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MEDICAL RESEARCH COUNCIL ANNUAL REPORT

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The Medical Research Council is the main government agency in the United Kingdom for the promotion of medical research. Originally set up in 1913 to administer funds provided for medical research under the terms of the National Insurance Act of 1911, it was incorporated under its present title by Royal Charter in 1920, a revised version of which was issued in 1966. The Council is financed mainly by an annual grant-in-aid from Parliament, received through the Department of Education and Science. It is not, however, a government department and has executive control of its funds as well as the freedom to pursue an independent policy.

It is the function of the MRC to promote the balanced development of medical and related biological research in this country, and it aims to provide support for new and promising lines of investigation, particularly at the growing points of knowledge; it is advised by three Boards—the Biological Research Board, the Clinical Research Board and the Tropical Medicine Research Board—and by many specialized committees. The Council employs its own research staff and also provides grants for other institutions and for individuals who are not members of its own staff, thus complementing the resources of the universities and hospitals. In addition the Council advises Government on matters relating to medical research and cooperates with Government departments and with other organizations in this country and overseas.

Report of the Medical Research Council 1 April 1968—31 March 1969

To the Secretary of State for Education and Science

The Medical Research Council submits the following report on its activities during the period from 1 April 1968 to 31 March 1969. This formal report includes a statement on the functions and policies of the Council, followed by a detailed report, prepared by a specially appointed committee of the Council, on the subject of radiobiology.

As a departure from the practice of previous years, the four articles following this report are designed as broad reviews of areas in which research under the Council's auspices has been particularly productive in the past two decades—over the period of Sir Harold Himsworth's secretaryship—rather than as accounts of narrowly defined subjects.

There follow summaries of the work of the Council's own establishments and of the projects that it has supported. The many publications by members of the Council's scientific staff and by others receiving support from the Council that have appeared in the medical and scientific journals provide a more complete picture of the research sponsored by the Council than can be given by the present report. These publications are too numerous to list here, but information about papers published by members of the Council's staff is available from the librarian of the National Institute for Medical Research.

Sir Henry Dale

Sir Henry Dale, first director of the National Institute for Medical Research, past President of the Royal Society and Nobel prize-winner, died on 23 July 1968 at the age of 93.

Dale's scientific career began at Cambridge, where he obtained a First Class in the Natural Sciences Tripos in 1898. By the time he had completed his medical degree at St Bartholomew's Hospital in 1903 he had already carried out some noteworthy physiological research, and in the following year he was appointed director of the Wellcome Physiological Research Laboratories, where he remained for ten years before becoming head of the Division of Physiology and Pharmacology at the newly founded National Institute for Medical Research.

Dale's principal scientific achievement grew from his collaboration with George Barger, while at the Wellcome Laboratories, in the pharmacological study of compounds isolated from ergot extract. These were mostly amines having physiological effects similar to those produced by stimulation of the sympathetic nerves, but in addition two compounds of special interest were obtained, namely histamine and acetylcholine, the latter producing the effects

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of stimulation of the parasympathetic nerves. It was some years later that H. W. Dudley's demonstration at the National Institute for Medical Research that acetylcholine was present in the animal body gave reality to the conception of its physiological importance, but in the meantime Dale, with a succession of physiological colleagues, had worked out the details of its mode of action. The whole investigation ultimately led to one of the great generalizations of physiology, namely that the physicochemical change that constitutes the nerve impulse causes either acetylcholine or noradrenaline to be discharged at the nerve endings; these substances then activate the next excitable structure—that is, the muscle or gland that the nerve controls.

The implications for both physiology and pharmacology were far-reaching; not the least of them was the realization that neither subject could in future be studied in isolation from the other. It was for this work that in 1936 Dale was awarded a Nobel Prize for medicine, jointly with Otto Loewi, who had reached similar conclusions by a different approach. Although Dale had not undertaken his physiological studies primarily with a view to developing new therapeutic methods, the discovery turned out to be of great value in clinical medicine. Its applications included the development of muscle relaxants for use in surgery and of many of the drugs now used to control hypertension.

Another discovery in which Dale played a major part was the dilator action of histamine on the capillaries and the latter's capacity for independent reaction. His interest in anaphylaxis went back to the beginning of his career, and in a series of experiments undertaken as part of a study of ' secondary wound shock ' at the end of the first world war he revealed, with Laidlaw, the role of histamine in anaphylactic shock—again, a whole new field of inquiry was opened up to future researchers.

Although he never held a teaching appointment Dale was an excellent lecturer and demonstrator. He had the capacity to transmit to others the enthusiasm for investigation that he himself possessed so abundantly. Generations of research workers were encouraged not only to follow in his footsteps but to break new ground of their own, and he was always willing to give help based on his own profound and extensive knowledge. His experimental demonstrations of his work were famous for their effectiveness, and his published papers are masterpieces of lucid argument and exposition.

Dale's association with the Medical Research Council goes back to 1914. Acting at first as chairman of the National Institute's committee of departmental heads, he was appointed as director in 1928. Throughout, Dale's administrative ability was seen to be commensurate with his scientific gifts and under his guidance the Institute flourished. Those who worked there carry an ineffaceable memory of a most happy team of research workers, whose endeavours were encouraged and whose troubles were shared by a director who was above all things a colleague.

While carrying on his research and directing the ever-increasing work of the National Institute Dale found time to concern himself with a problem that was becoming more acute as the use of potent biological agents in clinical medicine increased. Often there was no means of assessing the potency of vaccines and drugs of biological origin. Different firms produced sera varying so greatly that doctors had little idea of the appropriate dose for their patients. By 1922, on Dale's initiative, a standard for posterior pituitary extracts had been established.

He also organized the testing and standardization of commercially available neoarsphenamine, and when insulin was discovered the energy with which he organized its standardization much accelerated the commercial production of insulin of uniform activity. It was mainly at the instance of Dale, together with T. Madsen of Copenhagen, that the League of Nations Health Organization accepted biological standardization as an international obligation and at the same time entered into a formal agreement with the Council by which the latter undertook responsibility for international standards of all biological agents in medical use except serological products; this responsibility, which has much increased in recent years, the Council still holds under agreement with the World Health Organization. Legislative provision for proper methods of control of biological therapeutic and prophylactic agents within this country also owes much to the advice that Dale gave in the framing of the Therapeutic Substances Act of 1925.

On his retirement as director of the National Institute Dale served as a member of the Council until 1946; he was also chairman of its Committee on the Medical and Biological Applications of Nuclear Physics, the work of which led the Council to devote an increasing proportion of its resources to radiobiology in all its aspects. As chairman of the Scientific Advisory Committee to the War Cabinet he had been aware that the atomic bomb was being developed, but he was outspoken in expressing concern at its devastating power and also at the likelihood that the military potential of atomic energy would prevent the free exchange of information; as a scientist of international standing who had worked in collaboration with many scientists in other countries he deplored the creation of any barriers to contact between them.

As chairman of the Wellcome Trust Dale continued to be closely concerned with the development of medical research until 1960, sharing in the responsibility for the annual allocation of funds amounting to hundreds of thousands of pounds.

Dale was elected a fellow of the Royal Society in 1914; he was Biological Secretary of the Society from 1925 to 1935 and President from 1940 to 1945. He gave a great deal of his time and attention to the Society's affairs and initiated many developments in its policy.

Out of the long list of the honours conferred upon him, both British and foreign, mention may be made of his knighthood, awarded in 1932, the GBE, awarded in 1943, the Order of Merit, which he received in 1944, and the establishment by the Royal Society—with an endowment from the Wellcome Trustees—of the Henry Dale Research Professorship.

Those who knew Dale, and especially those who had the privilege of working with him, have a great sense of personal loss; mourning seems inappropriate, however, at the ending of a life so long and so full of achievement. He was a scientist whose outstanding intellect was combined with an almost unique breadth of knowledge and sound practical judgement; the Council looks back with pride on its association with one of the greatest of the world's scientists.

Retirement of Sir Harold Himsworth

At the end of September 1968 Sir Harold Himsworth retired from the Council's service. He had been Secretary since 1949 and latterly also a member and Deputy Chairman of Council. He was the third holder of the office of Secretary; and like each of his distinguished predecessors he has added new dimensions and

fresh lustre to the post from his own particular genius and experience. In all things he has brought wise guidance to the Council in its deliberations and skill to the direction of its affairs.

During the academic career that preceded his years with the Council, Sir Harold enhanced the already high reputation of University College Hospital Medical School for its scientific approach to clinical medicine. For 21 years after qualifying there he had a distinguished career at both the Hospital and the Medical School, being appointed Professor of Medicine and Director of the Medical Unit in 1939, at the early age of 34. His high scientific standing was recognized by his election to the Fellowship of the Royal Society in 1955.

In 1948 Sir Harold was appointed a member of the Council, but he served in that capacity for only a year before being appointed Secretary. During his period of office the scope and dimensions of the Council's organization have been greatly extended. Financial resources have increased tenfold and the number of research establishments directly controlled by the Council has risen by over 50 per cent. These developments have taken place over a wide scientific front, but there are certain sectors in which Sir Harold initiated major trends in policy. With his background, it was natural that he should be particularly anxious to improve the conditions for research in clinical science. Moreover, he assumed his post just when the National Health Service was taking shape, with all its promise of better opportunities in this field. His discussions with the Health Departments led to the publication of the White Paper *Clinical Research in Relation to the National Health Service* in 1953. To implement the policy therein announced, a Clinical Research Board was appointed to advise and assist the Council. Clinical research units and other projects to be supported centrally by the Council were inaugurated, and also decentralized research programmes within the Health Service. The Clinical Research Centre, designed as a major focus of such work and a clinical counterpart to the National Institute for Medical Research, is now in process of formation.

Sir Harold was also notably active in developing research in tropical medicine—or, as he himself prefers to term it, medicine in the tropics. He felt strongly that medical science was one and indivisible, so that no aspect of it could be neglected—or segregated—without detriment to the whole. He also saw that the newly independent countries within the Commonwealth might not at first be able to shoulder the whole burden of tropical medicine research, so that it would be all the more important for the United Kingdom to maintain and indeed increase its interest in this field. He successfully fostered various projects for this purpose; and throughout his period of office he was active as Chairman first of the Colonial Medical Research Committee and later of its successor the Tropical Medicine Research Board. He personally made numerous visits to territories in East and West Africa and the Caribbean, and frequently attended meetings of the regional councils or committees on medical research, which had been set up largely on his recommendation.

Sir Harold was fully conscious of the imperative need for the constant replenishment of the reservoirs of basic biomedical knowledge from which the more important practical advances are ultimately derived. Many research projects were promoted with this end in view in such subjects as virology, genetics and molecular biology; and the high quality of the work is attested by the award, during the period of his Secretaryship, of Nobel Prizes to no less

than six members of the Council's staff. This scientific policy has been linked with an administrative consideration, namely the Council's responsibility for supporting research in new fields before provision for them has been made in the universities. New or rapidly developing disciplines are thus 'seeded' in universities by means of grants, notably including subventions under the scheme of 'research groups' (as distinct from 'research units' of the Council's own staff) to develop promising research projects that universities are anxious to foster but cannot yet afford. In all this Sir Harold was at pains to cooperate closely with the University Grants Committee and with individual universities, considering the roles of the Council and the universities to be complementary in promoting research within the academic sphere.

Another aspect of the promotion of research is provision for the training of future investigators. Several new series of training awards, such as clinical research fellowships and junior research fellowships, were introduced during Sir Harold's time.

More generally, because of Sir Harold's appreciation of organizational problems in the field of medical research his advice was frequently sought by other countries; and the report *The Support of Medical Research* (1956), for which he was very largely responsible, is regarded as a blueprint for national medical research organizations. His views, as expressed in lectures and papers, have reflected a profound concern for the whole field of medical research and its relationship with government and society. He maintained close touch with the World Health Organization in its research interests, and he served on its Advisory Committee on Medical Research from the inception of the Committee in 1959 until 1964. In 1963 he accepted an invitation from the Government of New Zealand to visit that country for the purpose of advising on its provision for medical education and research.

The Council's advisory function, although not envisaged at the outset, became increasingly important as its prestige grew; and its effective fulfilment owed much to Sir Harold's personal qualities. The value of advice to the Government from an independent expert body, with a call on all the best opinions in the country, came to be fully recognized and valued. Subjects on which the Council's help was thus officially sought included radiation hazards, the introduction of poliomyelitis and other vaccines, and ethical considerations in medical research. It was in 1955 that HM Government turned to the Council for advice on the medical aspects of nuclear radiation, in view of widely expressed concern following the large number of tests of nuclear weapons at that time. Sir Harold was chairman of a committee set up by the Council to handle this difficult assignment. This committee's reports, published in 1956 and 1960, greatly advanced understanding of problems in this field and were acknowledged as being of immense value to the Government in its handling both of home affairs and of diplomatic negotiations.

All this Sir Harold could not have achieved had he not possessed great powers of vision and leadership and great administrative ability; but the matter does not end there. The success of his service to the Council owed much also to the personal relationships that he established with the scientific staff of the Council's establishments both in this country and overseas. This he did by seizing every opportunity that the preoccupations of his official work allowed to visit the Council's laboratories, and in the course of these visits he was at pains to meet individual members of the staff at all levels and to discuss their work with them.

These visits brought and maintained a realization throughout the whole of the Council's organization of the genuine enthusiasm for scientific investigation that Sir Harold himself felt and a sense of his keen interest in the efforts of individuals; this was a source of great encouragement. That part of his work was indeed by no means the least of Sir Harold's contributions as Secretary of the Council, and it is one for which he will be remembered with gratitude and affection by many.

The subjects of the four scientific reviews included in this volume—molecular biology, immunology, occupational health and toxicology and epidemiology (pp. 42–97)—have been selected because progress has been particularly striking in these areas of research during Sir Harold Himsworth's period of office.

The Council's Functions and Policies

Under its charter the Medical Research Council is charged with the responsibility of carrying out research directed to the advancement of medicine, using funds granted by Parliament together with the benefactions and donations it receives. Taking a broad view of what constitutes medical research, the Council is concerned to extend understanding of basic principles as well as to develop knowledge to the point where it may be used in medical practice. A second responsibility of the Council is to meet requests from official bodies for information about the state of knowledge in particular areas and, if appropriate, to give advice.

FACTORS DETERMINING THE COUNCIL'S ROLE

The factors determining the status and powers needed by the Council may be conveniently considered under the following five headings:

(i) the field and its unity
(ii) the research workers and their environment
(iii) the users and their needs
(iv) the independence of the Council
(v) cooperation with the other research councils.

The field and its unity

Advances in medicine require the study of normal and abnormal biological function at all levels of organization; this ranges from basic biological research at the molecular level and the extensive laboratory work that forms the scientific basis of the practice of medicine to the study of patients and epidemiological and population studies carried out in the field. Frequently a combination of approaches is needed to tackle a particular problem; for example, teams working on cancer include scientists studying interactions between host and viral nucleic acids, chemists and pathologists studying the nature and mode of action of substances with carcinogenic properties, clinicians making observations at the bedside and statisticians analysing data on populations. Similarly, in establishments concerned with rheumatism, clinicians will be found working closely with experts on various aspects of immunology and cell biology—subjects that are also important in cancer research. Indeed, research directed towards the solution of one problem may well turn out to be relevant to a quite different

subject, and numerous aspects of research are relevant to many different problems; this is because the solution of many of the most important problems in medical practice depends on further advances in our knowledge of cellular and subcellular processes. Deviations from the normal cannot be understood, at any level of biological organization, unless the normal itself is understood; indeed, cell biology relates to cellular disorders such as cancer and certain degenerative conditions in much the same way as traditional physiology relates to many aspects of clinical medicine.

It is this acceptance of the need for the closest coordination of research at all levels that has led to the recent reorganization of the medical side of the Council's own administration (see p. 263).

The research workers and their environment

The research workers may be members of the Council's own staff; many others, particularly university employees, are supported indirectly from the Council's funds. Of the Council's own staff, many work within universities. It is not only laboratory work that is closely associated with the universities; much of the clinical research undertaken in this country is carried out in university teaching hospitals and departments. There is good reason for this concentration of effort within the university environment. As has already been pointed out, all aspects of medical research are interrelated and it is thus important that research should not be fragmented. Moreover, any individual or team working in a given field is likely to need access to experts not only in a range of other aspects of biology but also in the non-biological sciences; such a range of expertise is most easily found within a university. This interdependence of the work of the Council and university research makes coordination of policies essential. Moreover, the Council depends on university departments for the training of junior research workers, an object to which it devotes a significant proportion of its funds.

The users and their needs

The principal users of the knowledge the Council seeks to obtain are individual members of the medical profession, who require that such information should be freely published and that they should have confidence in its source. Many Government departments and other corporate bodies—for example industrial organizations and trade unions—seek the advice of the Council. Obviously the health departments (which themselves sponsor some research) have a strong interest—not only the Department of Health and Social Security for England and Wales but also the Scottish Home and Health Department and the Northern Ireland Ministry of Health and Local Government; contact between these departments and the Council is maintained by common membership on boards and committees. Tropical medicine is looked after by the Council in collaboration with the Ministry of Overseas Development; the Council is not subject to territorial restrictions in the conduct of this work, and full use is made of this freedom in undertaking medical research in the tropics, a subject to which this country has contributed so greatly in the past. The welfare of Service personnel has for a long time been the concern of a number of Council committees, in which the Defence Departments participate. Other questions, particularly those of an industrial or environmental nature, have involved departments such as the Ministries of Agriculture, Fisheries and Food, Housing and Local Government, Power and Transport and the Post Office.

Government departments must be able to obtain advice on the implications of current knowledge and have research undertaken on the medical aspects of matters with which they are concerned; as might be expected in this period of great scientific activity, the occasions on which advice is requested become more frequent. Because of the breadth of the field covered by the Council's work, and because of its independent position and the wealth of medical and scientific expertise on which it can draw, it is usually in a good position to give the advice that is needed. In some instances the question raised may reveal the necessity of further research, and it is within the discretion of the Council to undertake such research—provided that, in the existing state of knowledge, a meaningful and reliable answer is possible.

The independence of the Council

Few today would dispute the importance of unrestricted publication of the results of scientific research, and the Council has always encouraged its staff to publish the results of their work promptly in the scientific journals. It is not generally acceptable that a decision to publish should be influenced by the possibility of repercussions on the policies of a Government department, and it is important that the Council should not only have but also, by virtue of its independent status, be seen to have real freedom to publish. Its independence also gives it freedom to plan for long-term as well as short-term research in medicine. It is on these freedoms that the confidence of both the medical profession and the research workers depends. The general public is also concerned. On occasion, when Government departments have been deeply involved, Parliament or some public body has asked for an independent review of a situation from the Council; an example of this was the Council's report on the possible effects on human health of the nuclear reactor accident at Windscale.

Cooperation with the other research councils

Since there is interaction between all aspects of science, particularly when the emphasis is on ' research ' rather than ' development ', it is manifestly desirable that the Council should remain in the closest possible touch with other Government-sponsored research organizations and with the medical and scientific community as a whole. The importance of this lies in the need for the Council, when making its own policy decisions, to be fully conscious of the overall national scientific policy and well informed of new trends in scientific activity, both in this country and abroad. The growing tendency towards international collaboration in research and the establishment of international organizations for the attack on major problems requiring an interdisciplinary approach and expensive facilities make liaison with other organizations all the more necessary. Special problems arise in relations with scientific bodies in other countries. Most developed countries have one or more research councils or similar bodies but the scientific coverage of such councils, and in particular the divisions of responsibility where more than one exists, may vary. Consequently in relations with foreign scientific organizations the research councils in this country often need to work in close cooperation.

The status and powers needed by any organization such as the Medical Research Council must be determined by the five factors discussed above. At the present time the Council has, in broad terms, the status it needs to fulfil its

functions. It has scientific independence and operates over the whole field of medical research, including basic biological research in areas relevant to medical problems. Associated as it is with the Department of Education and Science it cooperates closely, both in determining and in executing policies, with the universities and the other research councils. It is free to publish results and provide advice for a varied range of users, and it is in a position to cooperate with any Government department or other corporate body.

THE BASIS OF POLICY

Most of the major problems in medicine demand for their solution a continuing flow of original ideas. These may come from basic biological research or from observations made in the care and treatment of patients. They may be made possible by a fundamental finding or by the application of knowledge from one field to a problem in an entirely different one. In view of the central importance of original ideas, the first need of any research organization is the availability of individuals of high ability. The Council has been fortunate in recruiting such men and women over the past 50 years, and by giving such gifted scientists freedom to develop their own ideas it has demonstrated repeatedly that this is the best way to foster outstanding work.

This does not mean, however, that there is no place for scientific policy-making by the Council. Indeed, this is essential if research is to develop in a balanced way towards specific practical objectives. The Council can operate by specifying priorities and by organizing work in particular fields or initiating particular projects. While it is sound policy to encourage scientists of high originality to develop their own ideas, it does not follow that this is the best way to use all qualified manpower in medical research any more than in other fields. Moreover, even the best scientists can from time to time be encouraged to turn to unpopular and underdeveloped subjects.

The need for a scientific policy is related to the need to choose between competing claims for limited resources—a consideration which, in view of the relative rates of growth of science and of national resources, seems certain to be of increasing importance to all the research councils. To make the most productive use of its resources the Council must have adequate machinery, first, to form general policies; second, to deal with detail in particular fields; third, to assess the scientific merits of individual research programmes and, finally, to bring all these strands together in making a decision. Existing projects, whether supported directly or indirectly, have constantly to compete with new claims and needs since, broadly speaking, resources for new work must increasingly be found by discontinuing support for the old.

THE FORMULATION AND EXECUTION OF POLICY

The Council has evolved arrangements for formulating policy, for developing new projects and for terminating its support of others. None of these systems is immutable, however, and all are kept under review. Once a year the Council reviews the whole range of its work and then initiates further studies of particular fields as necessary. A report on one such study—namely on radiobiology—is included in this report (pp. 11–31); a similar study concerned with biochemical aspects of psychiatric illness is under way. Other committees and working parties deal in detail with special problems; these are listed at the

end of this report. A recent innovation is the creation of Grants Committees (see p. iv) to assess the scientific merit of applications for grants; the Biological Research Board and the Clinical Research Board, among their other duties, take into account both the individual assessments of the Grants Committees and the Council's policies in reaching a decision.

The initiative to undertake a line of research can come either from applicants for support or from the Council. In dealing with applications for support the first criterion to be applied is whether the work involved is genuinely in the highest class. If it is it will be supported, provided of course that it lies in the Council's field of operation; if it is not in the highest class current priorities are taken into account. At the present time the Council is anxious to increase its support for work, at all levels of biological organization, on arterial disease (particularly coronary thrombosis), population control and dependence on drugs (including nicotine). It is also anxious to encourage the development, particularly within the universities, of further research in the following fields: clinical neurology, psychiatry, obstetrics and gynaecology, dermatology, dentistry, virology and mycology. However, it must be emphasized that any proposal, if it is to be accepted, must show that the research has some prospect of obtaining meaningful results and that it is unlikely to give rise to false or misleading answers.

In initiating work on a major problem or programme the Council has power to set up a unit of its own if need be. Smaller-scale projects may be supported by short-term grants. Such projects are sometimes initiated by a Council working party, which may have defined the problem and arranged to keep it under review. Council staff may from time to time be asked to undertake such projects. However, this is an area in which the Council has had some difficulty in recruiting staff; these projects are usually short-term and have a practical object in view, and for these reasons they do not attract many research workers. There have indeed been instances where able scientists have been persuaded to undertake work of this kind with the satisfactory result that the desired answer has been obtained, and in the course of the work ideas for new and interesting research have emerged. The difficulty nevertheless remains, and to meet it the Council has recently decided to enter into research contracts, in cases where the need is great, with academic institutions or commercial firms for the development of projects of this kind.

One of the most important requirements of policy-making for a research organization is that it should be constantly forward-looking. It is necessary to base decisions on the most up-to-date evaluation of the current situation, but this is not enough; there is also need for a continuing attempt to identify areas of research that are at an early stage of development but where further advances might be expected to bring important results. In two instances at least the Council has been exceptionally fortunate in assessing future prospects correctly with little to guide it. First, the Council's policy over the years of fostering research in radiation biology resulted in the availability in this country of a body of knowledge and a sufficient number of trained workers for the British contribution to the solution of the biological problems resulting from developments in nuclear physics to be second to none; second, the early and rapidly expanded support given by the Council to the researches that have come together to form the subject of molecular biology kept this country in the forefront of this great scientific advance.

CONCLUSION

The circumstances in which research is carried out today underline the importance of certain continuing threads of Council policy. The restriction of resources makes it essential to terminate work if it is no longer fulfilling its earlier promise or if its priority has diminished, and to allocate the resources in the way likely to be most productive. Furthermore, the interdependence of research councils and universities demands close coordination of their administrative and sometimes of their scientific policies. The need of Government departments for sound information from an independent scientific source on which to base policies makes it necessary for the Council to make its advice available to all the relevant departments. Finally, the independence of the Council is an important factor in any confidence the medical profession, the scientific community and the public may have in the Council and its work.

Council Policy on Radiobiological Research

Over the last 20 years the Council has supported an expanding programme of research on the biological effects of ionizing radiations. By 1967 this programme accounted for roughly 6 per cent of the Council's budget, the major part of the sum being allocated to basic research on biological mechanisms and to the assessment of hazards rather than to radiotherapy. During this period, as a result largely of public anxiety arising from the use of nuclear weapons at the end of the second world war and their subsequent development and testing in the atmosphere, a massive research effort was also mounted in other countries and a considerable body of knowledge built up. The Council therefore considered that the time had come to assess the present state of knowledge, to identify the priorities within this field of work and to evolve a long-term research policy. Accordingly a committee* was appointed to carry out a review of the whole field and to make recommendations on policy. These have now been accepted by the Council.

REPORT OF RADIOBIOLOGY COMMITTEE

1. RADIATION PROTECTION

1.1 *Historical and organizational background*

Before radiobiological research in this country is considered in relation to protection against radiation hazards it is desirable to sketch the international and national framework into which it fits. Internationally the major body concerned is the International Commission on Radiological Protection (ICRP). This is a non-governmental organization, at present largely financed by subventions from the World Health Organization, the International Atomic Energy Agency and the International Society of Radiology, and by a grant from the Ford Foundation. The Commission has succeeded in bringing together experts from a wide range of countries and in securing to a remarkable degree agreement on underlying principles and protection standards, which have subsequently been adopted almost unaltered by the various adhering countries. Participation in all its activities and adherence to its recommenda-

* Members of Radiobiology Committee: Professor W. D. M. Paton FRS (*Chairman*); Professor D. A. K. Black; Professor A. R. Currie; Professor J. L. Gowans FRS; Dr J. A. B. Gray; Professor W. V. Mayneord FRS; Professor W. T. J. Morgan FRS; Professor C. H. Waddington FRS; Sir Brian Windeyer; Dr R. C. Norton (*Secretary*).

tions are voluntary. Other bodies concerned with radiological protection are the International Labour Office, the International Atomic Energy Agency of the United Nations, the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) and the European Atomic Energy Commission. The Medical Research Council has close links with all these bodies, and many members of the Council's own scientific staff and advisory committees* are also members of ICRP and its subcommittees.

These international bodies have little money of their own for research relevant to protection problems, and investigations are financed and carried out on their behalf by various agencies of member countries. In this country much of the research is financed by the Council. Council committees also perform an important role in collating, digesting and focusing attention on the results of such research.

In this country at present Government departments with executive responsibilities in the field of radiation are advised on various practical radiological matters by the Radioactive Substances Advisory Committee, which was set up under the Radioactive Substances Act, 1948. The Committee is consulted on draft regulations and orders and has also played a prominent part in the drawing up of Codes of Practice, which, although they do not have the force of law, are widely used as authoritative documents. A National Radiological Protection Board is to be set up (subject to the passing of the necessary legislation) and it is likely that this body, as well as assuming the functions of the Radioactive Substances Advisory Committee, will develop a research programme of its own.

While the Council does not have formal responsibility for laying down protection standards, the Government continues to rely on its advice on the underlying scientific principles and on the formulation of protection policy.

1.2 *Physical measurement of internal radiations and the fate of radionuclides in the body*

Exposure to radiation can arise from a number of different sources, both natural and man-made, and these are termed 'internal' or 'external' according to whether the source of radiation is inside or outside the body. The radium used in the luminizing industry and strontium-90 from fallout are probably the most notorious examples of internal radiation sources. They are 'bone seekers' and irradiate bone and bone marrow, thus giving rise to the risk of leukaemia and bone sarcomas. Iodine-131 is a further example of an internal source, being concentrated in the thyroid gland after medical administration or after ingestion of contaminated milk. Internal radiation sources present certain special problems. The first is that of dosimetry. The estimation of radiation dose requires elaborate mathematical analysis and physical methods of observation such as the use of whole-body counters, scanning devices or, more recently, electronic 'cameras'. Dosimetry of particulate radiation of low penetration presents special difficulties. Promising work is in progress, particularly in the Council's own establishments (the MRC Environmental Radiation Unit and the Radiological Protection Service), on the dosimetry of β-emitters such as strontium-90 in bone, using thermoluminescence techniques with lithium fluoride solid-state detectors. Techniques for the dosimetry of internal α-emitters are, however, insufficiently

* The Committee on Protection against Ionizing Radiations and its subcommittees.

developed. It is clear that considerable technical improvements are still possible—and desirable if radioactive isotopes are to be used safely and basic metabolic data are to be obtained. Work of this kind is of obvious relevance to recommendations on permissible levels of exposure.

The Council is supporting work in these fields in the MRC Radiobiology Unit, Environmental Radiation Unit and Cyclotron Unit and in the Radiological Protection Service. In addition, research mainly oriented towards operational procedures is carried out by the United Kingdom Atomic Energy Authority (UKAEA). Special problems arise in the use of plutonium, and the Council's advisory committees are currently evaluating the possible hazards from this source.

There are considerable gaps in our knowledge of the fate of radionuclides in the body, particularly of the bone-seeking isotopes and of trace elements. This subject is an extensive one since it involves the fate not only of the elements concerned but also of all the organic compounds into which they may be incorporated. The difficulty in developing such work is that it is at present regarded by most scientists as relatively unsatisfying. But the Committee believes that this may be partly a matter of fashion and that, given a scientist of originality who has established himself as a leader in this field, a transformation as striking as that seen, for instance, in the field of electrolyte metabolism could well take place.

1.3 *Physical measurement of external radiations*

Sources of external radiation include cosmic rays, radioactive substances in rocks, soils and building materials, caesium-137 from fallout deposited on the ground and X-rays used for medical (diagnostic or therapeutic) and industrial purposes. Techniques for the measurement of external radiations are reasonably well developed; they are, in general, sufficient for daily clinical use, but they require more development for studies of energy absorption in radiobiological research. There are outstanding problems in the dosimetry of neutron radiation produced by nuclear reactions or during certain therapeutic procedures. The difficulty lies with relatively low-energy neutrons; the proportion of this lower-energy radiation is sometimes significant and might quite considerably affect the estimate of dosage in radiotherapy or in the atomic industry.

A certain amount of physical research on more routine monitoring procedures has been carried out by the Radiological Protection Service, but this type of work is largely outside the direct responsibility of the Council. Much work is now carried out by the National Physical Laboratory (which is responsible for primary standards) and by such bodies as the UKAEA and the Central Electricity Generating Board, as well as in several laboratories in medical schools and universities. The present responsibilities of the Council (shared with other bodies) are mainly confined to the monitoring of the low levels of radioactivity to which the general population is exposed over long periods of time (carried out by the MRC Environmental Radiation Unit and the Radiological Protection Service) and to the provision of basic information and calibration facilities for the use of hospitals and medical research centres. The Council also has a broad responsibility for the identification and assessment of hazards from fallout resulting from nuclear tests.

The amount of radiation from diagnostic radiology to which the general population is exposed remains larger than the exposure from any other single artificial source and (despite greater care) is still increasing, though in this country it is still only some 15 per cent of the radiation due to natural radioactivity.

1.4 *The assessment of radiation risks*

Much remains to be learnt about the biological effects of radiation. At low dosage levels leukaemogenesis and carcinogenesis in general are at present accepted as the most serious risks for the individual, but there is evidence of other late effects following higher doses, for example cataract formation and possibly neurological damage and a general shortening of the life span. For the population as a whole genetic effects, both in the present and in subsequent generations, must also be taken into account.

It has only recently been possible to attempt quantitative estimates of the incidence of harmful effects (leukaemia and other forms of cancer and certain genetic effects) per unit dose of radiation, and even now the margins of uncertainty are very wide. In general, most knowledge has been gained of the effects of relatively large doses received at high intensity, notably from epidemiological studies of the survivors of Hiroshima and Nagasaki and of patients treated with radiation for ankylosing spondylitis; but even now these estimates are very imprecise. Useful and probably unique pathological studies have also been carried out at the MRC Radiobiology Unit on the whole-body exposure of limited numbers of animals, particularly mice and, more recently, large animals such as goats, to neutron and γ-irradiation from a nuclear reactor.

There is much less knowledge of the effects of small doses spread over long periods of time, yet these are the effects that are particularly important for the population at large. There are many uncertainties here—for example, the variation of sensitivity to radiation with age. It seems clear, however, that the foetus is exceptionally sensitive. It is not known whether the linear relationships that are now indicated between radiation dosage and the incidence of harmful effects at high dose levels apply also at low dose levels; the present estimates of risk from low dose levels are based on the assumption that a linear relationship does hold good and that there is no ' threshold ' of radiation exposure below which no effect is produced.

The work required to clarify the effects, both genetic and somatic, of prolonged exposure to small doses of radiation and to answer the question of whether there is a threshold is intrinsically laborious. So far most of the work on the lowest radiation levels has been concerned with genetic effects. A field study of rat populations in an area of high natural radioactivity (Kerala, South India), carried out by Professor H. Grüneberg and his colleagues*, failed to produce any positive evidence for genetic effects, though this does not prove that no such effects exist. However, it is improbable that similar field studies in any other part of the world would be more informative. Thus animal investigations must depend on laboratory studies, and major long-term experiments (based on the so-called ' megamouse ' approach) are in progress in the United States in an attempt to elucidate certain genetic effects. This type of experiment consists simply of exposing an extremely large number of animals to a radiation dose only a few times greater than that to which living beings on the earth's surface

* *A Search for Genetic Effects of High Natural Radioactivity in South India:* MRC Special Report No. 307, 1966.

have always been exposed. The animal population is then carefully scrutinized for the appearance of specific genetic changes.

The main objection to this kind of work is economic—the yield of knowledge is unlikely to be commensurate with the scale of expenditure involved. In addition, there are a number of practical difficulties: the work is liable to be impeded by epidemics among the animal populations, by inconsistency between the observations made by large numbers of individuals over periods of time, and by the difficulty of finding scientists dedicated enough to undertake and continue with it. Again, some experiments may be criticized on the grounds that the genetic markers used are not the most significant ones; and, lastly, there always remains the problem of extrapolation to human populations.

There is therefore considerable doubt, at least on practical grounds, whether this approach is likely to have more than limited success. However, if slightly higher dose rates are studied so that genetic effects can be obtained with smaller groups of animals, it may be possible to gain knowledge of the relationships between dose and genetic effects more readily. If the relationships were shown not to vary significantly, for instance with species, and if the limits of error could be reduced, then it should be possible to apply them with more confidence to human experience. Extrapolation to the effects of naturally occurring dose rates would still be needed, but this could then be carried out with greater confidence.

In view of the difficulties presented by experiments involving very large animal populations some alternative approaches have been suggested, though these all raise great problems of extrapolation. For example, it would in principle be far simpler to explore the effects of radiation on a million rapidly dividing cells than on a million animals, and results should emerge more quickly. Although such investigations at the cellular level may not be possible at the present time, continuing attempts should, in the Committee's view, be made to develop them; recent advances—for example in cell culture and typing—give hope that this kind of study may soon become feasible. Its success would be crucially dependent on there being at least some established links between the effects seen in cell culture and the genetic effects on whole animals. It may in the event be possible to establish such links initially only by carrying out parallel experiments on large numbers of animals. Nevertheless, the establishment of links for a few dose rates, by this or other methods, might eventually enable work to proceed much more rapidly and with greater confidence at the cellular level.

Another approach, applicable directly to man, might be based on a study of chromosome aberrations. These have been shown at the MRC Clinical and Population Cytogenetics Unit and Radiobiology Unit and elsewhere to occur after relatively low doses of radiation in lymphocytes (see §3.5), which can readily be sampled. There is evidence that they can also be found in other cell lines and it is assumed that they occur in germ cells (in which chromosome aberrations have been observed after high and moderate doses of radiation in animal experiments).

1.5 '*Maximum permissible levels*'

1.5.1. Radiological protection standards are usually specified in relation to:

(*a*) *Adults exposed in the course of their work* Adults exposed to radiation through their work include those working in atomic energy establishments, in

association with nuclear reactors, in industries using X-rays and radioactive isotopes, in hospitals and in some branches of research. Because of their occupation these individuals are likely to receive higher doses than does the general population and they are therefore under medical supervision. Moreover, they are subject to selection; the conditions of their employment are closely defined and records are kept of the cumulative dose of radiation to which they are exposed.

(*b*) *Members of the public* In the general population some groups receive higher radiation doses than others, for example infants up to the age of 2 years, in whose bones the highest concentrations of strontium-90 from fallout are to be found and who are at present assumed to be the group at greatest risk from this radiation source. Since members of the public are not under the same supervision as those who are occupationally exposed, the permissible levels at present recommended for individuals or small groups of individuals in the general population are one-tenth of the dose acceptable for occupational exposure.

When whole populations or large sections of populations are exposed it becomes necessary to consider not only the magnitude of risk to the individual but also the numbers of persons exposed: an exposure level carrying an acceptably small risk to an individual might give rise in a population to a burden of injury, both somatic and genetic, that could not be neglected. Consequently, further limitation of exposure—to one-third of the level specified for individuals in the population—is thought to be desirable when whole populations are exposed.

1.5.2 *The basis of ' maximum permissible levels '*

The setting of maximum permissible levels was originally based on the assumption that there was a dose of radiation below which harmful effects were negligible. The limits specified were arrived at by estimating the levels below which harmful effects were unlikely to be observed and then, because of the wide margins of uncertainty, scaling down substantially below these levels.

With increasing knowledge of the nature and extent of the risks associated with radiation, particularly genetic risks, it has been thought prudent to abandon the concept of the ' threshold ' dose, and to assume that even the lowest doses may involve a finite, though correspondingly low, probability of adverse effect. Now that it is becoming possible to make numerical estimates of risk (in terms, for example, of numbers of additional cases of leukaemia that might be expected to occur over and above the natural incidence per million of the population per rad per year) the possibility is also opening up of judging the degree of risk that might be acceptable in particular circumstances.

A quantitative estimate of risk at a particular dosage level would allow some comparisons to be made between the risks attributed to radiation and those associated with industrial hazards or with other hazards of modern everyday life, such as travelling in a car or being a pedestrian among traffic. Ideally, such judgements would involve balancing the benefits of, say, the peaceful uses of atomic energy against the risks of a given radiation exposure for the individuals, groups or whole population concerned. In the words of the International Commission on Radiological Protection*: ' The risks to members of the public

* Recommendations of the International Commission on Radiological Protection (adopted 17 September 1965): ICRP Publication 9, 47. Much of the discussion in §1.5 is based on these and other ICRP recommendations.

from man-made sources of radiation should be less than or equal to other risks regularly accepted in everyday life, and should be justifiable in terms of benefit that would not otherwise be received.' In the case of occupationally exposed persons and members of the public exposed to controllable sources of radiation, such a balancing operation would appear feasible provided that (*a*) the occurrence of the exposure could be foreseen and could be limited in amount by the development of proper operating procedures, and (*b*) the estimates, both of risk and of benefit, were sufficiently precise.

There are, however, differences in situations in which the exposure is accidental and in which it can be limited only, if at all, by remedial actions. Particularly in the case of fallout, it can be argued that no benefits accrue to the individuals concerned. The problem then involved in deciding on the point at which action should be taken is one of balancing the risks and social cost involved in any control or remedial measures against the estimated reduction of radiation risks.

Possibly for these reasons, and also because of the present lack of effective remedial measures (see below), radiobiologists appear to be increasingly unwilling to specify 'acceptable' or 'permissible' levels for involuntary exposure of the population at large to radiation. This tendency is apparent in the recent publications of ICRP, which gives scales or 'tariffs' of risk in relation to radiation exposure without specifying at what point action should be taken.

The Council's formal position is that it has accepted the general conclusion of ICRP that it is not feasible to recommend fixed levels, appropriate for all occasions, at which action should be taken. The Council has, however, gone on to say: 'The precise point at which it would be appropriate to take remedial action . . . would depend primarily on the general trend of contamination levels in a particular situation and on the current position regarding the development of remedial measures.'*

There are clearly very great difficulties involved in applying the principles discussed above, and these difficulties are not lessened by the concern of the public about radiation hazards or by their belief that the Council's 1960† 'maximum permissible levels' are in fact precise 'danger levels'. Nevertheless, if it can be shown that the hazard from a given type of radiation exposure is no more than a very small fraction of some commonly accepted everyday hazard, the radiation problem is put into perspective.

1.6 *Remedial measures and radioprotective drugs*

Work is proceeding in this country on the development of remedial measures against fallout, notably in the MRC Radiobiology Unit, at the Atomic Energy Research Establishment and at the National Institute for Research in Dairying. Certain measures, for example the administration of stable iodide, have been developed for use against a local short-term hazard from iodine-131, but no satisfactory remedial measure against fallout has yet been developed for use over long periods of time and for large sections of the population. A considerable effort has also been devoted both in this country and elsewhere

* *The Assessment of the Possible Radiation Risks to the Population from Environmental Contamination:* a report to the Medical Research Council by their Committee on Protection against Ionizing Radiations, 1964, p. 8.

† *The Hazards to Man of Nuclear and Allied Radiations:* A Second Report to the Medical Research Council by their Committee on the Hazards to Man of Nuclear and Allied Radiations (Cmnd. 1225), 1960, p. 47 (§177).

to the development of radioprotective drugs acting at the cellular level. Although work of this kind is of considerable theoretical importance nothing with any practical applications has so far emerged.

1.7 *Possibilities of further advances*

The Committee has in particular identified the following areas where further work relevant to radiological protection might usefully be carried out:

1. *Dosimetry of external radiation* The techniques of monitoring and dosimetry are, broadly speaking, adequate for external radiation sources. But, as with all other technologies, considerable improvement could be made if the equipment were smaller, lighter and cheaper as well as more sensitive, accurate and versatile, thus making possible large-scale epidemiological studies. There is perhaps a particular need for dosimetric studies of neutrons, though the need depends to some extent on the possibility (still not fully assessed) of using neutron radiation in therapy.

2. *Dosimetry of internal radiation sources* The promising research on techniques of thermoluminescence dosimetry should be pushed ahead, and there is a need for more work on α-emitters.

3. *The fate of radionuclides and their compounds in the body* It is strongly recommended that the Council should not hesitate to provide support for any research workers of talent. It is recommended that work on the development of counter-measures against ingestion of radioactivity and its removal if ingested (of the type that is in train at the MRC Radiobiology Unit and elsewhere) should be pursued as a matter of urgency.

4. *Pathological studies of whole-body exposure* There are possibilities of further advances in studies involving whole-body exposure of limited numbers of animals to various kinds of external radiation, including neutrons, along the lines of the MRC Radiobiology Unit's experiments.

5. *Long-term risks associated with low rates of exposure* The assessment of these risks and the question of a ' threshold ' still call for extensive research. Before the Council considers committing itself to large-scale genetic experiments, a detailed analysis should be made of how far such experiments can be replaced by other methods suitable for genetic analysis, using single cells or populations of cells in limited numbers of animals. It is possible that more intensified epidemiological work might contribute to this problem. If a large-scale approach seems to be called for, however, then it might form part of a dispersed international effort.

6. ' *Tariffs of risk* ' Apart from the question of what form of advice should be given to the Government (see conclusions, §4.1), the attempt to express the hazards of radiation by estimates of risks at various dose levels seems to be a logical approach and likely to be widely useful in a variety of situations. The work required to produce such statistical statements of risk should therefore be pushed forward.

7. *Risks from diagnostic radiology* There is a need for further work of the kind carried out by the Committee on Radiological Hazards to Patients (the Adrian

Committee), under the auspices of the Department of Health and Social Security, in order to keep a watch on the radiation from diagnostic radiology to which the general population is exposed.

2. RADIOTHERAPY

2.1 *Early development*

Radiotherapy developed empirically from clinical observations that X-rays and the radiations from natural radioactive substances, particularly radium, had profound biological effects. Some remarkable examples of beneficial effects were observed initially, particularly in the treatment of superficial malignant tumours; but there came a gradual realization that severe damage to normal tissues could also be caused. Clinical observation of this damage, both in patients and in radiologists themselves, was the starting point from which protection standards evolved.

Both the beneficial and the harmful effects of radiation seemed at first inconstant and uncertain, and it became necessary to develop accurate methods of dose specification and measurement, as well as to study the distribution of dose in the human body. This work was carried out mostly by physicists with a particular interest in the medical applications of ionizing radiations. This helped greatly to develop the practice of collaboration between the radiotherapist and the clinically trained physicist that exists today.

Radiotherapy has in the past been used for a wide variety of pathological conditions. With the introduction of more effective and safer methods of treatment for many of these its usefulness has become confined largely to various types of cancer and also some non-specific dermatoses, where it holds an important position.

2.2 *Development of apparatus*

Further developments in radiotherapy came about as a result of advances in high-voltage engineering and electronics. Originally all radiotherapy, other than radium therapy, was carried out with X-ray apparatus working at comparatively low voltage and therefore producing low quantum energy radiation. This apparatus was consequently incapable of delivering an adequate dose to deeply situated tumours without over-irradiation of surrounding normal tissues. However, with the construction of X-ray apparatus operating at much higher voltage and the development of more complex schemes of irradiation, it was possible to devise techniques by which an adequate dose could be delivered to a tumour situated in any part of the body with minimal irradiation of surrounding normal tissues. With the possible exception of neutron beam therapy, it seems unlikely that major advances in radiotherapy will now come merely from the further development of the apparatus.

2.3 *Possibilities of further advances*

The stage now appears to have been reached where advances will probably come from increased knowledge of the effects of radiation on tumours and on normal tissues—that is, from radiobiological studies oriented towards the needs of radiotherapy. Some examples of areas in which it seems at present that further advances might be made are:

1. *The 'oxygen effect'* An important advance has been the discovery that in general the higher the oxygen tension the more sensitive cells are to radiation.

The poorly oxygenated cells in the centre of the tumour may thus be relatively resistant to X- and γ-rays, and attempts are now being made to apply this knowledge to the treatment of patients—for example by administering radiotherapy to patients in specially constructed tanks with hyperbaric oxygen, or by using other methods to reduce the hypoxia of the tumour during irradiation. Many difficulties remain to be overcome.

2. *Neutron therapy* With neutron irradiation the oxygen effect is relatively slight, and it is therefore believed that the sensitivity to neutrons of the anoxic cells in the depths of the tumour is not so much reduced as is the sensitivity to other forms of radiation. The Council is already supporting therapeutic trials of neutron radiation produced by its cyclotron, and there may be a case for supporting similar work in other centres if cheaper and more easily handled sources of neutron radiation become available. If trials are undertaken in other centres it is desirable that they should be in collaboration with the MRC Cyclotron Unit.

3. *Fractionation of radiation dose* There are a number of areas in which fractionation studies may lead to further advances: examples are the effects of varying regimes on (i) intracellular recovery; (ii) the reoxygenation of tissues—see (1) above; (iii) alterations in the mitotic cycle; (iv) the cellular repopulation of skin and possibly other tissues, and (v) alterations in the vascularity of tissues.

4. *Cytotoxic drugs* The study of the effects of cytotoxic drugs, some of which have a radiomimetic action, is important for the elucidation of the effects of radiation. Moreover, it may be possible to produce greater radiosensitivity by using such drugs as an adjunct to radiotherapy, the two methods having a synergistic (mutually enhancing) effect. Work is proceeding in a number of centres on this possibility, and some further support for such investigations might well be considered by the Council if promising projects are put forward.

5. *Cell clones and immunology* A great deal of the present work in radiobiology is concentrated on clones of cells (i.e., cell populations directly derived from a single cell), their ' doubling times ' and the radiation doses necessary for their destruction under various experimental conditions. There is the possibility that immunological mechanisms are involved in the elimination of tumour cells in organized tissues, and immunological procedures are being used to increase the effectiveness of radiation in the destruction of tumours. Support might therefore be given to further work along both these lines.

Other fundamental radiobiological studies on the site and mode of action of the destructive effect of radiations in the cell are discussed below in the section ' Mechanisms of Radiation Injury '. Some of these may also have eventual applications in the field of radiotherapy.

2.4 *Need for clinical trials*

While it appears that a major improvement in survival rate is unlikely to be achieved quickly as a result of any of the radiobiological studies at present envisaged, such studies must nevertheless be regarded as the most probable basis for further advances. A small improvement in the treatment of cancer is difficult to demonstrate with any certainty unless large numbers of patients are investigated and adequate recording systems are used. It will thus be necessary to

conduct carefully controlled clinical trials to determine whether the application of knowledge gained from radiobiological studies has led to any increase in the efficacy of treatment. Such trials are complicated to organize and difficult to maintain over the necessarily prolonged trial period, but the Council's Committee on Evaluation of Different Methods of Cancer Therapy is in a position to provide considerable help. Such clinical investigations should be strongly encouraged, and every effort made to take advantage of recent technical advances in the keeping of records and their processing.

3. MECHANISMS OF RADIATION INJURY

3.1 *The primary interactions*

Ionizing radiations interact with biological materials by transferring energy to them. This frequently makes them highly reactive, and the resulting chemical reactions are the basis of the biological effects of radiation. In the case of electromagnetic radiations (γ- and X-rays) ejection of electrons is the most frequent primary event. Nuclear collisions are of significance as primary events with neutrons and heavy accelerated ions. Neutrons react mainly by collision with hydrogen nuclei, the protons from which then produce tracks of intense ionization—usually shorter than those made by primary electrons and analogous to those of α-particles. All these particles lose energy by creating secondary and tertiary ion pairs. In addition, the distribution of electric charge on adjacent molecules may be altered—a phenomenon known as excitation—and this too increases chemical reactivity. In general, the energy transfers are much more than enough to break many chemical (e.g., C–C) bonds if they are concentrated very locally. However, the energy is frequently transmitted along complex molecules, causing breaks at points other than the point of impact of the ionizing particle, or dissipated to adjacent molecules. These initial physical interactions last for periods of the approximate order of magnitude of 10^{-13} sec, while roughly 10^{-11} sec is required for approximate thermal equilibrium to be achieved and about 10^{-9} sec upwards for local diffusion of the initial products in watery media and for the chemical reactions involved.

The microorganization of the large molecules of living cells is liable to be destroyed by the impact of energetic particles, and concepts of solid-state physics such as quantum tunnelling are beginning to influence ideas about the consequent distribution of energy. Small changes of this kind in important molecules, notably DNA, may be of great consequence. However, the train of biochemical changes initiated by the primary events may have other far-reaching effects. Some of these arise from the highly reactive free radicals (structures with unpaired electrons) produced by the radiation, which it is now known may persist for many minutes or even hours, the time depending on the materials present and the environmental conditions. The commonest free radicals are those derived from water and oxygen (i.e., H, OH, $\bar{e}_{aq}$, HO_2^+ and many others) since these are far the most abundant molecules in living tissues. The instantaneous distribution of such chemical species in and along the tracks of the secondary particles is of great theoretical importance in predicting possible chemical sequences, and they are capable of a bewildering variety of reactions, the nature of which depends very much on the solutes and the ' scavengers ' that are present. Energy from the so-called activated water may increase the inactivating power of radiation on enzymes, thus causing an indirect effect as well as the direct effect of the radiation on the material. The study of all these initial reactions involves the use of

complex electronic techniques, such as electron-spin resonance. It is fairly easy to follow free radical formation and decay in simple model systems, but applications to cells and tissues are hampered by the difficulty of determining which among a complex set of signals are significant.

The effects of radiation have frequently been interpreted by the ' target theory '. In its simplest form this theory assumes a given biological effect to be due to one or more ionizations involving a particular ' target ' region. The theory has been of great utility and in simple cases leads to reasonable estimates of ' target size ' and also to the correct prediction of the dose of different radiations required to destroy a given target. In its simplest form, however, it does not take adequate account of the mechanisms of biochemical response by the irradiated tissue.

In general therefore, although the initial physical interactions between the radiation and the atoms it encounters are fairly well defined, the subsequent chemical and biochemical reactions are still poorly understood. It is important to elucidate these since knowledge of the specific reactions involved might open the way to a more effective chemical control of radiation effects—for example by the development of radioprotective drugs (§1.6).

3.2 *Cellular consequences*

Radiation damage may result in: (*a*) cell death, either during interphase or at mitosis—this response of course is the basis of radiotherapy and determines short-term radiation hazards; (*b*) mutation, leading to genetic effects; (*c*) induction of neoplasia, which may be consequent on ' somatic mutation '; (*d*) where there has been only a small number of ionizations there may be an effect on somatic cells that is normally not detectable and is revealed only by special tests—the cells can apparently still carry out their normal functions and they may or may not have repaired the damage. With small doses of radiation this last is the most likely course of events, the probability of detectable damage increasing with dose. A given biological outcome may be the result of a variety of initial ' lesions '. The biochemical lesions leading to cell death are not necessarily the same as those leading to mutation, and carcinogenesis may require a series of ' events ' before the production of an overt tumour.

The majority of radiobiological experiments have been concerned with lethality, and this is not surprising since the experiments have a clear endpoint and lead relatively rapidly to quantitative results. But the approach is often that of the ' black box ', with radiation dose as input and survival curves of a bacterial population, cell culture or animal colony as output. Some insight is obtained into the mechanism by which damage is produced, although the information may convey little but a guess about the number of ' hits ' per ' target '. A weakness of this approach is that it pays little attention to the fate of surviving units, which may hold important clues about the mechanisms of injury. A similar criticism applies to studies of arrest of mitosis at low radiation dosage. In both cases further studies are desirable.

3.3 *The influence of quality of radiation and dose fractionation*

The action of radiation depends not only on the dose administered but also on the time spacing of the dose; in general the effect decreases as the dose is spread over longer periods. The results of splitting a given dose into fractions are very complex and probably worthy of much more study. The effects are also determined by the physical nature of the radiation received, and particularly by the

density of ionization along the tracks of the secondary particles. This is related to the rate at which the ionizing particle loses energy per unit length of track (linear energy transfer—LET). The theoretical significance of LET lies in the spacing of ionizations in relation to the size of the biological 'target' under consideration, for example a critical molecule or atomic grouping within a molecule, since this determines the chance that one or more ionizations will occur within the target.

If radiations of low LET (e.g., γ-rays) are used it is found that:

(*a*) The dose–survival curve may have a 'shoulder', preceding an exponential decline in surviving units as the dose given increases.

(*b*) At low dose rates or when the dose is fractionated, the damage per unit dose may be lower than with higher dose rates or with single doses, possibly owing to repair processes.

(*c*) Raised concentrations of oxygen may increase the damage per unit dose.

By contrast it is found that with radiations of high LET (e.g., high-energy neutrons and α-particles):

(*a*) The dose–survival curves are more frequently exponential.

(*b*) Dose fractionation makes much less difference.

(*c*) The concentration of oxygen is of less significance.

A further characteristic of high-LET radiations is that they usually have a higher relative biological effectiveness (RBE) for a given energy absorbed than do lower-LET radiations. Although there is no universal correlation between LET and RBE, in a number of cases a maximum RBE is reached for an LET around 100 keV/μ, with a subsequent decline. Many unsolved problems exist, some of which—for example the values of RBE at low doses and low dose rates—are of considerable importance, particularly in relation to carcinogenesis. Studies of this kind are facilitated by the use of large machines (see §4.4 below).

3.4 *Biochemical changes*

Although it is established that radiation interferes with nucleic acid metabolism, antibody synthesis and enzyme activity, the search for specific biochemical changes has been disappointing. Interpretation of results is complicated by asynchrony of cell cycles, which creates a variation of sensitivity between different cells, and by the intervention of innumerable other mechanisms. Studies that use the techniques available to synchronize cell cultures hold out some promise of more clear-cut results.

The real difficulty, however, lies in the fact that the initial 'events' in the action of radiation are random in both space and time, whereas the basic cell processes require extreme precision for the complex synthesis, transport and orientation of material that are involved. The main hope seems to be in greatly increased basic knowledge of the biophysical chemistry, which should lead to more informed guesses about the probable results of interference with the mechanisms. Most of the cellular constituents are present in quantities that in molecular terms are large, so it is unlikely that a few randomly distributed, isolated lesions will affect sufficient of them to cause gross changes in cell behaviour. In contrast, only one or two specific DNA macromolecules are present in cells (except in the occasional polyploid cells), and they are moreover capable of being replicated, so that every lesion occurring in one of these can have an

important effect either immediately or within a few cell generations. Another example of a limited ' target ' that can produce a general cellular effect after a ' hit ' by radiation is the lysosome, since when damaged it releases hydrolytic enzymes.

There is very great difficulty in extrapolating from events in model biochemical systems to corresponding events *in vivo*. A similar caution is required in attempts to estimate the probable damage in man from radiation effects on populations of bacteria, cell cultures or even colonies of animals. Nevertheless, a great deal of our present-day information is necessarily derived from these simple systems.

3.5 *Effects on* DNA

Direct damage to the genetic material of the cell (DNA) has been an obvious field for study, in relation not only to the lethal effects of radiation but also particularly to mutation and carcinogenesis. Much attention has been given both to point mutation and to chromosomal damage, and both these types of study are important for the elucidation of the mechanisms of radiation effects. Studies of point mutation still depend almost wholly on conventional genetic procedures —for example, the exposure of colonies of animals and subsequent scoring of specific changes. Although laborious, such studies continue to hold out promise of further advances. There has moreover been considerable progress in the last few years in the study of chromosome damage. The study of aberrations in cultured lymphocytes damaged *in vivo* is proving of great interest, since this effect may be quantitatively linked to dose received, the incidence of dicentric and ring structure varying with radiation parameters in the same way as does cell death. The ready availability of human lymphocytes and their sensitivity and graded response hold considerable promise for human radiobiology.

Although ionizing radiations were the first agents shown to be capable of affecting the genetic material, we still know less in biochemical terms about their action than we do about the action of some other agents, such as ultraviolet radiation and mutagenic chemicals. This is chiefly because the effects of ionizing radiations are relatively drastic, owing to the high energy released; for instance, one-hit mutations in *Drosophila* involve the loss of several bands on a salivary chromosome—an effect too extensive to be within the range of a single active radical. As a result it seems rather unlikely that fundamental biologists would at present choose ionizing radiation as a preferred tool for analysing the mutagenic process in general, or that they would put any great effort into trying to unravel the complex issues involved in radiation mutagenesis. The main reasons for using ionizing radiations for investigations at the molecular level must be found in their technological and practical importance, rather than in their power or precision as tools of analysis. On the other hand certain of the effects produced by ionizing radiations are of considerable interest at the level of molecular genetics—for example, the mechanisms underlying arrest of mitosis and the ' repair mechanisms ' that produce partial recovery from radiation damage. It has been shown that damage produced by ultraviolet radiation may be repaired by light-activated enzymes, which are known to monomerize thymine dimers. There are, however, also dark-repair systems, probably of several kinds. Repair of chromosome breaks is usually carried out by a non-light-sensitive mechanism. It is not clear how large a stretch of damaged DNA can be repaired; but there is evidence (from dose rate studies) that at least a

sizeable fraction of X-ray-induced mutation can be repaired and, as we have seen, some of this damage is quite extended in space.

3.6 *Carcinogenesis*

The search for biochemical mechanisms of radiation injury has been concentrated particularly on carcinogenesis, but so far with little success. A widely held theory is that somatic mutation—a change in the DNA of somatic as distinct from germ cells—is associated with the proliferative and 'dedifferentiating' changes in neoplasia in that it destroys or alters cellular control mechanisms. At the present time there is great interest in the question of immunological response to specific tumour antigens that might arise from alterations in the DNA. But in the case of leukaemia at least—apparently the commonest form of radiation-induced neoplasia—and probably in other types of neoplasia as well, any simple theory of somatic mutation seems inadequate to fit the facts and more than one 'event' may be required. It is also well known that irradiation of chronic inflammatory conditions is particularly likely to lead to neoplasia, and it could be that some other pathological conditions are similarly sensitive to radiation. The effects of radiation on viral and other infections in the whole animal are particularly worthy of study.

3.7 *Other somatic effects*

Many changes follow whole-body irradiation, especially at relatively high dose levels. These are often due to the sensitivity of dividing cells with special functions—for example, cells of intestinal villi and bone marrow cells. Much more knowledge is needed of the natural history of such cell lineages and of the phases and nature of the radiation damage.

The sensitivity of lymphoid cells to radiation is of course the basis of the immunosuppressive effect. This is again due in part to the sensitivity of dividing cells; but an unexplained anomaly is the response of small lymphocytes, since most of these cells spend very long periods without dividing yet are extremely radiosensitive. This radiosensitivity is in fact of use in immunological research: radiation is used to dissect the various stages of immune responses on the basis of their relative radiosensitivities, and to provide animals for research whose immunological unresponsiveness permits the study *in vivo* of a variety of transplanted cells and tissues. Such work does not of course in itself throw light on mechanisms of radiation damage. Immunological studies are, however, proving important in many fields, including radiotherapy; for example, immunological attack on a tumour may be exploited to supplement attack by radiation (see §2.3).

Some obvious and important macroscopic effects of radiation deserve further study of their basic mechanisms with modern techniques. These effects can be graded, and need not be accompanied by cell death. Besides immunosuppression, examples are:

(*a*) Effects on the alimentary tract, as shown by the nausea and vomiting that follow whole-body irradiation and, in some cases, radiotherapy.
(*b*) Erythema—a striking radiation effect recorded in many of the early studies of radiation and dosimetry, but still not well understood.
(*c*) Effects on endocrine mechanisms.
(*d*) Effects on the lungs and on the vascular system.
(*e*) Cataract, particularly following irradiation by heavy particles.

The analysis of these complex responses in higher animals is important and deserves encouragement.

3.8 *Possibilities for further advance*

From the wide range of possible studies implied in the preceding discussion the Committee has in particular identified the areas listed below as ones in which the results of further work might be specially valuable. Attention is, however, drawn to the reservations expressed in §4.3 about the conditions under which such work might have the best chance of success.

1. *Lethality* A broad general account can now be given of lethality in cell or bacterial populations in relation to dose of radiation, dose rate and type of radiation. Microdosimetric studies have given a fairly detailed picture of the initial ionizing ' events ', and electronic computing methods might now make a valuable contribution to the estimation of biological damage. But the specific biochemical entities responsible for the damage and the chemical reactions in which they take part need to be identified.

2. *Effects on genetic material* Recent advances in the general field of molecular biology, and in the understanding of mutagenesis induced by ultraviolet radiation and chemicals, suggest that the time is ripe for a concerted attack by molecular biologists, quantum chemists and geneticists on the nature of the direct and indirect effects of ionizing radiations on the DNA of higher organisms as well as of microorganisms. The mechanisms capable of repairing radiation-induced damage to the genetic material also call for intensive study. Studies are also required of each stage of DNA replication, including transfer of materials and molecular orientation, and of the biochemistry of chromosome constituents, including histones.

3. *Ultrastructural effects* More experimental effort might also usefully be concentrated on radiation damage to the cellular ultrastructure. Such studies are relevant to theories of radiation damage due to the displacement of enzyme systems consequent on breakdown of cellular partitions.

4. *Damage to lysosomes* More knowledge is needed of the effects of radiation on extranuclear structures, particularly the lysosomes.

5. *Cellular repair mechanisms* Processes of repair of cellular damage deserve much more study since they may throw light on both primary lesions and normal mechanisms. Such studies may also assist materially in the interpretation of dose–response curves and in the enhancement of chemical ' protection '.

6. *High-*LET *radiations* There are prospects of further advances, particularly in understanding mechanisms of carcinogenesis, from continuing studies of high-LET radiations.

7. *Somatic effects* Further work should be developed at the higher levels of organization—in tissue, organ or whole animal—in the light of knowledge gained on simpler systems. With this should be associated the study by modern techniques of long known but relatively neglected somatic effects, such as damage to the alimentary tract, radiation erythema and cataract, and of the effects of radiation on lungs and blood vessels. It is at present uncertain whether there is a non-specific life-shortening effect, and this problem also requires investigation.

As already mentioned in the introduction to this report, the Committee's conclusions and recommendations are intended as a guide to the formulation of the Council's long-term policy for the support of research, perhaps over the next 10–20 years. In this context the assumption has been made that there will be no great change in the urgency of the problems of radiation hazards—as a result, for example, of a reversal of the present decline in environmental contamination from fallout attributable to nuclear weapon testing.

4.1 *Radiological protection*

The survey summarized in this report, together with a study of publications such as the Council's 1956 and 1960 reports on radiation hazards*, have convinced the Committee that the Council, through its committees and staff, plays an important part in organizing research, in collaborative assessment of the significance of results, in interpreting and focussing the major issues, in identifying new situations involving radiation risks, and in advising the Government. The Council's authoritative position has arisen from its unique capacity to obtain help from a wide range of experts, both in the radiation field itself and in the relevant branches of physical and biological science and medicine. The Committee believes that this position is of great value both nationally and internationally and that it should be maintained.

The advisory role that the Council has fulfilled in the past is well illustrated by the recommendations in its 1956 and 1960 reports on maximum permissible levels of strontium-90 in bone. Since that time, however, the increasing precision with which it is becoming possible to estimate radiation risks in quantitative terms has raised problems affecting the Council's future role. In the light of recent knowledge, it has been argued that it would be better not to recommend ' maximum permissible ' or ' acceptable ' levels, but rather to provide an estimate of the risks associated with any given level of radiation exposure, leaving the Government to decide at what point action may be necessary. On this basis it might be maintained that the scientific problem would be divorced from the political one and the question of precise levels at which action, if any, should be taken would no longer need to be the Council's responsibility. It seems more realistic, however, to argue that the Council would be expected to give some decisive advice on these secondary aspects as well as on the initial scientific problem, and the Committee considers that the Council would inevitably continue to be called on to give advice to the Government on the point at which action should be taken to protect the general population in case of nuclear accidents or rising radiation levels, as well as on protection policy in general.

The Committee takes the view that for the Council to fulfil an advisory role of the sort envisaged above it is necessary that it should continue to have its own staff actively working in the protection field. The nature of the research effort called for by the Council should, however, be primarily concerned with establishing the basic criteria on which protection standards rest. Thus the

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* *The Hazards to Man of Nuclear and Allied Radiations* (Cmd. 9780), 1956.

The Hazards to Man of Nuclear and Allied Radiations: A Second Report to the Medical Research Council by their Committee on the Hazards to Man of Nuclear and Allied Radiations (Cmnd. 1225), 1960.

Council's research programme should include work aimed at defining and, where possible, making quantitative estimates of the effects of radiation at all levels of biological organization—on intracellular constituents, cells, tissues, organs, whole animals and populations. In particular there is still room for further experiment relating low doses of radiation to their biological effects; but the Committee considers that such work should increasingly proceed by analytical methods defining the processes of damage and recovery, and that efforts should be made to reduce the need for exposing large animal populations to very low doses of radiation. There is also a need for continuing work on a number of special problems, for example hazards associated with the use of plutonium and carbon-14. The Council should not, however, be directly concerned with the implementation of protection procedures. This is the responsibility of Government departments having statutory functions and possibly, in the future, of the proposed National Radiological Protection Board.

However, the Committee has concluded that the scale of the Council's support of research relevant to radiological protection needs revision. It agrees with the view that the Council's 1956 and 1960 reports took the broad measure of the scientific problem of radiation protection and that further developments are likely to be concerned not so much with principle as with detail and quantitative adjustment. Practical maximum permissible levels covering a range of situations where the hazard can be controlled at source have been in force for a number of years and have apparently been satisfactory. It is true that these levels involve margins of safety that further work might modify; moreover, the lack of precise knowledge in this area may, on the one hand, lead to risk in special cases and, on the other, by overestimation of risk, hold up developments in medicine, scientific research and nuclear industry and have significant economic consequences. But if one takes account of the considerable body of knowledge relevant to radiation protection that has been built up since the war and particularly in the last decade, as well as of the extensive protection facilities that now exist and the currently declining levels of environmental contamination from fallout, the urgency of such work is evidently now considerably less than it was previously.

In considering the future scale of support by the Council for research relevant to protection the Committee has also been influenced by two other factors: first, it has noted that the Council's present expenditure in this field is high in relation to that in other fields and, second, it has been influenced by the likelihood that the proposed National Radiological Protection Board will need to build up its own programme of research. While the orientation of this programme may be expected to be mainly towards developmental and applied research, nevertheless the new organization may reasonably be expected to support some more basic work in addition. In the Committee's view it would be appropriate for the Council as well as the new organization to support such work; it is, however, essential that the two bodies should work in the closest collaboration.

The Committee therefore recommends that:

1. *Because the Council's advice in the field of radiological protection should be underpinned by continuing research, and because many aspects of such work cannot be expected to fit naturally into the research programmes of academic institutions, the Council must continue to undertake it directly in its own establishments.*

2. *It would be appropriate for the scale of future support, considered in relation to other claims within the radiobiological field, to become significantly less than it has been in the past.*
3. *Early consideration should be given to the question of how collaboration with the National Radiological Protection Board should be achieved.*

4.2 *Radiotherapy*

The Committee has been convinced that there is room for improvement in the techniques of radiotherapy as a treatment for cancer and that much of this improvement can be expected to result from increased understanding of the underlying scientific principles. Further work on the effects of different types of ionizing radiations and on the physiological conditions most favourable to selective action, as well as on methods of chemical sensitization to radiation, is particularly important. The Committee considers that this is an area of research that is unlikely to be adequately developed as a result of the spontaneous interest of those working in university departments, and that the Council, within its overall expenditure on radiation research, is at present spending a disproportionately small amount on research that is directly relevant to radiotherapy.

The Committee therefore recommends that *the Council should continue to participate directly in this field and, where opportunities present themselves, should consider increasing the scale of its support.*

4.3 *Fundamental studies on the effects of ionizing radiations*

In the section on the mechanisms of radiation injury (§3) a number of challenging areas for possible advance were noted. Work is already in train in some of these, both in the Council's own establishments and elsewhere; however, experience has shown that the majority of the problems are intrinsically very difficult and progress in, for example, the understanding of the earliest biological events is still rather disappointing. Moreover, it appears that fundamental studies have so far contributed relatively little to the solution of practical problems; their main value—which in the Committee's view should not be underrated—has been in providing some measure of understanding of empirical procedures. Nevertheless the Committee believes that fundamental work must be supported if further advances are to be made, and that the prospects would be improved if newer techniques could be applied and experts from other scientific disciplines brought together in an appropriate environment.

The Committee believes that the choice of environment for research of a mainly fundamental nature is a matter of particular importance. In this context it is useful to distinguish between two categories of work, namely that which can be seen to be directed towards the solution of problems of radiological protection and radiotherapy—which have already been discussed with particular reference to the role of the Council in §4.1 and §4.2 above—and that which is not specifically directed towards these ends but which involves the use of radiation as a means of investigating biological mechanisms in general.

In the case of work in the former category, the primary consideration should be association with research of a mainly developmental and applied nature. Such an association would be of value in that the applied research would provide material for investigation as well as maintaining the relevance of the more fundamental research and thus instilling a sense of purpose; moreover this fundamental work would have a feedback effect in creating a healthy scientific

atmosphere in which the more practical work could take place. It is also important where possible to maintain academic links, but with this category of work this may for practical reasons be difficult to achieve to the extent that the Committee would otherwise think desirable. For example, the main centres devoted to the developmental and applied problems of radiological protection will probably need to be close to centres providing regular protection services; similarly there are strong arguments for undertaking fundamental research relevant to radiotherapy near a radiotherapy department. It has already been noted that, in any event, work relevant to problems of protection and therapy cannot, as a rule, be expected to fit naturally into the research programmes of academic institutions, and the Committee has recommended that for this and other reasons (§4.1 and §4.2) the Council should continue to support establishments of its own to meet at least part of this need.

With regard to the more general use of ionizing radiation in biological research, arguments have also been put forward in favour of maintaining special radiobiological research centres. One argument is the need to provide special large radiation-producing machines, and this question is dealt with separately in §4.4 below. More generally, however, it has been argued that radiobiology is an independent scientific discipline calling for support in its own right. In favour of this view it can be claimed that ionizing radiation deserves study because it is a natural phenomenon affecting all biological material, and also that it has special advantages as a tool in biological research. For example, a precise dose, of known distribution and localized as required, can be administered at an exact time and in a painless manner from a distance, without disturbance of the experimental animal or preparation. It is true that at the molecular level the mechanisms of damage remain obscure and the action appears to be random in nature; but for producing controlled damage at higher levels of organization it offers real advantages with its possibilities of selective action. The Committee feels that these arguments carry a certain weight but that while radiation can undoubtedly be a useful tool in certain circumstances, and while certain applications and qualities of radiation do require special facilities, it is in general only one of a number of possible tools (with which it must be regarded, at least in terms of practical support, as being in competition). For example, in investigations on the mechanisms of carcinogenesis *per se*, the mitotic cycle or the origin of mutation, it is questionable whether the use of ionizing radiations is so superior to other fundamental methods of approach as to demand special consideration. In general therefore the Committee takes the view that where there are no direct links with research of a more practical orientation the need for an academically stimulating background should be the primary consideration in the choice of location for research. The support of such research in a mainly academic environment should provide everyday opportunities for critical discussion of current work as well as for actual collaboration.

In the light of all these considerations the Committee recommends that:

1. *Research of a fundamental nature that is specifically directed towards the solution of problems of radiological protection and radiotherapy should be supported primarily in association with centres undertaking work of a more practical nature in these fields. Active support should be given to projects arising from any promising new ideas in these areas. An academic stimulus such as might be provided by the proximity of a university or medical school is*

also important, but for practical reasons this must usually be a secondary consideration. In such circumstances a limited amount of work not specifically oriented towards practical problems would be justified to ensure the maintenance of the intellectual balance of the particular establishment.

2. *Work that cannot be seen to contribute more than generally to the solution of a problem of protection or therapy is, at the present time, best considered as coming from a particular speciality (e.g., biochemistry, cancer research, cell genetics) rather than from a still ill-defined overall radiobiology. Support for such work is best given where it will help to associate scientists using ionizing radiations more closely with those who are currently using other approaches to advance biology and medicine. Work in this category is in general better placed in a multidisciplinary environment such as is found in a university. It should not be given special priority, but should be judged in the usual way on its scientific merits with other research projects submitted to the Council for its support.*

4.4 *Large machines*

The Committee has given special consideration to the use of large machines such as nuclear reactors, cyclotrons and special linear accelerators for biological research purposes as distinct from clinical trials. These have some limited uses for the elucidation of the mechanisms of radiation damage and they also have more specialized uses in research directly relevant to radiological protection and radiotherapy. On the evidence put before it, the Committee does not feel that there is now, or is likely to be in the future, a large demand by research workers for radiations of special characteristics, which could be met only by additional machines. The Committee therefore recommends that:

1. *No additional very large high-energy machines for fundamental biological research purposes should be provided at present.*
2. *The machines maintained by the MRC Cyclotron Unit and, if possible, access to the facilities at Harwell should be retained.*
3. *The necessary steps should be taken to facilitate wider use by the academic community of these machines—for example, by the provision of laboratory facilities for visiting workers.*

Research supported by the Council

Full details of the research establishments and individuals supported by the Council and summaries of research programmes are given on pp. 99–252. Appendix IV (p. 273) provides information about the size of the Council's organization.

RESEARCH UNITS

New units

Three research units have been established during the past year and approval has been given for two more.

The *MRC Biochemical Parasitology Unit*, of which Dr B. A. Newton is the director, is accommodated in the Molteno Institute, Cambridge. The unit is to develop work on the biochemistry of protozoa, with special reference to human parasitic protozoa.

The *MRC Neurological Prostheses Unit* has been set up at the Institute of Psychiatry, Maudsley Hospital, London, with Professor G. S. Brindley FRS as honorary director. It will work on every aspect of the designing of electronic implants that may restore some degree of function in various types of disablement.

The *MRC Social and Applied Psychology Unit* has been established in the Department of Psychology at the University of Sheffield, with Professor H. Kay as honorary director; it will be concerned with the problem of complex judgements, in both practical industrial situations and controlled conditions in the laboratory, with special reference to the role of the computer in decision making.

The *MRC Statistical Research and Services Unit*, with Dr I. Sutherland as director, is to be established at University College Hospital Medical School, London.

The recently approved *MRC Leukaemia Therapy Unit* is to be set up at Hammersmith Hospital; Dr D. A. G. Galton is to be the honorary director. The unit's work will include clinical investigations into the treatment of the acute leukaemias and laboratory studies of blood cells.

Changes in units

Experimental Virus Research Unit	renamed *MRC Virology Unit;* Professor M. G. P. Stoker FRS succeeded as Honorary Director by Professor H. Subak-Sharpe
Infantile Malnutrition Research Unit, Uganda	renamed *MRC Child Nutrition Unit;* Professor R. A. McCance FRS succeeded as Director by Dr R. G. Whitehead
MRC Brain Metabolism Unit	Professor W. L. M. Perry (Honorary Director) succeeded by Dr G. W. Ashcroft as Director

Disbandment of unit

The *Cell Genetics Research Unit* has been disbanded on the resignation of the Honorary Director, Professor G. Pontecorvo FRS, to take up a post on the staff of the Imperial Cancer Research Fund.

RESEARCH GROUPS

A research group may be set up by the Council as a means of assisting a university in developing research within a particular department. The university then undertakes to assume financial responsibility for the group within an agreed period if the work is to continue. During the year 1968–69 three new groups were set up:

University	*Department and Director of Group*	*Title*
Liverpool	Department of Parasitology (*Professor W. Peters*)	Chemotherapy of Protozoal Diseases and Drug Resistance
London		
King's College Hospital Medical School	Department of Medicine (*Dr R. Williams*)	Metabolism and Haemodynamics of Liver Disease
Sussex	School of Biological Sciences (*Professor A. Korner*)	Mechanisms and Biosynthesis of Proteins and Nucleic Acids in Mammalian Tissues

The number of short-term research grants awarded by the Council continues to grow. Hitherto the Council's awarding bodies have been the Clinical and Biological Research Boards, which together have handled most applications, and the Tropical Medicine Research Board, which has dealt with a comparatively small number. Because of the heavy load of this work, over and above the Boards' other responsibilities such as advising the Council on projects for long-term support and reviewing progress reports of units and groups, it was decided that the Clinical and Biological Research Boards should each be assisted by two Grants Committees. Since January 1969 the majority of research grant applications have been referred for scientific assessment to one or other of these four committees. The Council has delegated to the Grants Committees powers to make awards within certain limits, though in some cases the decisions must lie with the Boards. The Boards will continue to exercise a general measure of control so as to ensure that awards reflect the Council's policies, including the priorities to be given to different subjects.

It is hoped that the new arrangements will provide more time for Council as well as Board members to consider major questions of policy and priorities, by relieving them of the more detailed work involved in the awarding of grants. At the same time it should be noted that these new Grants Committees include experts from all the appropriate fields, thus involving more of the scientific and medical community in the Council's work. Members of Grants Committees, like Council and Board members, will serve for a limited term. The present composition of the Committees is shown on p. iv.

From the list of grants on pp. 194–246 it will be seen that these awards cover a very wide range of topics.

Appendix IV (p. 273) contains a table showing the growth of the number of research grants over the years.

TRAINING AWARDS

The Council has always regarded the training of potential medical research workers as a most important aspect of its activities and various schemes of fellowships and scholarships exist for this purpose. The recently appointed Training Awards Committee considers applications for all awards except clinical research fellowships (which are awarded by the Clinical Research Board).

Clinical fellowships

The Council would welcome more applications for clinical research fellowships and Anglo–French clinical research scholarships, and qualified medical graduates are reminded of these opportunities of preparing themselves for a senior career in research. Under the clinical research fellowship scheme the Council is now able to pay stipends equivalent to the maximum point on the NHS Senior Registrar scale, in order to provide for more senior candidates than might otherwise apply.

Travelling fellowships

Competition continues to be keen for the Council's travelling fellowships and the associated awards for study overseas, for which nominations are made by the Council.

Junior research fellowships, scholarships for training in research methods, awards for further education and other awards

During the year major changes have been made in the arrangements relating to scholarships for training in research methods and awards for further education.

Until recently the Council has found it possible to offer research training scholarships to all candidates who appeared to be of a good standard (the normal criterion being a first or upper second class honours degree) and who proposed to work within the Council's field of interest. In the last year or two, however, the number of well qualified candidates has increased so sharply that a proportion of those who would have qualified in earlier years have not obtained awards. It was felt that the best course would be for the Council to control the distribution of awards between subjects by allocating specific numbers of awards to particular departments, leaving the chief responsibility for selecting individuals to fill those places with the heads of the departments. Accordingly, scholarships for the academic year 1968–69 were for the first time awarded on the basis of a scheme of allocations similar to the one used by the Science Research Council and the Social Science Research Council. Requests for quotas of scholarships far exceeded the number available. The scheme makes provision for some of the available awards to be made at a later stage ; this arrangement provides a second chance for departments whose hopes have been disappointed and for candidates who come forward after the allocated places have been filled.

In the allocation of the awards account is taken of the support offered by the other research councils—for example, by the Science Research Council in the general field of biology and by the Social Science Research Council in psychology.

The number of awards for further education has grown more rapidly than have research training scholarships in recent years. Increasing attention has been paid recently to the quality and scope of the courses that applicants wish to pursue, and the Training Awards Committee has now decided to restrict future awards to candidates who choose a course approved by the Council. This scheme will apply to awards made for the year 1969–70.

The Secretary of State for Education and Science has announced the withdrawal of the power of local education authorities to make postgraduate awards in fields covered by central government schemes, and the Council expects to take over, in 1969–70, a small number of awards that would under the previous arrangements have been made by these authorities.

More detailed information on the Council's awards will be found later in this report (pp. 247–52 and 273).

Finance

The Council's account for the financial year 1968–69 is shown in appendix I, which includes the corresponding figures for 1967–68 for comparison. A summary of receipts and payments over the last five years is given in appendix II, and from this the trends in expenditure on the different forms of research support can be seen. Appendix III shows the funds received by the Council from other bodies, either as grants or as reimbursements for work administered by the Council on behalf of Government Departments.

In the period of financial stringency following devaluation the Council could not expect to escape unscathed. The figure proposed by the Council for the

parliamentary grant-in-aid for 1968–69 was reduced by £291 000 by the Government, the approved grant being £15 339 000. During the year, as a result of further Government retrenchment, the Council was asked to reduce its budget by a further £108 345, leaving £15 230 655. The Council's budget was therefore some £400 000 less than the Council had proposed. In addition the Government requested the Council to reduce its commitments to make it possible to meet the full costs of unbudgeted pay awards without a supplementary grant. The effect of these reductions was to allow the Council, in real terms, only 6 per cent more in 1968–69 than in 1967–68. For the year 1969–70 the sum recommended for the Council's grant-in-aid has been reduced by the Government to a figure that represents an increase of about 9 per cent in real values above the provision for 1968–69.

From the following table it will be clear that with the funds provided for the years 1968–69 and 1969–70 the growth rate of research supported by the Council is lower than in the foregoing years.

	Parliamentary grant	*Percentage increase over previous year*	
		Actual	*Expressed in terms*
Year	£m.		*of constant prices*
1964–65	8.753	24.5	12.8
1965–66	10.088	15.3	10.3
1966–67	11.825	17.2	12.2
1967–68	13.758	16.3	13.0
1968–69	15.231	10.7	6.0
1969–70	17.141	12.5	9.0

The Council is concerned over the difficulty in planning its programmes under the present system of financial provision. The incidence of payments for long-term capital projects, once embarked on, is largely outside its control and cannot be evened out from year to year. If a project is delayed the funds allocated may not be spent in full. The unspent part must be surrendered and when the payment falls due in another financial year it must be made at the expense of short-term support; this system prevents the most effective use of the resources available for medical research.

A number of points may usefully be made about expenditure in 1968–69. The small decrease in expenditure on special grants does not indicate any change in policy but is due to the uneven incidence of payments for expensive pieces of apparatus. The increase in expenditure on new buildings is again largely accounted for by expenditure on the buildings for the Clinical Research Centre and the new development at the National Institute for Medical Research; expenditure on the buildings for the Clinical Research Centre during the year amounted to £1 million. As a result of the slow progress of building at the Centre mentioned in the 1967–68 report, the commissioning of phases I and II of the project may coincide in the financial year 1970–71 and thus create an abnormally large claim on the Council's resources in that year. The difficulty of absorbing the uneven cash demands caused by capital projects under the present system of budgeting has been referred to above.

The costs of the central administration showed a larger increase in expenditure in 1968–69 than in 1967–68, when it was very small (although the percentage of the total budget attributable to this head remains virtually the same); this is mainly due to increases in salary rates following the increases in Civil Service pay scales, to which the salaries of the Council's administrative staff are linked.

The percentage distribution of the Council's recurrent expenditure in 1968–69 compared with 1967–68 is shown in the table below.

	1968–69 %		1967–68 %	
Direct support				
National Institute for Medical Research	11.7		11.8	
Clinical Research Centre	3.2		2.1	
Research units and external scientific staff	47.4		48.9	
		62.3		62.8
Indirect support				
Special grants	5.4		5.9	
Research groups	3.2		3.5	
Short-term research grants	18.5		17.7	
Training awards	5.0		4.7	
International subscription	0.4		0.4	
		32.5		32.2
Administration	4.3		4.3	
Central expenses	0.9		0.7	
		5.2		5.0
		100.0		100.0

Benefactions

The Council is able to receive and administer private funds or properties entrusted to it by grants, gift or bequest, either for the general purposes of medical research or for research on specific subjects. A number of valuable additions to its resources were received during the year covered by this report and for these the Council wishes to make grateful acknowledgement.

Bequests and donations received during the year totalled £20 162. This includes bequests of £5000 from the late Mrs Flora Koch, in memory of her son, for research into mental diseases and disorders, and £1000 from the late John Farquharson for use in Scotland on cancer research. It also includes a donation of £8000 for research on mental retardation, generously donated by a member of the Council's staff, Dr N. O'Connor, from his prize as winner of the Kennedy International Award for service to the mentally retarded, and a further donation of $3000 (£1252) from Du Pont de Nemours International SA, Geneva, for the support of research at the MRC Laboratory of Molecular Biology.

Personnel

OBITUARY

The Council noted with much regret during the year under review the deaths of a number of those who had been associated with the MRC in one way or another over the years. A special tribute has already been paid (p. 1) to Sir Henry Dale, perhaps the most distinguished member of the MRC's staff and indeed of the Council itself.

Sir Charles Lovatt Evans

Sir Charles Lovatt Evans FRS, Emeritus Professor of Physiology in the University of London, former vice-president of the Royal Society and member of the Council from 1947 to 1950, died on 29 August at the age of 84.

Much of his long career, which included a spell at the National Institute for Medical Research between 1919 and 1922, was spent as professor of physiology at University College London. He made many notable contributions to his subject, being particularly concerned with the metabolism of the heart. He continued to publish the results of his research until 1967, working at Porton after his retirement.

Lovatt Evans was not only an outstanding research scientist and a member of numerous committees and advisory bodies, but a first-rate teacher whose lectures aroused an abiding interest in physiology in many of his students.

Professor W. M. Court Brown

Professor Michael Court Brown, who had been a member of the Council's staff since 1950 and since 1956 director of what later became the MRC Clinical and Population Cytogenetics Unit, died suddenly on 17 December 1968 at the age of 50.

His death was an immeasurable loss to research in the fields of radiation biology and cytogenetics, to both of which he made a series of outstanding contributions. In the former of these his best known work was perhaps the study, carried out in collaboration with Dr Richard Doll FRS, which established the correlation between radiation dose and leukaemia. This interest led him to cytogenetics, and he and his team of workers were responsible for discovering a variety of chromosome aberrations, notably abnormalities of the sex chromosome complement. A feature of their work has been the use of epidemiological techniques to determine the prevalence of these aberrations in specific groups and in the population as a whole.

That a whole new area of investigation has thus been opened up is due in large measure to Court Brown. He achieved this not only by the originality of his ideas but also by a combination of rare singleness of purpose and generous encouragement of his colleagues' work.

Dr R. C. Valentine

Dr Robin Valentine, who had been a member of the staff of the Biophysics Division of the National Institute for Medical Research since 1954, died on 10 October 1968.

Valentine began his scientific career as physicist but soon developed an interest in microbiology and became well known for his skilful use of the electron microscope to elucidate the structure of viruses. In particular he collaborated with Dr H. G. Pereira in a study of the morphology and antigenic composition of adenovirus type 5, in the course of which he produced a series of superb pictures revealing the significant features of the structure of the virus. More recently he had been working on problems of protein structure, publishing excellent electron micrographs of several crystallized enzymes, and had played a part in clarifying the structure of 7*S* immunoglobulin. His death at the early age of 40 cut short a career that was already distinguished.

Dr M. J. T. Adams

Dr Michael Adams, who was a medical officer on the Council's headquarters staff before moving to the Ministry of Health, died on 6 July 1968 at the age of 40.

Before joining the Council Adams had specialized in radiotherapy, being latterly senior registrar for the United Bristol Hospitals and tutor in radiotherapy in the University of Bristol. During his time with the Council he was accordingly concerned with radiobiology, and showed himself to be a delightful colleague as well as an able administrator whose loss will be severely felt.

HONOURS

During the period under review the Council learned with special pleasure of the following honours awarded by Her Majesty The Queen:

KG	Viscount Amory (*Chairman of Council*)
Knight Bachelor	Dr J. W. Howie (*Director, Public Health Laboratory Service*)
	Professor M. F. A. Woodruff FRS (*lately member of Clinical Research Board*)
CB	Dr R. H. L. Cohen (*Department of Health and Social Security; former member of Council's headquarters office staff*)
CBE	A. L. Cochrane (*Director, MRC Epidemiology Unit, South Wales*)
	Dr I. A. McGregor (*Director, MRC Laboratories, Gambia*)
	Dr G. F. Marrian FRS (*former member of Council*)
CMG	Professor B. G. Maegraith (*member of Tropical Medicine Research Board*)
OBE	Dr J. M. A. Lenihan (*Director, Scottish Centre, Radiological Protection Service*)
	Dr W. J. Meredith (*Director, Manchester Centre, Radiological Protection Service*)

The Council was also glad to note the following other honours:

Dr D. Bewley (*MRC Cyclotron Unit*): Röntgen Prize, British Institute of Radiology; Professor D. G. Evans (*member of Council and Biological Research Board*): BMA Stewart Prize; Professor J. L. Gowans FRS (*member of Council and Chairman of Biological Research Board*): Gairdner Award; Professor H. Harris FRS (*Honorary Director, MRC Human Biochemical Genetics Unit*): William Allan Memorial Award of the American Society of Human Genetics; Sir Harold Himsworth FRS (*former Secretary of Council*): Fothergillian Medal and Conway Evans Prize; Dr E. W. Ikin (*MRC Blood Group Reference Laboratory*): Oliver Memorial Award; Professor W. T. J. Morgan FRS (*member of Council and Biological Research Board*): a Royal Medal (Royal Society); Dr N. O'Connor (*Director, MRC Developmental Psychology Unit*): Kennedy International Award; Dr R. G. Whitehead (*Director, MRC Child Nutrition Unit*): Drummond Prize.

The Council noted with pleasure that the following had been made a Fellow of the Royal Society:

Dr A. Klug (*MRC Laboratory of Molecular Biology*)

MEMBERSHIP OF COUNCIL AND RESEARCH BOARDS

Council

Sir Edward Collingwood FRS, Professor Martin Roth and Professor A. R. Currie have retired from membership of the Council after completing their period of service; Professor D. A. Pond and Professor T. Symington have been appointed as scientific members. Dr Gray has also been appointed a member of the Council for the term of his secretaryship.

At the end of the present session Lord Amory will be succeeded as Chairman of the Council by the Duke of Northumberland.

Biological Research Board

Professor R. E. Coupland, Professor J. N. Davidson FRS and Professor D. Whitteridge FRS have retired as members of the Biological Research Board. Professor H. J. Evans and Professor C. G. Phillips FRS have been appointed as members. Professor J. L. Gowans FRS is continuing as chairman of the Board for a second year.

Clinical Research Board

Professor C. H. Gray and Professor Sir Michael Woodruff FRS have retired from membership of the Clinical Research Board and Professor R. Y. Calne and Professor T. Whitehead have succeeded them. Professor Roth and Professor Currie are now *ex officio* members of the Board since they have been appointed as chairmen of the Grants Committees. Professor Pond and Professor Symington also serve on the Board as clinical members of the Council.

Tropical Medicine Research Board

Professor D. V. Hubble, Professor A. M. Thomson, Professor T. Wilson and Dr F. J. Wright have retired as members of the Tropical Medicine Research Board and Dr Wallace Fox, Dr R. J. W. Rees and Dr J. H. Walters have been appointed in their places. Professor G. M. Bull has taken over the chairmanship of the Board on the retirement of Sir Harold Himsworth.

Assessors to Council and Boards

Through the appointment of assessors to Council other closely related organizations are able to be kept informed of developments taking place under the Council's auspices. The Chief Medical Officers of the Department of Health and Social Security and the Scottish Home and Health Department, the Chairman of the University Grants Committee, the Chairman of the Science Research Council and the Secretary of the Agricultural Research Council are, *ex officio*, assessors to the Council; a further assessor is nominated by the Royal Society on the Council's invitation. Sir George Godber (Department of Health and Social Security), Dr J. H. F. Brotherston (Scottish Home and Health Department), and Professor Sir John McMichael FRS (Royal Society, succeeding Sir Ashley Miles FRS) attend meetings in their capacity as assessors. The Chairman of the Science Research Council and the Secretary of the Agricultural Research Council receive papers on a reciprocal basis: papers are also exchanged with the Social Science Research Council and the Natural Environment Research Council.

The Chief Medical Officers of the Health Departments and the Chief Medical Officer of the Northern Ireland Ministry of Health and Local Government are assessors to the Clinical Research Board. Ministry of Overseas Development assessors attend meetings of the Tropical Medicine Research Board.

The members of Council, the three Research Boards and the Grants Committees are listed in full on pp. ii–iv.

RETIREMENTS AND RESIGNATIONS

Dr J. Walker

Dr James Walker, Head of the Division of Organic Chemistry at the National Institute for Medical Research, retired in March 1968 after thirty years in the Council's service. Dr Walker is distinguished for his work in a number of fields, particularly those of steroid chemistry, chemotherapy and the chemistry of antibiotics. He has a profound knowledge of chemistry, which he has always made readily available to others; his help in this respect will be greatly missed both by his colleagues at the National Institute for Medical Research and by the Council.

The following members of the Council's scientific staff have left to take up senior academic or hospital appointments:

Dr G. A. Foulds (*MRC Unit for Epidemiological Studies in Psychiatry*)	Visiting Professor, University of Western Ontario, Canada
Dr D. G. Harnden (*MRC Clinical and Population Cytogenetics Unit*)	Professor of Cancer Studies, University of Birmingham
Dr A. O. Langlands (*MRC Clinical and Population Cytogenetics Unit*)	Consultant, Western General Hospital, Edinburgh
Dr J. Lowy (*MRC Biophysics Unit*)	Professor of Biophysics, University of Aarhus, Denmark
Dr H. V. Thorne (*MRC Virology Unit*)	Professor of Microbiology, University of Sherbrooke, Canada

* * *

In submitting this report covering the Council's activities over the period 1 April 1968—31 March 1969, members of the Council wish to express their gratitude to all those, including the members of the staff, who have given help or advice, whether in an individual capacity or as members of special committees. This help has been of immense value in furthering the Council's programme of research.

AMORY

Chairman of the Medical Research Council

J. A. B. GRAY

Secretary of the Council

20 Park Crescent

London W.1

23 April 1969

Aspects of medical research, 1948–1968

The following reviews are intended to illustrate some notable achievements in selected fields of medical research during the period when Sir Harold Himsworth was Secretary of the Council. While the articles also refer to research not done in MRC establishments, the emphasis is essentially on the work carried out under the Council's auspices. The authors are all senior members of the Council's staff who have themselves been responsible for much distinguished work. Each article contains a personal assessment of the advances made in one particular area over the past twenty years or so, as well as of likely future developments.

Molecular biology

M. F. PERUTZ, CBE, PH D, FRS

Chairman of Governing Board, MRC Laboratory of Molecular Biology

EARLY BEGINNINGS

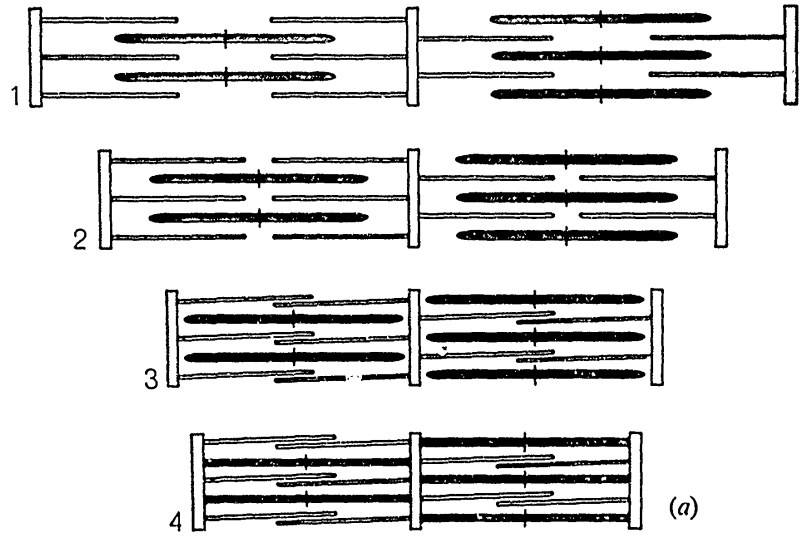
Molecular biology is the child of biochemistry and genetics, but it broke away from its parents under the influence of its godmother physics, by asking different questions and using different, often physical, methods to answer them. Biochemists mainly traced the course of the chemical reactions that build up living from non-living matter or convert food into energy; geneticists generally treated genes as abstract factors determining inherited features. Molecular biologists, on the other hand, have sought to explain the inheritance, development and behaviour of living organisms in terms of the atomic structure and interactions of certain large molecules. These molecules are mainly of three kinds: proteins, deoxyribonucleic acid (DNA) and ribonucleic acid (RNA).

Chemical reactions in cells proceed in a series of small steps, and each step is catalysed by a protein specifically adapted to that single purpose. Proteins possessing such catalytic properties are called enzymes. At first these were thought of as large molecules of indefinite structure, but in the late 1920's the Swedish physicist T. Svedberg showed that each enzyme has a definite size, and American biochemists were the first to crystallize some of them. Since crystallization is regarded as a criterion of chemical purity, this suggested that enzymes are molecules of definite structure. One of the great achievements of molecular biology in Britain has been the development of chemical and physical methods for determining the structure of enzymes, and the interpretation of their catalytic activity in precise atomic terms. Muscular movement is another biological activity that depends on the action of proteins and is beginning to be understood in molecular detail.

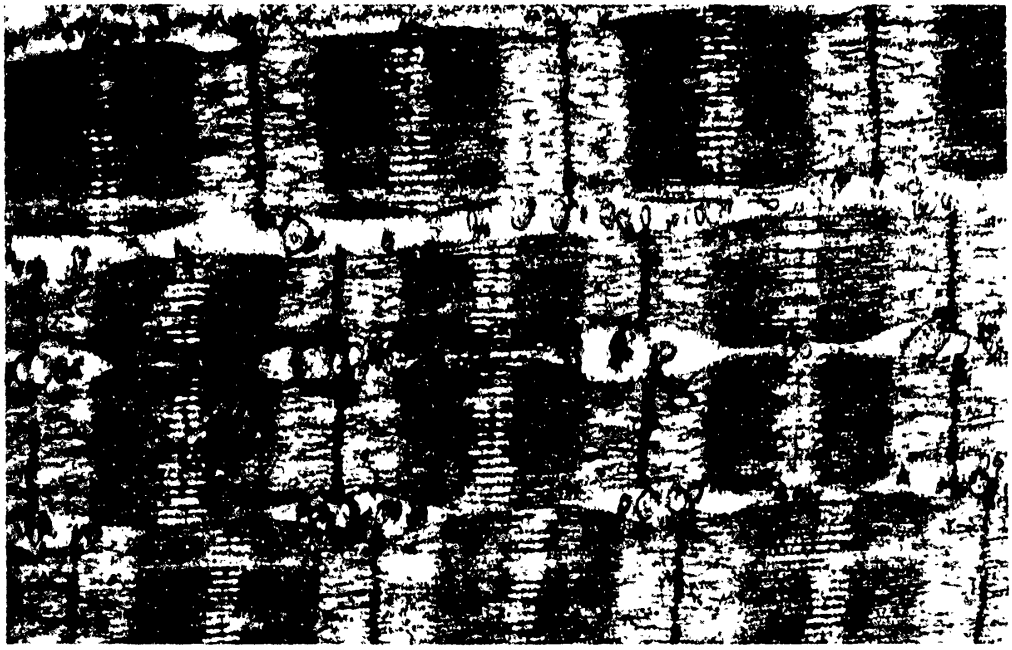
The transformation of genetics from an abstract to a molecular science has its roots in three independent lines of research that developed in the United States in the early 1940's. Mendel had shown that specific genetic factors control features such as the colour of flowers, but it had not been known how they exercise this control until G. W. Beadle and E. L. Tatum discovered that one genetic factor, or gene, apparently determines the production of one enzyme. This explained flower colour as a secondary genetic effect and suggested that the primary gene product was the enzyme that helped to make the flower pigment.

What are genes made of? They could not themselves be enzymes, since they would have to be made by yet more enzymes, and so on *ad infinitum*. The importance of deoxyribonucleic acids as the major constituents of chromosomes had been recognized correctly in the 19th century, but later their role had become controversial. In 1944 O. T. Avery and his colleagues in New York, following up observations by F. Griffith in London, discovered that DNA extracted from

PLATE I



(*a*)



(*b*)

1 2 μ

(*a*) Two segments (sarcomeres) of striated vertebrate muscle at four stages of contraction. The thin horizontal rods represent actin, the thick ones myosin and the vertical bars the membranes separating successive segments.

From H. E. Huxley (1965);
reproduced by courtesy of the Scientific American

(*b*) Ultrathin section through rabbit psoas muscle showing thin and thick filaments and membranes between successive segments. Note the regularly spaced cross-bridges linking thick and thin filaments.

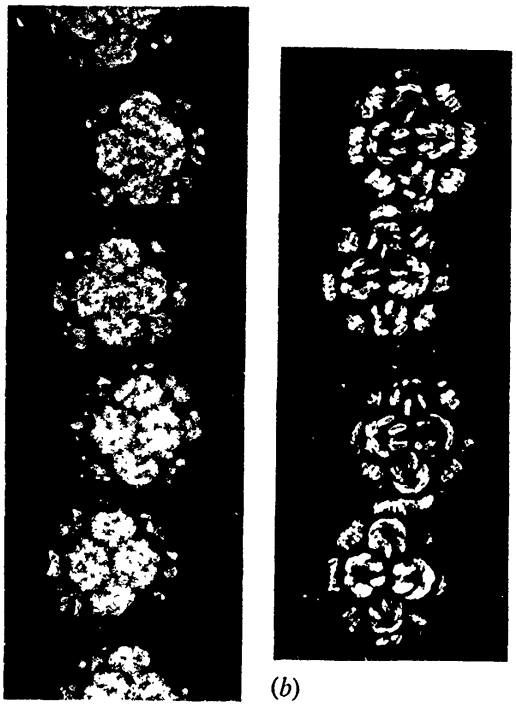
From H. E. Huxley (1957);
reproduced by courtesy of the Journal of Biophysical and Biochemical Cytology

PLATE II

Actin filaments from rabbit muscle with a precipitate of myosin cross-bridges attached to them, forming arrows. The ' knot ' at the centre represents a remnant of the membrane separating successive segments. Note how the arrows above the knot point upwards and those below the knot downwards. Negative staining shows up the fine details.

From H. E. Huxley (1963);
reproduced by courtesy of the Journal of Molecular Biology

PLATE III



(*a*) (*b*)

1000 Å

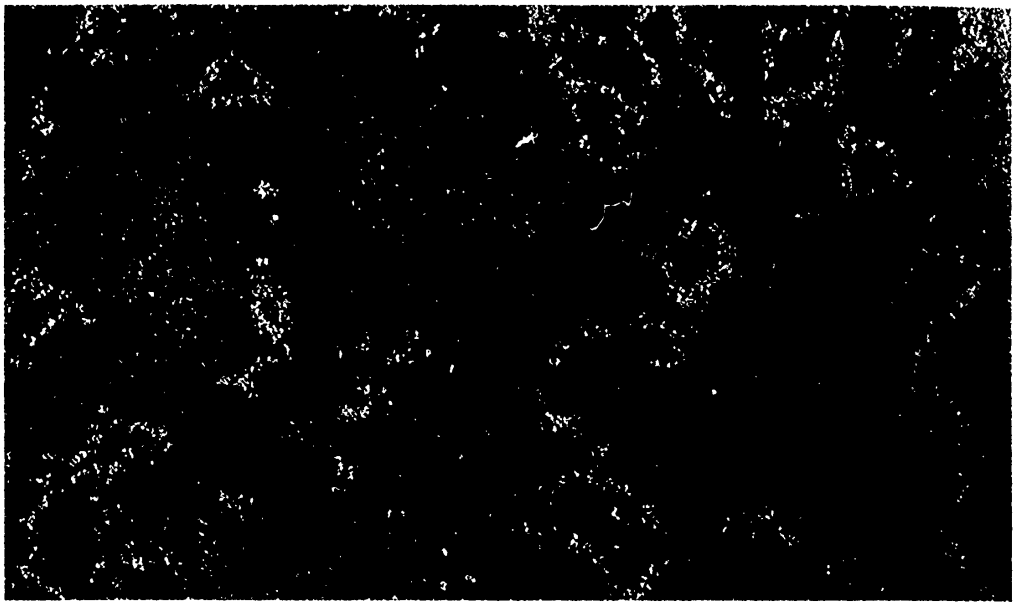
(*a*) Electron micrograph (negative stain) of turnip yellow mosaic virus particles, showing surfaces of regular hexagons and pentagons.

(*b*) Diagrammatic drawing of the arrangement of protein subunits as predicted by Caspar and Klug's theory.

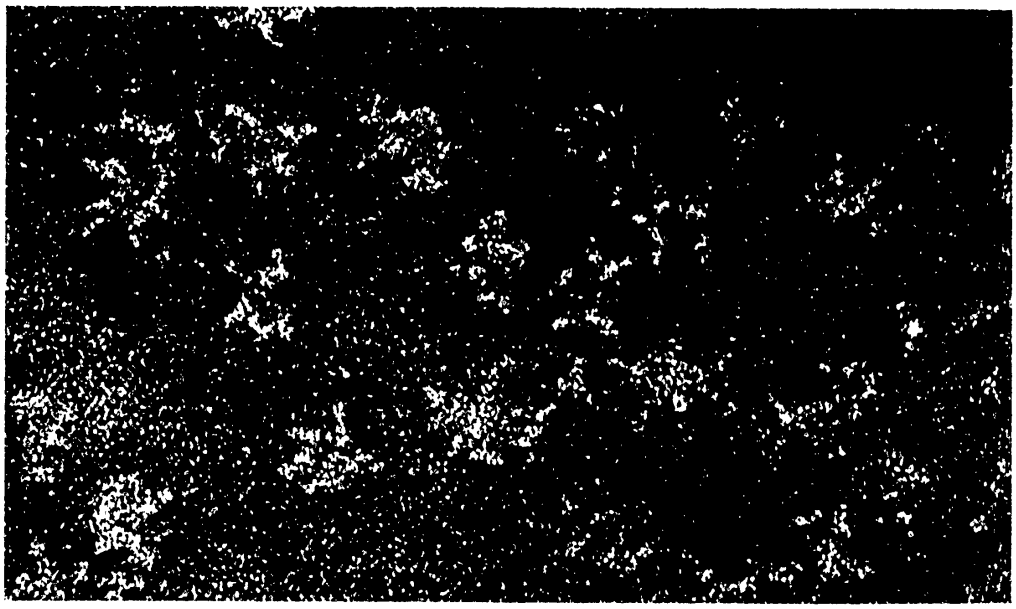
From J. T. Finch and A. Klug (1966);

reproduced by courtesy of the Journal of Molecular Biology

PLATE IV



(*a*)



(*b*)

(*a*) Electron micrograph (negative stain) of rabbit IgG antibody molecules, linked via their antigen-combining sites through a short bifunctional antigen molecule (invisible in the picture). The antibody molecules each have two hinged arms, at the end of which lie the combining sites. Three molecules are joined to form a triangle, four a rhomboid, five a pentagon, and so on. (× 500 000)

From R. C. Valentine and N. M. Green (1967);

reproduced by courtesy of the Journal of Molecular Biology

(*b*) Electron micrograph (negative stain) of rat IgM antibody molecules. No antigen is present. The molecules are seen to have a central core and five arms. (× 500 000)

Photographs by the late R. C. Valentine

one type of pneumococcus could effect a permanent genetic change in another type. This experiment was a turning point in the development of biology because it proved that a hereditary factor could be isolated in the test tube as a distinct chemical entity, DNA.

The third important line of research was initiated in 1943 by S. E. Luria's and M. Delbrück's discovery that inherited variations in bacteria are the result of spontaneous mutations and, three years later, by the discovery of genetic recombination in bacterial viruses, made independently by M. Delbrück and W. T. Bailey and by A. D. Hershey. The rigorous methods of studying the genetics of microorganisms that developed from these discoveries paved the way for the later analyses of genetic events at the molecular level. It remained for J. D. Watson and F. H. C. Crick to explain the nature of the genetic information and its transmission from parent to progeny in molecular terms.

So far nothing has been said about RNA, another kind of nucleic acid, which forms the chromosomes of certain small viruses, such as poliovirus, and acts as a go-between from genes to enzymes in higher forms of life. Its importance was first realized by J. Brachet in Belgium and T. Caspersson in Sweden about 30 years ago; but its functions in the synthesis of proteins have become understood only quite recently, when the intricate system of RNA and protein that constitutes the chemical machinery for the biosynthesis of enzymes was isolated in the test tube. This success has led to another great advance: the deciphering of the genetic code, which contains the information that is laid down in the chromosomes for translation into protein structure.

Viewed at the molecular level, life has a unity that makes molecular biology a coherent subject of great conceptual beauty. Its importance for medicine lies in allowing us to understand complex biological processes in terms of the simple laws of physics and chemistry, both in the parasites of man and, ultimately, in man himself. In the following pages I have tried to trace some of the contributions of the Council's staff to the development of its concepts and to set them into a general framework.

THE STRUCTURE OF PROTEINS

The chemical approach

Proteins appeared to play a key role in the metabolism of all living cells, and their structure seemed to many of us to be one of the central problems of biology. The great question was how it might be solved. Proteins were known to be giant molecules made up of 20 different kinds of amino acids linked together to form long chains, but their chemical structure and spatial architecture were obscure. Chemical methods for finding the amino acid composition of proteins were extremely laborious, and methods of working out the sequence of the different kinds of residues along the length of the chains did not yet exist.

In 1943 A. J. P. Martin and R. L. M. Synge in Leeds invented partition chromatography, which simplified and accelerated analysis of the amino acid composition of proteins enormously. F. Sanger was then working at the University Department of Biochemistry at Cambridge. In 1944 he introduced a chemical device which, together with the methods of Martin and Synge, allowed him to determine the sequence of amino acids in small protein fragments. He combined the free amino end-group of the chain fragment with a coloured compound; this labelled terminal amino acid could then be split off from the

remainder of the chain fragment and identified by partition chromatography. The process could be repeated on the remaining chain so that eventually the complete sequence of the fragment was determined.

Sanger applied this method to the study of insulin, because it was a pure protein of known amino acid composition. He first established that it consisted of two kinds of chains, one with 21 and the other with 30 residues, which were held together by sulphur bridges. In the course of ten years he and his colleagues succeeded in the formidable task of determining the complete sequence of the amino acid residues in the two chains and the positions of the three sulphur bridges.

Sanger's elucidation of the constitution of insulin was one of the milestones in protein chemistry. It removed the last shadow of doubt from the polypeptide hypothesis of protein structure enunciated by Hofmeister more than 50 years earlier. It established the fact that the amino acid residues really are arranged in a definite, genetically determined sequence, but disproved the widely held belief that this sequence was regular. It revealed the part played by sulphur bridges in the architecture of proteins and the chemical nature of species specificity. Most important of all, Sanger demonstrated that the complete formula of a protein can be determined by chemical methods and thereby stimulated a great volume of research all over the world. Insulin has recently been synthesized by teams in Germany, the United States and China, but the biochemical basis of its physiological action and its three-dimensional architecture are still unknown.

Since Sanger finished his work on insulin, he and others have improved the methods of sequence study and applied them to larger proteins. Two of the longest sequences have actually been worked out in the Council's Laboratory of Molecular Biology at Cambridge: chymotrypsinogen, with 245 residues in one chain, which was completed by B. S. Hartley in 1965, and glyceraldehyde phosphate dehydrogenase, with 333 residues in one chain, finished by J. I. Harris and his colleagues in 1967. C. Milstein has elucidated amino acid sequences of several immunoglobulins. A. G. Weeds is now working on the muscle protein myosin, which may contain over 2000 residues in one chain. The future of amino acid sequence analysis probably lies in automation, with the use of sophisticated physical methods such as mass spectrometry and computer analysis.

The physical approach

The chemical constitution of proteins suggested that they were long threads or fibres, but in fact most proteins behaved in solution as if they were spheres, which showed that the long chains of amino acids must be coiled or folded. To understand their catalytic activity, it seemed essential to know how the chains are folded, but chemical methods by themselves could not reveal this. What was needed, clearly, was a microscope sufficiently powerful to 'see' the arrangement of the chains, but they were 500 times thinner than the thinnest object a light microscope could reveal. Instead a physical method, introduced in 1913 by W. L. and W. H. Bragg, suggested itself. This was analysis of the X-ray diffraction pattern from crystals, which had unravelled the atomic arrangement in minerals and metals. The structure of some organic compounds had also been solved, but these were at least a hundred times smaller than the simplest enzymes.

Nevertheless J. D. Bernal, whom I joined as a research student in 1936, inspired all around him with boundless optimism about the powers of the X-ray method. In 1934 in the Cavendish Laboratory at Cambridge, he and his assistant Dorothy Crowfoot (now Hodgkin) had taken X-ray photographs of crystals of the enzyme pepsin and discovered that they gave X-ray diffraction patterns with sharp spots extending over a wide range of angles. At that time enzymes were still widely regarded as ' colloids ' of ill-defined structure, but the sharpness and extent of the diffraction pattern proved that pepsin molecules must be highly ordered and that most of their 5000 atoms must occupy definite positions.

However, pepsin proved too difficult a structure, and instead of pursuing it further Bernal in 1937 encouraged my plan to start X-ray studies of haemoglobin, the protein of the red blood cells. Crystals of horse haemoglobin gave excellent X-ray diffraction patterns; unlike pepsin they possessed a type of symmetry that made them most favourable for X-ray analysis. Besides, horse haemoglobin was easy to come by and simple to crystallize.

Rutherford's death in 1938 set in train a number of changes in the chairs of physics, as a result of which Bernal moved to London and W. L. Bragg, one of the founders of X-ray analysis, became Cavendish Professor at Cambridge. Bragg was at once fired with enthusiasm by my project and found me a grant from the Rockefeller Foundation. He and the late Professor of Biology, D. Keilin, helped me to carry on, with various interruptions due to the war, until the Medical Research Council began to support the project in 1947. At Bernal's suggestion the physical chemist J. C. Kendrew had joined me the year before. F. H. C. Crick and H. E. Huxley, both physicists, joined us soon afterwards. This group formed the nucleus of the Council's Research Unit for the Study of the Molecular Structure of Biological Systems, which, in 1962, joined up with Sanger's group to found the Laboratory of Molecular Biology.

In 1950 our interest was still concentrated almost entirely on discovering the structure of biological systems by X-ray diffraction. X-rays are diffracted by a crystal in a series of discrete reflexions which can be recorded on a photographic film in the form of a regular pattern. Each spot has a characteristic intensity that is related to the atomic arrangement in the crystal. However, there is generally no straightforward way of deriving the atomic arrangement from the diffraction pattern, because the intensities of the reflections constitute only half the required information. The other half consists of the phases and gets lost in the process of recording. Phase is a property of waves. Each spot in the X-ray diffraction pattern can be regarded as the imprint of a stationary wave originating from some arbitrary reference point in the crystal. The distance of the nearest wave crest from that reference point is known as the phase, and is a property that cannot be measured directly. (For a more detailed explanation of the meaning of phase, see Perutz, 1964.)

The atomic arrangement in crystals of simpler compounds can often be guessed, at least in part, by combining chemical information with the crystal symmetry and a few striking features of the diffraction pattern. A near guess allows the phases to be calculated with an accuracy sufficient to reveal the entire structure. So there were two avenues to the solution of a protein structure: either it had to be guessed or a way had to be found of measuring the phases

directly. This basic problem occupied Bragg, Kendrew, Crick and myself for many years. Our many approaches and disappointments are vividly described by W. L. Bragg in his lecture ' First Steps in the X-ray Analysis of Proteins ' or, as he sometimes prefers to call it, ' How Proteins were not Solved '.

Structure of crystalline proteins

In 1951 the Dutch crystallographer J. M. Bijvoet pointed out that the phase problem could be solved in principle by measuring the X-ray diffraction pattern from three crystals having exactly the same atomic arrangement but differing in the following way. Crystal 1 should contain the original compound under study; crystal 2 should contain the same compound, but chemically modified so that one of the light atoms in each molecule, a hydrogen say, is replaced by a heavier one such as mercury; crystal 3 should be similarly modified except that a different hydrogen atom in each molecule is to be replaced by an atom of mercury. The presence of the heavy atoms changes the relative intensities of the spots in the diffraction pattern in a way that allows the phases to be calculated. In theory, this seemed a hopeful approach to the problem of protein structure, but it was not clear at first how it could be applied in practice. To be successful, the heavy atoms would have to be attached without disturbing the arrangement of the protein molecules in the crystal. In crystallographers' language, the crystals with and without the heavy atoms would have to be isomorphous. In 1953 V. M. Ingram and I succeeded in preparing crystals with two atoms of mercury attached to each molecule of haemoglobin. When I developed the first X-ray diffraction picture I was thrilled to find that they were isomorphous with the crystals of pure haemoglobin and that the intensities of the spots had changed exactly as expected; at that moment I felt exuberantly confident that the structure of proteins would soon be solved. Shortly afterwards I obtained a picture of the haemoglobin molecule in projection on a plane, but to my great disappointment the only information this gave me was its external shape, which Bragg and I had already worked out by another method. Owing to the great thickness of the molecule its internal structure did not reveal itself. Clearly, I had to solve the structure in three dimensions but to do this I needed another set of isomorphous crystals with heavy atoms attached to a different pair of sites in each molecule. This proved very difficult and it took several years to find a solution.

In the meantime, Kendrew had made headway with the X-ray analysis of myoglobin, a simpler relative of haemoglobin that serves as an oxygen store in muscle. After a long search he and his collaborators had come across a crystal form of myoglobin extracted from the meat of sperm whales, which proved favourable for X-ray analysis, but there was no obvious way of attaching heavy atoms to the myoglobin molecules. In haemoglobin it had been possible to attach mercury to conveniently placed sulphur atoms, but these were absent in myoglobin. Eventually Kendrew and his colleagues found that myoglobin crystals contained several niches where compounds of gold, mercury or platinum accommodated themselves without actually entering into chemical combination with the protein molecules or disturbing their arrangement in the crystal. This solved the phase problem and allowed them to calculate the distribution of electron density in a series of sections cut through the myoglobin molecule, rather like the microtome sections through a tissue, but on a scale a thousand times smaller.

In many scientific investigations results accumulate undramatically like the drops of a filtrate, but in X-ray crystallography the measurement of thousands of diffracted spots conveys no meaning. Only after all the measurements have been combined in one grand mathematical synthesis does an image of the structure finally emerge. The first relevation of the structure of a protein molecule was a great moment, which made up for the many years of drudgery and frustration that had preceded it. Describing the model of the myoglobin molecule in his note to *Nature* Kendrew wrote: ' Perhaps the most remarkable features of the molecule are its complexity and its lack of symmetry. The arrangement seems to be almost totally lacking in the kind of regularities which one instinctively anticipates, and it is more complicated than has been predicted by any theory of protein structure.'

Kendrew's model was intensely exciting, even though it showed only the position of the haem (the red pigment that carries an atom of iron) and the general course of the polypeptide chain, but not the details needed to understand how myoglobin functions. To measure the intensities of about 5000 spots required for the first image of myoglobin had seemed a backbreaking job, but improving the image so as to distinguish details of the individual amino acids involved the measurement of about a quarter of a million spots. It still seems incredible that this feat should have been accomplished in two years.

In the meantime, my colleagues and I had also surmounted the chemical problems at first encountered in preparing a series of heavy-atom compounds of haemoglobin. In 1959 we obtained an excellent map, which showed the folding of the four chains and the positions of the haem groups. The chains were identical in pairs and each of them bore a strong resemblance to the single chain of myoglobin. Haemoglobin is a respiratory carrier that takes oxygen from the lungs to the tissues and facilitates the return transport of carbon dioxide. In 1963 Hilary Muirhead and I discovered that the entire haemoglobin molecule changes its shape every time oxygen is taken up or released, showing that the molecule is not so much an oxygen tank as a molecular lung, and that it is the change of shape that ensures its efficiency as a respiratory carrier. In 1967 Hilary Muirhead, Joyce Cox, Gwynne Goaman and I advanced another step and solved the structure of the oxygen-containing form in sufficient detail to map the positions of nearly all the 574 amino acids and to construct a model showing the positions of its 10 000 atoms. We hope that this model will lead to an understanding of the respiratory function in stereochemical terms.

In 1963 Bragg concluded his lecture ' The First Stages in the X-ray Analysis of Proteins ' with the prediction that ' it will be between five and ten years before this summit of precision (of the myoglobin structure) is reached by another party of investigators '; but today, only 5 years after his lecture, ten other structures have been solved at atomic or near-atomic resolution, the first of them in Bragg's own laboratory.

This was the structure of lysozyme, an enzyme that protects many body fluids from infection by dissolving the cell walls of bacteria. It was discovered by Sir Alexander Fleming in 1922. The structure was solved in 1965 by D. C. Phillips, A. C. T. North and their colleagues, working with Council support at the Royal Institution in London. The enzyme consists of a single chain of 129 amino acids irregularly folded and riveted by four sulphur bridges. Chemists had found that it attacks chains of sugar-like residues that make up

part of the bacterial cell walls. By attaching short fragments of such chains to the enzyme, Phillips and his colleagues discovered its catalytic site and deduced how it works.

The structures of two other enzymes were recently solved in the Council's Laboratory of Molecular Biology: chymotrypsin by D. M. Blow and his colleagues, and elastase by D. M. Shotton and H. C. Watson. Both are made in the pancreas and serve to digest other proteins. They are larger than lysozyme, and chymotrypsin is probably the most difficult structure yet solved by X-ray analysis.

What do these structures show? Have they really taught us to understand how enzymes bring about chemical changes in living cells? The first impression is of order combined with great complexity and a bewildering variety of forms. At the same time, some basic patterns seem to recur. The characteristic fold of the protein chain, first discovered in sperm whale myoglobin, seems to be common to the chains of all haemoglobin- and myoglobin-like proteins in both vertebrates and invertebrates. Enzymes that carry out chemically related functions seem to have closely similar structures in a great variety of species. The total number of different proteins may be very large, of the order of several thousand in a bacterium and several million in man, but they may be derived from a much smaller number of structural prototypes.

In myoglobin and haemoglobin more than three-quarters of the protein chain is coiled into a helix of a kind predicted by L. Pauling and R. B. Corey at Pasadena in 1951. Helices make up the straight segments of chain; at the corners the chains are folded irregularly. Kendrew and I now realize that we were fortunate in our choice of protein because the helical segments in myoglobin and haemoglobin stood out and immediately allowed us to trace the course of the chains from end to end. Most of the enzymes solved since contain little helix, which makes their X-ray maps much harder to interpret.

One feature common to all the known protein structures is the exclusion of water from their interior, which results from a concentration of water-attracting groups, such as acids and bases, on the surface and of hydrocarbon groups in the interior. The catalytic sites of enzymes are often located in clefts or pockets that fit the compound to be changed very exactly and draw it into the interior of the enzyme. In this situation electrical interactions between the enzyme and the compound to be changed are much stronger than they would be in water, and reactions that might proceed imperceptibly slowly in water are thus accelerated to high speeds. So far the catalytic action of enzymes can be interpreted on the basis of the simple laws of electrostatics, and no sophisticated or novel physical effects have to be invoked.

Several enzymes are flexible structures capable of clasping the compounds they attack. Haemoglobin, though strictly a respiratory carrier rather than an enzyme, undergoes large changes of structure on combining with oxygen; these serve to transmit information between its four subunits. There is reason to believe that certain biological control mechanisms discovered by F. Jacob and J. Monod in Paris, and by H. E. Umbarger, J. C. Gerhart, A. B. Pardee and others in the United States, depend on the interchange of signals between the subunits of large protein molecules, which change their shape in response to external chemical stimuli; haemoglobin may be the simplest prototype of a class of molecules possessing this ability.

THE STRUCTURE OF NUCLEIC ACIDS

The molecules of nucleic acids, like those of proteins, are long chains. The chain links consist of alternate phosphate groups and sugar-like rings (ribose in RNA and deoxyribose in DNA). Attached to each sugar is one of four different, disk-shaped bases.

DNA extracted from chromosomes can be drawn into crystalline fibres. From the X-ray diffraction pattern given by dried fibres of DNA, W. T. Astbury at Leeds had deduced that the bases are stacked at right angles to the fibre axis. When M. H. F. Wilkins and Rosalind Franklin and their collaborators took up the X-ray study of DNA in the MRC Biophysics Unit at King's College, London, in 1951, they discovered that the X-ray pattern improved and underwent striking changes when the DNA fibres were moistened. At the highest humidity the pattern was identical with one obtained from live sperm heads, so that it clearly corresponded to the structure of DNA in the chromosomes. This pattern was of the kind to be expected from a helix. At lower humidities another and more detailed pattern appeared, whose significance was not at first clear.

Like all X-ray diffraction patterns, that of DNA required information about the phases for its interpretation. The heavy-atom method, which was to solve the structure of proteins, could not be applied; the only alternative way was to build a molecular model, calculate its diffraction pattern, and see if it fitted the observed one. The X-ray pattern offered a certain amount of guidance by indicating the dimensions and geometry of the helix, the stacking of the bases and the general symmetry of the structure.

When J. D. Watson and Crick boldly attempted to build an atomic model they designed it to fit the X-ray data obtained at the MRC Biophysics Unit, also taking account of the chemical analyses of E. Chargaff in New York. These had shown that the four bases, which we may call A, T, G and C, always occurred in the ratio A:T=G:C=1.

Watson and Crick's double helical model with its paired bases was built in 1953. Improved X-ray patterns of the wet form of DNA, obtained at the Biophysics Unit at about the same time, proved that it must be substantially correct. However, lack of exact agreement between the model and the observed X-ray pattern led Wilkins and his colleagues to refine the structure. They also completed the X-ray analysis of the form taken up at lower humidities and found that it was a contracted version of the Watson–Crick helix, in which the bases, instead of lying at right angles to the fibre axis, are tilted to it at an angle of 70°.

Most RNA is single- rather than double-stranded, and gives X-ray patterns too poor to allow its structure to be solved, but in 1962 Wilkins and his colleagues discovered a double helical form of RNA extracted from yeast that gave a better X-ray pattern. Soon afterwards, a double helical RNA giving a similar but even better pattern was discovered in reoviruses by R. Langridge and P. J. Gomatos at the Children's Cancer Research Foundation in Boston; this was analysed in detail by W. Fuller, F. Hutchinson, M. Spencer, S. Arnott and M. H. F. Wilkins at the Biophysics Unit and by Langridge. Double helical RNA was also found in wound tumour virus of clover by K. Tomita and R. Rich at the Massachusetts Institute of Technology. Its structure is similar to the low-humidity form of DNA in which the bases are tilted to the fibre axis. Transfer and ribosomal RNA,

which are discussed below, probably contain double helical regions of this kind, but the helices may be discontinuous and alternate with molecular patterns that are still unknown.

The development of chemical methods for purifying nucleic acids and determining the sequence of bases along their length has proved even more difficult than the earlier attacks on proteins. In the 1940's Lord Todd and D. Brown and their colleagues in the University of Cambridge had elucidated the chemical constitution of coenzymes made up of not more than three nucleotides. R. W. Holley and his colleagues at Cornell University were the first to determine the sequence of bases in a long RNA chain. In 1965, after an effort lasting seven years, they isolated a chemically pure species of RNA from yeast (alanine transfer RNA—see below) and determined the nature of each of the 77 nucleotides along its length. In 1967 the sequence of a ribosomal RNA with 120 nucleotides in one chain was elucidated by G. G. Brownlee, Sanger and B. G. Barrell in our laboratory. Methods for determining the sequence of bases in DNA, which would be required to decipher genes directly, have not yet advanced so far.

THE GENETIC CODE*

Taken together, the genetic control of enzyme function and the definite sequence of amino acids in proteins implied that genes must determine the sequence of the amino acids along the polypeptide chain. This was first suggested in Watson and Crick's historic paper 'The Genetic Implications of the Structure of Deoxyribonucleic Acid' in *Nature* in 1953. After proposing the self-replicating mechanism which is implicit in their double helical model of DNA they state 'The phosphate–sugar backbone of our model is completely regular, but any sequences of the pairs of bases can fit into the structure. It follows that in a long molecule many different permutations are possible, and it therefore seems likely that the precise sequence of bases is the code which carries the genetic information'. Consequently, the sequence of the bases along the nucleic acid chain ought to be colinear with the sequence of the amino acids in the corresponding protein chain. This is known as the sequence hypothesis and is one of the fundamental postulates of molecular biology.

The form that the genetic code might take at first seemed problematical because DNA contains only four different bases, whereas proteins contain twenty different amino acids. The question of how a sequence of four different symbols can code for a sequence of twenty different items is a purely formal one. Supposing two bases coded for one amino acid, then the number of possible pairs of bases is $4^2=16$, too few to code for twenty amino acids. If three bases coded for one amino acid, then the number of possible triplets is $4^3= 64$, which would be too many.

In 1961 Crick, L. Barnett, S. Brenner and R. J. Watts-Tobin devised a series of genetic experiments that allowed the general nature of the code to be determined. Their results proved that a group of three nucleotide bases (or, less likely, a multiple of three bases) coded for one amino acid. This meant either that the majority of the 64 triplets would have to be without meaning or that many amino acids must be coded for by more than one triplet. They also

*Work quoted in the following sections has been done at the Council's Laboratory of Molecular Biology at Cambridge unless otherwise stated.

showed that there are no commas between triplets coding for successive amino acids, and that ambiguity is avoided by reading the sequence of bases from a fixed starting point. It had already been shown that the code is non-overlapping —that is, that separate triplets code for successive amino acids. Paradoxically, the sequence hypothesis on which the whole idea of the code was based took longer to prove than the unravelling of the general nature of the code, but in 1964 A. S. Sarabhai, A. O. W. Stretton, Brenner and A. Bolle finally succeeded in confirming it by genetic and biochemical experiments on virus-infected bacteria.

After the solution of the general nature of the genetic code, the initiative passed to the United States. M. Nirenberg, J. H. Matthei and P. Leder devised systems for testing the coding properties of different triplets outside the living cell. By a variety of ingenious methods they, H. G. Khorana and S. Ochoa and their colleagues determined the triplets coding for each of the twenty amino acids between 1961 and 1967. Strangely, some amino acids are coded for by as many as six triplets, and others by only one. Sixty-one of the triplets coded for amino acids, but the remaining three appeared to spell nonsense.

The meaning of these so-called nonsense triplets has been studied by Brenner, Stretton, S. Kaplan and others with biochemical and genetic techniques quite different from those employed for the deciphering of the amino acid code. They came to the conclusion that all three nonsense triplets code for chain termination. 'Nonsense' suggests that the synthesis of the chain stops passively at a triplet devoid of meaning, but M. S. Bretscher has recently shown that this is not so; chain termination is an active process, though its nature is still obscure.

THE TRANSLATION OF THE GENETIC MESSAGE

Most proteins in the cell are coded for by the DNA in the nucleus, but they are made in cytoplasmic particles known as ribosomes. An intermediary is therefore necessary to transfer the information from the nucleus to the cytoplasm. Since ribosomes consist of protein and RNA, it was at first thought that the ribosomal RNA itself contained this transcript of the genetic message. However, F. Jacob and J. Monod in Paris pointed out in 1961 that all the observations could be better explained if the ribosomes merely served as machines for the assembly of proteins and the template itself was *another* RNA, which they called messenger RNA.

In collaboration with Jacob and M. Meselson, Brenner tested this hypothesis on viruses that infect bacteria. They found that an RNA transcript of the viral DNA attached itself to the ribosomes of the bacterial host. The bacterial ribosomes then manufactured viral protein. This experiment proved the non-specificity of the ribosomes and the existence of the messenger RNA. F. Gros and others at Harvard University proved that this form of information transfer from chromosomes to ribosomes was not peculiar to viral infection, but also occurred in uninfected bacteria; it has since been found in organisms of all kinds.

Another problem connected with the biosynthesis of proteins had arisen at an earlier stage. There is no stereochemical correspondence between amino acids and nucleic acid chains that would help amino acids to find their correct places on an RNA template. Crick suggested that this difficulty might be overcome if there were special enzymes (activating enzymes) that combined each amino acid with a nucleotide adaptor. This adaptor would contain the

' anticode ' for the amino acid. The anticode, a triplet of bases, would find the right coding triplet on the messenger RNA by complementary base pairing.

Crick's hypothesis was borne out by the discovery in 1955–56 of the adaptor (transfer RNA) and of the necessary activating enzymes by M. B. Hoagland and by P. Berg in the United States. For each amino acid, cells contain at least one specific activating enzyme and one or more specific transfer RNA's. Proteins are assembled in three main steps. First the activating enzyme links its specific amino acid to the appropriate transfer RNA. In the second step the transfer RNA with the amino acid attached finds the right place on the messenger RNA chain. In the third step, the chemical machinery of the ribosome and of the cytoplasm incorporates the amino acid into the growing protein chain and releases the transfer RNA for further use.

In the early 1960's Sanger began to develop chromatographic methods for determining the sequence of bases in RNA. Transfer RNA, consisting of single chains of only 70–80 nucleotides, seemed the simplest material to begin with. This led him and K. A. Marcker to a discovery of the greatest importance for our understanding of protein synthesis.

When trying to isolate the transfer RNA for the amino acid methionine, they came across two different kinds: one carrying normal methionine, and another carrying a methionine so modified that it was like a railway carriage with its front coupling blocked. This blocked amino acid could clearly form only the first amino acid of a growing chain, which suggested that it acts as the initiator of protein synthesis. This expectation was borne out by an experiment of J. M. Adams and M. R. Capecchi at Harvard University. So far, however, this initiator has been found only in microorganisms, and in certain organelles contained in the cells of higher organisms: these are the mitochondria, which turn food into energy, and the chloroplasts, which make starch from carbon dioxide and water, using sunlight as a source of energy. Only relatively few enzymes, however, are made in these organelles. The mechanism of chain initiation of the majority of enzymes made in other parts of the cells of higher organisms is still unknown.

This discovery has acted as the initiator for much of the biochemical work in our new laboratory. Marcker, B. F. C. Clark, Bretscher and others found that the two forms of methionine transfer RNA responded differently to certain coding triplets and entered different sites on the ribosomes. The complete base sequences of both forms have now been determined and turn out to be markedly different from each other, even though both respond to the same activating enzyme. This is a strange feature that is still unexplained.

Like messenger RNA, ribosomal and transfer RNA's are generated by transcription from chromosomal DNA, which contains certain genes specifying the structure of these RNA's. A mutation in one of these genes, consisting in the replacement of one base for another in DNA, would therefore be expected to result in a complementary base change in the RNA determined by that gene. If that mutation changes the anticoding triplet in a transfer RNA, it may alter the transfer RNA's response to the code laid down in the messenger. For instance, a mutated transfer RNA may misread a triplet spelling ' chain termination ' for a triplet that codes for an amino acid. Brenner, J. D. Smith and others have proved that such misreading does occur and that it can be brought about by the change of a single nucleotide base in the ' anticoding ' triplet.

Ribosomes are complex organelles made up of three different RNA's and over 20 different proteins. It will be a long time before their three-dimensional structure can be determined. Transfer RNA, on the other hand, is a relatively small molecule. Since it appears to fit into appropriate slots in the ribosomes, its structure might tell us something indirectly about that of the ribosomes themselves. However, structure analysis by X-ray diffraction can be applied only to substances available in crystalline form and up to 1968 transfer RNA had defied efforts at crystallization. By crystallizing the initiating methionine transfer RNA, Clark and his colleagues have now opened the way to the determination of its three-dimensional structure.

EFFECTS OF MUTATIONS ON PROTEIN STRUCTURE

In their paper 'The Genetic Implications of the Structure of DNA', Crick and Watson suggested that mutations might arise by mispairing of bases during replication. If this occurred in a gene coding for a protein, it could result in a triplet that spells out a wrong amino acid. A suitable system for testing this hypothesis presented itself in sickle-cell anaemia, a human congenital disease, which in 1949 L. Pauling, J. A. Itano and others at Pasadena had shown to be associated with the appearance of an abnormal haemoglobin. At this time J. V. Neel in the United States and E. A. Beet, an Officer in the Colonial Medical Service in Zambia, had independently proved that the disease was inherited in a simple Mendelian fashion, suggesting that it was due to a single mutational step in a chromosomal gene. In people afflicted by it, the red cells in the arteries are normal, but in the veins, where the haemoglobin carries no oxygen, they become elongated or sickled.

In 1950 J. M. Mitchison and I discovered that the deformation of the red cells was caused by the insolubility of sickle-cell haemoglobin in its oxygen-free form. When V. M. Ingram joined the staff in 1953, he first wondered whether this strange property might be due to a change in the number of sulphur-containing amino acids, but he found this to be the same in sickle-cell and in normal haemoglobin. Analyses of the total amino acid content of the two proteins had also failed to show any differences. Ingram then developed an elegant chromatographic technique that he called fingerprinting; this enabled him to detect a change in the electric charge or solubility in any one of 30 or more fragments produced by partial breakdown of a protein. He discovered in 1957 that the disease was due to a change of a single one among the 287 pairs of amino acids in the haemoglobin molecule. This proved for the first time that a mutation can cause the change of a single amino acid in a protein chain.

Since then about a hundred abnormal haemoglobins have been discovered, many of them by H. Lehmann in the MRC Abnormal Haemoglobin Unit. A few of these involve deletions of short stretches of the protein chain, but all the others consist of changes of single amino acids. This finding raised a fundamental point. If each amino acid change was due to a single mutational event it should be possible to correlate it with the replacement of a single base in a coding triplet. However, the code had been determined in microbes and was not necessarily the same in man. If each of the amino acid changes in the abnormal haemoglobins turned out to be compatible with a single base change, this would argue strongly in favour of the universality of the genetic code. In fact, this was found to be true of all but one of the amino acid changes, and the one exception later proved to be due to an error in chemical analysis.

Many of the abnormal haemoglobins give rise to pathological changes, some of them severe. The recent construction of an atomic model of haemoglobin offered Lehmann and myself the opportunity of studying the causes of the abnormalities in atomic detail. One by one, we replaced normal amino acids in the model by their mutant counterparts and examined the stereochemical consequences of the replacement. We found the haemoglobin molecule to be insensitive to replacements of most amino acid residues on its surface, but extremely sensitive to even quite small alterations of residues forming internal contacts. Such alterations are liable to make the haemoblobin molecules unstable and to cause haemolytic anaemia. Replacements near the red pigment groups and at contacts between neighbouring protein chains impaired the oxygen-carrying function. We were pleased to be able to explain disease in precise stereochemical terms, but discouraged at the same time, because our findings do not hold out any hope that lesions in mutant proteins could be repaired directly. Repair would have to be carried out at the genetic level, or by replacement of the organ that makes the protein; to make healthy haemoglobin the bone marrow would need replacement.

THE MECHANISM OF MUSCULAR CONTRACTION

The mechanism of muscular contraction has long been one of the fundamental problems to be studied by X-ray diffraction. At first it seemed obvious to suppose that muscle bears some resemblance to rubber, where contraction is caused by random coiling of molecular chains. Such coiling, or any kind of systematic folding, should manifest itself by changes in the X-ray diffraction pattern.

In the course of his pioneering studies of protein fibres, W. T. Astbury at Leeds had taken X-ray diffraction photographs of muscle dried at various stages of contraction, but had found no evidence of any systematic change in the folding of the protein chains. Soon after H. E. Huxley joined us he began an X-ray study of wet muscle fibres under experimental conditions capable of revealing fine structure that Astbury would not have been able to detect. Between 1950 and 1952 he found evidence of two interpenetrating kinds of filaments of submicroscopic dimensions, but paradoxically neither of these filaments seemed to shorten when muscle contracted.

The paradox was resolved in 1953 by Huxley and Jean Hanson (of the MRC Biophysics Unit) while they were both working at the Massachusetts Institute of Technology and, simultaneously and independently, by A. F. Huxley and R. Niedergerke at the Physiological Laboratory at Cambridge. Muscle was found to contract not by a shortening of its protein chains but by a sliding motion of the two interpenetrating sets of protein filaments (plate I). This concept was so new and revolutionary that very few workers in the field were willing to believe it. Stimulated by their scepticism, H. E. Huxley refined the methods of preparing specimens for electron microscopy and revealed the structure of muscle in a degree of detail never attained before. His classic paper in 1957 on ' The Double Array of Filaments in Cross-striated Muscle ' piled proof on proof in favour of the sliding filament model. In the years that have followed it has become universally accepted.

Since then Huxley has studied the detailed mechanism of sliding. To explain his work, the structure of muscles must first be described, at least in outline.

Striated muscle is divided into segments by a series of regularly spaced disks. Attached to each side of the disk are the thin filaments, which consist mostly of the protein actin. Half-way between two disks lies a set of thick filaments, which consist of the protein myosin. Changes in the length of the segment are brought about when the thin filaments slide in and out between the array of thick ones (plate I). What causes the sliding? Huxley's photographs show bridges extending from the filaments of myosin towards those of actin; these bridges might pull on the actin like a series of ratchets. However, this idea poses a problem of direction. To pull the actin filaments inwards, the two halves of the myosin filaments would have to pull in opposite ways. Huxley found the explanation by dissolving myosin and allowing it to reaggregate into filaments; he found that the myosin molecules grow outwards from the middle of the filament so that the bridges at each end of the filament point in opposite ways. Next he allowed myosin molecules to precipitate on filaments of actin; he found that they formed arrow-shaped bridges that pointed in opposite ways on the actin filaments attached to opposite sides of the disk (plate II). These experiments proved that both the actin and the myosin filaments possess the polarity needed to allow the two halves of each segment to pull in opposite directions.

The structure of the actin filaments has been studied by Jean Hanson and J. Lowy at the MRC Biophysics Unit. On electron micrographs each filament looks like an open necklace made up of two strings of beads twisted around each other, but the polarity of the beads is not yet apparent in these pictures.

So far there had been little indication that the bridges actually move. In the early days such evidence was hard to obtain since it used to take 20 hours' exposure to get an X-ray diffraction picture from a live muscle. Now, thanks to new techniques developed by H. E. Huxley, K. C. Holmes, W. Brown and W. Longley at this Laboratory and by G. F. Elliott, C. R. Worthington and B. M. Millman at the MRC Biophysics Unit, that time has been reduced to about 20 minutes, making it possible to take X-ray pictures of muscle during a series of short twitches. In parallel and independent experiments, Elliott, Lowy and Millman in London and Huxley, Brown and Holmes in Cambridge showed that even during an active twitch neither the myosin nor the actin filaments undergo any contraction. The Cambridge group then discovered a difference between the arrangement of the myosin bridges in resting and contracting muscle, which was confirmed by the group in London. While the bridges in resting muscle form an orderly array, their arrangement in actively contracting muscle is more random, as might be expected if they moved backwards and forwards like a set of non-synchronized ratchets trying to pull the actin fibres inwards.

STRUCTURE OF SMALL VIRUSES

The present research in this Laboratory by A. Klug and his colleagues on the structure of small viruses is a direct continuation of Bernal's X-ray studies on crystalline virus preparations in the late 1930's, and some of it is still concerned with the same two plant viruses first examined by Bernal: tobacco mosaic and tomato bushy stunt. One is rod-shaped and the other spherical, and both consist of only RNA and protein. Between them they typify the simplest forms of living matter.

Bernal and Fankuchen discovered in 1941 that each individual particle of tobacco mosaic virus diffracted X-rays as though it were a tiny crystalline rod

made up of identical subunits regularly arranged along its length. The problem was then left to hibernate until 1952, when W. Cochran and Crick developed a mathematical theory of diffraction from helical chain molecules in order to test the helical model of the protein chain proposed by Pauling and Corey the previous year. In 1952 J. D. Watson resumed the X-ray work and, with the help of Cochran and Crick's theory, found that the subunits are arranged along a helix with a pitch of 23 Å. The exact number of particles per turn and the relative positions of protein and nucleic acid were later determined by Rosalind Franklin in Bernal's laboratory at Birkbeck College, London, where Klug joined her in 1954. Their results made it clear that the virus consists of a long, helically wound filament of RNA, protected by a coat of small, identical and helically arranged protein molecules.

Franklin and Klug's work stimulated Watson and Crick to formulate a general theory of virus structure in 1956. They argued that the amount of RNA present in a small virus is not enough to code for more than a very few protein molecules, so that it would be most economical, in terms of genetic information, if the coat of a virus were made of small protein molecules that are all alike. Now identical particles tend to arrange themselves regularly, so that their surroundings are all the same; it can be shown that this condition imposes certain geometrical restrictions, forcing the protein molecules to arrange themselves in regular patterns on the surface of either a cylinder or a sphere. In the first case they would have to grow along a cylindrical surface in the form of a helix, but the theory imposes no geometric restriction on the pitch of the helix or the number of particles per turn. If they aggregated on the surface of a sphere, on the other hand, geometry shows that they can do so only in multiples of 12, 24 or 60. Each of these three types of aggregate would possess a different type of symmetry, which could be detected by X-ray analysis. The symmetry predicted for a particle containing a multiple of 60 subunits was first detected in X-ray diffraction pictures of tomato bushy stunt virus by D. L. D. Caspar in 1956. It has since been confirmed in all spherical viruses, including poliovirus and several others of medical interest.

However, at first only the X-ray evidence agreed with the theory, while electron microscope data suggested that certain viruses are made up of numbers of subunits that are not multiples of 60. Caspar and Klug have brought these apparently divergent results into an orderly system by an ingenious extension of Watson and Crick's theory. In 1962 they predicted that identical particles form solid surfaces by arranging themselves in patterns of pentagons and hexagons. These patterns fall into distinct classes of gradually increasing complexity.

The predicted patterns were on so small a scale that they could not have been resolved by the techniques of electron microscopy used in the early 1950's, but the method of negative staining, first introduced by H. E. Huxley in 1956 and by Brenner and R. W. Horne in 1959, brought out striking new details in biological specimens. With its help, Klug and J. T. Finch verified that the subunits in all the small spherical viruses are arranged in accordance with one or the other of the predicted patterns, so that each virus can be assigned to a morphological class (plate III). The number of protein subunits is a multiple of 60 in all cases, though these may be grouped into clusters to give a mulberry-like appearance to the surface of the particle; in one plant virus, for instance,

the number of clusters is 32. This work has proved that the simplest forms of life possess regular structures that conform to a limited number of types and are dictated by the laws of solid geometry.

Larger viruses also form regular polyhedra, but their coats may be composed of more than one kind of protein subunit. This was first shown in 1965 by R. C. Valentine and H. G. Pereira at the National Institute for Medical Research when they studied the anatomy of the adenovirus in the electron microscope. This virus is a regular polyhedron with 20 faces. The protein subunits covering the faces and edges of the polyhedron look spherical, but the protein subunits at the corners look like spheres with long antennae attached to them. Valentine and Pereira separated the two kinds of subunits and showed that the virus uses the antennae to attach itself to its host cell.

Further great advances in the analysis of periodically repeating structures by the electron microscope have recently been made by Klug and D. J. DeRosier. They found that the optical diffraction patterns obtained from electron microscope images are capable of revealing features that are not apparent to the eye. They interpret these diffraction patterns by methods similar to those used in the analysis of X-ray diffraction patterns from crystals, though fortunately they are not plagued by the phase problem.

The internal structure of the protein subunits is still unknown. For the past few years, Klug, Holmes, Finch, R. Leberman and others have tried to solve the structure of virus proteins by X-ray analysis, using the method of isomorphous replacement with heavy atoms described earlier. They have obtained a tentative electron density map of the protein subunit of the tobacco mosaic virus, but so far this has defied interpretation in chemical terms.

PRESENT AND FUTURE

Now that the genetic code is known, Sanger and his group are developing methods for reading the genetic message itself. By doing so they hope to discover more about the mechanisms that control its transcription from gene to messenger RNA and its translation from messenger RNA to protein. The sequence of coding triplets that specifies the amino acid sequence of a protein may be preceded by a prefix and possibly followed by a postscript. Both these may be concerned with control but their nature and function are still unclear. Molecular biologists also suspect that the multiplicity of triplets that code for certain amino acids may serve to control the rate of protein synthesis: for instance, a particular coding triplet could slow down the rate of synthesis if the corresponding transfer RNA were present only in very low concentration.

Methods for the synthesis of genes are also developing fast. H. G. Khorana hopes that he will shortly have synthesized the gene for a transfer RNA, comprising about 80 nucleotides in a DNA chain. To make the gene for a small enzyme would require no more than a five-fold increase in Khorana's present effort, but even if such a gene were synthesized now, it might fail to function because we do not yet know the prefix needed to get enzymes to transcribe it and translate it into protein structure. Methods for assembling polypeptide chains by organic chemistry are also progressing apace, and the enzyme ribonuclease, with 124 amino acids in one chain, is reported to have been synthesized by two groups of chemists in New York.

In the long run this kind of work may lead to the design and synthesis of new kinds of enzymes and of the genes required to make them *in vivo*, and ultimately to their introduction into higher organisms. But first we must learn how protein chains of a given amino acid sequence fold up spontaneously to form a complex and uniquely ordered structure and how that structure determines a particular kind of catalytic activity. The great expansion and acceleration of protein crystallography that is now taking place should lead to solutions of these problems.

Certain fields of molecular biology have become overcrowded, especially microbial biosynthesis and control. This was one of the reasons that caused Brenner and Crick to switch research to growth and differentiation of higher organisms. Brenner has selected a small nematode worm which contains only 1000 cells, has a life cycle of $3\frac{1}{2}$ days, lives on bacteria and is fully differentiated into skin, muscle, gut and nerve cells. It possesses six pairs of chromosomes and reproduces either as a self-fertilizing hermaphrodite or by fertilization of the hermaphrodites by sexually differentiated males. The existence of these two alternative modes of reproduction makes this worm an ideal subject for genetic studies: either a large progeny can be raised from a single individual or, alternatively, crosses can be made of selected mutants. Thanks to the small size of the worm its entire anatomy can be explored on a scale much finer than would be possible even for an isolated part of a larger organism; in principle the development of every cell could be traced from the early embryo to the adult. At the moment the main interest is the growth of the nervous system and its genetic control.

At the time of writing, the Council supports research over a much wider field of molecular biology than is covered by this short review. This support includes the genetics and metabolism of a great variety of microorganisms, ranging from cancer-producing viruses and the common cold viruses to bacteria that have developed resistance against penicillin and other antibiotics; some of the Council's research on human genetics, on the genetic effects of radiations and on chemical mutagens also falls into the field of molecular biology (see, for example, Annual Reports for 1961–62 (p. 33), 1966–67 (p. 55) and 1967–68 (p. 57). In general, one can foresee that the great unsolved problems of medicine, such as cancer and cardiovascular and degenerative diseases, may have to be approached by seeking an understanding of pathological events at the molecular level. This suggests that the frontiers of molecular biology should be extended towards medicine and the biology of higher organisms.

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Immunology

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Twenty-five years ago the main and almost sole raison d'être of immunology was the study of immunity against infectious diseases, carried out mostly in departments of bacteriology or pathology. Today, although protection against infectious disease remains a very important aspect of their collective endeavour, immunologists are also to be found in departments of biochemistry, molecular biology, cell biology, dermatology, genetics, haematology, medicine, surgery and zoology and even in departments styled simply ' immunology '. Their field of research may broadly be defined as the study of the specific responses of the body to the introduction of foreign materials or—as Sir Macfarlane Burnet has put it—of the distinction by the body between ' self ' and ' not self '. The qualifying term ' specific ' is needed to emphasize that each immunizing material elicits its own unique response. The term ' foreign ' implies that the molecules are recognizably different from those normally present in or part of the individual's make-up. Among substances foreign in this sense are some, such as drugs or poisons, that possess biological activities of their own, whose investigation is more the concern of pharmacologists and toxicologists than of immunologists; most foreign substances, however, are essentially bland, and yet the body responds to them as readily as it does to those substances that are more obviously harmful or dangerous. It is the response to foreign molecules *per se* that is the concern of immunology. The subject has come to be considered virtually as a discipline in its own right, and it now accounts for a considerable part of the Council's research endeavour. This review attempts to explain how, during a period in which research in biology and medicine as a whole have developed greatly, there has come to be an increasing emphasis on immunology. The article is mainly concerned with applications to medical practice, and will not discuss the many ways in which immunological techniques, with their remarkable specificity and sensitivity, have become established as useful tools in diagnostic medicine and in many branches of biological research.

THE IMMUNE RESPONSE

All vertebrates, including even the most primitive, have two operationally distinct ways of responding to the introduction of foreign molecules by routes other than into the digestive system. Molecules that evoke responses of these kinds must generally be above a certain size—that is, macromolecules—and they are termed collectively *antigens*. The two responses that they evoke involve the production of entities with the capacity to react specifically with the antigen causing them. The first of these entities are lymphocytes, cells that are normally present in the blood and in lymphoid tissues, and of which an average human being contains about a million million. The second are antibodies, which are proteins secreted into the blood and the tissue fluids by specialized cells derived

from lymphocytes. Antibodies constitute the fraction of blood plasma proteins defined as γ-globulin, and proteins of this kind have come to be termed *immunoglobulins.*

The interaction between antigens and antibodies has been studied in great detail, and much of the earlier work was summarized in an admirable Council monograph (*The Chemistry of Antigens and Antibodies* by J. R. Marrack, 1938). More recent work has largely refined and given precision to the ideas already current before the war, namely that antibody molecules have *combining sites*, or areas of their surface whose configuration is complementary to that of defined areas on the surface of the antigen, which are termed *antigenic determinants.* The latter are quite small in relation to the total surface area, and on a complex macromolecule there may be many distinct determinants, each able to evoke an antibody response peculiar to itself. Their complementary configurations allow the antigen and antibody molecules to approach very closely at these sites, and powerful intermolecular attractive forces come into play. The actual strength of the attraction depends on the goodness of fit, and may range from relatively weak to very strong indeed. If the antigen is a microbial toxin (which is often an enzyme) or a virus, combination with antibody prevents the toxin or virus from combining with its normal target materials in the body fluid or cells, and effectively neutralizes the microbial agent. When the antigen is part of the surface of a bacterium, the latter becomes coated with antibody and is then much more susceptible to killing by phagocytic cells of the body or by the action of ancillary serum factors collectively termed *complement.* Because their antigenic determinants are generally different each antigen tends to evoke a highly specific antibody response; thus antibodies against diphtheria toxin do not combine with tetanus toxin, nor do antibodies against poliomyelitis virus combine with measles virus, or *vice versa.*

Much less is known about the nature of the specific interaction between antigens and lymphocytes. These cells do not secrete substantial amounts of antibodies such as can conveniently be studied in a test tube, and their properties can be studied only by indirect means. However, there are several reasons, none of which is conclusive but the total weight of which is compelling, for supposing that lymphocytes have at their surface specific *receptors* capable of combining with determinant sites on the antigen, and that the receptors are antibody molecules made, but not freely secreted, by these cells. There are also grounds for supposing that an individual lymphocyte at any given time possesses only a limited number of different kinds—possibly only one kind—of antibody-like receptor at its surface: that is to say, an antigen is able to interact only with those members of the total lymphocyte population that possess specific receptors for it.

There are now recognized to be three ways in which an individual lymphocyte may respond when it interacts with the antigen. First, it may, paradoxically, be rendered unresponsive to the antigen in question, the result being a state of immunological *tolerance* or paralysis. It is unknown at present whether the lymphocyte is eliminated or inactivated in this process. Secondly, it may be stimulated to enlarge and to develop in its cytoplasm the more elaborate apparatus necessary for increased protein synthesis and cell division. The cell may then divide once or more than once to produce a family of daughter lymphocytes possessing an equal or increased capacity to interact with the original antigen. These cells may live for a long time, and can in turn be

stimulated by further contact with the antigen. Since there are now more of them, the overall response will be correspondingly greater than on the first occasion, and this phenomenon is often referred to as immunological memory. Thirdly, the stimulated lymphocyte may divide several times and finally differentiate into cells highly specialized for secreting protein, termed *plasma cells*. Such cells were first recognized by Fagraeus in Sweden, as recently as 1946, as those primarily responsible for making the antibodies that are liberated into the body fluids. The outcome of the third process is a rise in the level of antibody that is maintained so long as the population of specific plasma cells persists. In general this level slowly declines with time, but rapidly rises again on further contact with the antigen.

The three effects described above may be, and commonly are, produced on different individual members of the population of specifically competent lymphocytes simultaneously, and the outcome depends on the balance between them, which appears to be determined by the nature, physical state and route of entry of the antigen. A number of empirically discovered agents known as *adjuvants* increase the size of the response to antigens, partly by causing the antigen to be retained for prolonged periods without being destroyed, and partly by encouraging the proliferation of the lymphocytes. On the other hand, agents that destroy lymphocytes (e.g., X-rays, antilymphocyte serum) or interfere with their multiplication (e.g., antimitotic and antimetabolite agents) diminish or abolish their ability to respond to antigens and instead facilitate the production of specific tolerance.

This brief account of the general nature of the immune response may serve as a background to the following account of some of the more directly practical applications of immunology. Very little of this account could have been written 25 or even 10 years ago. The knowledge on which it is based derives from work done in many laboratories in many countries; important contributions have been made by workers in this country, most of them supported by the Medical Research Council (especially at the National Institute for Medical Research and in the MRC Immunochemistry, Cellular Immunology and Radiobiology Units and the Basic Immunology Research Group).

PROPHYLACTIC IMMUNIZATION

The purpose of prophylactic immunization is to stimulate antibody formation by introducing the antigens of infective agents in a suitably controlled and harmless form, so that when a person is subsequently exposed to the infective agent or its toxins in a virulent form a sufficient level of preformed antibody, or enough specifically responsive lymphocytes capable of making antibody rapidly, are available to neutralize the agent before it can cause significant damage. The one-time scourges diphtheria, smallpox and yellow fever were already capable of complete control by this means before the period under review. The list now includes tetanus, poliomyelitis and measles as well as anthrax, plague and some other diseases less immediately relevant to this country. Highly—though not completely—effective vaccines have been developed against whooping cough, tuberculosis, influenza and typhoid fever. The most important role of the Council in these developments has been in organizing large-scale trials with the cooperation of the Department of Health and Social Security, and sometimes in conjunction with the World Health Organization, to test the efficacy of the vaccines in the field, and to control their quality through the Immunological

Products Control Division of the National Institute for Medical Research. The early Medical Research Council trials of BCG and whooping cough vaccines were widely acclaimed as models of statistically controlled trials. Active immunization is likely to be extended to include some other infectious diseases, such as rubella, which can either be clinically severe or have serious side-effects. Unfortunately, as the work of the Common Cold Research Unit has shown, the prospects of successful immunization against the common cold appear remote because of the large number of different viruses involved.

There are some very important tropical diseases, such as malaria, trypanosomiasis and leishmaniasis (protozoal infections), schistosomiasis (a helminth infection) and trachoma (caused by an unusual kind of intracellular bacterium) to which members of affected populations can eventually become immune, but the development of immunity involves prolonged or repeated infections and a high morbidity. Prevention of these diseases by the eradication of vectors and improved sanitation is proving to be a slow and difficult business, and their cure by chemotherapy is at present beyond the means of many of the countries most severely affected. There is therefore a strong incentive to develop ways of achieving by controlled immunization the level of immunity that can result from natural infections. The Council has supported pioneer studies on the mechanisms of immunity involved, notably in the case of malaria and trachoma at the MRC Laboratories in the Gambia, at the MRC Trachoma Unit in the Gambia and London and at the National Institute for Medical Research. Because of the complicated life cycles of some of the parasites and the existence in some diseases of numerous antigenically different strains, this field of research is particularly difficult and challenging.

IMMUNOCHEMISTRY

Practically all our present knowledge about the detailed nature of antibodies has been gained during the last 25 years. They are now recognized as forming part of a uniquely complex population of molecules, the immunoglobulins. The complexity is due to the fact that not only does an individual possess antibodies against a very wide variety of antigens, but also any individual is able to make a number of different antibodies against a given antigen. These may even be all directed against the same antigenic determinants, but they vary both in the exactness with which they fit these determinants and in the class of immunoglobulin (see below) to which they belong. This has meant that antibodies as isolated from the blood, however carefully purified, are not normally homogeneous, and not readily amenable to detailed examination by the techniques brilliantly used by chemists and physicists to elucidate the structure of other proteins. However, a very important discovery was made in 1958 by R. R. Porter, working at the National Institute for Medical Research, when he showed that antibody molecules could be split by enzymes so as to separate the parts of the molecule containing the sites specifically combining with the antigen from the remainder of the molecule, which had no antibody activity and appeared to be common to many different sorts of antibody. Shortly afterwards G. M. Edelman at the Rockefeller Institute showed that antibody molecules contained two kinds of polypeptide chain, which could be separated by splitting a small number of disulphide (S–S) bonds that evidently held the chains together. Porter succeeded in isolating the chains in soluble form, and was able in 1961 to propose a general model for the structure of antibody molecules, which has

been amply verified by later work. A more recent version of the model is shown in figure 1; the extent to which this model resembles actual antibody molecules can be seen if it is compared with the electron micrograph of IgG antibody taken by the late R. C. Valentine at the National Institute for Medical Research (plate IV*a*). The important features are that there are two kinds of chain, the smaller termed L (light) and the larger H (heavy), which are linked in pairs. The antibody-combining site is made up of part of the H and part of the L chain, while other important biological properties of antibodies, referred to below, depend on the structure of the rest of the H chain.

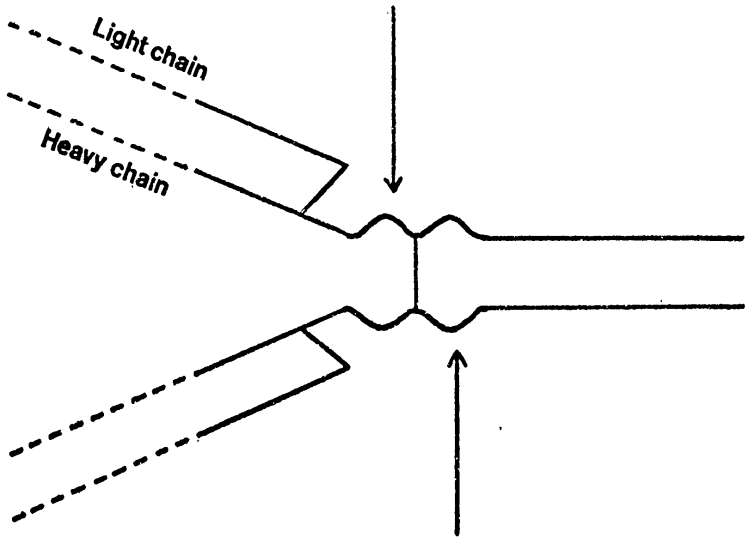

FIGURE 1

Diagrammatic representation of the four-chain structure of IgG, in which the chains are linked by three disulphide bridges. The broken lines indicate stretches of the chains in which heterogeneity occurs within a given chain type; these stretches include the antibody-combining sites. The undulating portion of the heavy chain represents a portion susceptible to cleavage by proteolytic enzymes (papain at the point marked by the upper arrow and pepsin at the point marked by the lower arrow).

In certain (fortunately rare) individuals a single immunoglobulin-producing cell may begin to proliferate at random and give rise to a tumour, termed a *myeloma*, composed of daughter cells that secrete a completely homogeneous immunoglobulin into the blood in such large amounts that it can easily be prepared almost pure, thus permitting a detailed structural analysis that is normally impossible. Analysis of the chemical and immunological properties of such myeloma proteins has revealed that the amino acid sequence at one end of both L and H chains is extremely variable from one immunoglobulin to another, and it is from this variability that the extraordinary range of antibody specificities arises. The amino acid sequence of the other part of the chains, however, may be practically identical in many immunoglobulins, provided that these belong to the same class. The class is an attribute determined by the 'constant' parts of the H and the L chains. Five main classes, depending on different kinds of H chains, have been described in man, and antibodies within each class show distinct and characteristic biological properties.

THE BIOLOGICAL PROPERTIES OF ANTIBODIES

The five main classes are termed G, A, M, D and E. Very similar classes have been found in other species, and this fact alone suggests that they must each have some important biological functions. In fact striking differences have been observed between antibodies of the various classes in respect of their transmission from mother to infant before birth, their persistence and distribution in the body fluids and secretions, and their ability to kill microorganisms and to cause inflammation when they react with antigen. For example, only IgG (immunoglobulin G) and IgM antibodies activate complement, which greatly increases their efficiency in promoting phagocytosis or direct killing of microbes and at the same time causes a powerful local inflammatory reaction. IgM antibodies are five times larger and have correspondingly more binding sites than IgG (see plate IV*b*), which makes them well adapted for combining with antigens spread over the surface of cells but less well adapted for combining with molecules, such as bacterial toxins, in solution; IgA antibodies have recently been found to be selectively concentrated in mucous secretions, and there is increasing evidence that they may serve a special function in protecting mucous surfaces against microbial invasion. IgE antibodies, which were finally identified only in 1967, have the peculiar property of attaching firmly to the surface of mast cells, which are widely distributed in the body and are loaded with specialized granules containing the pharmacologically active agent histamine. When the antigen reacts with such antibodies on mast cells these discharge their histamine; on a small scale this causes increased local circulation, but on a larger scale it causes urticaria (' hives '), hay fever, asthmatic symptoms or even acute anaphylactic shock. No obvious biological advantage has yet been discerned for this reaction, although it is plausible to suppose that an increased local circulation would help to concentrate the body's defences where they were most needed. Since the varieties of immunological response were certainly evolved many thousands of years ago, there is of course no reason why they should all still be beneficial to us in the present day.

CELL-MEDIATED SPECIFIC IMMUNITY

Lymphocytes that are specifically responsive to an antigen, but do not themselves secrete antibody, are responsible for an important biological defence reaction known as ' delayed type ' hypersensitivity or, more appropriately, cell-mediated immunity. Reactions of this kind familiar to many people are the tuberculin skin test used to assess the state of immunity to tuberculosis, or chronic dermatitis due to chemical irritants, whose defensive role in this context is not obvious. The association of these reactions with lymphocytes was first recognized by K. Landsteiner and M. W. Chase at the Rockefeller Institute, New York, in 1942, but their mechanism has only really begun to be elucidated in the last ten years, mainly as the result of work done in America, Scandinavia, Czechoslovakia and Great Britain (largely under the auspices of the Council, and notably at the National Institute for Medical Research and at the MRC Rheumatism and Cellular Immunology Units). It appears that when the reactive lymphocytes interact with antigen on the surface of other cells the latter are killed, and at the same time a substance is released that causes macrophages in the neighbourhood to become activated.

The importance of this mechanism is twofold. On the one hand it can act to destroy the body's own cells parasitized by intracellular organisms, such as those

of tuberculosis, leprosy, leishmaniasis and probably some viral infections, and in this way can limit their spread; on the other it can destroy cells that are in some way recognizably foreign to the host. The most obvious and now well known example is the rejection of a tissue graft from another individual, and indeed the cell-mediated immunity reaction is the main barrier to successful transplantation. However, a less obvious but biologically more important example may be the rejection of mutant cells, notably tumour cells, which is discussed further below.

DISEASES DUE TO ALLERGY

Since the beginning of this century it has been recognized that immunological reactions are not always beneficial, and that the introduction of an otherwise bland substance into a person already immunized by previous contact with it may result in local inflammation or a local or general acute anaphylactic reaction. For example, insect bites owe most of their effects to acquired hypersensitivity to components of the insect's saliva and not to intrinsic irritant properties of these substances. Considerable knowledge has been gained about the mechanisms of these hypersensitivity reactions during the past 15 years, much of it through the work of Council staff. Three distinct mechanisms may all play a part. One is the explosive release of histamine and other pharmacologically active substances described above, especially in persons who have developed antibodies in the class IgE. Another is the cell destruction that occurs in persons who have developed cell-mediated specific immunity. A third is due to the formation of antigen–antibody complexes within the body fluids. These react with complement, and are ingested by polymorphonuclear white blood cells. The latter in turn liberate considerable quantities of stored hydrolytic (digestive) enzymes, which may cause considerable—even irreparable—local tissue damage.

The knowledge of these mechanisms, derived from experiments on animals, revealed that the pathological features of an unexpectedly large number of hitherto unexplained human diseases were very similar to those of the experimental lesions. Apart from the well recognized ailments such as hay fever and so-called ' extrinsic ' asthma, due to sensitization by inhaled antigens such as pollens, moulds and the mites of house dust, there can now be included a variety of respiratory diseases such as farmer's lung and byssinosis (cotton spinners' disease), which were studied in the Council's former Clinical Immunology Research Group (see p. 80 and also the Annual Report for 1966–67, pp. 74–82). Various forms of acute and chronic inflammation of the kidney and acute inflammation of the blood vessels are also best explained by the presence of antigen–antibody complexes. Although the recognition that these diseases have an immunological basis has not so far helped to prevent their occurrence, it has made it much easier to treat them rationally.

IMMUNOLOGICAL TOLERANCE AND AUTOIMMUNE (AUTOALLERGIC) DISEASES

The preceding discussion has assumed that no animal would make an immunological response against components of its own body fluids or tissues. This assumption seems so self-evident that it was made for many years without questioning by what mechanism responses against foreign molecules could distinguish very fine shades of difference, such as those between the egg white proteins of a hen and a turkey, while no response was made against quite similar molecules present in the animal itself. The first attempt to suggest a mechanism

was made by F. M. Burnet and F. Fenner in 1949. Although their detailed suggestions would not be acceptable today, they made the point that animals do not as a rule make an immunological response against substances present in the body during foetal life, when the immunological apparatus is still immature, and put forward the hypothesis that this was the basis of self-tolerance. This hypothesis was apparently confirmed by the experiments of R. E. Billingham, L. Brent and P. B. Medawar in 1953, who injected spleen cells from one inbred strain of mice into newborn mice of a different inbred strain and showed that when the latter grew up they would accept skin grafts from the first strain permanently, instead of rejecting them by an immunological reaction after a few days as would normally have been expected. Later experiments have shown, however, that tolerance can be induced in adult as well as in immature animals. At the MRC Radiobiology Unit it was found possible to keep alive adult mice whose immunological capacity had been destroyed by X-irradiation, and such mice would accept skin grafts from another strain. More recently D. W. Dresser and N. A. Mitchison at the National Institute for Medical Research showed that tolerance to certain foreign antigens can be induced in adults even without the use of X-rays or immunosuppressive drugs, provided that the antigens are administered in such a way as to minimize their immunizing effect. This can sometimes be achieved by repeated and prolonged administration of very minute quantities of antigens, which cause paralysis of the potentially responsive cells (as mentioned above) without stimulating a significant proportion of these to respond by differentiation to ' memory ' cells or to antibody-forming cells. A similar final result can also be achieved by administration of a very large quantity of antigen (so large as often to be unattainable in practice). The second procedure probably works by stimulating all the responsive lymphocytes to differentiate into plasma cells, which eventually die off and leave the animal exhausted of cells able to respond to the antigen in question. It is likely that it is by the former mechanism that an animal normally becomes tolerant of its own constituents.

Such a mechanism can only operate, however, if those constituents and the lymphocytes are able to come into effective contact with one another. There are specialized tissues that are normally kept permanently separated by anatomical barriers from direct contact with cells in the circulation; such tissues are the lens of the eye, spermatogenic cells and myelinated nerves in the brain, and each contains at least some constituents unique to itself. It had been observed during the 1930's—predictably, by hindsight—that when experimental animals were injected with these particular tissues, derived from other animals of the same species, they could be induced to make antibodies that could react against their own corresponding tissues—that is, autoantibodies. Such antibodies, however, were not obviously harmful, and they were generally regarded as occurring only in very special circumstances and as unlikely to be relevant to human disease.

A major change of attitude has since occurred, mainly as the result of two observations. The first was the discovery by R. R. A. Coombs, A. E. Mourant and R. R. Race in 1945 of autoantibodies attached to human red cells in an unexplained form of anaemia accompanied by excessive destruction of the red blood cells. Secondly, in 1956 I. Roitt and D. Doniach found that patients with an uncommon thyroid disease (Hashimoto's disease) had large amounts of circulating antibody against thyroglobulin, the characteristic protein made by

the thyroid gland, and E. Witebsky and N. Rose in the United States showed that rabbits could be caused to make antibodies against their own thyroglobulin and to suffer a transient inflammation of the thyroid after injection of rabbit thyroglobulin mixed with a suitable adjuvant. These observations stimulated a widespread search for autoantibodies in numerous diseases of unexplained aetiology, and for experimental animal models for such diseases. The result has been an almost embarrassing harvest of evidence for the presence of antibodies and cell-mediated immunity against specific tissue constituents in a wide variety of diseases such as rheumatic fever, rheumatoid arthritis, pernicious anaemia, systemic lupus erythematosus, nephrosis, multiple sclerosis, Addison's disease (of the adrenal glands) and pemphigus, as well as in haemolytic anaemia and thyroiditis. In some of these diseases the autoimmunity is almost certainly a secondary consequence of some other disease process in the tissues, which causes altered or normally inaccessible components to stimulate lymphocytes to respond to them, but in others it appears that an unexplained breakdown of self-tolerance is the primary cause of the disease as well as of the occurrence of immunization.

Autoimmunity was the subject of a special article in the Council's Annual Report for 1959–60, and the immunology of rheumatoid arthritis (with special reference to induced autoimmune diseases in animals that appear to be analogous) was discussed in the Report for 1967–68. Although much remains to be discovered before it can be completed, a new chapter has been begun in the history of medicine. There are grounds for hoping that in some conditions carefully controlled suppression of the immune response will prove to be an effective method of treatment.

IMMUNOLOGICAL DEFICIENCY DISEASES

The advent of chemotherapeutic agents effective against most bacterial infections has made it possible to keep alive children who appear to lack the normal mechanisms of resistance to such infections, many of whom would undoubtedly have died in infancy 25 years ago. One consequence has been the recognition of several deficiencies, often hereditary, involving the development of lymphocytes or their capacity to make antibodies (or both). Although apparently rare, these may well prove to be more frequent causes of unexplained death in infancy than is at present recognized. The deficiency first recognized and most extensively studied is hypogammaglobulinaemia, in which the capacity to develop cell-mediated specific immunity is apparently intact but the capacity to make antibodies is seriously impaired. Over the past ten years a number of other immunity deficiency syndromes have been recognized, including a syndrome combining loss of ability to make antibodies with lack of cell-mediated immunity, which is almost invariably fatal, and a syndrome involving loss of cell-mediated immunity only.

Many of these conditions are genetically controlled, and some are sex-linked. Characteristically the children, once the level of antibodies passively transferred from the mother has fallen, develop recurrent bacterial infections, many of them eventually fatal. The children suffering from hypogammaglobulinaemia can be kept in good health by giving them regular injections of the immunoglobulin fraction prepared from pooled adult blood plasma, which supplies enough of the antibodies that they cannot make themselves. The Council has been responsible for an extensive trial and long-term follow-up study of this treatment and of the

features of the hypogammaglobulinaemia syndrome and it also supports work on other immunological deficiency diseases. Apart from any practical results the study of these diseases promises to shed considerable light on the nature of the immunological response.

TRANSPLANTATION OF ORGANS AND TISSUES

Thanks to the publicity given to heart transplantations during the past year, most members of the public are now aware that the barrier to successful transplantation of organs and tissues is not lack of surgical expertise but rejection of the transplant as a result of an immunological response made against it by the host. This was first clearly shown by Medawar in 1944 from his studies of skin grafts in rabbits. Except for identical (uniovular) twins, or for pure-line strains of animals obtained as the result of prolonged inbreeding by brother–sister mating, all individuals are likely to differ from one another in respect of some of the components that compose the surface of all the living cells of their body. These components are the ' transplantation ' or ' histocompatibility ' antigens. Like the better known blood group antigens on the surface of red cells, the transplantation antigens are strictly determined by heredity. At least six separate genetic loci are already recognized in man; there are several possible variations at each and they can occur in different combinations, so the probability that any two persons will have precisely the same make-up is exceedingly small, although the differences between close relations will be fewer than the differences between persons chosen at random.

It has become clear from animal experiments that the recipient of a graft is liable to make an immunological response against any transplantation antigen represented in the grafted cells but not in its own cells. Some transplantation antigens, however, evoke a more intense and regular response than others, and these are the most important in determining the duration of survival of the graft. Both a cell-mediated immune reaction (involving an increase in reactive lymphocytes) and an antibody reaction are evoked, but it is the cell-mediated immunity reaction that is generally responsible for destroying the grafted cells. In certain circumstances the antibodies may assist in this process, but in others it appears that they may actually help to protect the graft by coating the cells and preventing access of the lymphocytes.

The immunological problem of obtaining successful grafts, other than between identical twins, can be approached in three ways. One is to select donors with the minimum number of differences in important (' major ') transplantation antigens. To do this requires a method for determining the types of transplantation antigen, and thanks to a cooperative effort between workers in Holland, France, Italy, the United States and Britain this can now be done, the white blood cells being used for testing. The method is based on studies in mice that applied serological techniques devised by P. A. Gorer in England to genetically pure lines of mice bred at Bar Harbor, Maine.

The second approach is to diminish the intensity of the immunological response made by the recipient of the graft. This again can be done, by the use of cortisone and its analogues and of drugs that prevent the cell division necessary for the production of new reactive lymphocytes. However, there is a major drawback to this line of treatment, namely that it tends to suppress all immune

responses simultaneously, and to leave the patient a prey to fatal invasion by microbes to which he would normally not be susceptible. Consequently much interest has been aroused by the possibility of using an entirely different immunosuppressive agent, namely ALS (antilymphocyte serum), an antiserum developed by immunizing animals, usually horses, with human lymphocytes. This type of agent, whose study in experimental animals was pioneered in Edinburgh, Boston and London (at the National Institute for Medical Research), is able to incapacitate the lymphocytes that would otherwise damage the graft, while leaving the essential antibody-forming mechanism largely intact. ALS is still in the development stage, but it has been used in conjunction with more conventional immunosuppressive agents in a singularly successful series of kidney transplantations in the United States, and a Council Working Party is coordinating the arrangements for using it on patients in Britain.

The third possible approach is to devise a means for making the recipient tolerant of the donor's transplantation antigens beforehand. Some success in this direction has indeed been achieved in animal experiments, and rapid progress is being made in the identification and isolation of the human transplantation antigens that would be needed to extend such success to man.

It is probable that by a combination of the three approaches mentioned, even without the aid of any totally unforeseen discovery, the immunological barriers to transplantation of organs from man to man will be surmountable in cases where adequate preparation is possible. Even on the basis of existing knowledge the prognosis for kidney transplantation in suitable combinations of donor and recipient has become reasonably good. Most of the British research has been supported by the Council, and the subject was reviewed at greater length in the Council's Annual Report for 1962–63.

IMMUNOLOGY AND CANCER

Cancer research and immunology have moved steadily closer to one another during the past 15 years. The process was accelerated by the demonstration by N. A. Mitchison in 1953 that tumours transplanted between inbred strains of mice could be rejected by the action of sensitized lymphocytes but not serum antibodies of the host. Although it was first demonstrated with tumours, this is in fact the same mechanism that causes rejection of homografts of normal tissues. It has since been shown that cancer cells contain the normal transplantation antigens of their host, but often possess additional antigens that differ from those of the corresponding normal cells. In virus-induced cancers in animals (or cells that have acquired cancer-like properties in culture) the new antigens are characteristic of the infecting virus (see Annual Report for 1966–67), but in tumours induced by a given chemical carcinogen the new antigens may differ from one tumour to another, even in the same animal. In the case of spontaneously arising human cancers experiment is obviously impossible, but in a few instances abnormal antigens have been demonstrated by other means. There is in fact enough evidence from experimental cancer research to render tenable the hypothesis that many, if not all, cancers may possess abnormal antigens and that they should therefore evoke some degree of immunological reaction from the host. On this hypothesis, a cancer grows progressively because the immunological response of the host has been inadequate to prevent it from doing so, while any incipient cancer that does provoke an adequate response will be nipped in the bud before it can become apparent. Indeed, the elimination

of aberrant cells has been proposed as the main reason why the capacity to mount a vigorous homograft reaction is well developed in animals at all stages of evolution. Inadequacy of the immunological response can in principle be due to inaccessibility or excessively rapid growth of the tumour cells, to the stimulation of only a weak cell-mediated immunity by the hypothetical tumour antigen, or to protection of the tumour from the lymphocytes because its host has developed so-called ' enhancing ' antibodies, which coat the tumour cells without damaging them. There is experimental evidence to support all three possibilities in particular cases.

Early diagnosis and surgery, specific chemotherapy and X-ray treatment will undoubtedly remain the methods of choice for treating cancers for some time to come. The prospects of increasing the immunological response against an established tumour, or even, in the case of those tumours that may ultimately prove to be caused by viruses, of immunizing against them prophylactically, are sufficiently promising to justify continued effort in this direction. The greatest need at present is to learn more about the aetiology of cancers and about the control of immunological responses.

ISOIMMUNIZATION DURING PREGNANCY

One very successful form of transplant, which occurs without the intervention of surgeon or physician, is the foetus in its mother's womb. Since half its genes are derived from the father and half from the mother the foetus is certainly foreign to the mother, and animals have in fact been shown to reject skin grafts from their newborn offspring—and newborn animals grafts from their parents—quite readily. One of the very interesting problems of immunology and reproductive physiology is how the mother avoids making an immunological response to her foetus *in vivo*. It seems that there must be some barrier that prevents the passage of transplantation antigens across the placenta, although permitting molecules such as maternal antibodies of the IgG variety to cross readily. Some recent evidence suggests that the barrier may consist of a layer of acid mucopolysaccharide lining the maternal side of the foetal tissues.

However, there is clear evidence that foetal red and white blood cells may cross the placenta and enter the mother, especially during labour, and that the mother is sometimes immunized by antigens in them that she does not possess herself. This ' isoimmunization ' can have serious consequences in subsequent pregnancies, since her antibodies can cross the placenta and react with any antigens in the foetal cells against which she is immunized, causing a severe and possibly fatal haemolytic anaemia in the baby; until recently this could be cured only by giving a transfusion to replace the baby's red blood cells with those of the mother's group. Isoimmunization occurs most commonly with Rh-negative women, who run a risk of somewhat under 1 in 10 of becoming immunized by the Rh antigens of a Rh-positive foetus. However, it was discovered simultaneously in Liverpool and the United States in 1967 that administration of sufficient human anti-Rh antibodies to a Rh-negative mother shortly after labour caused any Rh-positive red cells present in her circulation to be rapidly removed and prevented her from becoming actively immunized against the Rh antigen. Since there are estimated to be some 64 000 women at risk annually in Britain alone, and since the supply of human anti-Rh antibodies is at present limited, the minimum effective quantity must be carefully assessed, and a clinical trial for this purpose has been organized by a Council working party.

To obtain a fuller understanding of the fundamental nature of the immune response represents an obvious challenge. This response is the main mode of reaction developed by vertebrates in the course of evolution to defend their integrity against any foreign materials, dead or alive, that penetrate their protective mechanical barriers. Furthermore, without such an understanding it is difficult to try to control the immune response at will, whether it is desired to intensify it for the purposes of protective immunization or to depress it selectively in autoimmune diseases or for the purposes of transplantation. Of the many approaches to this problem the one that has had the most spectacular success so far is the detailed analysis of the chemical structures of immunoglobulin molecules. The finding that the specific properties of antibodies are uniquely controlled by the sequence of the amino acids in the chains rules out any theory that the molecules are made in some plastic form and can acquire their specific properties by subsequent internal rearrangement. Moreover, each individual immunoglobulin has unique amino acid sequences in part of its chains, which means that the synthesis of each distinct immunoglobulin must be controlled by one or more distinct genes. This poses the problem whether every gene for every possible immunoglobulin is already present in the fertilized ovum, or whether the different genes arise later as a result of ' somatic mutation ' in individual lymphocytes of a much smaller number of genes controlling the synthesis of the immunoglobulin chains. Many workers prefer the second alternative, for a variety of reasons—for example, it is hard to envisage how, according to the first hypothesis, the capacity to respond to antigens that are not normally present in the environment could have survived the selective processes that tend to eliminate useless genes during the course of evolution.

However, the rate of mutation required by the second hypothesis is much greater than is known to occur in any other system, and there would need to be some quite unusual mechanism to bring it about. Fortunately immunoglobulin molecules possess a number of recognizable hereditary characters, which obey the ordinary rules of genetics; thus by the patient accumulation of sufficient information about a large enough number of different immunoglobulin molecules it will be possible to decide which, if any, of the hypotheses can accommodate all the facts. It has already been found that a large number of amino acids occur at identical positions in the immunoglobulin chains of species as far apart as the mouse, the horse and man. This is strong evidence that the general structure of these chains must have evolved from some common ancestral gene in the early evolution of mammals and have suffered relatively little change during their subsequent evolution. There is little doubt that by combining genetic, chemical and immunological studies the problem will be solved—though the nature of the final solution may be unexpected.

Studies of this kind are concerned with general principles, and make no predictions about the behaviour of individual lymphocytes. There is a need for maintaining lymphocytes (especially populations derived from a single cell) alive and functioning for long periods of time in tissue culture outside the body, so that their capacities can be studied—for example, in order to find out whether a given lymphocyte is restricted to producing only a single kind of immunoglobulin molecule—an important problem, particularly in relation to the induction of tolerance. Success in this field would also open up the possibility

of producing large amounts of immunoglobulin and even of specific antibody *in vitro*. Furthermore, large-scale cultures of lymphocytes might also provide a convenient source for preparing transplantation antigens for the purpose of inducing tolerance or active immunization.

Although all lymphocytes look much alike, and are originally derived from stem cells in the bone marrow, they contain at least two different populations, which proliferate in different compartments of lymphoid tissues. One population, called thymus-dependent because it fails to develop in the absence of the thymus, contains the long-lived lymphocytes, which are primarily responsible for cell-mediated immunity. The other population, about whose life cycle much less is known, is primarily concerned with making immunoglobulins. In the case of certain antigens efficient development of antibody production and of immunity appears to depend on some kind of cooperation between the two populations. It may be hoped that studies on children with congenital deficiencies of one or other of the lymphocyte populations will supplement current work on animal models to reveal the nature and biological significance of this cooperation.

Despite the advances of the past 25 years it is still uncertain what determines whether an antigen will elicit a strong or a weak immunological response. Attention has recently been turned to the part played by macrophages, the cells by which most antigens are taken up and sooner or later digested, and it appears that these cells have a marked effect in causing lymphocytes to respond to the antigens that they have ingested. These studies promise to throw light on the important practical question of how adjuvants work. Adjuvants are at present devised empirically, and those most effective in animals unfortunately produce unacceptably severe local reactions in man. Their improvement is highly desirable for two reasons—first, in order to facilitate a 'single shot' active immunization that is effective over a long period, especially of people in the developing countries and elsewhere who are not in a position to receive repeated injections to boost their immunity; and, secondly, because the use of adjuvants makes it possible to economize enormously on scarce or expensive immunizing agents (e.g., new epidemic strains of virus and synthetic 'tailor-made' or highly purified antigens such as may become the agents of choice in the future).

Even if adjuvants are not greatly improved, on the basis of past achievements continued progress in immunization against infectious diseases can be predicted. The major gaps in prophylactic immunization relate to what are mainly tropical diseases—cholera, enteric fevers, leprosy, trypanosomiasis, leishmaniasis, filariasis, schistosomiasis and malaria. Britain has had in the past a strong tradition of research in this field. It is now evident that the developing countries (and the World Health Organization) need and welcome the continuation of this tradition. In recent years there has been a marked revival of interest in the possibility of prophylactic immunization against some of these diseases, and the cooperation that has developed between parasitologists and immunologists has at least served to delineate much better the problems involved.

Another question to be answered is what determines the extent of cell-mediated immunity and the production of the various classes of antibody mentioned earlier. The need to control this aspect of the immunological response is likely to increase as more is learned about the biological significance of the

different classes of antibody. For example, IgE antibodies are responsible for anaphylactic phenomena, but in the presence of sufficient IgG antibodies the antigen is pre-empted and anaphylaxis is prevented. The aim of ' desensitization ' treatment, practised for many years, is now recognized as being selectively to increase the IgG antibody levels. Similarly ' enhancing ' antibodies, which can protect against the effects of cell-mediated immunity and about whose nature insufficient is known, may be desirable under some circumstances but detrimental under others. Identification and measurement of the different classes of antibody depend on specific reagents (antisera), some of which are at present scarce and difficult to prepare; but as such reagents become available it is almost inevitable that the role of various antibodies, protective or otherwise, will be clarified in microbial and parasitic infections as well as in autoimmune diseases and other conditions, such as cancer.

Another related problem is how the reaction of antigens with some, though not all, classes of antibody activates the auxiliary factors known as ' complement ' already mentioned. Studies carried out in America have shown that there are at least nine components of complement, which act in series. Partial activation of the series causes local inflammation, while activation all the way along the series at a cell surface kills the cell. Because the various components of complement are difficult to purify and to estimate their study has been limited to a very few groups of workers. As the methods are simplified and reagents become more readily available we may expect to understand better under which circumstances these reactions are protective and under which they actually cause disease.

The autoimmune diseases currently present a picture that has become less rather than more clear as observations have accumulated. Some of these diseases show a marked familial tendency and also tend to be associated with one another, while others appear to arise quite separately and without any hereditary predisposition. It seems likely that the former are linked with some instability of the immunological mechanism, while the latter are due in the first instance to wholly exogenous causes. Clarification may depend on gaining a better understanding of the genetic control of the immune response in man and in animals, and on developing animal models for these diseases. A strain of mice that has provided the one animal model for a hereditary autoimmune disease has proved to be congenitally infected with a virus. Whether this infection plays any part in the disease process remains to be discovered, but the possibility that viral infection of lymphoid tissues may cause immunological abnormalities cannot be neglected.

Subject to the need to learn more about the fundamental nature of the immune response, guide lines have already been laid down for progress in transplantation, and in principle (though not to a great extent in practice) towards an immunological approach to cancer. However, there is need for the continued development of means that are more selective than those at present available on the one hand for suppressing the immune response without interfering with cell division in other respects, and on the other for suppressing tumour cell division without damping down the immune response. The discovery of antilymphocyte serum, although it may not prove to be the final answer, has shown that the former is possible; the latter may be achieved as a result of greater knowledge of the biochemical peculiarities of tumour cells.

It is even more difficult to discuss future trends adequately in a short review than it is to do justice to all the interesting discoveries and applications that have been made during the past quarter of a century. The period has been one of great advance. For the past 15 years papers on immunology have composed some 10 per cent of the work presented at the annual meetings of the Federation of American Societies for Experimental Biology, and it seems likely that the momentum achieved will be maintained for some time to come.

Occupational health and toxicology

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Research in occupational health and toxicology covers a wide field. In this account many important aspects of the research supported by the Council have had to be omitted—the work in applied psychology, on the causes and treatment of accidents*, on ergonomics and heat stress and on the effects of noise on hearing and performance. Ionizing radiation is mentioned in the article on epidemiology (p. 90).

Environmental factors are involved in the aetiology of many diseases and research in occupational health is concerned with those diseases where a cause and effect relationship is suspected or known but where the extent of the damage produced, or the nature of the environmental factors, is ill defined. Much of the work aims at establishing a quantitative relationship between the harmful factors and the ill-effects produced on which to base logical preventive measures. This can be done in the absence of a full understanding of the mechanism by which the environmental factors act, but the investigation of these can lead to a deeper understanding of disease processes, including those not related to occupation. Such problems demand a multidisciplinary approach for their solution, and success can be achieved only by a body having no vested interests in one particular professional skill or one administrative authority. The independent status and the broad scientific coverage of the Medical Research Council have made this possible, and indeed the Council—and the Medical Research Committee before it—have been concerned with occupational health for more than 50 years. This account outlines the role of the Council and some of the research it has supported in this field over the past 25 years.

In 1943 the Department of Research in Industrial Medicine was set up by the Council at The London Hospital under D. Hunter. At the end of the war people trained to use new techniques developed in the Services were ready to start attacking problems in occupational health on a wider front. The Council established several more units with broad terms of reference, and the staff were encouraged to develop their own lines of research. Ideas and methods that started in the ward and laboratory were carried into the factory and mine and later to the general population, and many different disciplines—clinical medicine, epidemiology, physiology, biochemistry, chemistry, physics and statistics—were involved. Even when clinical contact was less close, reports of occupational hazards provided the starting point for research on physiological, biochemical and immunological mechanisms. Every encouragement was given to Council staff to use their unique position in relation to universities, government departments, industry and the trade unions to ensure rapid advance in knowledge and the early publication of results. This position of independence

* The Council's Report for 1963–65, pp. 68–78, includes review articles on some aspects of applied psychology and on accidents.

combined with the mutual trust prevailing between the Council and the many bodies concerned has been perhaps the greatest single factor in the successes achieved.

Research in occupational health is affected by economic and social pressures. Consequently it is difficult to judge what balance of effort is needed between short-term work on specific problems and basic research with long-term objectives. Here the broad view of the whole field of medical research available to the Council is of special value.

It is becoming increasingly hard to differentiate between the effects on health of the working and general environments. Conditions in the factories improve; conditions outside get better in some respects and worse in others. For example, the carbon monoxide levels have decreased in steel works but have increased in the traffic jams encountered on the way to and from work, and even there the blood carboxyhaemoglobin level is influenced far more by the cigarette smoke inhaled than by the amount of carbon monoxide in the air. Before the war asbestos dust was largely a problem arising from asbestos textile mills and from pipe lagging. Since the war there has been a fivefold expansion in the use of asbestos, so that many more people are exposed to small amounts of the dust. The pollution of the environment by lead from motor fuels is a source of current controversy. This needs further investigations in the light of knowledge of the effects of lead on those occupationally exposed to it.

INDUSTRIAL MEDICINE

The main work of the Department of Research in Industrial Medicine at The London Hospital was the recognition of diseases attributable to toxic substances encountered in industry. Many of the investigations—for example the hazard to electrical workers making mercury switches—started from detailed industrial histories taken in the outpatient clinic. Reports of illness of sheep and cattle near an aluminium smelter led to a full investigation of a possible fluoride hazard to the workers and those living in the neighbourhood. A risk of lung cancer in chromate workers reported from the United States was confirmed in the United Kingdom. In several instances new techniques were developed for making environmental measurements. A study of the hazards to agricultural workers using new pesticides led to legislation, which has been strikingly successful in preventing injury to workers from these materials despite the great expansion in their use. The Department achieved its aim of increasing industry's awareness of potential hazards, and it was disbanded in 1963 on the retirement of the Director.

Dust diseases

In 1945 nearly 6000 coalminers with pneumoconiosis were suspended from work in the mines. The Medical Research Council set up the Pneumoconiosis Unit under C. M. Fletcher in South Wales, where the problem was most acute. The main aim was to acquire sufficient knowledge to set a safe ' dust level ' and, if possible, to detect slight changes from the normal in the worker before a progressive disease had started. The complete elimination of the dust from mines and most other work places is impracticable. The more stringent the 'dust standard' the greater the cost, so a compromise between what is medically desirable and what is economically and socially acceptable has to be struck. To do this the nature and the full extent of injury to health must be established

and related to the dose of dust. But both the dose and the response to it have to be measured over a period of many years because, in general, pneumoconiosis develops only slowly.

In the development of methods of measuring the dust and assessing the response to its inhalation, the dust particles were at first counted. Miners were selected at random from the colliery list and accompanied for the whole shift. In this way it was possible to get an unbiased estimate of each man's exposure since no samples were collected when he was absent. This sampling procedure formed the basis of the scheme used by the National Coal Board in its 15-year prospective study of 25 000 miners, which was the logical development of the earlier retrospective studies by the MRC Pneumoconiosis Unit. Particle counting is laborious and subject to many errors. Direct measurement of the mass of respirable particles able to reach the alveoli, where they are retained, became possible when a method (suggested by the National Coal Board) of separating particles on the basis of their falling speeds was developed into a practical technique by the Pneumoconiosis Unit. The exchange of ideas at meetings of committees of the Council has been an important factor in the present trend in this and other countries to change from particle counting to direct gravimetric estimates of the respirable mass of the dust, which are both more efficient and biologically more appropriate. In the future, when the equipment has been perfected, sampling will be within the breathing zone of the man, where the concentration of dust may be several times the concentration a few feet away. The next main problem in this field is how to sample fibrous dusts, such as asbestos. There is at present insufficient basic knowledge of the factors influencing the deposition of such elongated particles in the lung and of the influence of particle size and shape on the fibrotic and neoplastic changes produced by this dust.

The effects on health are also difficult to measure. Should clinical, radiological, physiological or pathological indices be used? Should these measurements be made on men in hospital, on those at work or on those who have left the ' dusty ' occupations? Other factors, such as age, general air pollution and cigarette smoking, have to be taken into account. The MRC Pneumoconiosis Unit started the systematic assessment of the reproducibility, validity and inter-relation of a range of indices in progressively better and more representative samples of the population of miners and ex-miners, and later the general public, as the epidemiological techniques were improved. The further use of these methods for other purposes by the MRC Epidemiology Unit (South Wales) is described in the article on epidemiology.

A system of classification of the radiographic appearances of coalworkers' pneumoconiosis, developed at the Pneumoconiosis Unit, was recommended by the International Labour Office in 1950. The scheme was revised in 1958. Recently the unit has been working with research groups in several countries to develop a system of wider relevance, which can be applied to workers exposed to asbestos. The work on observer variation, first applied to pneumoconiosis, was a source of much controversy but is now widely accepted and applied in other branches of medicine.

The systematic recording of chest symptoms was started and led in 1960 to the MRC questionnaire on respiratory symptoms. This is the most widely used scheme for studying bronchitis and has been translated into more than 12 languages; there are more than 60 studies using it.

Symptoms are subjective and not easily graded. Research on lung function, started at the end of the war to measure disability in occupational chest disease, has expanded very rapidly and has led to the development of several objective and sensitive indices of various components of lung function. Its contribution to the diagnosis of non-occupational chest diseases, to the treatment of acute and chronic respiratory failure and to an understanding of the physiology of the lung—for example the balance between the ventilation and the perfusion of the blood, and the factors influencing capacity for exercise—now far exceeds its contribution to occupational health. The Pneumoconiosis Unit has designed instruments for testing lung function, which are now in wide use in clinics and in the field. The International Biological Programme on Human Adaptability is using these new methods, and the ILO's 1966 recommendations on respiratory function tests in pneumoconiosis made extensive use of the experience of the Pneumoconiosis Unit. While the tests cannot always be used as proof of a dust effect, the more specific changes in asbestosis, beryllium disease and farmer's lung are helpful in diagnosis.

Many surveys in representative samples of the general population and in workers exposed to dust in mines, foundries and factories have been made using these methods. The severity of simple pneumoconiosis seen on the chest radiograph, which from other evidence is known to relate well to the amount of dust in the lung, is not at all closely related to the incidence of bronchitis. Regional differences were discovered. For example, the difference between miners and those without mining experience in frequency of symptoms and degree of impairment of lung function was greater in South Wales than in Derbyshire, where the effect of mining was small. In all surveys the effects of cigarette smoking are very marked and tend to swamp any direct effect of the dust. In the future the National Coal Board Pneumoconiosis Field Research Scheme may supply essential data for relating the dose of dust to the amount of bronchitis in working miners.

Although the category of ' simple ' pneumoconiosis is poorly related to bronchitis, long-term studies in South Wales showed that it involved a risk of ' complicated ' pneumoconiosis, which can cause severe disability and shorten life. Fortunately it is possible to detect dust accumulation in the lung radiologically before the risk of a progressive disease is appreciable. Improved methods of assessing early changes in the chest film now provide a means of protecting the individual and, when applied to the group, of assessing the adequacy of dust control.

The discovery of the differences between simple and complicated pneumoconiosis in coalworkers made it no longer necessary to suspend from further work all miners with pneumoconiosis and the change in practice was introduced with the Industrial Injuries Act, 1948. The mechanisms responsible for complicated pneumoconiosis are still not clear despite much research. This has included a major epidemiological project to compare the development of complicated pneumoconiosis in two mining communities in South Wales with differing incidence of tuberculosis. It now seems likely that this form of pneumoconiosis has more than one cause, of which tuberculosis is one, another being linked, in some way not yet clear, with the factors concerned in the development of rheumatoid arthritis.

The continuous research effort by the National Coal Board and the Council and the application of the new knowledge—both medical and engineering—

have produced great improvements. In 1967 the number of new cases of pneumoconiosis in coalminers had fallen to 741—about one-eighth of the number in 1945.

The research effort is now shifting to the more complex problem of asbestos dust (see Annual Report, 1967–68, pp. 70–76). Several years of work will be needed before knowledge of the effects of asbestos matches that of the effects of coal and mixed mineral dusts.

In the last 15 years knowledge of the effects of organic dusts has advanced rapidly (see Annual Report for 1966–67, pp. 74–82). There are two broad groups of diseases: those due to dusts arising from the processing and spinning of natural fibres (cotton, flax, hemp, jute and sisal) and those due to dusts produced by the moulding of vegetable matter (hay, straw, corn and crushed sugar cane or bagasse).

Byssinosis, the disease caused by cotton, flax and hemp, used to be regarded as a rarity except in Lancashire and Northern Ireland. Epidemiological studies, using techniques developed by R. S. F. Schilling (Department of Occupational Health, London School of Hygiene and Tropical Medicine) and by the MRC Pneumoconiosis Unit, have shown that byssinosis is in fact a world-wide problem wherever these fibres are processed. Severe respiratory disability has been produced though its cause has not been recognized in the past. There are no radiographic changes; epidemiological studies therefore have to be based on symptomatology and on tests of lung function, which alters during the course of a shift worked in a dusty atmosphere. These changes can be used to monitor the exposures of groups of workers and thus to detect the most susceptible subjects. Provisional values for acceptable dust levels have been set. The mechanisms causing byssinosis are not yet clear. Antigens in the cotton dust, bacterial endotoxins and pharmacologically active agents may all be concerned, and research continues.

Diseases of the second group—due to dusts from mouldy vegetable matter—were shown, by work at the former MRC Clinical Immunology Research Group under J. Pepys, at the Institute for Diseases of the Chest in London, and by P. H. Gregory and his colleagues at Rothamsted Experimental Station, to have a common immunological basis. The majority are caused by delayed hypersensitivity to thermophilic actinomycetes. These organisms will grow only at high temperature and humidity, conditions that follow the baling of hay and bagasse and the storing of wet grain. Inhalation of dusts from such mouldy materials produces characteristic clinical and radiographic changes and alterations of lung function. The blood contains precipitating antibodies to the actinomycetes. Once sensitized the individual is likely to relapse on further slight exposure. Prevention depends on reduction of moulding in crops, avoidance of inhalation of spores and, since the periods of exposure to dust are usually short, the use of efficient masks. This work provides an opportunity for applying the techniques of occupational hygiene to some farming operations.

Since many dust diseases are caused by the retention of the dust in the alveoli or respiratory bronchioles, a means of accelerating removal of the dust could be of great value. No means of doing this has yet been discovered. The possibility of influencing the action of the dust once it is in the lung has been improved by the discovery in Germany that polyvinylpyridine-*N*-oxide powerfully inhibits the fibrogenic action of silica, both *in vivo* and in tissue culture. Experiments at the National Institute for Medical Research have shown that this polymer acts

by preventing silica particles from destroying the phagosome membrane in the phagocytic cells. Unfortunately it has little effect on asbestos dust.

Skin diseases

The skin is vulnerable to many of the agents used in industry. Diseases of the skin cause much incapacity, though rarely serious illness. J. R. Squire, first Director of the MRC Industrial Medicine Unit, set up in Birmingham in 1946, investigated the incidence and causes of skin disease in a variety of industries. The work's first aim was a reduction of time lost, and basically simple problems, such as the cleaning of the skin and the value of protective creams, were examined as well as the problem of skin cancer (see below).

The early studies on damage to the skin by industrial chemicals revealed a great lack of basic knowledge of many of the biological properties of this tissue. In 1952 the Council established a Unit for Research on the Experimental Pathology of the Skin, and much information on the ways in which the skin responds to a variety of damaging agents has been acquired. The biochemical activity of skin, including lipid and mucopolysaccharide metabolism, is now becoming clearer. The work has been extended to the action of parasitic fungi and to the immunological responses of the skin.

Hazards from carcinogenic substances

The substances already known or suspected to be carcinogenic are surprisingly diverse and predictions about the likely carcinogenicity of new substances cannot be made with certainty. Constant vigilance is needed to detect occupational cancers, which may occur many years after first exposure to the substance or environment concerned. Examples are the recently discovered pleural and peritoneal tumours associated with exposure to asbestos and the nasal cancers in wood machinists. Efforts are now being made to identify the carcinogens. Prevention through improved occupational hygiene can start at once, though it is rarely possible to plan this economically without a knowledge of the nature of the agent.

An unusually high incidence of skin cancer among some engineers exposed to mineral oils was discovered by C. N. D. Cruickshank and J. R. Squire during the investigations of the MRC Industrial Medicine Unit. A large and protracted study by experimental pathologists, organic chemists and physical chemists, with advice from experts in the oil industry, was carried out to identify the carcinogenic substances in various oil fractions. The full report (MRC Special Report No. 306) was published in 1968. The aim of developing a rapid and reliable method for detecting carcinogens in oils was not fully achieved. This was not surprising in view of the complexity of the oils (the identification of all the carcinogens in cigarette tobacco smoke has defied an even greater investigative effort). However, the problem of skin cancer associated with cutting oil demanded an immediate answer, and once the hazard was recognized protection and early detection could be provided even though elimination of the causative agent was not possible.

Observations 30 years ago that workers in a large nickel refinery had an unusually high incidence of nasal cancer did not lead to the identification of the causative agent, but a follow-up study showed that only men who worked with

a process now obsolete developed the lesion. The subsequent experimental demonstration that nickel carbonyl is carcinogenic in rats is possibly irrelevant since the refinery still produces large quantities of this compound.

Work at the MRC Air Pollution Unit illustrates one difficulty of relating cause and effect in occupational cancer. Coke oven workers are exposed to a high level of benzopyrene, a well known skin carcinogen in animals, yet the incidence of lung cancer in these men is not exceptional.

An investigation of dimethylnitrosamine and its safety or otherwise as an industrial solvent led to the discovery in the MRC Toxicology Unit that it was very toxic. But it was also shown to be the first of a large newly discovered group of carcinogens—nitrosamines and nitrosamides—which produce a wide range of tumours in many species, including primates. The industrial uses of these compounds can be controlled, but the possibility that nitrosamines may be formed occasionally in food processing and the discovery that they occur naturally in some plants and microorganisms emphasized their wider importance. Their chemical simplicity and high carcinogenic activity, even in single doses, make them especially useful for studies on the mechanisms of carcinogenesis.

STUDIES IN LABORATORY ANIMALS

Too often occupational health research starts with the detection of disease in man. As its prime aim is prevention, an attempt must also be made to detect and study experimentally substances to which people will be newly exposed. So much attention is now paid to testing the safety of drugs, pesticides and food additives by animal experiments that it is easy to forget that 25 years ago a substance might be introduced into industry without any investigation of possible hazards. The chemical industry asked the Medical Research Council in 1947 to set up a unit to study the toxic properties of potentially useful materials where information was inadequate. The MRC Toxicology Unit has broad terms of reference and it has the general aim of providing a more complete picture of the nature and variety of chemical injury. It was not intended to provide a testing service. The big chemical manufacturers had already started to do tests on chemicals they were selling or using, but there were substances of potential interest to industry and agriculture about whose toxicity little was known. These have provided the starting points for all the research work undertaken by the MRC Toxicology Unit.

Beryllium was one of the first substances studied and affords a good example of the practical and theoretical problems. It was not difficult to establish by simple experiments that it was toxic and therefore that protection of workers was necessary. The much more difficult problem was to assess a safe degree of exposure. If a safe substitute for a toxic substance can be found complete removal is a practical solution—as in the case of some of the compounds known to produce bladder cancers. But if an indispensable substance is of great economic importance, as beryllium appeared at one time to be to the atomic energy industry, some continuing exposure of workers will occur. Where compounds are highly toxic it becomes of especial importance to discover the mechanism concerned, because some people may be affected at even very low dosage. Beryllium and isocyanates (used in the production of foamed plastics) may be examples of such compounds. Surveys of workers exposed to these substances are now in progress.

The experimental methods used are determined by the nature of the substance concerned and the type of response it elicits. With beryllium the toxicity of the ions was quickly established. Later work designed to pin-point its site of action in sensitive tissues made it possible to suggest a basis for its toxic action in humans, who develop a disease that is not reproducible in animals. The highly specific binding of beryllium to a few proteins, and the discovery that in guinea pigs genetic factors may influence the skin response, suggest that an immune mechanism may underlie the severe reactions seen in some people exposed to the dust. Immune responses, now being so thoroughly explored in other fields, have received little attention as a mechanism in the reactions to poisons.

Sometimes investigations have shown that the suspected agent may not be toxic in itself. For instance, dimethylnitrosamine, triorthocresylphosphate and tetraethyl lead are not themselves toxic, but after absorption they are metabolized by the liver to new toxic molecules. This clearly limits the value of purely *in vitro* techniques for detecting toxic substances.

Many investigations may be expected to throw light on basic cellular processes. Trialkyl tin salts were originally examined because they were potentially useful fungicides; the problem was whether they would present the same hazards as the alkyl mercury compounds, which cause irreversible brain damage in man. The trialkyl tin compounds produced in animals a reversible oedema of the brain, suggesting that they would be less hazardous than an alkyl mercury fungicide. This has subsequently been confirmed by experience. Further studies revealed that triethyl tin salts were very active inhibitors of oxidative phosphorylation, a vital process in the life of every cell. Since triethyl tin combines with only a few macromolecules, a detailed examination of the molecular basis of this affinity may throw light on the unknown steps in this important biological process.

Mercury and its compounds are still an important occupational hazard. Studies on its binding in tissues and on the factors that determine the distribution of various forms of mercury in the body explain why poisoning by the vapour of the metal affects the brain, while mercuric salts damage the kidney. This work suggested a simplified method for measuring the mercury in urine—an essential safeguard for mercury-exposed workers—and a tedious method taking many hours was reduced to a simple semi-automatic procedure taking a few minutes.

Early work on reactions between the organophosphorus insecticides and esterases has been used by others to develop the nucleophilic oximes for therapy in poisoning by many organophosphorus compounds. This knowledge of the reactions between esterases and organophosphorus inhibitors now forms the basis of a current study of the mechanism of delayed structural damage to the brain by triorthocresylphosphate and other organophosphorus compounds. A protein that is phosphorylated by such compounds appears to be involved. It is hoped that the way in which this protein with esterase activity performs its vital role in the maintenance of neurones with long axons will be explained later.

Acrylamide has been studied because of a hazard to engineers using it for waterproofing soil during mining and tunnelling. It produces in animals a peripheral neuropathy that is largely reversible when exposure ceases. The first human cases occurred in chemical plants using the material and the effects were similar to those seen in laboratory animals. The site of reaction of

acrylamide within the nervous system is now being studied. The effect is very localized and apparently produced only by acrylamide and not by molecules that are closely related chemically.

Knowledge of the action of poisons on the nervous system, both reversible and irreversible, can give clues linking biochemical and behavioural changes. Both triethyl tin (a useful fungicide) and triethyl lead, which is the toxic molecule formed when tetraethyl lead (the petrol additive) is absorbed, apparently have the same biochemical activity, which is directed against cell organelles in isolated tissues, including the brain. Yet triethyl tin poisoning in man and animals leads to weakness and lassitude with brain oedema, while triethyl lead causes wild excitement and convulsions and no brain oedema. Further study of these two chemically similar compounds may explain their different effects. Neither produces the irreversible damage in the brain seen with alkyl mercury compounds.

An alteration of response in the nervous system is widely held, especially in the Soviet Union, to be a sensitive index of toxicity. Comprehensive behaviour studies in animals treated with a limited number of substances have been made in collaboration with staff of the MRC Unit on Neural Mechanisms of Behaviour. Even with compounds having toxic effects virtually confined to the nervous system, this does not appear to be a particularly sensitive method. But the effects on behaviour in man might be important for discovering the concentration at which certain poisons such as carbon monoxide produce toxic effects. The MRC Air Pollution Unit is investigating the behavioural effect of carbon monoxide (since it is present in cigarette smoke and is a common industrial and urban pollutant) at concentrations generally held to be too small to produce symptoms; the tests being used for this were developed by the MRC Applied Psychology Unit to assess performance of demanding tasks, judgement and vigilance. A method of estimating carbon monoxide in minute samples of blood was developed for this work.

Experimental work on toxic substances is not limited to an attempt to predict hazards. For example, work has recently started on carbon disulphide, because of an interesting finding in industry that people exposed to what had been thought to be a safe level may have an increased risk of ischaemic heart disease. It is too early to say whether closer study of the toxic effects of carbon disulphide will throw useful light on the general aetiology of ischaemic heart disease; but the work is opening up the question of whether occupational hazards can manifest themselves as increased susceptibility to what may be called natural diseases—a point that is discussed further below.

The use of toxic substances as tools in biological research is well established. Physiologists have made valuable use of vegetable poisons known to primitive man, such as nicotine, curare and eserine, and this should encourage rather than deter efforts to put new materials synthesized by chemists (such as those referred to above) to similar useful purposes.

Experiments in animals have helped to elucidate mechanisms in pneumoconiosis. An elegant set of experiments by E. J. King and G. Nagelschmidt defined the relative importance of mass, number and surface area of particles in the production of silicosis. The results were of immediate use in the design of dust-sampling instruments. A long series of experiments showed that mycobacteria of low virulence, when combined with coal dust, produced a disease with some of the features of complicated pneumoconiosis of coalworkers.

Improved methods of dispersing and measuring dusts in animal chambers have opened up the possibility of work on the quantitative aspects of inhalation. This provides a means of comparing the deposition and elimination of different dusts—for example the principal types of asbestos or coals of different ranks—as the particles retained in the rat's lung are similar in size to those retained in the human lung.

FUTURE DEVELOPMENTS

The future trends of research on the aspects of occupational health covered in this article will depend greatly on advances in the basic sciences of biochemistry, physiology, genetics, molecular biology and immunology, as well as on the development of new products and methods in industry. When the first work on beryllium, for example, was started modern immunology was only just developing; but now new knowledge should make further progress possible. It is, however, possible to forecast the type of problem to which particular attention will be given.

First, the increasing awareness of potential chemical hazards in our environment will stimulate research to detect at the earliest stage minor deviations from normality—in particular, the possible role of a mild but protracted exposure to a toxic substance in altering the course or frequency of ' natural ' diseases. The effects of lead are an example. An occupational disease of lead workers has been recognized for centuries; some of the symptoms of lead intoxication are quite specific, but in a milder degree the effects of lead may result only in a greater tendency to develop hypertension or cerebrovascular disease. Everyone ingests a certain quantity of lead, mainly from food and some drinking water. While one approach to the study of possible effects of such minor exposure is by epidemiological studies, another would be to look for a minimal deviation from normal in some biochemical cellular process caused by lead. The best approach is to link experimental toxicological studies on animals with refined epidemiological investigations on people with varying degrees of exposure or ' body burden '. Such studies are difficult and may need to extend over many years, so that the final assessment may be possible only after those who initiated them have retired from active work. It is therefore essential that the continuity of such investigations should be maintained.

Another aspect of this problem is the linking of full and accurate information about occupation to national mortality and, later, morbidity records. An important problem is how to achieve the earliest possible detection of the late effects of occupational exposures—for example cancers that may appear only 20 or more years after first exposure. There is an immediate need for an efficient centralized system by which those in certain occupations with a recognized long-term risk can be followed to establish the cause of death. Only in this way will it be possible to discover whether the preventive measures now being taken are effective. Once started such a scheme could be extended to other groups in which the evidence of a long-term risk was less certain. The records could also be used to show the contribution of occupational factors to ' natural ' diseases. Much of the information for this type of occupational health research already exists but it is not assembled in a form in which the essential data can be interrelated. Computers now make this kind of correlation technically easy once the administrative scheme necessary for the efficient assembling of the data has been perfected.

In the future it seems probable that more attention will be given to the characteristics of the individual that contribute to the manifestations of an occupational ' disease '. At present, when safe levels of, for example, dusts and many toxic chemicals are being established, the variation of sensitivity from one individual to another is assumed to be random and inexplicable. If it is not, and if a few individuals, for genetic or other reasons, are highly susceptible and others perhaps completely immune, it may become possible to identify these people in advance by biochemical or other techniques. A further marked reduction in occupational diseases might thus be achieved.

Occupational health research, by the pressure it applies to improve conditions in industry, is constantly bringing these closer to the general environment. Consequently there is a blurring of the edges between occupational health research and research in general medicine. The advances in epidemiology and other disciplines stimulated by occupational health research are finding wide applications in general medicine. Moreover, the discoveries in toxicology stimulated by industry's need to use powerful chemicals have added greatly to the knowledge of normal biochemical processes in the cells. This, in turn, contributes to understanding of the mechanisms of diseases that are not known to be related to any occupation.

Epidemiology

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Epidemiology can be defined as the study of the frequency with which disease occurs in different populations. As a method of research it has four principal applications. First, it may help to provide a balanced picture of the natural history of disease, by demonstrating the frequency with which signs and symptoms may be found in the population as a whole, including people who have not yet sought medical advice. Secondly, it may suggest a clue to causation, by demonstrating differences in the incidence of a disease under different conditions. Thirdly, it may test the value of a hypothesis about the cause by carefully designed observations relating the occurrence of the disease to the personal or environmental characteristics of affected and unaffected individuals. Finally, if the evidence is strong enough, epidemiological methods may be used to test a hypothesis in practice, by showing whether the disease is prevented by removing the agent or protecting against it.

THE CAUSES OF DISEASE

Epidemiological techniques were first developed for the study of infectious diseases, and their use led to the discovery of many of the principal infectious agents and to the control of the diseases they produced. Later, these methods began to be adapted to the study of other conditions, and they played a large part in the discovery of vitamins and the diseases caused by vitamin deficiency and of the effects of many industrial poisons. It was not until after the second world war, however, that epidemiology was generally applied to the study of such conditions as cancer, arteriosclerosis, malformations and psychiatric illness and of juvenile delinquency and accidents. By then it had become apparent that the common causes of death were very different from those that had been common 20 or 30 years previously. Some diseases had been brought under control, but others were becoming both relatively and absolutely more important. These included cancer of the lung, coronary thrombosis, leukaemia and duodenal ulcer.

Cancer of the lung

The death rate in men from cancer of the lung had risen from 9 per million per year in 1905 to 27 per million in 1925, and 289 per million in 1945. This rise was so dramatic that in 1947 the Medical Research Council called a conference to consider the reasons for it. At the time, it seemed possible that the increase might be largely an artefact due to improved methods of diagnosis and to advances in chemotherapy which, by preventing patients from dying of pneumonia while the cancer was still in an early stage, enabled the disease to develop until it was more easily diagnosed. The conference could not exclude

this explanation, but neither could it exclude the possibility that the increase in mortality reflected a real increase in the incidence of the disease, and it seemed sensible to review the changes that had taken place in the environment to see whether any of them could have been responsible.

An investigation was therefore undertaken by Sir Austin Bradford Hill and R. Doll of the MRC Statistical Unit, with the advice of Sir Ernest Kennaway and P. Stocks. Altogether some 5000 hospital patients, including almost 1500 with lung cancer, were interviewed. Inquiries were made about the extent to which the patients had been exposed to any of the factors that were under suspicion (coal smoke, the exhaust fumes of motors, specific occupational hazards, tobacco smoke and respiratory infections) and comparisons were made of the information obtained from patients with different diseases. The preliminary results, reported in 1950, revealed only one striking contrast between those with and those without lung cancer: namely a difference in smoking habits.

This difference was confirmed when the study was completed and a new investigation was begun to test the correctness of the conclusion by a different method. At the end of 1951, a questionnaire was sent to all members of the medical profession in the United Kingdom asking for brief details of their smoking habits. Over 40 000 doctors replied and were classified, on the basis of their answers, into broad groups according to the amount of tobacco they smoked, their method of smoking it, and whether they had given up smoking or were continuing to smoke. These groups have now been followed for more than 17 years and information has been obtained about changes in their smoking habits by further questionnaires sent out in 1957 and 1966. Information on deaths has also been obtained and the death rates for different causes of death have been calculated for each group.

By 1956 enough information had been obtained to confirm that the death rate from lung cancer was substantially higher in men who smoked than in non-smokers, and that it was higher in cigarette smokers than in other smokers, in heavy cigarette smokers than in light, and in men who continued to smoke than in those who had given up. Similar results were reported from other countries and in 1957, after a review of all the relevant facts, the Medical Research Council reached the conclusion that smoking, and particularly cigarette smoking, was one of the principal causes of the disease. In its absence the male death rate from lung cancer, which by 1966 had risen to 962 per million and was four times the rate attributable to traffic accidents, might be expected to be reduced by about 90 per cent.

In 1964, the results of ten years' observation on doctors were available. By then nearly 5000 deaths had occurred and it was possible to make quantitative estimates of the relationship between smoking and mortality from a large number of other diseases besides lung cancer. Approximately two-thirds of all deaths were attributed to causes that did not appear to be related to smoking, the death rate from these causes being practically the same in smokers and non-smokers. The remaining third were attributable to coronary thrombosis, chronic bronchitis, pulmonary tuberculosis, peptic ulcer, cirrhosis of the liver, and cancers of the upper digestive and respiratory tracts as well as cancer of the lung, and deaths from all these diseases were significantly more frequent among smokers than among non-smokers. How far smoking is a cause of these other

diseases remains to be shown. In the case of cirrhosis of the liver, the association is presumably incidental and secondary to an association between smoking and the consumption of alcohol. It seems likely, however, that smoking is a principal cause of chronic bronchitis and one of the factors responsible for mortality from coronary thrombosis, at least at ages under 65 years.

Coronary thrombosis

This last disease, like cancer of the lung, occurs characteristically in men and the mortality attributed to it has increased enormously in the last 40 years. How much of this increase is real is, however, difficult to decide. The clinical condition was clearly described for the first time only in 1912, and there can be no serious doubt that much of the apparent increase is an artefact due to changes in diagnostic fashion. In 1951, however, J. N. Morris, of the MRC Social Medicine Unit, showed that much of the increase was almost certainly real. Detailed examination of the published mortality statistics showed that the increase in the number of deaths attributed to coronary thrombosis was, at each age, greater than the decrease in those other conditions that might have provided an alternative diagnosis and that the rate of increase was much greater in men than in women. A similar increase was also found in the necropsy records of The London Hospital, where successive pathologists had had a special interest in arterial disease over a period of 40 years. Even more striking was the increase in the number of cases of spontaneous rupture of the heart. This condition, which is the most obvious manifestation of a severe thrombosis, causes sudden death and is found most often at a coroner's necropsy. It can hardly be overlooked or confused with any other; yet, over a wide area of the country, the number of occasions on which it was diagnosed increased two-and-a-half times between 1932 and 1949.

Despite this evidence of an increase in the number of fatal cases of coronary thrombosis, Morris was unable to find any evidence of an increase in the amount or severity of coronary arteriosclerosis. On the contrary, the necropsy records of The London Hospital showed that the recorded prevalence of advanced coronary arteriosclerosis had decreased in all pathological categories in all the relevant age groups and in both sexes. It seemed therefore that disease of the coronary arteries, although important, was not the only factor in producing coronary thrombosis (or infarction) and that other factors also had to be considered.

One clue was derived from the study of populations at different stages of social and economic development. This showed that a high incidence of coronary heart disease was characteristic of highly developed countries and suggested the possibility that diet, and particularly the content of animal fat in the diet, might be an important cause. Much laboratory work has been devoted to this aspect of the subject, but it has not been possible to define the precise role of any one factor.

Several large studies, carried out in the United States, have shown that the morbidity from coronary heart disease is closely related to the level of the blood pressure and the blood cholesterol as well as to the amount smoked. To these factors Morris and his colleagues have added the degree of physical activity. In their first study, the incidence of coronary disease was compared in men who were employed by the London Transport Executive and the Post Office and other Government departments. Within these categories of employment, the

incidence of coronary thrombosis and, more particularly, of severe thrombosis leading to early death was highest, at each age, in the groups whose work required the least physical activity. In bus drivers the mortality from a first episode of coronary disease was twice that in conductors; in Post Office telephonists and in Civil Service executives and clerks it was twice that in postmen; and in Post Office counter-hands and postal supervisors, whose work was intermediate in activity, the mortality was also intermediate. When the national mortality rates recorded by the Registrar General for men in different occupations were re-examined in the light of these findings, differences in physical activity at work were found to be capable of accounting for a large part of the differences in mortality between the different socioeconomic classes. Within each class, the mortality was greatest in sedentary workers and least in those whose work was physically heavy.

The hypothesis that physical inactivity was an important factor was later confirmed when Morris and M. D. Crawford carried out a survey of post-mortem findings throughout the country. Some 200 pathologists each contributed reports of 25 consecutive necropsies, irrespective of the cause of death or of the reasons for carrying out the necropsy. The results showed that fibrous scars (the result of previous episodes of the disease) were far commoner in the heart muscles of ' light ' workers than in those of ' heavy ' workers, and that this applied particularly to the most severe type of scarring and to the relatively young age group 45–59 years.

Another factor appears to be related, in some way, to drinking water and Morris, Crawford, and M. J. Gardner have sought to characterize it by investigating the mortality and the water supply in the 61 largest county boroughs in England and Wales. The results show that in middle age and early old age the death rate from all causes, but particularly from cardiovascular disease, fell approximately in inverse proportion to the hardness of the drinking water and the amount of calcium it contained. No evidence could be obtained that the relationship with water hardness reflected some other environmental factor. Chemical studies of trace elements in water from consumers' taps showed none at a concentration that could be considered toxic, whether the water was very soft or very hard. Analysis revealed that the quantities of several other elements present varied with the softness or hardness of the water, but it was not possible to relate mortality rates as closely to any of these as to the quantity of calcium present.

Radiation and cancer

The third greatest rise in mortality, after cancer of the lung and coronary thrombosis, was that due to leukaemia. From 1931 to 1954 the mortality from leukaemia increased nearly threefold and in December 1954 the Council held a conference to discuss the reasons for it. By that time the evidence from Hiroshima and Nagasaki, and from laboratory studies on irradiated animals, had focussed interest on the effect of ionizing radiations, and the working party appointed under the chairmanship of L. J. Witts began its work by organizing an investigation into the role of radiation as a cause of childhood leukaemia.

The investigation was directed by Alice Stewart, of the University Department of Social Medicine, Oxford, and was supported in part by the Council. It was developed to include the study of childhood cancers of all types and copies were obtained of the death entries for all children under 10 years of age who

had died of cancer in England since the beginning of 1953. Information about the past history of the children was sought at interviews with their mothers and similar information was sought, for comparison, from the mothers of living children of the same sex who were born about the same date in the same locality. By 1957, data had been obtained for 1299 pairs of children and one major difference was demonstrated. Of the children who had died from leukaemia or from other forms of malignant disease, 13.7 per cent had been exposed to ionizing radiations *in utero* (when X-ray examinations had been made of their mother's abdomen) compared with only 7.2 per cent of the children who had survived. Similar differences were not found when comparisons were made between the X-ray exposure of the mothers before the children's conception or of the children after birth, or when comparisons were made between previous illnesses in the two groups and the treatment given for them, or between any of the other personal characteristics that were examined. When checks were made on the reliability of the mother's memory of X-ray exposures, no differences were found between the cancer group and the controls, and it was concluded that the X-ray exposure was likely to have been the cause of approximately 7 per cent of all deaths from cancer in young children in the country as a whole.

The importance of this finding lies not only in the clue it provides to a means of preventing cancer in children, but also in the indication that small doses of radiation, of the order of 1–2 rads, may be capable of causing cancer. The foetus may be more susceptible to the induction of cancer than either the child or the adult; but the mechanism of cancer induction is presumably similar at the different stages of life, and if such small doses of radiation can cause cancer in the foetus it is likely that they can also do so after birth, though less frequently.

Ionizing radiations have been present in the environment since life began to appear on earth, but they have assumed a new importance with the development of their use for medical and industrial purposes and with the utilization of atomic energy. The need for knowledge of the effect of small doses became even more urgent when the atmosphere was polluted by fallout from test explosions of atomic weapons and in March 1955 the Council was asked to review the scientific evidence on the medical aspects of nuclear and allied radiations. The committee appointed to do this paid particular attention to the relationship between radiation and leukaemia, and sponsored a nation-wide survey of the incidence of leukaemia among patients treated with X-rays for ankylosing spondylitis (a form of rheumatism) so as to obtain some understanding of the relationship between the dose of radiation and the development of malignant disease.

Evidence that leukaemia might be produced among patients treated with X-rays for ankylosing spondylitis had already been obtained when W. M. Court Brown and J. D. Abbatt, then members of the Council's external staff, found that the mortality from leukaemia among nearly 10 000 patients treated for ankylosing spondylitis was between 5 and 10 times the rate among the general population. A more extensive and more detailed investigation was therefore undertaken by Court Brown and Doll with the temporary assistance of many other members of the Council's staff. More patients were traced and a random sample of approximately 1 in 6 of the patients was selected to provide data that would enable estimates to be made of the number who had been exposed to different amounts of therapeutic radiation. The amount of radiation received by the red marrow of the spine was then estimated by the use of conversion

factors obtained from an investigation on a model carried out by R. E. Ellis of the Middlesex Hospital, D. E. A. Jones of Mount Vernon Hospital, B. M. Wheatley of the Institute of Cancer Research, and J. H. Mulvey of the MRC Radiobiology Unit. The results of this more detailed study showed that the leukaemia mortality among the patients was about 10 times that expected and that the incidence of leukaemia was, with these levels of exposure, approximately proportional to the dose received. From the data it was calculated that the additional risk of developing leukaemia might be approximately 20 per million for each rad of dose received by the red marrow, a figure that agreed closely with an estimate that was made in America by a similar method based on data from survivors of the Hiroshima and Nagasaki explosions. Further observations on a larger group of patients, followed up until the end of 1962, subsequently showed that additional mortality occurred not only from leukaemia, but also from cancer of all parts of the body that had been directly irradiated. The increase in risk, however, was much smaller than for leukaemia and the total risk of mortality from all other cancers added together was estimated to be about the same as the risk of dying from leukaemia. The results of this study therefore, like those of Stewart's, suggested that all amounts of irradiation, no matter how small, might be capable of causing cancer. But even if they were, the size of the risk to which people were exposed from the diagnostic use of X-rays and the still smaller amounts of radiation from other sources was so small that it could not normally be recognized.

Chronic bronchitis

Evidence of the effect of another type of environmental hazard was obtained in 1948, when London experienced its worst fog for many years and there was a sudden rise in total mortality. Four years later, in December 1952, when polluted fog again enveloped London, the increase in the death rate was greater than in any previous episode and 4000 extra deaths were attributed to it. The deaths occurred chiefly among elderly people with bronchitis and it seemed probable that they were due primarily to the effects of pollution by coal smoke and sulphur compounds. Since then many investigations have been carried out, both on the acute effects of atmospheric pollution and, more generally, on the causes of bronchitis.

By relating day-to-day changes in the health of bronchitis patients living in the London area to weather conditions and pollution levels P. J. Lawther and R. E. Waller, of the MRC Air Pollution Unit, were able to established that pollution, rather than bad weather, made the condition of patients more acute. Since the Clean Air Act of 1956 smoke concentrations have fallen to about 15 per cent of the 1958–59 level. Sulphur dioxide concentrations remain about the same, but the fact that the last major ' smog ', in December 1962, caused only one-fifth of the 1952 increase in deaths seems to suggest that smoke rather than sulphur dioxide is the decisive factor in the exacerbation of bronchitis.

These findings appear to be confirmed by a prospective study of the smoking habits and respiratory symptoms of a group of London working men aged 30–59 years, carried out with Council support by C. M. Fletcher. This survey, although still incomplete, has already revealed an improvement in the men's respiratory symptoms irrespective of any change in smoking habits, due apparently to the decline in air pollution.

Further information about the effects of general atmospheric pollution, cigarette smoking and occupational exposure to industrial dusts has been obtained by surveys of populations living under different environmental conditions. Such surveys have provided one of the classical methods of epidemiological investigation and have long been used for the study of infectious diseases and industrial poisoning. Their application to chronic and degenerative disorders, however, has presented many difficulties and it is largely due to the work of A. L. Cochrane and his colleagues of the MRC Epidemiology Unit (South Wales) and the Pneumoconiosis Unit that it has now become possible to use them successfully for this purpose.

One difficulty was that a chronic disease might cause an individual to change his way of life, so that a survey of miners, for example, might fail to show a close relationship between pneumoconiosis and work in a particular pit, because the men who were most severely affected had been forced to change their jobs. In theory, this difficulty can be overcome by examining an entire community rather than the particular members employed, at a given point in time, in a particular industry, and in 1953 Cochrane and his colleagues showed that this method was also a practical possibility. In that year they made a census of the population of the Rhondda Fach and succeeded in obtaining the cooperation, for the purpose of X-ray examination, of 90 per cent of the entire population aged 5 years and over, amounting in all to nearly 25 000 persons. One result of this survey was the demonstration that the electoral roll could be used as an adequate sampling frame if corrected by the collection of personal information, and survey techniques have been developed that use either the results of a personal census or a corrected electoral roll as the basis for the selection of smaller random samples of individuals for detailed examination.

Another difficulty is that more than one observer may have to be employed to examine large populations or to examine different populations speaking different languages in widely separated parts of the world, with the consequent risk of error due to differences in the standards applied. Such differences, both between observers and between the same observer's performance on different occasions, were shown to be much greater than had been anticipated and methods of examination that could be shown to be reproducible and independent of observer bias were therefore developed in pilot studies. Standard methods were laid down for the taking and reading of X-ray films, for example, and a standard questionnaire for recording respiratory symptoms—which has subsequently been used for studies in many countries—was developed by the MRC Pneumoconiosis Unit in cooperation with C. M. Fletcher and D. D. Reid.

With these techniques studies have been made of such diverse conditions as bronchitis, rheumatoid arthritis, raised blood pressure, ischaemic heart disease, anaemia, bacteriuria, glaucoma, cataract, goitre, migraine, cancer of the cervix, psychiatric abnormality and juvenile delinquency, and their prevalence in different communities has been compared with other characteristics of the population or environment. The data obtained have also been used to provide a much clearer picture of the natural history of certain conditions. This approach has demonstrated, for example, the spread in the distribution of blood pressures throughout the population, the progressive rise in blood pressure with age, and the multifactorial character of the relationship between the levels of blood pressure in relatives.

Among the many changes that have taken place in the environment in the last 20 years few have exerted so much effect as the introduction of new drugs and new methods of prophylaxis. To assess their value it has sometimes been necessary to undertake large-scale trials in which many doctors have cooperated and thousands of people have been treated and kept under observation—sometimes for several years. Many trials of this type have been organized by the Council: for example, trials of poliomyelitis and measles vaccines, of BCG vaccine in the prevention of tuberculosis, of streptomycin, isoniazid and other agents in the treatment of tuberculosis, and of cortisone in the treatment of ulcerative colitis and rheumatoid arthritis.

The use of oxygen in premature babies

The control of disease, however, has not always proceeded smoothly and side-effects have been produced that have been recognized only after intensive investigation. Perhaps the most dramatic of these effects was the epidemic of blindness in prematurely born children that was noticed in 1942 by an American ophthalmic surgeon, T. L. Terry. Sporadic cases of retrolental fibroplasia, as the condition was called, had occurred previously, but never in numbers comparable to those that began to appear in clinics for premature babies in the United States and Great Britain, and to a less extent elsewhere in Europe, America, South Africa and Australasia. Many hypotheses were advanced to explain the cause of the disease, including the direct action of light in the premature eye, a lack (or an excess) of vitamins, impurities in food, metabolic disturbances affecting the premature infant, a virus infection, and too much (or too little) oxygen. No substantial evidence, however, was produced in favour of any particular agent, and in 1952 the Council arranged a conference under the chairmanship of Sir Stewart Duke-Elder to organize the collection of data and to conduct investigations into the problem. In the event, two lines of research led to the same conclusion. First, N. H. Ashton and his colleagues at the Institute of Ophthalmology in London carried out a series of experiments in which kittens were exposed soon after birth to atmospheres containing various amounts of oxygen. These experiments showed that lesions, closely resembling the early stages of retrolental fibroplasia, were produced when the oxygen concentration was high (70–80 per cent). Secondly, information was sought on all babies weighing 4 lb (1.8 kg) or less who were admitted to a number of premature baby clinics during a two-year period. The disease was found in 7.7 per cent of the 1095 babies studied, the most immature babies having the highest risk of being affected. The main cause was found to be exposure to oxygen. There were no cases among the 344 babies who had no oxygen, and the proportion of affected babies was related to the length of time for which the oxygen was given. Moreover, nurseries that used little oxygen did not on average show inferior survival rates. The administration of oxygen to premature babies was then drastically curtailed and the epidemic disappeared even more quickly than it arose.

Oral contraceptives

More recently anxiety began to be felt about the possible side-effects of oral contraceptives (which by 1967 were being used by an estimated 12 per cent of all married women under 45 years of age). Soon after their introduction reports

began to come in of conditions liable to cause permanent injury or death among women taking them. These were chiefly jaundice, raised blood pressure, cerebral thrombosis, venous thrombosis and pulmonary embolism, the last two being the most common. In an attempt to decide whether or not these could be attributed to oral contraceptives, complementary investigations (covering consultations with general practitioners, admissions to hospitals and deaths) were undertaken by the Royal College of General Practitioners, with support from the Council, by M. P. Vessey and R. Doll of the MRC Statistical Unit, and by W. H. W. Inman of the Committee on the Safety of Drugs. It was found that the proportion of women suffering from thromboembolic disorders (other than coronary thrombosis) among women using oral contraceptives was about eight times higher than among those not using them. Between the ages of 20 and 34 years the risk of death from pulmonary embolism or cerebral thrombosis among married women that could be attributed to oral contraceptives was estimated to be about 1.3 per 100 000 women using the contraceptives—that is, about a quarter of the risk of dying from a motor accident and about 2 per cent of the risk of death from all causes. There must certainly be some other risks from oral contraceptives, but the total risk is likely to remain small.

Cross-immunity between mycobacteria

With the control of tuberculosis, a further source of mycobacterial infection in Britain was recognized by the work of the MRC Tuberculosis and Statistical Units, which was coordinated by P. M. D'Arcy Hart. The occurrence of these other mycobacterial infections, which are antigenically related to avian tuberculosis, was established in a series of surveys of delayed hypersensitivity reactions to human and avian tuberculins in RAF recruits and other subjects. Moreover, the results of the Council's tuberculosis vaccine trials indicated in 1956, for the first time, that infection with these mycobacteria conferred some natural immunity to subsequent infection with the human tubercle bacillus. Subsequently, it was found that other cross-immunizations between different types of mycobacteria existed, and J. A. Kinnear Brown and I. Sutherland showed in particular that infection with tubercle bacilli conferred some immunity to leprosy in Uganda. The immunological relationships between these mycobacteria will probably help to explain some of the geographical variations in mycobacterial disease throughout the world; moreover, they are of considerable theoretical interest because cross-immunity between infections, whether bacterial or viral, is normally so weak.

NATIONAL SURVEY OF HEALTH AND DEVELOPMENT

In the great majority of the investigations that have been discussed, a clue to the cause of disease had been provided either by a change in the incidence or mortality of a particular disease, or by a change in the environment to which the population of the country had been exposed. In the absence of such clues the use of epidemiological methods is still possible, but it may be much more difficult to frame a fruitful hypothesis. An example of the way epidemiological methods have been applied to identify the factors responsible for a wide range of conditions in the tangled skein of twentieth century life, without starting from known changes in the environment or in disease incidence, is provided by the work of J. W. B. Douglas and the MRC Unit for the Study of Environmental

Factors in Mental and Physical Illness. Douglas's work with the National Survey of Health and Development began in 1946 and has been supported by the Council since 1962. Records were made of more than 5000 children who were born in Britain between 3 March and 9 March 1946, including all the legitimate single births that occurred in middle class and agricultural workers' families and a quarter of the legitimate single births that occurred in other families. All the children have been followed individually and contact has been maintained with about 90 per cent of them. At various times during the 23 years they have been studied information has been obtained about the children's parents, homes, educational progress, behaviour, jobs and health. Much information relating the social and economic circumstances of the families to the occurrence of accidents, infectious diseases and hospital admissions and to the education and social progress of the young people has been published in three books (*Children under Five*, 1958; *The Home and the School*, 1964; *All our Future*, 1968) and more has been published in recent scientific papers.

In one of these studies the pattern of respiratory illness among the children was related to the degree of air pollution in the areas where they lived. The frequency of upper respiratory infections did not vary, but lower respiratory tract infections were two to three times as common in the most polluted area as they were in the least polluted one. Neither sex nor social or economic circumstances affected the difference.

When the frequency of delinquency among boys was related to their family backgrounds it was found to be seven times greater in families in which the father was a manual worker, and both parents had had only elementary schooling and had been brought up in manual working class families, than in those in which the father was not a manual worker and both parents had been to secondary school or had been brought up in middle class families. Divorce or separation of the parents entailed an even greater risk of delinquency.

FUTURE PROSPECTS

In the future, as in the past, one of the main contributions of epidemiology is likely to derive from monitoring changes in the incidence of disease or in the characteristics of the environment. Special opportunities, however, may be expected from the opening up of large areas in Africa, Asia and South America to modern methods of medical research. Much was learnt about the cause of infectious diseases from a study of their geographical limitations and equally important clues may be obtained by studying the characteristics of populations that are still relatively free from the common degenerative diseases of Europe and North America. In particular, such populations may provide important clues to the causes of vascular disease and of many types of cancer.

Another important contribution is likely to arise out of the interaction of epidemiology and genetics. The direction from which advances might come has been indicated by the discovery that individuals who carry one gene for the production of an abnormal type of haemoglobin show an increased resistance to malaria, while those who carry two genes for the same condition develop sickle-cell anaemia. It is now known that several genes are found in two or more variant forms and it seems likely that some of these forms, for example those producing the different ABO blood group antigens, are maintained in the population by unknown advantages for the heterozygote, which compensate for the disadvantages that may occur when both the relevant genes are abnormal.

The fact that duodenal ulcer is now known to occur more commonly among group O people who are genetically incapable of secreting the corresponding antigen into their gastrointestinal juices and that multiple adenoma of the thyroid occurs more commonly in people who are genetically incapable of tasting phenylthiocarbamide does not reduce the need for epidemiological study of these conditions; on the contrary, it helps to define groups of people among whom the effect of an environmental agent may be most clearly discerned.

Advances may also be expected from the improved facilities for the collection of medical data that would follow the introduction of a national system for linking medical and vital records. Proposals for such a system were made by the Council in 1964, following the successful pioneering work of the Oxford Record Linkage Study. In the first instance, the suggested scheme would embrace birth, marriage and death records and selected data of long-term interest from hospital in-patient records. Even such a limited scheme would facilitate the discovery of new relations between diseases and—a point of increasing importance—between the treatment of one disease and the development of another. Among many other advantages, it would greatly facilitate large-scale prospective studies of individuals classified, for example, according to their genetic characteristics or their exposure to occupational hazards.

But perhaps the main advance will come from the more extensive use of the experimental method. This is not easy as it requires the disciplined cooperation of large numbers of people in an experiment, the value of which is of necessity uncertain. The method was used with great success when fluoride was added to the water supplies of three communities and withheld from the supplies of three others. It has been widely used for testing the value of prophylactic inoculations and has been pioneered by Cochrane as a means of testing the significance of what appear to be the early signs of disease. If it had been adopted when cytological examination was first introduced for the detection of carcinoma-in-situ of the uterine cervix, we might now be in less doubt about the value of the service and the interval required between examinations.

Research supported by the Medical Research Council

The following section of the report takes the form of a handbook providing information about the activities of Council establishments and of members of the external scientific staff. In each case the summary of research is preceded by a list of staff employed by the Council and of others who have worked in association with the establishment in question. In addition to members of the Council's scientific staff, these lists include the names of those working in the following categories: Senior Technical Officers; Technical Officers; Chief Technicians II; Technical Research Assistants (Higher); Senior Executive Officers and Higher Executive Officers (including library staff of equivalent grades). Units that were disbanded and staff who left the Council's service before 1 January 1969 are not included in this report.

The lists of the Council's own establishments and external staff are followed by information about other work supported by the Council under various schemes of grants and training awards—namely, block grants to institutions, research groups, short-term research grants, fellowships and scholarships.

National Institute for Medical Research

Mill Hill, London N.W.7

(01–959 3666)

The National Institute for Medical Research, the largest of its kind in the Commonwealth, is the Council's principal research establishment. It was originally set up in 1920 in Hampstead (at the former Mount Vernon Hospital), but in 1950 the main Institute moved into its present building at Mill Hill. Most of the Institute's divisions are housed at Mill Hill but, as indicated below, three divisions and three laboratories are at Hampstead.

The first Director of the Institute was Sir Henry Dale, OM, GBE, FRS. *He was followed in 1942 by Sir Charles Harington,* KBE, FRS, *who retired in 1962 and was succeeded by the present Director.*

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J. H. Humphrey, MD, FRS

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E. J. Toms
C. C. Widnell, PH D
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*Mrs R. V. Pitt-Rivers, PH D, FRS, becomes Head of the Division of Organic Chemistry from April 1969 after Dr Walker's retirement.

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* On leave of absence at Institute of Neurophysiology, University of Oslo.

† On secondment for work in Malaysia.

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† On leave of absence at Massachusetts General Hospital, Boston.

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R. J. Moore, ALA

ADMINISTRATIVE STAFF

J. H. Platts (*Administrative Officer*)
T. J. Jarrett (*Finance Officer*)
Mrs M. E. A. Lang (*NIMR Hampstead Laboratories*)
Miss P. M. Townend (*Director's secretary*)
J. H. Woodcock, BA (*Personnel Officer*)

WORKS AND MAINTENANCE

J. Cree (*Works Superintendent*)
K. R. Watts (*Deputy Works Superintendent*)
J. C. Tyler (*Maintenance Engineer; NIMR Hampstead Laboratories*)

The work of the Institute covers as wide a field as possible in basic non-clinical medical research, and is mostly of a long-term character. In some areas, such as research on virus vaccines, labelled blood proteins and immunosuppressive agents, the work verges on the clinical field, and members of the scientific staff often collaborate in clinical developments arising from their discoveries. Certain major themes, such as climatic physiology, the mechanisms of protein synthesis, the actions of viruses on cells and the nature and control of the immunological response, are constantly under study. Other major themes are largely determined by the particular interests of the senior members of the staff—for example investigations on the growth of leprosy organisms, the transplantation of tissues, the action of pharmacological agents infused into the cavity of the brain and the neurological basis of pattern recognition. Special tasks such as those relating to biological standards and the epidemiology of influenza, which the Council undertakes for the World Health Organization, are interwoven with the normal research activities of appropriate divisions throughout the Institute.

The researches enumerated in the following summary often represent the joint work of members of more than one division; the summary is constructed on a scientific and not on an administrative basis.

ORGANIC CHEMISTRY, BIOCHEMISTRY AND BIOPHYSICS

1. Chemistry of substances of lower molecular weight: (*a*) biosynthesis of thiamine; (*b*) thiazoles derived from cysteine; (*c*) phospholipids, glycolipids and sphingolipids; (*d*) muramic acid and derivatives; (*e*) preparation of radioiodinated oligosaccharide derivatives.
2. Nucleic acids: (*a*) structure of ribosomal RNA and ribosomes; (*b*) purification of messenger RNA; (*c*) mitochondrial nucleic acids.
3. Hormones: effects on nucleic acid, phospholipid and protein turnover; hybridization techniques in study of hormone-induced changes in RNA metabolism.
4. Protein biosynthesis: (*a*) by liver mitochondria; (*b*) of immunoglobulin.
5. Protein structure: (*a*) use of bifunctional ligands; (*b*) thyroglobulin; (*c*) antibodies; (*d*) molecular basis of antigenicity; (*e*) spectroscopic characterization; (*f*) genetically determined haemoglobin variants; (*g*) crystalline viral proteins.
6. Plasma proteins: (*a*) tissue damage and rate of synthesis; (*b*) site of catabolism; (*c*) role of lysosomes and liver subcellular particles in catabolism; (*d*) venom-induced hypofibrinogenaemia.
7. Subcellular organelles: (*a*) ribosomes; (*b*) development of endoplasmic reticulum and function in amphibian metamorphosis.
8. Biochemistry of viruses: (*a*) control of replication by interferon; (*b*) synthesis of Semliki virus proteins in cell-free systems; (*c*) changes in host cell metabolism immediately after infection.
9. Development of special techniques: (*a*) ultracentrifugal analysis; (*b*) acrylamide gel electrophoresis; (*c*) thin-layer chromatography; (*d*) microcountercurrent distribution analysis; (*e*) radioimmunoassay.

MICROBIOLOGY

1. Adenoviruses: (*a*) purification and characterization of viral components; (*b*) biochemistry of infected cells; (*c*) virus neutralization by antibody; (*d*) carcinogenic transformation by adenoviruses.
2. Arboviruses: (*a*) growth in mammalian cells *in vitro;* (*b*) characterization of Group B; (*c*) specificity of antibodies neutralizing Group B.
3. Antibiotics: (*a*) mode of action of antibiotics interfering with biosynthesis of cell walls; (*b*) micrococcin variants; (*c*) action of vancomycin; (*d*) relative assessment of penicillin and derivatives.
4. Bacterial surface structures: control of biosynthesis of cell surface components; structure of cell walls and membranes; relationship of cell wall and membrane formation to cell division and growth; chemistry of muramic acid and derivatives.
5. Genetics: (*a*) genetics of *Ustilago*—recombination, radiation-sensitive and nuclease-deficient mutants; (*b*) cytoplasmic inheritance and ageing in fungi; (*c*) physiology and genetics of coliphage λ; (*d*) transfer of influenza virus antigens by recombination.
6. Influenza: structure of virion; antigenic specificity and functions of viral components; comparative study of human and animal viruses.
7. Interferon: production, mode of action and standardization; effect on cellular metabolism.
8. Mycobacteria: (*a*) *Myco. lepraemurium* and *leprae* in cell cultures; (*b*) human leprosy in experimental animals; (*c*) non-specific immune responses in mycobacterial diseases; (*d*) intracellular defence mechanisms against tubercle bacilli; (*e*) mycobacterial cell walls.
9. Poliovirus: assessment of its neurovirulence and correlation with *in vitro* marker tests.
10. Yeast cell division: nucleic acids in synchronized cultures; satellite DNA; development of mitochondria in cell cycle; nuclear fine structure.
11. Bacteriostatic effects of serum and serum fractions *in vitro*; effect of iron compounds.
12. Detection of oncogenic viruses and tumour-forming cells.

IMMUNOLOGY

1. Mechanism of cell damage by complement.
2. Fate of radioactively labelled antigens and haptens in relation to antibody production, cell-mediated immunity and induction of tolerance.
3. Origin and function of germinal centres; route of entry of lymphocytes.
4. Structure, biosynthesis and sequence analysis of immunoglobulins; role of carbohydrate.

5. Immunological response systems: (*a*) cellular receptors for antigen; (*b*) subcellular mechanisms; (*c*) cell–cell interactions; (*d*) *in vivo* and *in vitro* responses of individual cells: (*e*) physiology of lymphocytes; (*f*) mechanisms of tolerance; (*g*) population dynamics of lymphoid populations.
7. Tissue transplantation: action of antilymphocytic antisera; tolerance of heterografts and role of antibody.
8. Freeze substitution techniques for subcellular localization of antigens and antibodies.

SPECIAL CYTOLOGY

1. Electron microscopy and function of frozen and thawed smooth muscle.
2. Cell markers in study of tumour growth mechanisms.
3. Karyology of human diploid cell strains.
4. Techniques of fluorescence microscopy.

PHYSIOLOGY AND PHARMACOLOGY

1. Neural control of release of vasopressin and oxytocin.
2. Oxytocin: inhibition by analogues; nature of receptor protein.
3. Ionic permeability of skeletal and cardiac muscle.
4. Microinfusion of drugs into brain.
5. Central control of the motor neurones of the spinal accessory nerve.
6. Regulation of body temperature: (*a*) action of monoamines; (*b*) function of hypothalamic neurones.
7. Behaviour of neurones in cerebral cortex when excited by pattern vision.
8. Relation between learning and persistent changes in conductivity of cortical synapses; effects of anaesthetics on conductivity of cortical synapses.
9. Mechanism of action of calcitonin and parathyroid hormone.
10. Physiology of erythropoietin secretion.

HUMAN PHYSIOLOGY AND BIOMECHANICS

1. Thermoregulation: (*a*) physiological responses in controlled hyperthermia; (*b*) mechanisms of heat acclimitization; (*c*) thermal radiation areas; (*d*) thermoregulation in athletes.
2. Environmental studies: (*a*) in Antarctica; (*b*) related to the International Biological Programme.
3. Circadian rhythms in children and in blind subjects.
4. Peripheral circulation: effects of temperature; circulation in skin grafts.
5. Effects of exercise: measurement of cardiac output and oxygen consumption; circulatory and respiratory effects limiting athletic performance.
6. Biomechanics: analysis of movement in work and athletic activity; effects of prolonged inactivity and sitting; effects of impact.
7. Functional anthropometry of industrial populations.

PARASITOLOGY

1. Malaria: (*a*) experimental immunology; (*b*) 24- and 48-hour cycles in blood; (*c*) action of chloroquine on endoerythrocytic parasites; (*d*) resistance to chloroquine; (*e*) cultivation of endoerythrocytic parasites; (*f*) lipid constitution and metabolism of parasites.
2. Trypanosomiasis: (*a*) immunology; (*b*) effect of trypanocidal drugs; (*c*) lipid constitution and metabolism in mammalian and insect forms.
3. Amoebae: taxonomy, ultrastructure and culture of potentially pathogenic small amoebae.
4. Filariasis: (*a*) periodicity; (*b*) control by drugs; (*c*) fine structure; (*d*) immunological reactions.
5. Immunology of helminth infections: (*a*) schistosomiasis—adaptive phenomena and antigenic mimicry, fractionation of antigens, characterization of antibodies; (*b*) *Nippostrongylus*—cellular basis of immunity, characterization of protective antigens and antibodies.

1. Advisory and control work for the Department of Health and Social Security (under the Therapeutic Substances Act) and the British Pharmacopoeia Commission and European Pharmacopoeia.
2. Standards and reference preparations: preparative and assay work for 30 WHO and 20 British national or research standards and reference preparations.
3. Assay and characterization of heparins of various origins; assay, characterization and clinical trials of pituitary hormones.
4. Radioimmunoassay: (*a*) development of techniques and characterization and supply of reagents; (*b*) estimation of erythropoietin and species-specific insulins in mixtures.
5. Control testing: inactivated poliomyelitis vaccine, oral poliomyelitis vaccines, inactivated measles vaccine, live attenuated measles vaccines, influenza vaccines, yellow fever, smallpox, diphtheria, tetanus, pertussis and BCG vaccines; development of new methods for control of rubella vaccine.
6. Methods of assay of combined vaccines; investigations of toxicity of pertussis vaccines
7. Assessment of neurovirulence of poliomyelitis virus and its correlations with *in vitro.* marker tests.
8. Tissue culture: (*a*) provision of national tissue culture service; (*b*) investigation of human diploid cell cultures for preparation of virus vaccines; (*c*) karyology of human diploid cell strains.
9. Under the auspices of WHO, collaborative studies with international control authorities on the potency assay of immunological products.

BIOLOGICAL ENGINEERING AND INSTRUMENTATION

1. Simulation of biosystems using analogue, digital and hybrid computation; programming; on-line computation in laboratory experiments.
2. Design and construction of equipment for measurement, control and automatic processing of data and materials.
3. Specialized techniques and devices, including: (*a*) variable refraction spectacles; (*b*) cryogenic probes for neurosurgery, ENT and ophthalmic surgery; (*c*) breath alcohol analysis; (*d*) molecular models; (*e*) two-phase vibratory pumps; (*f*) portable sensitive man balance.
4. Design and manufacture of miniature and subminiature telemetry equipment.
5. Development and application of new sensing systems for automatic patient-monitoring equipment and very small recording instruments suitable for population studies (SAMI).
6. Fast-access literature retrieval system.

Clinical Research Centre

(To be at Northwick Park, Harrow, Middlesex)

Present address: 164 Tottenham Court Road, London W.1
(01–387 5381)

The Clinical Research Centre, which is now under construction in association with a new district general hospital being built by the North-West Metropolitan Regional Hospital Board at Northwick Park, Harrow, will form the clinical counterpart of the National Institute for Medical Research. While the Centre is being constructed, teams of scientific and supporting staff are already being built up in the form of 'shadow' divisions or sections, some of which have already started their research programmes while temporarily housed elsewhere. A number of other clinicians and scientists have been designated for work at the Centre and will be taking up their appointments in the future. The Council has also decided that a substantial part of the research programme of the Division of Biomedical Engineering of the National Institute for Medical Research should be transferred to the Clinical Research Centre at Northwick Park in 1970. In this report, however, the research programme of this Division continues to appear under the National Institute (p. 103).

Director
Professor G. M. Bull, MD, FRCP

Deputy Director
Richard Doll, OBE, MD, D SC, FRCP, FRS (*until 30 June 1969*)

DIRECTOR'S DIVISION

Senior staff

Clinical Research Centre Laboratories, National Institute for Medical Research, London N.W.7

(01–959 3277)

R. Hoffenberg, MD, PH D, MRCP (*part-time*)
Miss E. G. Black, B SC
E. B. D. Dowdle, MD, MRCP*
Miss J. E. Inwood, B SC

University College Hospital Medical School, London W.C.1

M. Friedman, MD, MRCPE
Miss H. T. Cory, B SC

Whittington Hospital, London N.19

T. Freeman, BM, MC PATH
Miss H. G. M. Clarke, MB, D OBST RCOG (*part-time*)

Royal Free Hospital, Liverpool Road, London N.1

J. S. Garrow, MD, PH D, MRCPE
D. Halliday, PH D*

St Bartholomew's Hospital, London E.C.1

R. W. E. Watts, MD, PH D, FRCP*
Miss D. A. Gibbs
Miss W. J. Westwick, PH D

---

* Designated staff, who have not yet taken up their appointments.

DIVISION OF CELL PATHOLOGY

Clinical Research Centre Laboratories,
National Institute for Medical Research, London N.W.7
(01–959 3277)

Senior staff

A. C. Allison, BM, D PHIL (*Head of Division*)
N. L. Gregory, M SC
A. Griffiths, PH D (*until Jan. 1969*)
F. Grover, FIST
Miss J. J. Harvey, PH D
Miss G. R. Paton, B SC
S. de Petris, DR SCI
Mrs B. Zisman, M SC

DIVISION OF LOW TEMPERATURE BIOLOGY

Clinical Research Centre Laboratories,
National Institute for Medical Research, London N.W.7
(01–959 3277)

Senior staff

Miss A. U. Smith, MD, D SC (*Head of Division*)
B. C. Elford, B SC
J. Farrant, PH D
M. Laurence, MB, FRCS (*part-time*)
D. Lee, PH D
D. E. Pegg, MD
P. Ward

DIVISION OF COMMUNICABLE DISEASES

MRC Common Cold Unit,
Harvard Hospital, Coombe Road, Salisbury, Wilts.
(0722 22485)
and
Clinical Research Centre Laboratories,
National Institute for Medical Research, London N.W.7

*Senior staff**

D. A. J. Tyrrell, MD, FRCP, MC PATH (*Head of Division*)
Sir Christopher Andrewes, MD, FRCP, FRS (*Consultant Adviser*)
Miss J. P. Addey, B SC
A. S. Beare, MB, MC PATH, DTM & H
A. F. Bradburne, B SC
M. L. Bynoe, MB, DTM & H, D OBST RCOG
F. W. Clothier, AIST
R. J. Manchee, B SC
Miss S. E. Reed, MB
D. M. Sharpe, MB (*until Jan. 1969*)
E. J. Stott, PH D
D. Taylor-Robinson, MD, MC PATH

ANIMAL DIVISION

Clinical Research Centre Laboratories,
National Institute for Medical Research, London N.W.7

Senior staff

C. R. Coid, PH D, MRCVS (*Head of Division*)

DIVISION OF ANAESTHESIA AND RECOVERY

Department of Anaesthesia,
Hammersmith Hospital, London W.12
(01–743 2030)

Senior staff

Professor J. F. Nunn, MB, PH D, FFARCS, DA (*Head of Division*)
G. H. Hulands, MB, FFARCS

*Dr Tyrrell works partly in London and partly in Salisbury; the other staff all work in Salisbury.

DIVISION OF COMPUTING AND STATISTICS

172 Tottenham Court Road, London W1P 9LH
(01–387 0201)

Senior staff

M. J. R. Healy, BA (*Head of Division*)
A. J. Fox, B SC*
A. V. Swan, M SC
P. Vitek, B SC, GRAD ENG

DIVISION OF CLINICAL CHEMISTRY

2 Forrest Road, Edinburgh 1
(031–225 3186)

Senior staff

F. L. Mitchell, PH D, FRIC, MC PATH (*Head of Division*)

DIVISION OF BIOENGINEERING

Medical Research Council Laboratories,
Holly Hill, Hampstead, London N.W.3
(01–435 2232)

Senior staff

H. S. Wolff, B SC† (*Head of Division*)
D. C. Pressey, B SC

DIVISION OF IMMUNOLOGY

Senior staff

G. L. Asherson, DM, MRCP, MC PATH†
A. M. Denman, MB, MRCP‡

ELECTRON MICROSCOPY SECTION

Senior staff

R. R. Dourmashkin, BA, MD (*Head of Section*)

RADIOISOTOPE SECTION

Guy's Hospital Medical School,
St Thomas's Street, London S.E.1
(01–407 7600)

Senior staff

N. Veall, B SC, F INST P (*Head of Section*)
J. C. W. Crawley, B SC
J. D. Pearson, B SC
G. Rahmani

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* Working in the Department of Mathematics, Imperial College, London.
† Designated staff, who have not yet taken up their appointments.
‡ On study leave at the Karolinska Institute, Stockholm.

CLINICAL RADIOLOGY SECTION

The Royal Free Hospital, Gray's Inn Road, London W.C.1
(01–837 6411)

and

New End Hospital, London N.W.3
(01–435 7131)

Senior staff

L. Kreel, MB, MRCP, FFR, DMRD (*Head of Section; part-time*)*

Attached workers

M. S. Hirsch, MD (*National Cancer Institute, Maryland*)
W. Ptak, GRAD MED (*National Academy, Krakow*)
F. E. Speizer, MD (*US National Communicable Disease Center*)

LIBRARY

Clinical Research Centre,
164 Tottenham Court Road, London W1P 9LH
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L. C. G. Manwaring, FLA (*Librarian*)

ADMINISTRATIVE OFFICE

Clinical Research Centre,
164 Tottenham Court Road, London W1P 9LH
(01–387 5381)

F. Rushton (*Administrative Officer*)
P. G. Daly (*Personnel Officer*)
J. B. Towell (*Finance and Supplies Officer*)
Mrs L. E. Hill, MD, MRCP, DCH (*Medical Administrative Officer*)

The intention is to bring together in the Clinical Research Centre a variety of clinical and related disciplines that will facilitate a programme of collaborative research. The full extent of the research to be undertaken is not yet decided but the staff appointed or designated have already begun a number of projects that will form the basis of their later research programmes.

DIRECTOR'S DIVISION (MEDICINE)

1. Factors influencing the movement of schistosomes during the various stages of their life cycle.
2. Control of synthesis of foetal haemoglobin.
3. Identification of individual proteins using a technique of crossed immunoelectrophoresis and study of their metabolism by means of iodine trace labels.
4. Effect of steroids on growth in children.
5. Synthesis and catabolism of liver-produced plasma protein; thyroxin turnover studies.
6. Development of external scintillation counting techniques for the measurement of tissue protein turnover in man.

CELL PATHOLOGY

1. Lysosomes in relation to cell damage and carcinogenesis.
2. Role of immunosuppression and of tolerance in oncogenesis.

* Designated staff, who have not yet taken up their appointments.

LOW TEMPERATURE BIOLOGY

1. Effects of cooling and thawing on the survival of various tissues and their intracellular structures, with special reference to the role of protective agents in different concentrations.
2. Construction of programmed apparatus for the automatic control of temperature and concentration of protective agents.
3. Study of conditions required for the formation of glomerular filtrate in the isolated kidney.

COMMUNICABLE DISEASES

1. Propagation and study of viruses and mycoplasmas in organ culture and their clinical effects on human volunteers.
2. Development of techniques of vaccination against influenza and of chemotherapy in virus infections.

LABORATORY ANIMALS

1. Design of cages and supply, breeding and maintenance of experimental animals.
2. Study of viruses in specific pathogen-free colonies and of transplacental transmission of viruses.

ANAESTHESIA

1. Factors affecting respiratory mechanisms and pulmonary blood flow during anaesthesia.
2. Cellular effects of anaesthesia.
3. Evaluation of gas analysis apparatus and other anaesthetic apparatus.

COMPUTING AND STATISTICS

1. Analysis of multivariate data.
2. Statistical computer programs.
3. Statistical problems of clinical chemistry.

CLINICAL CHEMISTRY

1. Steroid metabolism in the foeto-placental unit and in the newborn infant.
2. Application of automation to clinical chemistry.

RADIOISOTOPES

1. Investigation of blood flow using radioisotopes.
2. Miscellaneous clinical applications of radioactive tracers.

Research Units

One of the chief means adopted by the Council for the long-term support of research has been the creation of research units in which its own staff work. Such units may be set up to further research into a new subject not yet appropriate for inclusion in the university framework, or to develop a subject which requires support on a scale beyond the resources of a university or hospital or which has been hitherto neglected. The principal requirement is that there should be a scientist of proven ability to lead a team working within fairly wide terms of reference in a particular field. The majority of the Council's units are situated within or in close proximity to a university or hospital, but they are normally independent of the host institution both in function and in administration.

It has recently been decided to prefix the words 'MRC' (or 'Medical Research Council') to the title of each unit, omitting the word 'Research' before 'Unit'. This change has accordingly been made throughout the present report.

MRC DEPARTMENT OF CLINICAL RESEARCH

University College Medical School,
University Street, London W.C.1
(01–387 5861)

Director

E. E. Pochin, CBE, MD, FRCP*

Senior staff

A. G. Cronquist, FBHI, DIP STA
C. J. Edmonds, MD, B SC, MRCP
D. A. W. Edwards, MD, FRCP†
B. M. Jasani, M SC
Miss J. C. Marriott, B SC
E. N. Rowlands, MD, B SC, FRCP†
B. D. Thompson, PH D

Attached workers

C. F. Barnaby, PH D (*Pugwash, London*)
E. R. Beck, MB, B SC, MRCP (*University College Hospital, London*)
R. C. Godfrey, MB, MRCP (*University College Hospital, London*)
R. J. T. Orton, B SC (*Hertfordshire County Council*)

The clinical work of the Department and its laboratory facilities give opportunities for the detailed study of certain diseases, and for investigating methods of diagnosis and treatment.

Summary of research

1. (*a*) Metabolism of the normal and of the overactive thyroid gland, and particularly of thyroid cancers, studied largely by observations on the metabolism of radioiodine; (*b*) methods of locating and measuring radioactive isotopes in man, including the use of liquid scintillation counters as sensitive and economical detectors of the body content of various radioisotopes.
2. Gastrointestinal tract: (*a*) mechanisms of production of symptoms in dysphagia; (*b*) development of algorithms for diagnosis of dysphagia and incorporation in automated patient interrogation system; (*c*) mechanism of absorption of different substances through the wall of the gut.

* Salary of post partly met by permanent endowment from the Rockefeller Foundation.

† Dr Rowlands is Director of the MRC Gastroenterology Unit at the Central Middlesex Hospital, London (p. 114); Dr Edwards is also a part-time member of this Unit.

MRC GASTROENTEROLOGY UNIT

Central Middlesex Hospital,
Park Royal, London N.W.10
(01–965 5733)

Director

E. N. Rowlands, MD, B SC, FRCP*

Senior staff

D. A. W. Edwards, MD, FRCP*
T. D. Kellock, MD, FRCP (*honorary*)
J. E. Lennard-Jones, MA, MD, FRCP (*part-time*)
J. J. Misiewicz, MB, B SC, MRCPE
R. I. Russell, MB, MRCPE, MRCPG
Mrs M. Shiner, MRCP, DCH (*part-time*)
T. Smith, M SC
Miss S. L. Waller, MB, B SC, MRCP, MRCPE
H. S. Wiggins, PH D

Attached workers

P. Cannon, MB, MRCP (*London Hospital*)
B. S. Drasar, PH D (*Wright-Fleming Institute*)
J. H. Jones, MB, MRCP (*St Mark's Hospital, London*)
P. C. Richardson, MB, MRCP (*London Hospital*)

The Unit is studying the motility of the alimentary tract in health and disease, mechanisms of fat absorption, the bacterial flora of the gut, and the pathogenesis and treatment of certain gastrointestinal disorders.

Summary of research

1. Pathogenesis of pharyngo–oesophageal diseases and hiatus hernia.
2. Development of algorithm with automated interrogation system for computer-assisted diagnosis of dysphagia and chest pain.
3. Effects of drugs and hormones on gastrointestinal pressures and transit in health and disease.
4. *In vitro* pharmacological studies on strips of muscle removed at operation.
5. Investigation of malabsorption by biochemical, bacteriological and electron microscope techniques and by the study of motility.
6. Therapeutic trials in peptic ulcer, and inflammatory disorders of the intestine.
7. Pathogenesis and management of Crohn's disease and colitis.
8. Measurements of low levels of radioactivity in man by whole-body counting.

MRC CLINICAL ENDOCRINOLOGY UNIT

2 Forrest Road, Edinburgh 1
(031–225 3186)

Director

John A. Loraine, MB, D SC, FRCPE

Senior staff

H. K. Amin, MB, FRCSE
H. A. F. Blair, AIST
Mrs J. M. Cooper, M SC
G. Court, PH D
G. P. Crean, MB, PH D, FRCPE (*part-time*)
D. W. Davidson
Mrs M. M. Evans, B SC
P. C. Ganguli, MB, MRCPE
W. M. Hunter, PH D
W. J. Irvine, MB, B SC, FRCPE (*part-time*)
A. A. A. Ismail, PH D
Miss A. B. Jurewicz, B SC
J. R. Kalden, DR MED
R. W. Kelly, PH D
K. E. Kirkham, PH D
D. N. Love
S. F. Lunn, FIAT
Miss M. A. Mackay, FATA, AIST
Mrs R. M. Monaghan, M SC (*part-time*)
A. D. Papanicolaou, DR MED
J. Robinson, B SC
R. D. E. Rumsey, M SC
Mrs P. M. Stevenson, PH D

* Dr Rowlands and Dr Edwards work also in the MRC Department of Clinical Research (see p. 113).

Attached workers

D. Adamopoulos, MD (*University of Athens*)
Mrs M. Chan, MB, MRCP (*University of Hong Kong*)
J. R. Kalden, DR MED (*University of Tübingen*)
M. Y. Sukkar, MB (*University of Edinburgh*)
Miss M. Willmott, MS, DGO (*University of Edinburgh*)

The main research interests of the Unit are the development of assay methods for the quantitative determination of hormones and their metabolites in body fluids, the application of such methods to clinical problems, investigations on the mechanism of action of hormones, and studies in clinical and experimental gastroenterology and in autoimmunity.

Summary of research

1. Steroidogenesis and energy relationships in the ovary (with Dr G. S. Boyd, University of Edinburgh); gonadotrophin-induced ovulation in the rat; lipotrophic activity of pituitary glycoproteins.
2. Developmental work on radioimmunoassays for follicle-stimulating hormone (FSH), luteinizing hormone (LH), insulin, gastrin, and glucagon; application of radioimmunoassays for human growth hormone (HGH) and insulin to clinical problems, including dwarfism, acromegaly and diabetes mellitus; clinical application of radioimmunoassay for ACTH (with Professor J. Landon and Dr G. M. Besser, St Bartholomew's Hospital, London, and Dr D. R. Cullen, Royal Infirmary, Edinburgh).
3. Measurement of thyroid-stimulating hormone (TSH) and the long-acting thyroid stimulator (LATS); assessment of various thyroid function tests in normal subjects and in pathological conditions (with Dr J. Milne, Royal Victoria Hospital, Edinburgh, and Dr R. Hall, Royal Victoria Infirmary, Newcastle upon Tyne).
4. Isolation, identification and chemical synthesis of unknown steroid-like compounds associated with intrauterine life and infancy, and investigation of the metabolism and mechanism of action of these and related substances.
5. Use of new techniques for investigation of steroid profiles at various stages of human life and in pathological conditions; establishment of new assay method for testosterone and related C-19 steroids; development of full automation for steroid assays (with Atomic Weapons Research Establishment, Aldermaston).
6. Endocrinology of puberty in girls, of the menopause and of patients with an abnormal sex chromosome constitution, hirsutism, premenstrual tension, impotence and homosexuality (with Professor J. O. Forfar, Department of Child Life and Health, University of Edinburgh, Dr G. A. Dove, London, and Drs J. A. Cooper and C. Smith, University of Edinburgh).
7. Assay of FSH, LH and urinary steroids in patients receiving treatment with various types of oral contraceptives and with clomiphene in an attempt to elucidate the site and mode of action of these compounds (with Professor D. Charles, Boston University School of Medicine, USA, Dr G. L. Foss, Bristol Royal Hospital, Dr M. C. N. Jackson, Exeter, and Dr A. B. Loudon, Family Planning Centre, Edinburgh).
8. Experimental and clinical gastroenterology: (*a*) factors regulating growth of the gastric and intestinal mucosa in rats; (*b*) physiology of gastric secretion in rats; (*c*) bioassay of gastrin; (*d*) endocrine function in patients with gastrointestinal diseases.
9. Autoimmunity in relation to abnormalities of the adrenal, ovary, thyroid, stomach and parathyroid; incidence of organ-specific autoimmunity in diabetes mellitus; production of myasthenia gravis in experimental animals by immunological techniques; autoimmunity in NZB mice.

MRC RHEUMATISM UNIT

Canadian Red Cross Memorial Hospital,
Taplow, Maidenhead, Berks.
(06–286 4411)

Director
Professor E. G. L. Bywaters, MB, FRCP

Deputy Director
L. E. Glynn, MD, B SC, FRCP, FC PATH

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Senior staff

Miss B. M. Ansell, MB, FRCP (*part-time*)
J. C. Brown, MB, MRCP
Mrs P. C. Brown, MD
R. Consden, PH D, FRIC
Mrs E. J. Denman, MB*
J. Dorling, FIMLT
E. J. Holborow, MD, MC PATH
A. Howard, B SC†
G. D. Johnson, FIMLT
Mrs E. W. Kasp-Grochowska, PH D
G. Loewi, DM, MC PATH
J. N. McCormick, MB
J. E. Scott, D SC
Miss A. S. Temple, HNC
D. P. Page Thomas, MB, MC PATH

Attached workers

B. M. Greenwood, MB, MRCP (*Wellcome Research Fellow*)
Mrs E. M. Herrick, MB (*Wellcome Research Fellow*)
D. Kingston, MA (*MRC External Staff*)
I. C. M. MacLennan, MB, B SC (*Arthritis and Rheumatism Council grant-holder*)
D. A. Rajapakse, MB, MRCP (*Arthritis and Rheumatism Council grant-holder*)
J. H. Schwab, PH D (*University of North Carolina*)
B. T. Thomas, MD (*University of Athens*)
M. Ünlü, MD (*Gulhane Medical-Military Academy, Turkey*)

The Unit is carrying out clinical and laboratory investigations on the nature, course and treatment of rheumatic diseases; these involve studies of both normal and abnormal connective tissue, with special emphasis on autoimmune reactions.

Summary of research

1. Changes in connective tissue with age and disease.
2. Use of immunofluorescence methods to detect autoantibodies in human and animal sera, to investigate the distribution in the tissues of native and foreign antigens and of antibody and to study immune responses at a cellular level.
3. Experimental study of autoantibodies and autoimmune disease.
4. Nature of immune responses to polysaccharide-containing antigens.
5. Family study of rheumatic fever, systemic lupus erythematosus and Still's disease, with reference to genetic constitution.
6. Long-term surveys of the course of rheumatic fever and rheumatoid arthritis in children.
7. Effects of prophylaxis in the prevention of rheumatic fever recurrences.
8. Controlled therapeutic trials in various connective tissue diseases.

MRC IMMUNOCHEMISTRY UNIT

University Department of Biochemistry,
South Parks Road, Oxford
(0092 59214)

Honorary Director

Professor R. R. Porter, PH D, FRS

Scientific staff

G. W. J. Fleet, BA
Miss E. M. Press, B SC
G. T. Stevenson, MD, D PHIL
J. M. Wilkinson, PH D

Attached workers

H. N. Eisen, MD (*Washington University School of Medicine*)
B. Frangione, MD (*New York University School of Medicine*)
M. A. Fried, PH D (*Wellcome Research Fellow*)
Mrs R. G. Fruchter, PH D (*Wellcome Research Fellow*)
Miss N. M. Hogg, M SC (*Commonwealth Scholar*)
S. V. Hunt, BA (*MRC Scholar*)
N. E. Hyslop, MD (*Harvard Medical School*)
M. E. Lamm, MD (*New York University School of Medicine*)
L. Mole, B SC (*MRC Scholar*)
I. J. O'Donnell, B SC (*CSIRO Division of Protein Chemistry, Australia*)
W. Palm, PH D (*British Council Scholar*)

* On leave of absence from February 1969 at the Karolinska Institute, Stockholm.

† Seconded to the Department of Experimental Pathology, University of Birmingham, until May 1969.

The research programme of this Unit is concerned with the structural basis of the specific affinity of antibodies.

Summary of research

1. Comparative amino acid sequences of the heavy chain of pathological human IgG.
2. Amino acid sequences of the Fd fragment of normal rabbit IgG and rabbit antibody.
3. Fractionation of lymphoid cells.

MRC REPRODUCTION AND GROWTH UNIT

Princess Mary Maternity Hospital, Newcastle upon Tyne NE2 3BD

(0632 814352)

Director

Professor A. M. Thomson, MB, B SC, FRCOG, DPH

Honorary Consultant in Obstetrics

Professor J. K. Russell, MD, FRCOG

Senior staff

W. Z. Billewicz, M SC
Miss A. E. Black, B SC (NUTRITION)
G. A. Cheyne, FIMLT
Mrs H. M. Fellows, MB (*part-time*)
Miss R. M. Holliday
Mrs C. A. Hytten, MB (*part-time*)
F. E. Hytten, MD, PH D
T. Lind, MB, MRCOG

Attached workers

G. H. Rannie, BA (*University of Newcastle upon Tyne*)
E. G. Robertson, MB, MRCOG (*University of Newcastle upon Tyne*)

The Unit undertakes research on human reproduction and on the development of children, in collaboration with the Departments of Obstetrics and Gynaecology and of Child Health, University of Newcastle upon Tyne.

Summary of research

1. Growth, health and immunoglobulin levels of children in Africa (with the Council's Laboratories in the Gambia).
2. Physical growth and development of pre-school children in Newcastle upon Tyne.
3. Measurement and natural history of oedema during pregnancy, and related aspects of body fluid compartments and blood composition.
4. Measurement of total body fat with ^{85}Kr.
5. Changes in renal function during pregnancy, with particular reference to the excretion of nutrients.
6. Volume and composition of liquor amnii.

MRC MINERAL METABOLISM UNIT

The General Infirmary, Great George Street, Leeds 1

(0532 32799)

Director

B. E. C. Nordin, MD, PH D, FRCP

Assistant Director

A. Hodgkinson, D SC, FRIC

Senior staff

L. Bulusu, MA, FSS
T. H. Campion, PH D
M. Cochran, MB
A. Horsman, BA
C. F. Knowles, FIMLT
M. Peacock, MB, MRCP
W. G. Robertson, B SC
C. J. Schorah, PH D
R. Wilkinson, B SC
Miss M. M. Young, MB
Mrs J. M. Zanelli, B SC
P. M. Zarembski, PH D, FIMLT

Attached workers

P. Clark, FRCS (*University of Leeds*)
F. G. E. Pautard, PH D (*University of Leeds*)
P. Smith, FRCS (*University of Leeds*)

The Unit is studying various aspects of mineral metabolism, with particular reference to calcium, strontium, magnesium, and certain trace elements. Its clinical work centres on renal stone disease and osteoporosis.

Summary of research

1. Ionic products of calcium phosphate and calcium oxalate in urine of normal subjects and patients with renal calculus.
2. Experimental production of renal calculi in animals.
3. Crystal formation and aggregates in urine.
4. Quantitative bone radiology, including spine densitometry.
5. Effects of hormones and other agents on bone metabolism in tissue culture.
6. Calcium absorption studied by isotopic and balance techniques.
7. Determination of ultrafiltrable and ionic calcium in plasma.
8. Determination of tubular reabsorption of calcium in animals and man.
9. Bone ageing studied by bone density fractionation.
10. Metabolism of oxalic acid in relation to renal calculi.
11. Acid-base balance, with particular reference to renal tubular acidifying power.

MRC DEMYELINATING DISEASES UNIT

Newcastle General Hospital, Westgate Road,
Newcastle upon Tyne NE4 6BE
(0632 35251)

Honorary Director

Professor E. J. Field, MD, MS, PH D, FRCP

Honorary Clinical Adviser

Professor Henry Miller, MD, FRCP, DPM

Senior staff

D. H. Adams, D SC, FRIC
E. A. Caspary, M SC
D. Hughes, B SC
A. Peat, B SC

Attached worker

M. Saunders, MB, MRCP, MRCPE (*Wellcome Research Fellow*)

The Unit is concerned with aetiological factors in multiple sclerosis. The biology of glial cells is an important subject of study.

Summary of research

1. Electron microscope study of multiple sclerosis, kuru and scrapie.
2. Protein synthesis in the nervous system, with special reference to the developing brain and myelin.
3. Pathogenicity for animals (especially sheep, goats and mice) of material from cases of multiple sclerosis.
4. Cellular immunity in multiple sclerosis and experimental encephalomyelitis.

MRC UNIT ON THE EXPERIMENTAL PATHOLOGY OF SKIN

The Medical School, University, Birmingham 15
(021–472 2103 and 1301)

Director
C. N. D. Cruickshank, MD, MRCP, MC PATH, DIH

Senior staff

J. R. Cooper, FIMLT
M. A. Cowan, MD, MRCP (*honorary*)
A. E. Fairburn, MD, MRCP (*honorary*)
A. R. H. Hastie, MB, D CH
Mrs E. A. Hell, D PHIL
C. Hodgson, MD, MRCP (*part-time*)
C. C. Lim, MB, MRCP
V. J. W. Long, PH D
Mrs P. R. Mann, M SC
R. Summerly, MB, MRCP
M. D. Trotter, PH D
H. J. Yardley, PH D

Attached workers

A. J. Brockas, B SC (*MRC Scholar*)
M. A. Cooke, MB (*Skin Hospital, Birmingham*)
B. V. M. Corps, MB, FRCS (*Birmingham Regional Plastic Surgery Unit*)
M. T. Withnall, B SC (*MRC Scholar*)

The aim of the Unit is to achieve a better understanding of the structure and functions of the skin in health and disease. Considerable emphasis has been placed on the study of metabolic processes *in vitro* and on a study of allergy.

Summary of research

1. Metabolism of lipids in skin under varying conditions.
2. Sulphated mucopolysaccharides in skin.
3. Factors associated with the initiation of DNA synthesis in normal and psoriatic skin.
4. Biology of allergic skin reactions.
5. Dermatophytes, particularly their allergenic glycopeptides.
6. Clinical investigation of selected patients.

MRC BODY TEMPERATURE UNIT

Department of the Regius Professor of Medicine, Radcliffe Infirmary, Oxford
(0092 49891)

Honorary Director
Professor Sir George Pickering, MD, FRCP, FRS

Assistant Director
K. E. Cooper, MA, MB, M SC

Senior staff
J. Stein, BM, B SC

Attached workers

A. J. Honour, D PHIL (*University of Oxford*)
P. J. Teddy, B SC (*MRC Scholar*)

The Unit is concerned with body temperature regulation, in both man and animals. It is studying patients with neurological lesions affecting one or more components of the temperature-regulating mechanisms. The mechanisms whereby pyrogens are produced from leucocytes and their mode of action in the hypothalamus are being studied.

Summary of research

1. Action of endogenous pyrogens within the hypothalamus.
2. Mode of action of antipyretics.
3. Studies of patients with abnormalities of temperature regulation.

MRC EXPERIMENTAL HAEMATOLOGY UNIT

St Mary's Hospital Medical School, London W.2

(01–723 1252)

Director

Professor P. L. Mollison, MD, FRCP, FC PATH, FRS (*part-time*)

Senior staff

I. Chanarin, MD, B SC, MC PATH (*honorary*)
Miss P. E. Crome, MB, MC PATH (*honorary*)
N. C. Hughes-Jones, DM, PH D
R. S. Lane, MB*
Miss J. T. Perry, B SC
M. S. Rose, MB

The Unit's aim is to link experimental and clinical studies in the field of haematology. The Unit is recognized as a World Health Organization Reference Centre for the Use of Immunoglobulin Anti-D for the Prevention of Rh Sensitization.

Summary of research

1. Suppression of primary immunization to red cell antigens by passively administered antibodies.
2. Detection of very low concentrations of red cell antibodies *in vitro* and *in vivo*.
3. Equilibrium constant and concentration of anti-Rh in immunized volunteers.
4. Folate and vitamin B_{12} interrelationship in man.
5. Effects of antibodies in pernicious anaemia.
6. Typing of lymphocytes with oligospecific antisera.

MRC BLOOD GROUP UNIT

Lister Institute of Preventive Medicine,

Chelsea Bridge Road, London S.W.1

(01–730 4042)

Director

R. R. Race, PH D, FRCP, FRS

Senior staff

Mrs C. A. Gooch, B SC
Miss E. J. Gavin, B SC
Miss R. A. Sanger, PH D
Miss P. A. Tippett, PH D

The Unit is searching for unrecognized blood group antigens and studying the inheritance of those already known. All the investigations listed below have been carried out in collaboration with numerous colleagues in this country and abroad.

Summary of reasearch

1. The X-linked blood group system Xg; use of Xg in investigation of abnormalities of form or number of the sex chromosomes and in the mapping of genes on the X chromosome.
2. Blood groups and abnormalities of the autosomes.
3. Blood groups and problems of twinning, chimerism, mosaicism and dispermy.
4. Background of the Rh and MNSs systems.
5. The antigens Ul^a and En^a.

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* On leave of absence, working in the University of Washington.

MRC BLOOD GROUP REFERENCE LABORATORY

(Administered by the Council for the Department of Health and Social Security)

Gatliff Road, off Ebury Bridge Road, London S.W.1

(01–730 2152)

Director

K. L. G. Goldsmith, MB, PH D, MC PATH

Senior staff

J. B. Dawes, B SC
Miss C. M. Giles, PH D
Miss E. W. Ikin, PH D
Mrs T. T. B. Phillips, MB

The Laboratory is responsible for large-scale processing of blood grouping serum of human origin and for issuing it to the National Blood Transfusion Service, the Defence Services and hospitals in the United Kingdom and overseas, and for the production of animal sera both for routine issue and for experimental purposes. The Laboratory is also the International Blood Group Reference Laboratory of the World Health Organization. Technical and clinical advice and instruction are given to visiting workers, and general assistance over a wide field is given to a large number of laboratories, transfusion centres and research institutes.

Summary of activities

1. Large-scale production and issue of blood grouping reagents of human, animal and plant origin, and preparation of International Standards.
2. Production of immunofluorescent anti-human-globulin serum.
3. Provision of reference facilities, including red cell grouping of laboratory and hospital staffs for control purposes and the investigation of human and animal sera submitted by laboratories for checking prior to their use as grouping sera.
4. Full red cell grouping of donors of the National Panel of Donors of Rare Blood Types and of the International Panel of Donors of Rare Blood Types (records of both panels are maintained and revised Panel lists are issued).
5. Investigation of ' new ' blood group antigens and antibodies.

MRC ABNORMAL HAEMOGLOBIN UNIT

University Department of Biochemistry,

Tennis Court Road, Cambridge

(0223 63240 and 51781)

Honorary Director

Professor H. Lehmann, MD, SC D, FRCP, FRIC, FC PATH

Senior staff

P. J. Gaffney, PH D
Miss J. Goldstein, M SC
P. A. Lorkin, BA

Attached workers

Mrs D. Charlesworth, PH D (*Addenbrooke's Hospital, Cambridge*)
Mrs S. Ducastaing (*University of Bordeaux*)
E. Gallo, MD (*University of Turin*)
K. Murawski, MD (*University of Warsaw*)

This Unit investigates the chemical nature of abnormal haemoglobins and variants of serum proteins and enzymes, which are collected from all parts of the world. The Unit is recognized as a World Health Organization Reference Centre for Abnormal Haemoglobins.

Summary of research

1. Identification of new abnormal haemoglobin variants in man; partial investigation of other abnormal haemoglobins in man and animals.
2. Investigation of human pseudocholinesterase variants and of animal cholinesterases.
3. Surveys of haemoglobin variants and other inherited characters in samples collected from populations in various parts of the world.
4. Reference work on abnormal haemoglobins and pseudocholinesterases for laboratories in the United Kingdom and overseas.

MRC BLOOD PRESSURE UNIT

Western Infirmary, Glasgow W1
(041–339 8822)

Director

A. F. Lever, MB, B SC, FRCP

Scientific staff

C. J. W. Brooks, PH D, DIC (*honorarium*)
J. J. Brown, MB, B SC, MRCP
R. H. Chinn, MB
Miss G. Düsterdieck, DR CHEM
R. Fraser, PH D
R. I. Gleadle, MB, MRCP
W. D. Mitchell, PH D
J. I. S. Robertson, MB, B SC, MRCP
M. Tree, B SC
R. J. Wier, MB, MRCPG
Miss J. Young

This Unit is concerned with the clinical and biochemical aspects of renin, angiotensin and the adrenal steroids, particularly in relation to their role in controlling blood pressure and sodium balance.

Summary of research

1. Factors controlling the release of renin from the kidney and of aldosterone from the adrenal cortex.
2. Clinical studies of aldosterone, renin and sodium in heart failure, renal disease, adrenal cortical disease (particularly Conn's syndrome) and hypertension.

MRC CARDIOVASCULAR UNIT

Royal Postgraduate Medical School of London,
Ducane Road, London W.12
(01–743 2030)

Director

Professor J. P. Shillingford, MD, FRCP (*part-time*)

Scientific staff

I. T. Gabe, MD, MRCP
C. J. Mills, B SC
L. H. Opie, DM, D PHIL, MRCP
M. Thomas, MD, MRCP
R. C. Young, PH D

Attached workers

A. A. Gabor, MD (*Hungarian Ambulance Service*)
D. K. Gupta, MD, MRCP (*All-India Institute of Medical Sciences*)
P. J. B. Hubner, MB, MRCP (*MRC Junior Research Fellow*)
D. E. Jewitt, MB, B SC, MRCP (*Hammersmith Hospital*)
V. Jurkovič, MD
B. J. Maurer, MB (*Hammersmith Hospital*)
G. Noseda, MD (*University of Zurich*)
R. Samson, MB (*University of Cape Town*)
P. Toutouzas, MD (*University of Athens*)

The Unit is concerned with the study of the circulation in health and disease, with special emphasis on coronary heart disease and its early diagnosis. The clinical investigations are augmented by basic laboratory studies, including research into the biophysics of the circulation.

Summary of research

1. Circulatory, respiratory, renal and biochemical changes taking place in patients with acute myocardial infarction.
2. Methods for improving treatment in acute myocardial infarction.
3. Development and use of electromagnetic flowmeter for the study of the circulation in disease.
4. Study of the circulation by indicator substances, including radioisotopes.

MRC TUBERCULOSIS AND CHEST DISEASES UNIT

Brompton Hospital, Fulham Road, London S.W.3
(01–352 1043)

Director
Wallace Fox, MD, FRCP

Scientific staff

G. C. Ferguson, MB, MRCP
G. C. Gould, MB†
Miss J. F. Heffernan, MB, DPH
A. B. Miller, MB, MRCP
D. N. Mitchell, MD
A. J. Nunn, M SC
H. Stott, MD, MRCP, DPH, DTM & H, DIH
Miss R. Tall, B SC

Attached workers

J. R. Mikhail, MRCS
J. E. Stark, MD, MRCP

The chemotherapy of tuberculosis and other chest diseases and associated problems are being studied by the Unit, the work being increasingly orientated to the community rather than the individual. The Unit cooperates closely with the MRC Unit on Drug Sensitivity in Tuberculosis and with the Statistical Unit.

Summary of research

1. Chemotherapy of tuberculosis in Britain, in East Africa (with the East Africa Tuberculosis Investigation Centre), in South India (with WHO, the Indian Council of Medical Research and the Madras State Government, at the Tuberculosis Chemotherapy Centre, Madras), in Hong Kong (under an agreement with the Hong Kong Government), in Singapore (with the Government Tuberculosis Service) and in Czechoslovakia (with WHO and the Tuberculosis Services of the Central Bohemian Region and Prague).
2. Prevalence of drug resistance in newly diagnosed cases in Tanzania (with the East Africa Tuberculosis Investigation Centre).
3. One-year evaluation of the routine results of chemotherapy in newly diagnosed cases in Kenya (with the East Africa Tuberculosis Investigation Centre).
4. Protection afforded by BCG and vole bacillus vaccines in adolescence and early adult life in Britain.
5. Comparison of methods of treatment of tuberculosis of the spine (investigations initiated through the Orthopaedic Tuberculosis Subcommittee of the Council's Committee for Research on Tuberculosis in the Tropics).
6. Investigation of isoniazid as a possibly carcinogenic agent.
7. Treatment of carcinoma of the bronchus with two cytotoxic agents.
8. Therapy of asthma (with the consultant staff of the Brompton Hospital).
9. Aetiology and prevalence of sarcoidosis in young adults; mechanism of the Kveim test; standardization of Kveim test material; immunological aspects; investigation of animal experimental models.
10. Methodology of controlled clinical trials.

† Working in Nairobi.

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MRC UNIT ON DRUG SENSITIVITY IN TUBERCULOSIS

Royal Postgraduate Medical School, Ducane Road, London W.12

(01–743 2030)

Honorary Director

Professor D. A. Mitchison, MB, MRCP, MC PATH

Senior staff

J. K. Clancey, FIMLT*
Mrs A. Csillag-Szekely, D PHIL
Miss J. M. Dickinson, LRCP & SI
E. A. Edwards, AIMLT*
G. A. Ellard, PH D
Miss P. T. Gammon, B SC
P. S. Jackett, B SC
A. B. Keyes, AIMLT*
M. J. Lefford, MB

The Unit studies the bacteriological aspect of mycobacterial infections in man. Particular attention is given to bacteriological methods in the chemotherapy and epidemiology of tuberculosis. The Unit works in close association with the MRC Tuberculosis and Chest Diseases Unit.

Summary of research

1. Provision of centralized bacteriological services for studies of primary regimens of chemotherapy for tuberculosis in Britain and of different policies of chemotherapy and sensitivity testing in Hong Kong.
2. *In vitro* and animal experiments on intermittent chemotherapy in tuberculosis.
3. Improvements in diagnostic and sensitivity test methods.
4. Immunity in tuberculosis and related infections.
5. Pharmacology of antimycobacterial drugs.
6. Life cycle of mycobacteria.

DUNN NUTRITIONAL LABORATORY

Milton Road, Cambridge CB4 1XJ

(0223 63356)

Director

E. H. Kodicek, MD, PH D

Senior staff

D. R. Ashby
D. C. Barker, PH D
M. J. Barnes, PH D
C. J. Bates, D PHIL
P. A. Bell, PH D
B. J. Constable
K. C. Day
D. R. Fraser, PH D
D. E. M. Lawson, PH D
C. I. Levene, MD, MC PATH
J. B. Mason, BA
B. Pelc, ING CHEM, C SC
I. M. Sharman, PH D, FRIC
Mrs K. J. I. Thorne, PH D
P. W. Wilson

Attached workers

Miss E. M. Cruickshank, PH D (*University of Aberdeen*)
H. G. Martin, B SC (*MRC Scholar*)
E. Morava, MD (*Institute of Nutrition, Budapest*)
Miss A. M. Shaw, PH D (*Ames Research Center, California*)
Miss C. Short, B SC (*MRC Award for Further Education in the Medical Sciences*)

* Working on the East African Tuberculosis Chemotherapy Trials (Mr Clancey in Uganda, Mr Edwards in Kenya and Mr Keyes in Tanzania).

INFANT NUTRITION RESEARCH DIVISION

Senior staff

Miss E. M. Widdowson, D SC (*Head of Division*)
P. H. Adams, MB, MRCP
G. C. Kennedy, MB, PH D
K. G. McCullagh, B V SC, MRCVS
D. A. T. Southgate, PH D
R. A. Spires, FIST

Attached workers

Miss R. Schemmel, MS, PH D (*Michigan State University*)
Miss L. H. Stone, B SC (*University of Nottingham*)

The Unit is engaged in research on vitamins and other nutrients, including elucidation of the biochemical and physiological processes underlying their mode of action and of the effects of deficiency and the development of methods for their estimation in tissues. The Infant Nutrition Research Division studies the regulation of growth and development, the physiology of the newborn and the effects of protein and calorie deficiency.

Summary of research

1. Vitamin C studies in relation to (*a*) collagen and mucopolysaccharides, with particular reference to their formation in tissue culture and nutritional requirements of fibroblasts; (*b*) hydroxylation mechanisms in collagen and elastin biosynthesis; (*c*) ultrastructural changes associated with connective tissue, and the biosynthesis of collagen and elastin.
2. Niacytin (the bound nicotinic acid in cereals): elucidation of chemical structure and biochemical pathways.
3. Distribution, mode of action, metabolism and estimation of tritiated and ^{14}C-labelled vitamin D and metabolites: (*a*) in animal tissues, particularly intestines; (*b*) effect on nucleic acid metabolism and protein synthesis; (*c*) electron microscope autoradiography of labelled vitamin D; (*d*) gas–liquid chromatography of vitamin D.
4. Nutritional status of the elderly with respect to riboflavin.
5. Vitamin A and vitamin E: (*a*) mode of action, particularly at the subcellular level; (*b*) effects of deficiency; (*c*) blood levels in human subjects.
6. Structure and function of bacterial mesosomes and membranes in relation to bactoprenol.
7. Ultrastructure of chromosomes; (*b*) electron X-ray and optical diffraction of crystalline ribosomes.

INFANT NUTRITION RESEARCH

1. Physiology and biochemistry of development of the mammal, *in utero* and in the neonatal period, with special reference to fat and mineral metabolism.
2. Growth and development of pigs after experimental resection of the intestine.
3. Effects of environmental temperature on metabolism of man.
4. Effects of deficiencies of calories and protein in man and animals.
5. Hypothalamic regulation of water and energy expenditure.
6. Nutrition and pathology of the African elephant.

MRC CHILD NUTRITION UNIT

Mulago Hospital, P.O. Box 7051, Kampala, Uganda
(Telegrams: Medresco, Kampala, Uganda)

Director

R. G. Whitehead, PH D

Honorary Clinical Consultant

J. P. Stanfield, MD, MRCP, DCH

Senior staff

J. G. Ablett, MB
Mrs D. G. Coward, PH D
W. A. Coward, PH D
R. S. Crowne, AIST
R. F. Grimble, PH D
J. M. Parkin, MB, MRCP
Miss E. M. E. Poskitt, MB, MRCP
Miss I. H. E. Rutishauser, B SC(NUTRITION)
M. B. Sawyer

Attached workers

Miss S. Cookson, B SC (*MRC Scholar*)
T. T. S. Hall, MBE, MD, D OBST RCOG (*MRC grant-holder*)

The Unit studies the development of young children who are growing up under rural conditions and are being fed the traditional low-protein diets of Uganda. Some of these children are studied in the Unit's own ward and others in various outpatient clinics.

Summary of research

1. Progressive effects of chronic protein malnutrition on tissue structure and metabolic function in young children and experimental monkeys.
2. Development of biochemical tests for assessment of nutritional status in young children who are living on a diet believed to be inadequate.
3. Effects of malnutrition in early childhood on the maturation and function of the brain in later years.
4. Objective assessment of the long-term effectiveness of various nutrition and education programmes in a rural community.
5. Evaluation of immunization schedules appropriate to developing countries.

TROPICAL METABOLISM RESEARCH UNIT

University of the West Indies, Mona, Kingston 7, Jamaica

(Telegrams: Tropmetres, Kingston, Jamaica)

Director

Professor J. C. Waterlow, MD, SC D, FRCP

Senior staff

G. A. O. Alleyne, MD, MRCP
Miss A. Ashworth, PH D
P. J. Garlick, BA
D. J. Millward, B SC
R. D. G. Milner, MB, PH D, MRCP
D. I. M. Picou, MB, PH D
Mrs H. A. S. Seakins, BA
Miss J. M. L. Stephen, PH D*

Attached workers

H. Besterman, B SC (*St Mary's Hospital Medical School*)
G. Scullard, B SC (*St Mary's Hospital Medical School*)
T. Taylor-Roberts, B SC (*St Mary's Hospital Medical School*)

The Unit is concerned mainly with the clinical and biochemical effects of malnutrition in infants and young children, and particularly with the study of protein metabolism and body composition. It collaborates with the World Health Organization, with members of the staff of the Faculty of Medicine of the University of the West Indies and with the Government of Jamaica in the study of practical nutritional problems.

Summary of research

CLINICAL STUDIES

A. Studies on malnourished infants:

1. Biochemical and clinical criteria for the assessment of the severity of protein depletion and for prognosis.
2. Measurement of body and tissue composition in malnutrition.
3. Potassium deficiency measured with the whole-body counter.
4. Acid–base metabolism.
5. Endocrine changes: corticosteroids and insulin.
6. Factors affecting the absorption of iron.
7. Protein turnover studied with ^{35}S- and ^{15}N-labelled amino acids and with ^{131}I-labelled proteins.
8. Activity of tissue enzymes.
9. Calorie requirement for growth.
10. Oxygen consumption.
11. Carbohydrate metabolism.

B. Studies on adults: acid–base metabolism in adult sickle-cell anaemia patients.

* Seconded to the Jamaican Ministry of Health.

1. Mechanism of fatty liver in protein deficiency.
2. Adaptation to low protein intakes in the rat.
3. Mechanism and control of protein catabolism.
4. Effects of different levels of protein and carbohydrate intake on hepatic metabolism in the rat.
5. Effects of acid-base changes on renal intermediary metabolism in the rat.

MRC LABORATORIES, THE GAMBIA

Fajara, nr Bathurst, The Gambia, West Africa
(Telegrams: Tropmedres, Bathurst)

Director
I. A. McGregor, CBE, FRCP, DTM & H

Senior staff
H. A. Garling (*Administrative Officer*)
P. J. Hall, FIMLT
A. B. G. Laing, MB, DTM & H
A. W. Logie, MB, D OBST RCOG, DA
R. J. M. Wilson, PH D*

Attached workers
M. T. Gillies, MB (*University of Sussex*)
W. F. Snow, B SC (*University of Sussex*)
T. J. Wilkes (*University of Sussex*)

The staff of the Laboratories work on problems related to the tropical diseases of the Gambia. Visiting workers carry out their own research programmes and are given laboratory facilities. The MRC Trachoma Unit (p. 130) has a permanent field station at the Gambia Laboratories.

Summary of research

1. Malaria: (*a*) epidemiology, serology and pathology in Gambians; (*b*) characterization of malarial antigens and antibodies; (*c*) *in vitro* cultivation of *P. falciparum*; (*d*) effects of placental infection; (*e*) chemotherapy—efficiency of different antimalarials, alone and in combination, and field assessment of repository antiplasmodial drugs.
2. Immunoglobulins: factors influencing levels of the various immunoglobulins in the sera of Africans (with Dr D. S. Rowe, WHO Immunoglobulin Reference Laboratory, Lausanne, and members of the Pasteur Institute, Dakar, Senegal).
3. Child health: patterns of growth, morbidity and mortality in rural Gambian children (with the MRC Reproduction and Growth Unit).

MRC BIOCHEMICAL PARASITOLOGY UNIT

Molteno Institute, Downing Street, Cambridge CB2 3EE†
(0223 50577)

Director
B. A. Newton, PH D

Senior staff
to be appointed

Attached worker
Miss S. K. Pearsall (*MRC Scholar*)

The Unit is concerned with the biochemistry of parasitic protozoa, host–parasite relationships and the mechanism of action of antiprotozoal drugs.

* Seconded from the Parasitology Division of the National Institute for Medical Research.
† Temporary address: 5 Shaftesbury Road, Cambridge CB2 2BW.

Summary of research

1. *In vitro* cultivation of pathogenic trypanosomes.
2. Protein and nucleic acid metabolism in trypanosomatid flagellates.
3. Characteristics and function of extranuclear DNA in trypanosomes.
4. Mode of action of trypanocidal drugs and the mechanism of drug resistance.

MRC EPIDEMIOLOGY UNIT (JAMAICA)

University of the West Indies, Mona, Kingston 7, Jamaica
(Telegrams: Epidres, Kingston, Jamaica)

Director
W. E. Miall, MD*

Senior staff
M. T. Ashcroft, DM, DPH, DTM & H
Miss R. A. Bell, B SC
G. J. Miller, MB, MRCP

Attached worker
L. R. Carrillo, MD (*Peruvian University*)

The Unit is carrying out long-term epidemiological studies of cardiovascular and pulmonary disease in adults and growth and development studies of children in samples of the general population in Jamaica and other territories in the Caribbean.

Summary of research

1. Cardiovascular studies: (*a*) longitudinal study of the influence of environmental and genetic factors on arterial pressure, and of the relationship between arterial pressure levels and prognosis in Jamaica and South Wales; (*b*) role of bacteriuria in the aetiology of hypertension in Jamaica and South Wales (with Dr E. H. Kass, Harvard Medical School, and Professor K. L. Stuart, University of the West Indies); (*c*) clinical, electrocardiographic and radiological studies of heart disease in Jamaican and Guyanese populations.
2. Pulmonary function studies: (*a*) comparison of different ethnic groups in the Caribbean; (*b*) Jamaican patients with chronic pulmonary disease; (*c*) pulmonary fibrosis in blackfat tobacco smokers in Guyana.
3. Studies on child development: (*a*) factors influencing development in a rural population in Jamaica; (*b*) anthropometry of infants and schoolchildren throughout the Caribbean; establishment of standards for international and secular comparisons.

MRC EPIDEMIOLOGY UNIT (SOUTH WALES)

4 Richmond Road, Cardiff CF2 3AS
(0222 20376)

Director
A. L. Cochrane, CBE, FRCP, DPH

Honorary Assistant Director
W. E. Miall, MD

Senior staff
J. C. Bignall, MB
H. Campbell, MB FSS (*part-time*)
G. F. Cory (*Administrative Officer*)
P. C. Elwood, MD, DPH, DCH
P. A. Graham, FRCS (*honorarium*)
Miss J. B. Landsman, MB, FRCPG
P. M. Sweetnam, B SC, SD
W. E. Waters, MB, DIH
Miss J. M. Weddell, MB, DTCD

* Also Honorary Assistant Director of the MRC Epidemiology Unit (South Wales).

This Unit is using epidemiological techniques to study the attack rate, prevalence and progression of many diseases, and to test hypotheses about aetiology and prevention.

Summary of research

1. Epidemiology, prevention and assessment of importance of iron deficiency in the community.
2. Epidemiology of folate and vitamin B_{12} deficiencies in the elderly.
3. Methods of surveying random samples of the Welsh population.
4. Epidemiology of ophthalmological abnormalities, with particular reference to glaucoma, squint and lens opacities.
5. Epidemiology of varicose vein, associated with a randomized control study of in-patient and out-patient treatment of varicose veins (with Mr Hugh Jones, Cardiff Royal Infirmary).
6. Epidemiology of carcinoma of the cervix in Cardiff (part of a large collaborative study), including studies of error and a case-control comparison.
7. Genetics of porphyria variegata and porphyrin metabolism (with Professor R. Mahler).
8. Observer variation in the radiological diagnosis of osteoporosis and validation of osteoporotic indices (with the Medical Unit and Department of Radiology, Cardiff Royal Infirmary).
9. Randomized controlled therapeutic trial in males and females with slightly raised diastolic pressures (with Dr G. S. Kilpatrick, Medical Unit, Cardiff Royal Infirmary).
10. Epidemiological studies of urinary tract infection in women and of the effect of analgesic consumption on kidney function.
11. Epidemiology of headache in several areas in Wales.
12. Follow-up survey of the stratified random sample of men and women examined in the Rhondda in 1958 to test hypotheses about the aetiology of coronary disease, bronchitis, rheumatoid arthritis and progressive massive fibrosis, and to study the changes in a variety of biochemical and haematological variables (with the Arthritis and Rheumatism Council Field Unit and the Welsh National School of Medicine).
13. Statistical assistance for other research projects in South Wales.

MRC DENTAL UNIT

Dental School, Lower Maudlin Street, Bristol BS1 2LY
(0272 26884)

Honorary Director

Professor A. I. Darling, DD SC, MDS, FDSRCS, MRCS, FC PATH

Senior staff

G. H. Dibdin, PH D
H. N. Newman, MA, BDS
D. F. G. Poole, PH D
M. V. Stack, PH D
W. E. Starkey, OBE, LDS
J. E. Tyler, ARIC, M SC

Attached workers

G. F. Howden, BDS, PH D (*University of Bristol*)
T. Tolidis, DD (*University of Thessalonika*)

The Unit is principally concerned with the pathology of dental caries.

Summary of research

1. Histological studies: (*a*) ultrastructure of developing, mature and carious enamel; (*b*) autoradiography of developing enamel; (*c*) simulation of enamel caries *in vitro*; (*d*) scanning electron microscopy of fractured and etched enamel.
2. Chemical studies: (*a*) gas chromatography of organic acids associated with enamel lesions; (*b*) determination of enamel surface area.
3. Physical studies: (*a*) porosity and water structure of normal and carious enamel as shown by sorption techniques; (*b*) surface interactions of enamel studied by flow microcalorimetry.

MRC VISION UNIT

Institute of Ophthalmology, Judd Street, London W.C.1
(01–387 9621)

Director
H. J. A. Dartnall, D SC, FRIC

Senior staff

J. N. Lythgoe, PH D
J. D. Moreland, PH D
Mrs P. H. Silver, PH D

The Unit is concerned with the photochemical, physiological and psychophysical bases of vision in man and animals and with the evolutionary adaptation of the visual apparatus to various light-climates.

Summary of research

1. Visual pigments in vertebrates, and correlation with light environment.
2. Effects of changing environment, e.g. influence of day length, light intensity and quality and water salinity, on visual pigments in migratory and non-migratory fishes.
3. Visual pigments in rod and cone preparations.
4. Measurement of visual sensitivities with automatic apparatus.
5. Measurement of lens and corneal pigmentation.
6. Purkinje's blue arcs.
7. Relationship between the fine structure of photoreceptor outer segments and photochemical data.
8. Effect of drugs on colour vision in humans.
9. Human peripheral colour vision.
10. Underwater vision: measurement of optical characteristics of natural waters.

MRC TRACHOMA UNIT

Lister Institute of Preventive Medicine,
Chelsea Bridge Road, London S.W.1
(01–730 2181)

Medical Research Council Laboratories,
Fajara, Bathurst, The Gambia

Honorary Director
Professor L. H. Collier, MD, D SC, MRCP

Senior staff

Miss A. Barton, B SC
W. A. Blyth, PH D
A. J. Garrett, PH D
Mrs A. E. Mogg, B SC
J. Sowa, M SC (*Gambia*)
Mrs S. C. I. Sowa, MB, DO (*Gambia*)
Mrs J. Taverne, PH D (*part-time*)

At the Lister Institute trachoma and related microorganisms are studied, with particular attention to their mode of replication, antigenic structure and pathogenicity, and to the possibility of producing a trachoma vaccine.

In the Gambia research is undertaken on diagnostic methods for trachoma, on the serological response to infection and on the pathogenesis of the corneal lesions.

Summary of research

1. Trachoma and inclusion conjunctivitis agents: (*a*) purification methods; (*b*) mode of replication; (*c*) antigenic structure and immunogenicity; (*d*) pathogenicity for various hosts.
2. Field studies: (*a*) diagnostic methods; (*b*) serological response to infection; (*c*) pathogenesis of trachomatous lesions.

MRC RADIOBIOLOGY UNIT

Harwell, Nr. Didcot, Berkshire

(Rowstock 393)

Director

J. F. Loutit, CBE, DM, FRCP, FRS

Deputy Director

G. E. Harrison, D SC, F INST P

DIRECTOR'S SECTION

Senior staff

M. J. Ashwood Smith, PH D
D. W. H. Barnes, MA, BM, FC PATH
T. R. L. Bigger
M. R. Bland, B SC
R. O. Jones, PH D
D. R. Lucas, ND, FC PATH
D. G. Papworth, B SC
Miss E. M. Peakman
D. Scott, PH D*
V. S. Šljivić, DR MED, DR PHIL
L. A. Stocken, D SC, FRIC (*honorarium*)
J. Wilcockson, B SC

CHEMISTRY

Senior staff

G. E. Harrison, D SC, F INST P (*Head of section*)
P. J. V. Adams
J. H. Barnes, M SC, FRIC
G. W. Bazill, B SC†
T. E. F. Carr, B SC
Mrs A. Harrison, PH C
J. V. Horgan
G. R. Howells
E. R. Humphreys, PH D
J. Nolan, B SC
G. Patrick, BA, D PHIL
A. J. P. Phillips, PH D
J. T. Triffitt, PH D

EXPERIMENTAL PATHOLOGY

Senior staff

R. H. Mole, BM, FRCP, MC PATH (*Head of section*)
P. W. Edmondson, MRCS, FC PATH
E. V. Hulse, MD, MC PATH
Mrs A. Kendall, PH D
Mrs P. L. F. Litchfield, BM

BIOPHYSICS

Senior staff

G. J. Neary, SC D (*Head of section*)
D. A. Bance
A. L. Batchelor, PH D
B. A. Bridges, PH D
M. J. Corp, MSR
P. Gray
H. D. Maccabee, PH D
D. G. Martin
J. G. Mitchell, PH D (*until Feb. 1969*)
R. J. Munson, PH D
R. J. Preston, BA
J. R. K. Savage, PH D
W. S. G. Weal
C. F. Wright, FIST

GENETICS

Senior staff

Miss M. F. Lyon, SC D (*Head of section*)
K. F. Dyer, B SC
T. Morris, M SC
Miss R. J. S. Phillips, B SC
A. G. Searle, D SC

CYTOGENETICS

Senior staff

C. E. Ford, D SC, FRS (*Head of section*)
G. Breckon
R. S. K. Chaganti, PH D
E. P. Evans, PH D
C. McKenzie, PH D
Miss G. E. Roberts, B SC

Attached workers

Miss R. Born, B SC (*Institute of Biology, Munich*)
Major J. F. P. Clemenger, B VET MED, MRCVS (*Ministry of Defence*)
A. Durakovič, MVD, M SC (*Institute of Medical Research, Zagreb*)
S. Igali, PH D ('*Frederic Joliot Curie*' *National Institute for Radiobiology and Radiohygiene, Budapest*)
H. Simpson-Gildemeister, B SC (*University of Oxford*)
G. Siracusa, MD (*Laboratory of Animal Radiobiology, Rome*)

* * *

F. D. Bushell (*Administrator*)
J. H. Martin, ALA (*Librarian*)

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* On leave of absence at the University of California.

† Seconded to the MRC Microbial Genetics Unit.

The Unit is studying the action of ionizing radiations on living cells. The various sections, separately and in collaboration, give special attention to fast neutrons and to X- and γ-radiation.

Summary of research

DIRECTOR'S SECTION

1. Turnover, maturation and migration of haemopoietic stem cells.
2. Sensitivity of lymphocytes, animal and human, to irradiation and radiomimetic agents.
3. Correlation of histological, ultrastructural and metabolic changes in normal tissue and in organ cultures *in vitro*.
4. Correlation of biological damage from ultraviolet radiation with biochemical changes.

CHEMISTRY

1. Effects of dietary supplements on the uptake of radioactive strontium and some heavy elements in man and rats (the latter in conjunction with Dr K. Kostial, Institute for Medical Research, Zagreb).
2. Radiosensitization and mechanisms of radioprotection.
3. Enzymes concerned with replication of biologically active DNA.

BIOPHYSICS

1. Effects and mechanisms of action of ionizing radiations on the genetic material of cells: physicochemical changes in DNA, biochemical mutations, chromosome aberrations and cell killing.
2. General responsibility for irradiation techniques and equipment.

EXPERIMENTAL PATHOLOGY

1. Quantitative aspects of recovery from whole-body irradiation and its cellular basis.
2. Quantitative comparisons of lethal and other effects of fast neutron radiation and γ-radiation in large and small mammals.
3. Delayed effects of whole-body irradiation of mice and their modification by cell grafting.

CYTOGENETICS

1. Cell population studies using chromosome markers in the mouse.
2. Cytogenetics of neoplasia in experimental animals.
3. Cytogenetics of chromosome rearrangements in the mouse.

GENETICS

1. Induction of genic and chromosomal mutations in mice and other mammals by chronic γ-irradiation, acute X-irradiation and neutron irradiation: effects of dose fractionation.
2. Genetics and effects on soma and fertility of mouse mutants and chromosome abnormalities.
3. Genetics of irradiated populations.

Dr L. A. Stocken, Department of Biochemistry, University of Oxford, who receives a Council honorarium, is working on the relationship between changes in microstructure of histones and the mitotic process after irradiation.

MRC EXPERIMENTAL RADIOPATHOLOGY UNIT

Hammersmith Hospital, Ducane Road, London W.12

(01–743 4594)

Director

Miss T. Alper, MA, MS (ED), F INST P

Senior staff

Miss E. Blum, DR PHIL
P. E. Bryant, M SC
W. A. Cramp, PH D
Miss B. M. Cullen, B SC
D. Dowson
N. T. S. Evans, PH D
A. J. Forage, PH D
A. I. Hashmi, M SC
M. J. Hedges
Mrs S. Hornsey, B SC
Mrs B. Knowles (*part-time*)
R. J. Littleton, B SC
N. J. McNally, M SC
S. J. Pocock, M SC (*until Jan. 1969*)
R. H. Thomlinson, MB
D. K. Watkins, PH D

Attached workers

Mrs M. Elgate (*Israel Institute for Biological Research*)
J. Ginsburg, MD (*Royal Free Hospital Medical School, London*)
P. F. D. Naylor, MD (*St Thomas's Hospital and Medical School, London*)
J. M. Rudé, MA (*University of Illinois*)

Investigations on the effects of radiation on living organisms are aimed at elucidating basic mechanisms of action of ionizing radiation, especially with reference to the bearing of such studies on radiotherapy.

Summary of research

1. Mechanisms of radiation action on macromolecules, cells and tissues and their interrelationships (test systems ranging from microorganisms to animals); effects of modifying agents (e.g. sensitizers, protectors) and techniques (e.g. change in LET and dose rate, dose fractionation).
2. Relevance of these mechanisms to radiotherapeutic practice, with normal and neoplastic tissues as test systems; tumour biology and its relation to radiation response.
3. Radiation as a tool for investigating macromolecular structure and immunological phenomena.

MRC ENVIRONMENTAL RADIATION UNIT

University Department of Medical Physics,
The General Infirmary, Leeds 1
(0532 32799)

Honorary Director
Professor F. W. Spiers, CBE, D SC

Deputy Director
P. R. J. Burch, PH D

Senior staff

D. B. Appleby
L. Burkinshaw, PH D
L. D. Davis, MA
D. Gvozdanovic, GRAD IN SCI
Mrs. S. Gvozdanovic, GRAD IN SCI
D. H. Marshall, PH D
B. Oldroyd
C. B. Oxby, PH D
Miss J. R. Whitwell
G. D. Zanelli, B SC

Attached worker
W. Sewchand, BA (*MRC grant-holder*)

The aims of the Unit are to assess the dose received by human tissues from environmental ionizing radiations, and to consider the biological significance of this dose.

Summary of research

1. Measurement of total-body potassium in normal and pathological conditions.
2. Measurement of acquired radioisotopes in the human body.
3. Whole-body retention of γ-emitting radioisotopes; studies of calcium metabolism.
4. Continuous recording of external γ- and cosmic-ray intensities at a fixed site.
5. Measurement of radioactivity in soils and biological specimens.
6. Theoretical and experimental studies on radiation dosimetry in bone.
7. Theoretical studies of the mechanisms of 'natural' and radiation-induced diseases and of ageing.

RADIOLOGICAL PROTECTION SERVICE

(jointly with the Department of Health and Social Security)

Clifton Avenue, Belmont, Sutton, Surrey

(01–643 5441)

Director

W. Binks, CBE, M SC, F INST P

Deputy Director

E. E. Smith, B SC, A INST P

Senior staff

P. N. Baggott
T. V. Bird
L. J. F. Brotherton
K. Callowhill, AMIEE
P. N. Casbolt
Miss J. E. Challiss, B SC
J. J. Cleary
B. L. Davies, B SC, A INST P
M. J. Duggan, B SC
A. A. Edwards, M SC
B. E. Godfrey, M SC, A INST P
S. G. Goss, B SC
E. Greenslade
A. E. Greinig, M SC
E. I. Hamilton, D PHIL
R. T. Hankins
C. L. Harvey
T. E. Hilditch, B SC
Miss C. A. Howell, B SC
B. E. Jones, B SC, F INST P
D. G. Jones, PH D
A. Knight, M SC
B. E. Lambert, M SC
T. O. Marshall, B SC
Miss M. J. Minski, B SC
M. C. O'Riordan, B SC
N. Patla, PH D
P. B. Roberts, AIST
J. Rydygier, M PHIL
R. Seymour, PH D
P. J. Soilleux, M SC
J. W. Stather, PH D
J. Vennart, B SC, F INST P
Miss M. E. Walton (*Administrative Officer*)
P. D. J. Whetmath
M. J. Whillock
Miss V. Williams, M SC

BIRMINGHAM REGIONAL CENTRE

Queen Elizabeth Hospital, Edgbaston, Birmingham 15

(021–472 3705)

Honorary Director

R. F. Farr, MA, F INST P

Senior staff

R. Gelder, B SC
G. S. Greaves, B SC
R. C. Hampton
D. L. O. Humphreys, M SC
D. T. Mullarkey, DIP TECH
D. L. Speight, M SC
G. N. Stradling, PH D

LEEDS REGIONAL CENTRE

29 Clarendon Road, Leeds 2

(0532 32799 or 0532 30811)

Honorary Director

Professor F. W. Spiers, CBE, D SC

Senior staff

T. Ashton, B SC, A INST P
B. P. Danbury
R. D. Harden, B TECH
A. P. Hudson, B SC
J. Sellars, PH D

MANCHESTER REGIONAL CENTRE

Christie Hospital and Holt Radium Institute, Withington, Manchester 20

(061–445 8123)

Honorary Director

W. J. Meredith, OBE, D SC, F INST P

Senior staff

W. F. Bland, B SC, A INST P
J. R. Croft, B SC
G. C. Roberts, B SC
D. C. Thomas

SCOTTISH CENTRE

(jointly with Scottish Home and Health Department)

9 West Graham Street, Glasgow C.4

(041–332 6061)

Honorary Director

J. M. A. Lenihan, OBE, PH D, FRSE, F INST P

Senior staff

P. C. Escott, B SC
A. Gall
N. T. Harrison, B SC, A INST P
G. C. Jardine, GRAD, IERE
E. W. Mason, PH D
D. Robertson, B SC

The aims of the Service are to carry out research, mostly of a physical nature, into problems concerning the protection of workers and of the public from the effects of ionizing radiations, and to act as a central organization for the control of radiation hazards.

Summary of activities

COLLECTION AND DISSEMINATION OF INFORMATION

1. Assistance to the Council's Committee on Protection against Ionizing Radiations and to its subcommittees and panels in the preparation of recommendations on the permissible levels of external and internal radiation for radiological workers and for certain groups of the general public.
2. Assistance to the Radioactive Substances Advisory Committee and its panels and also to various government committees in the preparation of codes and regulations for the control of radiation hazards.
3. Participation in the work of the International Commissions on Radiological Protection and on Radiological Units and Measurements.
4. Collection of data on the metabolic behaviour of radionuclides and stable elements in humans, and the assessment of maximum permissible body burdens and of concentrations in air and in water of a number of radionuclides.
5. Collection of data on the effects of radiation; estimates of risk per unit dose.
6. Assistance to various committees of the British Standards Institution and to other national and international bodies.

RADIATION MONITORING AND ADVISORY SERVICES

1. Operation of a personnel radiation-monitoring service utilizing photographic films and thermoluminescent powder.
2. Measurements of radioactivity in the body *in vivo* and by analysis of excreta.
3. Inspection of departments and sites having possible radiation hazards (from normal operating procedures or accidents).
4. General advice on the design of radiation departments and the reduction of hazards in new uses of radioactive isotopes.
5. Calibration of radiation-monitoring instruments.
6. Leakage testing of sealed radioactive sources.
7. Measurement of amounts of various nuclides deposited in the bodies of persons exposed to unsealed radioactive materials.
8. Miscellaneous measurements of environmental radioactivity, e.g. continuous measurement of the local γ-radiation due to fallout and measurement of the natural radioactivity of some drinking waters.
9. Tests of the effectiveness of protective materials.
10. Advice on design of radiochemical laboratories.

MISCELLANEOUS INVESTIGATIONS

1. (*a*) Improvement of the accuracy of techniques for measuring external radiation received by workers (film dosimetry, thermoluminescence dosimetry and track-plate methods for neutron dosimetry); (*b*) automation in film densitometry and dose evaluation.
2. (*a*) Radium in persons formerly employed in the luminizing industry (with MRC Statistical Unit); (*b*) ^{40}K in relation to various factors and diseases (with Queen Elizabeth College, MRC Neuropsychiatry Unit and Kings College Hospital); (*c*) ^{59}Fe in studies of iron metabolism (with Kings College Hospital); (*d*) ^{137}Cs in the population.
3. Radioactivity in animals: (*a*) following neutron activation *in vivo* (with Kings College Hospital); (*b*) metabolism of radium compounds; (*c*) distribution and retention of ^{14}C- and ^{3}H- labelled compounds; (*d*) comparison of effects of tritiated thymidine, tritiated water and X-rays; (*e*) metabolism and distribution in the skeleton of bone seeking radionuclides.
4. Environmental radioactivity: (*a*) radon in the atmosphere at different sites, e.g. in mines; (*b*) particle size distribution of radon decay products; (*c*) plutonium in various materials, including animal tissues; (*d*) radioactivity in building materials.
5. Measurement of stable elements in human tissues using mass spectrometry and X-ray fluoroscopy.
6. Development of electronic equipment for radiation measurements, particularly utilizing transistors.
7. Theoretical and practical studies of methods of achieving low background radiation in measurements of radioactive materials.

8. Theoretical and practical studies on the scattering of X- and γ-radiation from surfaces and volumes; design of maze entrances; investigation of airshine.
9. Investigations into problems of measurement and dosimetry of β-radiation and Bremsstrahlung.
10. Protective properties of various materials (e.g. water, concrete, paraffin wax) against fast neutrons.
11. Investigation on the performance of available neutron site-monitoring equipment and the development of new designs, with emphasis on improved portability and sensitivity.

MRC CYCLOTRON UNIT

Hammersmith Hospital, Ducane Road, London W.12
(01–743 4594)

Director

D. D. Vonberg, B SC

Senior staff

L. C. Baker, FIST
D. K. Bewley, PH D
P. D. Buckingham
G. Burton, B SC
M. A. Chaudhri, D PHIL
J. C. Clark, B SC
M. B. Coyne
S. B. Field, PH D*
K. Finding, AMI MECH E
Professor J. F. Fowler, PH D, F INST P (*honorarium*)
A. W. G. Goolden, MB, DMRT (*honorary*)
G. F. S. Harding
T. Jones, M SC
R. L. Morgan, MB, B SC, DMRT, FFR (*part-time*)
C. J. Parnell, B SC
R. J. Post, MIEE
T. E. Saxton, B SC
J. Sharp, B SC
D. J. Silvester, PH D
I. A. Watson, M SC†

This Unit has three main functions: to produce with the cyclotron those radioactive isotopes not available from other sources and to collaborate in the investigation of their clinical value; to provide facilities for collaborative radiobiological investigation using the radiations from the cyclotron, linear accelerator and the Van de Graaff machine, and to provide facilities for research in fast-neutron therapy with the cyclotron.

Summary of research

1. Clinical use of the following radioisotopes and labelled compounds prepared with the cyclotron: $C^{15}O$, ^{13}N, ^{11}CO, ^{18}F, ^{81}Rb, ^{52}Fe, ^{123}I, ^{43}K (with the Royal Postgraduate Medical School, Hammersmith Hospital and other hospitals).
2. Investigation in preparation and applications of ^{62}Zn, ^{85m}Kr, ^{90}Nb, ^{117}Sb, ^{203}Pb as tracers in medical and biological studies.
3. Development of new methods of production of isotopes and labelling of compounds to give higher purity and greater specific activity; absolute standardization of isotopes.
4. Radiobiological investigations using charged particle beams from the cyclotron to study the variation in response of mammalian and plant cells and bacteria to radiations of different linear energy transfer (LET) (with the MRC Experimental Radiopathology Unit and the Royal Postgraduate Medical School).
5. Clinical trial of radiotherapy with fast neutrons.
6. Dosimetry of fast neutrons, neutron spectrometry and distribution of LET in tissue.
7. Comparison of X-rays and fast neutrons in transplanted tumours in rats and determination of relative biological effectiveness in various biological systems (with the MRC Experimental Radiopathology Unit, the Churchill Hospital, Oxford, the Royal Free Hospital Medical School, London, St Bartholomew's Medical College, London and the Royal Postgraduate Medical School).

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* On leave to work at the Department of Radiology, University of Stamford, California.

† On leave to work at the Sloan Kettering Institute for Cancer Research, New York.

8. Dose rate effects and protection by anoxia using 7-MV X-rays and electron beams (with the MRC Experimental Radiopathology Unit).
9. Engineering studies: (*a*) increased stability of cyclotron beam using improved techniques with solid state devices; (*b*) use of ion pumps and cryosorption pumps in a hydrocarbon-free pumping system for the Van de Graaff machine; (*c*) use of television methods for automatic area counting; (*d*) design of an improved ion source for the cyclotron; (*e*) feasibility of a 'beam-sharing' beam transport system for the cyclotron.

MRC CELLULAR IMMUNOLOGY UNIT

Sir William Dunn School of Pathology, Oxford OX1 3RE

(0092 57321)

Honorary Director

Professor J. L. Gowans, MB, D PHIL, FRS

Senior staff

Miss S. T. Ellis, PH D
W. L. Ford, MB, D PHIL, MRCPE
J. C. Howard, BA

Attached workers

W. R. Bowers, PH D (*Rockefeller University*)
J. W. Hollingsworth, MD (*Yale University*)
B. J. Roser, MB, PH D (*University of Sydney*)
N. L. Tilney, MD (*Harvard University*)

This Unit is concerned with the physiological and immunological functions of lymphoid tissue.

Summary of research

1. Cellular basis of antibody formation.
2. Immunological significance of lymphocyte recirculation.
3. Mechanism of homograft reaction.

MRC MUTAGENESIS UNIT

Institute of Animal Genetics, West Mains Road, Edinburgh 9

(031-667 1011)

Honorary Director

Professor Charlotte Auerbach, D SC, FRS

Senior staff

M. J. Allison, PH D (*until Jan. 1969*)
J. Corran, MA
Mrs M. E. Griffiths, B SC (*part-time; until Feb. 1969*)
B. J. Kilbey, PH D
B. M. Slizynski, DR PHIL

Attached workers

A. Abbondandolo, DIP AGRIC (*University of Pisa*)
Mrs C. Queiroz, B SC (*University of Lisbon*)
W. Ratnayake, B SC (*University of Ceylon*)
D. M. Shankel, PH D (*University of Kansas*)
R. Sram, MD (*University of Prague*)

The Unit is engaged in an analysis of the process of mutation, with particular emphasis on the events leading from the primary lesion in DNA to the emergence of the mutant cell.

Summary of research

1. Analysis of the effect in bacteria and fungi of secondary cellular processes such as repair on dose-response curves following treatment with a variety of mutagens and on observed cases of mutagen specificity.
2. Cytological basis for repair of premutational damage during spermatogenesis in mice.

MRC EXPERIMENTAL GENETICS UNIT

Department of Animal Genetics, University College London,
Wolfson House, 4 Stephenson Way, London N.W.1
(01–387 0871)

Honorary Director
Professor H. Grüneberg, MD, D SC, FRS

Senior staff

M. S. Deol, D SC
D. M. Hunt, PH D
D. R. Johnson, PH D
Mrs H. M. Murphy, PH D
Miss G. M. Truslove, PH D

Attached worker
Professor W. Landauer, DR PHIL NAT

The Unit is concerned with the mechanisms of gene action, with special reference to the origin of inherited diseases in animals and man. The abnormalities studied in vertebrates and insects are both morphological (including ultrastructural) and biochemical.

Summary of research

1. Pathology of development of skeletal mutants, including biochemical studies, and relations between body size and minor skeletal variants.
2. Physiology, morphogenesis and cytodifferentiation of the inner ear in relation to the central nervous system and to abnormalities of pigmentation.
3. Role of the amniotic fluid in pathological development.
4. Hair structure and ultrastructure in mouse mutants.
5. A search for effects in adult life of genes ascertained through their effects in early development.
6. Gene action in the mammalian X chromosome.
7. Environmental factors affecting gene manifestation in *Drosophila*.

MRC CLINICAL GENETICS UNIT

Institute of Child Health,
30 Guilford Street, London W.C.1
(01–242 9789)

Director
C. O. Carter, DM, FRCP

Senior staff

Miss I. H. M. Blyth, MB, D OBST RCOG
Mrs K. A. Evans, AIMSW
Mrs I. Gal, DR MED
D. J. Mantle, MRCS (*until Jan. 1969*)
Mrs J. Slack, BM, DCH (*part-time*)
J. Wilson, MB, PH D, MRCP (*part-time*)

Attached workers

Miss S. Bundey, MB, MRCP, DCH (*National Fund for Research into Crippling Disease grant-holder*)
C. J. Vesey, M SC (*Wellcome Trust grant-holder*)
J. Wilkins, MB, MRCPE, DCH (*MRC Clinical Research Fellow*)

The main work of the Unit falls under two headings: (1) the study of genetic and other factors in the causation of developmental abnormalities in man; and (2) investigation of the role of inheritance in the causation of common diseases, with some parallel studies on normal human variation. A genetics counselling clinic is held weekly at The Hospital for Sick Children.

Summary of research

1. Common congenital abnormalities: pyloric stenosis, spina bifida cystica, congenital dislocation of the hip, Hirschsprung's disease, Down's syndrome and polycystic kidneys.
2. Coronary artery disease, including estimations of serum lipoprotein lipase and sugar tolerance in families.
3. Genetics and biochemistry of Leber's optic atrophy, dystrophia myotonica and tuberose sclerosis.
4. Genetics of childhood muscular dystrophies.
5. Genetics of mental retardation.

MRC POPULATION GENETICS UNIT

Old Road, Headington, Oxford OX3 7LE

(0092 62834)

Director

A. C. Stevenson, MD, B SC, FRCP, DPH

Scientific staff

A. Barr, PH D (*part-time*)
Mrs J. Bedford, B SC
M. Bobrow, MB, B SC
G. Clarke, AIMLT
Miss B. C. C. Davison, MB, DPH, D OBST RCOG
A. C. W. Lewis, MB, MRCOG
M. W. Oakes, M SC
P. L. Pearson, PH D
Mrs A. E. Unrau, B SC

The Unit is concerned primarily with work designed to illuminate the genetic structure of human populations by means of the pattern of distribution of traits of medical importance. The cytological laboratory is concerned with the relationship of chromosomal aberrations to developmental anomalies, abortions and infertility. Advice and referral clinics are held in the hospitals of the Oxford Regional Hospital Board.

Summary of research

1. Cytology and cultural characteristics of normal chorion and hydatidiform mole.
2. Analysis of cytological and clinical findings in primary amenorrhoea.
3. Clinical and genetic studies of the testicular feminization syndromes.
4. Culture of cells from amniotic fluid.
5. Study of offspring of incestuous unions.
6. Follow-up study of families where genetic risk estimates have been given over the last ten years.
7. Meiotic studies on testicular material, with special reference to chiasma frequency in relation to age.
8. Male infertility, meiotic and mitotic cytology and distribution of DNA content in sperm.
9. Penetration of sperm into somatic cells.
10. Chromosome studies on psychopathic prisoners.

MRC CLINICAL AND POPULATION CYTOGENETICS UNIT

Western General Hospital, Crewe Road, Edinburgh 4

(031–332 1361)

Derbyshire House, St Chad's Street, London W.C.1

(01–278 2890)

Acting Director

Miss P. A. Jacobs, D SC*

Honorary Consultant Physician

Professor J. A. Strong, MBE, MD, FRCP, FRCPE

* The Director, Professor W. M. Court Brown, died in December 1968 (see p. 37); Professor H. J. Evans will become Director from October 1969.

DIRECTOR'S SECTION

Senior staff

J. Aitken, MB
Mrs M. E. A. Brunt, MB, D OBST RCOG (*part-time*)
T. R. Elsdale, PH D
T. K. Maclachlan, MB, MRCP, DPM
Miss M. S. Newton, MB, D OBST RCOG
W. H. Price, MB, B SC, MRCPE (*part-time*)
P. G. Smith, DIP TECH

CYTOGENETICS SECTION

Senior staff

Miss P. A. Jacobs, D SC (*Head of Section*)
Miss K. E. Buckton, B SC
M. J. W. Faed, PH D
J. Foulkes, M SC
Mrs S. G. Ratcliffe, MB, MRCPE, D CH (*part-time*)
G. Spowart, HNC
Mrs A. S. Watson, BM B SC (*part-time*)

EXPERIMENTAL STUDIES SECTION

Senior staff

D. G. Harnden, PH D (*Head of Section; until March 1969*)
Miss A. Kingston, B SC
Mrs S. McBeath, FIMLT (*part-time*)
J. K. McDougall, M INST BIOL
Miss M. L. O'Riordan, M SC
A. Ross, FIMLT
D. E. Young, PH D

PATTERN RECOGNITION AND AUTOMATION SECTION*

Senior staff

D. Rutovitz, PH D (*Head of Section*)
J. Cameron, HNC
A. S. J. Farrow, B SC
Miss R. Goldberg, B SC
D. K. Green, PH D
Miss C. J. Hilditch, B SC
D. C. Mason, PH D
B. Stein, BA

Attached worker

C. M. Steel, B SC, MB, MRCPE (*University of Edinburgh*)

The Unit undertakes research on (1) human genetics, with particular emphasis on cytogenetics; (2) pattern recognition, with special emphasis on computer-aided chromosome analysis, and (3) genesis of tumours, with particular reference to radiation, viruses, ageing and morphogenetic factors.

Summary of research

CYTOGENETICS

1. Genotype-phenotype relationships in patients with abnormal chromosome complements.
2. Cytogenetic studies on selected populations.
3. Study of human meiotic chromosomes.
4. Organization of a registry of individuals and families wtih an abnormal karyotype for epidemiological and genetic research.
5. Investigation of the effects of chromosome-damaging agents *in vivo* and *in vitro*.

PATTERN RECOGNITION AND AUTOMATION

1. Development of a fully automatic system of screening for chromosomally abnormal individuals by computer analysis of a sequence of mitotic cell photomicrographs.
2. Investigation and planning for second-generation scanning equipment and a computer-controlled microscope.

EXPERIMENTAL STUDIES

1. Genotypic factors in the sensitivity of human cells to viral transformation *in vitro*.
2. New approaches to the study of genetic factors in human cancer.
3. Morphogenesis in fibroblast cultures.

* Derbyshire House, St Chad's Street, London W.C.1

MRC VIROLOGY UNIT

Institute of Virology, Church Street, Glasgow W.1
(041–339 8855)

Honorary Director
Professor J. H. Subak-Sharpe, PH D

Senior staff

D. Bell, PH D
E. A. C. Follett, PH D
Mrs J. C. M. Macnab, B SC
Mrs N. F. Miller, B SC
T. H. Pennington, MB, PH D
C. R. Pringle, PH D
G. J. Russell, M INST BIOL
J. F. Szilagyi, D PHIL
H. V. Thorne, PH D (*until Feb. 1969*)
J. S. White, FIMLT
N. M. Wilkie, PH D
J. F Williams, PH D
W. H. Wunner, PH D

Attached workers

A. A. Combiescu, MD (*Cantacuzino Institute, Bucharest*)
Mrs R. L. Edwards, M SC (*MRC Junior Research Fellow*)
R. D. Goldman, PH D (*Princeton University*)
Miss M. I. Irving, B SC (*University of Glasgow*)
N. S. Lockhart, B SC (*MRC Scholar*)
Miss S. M. Mitchell, B SC (*MRC Scholar*)
D. A. Ritchie, PH D (*University of Glasgow*)
R. A. Roosa, PH D (*Wistar Institute, USA*)
Mrs M. C. Timbury, MD, PH D (*University of Glasgow*)

The Unit carries out research on the structure, function and information content of viruses, with particular reference to changes in animal cells infected by lytic and tumour viruses.

Summary of research

1. Mechanism of neoplastic transformation by polyoma and SV40 viruses and adenoviruses studied in cell culture.
2. Characteristics of the DNA and protein components of tumour viruses.
3. Characteristics of neoplastic cells induced by viruses compared with those of normal and of spontaneously appearing neoplastic cells investigated in cell culture and by electron microscopy.
4. Genetically stable biochemical variants of a stable mammalian cell line.
5. Production and analysis of conditional lethal mutants of herpes group viruses, adenoviruses, papovaviruses and arboviruses.
6. Identification of RNA's and proteins specified by the herpes virus genome in infected cells.
7. Analysis of virus–virus and virus–host relationships using the 'nearest neighbour' nucleotide patterns in the nucleic acid (with the Department of Biochemistry, University of Glasgow).
8. Mechanism of the antiviral activity of the antibiotic rifampicin.

MRC MICROBIAL GENETICS UNIT

University Department of Molecular Biology,
King's Building, West Mains Road, Edinburgh 9

Honorary Director
Professor W. Hayes, MB, D SC, DPH, FRCPI, FRS

Senior staff

G. W. Bazill, B SC*
P. M. A. Broda, PH D
W. D. Donachie, PH D
S. W. Glover, PH D
J. D. Gross, PH D
R. S. Hayward, PH D
D. Karamata, PH D
Miss M. Masters, PH D
Miss M. Monk, PH D
E. E. M. Moody, B SC
Mrs N. E. Murray, PH D
J. G. Scaife, PH D
N. S. Willetts, PH D

* Seconded from the MRC Radiobiology Unit.

Attached workers

G. Alfaro, MD (*National University of Mexico*)
S. J. Austin, B SC (*MRC Scholar*)
Miss D. Bannister, B SC (*MRC Scholar*)
Miss R. M. Hall, B SC (*University of Sydney*)
J. Hubáček, B SC (*Institute of Microbiology, Prague*)
W. S. Kelley, PH D (*Tufts University, Boston*)
P. M. Leighton, M SC (*Wellcome Trust Fellow*)
A. Lukin, PH D (*University of Moscow*)
D. T. Martin, B SC (*MRC Scholar*)
A. F. Morgan, B SC (*MRC Scholar*)
R. Schekman (*University of California, Los Angeles*)
T. Tsuji, MD (*University of Alabama Medical Center*)
J. A. Wechsler, PH D (*Yale University*)

The Unit is undertaking detailed study of the fine structure of genes and chromosomes in microorganisms and the mechanisms of their replication and transfer to other cells (i.e. sexuality). Research is concerned primarily with the genetics of bacteria and their viruses, which are relevant to such problems as resistance to antibiotics and host–virus relationships.

Summary of research

1. Isolation of temperature-sensitive mutants of *Bacillus subtilis* having defects in DNA synthesis, and their analysis with a view to extending knowledge of the nature of chromosome replication.
2. Regulation of cell division in *Escherichia coli*.
3. Genetic and physiochemical basis of host-induced modification in bacteria and bacteriophages.
4. Nature and behaviour of resistance transfer factors and other episomal genetic elements.
5. Mechanism of genetic recombination in bacteria and bacteriophages.
5. Mutational study of the regulation of the lactose operon in *E. coli*.
7. Interactions of RNA polymerase with DNA.

MRC MICROBIAL SYSTEMATICS UNIT

Adrian Building, University Road, Leicester LE1 7RH
(0533 50000)

Director

P. H. A. Sneath, MD, DIP BACT

Senior staff

Mrs D. Wood, PH D, DIP BACT

Attached workers

Professor J. W. Carmichael (*University of Alberta*)
M. Goodfellow, PH D (*MRC Research Fellow*)

This Unit is engaged in research on the classification of microorganisms, with special reference to numerical taxonomy and computer methods. The application of these methods to other fields of medical and biological science is also being explored.

Summary of research

1. Systematics of pseudomonads, pasteurellas and related bacteria, coryneform bacteria and the *Nocardia* group.
2. Influence of environment on the classification of bacteria.
3. Systematic study of primary structure of proteins.
4. New statistical methods in taxonomy.
5. Development of computer programs for systematics.

MRC HUMAN BIOCHEMICAL GENETICS UNIT

The Galton Laboratory, University College London, Wolfson House,
4 Stephenson Way, London N.W.1
(01–387 0871)

Honorary Director
Professor Harry Harris, MD, FRS

Senior staff

T. E. Cleghorn, MD (*honorary*)
P. J. L. Cook, MB
G. Corney, MD, D OBST RCOG, DCH
Miss R. A. Fisher, MB, M SC
D. A. Hopkinson, MD
W. H. P. Lewis, PH D (*until Feb. 1969*)
Miss J. M. Parrington, B SC
Mrs N. J. Parry-Jones
Miss E. B. Robson, PH D
K. P. Sinha, MD, MSC
Miss A. L. Stewart, MB, DCH (*part-time*)

Attached workers

Miss C. A. Chilcot, B SC (*MRC Scholar*)
Miss L. J. Donald, B SC (*Queen's University, Kingston, Ontario*)
Mrs Y. H. Edwards, B SC (*MRC Scholar*)
M. Kirjarinta, B SC (*University of Helsinki*)
Miss P. J. McAlpine, MA (*University of Toronto*)
P. S. Moorhead, PH D (*Wistar Institute, Philadelphia*)
Miss J. Peters, B SC (*MRC Scholar*)
Miss S. Rapley, PH D (*Drummond Fellow*)
Miss D. M. Swallow, B SC (*MRC Scholar*)
Miss D. M. Thomas, B SC (*MRC Scholar*)

The aim of the Unit is to study the biochemical genetics of human variation and of inherited disease.

Summary of research

1. Biochemical diversity in human populations: its genetical and biochemical basis and clinical significance.
2. Biochemical studies on cells grown in tissue culture.

MRC BIOPHYSICS UNIT

Department of Biophysics, University of London, King's College,
26–29 Drury Lane, London W.C.2
(01–836 8851)

Director
Professor Sir John Randall, D SC, FRS (*part-time*)

Deputy Director
Professor M. H. F. Wilkins, CBE, PH D, FRS

Senior staff

T. C. Appleton, PH D
S. Arnott, PH D
D. L. Back
Miss A. I. Bailey, PH D
Mrs A. V. W. Brown, D PHIL (*part-time*)
G. L. Brown, PH D
D. H. Burrin, PH D
A. Cooper
H. G. Davies, PH D
Miss E. J. Evans, B SC
W. B. Gratzer, PH D
Professor Jean Hanson, PH D, FRS
Mrs M. E. Haynes, B SC
D. E. Hookes, BA
J. M. Hopkins
Miss R. D. Hynes
H. Isenberg, M SC
M. Jacobs, PH D
Z. Kosinski, M SC
H. R. Munden, FIST
E. J. O'Brien, PH D
S. R. Pelc, D PHIL
E. G. Richards, PH D
Miss E. M. Rome, PH D
M. Spencer, PH D

Attached workers

A. E. Blaurock, PH D (*University of Michigan*)
P. Carl, PH D (*University of California, Berkeley*)
Mrs R. I. Collinson-Jones, B SC (*MRC Scholar*)
D. M. Engelman, PH D (*US National Institutes of Health Fellow*)
Miss S. B. Hills, B SC (*MRC Scholar*)
Miss A. Hodgson, B SC (*MRC Scholar*)
Y. K. Levine, BA (*MRC Scholar*)
Miss V. Mautner, B SC (*MRC Scholar*)
P. J. Pond, B SC (*MRC Scholar*)
P. J. Vibert, B SC (*MRC Scholar*)
N. G. Webb, B SC (*MRC Scholar*)

The Unit studies large molecules and the structures into which they are organized in cells and tissues, in order to gain insight into the ways in which cells work.

Summary of research

1. Nucleic acid and protein structure and function: (*a*) X-ray diffraction and molecular structure of RNA, DNA, nucleoprotein, ribosomes and chromosomes; (*b*) interaction of nucleic acids with antimetabolites; (*c*) computer refinement of molecular structure of polymers; (*d*) primary and secondary structures of transfer RNA, ribosomal RNA and RNA of bacteriophages; (*e*) active sites in RNA's; role of minor nucleotides in control of viral synthesis; (*g*) isolation and characterization of low-molecular-weight RNA; (*h*) physical chemistry of polynucleotides, RNA and ribosomes—conformations in solutions by optical rotation, spectrophotometry and ligand binding; (*i*) conformational changes and subunit interaction in activator-controlled enzymes; (*j*) thermodynamic and kinetic studies of conformation and aggregation equilibria in proteins.
2. Molecular basis of contractility in muscle, studied by X-ray diffraction, electron microscopy and physicochemical methods.
3. Cilia: biochemical, genetic and morphogenetic studies and determination of macromolecular organization.
4. Membrane structure and function.
5. Structure and composition of single cells (including cells synthesizing haemoglobin in embryo and adult), nerve membranes and chromosomes and the relation to function: electron and quantitative light microscopy; electron microscopy of ribosomes.
6. Autoradiography: (*a*) development for soluble compounds; (*b*) renewal of DNA in non-dividing cells; (*c*) effect of ionizing radiations on renewal of DNA.
7. Structure and function of macromolecular systems in nerve cells.

MRC LABORATORY OF MOLECULAR BIOLOGY

University Postgraduate Medical School, Hills Road, Cambridge CB2 2QH
(0223 48011)

*Chairman of Governing Board**
M. F. Perutz, CBE, PH D, FRS

Deputy Chairman
J. C. Kendrew, CBE, SC D, FRS

Honorary Adviser
Sir Lawrence Bragg, CH, OBE, MC, MA, FRS

STRUCTURAL STUDIES

Senior staff

J. C. Kendrew, CBE, SC D, FRS (*Head of Division*)
U. W. Arndt, PH D
D. J. Battison
D. M. Blow, PH D
W. Bolton, PH D
J. N. Champness, PH D
Miss J. M. Cox, BA
R. Diamond, PH D
J. T. Finch, PH D
T. H. Gossling, MA
J. C. Haselgrove, B SC
H. E. Huxley, MBE, SC D, FRS
J. V. Kilmartin, BA
Mrs P. L. King, BA
A. Klug, PH D, FRS*
R. Leberman, PH D (*until Jan. 1969*)
J. Barrington Leigh, MA
A. D. McLachlan, PH D
J. F. W. Mallett, BA
J. K. Moffat, B SC
Miss H. Muirhead, PH D
Miss L. A. Richardson, BA
P. N. T. Unwin, PH D
J. Weinzierl, PH D

* The Heads of Divisions, and Dr Huxley and Dr Klug form the governing board of the Laboratory.

Attached workers

J. J. Birktoft, CAND SCIENT (*Carlsberg Laboratory, Copenhagen*)
G. G. Borisy, PH D (*University of Chicago*)
D. L. D. Caspar, PH D (*Harvard Medical School and Children's Cancer Research Foundation*)
D. J. De Rosier, PH D (*University of Chicago*)
A. C. H. Durham, BA (*MRC Scholar*)
H. P. Erickson, PH D (*Johns Hopkins University*)
P. F. C. Gilbert, BA (*MRC Scholar*)
J. Greer, AB (*Princeton University*)
R. Henderson, B SC (*MRC Scholar*)
R. Josephs, PH D (*John Hopkins University*)
M. Levitt, B SC (*MRC Scholar*)
P. B. Moore, PH D (*University of Geneva*)
O. D. Moorhouse, BA (*University of Toronto*)
Miss S. J. Morris, PH D (*Max-Planck-Gesellschaft*)
T. Steitz, PH D (*Harvard University*)
P. M. Wassarman, PH D (*Brandeis University*)

MOLECULAR GENETICS

Senior staff

F. H. C. Crick, PH D, FRS } (*Joint Heads*
S. Brenner, MB, D PHIL, FRS } *of Division*)
Mrs L. Barnett, B SC
M. S. Bretscher, PH D
B. F. C. Clark, PH D
A. J. Munro, PH D
J. D. Smith, PH D
A. O. W. Stretton, PH D

Attached workers

J. N. Abelson, PH D (*Johns Hopkins University*)
Miss S. Cory, M SC (*University of Melbourne*)
R. W. Davies, BA (*Science Research Council Scholar*)
B. P. Doctor, PH D (*Walter Reed Army Institute of Research, Washington*)
M. L. Gefter, PH D (*Albert Einstein College of Medicine, Bronx*)
D. I. Hirsh, PH D (*Rockefeller University*)
M. L. Hooper, BA (*MRC Scholar*)
E. R. Katz, B SC (*Churchill Scholar*)
A. Landy, PH D (*University of Illinois*)
H. Lodish, PH D (*Rockefeller University*)
Miss P. C. Marrack, BA (*Science Research Council Scholar*)
G. S. Martin, BA (*MRC Scholar*)
P. S. Rudland, BA (*MRC Scholar and Salters Scholar*)
R. L. Russell, PH D (*Cornell University*)
Mrs J. Argetsinger Steitz, PH D (*Harvard University*)
A. A. Travers, BA (*MRC Scholar*)
A. Yudelevich, PH D (*Albert Einstein College of Medicine*)

PROTEIN AND NUCLEIC ACID CHEMISTRY

Senior staff

F. Sanger, CBE, PH D, FRS (*Head of Division*)
G. G. Brownlee, PH D
P. J. G. Butler, PH D
J. I. Harris, PH D
B. S. Hartley, PH D
R. Jakes
G. M. T. Jones, BA
S. M. E. Magnusson, DR MED
K. Marcker, DR PHIL
C. Milstein, PH D
J. R. L. Pink, BA
A. G. Weeds, PH D

Attached workers

J. M. Adams, PH D (*Harvard University*)
C. J. Bruton, BA (*MRC Scholar*)
S. H. Buttery, B SC (*University of Melbourne*)
J. E. Dahlberg, PH D (*University of Chicago*)
S. Dube, PH D (*Roswell Park Memorial Institute, Buffalo, USA*)
P. Fellner, BA (*MRC Scholar*)
B. Frangione, MD (*New York University School of Medicine*)
P. G. N. Jeppesen, BA (*MRC Scholar*)
H. Kaplan, PH D (*Sussex University, Ottawa*)
W. C. Kenney, PH D (*University of California*)
F. Labrie, MD (*Laval University, Quebec*)
J. L. Nichols, PH D (*University of Alberta*)
P. W. J. Rigby, BA (*MRC Scholar*)
D. M. Shotton, BA (*MRC Scholar*)
A. E. Smith, BA (*MRC Scholar*)
J. Svasti, BA (*Trinity College, Cambridge*)
Miss M. Szekely, PH D (*Institute of Medical Chemistry, Budapest*)
Miss J. Thomas, PH D (*University College of Swansea*)
R. J. Wolverson, BA (*MRC Scholar*)

* * *

Miss A. C. Martin (*Administrative Staff*)

The aim of the Laboratory is the study of the structure, function and synthesis of large molecules of biological importance.

Summary of research

STRUCTURAL STUDIES

1. X-ray studies of the structure of haemoglobin, myoglobin, chymotrypsin, elastase and glyceraldehyde phosphate dehydrogenase.
2. Determination of virus structure by X-ray diffraction, electron microscopy and chemical analysis, with particular reference to tobacco mosaic, turnip crinkle, human wart, rabbit papilloma and tomato bushy stunt viruses.
3. X-ray and electron microscopy studies of muscle and muscle proteins.
4. Theoretical work in protein crystallography.
5. Developments in techniques and instrumentation for X-ray analysis, electron microscopy and 3-dimensional electron microscopy.

MOLECULAR GENETICS

1. Genetic and biochemical studies of a suppressor tyrosine transfer RNA.
2. Isolation and structure of transfer RNA's from *Escherichia coli.*
3. Mechanism of protein synthesis.
4. Genetics, structure and behaviour of nematode worms.
5. Antibody formation.
6. Theory of pattern formation.

PROTEIN AND NUCLEIC ACID CHEMISTRY

1. Structure and activity of yeast glyceraldehyde phosphate dehydrogenase and yeast and alcohol dehydrogenase.
2. Chemical modification and reactivity of amino acid side-chains in proteins.
3. Primary structure of bovine thrombin, prothrombin and porcine elastase.
4. Purification and properties of amino-acyl-tRNA synthetases.
5. Constancy and variability, and the nature of the variability, of amino acid sequences of immunoglobulins.
6. Nucleotide sequences in the two methionyl transfer RNA's (with the Molecular Genetics Division) and in valine transfer RNA.
7. Methods for fractionation and sequence determination of RNA and DNA.

MRC MOLECULAR PHARMACOLOGY UNIT

Old Press Site, Mill Lane, Cambridge

(0223 50703)

Honorary Director

Professor A. S. V. Burgen, MD, FRCP, FRS

Senior staff

K. J. Dorrington, PH D
R. W. King, PH D
J. C. Metcalfe, PH D
G. C. K. Roberts, PH D
R. W. Stoddart, PH D

Attached workers

K. K. Adjepon-Yamoah, MB (*Government of Ghana Research Fellow*)
M. C. Colley, BA (*MRC Scholar*)
T. Nogrady, PH D (*Loyola College, Montreal*)
R. F. Randall, B SC (*Canadian MRC Fellow*)
P. Taylor, PH D (*US National Institutes of Health Fellow*)

The Unit is concerned with the molecular basis of interactions between drugs and biological structures. It is especially interested in the application of spectroscopic methods for studying drug complexes and the investigation of kinetic aspects of drug combinations.

Summary of research

1. Investigation of drug antibodies as model systems for drug receptors and for studies of alterations in conformation.
2. Nature of the molecular changes in cell membranes produced by anaesthetics.
3. Examination of enzyme structure and the spectral changes occurring in combination with substrates and inhibitors by nuclear magnetic resonance.
4. Relationship of the structure of inhibitors of carbonic anhydrase to the enzyme structure and the determinants of the kinetic rate constants for association and dissociation of the enzyme–inhibitor complex.
5. Isolation and characterization of proteins of cell membranes; measurements of drug binding and effects on conformation.

MRC METABOLIC REACTIONS UNIT

Department of Biochemistry, Imperial College, London S.W.7
(01–589 5111)

Honorary Director
Professor E. B. Chain, D PHIL, FRS

Senior staff

H. F. Bradford, PH D
C. Chlouverakis, DR MED
K. Corbett, B SC
Miss H. Gould, PH D
H. W. S. King, B SC
A. E. Lowe
K. R. L. Mansford, PH D, FRIC, M INST BIOL
K. A. Rookledge, M INST BIOL
S. P. R. Rose, PH D

The research programme of this Unit is concerned with the mode of action of hormones, in particular insulin and glucagon, brain metabolism, and the control of protein biosynthesis.

Summary of research

1. Hormonal control of intermediary metabolism in the perfused heart, diaphragm muscle, intestine and liver and the influence of streptozotocin diabetes on glucose metabolism in these tissues.
2. Anaerobic metabolism in myocardial infarction (with the MRC Cardiovascular Unit).
3. Methods of preparing glucagon and insulin antibodies for sensitive immunoassays.
4. Glucose metabolism in isolated muscle from reptiles.
5. Metabolic studies and hormonal sensitivity in obese hyperglycaemic mice.
6. Control of protein biosynthesis in avian reticulocytes, mammalian muscle and *Bacillus thuringiensis*.
7. Brain metabolism: carbohydrate metabolism in mammalian, snail and octopus brain, isolated nerve-ending particles, neurons and glia, with particular reference to amino acid and protein synthesis.
8. Instrumentation: radioactive gas chromatographic methods; computer evaluation of data from automated column chromatography.

MRC BRAIN METABOLISM UNIT

Department of Pharmacology, University Medical School, Teviot Place, Edinburgh 8
(031–667 1011)

Director
G. W. Ashcroft, MB, MRCPE, D OBST RCOG, DPM

Scientific staff

H. M. Adam, MB (*honorary*)
Miss I. M. Blackburn, MA
T. B. B. Crawford, PH D (*honorary*)
A. J. Dewar, M SC
D. Eccleston, MD, PH D, DPM
I. Laszlo, GRAD IN MED, PH D
A. T. B. Moir, MB, PH D
I. A. Pullar, B SC
H. W. Reading, PH D, DIP MICROBIOL
Miss E. E. Robertson, MB, FRCPE, DPM (*honorary*)
Miss C. M. Yates, PH D

Attached workers

Miss M. Burden, PH D (*W. H. Ross Foundation Fellow*)
R. L. Cundall, MB, DPM (*Wellcome Trust Research Fellow*)
Miss A. C. Geddes, B SC (*University of Edinburgh*)
J. Halliday, B SC (*University of Edinburgh*)
S. H. Shariff, MB, M SC (*Pakistan Council of Scientific and Industrial Medicine*)
R. F. Sugden, B SC (*University of Edinburgh*)

The Unit carries out studies on cerebral metabolism in animals and man, with special reference to neurological and psychiatric disorders.

Summary of research

ANIMAL STUDIES

1. Cerebral metabolism in the intact animal.
2. Properties of the blood-brain-cerebrospinal fluid barrier systems.
3. Metabolic pathways in the brain and the effect of electrical stimulation and psychotropic drugs on them; regional differences in cerebral metabolism.
4. Retinal metabolism.
5. Development of cytochemical techniques.

CLINICAL STUDIES

(at the Royal Edinburgh Hospital in the Unit's own ward, at the Western General Hospital with Professor F. J. Gillingham, and at the Northern General Hospital with Dr J. B. Stanton).

1. Manic–depressive psychosis: changes in renal and cerebral transport functions and amino acid and electrolyte transport in the erythrocyte.
2. Depressive illness: changes in cerebral amine metabolism.
3. Parkinsonism: changes in cerebral dopamine and 5-hydroxytryptamine metabolism.
4. Biochemical studies in patients with degenerative diseases of the nervous system.
5. Epilepsy: blood–brain barrier changes; release of possible transmitter substances.

MRC NEUROENDOCRINOLOGY UNIT

University Department of Human Anatomy, South Parks Road, Oxford OX1 3QX

(0092 58686)

Honorary Director

Professor G. W. Harris, CBE, MD, DM, SC D, FRS

Senior staff

K. Brown-Grant, MD, SC D
C. S. Corker, B SC
D. J. El Kabir, MB
D. Exley, D PHIL
K. Farrington, B SC
C. W. Graham
Miss M. Reed, PH D
A. W. Rogers, MB, PH D

Attached workers

I. W. Bayman (*Queen's College, Oxford*)
P. Dandona, MB (*Rhodes Scholar*)
H. H. Feder, PH D (*US Public Health Service Research Fellow*)
Mrs D. Hollingsworth, MD (*Yale University School of Medicine*)
Y. Manabe, MD (*Kyoto, Japan*)
A. Munck, PH D (*Dartmouth Medical School, Hanover, USA*)
F. Naftolin, MD (*University of Washington*)
P. M. Packman, MD (*University of Washington*)
Miss R. Prasad, MB
K. B. Ruf, MD (*University of Basle*)

The Unit is concerned with investigations into anatomical, physiological and behavioural relationships between the central nervous system and the endocrine glands.

Summary of research

1. Effect of hormones on the development and differentiation of the central nervous system.
2. Chemical mediators by which the hypothalamus regulates the activities of the anterior pituitary gland.
3. Development of methods for estimation of steroid hormones in body fluids.
4. Cyclic endocrine activity in normal and psychiatrically abnormal individuals.
5. Mode of action of the progestational compounds and other contraceptive steroids in blocking ovulation.
6. Estimation of thyrotrophic hormone in blood; properties of the long-acting thyroid stimulator; thyroid–ovarian interrelationships.
7. Neuroendocrine factors in induced ovulation.
8. Development of autoradiographic techniques.

MRC NEUROPHARMACOLOGY UNIT

Department of Experimental Neuropharmacology, The Medical School,
Birmingham 15
(021–472 1642)

Honorary Director
Professor P. B. Bradley, D SC

Senior staff

M. F. Beeson, B SC
R. W. Blunn, HNC
R. J. Boakes, B SC
D. H. Hands, MB
B. J. Key, PH D (*honorary*)
A. R. King, PH D
M. I. Phillips, PH D*

Attached workers

I. Briggs, PH D (*University of Birmingham*)
A. Dray, B SC (*MRC Scholar*)

The Unit is studying the actions of drugs on the central nervous system, with particular reference to the correlation between electrophysiological and behavioural effects and to interactions with sensory stimuli, and also the sites of action of drugs in the brain, particularly in relation to synaptic transmission. The drugs studied are those with known effects on mental function and also substances that may be important as neurohumoral agents.

Summary of research

1. Effects of drugs on recent memory, attention and habituation to sensory stimuli in animals and on the inflow and integration of sensory information in the brain.
2. Effects of drugs on the performance of animals in situations controlled by aversive and appetitive stimuli.
3. Effect of electrical stimulation of the brain on the behaviour of animals.
4. Effects of drugs on the activity of single neurones in the brain when applied by iontophoresis.

MRC UNIT ON NEURAL MECHANISMS OF BEHAVIOUR

Department of Psychology, University College London,
Gower Street, London W.C.1
(01–387 7050)

Honorary Director
Professor G. C. Drew, MA

Deputy Director
I. S. Russell, PH D

Senior staff

D. A. Oakley, B SC
R. M. Pigache, MB, BS
H. C. Plotkin, PH D
G. A. Tolliver, MA

Attached workers

Mrs S. Cunnold, B SC (*MRC Scholar*)
Mrs I. Kennedy, BA
D. Kleinman, B SC
J. Murrell, BA (*part-time*)
L. Nadel, PH D (*US National Institute of Mental Health Fellow*)
J. Odling-Smee, BA
A. G. Yeo, B SC (*Science Research Council Student*)

* On leave of absence at the Department of Psychology, University of Michigan.

The Unit is primarily studying the role of the cerebral cortex in learning and memory. Other work is concerned with cortical–subcortical interactions in such neural processing as the encoding, storage and retrieval of information during learning and memory processes.

Summary of research

1. Validation and standardization of different conditioning procedures: distraction and exploratory measures of habituation; Pavlovian conditioning procedures such as passive avoidance, conditioned emotional response, conditioning of nictitating membrane in rabbit; instrumental conditioning involving avoidance procedures and various positive reinforcement schedules; 'go, no-go' learning reversals and extinction; fractionation and synthesis of complex conditioned performances.
2. 'Spreading cortical depression' as a technique of functional ablation of cortex: use in chronic preparations; comparison with surgical procedures; effects on subcortical structures; effects on learning and memory.
3. 'Split-brain' function in relation to the formation of memory traces: learning in normal and 'split-brain' animals; lateralization of various types of learning; comparison of learning between hemispheres.
4. Use of brain lesions to study defects of memory; role of frontal cortex; hemidecortication; learning in decorticate animals.

MRC UNIT FOR METABOLIC STUDIES IN PSYCHIATRY

University Department of Psychiatry, Middlewood Hospital, PO Box 134, Sheffield S6 1TP
(0742 349491)

Honorary Director

Professor F. A. Jenner, MB, PH D, DPM, MRCP

Senior staff

P. A. Bond, PH D
N. E. Chard, AIMLT
L. Grant, AIST, MRSH
R. J. Pollitt, PH D

Attached workers

N. J. Birch, B SC (*University of Sheffield*)
D. Ellis, B SC (*MRC Scholar*)
J. A. C. Empson, BA (*MRC Scholar*)
S. M. Hanna, MB, MRCP, DPM (*United Sheffield Hospitals*)
Miss C. A. Harris, B SC (*MRC Scholar*)
R. J. Kerry, MRCS, DPM (*Middlewood Hospital, Sheffield*)
C. R. Lee, B SC (*University of Sheffield*)
U. T. Place, MA, DIP ANTH (*University of Leeds*)
C. P. Seager, MD, DPM (*University of Sheffield*)
P. D. Stonier, B SC (*MRC Scholar*)
M. J. Wheeler, B SC (*MRC Scholar*)

The aims of this Unit are to investigate possible biochemical, humoral and electrophysiological abnormalities in patients with mental disorders, and aspects of physiology, biochemistry and animal behaviour that may have a bearing on these problems.

Summary of research

1. Investigation of the hierarchy of events underlying the recurrent changes in behaviour, EEG, electrolytes, water metabolism, catecholamines, steroids and vasopressin.
2. Investigation of apparently analogous abnormal rhythms of activity and metabolism in rats to assess whether they are useful models of the periodic psychoses.
3. Chemical study of inborn errors of metabolism in mentally subnormal persons, especially aspartylglycosaminuria, argininosuccinic aciduria and a defect involving abnormalities of hair proteins.

MRC NEUROPSYCHIATRY UNIT

Medical Research Council Laboratories, Woodmansterne Road, Carshalton, Surrey
(01–643 4461)

Clinical Investigation Ward, Greenbank, West Park Hospital, Epsom, Surrey
(01–39 24771)

Director
D. Richter, PH D, MRCP

Senior staff

R. Balázas, DR MED, DR PHIL
J. B. Brierley, MD, FC PATH
B. W. L. Brooksbank, PH D
A. W. Brown, B SC
J. A. Cocks, M INST BIOL
A. J. Coppen, MD, DPM (*part-time*)
M. K. Gaitonde, PH D
A. L. Johnson, B SC
D. A. MacSweeney, MB, MA
B. S. Meldrum, MB, PH D
Mrs M. Metcalfe, DIP DE PSYCHOL (*part-time*)
G. W. Morris
Mrs R. O'Keeffe, B PHARM
D. M. Shaw, MB, PH D, MRCP, DPM
J. C. Watkins, PH D
P. C. Whybrow, MB

Attached workers

T. Arnfred, CAND SCI (*University of Copenhagen*)
V. Bhargava, MD (*Medical College, Gwalior, India*)
Miss M. Carter-Pedler, B SC (*MRC Scholar*)
A. E. Gordon, B SC (*University of London*)
Mrs B. Herzberg, MB, MRCP, DPM (*Brunner Research Fellow*)
I. A. Khan, MB, M PHIL (*University of Karachi*)
S. Kovács, MD (*Hungarian Academy of Science*)
A. J. Patel, PH D (*University of Baroda*)
A. J. Prange, MD (*University of North Carolina*)
E. H. Reynolds, MB, MRCP (*The National Hospital, London*)

The Unit carries out basic and clinical research on the causes and treatment of mental disorders. At West Park Hospital, Epsom, special metabolic investigations not ordinarily available in mental hospitals are carried out in a clinical investigation ward.

Summary of research

1. Biochemical and biophysical factors related to depressive illness and schizophrenia.
2. Biochemistry of the brain in normal subjects and in mental hospital patients.
3. Metabolic changes associated with maturation and with the functional activity of the brain.
4. Action of drugs and electrical shock treatment on the brain.
5. Anoxic damage to the brain during birth asphyxia and open-heart surgery.
6. Characteristics of evoked electrical responses in the brain.
7. Neurological sequelae of meningoencephalitis.
8. Metabolic factors related to mental subnormality and to epilepsy.
9. Central transmitter mechanisms in the brain.
10. Factors affecting RNA and protein metabolism of the brain.
11. Electrolyte changes in affective disorders.
12. Effects of hypoglycaemia and hypotension on the functions of the brain in rhesus monkeys and in human subjects.

MRC PSYCHIATRIC GENETICS UNIT

Institute of Psychiatry, Maudsley Hospital, Denmark Hill, London S.E.5
(01–703 9600 or 8585)

Director
E. T.O. Slater, CBE, MD, FRCP, DPM (*part-time*)

Senior staff

Mrs V. A. Cowie, MD, PH D, DPM (*part-time*)*
J. Kahn, PH D
J. S. Price, BM, DPM
Miss V. G. Seal (*part-time*)
J. Shields, BA

* On leave of absence at the National Institutes of Health, Bethesda, Maryland, from September 1968.

Consultant Adviser

J. L. Hamerton, D SC (*honorarium*)

The work of the Unit deals with the effect of genetic factors in producing any type of mental ill-health.

Summary of research

1. Follow-up study of monozygotic and same-sexed dizygotic twin pairs of which one member has been under treatment at the Maudsley Hospital for neurosis, personality disorder or schizophrenia since 1948.
2. Nature of personality resemblance in normal monozygotic twins and influences affecting it.
3. Familial factors in mental illness, including a study of bipolar affective psychosis.
4. Fertility and chromosome studies on parents of mongols and control populations.
5. Chromosome studies on systematic samples of boys from a remand home and the boys' wing of a prison and of women from a prison.

MRC CLINICAL PSYCHIATRY UNIT

Graylingwell Hospital, Chichester, Sussex

(0243 85171)

Director

P. Sainsbury, MD, MRCP, DPM

Senior staff

B. M. Barraclough, MB, MRCAP, DPM
Miss J. S. Bunch, MA
Mrs J. C. de Alarcon, PH D
R. de Alarcon, DR MED, DPM
A. I. M. Glen, MB, MRCP, DPM
J. D. Haines
B. E. Heine, MB, DCH, DPM
A. B. Levey, MA
Miss B. Nelson, DPSA
G. C. Ongley
J. C. Shaw, B SC

Attached worker

Professor D. Levine, PH D (*University of Nebraska*)

The Unit is concerned with the investigation of clinical problems in a psychiatric hospital and its community services. The main subjects of research are (1) clinical measurement of behaviour; (2) factors in the patients' social and family environment that relate to psychiatric illness; (3) suicide and its prevention, and (4) neurophysiological mechanisms underlying psychiatric symptoms.

Summary of research

1. Evaluation of a community psychiatric service; effects of clinical outcome and attitudes to mental illness.
2. Clinical and epidemiological aspects of suicide and its prevention.
3. Heroin dependency: prevalence and mode of spread; social and clinical characteristics of the heroin user.
4. Psychophysiological disorders: (*a*) prolonged anxiety and hypertension; (*b*) changes in membrane ion transport in the salivary duct in depression and other clinical conditions; (*c*) measurement of expressive movements and their psychological relationships.
5. Development of techniques for the spatial analysis of EEG and their application to clinical records.
6. Analysis of the conditioned eyeblink response to develop measures of its efficiency and to determine its relation to personality and maladaptive behaviour.

MRC SOCIAL PSYCHIATRY UNIT

Institute of Psychiatry, De Crespigny Park, London S.E.5
(01–703 5411)

Director
J. K. Wing, MD, PH D, DPM

Senior staff

C. R. Bagley, MA
J. L. T. Birley, BM, MRCP, DPM (*part-time*)
Miss J. M. Clarke, B SC (ECON)
Mrs A. M. Hailey, BA
J. P. Leff, B SC, MRCP, DPM
Miss E. J. Sproule, M SC
Miss B. C. Stevens, PH D

Attached workers

A. Binitie, MB, DPM (*University of Ibadan*)
M. Foncerrada, MD (*Paediatric Hospital National Medical Centre, Mexico City*)
A. Hakki, MB, DPM (*North East Metropolitan Regional Hospital Board*)
C. Schooler, PH D (*US National Institute of Mental Health*)
Mrs L. G. Wing, MD, DPM (*MRC External Staff*)

The Unit gives special attention to the measurement and classification of social and clinical abnormalities of the mentally ill and subnormal and to the evaluation of the effects of social methods of treatment.

Summary of research

1. Schizophrenia: (*a*) factors affecting social and clinical outcome in schizophrenic patients admitted to hospital for the first time; (*b*) clinical and social handicaps of schizophrenic patients in a London borough, and their need for services; (*c*) incidence of mental illness in close relatives of schizophrenic patients; (*d*) efficacy for out-patients of maintenance drug treatment compared with placebo; (*e*) verbal abnormalities in parents of schizophrenic patients compared with parents of patients with affective disorders; (*f*) symptomatology of schizophrenia in nine areas of the world (in collaboration with WHO).
2. Cumulative psychiatric disease reigster based on the population of a London borough (with grant from the Department of Health and Social Security).
3. Standardized diagnostic categorization of functional psychoses.
4. Development of autistic, aphasic, mongol and partially blind–partially deaf children.
5. Experimental evaluation of a psychiatric rehabilitation unit.
6. Comparison of matched patients admitted to a general hospital psychiatric unit and a mental hospital respectively.
7. Comparison of social milieu provided by different types of psychiatric ward.

MRC DEVELOPMENTAL PSYCHOLOGY UNIT

Drayton House, Gordon Street, London W.C.1
(01–387 4692)

Director
N. O'Connor, PH D

Senior staff

R. F. Cromer, PH D
Mrs U. Frith, PH D
Mrs B. M. F. Hermelin, PH D

Attached workers

Mrs N. Grieve, MD, DIP ED (*University of Melbourne*)
O. Petrovic, PH D (*University of Ljubljana*)

This Unit is studying the psychopathology of cognitive development, and is particularly concerned with the perceptual problems and the physiological responses of psychotic children and the neuropsychology of disturbed children.

Summary of research

1. Development and use of psychological and physiological methods of measuring the intellectual, behavioural and physiological responses of normal and handicapped children.
2. Analysis of patterns of intellectual and behavioural function and dysfunction that might lead to a more accurate diagnosis of abnormal and subnormal developmental states.
3. Planning of appropriate educational procedures on the basis of these patterns.

MRC UNIT FOR EPIDEMIOLOGICAL STUDIES IN PSYCHIATRY

University Department of Psychiatry, Royal Edinburgh Hospital,
Morningside Park, Edinburgh 10
(031–447 7489)

Honorary Director
Professor G. M. Carstairs, MD, FRCPE, DPM

Asistant Director
N. B. Kreitman, MD, DPM

Senior staff

Miss D. Buglass, BA, M PHIL
J. A. Clarke, MB, DPM
Miss P. Dugard, BA, SD (*part-time*)
Miss K. Friedlander, MA
P. F. Kennedy, MB, DPM
Miss I. M. K. Overstone, MB, DPH, DPM
A. E. Philip, PH D, DCP
A. Robertson, MA

Attached workers

Miss N. P. Chowdhury, B SC (*University of Edinburgh*)
J. C. Ebie, MB, DPM (*University of Ibadan*)
R. Hicks, MB, DPM (*University of Edinburgh*)
R. L. Kapur, MB, DPM (*University of Edinburgh*)
P. W. McTurk, MB (*Royal Edinburgh Hospital*)
I. Oswald, MB, D SC, DPM (*University of Edinburgh*)
J. Warder, BA (*University of Edinburgh*)

The Unit studies sections of the population in which there is a high risk of particular psychiatric illnesses and examines clinical, social and psychological features of illness in order to develop aetiological hypotheses. The long-term aim is to pave the way for preventive action.

Summary of research

1. Attempted suicide: epidemiology; psychological, cultural and ecological studies; suicidal behaviour in families; prediction of repetition; experimental assessment of after-care programme.
2. Agoraphobic housewives: clinical, familial, psychological and social aspects.
3. Neurosis in men and the psychiatric, psychological and social characteristics of their wives.
4. Adolescent psychiatric disorders: social and family adjustment; self-concept and perception of others.
5. Prison populations: prevalence of psychiatric illness; psychological classification of convicted prisoners; characteristics of violent offenders.
6. Data processing of in-patient and day hospital records.
7. Problem families: identification and service needs.
8. Classification of personality disorders in a hospital population.
9. Psychiatric wards: social structure and symptom fluctuation.
10. Student health: cultural, demographic, psychiatric and psychological prediction of student wastage and academic failure.

MRC UNIT ON ENVIRONMENTAL FACTORS IN MENTAL AND PHYSICAL ILLNESS

London School of Economics and Political Science, Houghton Street, Aldwych, London W.C.2
(01–405 7686)

Director

J. W. B. Douglas, BM, B SC

Senior staff

S. K. Bhattacharyya, M SC
A. J. Costello, MB, D OBST RCOG, DPM
J. D. Ingleby, BA
Mrs P. J. Leach, PH D
Miss J. M. Ross, B SC
M. E. J. Wadsworth, BA

Attached workers

Miss N. Cherry, B SC (*Population Investigation Committee*)
Mrs B. Dawson, MA (*City University, New York*)
D. Nelson, MA (*University of Edinburgh*)

This Unit was set up to study problems on the borderline of medicine and sociology and one of its aims is to promote the cooperation of doctors, sociologists and psychologists in joint research and in the development of new techniques.

Summary of research

1. National Survey of Health and Development—a longitudinal study of 5000 children born in March 1946: (*a*) environmental factors in education (with Rothamsted Experimental Station); (*b*) delinquency and maladjustment (with grant from the Home Office).
2. Vocational training and technical education (with grant from the Population Investigation Committee).
3. Development of observational techniques for assessing the social and intellectual development of children.
4. Factors influencing child-rearing patterns.

MRC MEDICAL SOCIOLOGY UNIT

Centre for Social Studies, Westburn Road, Aberdeen AB9 2ZE
(0224 23423)

Honorary Director

Professor Raymond Illsley, PH D

Senior staff

Miss J. Aitken-Swan, AIMSW, AHA
Professor Sir Dugald Baird, MD, BS C, FRCOG, DPH (*honorary*)
Miss S. H. M. Burt, MA
W. R. Bytheway, B SC
G. W. Horobin, B SC (ECON)
D. J. Oldman, MA
Miss E. D. B. Thompson, PH D

Attached workers

J. Cater, MB, CH B, MRCPE (*Action for the Crippled Child grant-holder*)
K. R. Davidson, MA (*St Francis Xavier University, Nova Scotia*)
C. Farmer, MA (*St Patrick's College, Ottawa*)
Miss L. S. Feldman, BA (*Harvard University*)
D. Gill, BA (*Scottish Education Department grant-holder*)
Mrs J. Kennedy, BA (*Association for the Aid of Crippled Children grant-holder*)
D. R. May, BA (*Scottish Home and Health Department grant-holder*)
J. B. McKinlay, BA (*Nuffield Provincial Hospitals Trust grant-holder*)
H. G. Popplestone, M SC (*Nuffield Provincial Hospitals Trust grant-holder*)
Miss M. Voysey, BA (*Nuffield Provincial Hospitals Trust grant-holder*)
A. J. Wootton, M SC (*Association for the Aid of Crippled Children grant-holder*)

The Unit collaborates with the University Departments of Obstetrics and Gynaecology, Child Health and Sociology in studies of the sociology of reproduction and child development and of the organization of related health and education services.

Summary of research

1. Social and obstetric factors in the history of handicapped children and family reactions to handicap.
2. Social antecedents and developmental consequences of complications of pregnancy and delivery.
3. Factors influencing differences in values, behaviour and intellectual attainment of children.
4. Fertility and family growth and planning in Aberdeen.
5. Social factors in illegitimate maternities and the process and consequences of adoption.
6. Patterns of marriage and fertility in tropical Africa and their obstetric and paediatric implications.
7. Therapeutic abortion in Aberdeen : the decision-making processes; characteristics of the women concerned and effects of the decision made.
8. Distribution of health problems in Aberdeen and the utilization of health services.

MRC UNIT ON OCCUPATIONAL ASPECTS OF AGEING

University Department of Psychology, 7 Abercromby Square, Liverpool 7
(051–709 5351)

Honorary Director
Professor L. S. Hearnshaw, MA

Honorary Medical Adviser
Professor A. B. Semple, CBE, VRD, MD, DPH, QHP

Honorary Scientific Advisers
D. B. Bromley, PH D*
M. G. Davies, PH D (*until Mar. 1969*)

Senior staff
Miss H. M. Cameron, MA
Mrs G. R. Hearnshaw, PH D (*part-time*)
Mrs A. C. Owens, MBE, PH D (*part-time*)
R. Slater, M PHIL
J. M. Smith, BA
Miss J. S. Sullivan, BA

Attached workers
Mrs A. D. M. Davies, PH D (*University of Liverpool*)
H. H. Whincup, MB (*Treasury Medical Service*)

The Unit is studying the psychological changes that accompany increasing chronological age, particularly the changes in those over 40 years considered likely to be of occupational importance. Both laboratory and field investigations are carried out.

Summary of research

1. Vigilance behaviour and temporal expectancy, with special reference to ageing.
2. Adult learning and the problems of retraining and rehabilitation of older persons.

MRC APPLIED PSYCHOLOGY UNIT

15 Chaucer Road, Cambridge CB2 2EF
(0223 55294)

Director
D. E. Broadbent, SC D, FRS

Assistant Directors
R. Conrad, PH D†
E. C. Poulton, MB

* On leave of absence at the Philadelphia Geriatric Center.

† Seconded to the Nuffield Hearing and Speech Centre, Royal National Throat, Nose and Ear Hospital, London.

Senior staff

Mrs P. M. E. Altham, BA
I. D. Brown, PH D
A. Carpenter, MB
W. P. Colquhoun, PH D
D. W. J. Corcoran, PH D
A. Davidson
Miss K. E. M. Fox, B TECH
Mrs M. H. P. Gregory, MB
P. Hamilton, PH D
M. Hammerton, PH D
L. R. Hartley, B SC
G. R. J. Hockey, B SC
C. M. Holloway, PH D
J. N. T. Martin, MA
J. Morton, PH D
S. D. G. Stephens, MB, B SC
R. T. Wilkinson, PH D
Miss M. M. Woodhead
Miss P. A. M. Wright, PH D

Attached workers

Miss N. S. Anderson, PH D (*University of Maryland*)
Miss S. A. Fisher, B SC (*MRC Scholar*)
G. J. Hitch, M SC (*MRC Scholar*)
H. Loess, PH D (*College of Wooster, Ohio*)
M. I. Posner, PH D (*University of Oregon*)
R. O. Rouse, PH D (*Williams College, Massachusetts*)
A. J. Sanford, B SC (*MRC Scholar*)

The Unit observes and measures human behaviour, usually by experiment. The aim is to establish general principles governing healthy human performance in various types of work and various environments.

Summary of research

1. Perception: (*a*) alertness during prolonged listening and looking; (*b*) relationship between attention and evoked cortical responses; (*c*) experimental comparisons of different type faces and printed layouts; (*d*) effect of response bias on sensory judgments; (*e*) factors affecting conversation and the intelligibility of speech; (*f*) identification of complex patterns; (*g*) design of currency conversion tables.
2. Thinking and memory: (*a*) decision theory in relation to human performance; (*b*) speed and load stress in decision taking; (*c*) design of computer codes; (*d*) factors affecting immediate memory; (*e*) verbal learning; (*f*) pupil size as an index of mental effort.
3. Response: (*a*) factors affecting control by man as an element in a servo system; (*b*) experiments on car driving performance; (*c*) performance in use of the national telephone system.
4. Working conditions: (*a*) achievement after reduced amounts of sleep; (*b*) efficiency on first being woken up; (*c*) effects of high intensity noise, heat, small doses of alcohol, other drugs and toxic substances; (*d*) effects of combined stresses.
5. Methods: (*a*) assessment of degree of confidence in experimental results; (*b*) mathematical models for human performance; (*c*) development of portable apparatus for assessing deterioration of skill; (*d*) automatic data reduction techniques.

MRC SOCIAL AND APPLIED PSYCHOLOGY UNIT

Department of Psychology, University of Sheffield, Sheffield S10 2TN
(0742 78555)

Honorary Director
Professor H. Kay, PH D

Assistant Director
P. B. Warr, PH D

Senior staff

R. G. Crabtree, M SC
G. W. A. Hespe, B SC
A. J. Little, BA
M. E. Sime, BA

The Unit's primary interest is in complex judgment and decision-making. These processes are being investigated in industrial and other settings to develop models with practical significance as well as theoretical value. Field studies are particularly emphasized, but laboratory projects also form an important part of the Unit's work.

Summary of research

1. Integrated computer–manager systems of decision-making.
2. Probability and pay-off variables in risk-taking situations.
3. Judgments about industrial participation and productivity.
4. Achievement motivation and other personality variables.
5. Judgments about people.

MRC SPEECH AND COMMUNICATION UNIT

University of Edinburgh, 31 Buccleuch Place, Edinburgh 8
(031–667 1011 and 5265)

Director
Professor R. C. Oldfield, MA

Senior staff

Mrs C. M. Armstrong, B SC
Mrs E. A. Carswell, PH D
Miss C. V. Gamsu, BA
G. R. Kiss, B SC
J. C. Marshall, PH D
T. F. Myers, B SC

Attached workers

J. Hosier, BA (*MRC Scholar*)
Miss L. Lane, B SC (*MRC Scholar*)
S. H. McDonough, BA (*MRC Scholar*)
P. V. Mathews, B SC (*MRC Scholar*)
T. J. Powell, BA (*MRC Scholar*)
T. G. Steward, BA (*MRC Scholar*)
R. J. Wales, B SC (*University of Edinburgh*)

The aim of the Unit is the investigation of psychological processes underlying language and other forms of communication in both normal and pathological conditions.

Summary of research

1. Psychological processes connected with grammatical, syntactical and semantic aspects of normal and disordered speech.
2. Object identification and object naming in normal and brain-injured individuals.
3. Factors affecting control of amount, speed, loudness and articulation of speech.
4. Disorders of language development in children.
5. Speech in Parkinsonism and other disorders of the basal ganglia and brain stem.
6. Cerebral dominance and handedness in relation to speech and musical functions.
7. Structure and function of verbal association networks.
8. Some linguistic and some non-linguistic factors in speech perception.

MRC SOCIAL MEDICINE UNIT

London School of Hygiene and Tropical Medicine, Keppel Street, London W.C.1
(01–636 8636)

Honorary Director
Professor J. N. Morris, D SC, FRCP, DPH, DCH

Assistant Director
J. A. Heady, PH D

Senior staff

J. S. A. Ashley, MB
R. T. Benn, M SC
S. P. W. Chave, PH D (*honorary*)
Miss J. Cooper, AIS (*honorary*)
Mrs M. D. Crawford, MD (*part-time*)
M. J. Gardner, B SC, DIP MATH STAT
T. Griffith, BA
Miss J. W. Marr, MBE, SRD
T. W. Meade, MRCP (*honorary*)
M. J. Power, DIP SS
Mrs E. A. J. Scott, MB (*part-time*)

Attached workers

A. B. Ford, MD (*Case Western Reserve School of Medicine, Cleveland*)
M. Kramer, S CH (*US National Institutes of Health*)
Professor C. B. Kerr, MB, D PHIL, MRACP (*University of Sydney*)

The Unit investigates the influence of social factors on health and sickness, and the relationship of social to other factors. Studies are made of populations and their environments, and individuals are studied in relation to these.

Summary of research

1. Cardiovascular studies: (*a*) incidence and prediction of ischaemic heart disease in London busmen in relation to nature of work and other factors, including physique and obesity, diet, blood pressure, blood lipids and family history; (*b*) trial of reduction of high blood lipid levels in healthy men—prospective study of ischaemic heart disease (with Edinburgh Royal Infirmary, Edinburgh Blood Transfusion Service, Institute for Cardiovascular Research, Prague, and Hungarian Institute of Cardiology, Budapest); (*c*) relationship of leisure activity to health in middle-aged men—prospective study in executive class civil servants; (*d*) relationship of cardiovascular disease to hardness of water and other local factors in British towns; (*e*) epidemiology of peripheral vascular disease.
2. Social studies: (*a*) patterns of leisure in middle-aged men; (*b*) juvenile delinquency in East London—clinical and epidemiological prediction of chronicity.
3. Current trends in morbidity and mortality: (*a*) incidence of ischaemic heart disease and duodenal ulcer in physicians; (*b*) death rates in British towns in relation to social features.
4. Working of the health services: hyperplasia of prostate in several teaching and non-teaching hospitals—background of the patients, their condition on admission, the care received and the outcome.

MRC ENVIRONMENTAL PHYSIOLOGY UNIT

London School of Hygiene and Tropical Medicine, Keppel Street, London W.C.1

(01-636 6084)

Director

Professor J. S. Weiner, PH D, MRCS

Senior staff

C. R. Bell, BA
K. J. Collins, D PHIL
G. W. Crockford, B SC
M. J. Crowder, B SC
C. T. M. Davies, PH D
J. D. Few, M SC
K. G. Foster, B SC
Miss J. L. Hubbard, B SC
E. S. Reeves
A. J. Watts, B SC (ECON)

Attached worker

G. J. Davies, B SC (*Sports Council Bursar*)

The investigations of the Unit are concerned with anatomical, physiological and ergonomic problems arising in the working environment.

Summary of research

1. Limits of tolerance for work at high temperatures and humidity, with reference to different patterns of work and posture, and in relation to age and physique.
2. Physiology of muscular work, including athletic performance.
3. Survey of fitness as measured by work capacity in various groups, e.g. schoolchildren, industrial workers, sportsmen.
4. Relationship of raised body temperature to performance in high-temperature environmental conditions.
5. Intense radiant heat in relation to the development of protective clothing.
6. Biochemistry and histochemistry of sweat gland activity in man and animals.

7. Growth and heat tolerance of animals at high temperatures, with particular reference to genetic factors.
8. Role of endocrine glands in heat adaptation.
9. Fluid and electrolyte balance during heat exposure in man.
10. Neurological basis of temperature regulation.
11. Development of sweat responses in the newborn human.

MRC TOXICOLOGY UNIT

Medical Research Council Laboratories, Woodmansterne Road, Carshalton, Surrey

(01-643 4461)

Director

J. M. Barnes, CBE, MB

TOXICOLOGY

Senior staff

W. H. Butler, MB
E. B. Casey, MB, MRCP
Miss V. M. Craddock, PH D
R. C. Emery
Miss P. M. Fullerton, DM, MRCP (*part-time*)
S. Gibbard, M SC
G. C. Hard, B V SC, PH D
J. A. E. Jarvis
C. R. Kennedy, AIMLT
R. F. Legg, AIMLT
L. Magos, DR MED
A. R. Mattocks, PH D
Miss M. J. Ord, PH D*
Miss R. Schoental, D SC
C. Turberville, BA
J. M. A. Vacher, DR MED

Attached worker

W. Dieckmann, D VET MED (*Research Fellow, European Society for Study of Drug Toxicity*)

BIOCHEMICAL MECHANISMS

Senior staff

W. N. Aldridge, PH D (*Head of Section*)
Miss J. E. Cremer, PH D
F. De Matteis, PH D, LAUREA MED CHIR
A. R. Henderson
M. K. Johnson, PH D, ARCS, ARIC
P. E. Morrow, PH D
V. H. Parker, B SC
M. S. Rose, PH D
M. D. Stonard, B SC
B. W. Street, AIMLT

Attached workers

R. R. G. Lauwreys, MD (*University of Louvain*)
Miss E. Reiner, PH D (*Institute for Medical Research, Zagreb*)

EXPERIMENTAL PATHOLOGY OF TRAUMA

Senior staff

H. B. Stoner, MD, B SC, MC PATH (*Head of Section*)
R. N. Barton, B SC
Mrs P. L. Corney, B SC
D. F. Heath, D PHIL
R. A. Little, B SC
R. Plestina, DR MED
C. J. Threlfall, B SC
K. D. Wilford

The aim of the Unit is to establish the basic concepts necessary for explaining at a molecular level the mechanisms of toxicity and of chemical and physical tissue injury.

Summary of research TOXICOLOGY

1. Changes in nucleoproteins and histones induced by nitrosamines.
2. Early cellular damage produced by liver poisons.
3. Evolution of renal tumours induced by dimethylnitrosamine.
4. Metabolism of pyrrolizidine alkaloids.
5. Toxic effects of carbon disulphide in rats.

* Working in the University of Southampton.

6. Immune responses to beryllium in guinea pigs.
7. Toxic substances in woods.
8. Clinical features of toxic neuropathies.
9. Identification of the sites of action of toxic substances in *Amoeba proteus* (at the University of Southampton).

BIOCHEMICAL MECHANISMS

1. Sites of interaction of trialkyl tins and beryllium with specific proteins.
2. Disturbances of oxidative phosphorylation produced by trialkyl tins, uncoupling agents, dichlorovinylcysteine, alkylating agents etc.
3. Phosphorylation of proteins and the delayed neurotoxicity produced by certain organophosphorus compounds.
4. Nature of metabolic compartments in brain derived from studies of drugs acting on the central nervous system.
5. Biochemical effects of acrylamide *in vivo* and *in vitro*.
6. Control of liver δ-aminolaevulate synthetase and the metabolic fate of liver haem, with particular reference to cytochrome *p*-450.

EXPERIMENTAL PATHOLOGY OF TRAUMA

1. Effects of environment, including cold acclimation, and of drugs acting on the metabolism of the sympathetic nervous system after injury from limb ischaemia and scalds.
2. Quantitative studies on carbohydrate and fat metabolism in rats in pathological states.
3. Responses to injury in the newborn rabbit.

MRC PNEUMOCONIOSIS UNIT

Llandough Hospital, Penarth, Glamorgan CF6 1XW
(0222 708761)

Director

J. C. Gilson, CBE, MB, FRCP

Senior staff

G. Berry, MA
N. E. Bevan, M SC
W. G. Clarke, MSR (*honorarium*)
Mrs J. A. Cobb, MB, DA (*part-time*)
Miss M. M. Collins
G. F. Cory (*Administrative Officer*)
J. E. Cotes, DM, FRCP
A. S. Davies, B SC
S. E. Davies, MB, B SC
S. Y. Ghobrial, DR MED
C. Gold, MB, D OBST RCOG
Mrs M. McDermott, B SC
C. B. McKerrow, MD, FRCP
T. G. Morris, PH D
J. M. Müller, DR MED
P. D. Oldham, MA
J. A. Reynolds, AMIERE
C. E. Rossiter, MA
M. J. Saunders
J. W. Skidmore
V. Timbrell, PH D, F INST P
Chang-hyun Um, DR MED
J. C. Wagner, MD, MC PATH

Attached worker

Mrs M. M. F. Wagner, MB, MC PATH (*Welsh Hospital Board Research Fellow*)

The Unit uses a multidisciplinary approach to discover the effect of industrial dusts and fumes on the lungs, the type of disability caused and the natural history of the associated diseases. The work covers studies in epidemiology, lung function, dust physics and chemistry, morbid anatomy, immunology, experimental pathology, biochemistry, radiology, treatment and statistics. Many of the projects are cooperative investigations with other workers in this country and overseas.

Summary of research

1. Asbestos: national and international surveys of the health hazards of asbestos dusts; investigation of the carcinogenic and fibrogenic action of the principal types of asbestos following intrapleural injection and quantitative inhalation in rats.
2. Beryllium: survey of beryllium workers and treatment of those with early beryllium disease.

3. Cotton dust: prospective surveys of byssinosis in cotton workers; studies of the mode of action of cotton and other dusts by experimental inhalation.
4. Foundry and mixed dusts: determination of the dose–response relationship of radiological pneumoconiosis and bronchitis in a UK survey of foundry workers; relationship of radiological category of pneumoconiosis to dust content and other variables in the lungs.
5. Isocyanates: immediate and long-term effects on lung function following exposure to foaming agents.
6. Effect of shape, size and aerodynamic properties of fibres on their penetration into the lungs; preparation, characterization and distribution of UICC reference samples of asbestos.
7. Assistance to the International Biological Programme in development of tests of lung function and exercise capacity for use in diverse ethnic groups.
8. Ventilation–perfusion imbalance in early chronic bronchitis; relation of the transfer factor of carbon monoxide to the type of simple pneumoconiosis.

MRC AIR POLLUTION UNIT

St Bartholomew's Hospital Medical College, Charterhouse Square,
London E.C.1
(01–253 1537)

Director
Professor P. J. Lawther, MB, FRCP

Senior staff
B. J. Biles
A. G. F. Brooks
B. T. Commins, PH D, FRIC
Miss T. Davies, B SC
C. J. Derrett, B SC
J. McK. Ellison, PH D, F INST P
R. E. Waller, B SC

The Unit is concerned primarily with the investigation of the clinical aspects of air pollution as it affects general and industrial populations. Studies are being made on the physical and chemical characteristics of pollutants and on the significance of polluted air, especially in relation to lung cancer and chronic bronchitis. The Unit is designated the WHO International Reference Centre on Air Pollution.

Summary of research

1. Physical and chemical characteristics of pollution.
2. Analytical techniques for determination of pollutants in urban atmospheres.
3. Possible adsorption of sulphur dioxide on particles and its oxidation to sulphuric acid.
4. Determination of carcinogenic substances in town air and in industrial atmospheres.
5. Health hazards of emissions from motor vehicles, with special attention to polycyclic hydrocarbons and carbon monoxide.
6. Effects of pollutants on pulmonary function.
7. Variations in mortality, in the demands for hospital admission and in the clinical condition of patients with chronic bronchitis and emphysema in relation to daily changes in weather and air pollution.
8. Analysis of data on lung cancer mortality in relation to urban factors.
9. Daily variations in the respiratory function of normal subjects.
10. Respiratory function in patients with occupational disease of the lungs.
11. Chemical constitution of irritant and toxic chemicals, including carcinogens, and their mode of action.
12. Optical methods of assessing particulate pollution and of identifying pollutants.
13. Theoretical study of the lung as a pneumatic system.
14. Chemical and physical properties of various forms of asbestos in relation to their carcinogenicity.
15. The possible effects of air pollutants on the growth and morphology of *Haemophilus influenzae* and other respiratory pathogens.

MRC INDUSTRIAL INJURIES AND BURNS UNIT

Birmingham Accident Hospital, Bath Row, Birmingham 15
(021–643 7041)

Director
J. P. Bull, MD, FRCP

Senior staff

G. A. J. Ayliffe, MD, MC PATH
Miss S. Baar, PH D, FRIC
Mrs S. A. Carney, PH D (*part-time*)
J. W. L. Davies, PH D
Miss S. P. Farrow, M SC
M. Hall, AIMLT
D. MacG. Jackson, MD, FRCS (*part-time*)
R. J. Jones, PH D
J. C. Lawrence, PH D
H. A. Lilly, FIMLT
E. J. L. Lowbury, DM, FC PATH
Miss F. A. Pettit, B SC
C. R. Ricketts, D SC

Attached worker
Miss M. B. Leeming, MB, DA, FFARCS (*MRC grant-holder*)

The Unit studies the causes, local and general pathology, complications and treatment of burns and other injuries. There is close liaison with the staff of the Birmingham Accident Hospital; special studies of hospital infection are made in the Hospital Infection Research Laboratory at Summerfield Hospital under the supervision of Dr Lowbury.

Summary of research

1. Causes and prevention of common injuries.
2. Characterization and circulatory effects of infused colloids; their use for measuring permeability.
3. Metabolic changes in injured patients; effects on the turnover of plasma proteins; modification of metabolic changes by therapy.
4. Assessment of patient-monitoring equipment for severe injuries and burns.
5. Biochemical changes in heated red cells and in the red cells from burned patients.
6. Metabolic changes in cultured skin injured by toxic substances, heat and radiation from laser, microwave and ultrasonic sources.
7. Effects of bacterial infection on patients with burns; antigenic and enzymic components of *Pseudomonas aeruginosa* and their immunizing properties in animals and man.
8. Epidemiology of infection of burns and wounds; its relation to theatre and ward hygiene; controlled trial of isolators.
9. Survival of pathogens in different environments and methods of control.
10. Controlled trials of local chemotherapy and chemoprophylaxis for infection of burns and wounds.
11. Epidemiology of respiratory infection in patients with tracheostomies after severe injury.

MRC POWERED LIMBS UNIT

West Hendon Hospital, Goldsmith Avenue, The Hyde, London N.W.9
(01–205 6363)

Director
A. B. Kinnier Wilson, MB, MRCP, DPM

Senior staff

J. C. Chapman, B SC
W. Godfrey, MIST
R. P. J. G. McWilliam, BA
S. R. Montgomery, SC D (*part-time*)
R. E. Reilly, M SC

Attached workers

G. E. Fulford, MB, FRCS (*Princess Margaret Rose Orthopaedic Hospital and Western Hospital, Edinburgh*)
Miss A. R. Carter, BA (*University of Cambridge*)

The Unit conducts research on therapeutic engineering for the limbless and paralysed, and for this purpose it adopts a multidisciplinary approach, involving aspects of both biology and engineering, to the development of advanced motorization and control systems for artificial limbs and splints.

Summary of research

1. Development of a comprehensively designed gas-powered artificial arm for 7–12 year-old patients, with special attention to fitting the movements and forces used to the tasks of everyday life and suiting the controlled prosthetic outputs to the controlling actions of the patient.
2. Development of (*a*) implanted externally energized EMG sensors; (*b*) the control logic and power systems for a multijoint myoelectrically controlled artificial arm.
3. Development of further improved powered arm splints for ambulant patients.
4. Development of electrohydraulically powered arm splints for chair-bound patients.
5. Systems analysis of the forces, powers and work required from powered limbs and of the associated energy storage and conversion problems.

MRC NEUROLOGICAL PROSTHESES UNIT

Institute of Psychiatry, De Crespigny Park, Denmark Hill, London S.E.5
(01–703 5411)

Honorary Director
Professor G. S. Brindley, MD, MRCP, FRS

Consultants in Neurosurgery
M. A. Falconer, M CH, FRCS, FRACS
W. S. Lewin, MS, FRCS

Senior staff
P. E. K. Donaldson, MA

The Unit is working towards the development of implantable protheses to replace tracts of nerve fibres of the central nervous system that have been destroyed, or have been made useless because of the destruction of sense organs.

Summary of research

1. Construction, insertion and investigation of radio-controlled stimulators of the human striate cortex.
2. Experiments on animals directed towards the development of implantable prostheses for the partial replacement of destroyed tracts of cerebral or spinal white matter.

MRC STATISTICAL UNIT*

University College Hospital Medical School,
115 Gower Street, London W.C.1
(01–387 7651)

Director
W. R. S. Doll, OBE, MD, D SC, FRCP, FRS

Scientific staff
J. T. Boyd, MB, DPH
Miss P. J. Cook, MA, B LITT
Miss C. Duncan, B SC
Mrs P. M. Fraser, MB
R. Peto, M SC
M. C. Pike, PH D†
I. Sutherland, D PHIL
M. P. Vessey, MB

Attached workers
F. E. Speizer, MD (*University of Stanford, California*)
M. Stukonis, MD (*Oncological Research Institute, USSR*)

* Certain aspects of the programme of the Statistical Unit are to be incorporated in the work of the Clinical Research Centre (p. 108) and others in the work of a new Statistical Research and Services Unit (under the direction of Dr. I. Sutherland).

†Seconded to Makerere University College, Kampala, Uganda.

The Unit is concerned with the development and application of statistical methods in medicine and in the associated sciences, including research into the epidemiology and aetiology of disease, the promotion and analysis of vital statistics, the design and analysis of therapeutic trials of new drugs and other agents, the design and analysis of field trials of prophylactic agents and the application of mathematical–statistical techniques to the solution of laboratory and epidemiological problems. The investigations listed in the summary of research include collaborative work undertaken with other Council units, Council committees and other scientific workers.

Summary of research

EPIDEMIOLOGY AND AETIOLOGY OF DISEASE

1. Aetiology of cancer of the lung and chronic bronchitis, with particular reference to smoking, air pollution and occupation.
2. Epidemiology of various cancers, including leukaemia, Burkitt's lymphoma and cancers of the bone, nasal sinuses, cervix uteri and oesophagus.
3. Incidence of cancer in tropical countries, particularly East Africa and Fiji.
4. Mechanism of carcinogenesis.
5. Long-term effects of smoking, ionizing radiations, industrial employment (e.g. in asbestos and gas industries) and oral contraceptives.
6. Causes of death in asthmatics.
7. Epidemiology of pulmonary tuberculosis, mycobacterial infections in East Africa, measles and whooping cough.
8. Analysis of secular trends in the transmission of tuberculosis infection.

THERAPEUTIC AND PROPHYLACTIC TRIALS

1. BCG and vole bacillus vaccine in the prevention of tuberculosis; BCG vaccines in the prevention of leprosy and *Mycobacterium ulcerans* infection.
2. (*a*) Treatment of cancer, including leukaemia, myelomatosis, malignant melanoma and Burkitt's lymphoma; (*b*) use of radiotherapy under high-pressure oxygen; (*c*) treatment of *Mycobacterium ulcerans* infection, tetanus, myocardial infarction, gastric ulcer and depressive illness.
3. Effectiveness of intrauterine contraceptives in Britain and Africa and of oral progestogen contraceptives in Slovenia.

MATHEMATICAL STATISTICS AND COMPUTER SCIENCE

1. Fitting mathematical models to observations on cancer incidence.
2. Application of bioassay techniques to radiobiology.
3. Computer-aided diagnosis of hypercalcaemia and liver disease.
4. Recognition of small epidemics of endemic diseases.
5. Efficient analysis of randomized clinical trials.

MRC COMPUTER UNIT (LONDON)

242 Pentonville Road, London N.1

(01–837 7842)

Director

C. C. Spicer, MRCS, DIP BACT, FSS

Senior staff

R. Ellams, M SC
R. M. Greenwood, MB, PH D
I. D. Hill, B SC
J. R. Jagoe, BA
Mrs J. Pateman, B SC
K. Paton, PH D
Mrs A. Williamson, MS (*part-time*)

Computer Manager

B. J. Paton

The computer finally passed its acceptance tests at the end of November 1968. Most of the year has had to be spent in writing service programs and in testing the software associated with the machine, but computing and statistical assistance has been given to the Council's staff.

MRC LABORATORY ANIMALS CENTRE

Medical Research Council Laboratories, Woodmansterne Road, Carshalton, Surrey
(01–643 4461)

Director
J. Bleby, B VET MED, MRCVS

Senior staff
D. K. Blackmore, PH D, FRCVS
M. F. W. Festing, PH D
J. L. Izard
Miss D. G. Owen, M SC
G. Porter, M INST BIOL
M. Robinson, BA, M INST BIOL
G. H. Townsend, MRCVS, DTVM, DVSM

Attached workers
G. M. F. Juldeh (*Nigerian Institute for Trypanosomiasis Research*)
U. Thein Han, B SC (*Laboratory Animals Breeding Unit, Burma Pharmaceutical Industry*)
M. Varga (*Laboratory Animals Institute, Godollo, Hungary*)
S. Zidek (*Czechoslovak Academy of Sciences*)

The Centre's object is to make more readily available to laboratories animals of a type and quality best suited to their requirements. It has four main functions: (1) to act as an exchange for information and to advise on all problems concerning laboratory animals and their housing and to maintain liaison with similar organizations in other countries, for which purpose it prepares newsletters, catalogues, handbooks, films and other material for distribution to other laboratories, and administers an accreditation scheme for commercial breeders; (2) to maintain, under controlled (pathogen-free) conditions, primary-type colonies of special strains for issue as breeding nuclei; (3) to conduct relevant research; (4) to train staff, both graduate and technical.

Summary of research

1. Genetics of reproductive performance of mice and methods of large-scale production of mice and rats conforming to a given genetic specification and to certain standards of health and nutrition, including the development of specific-pathogen-free (SPF) colonies.
2. Control of health in large laboratory populations of high density, especially in conditions of rigorous isolation.
3. Combined morbid anatomical and microbiological studies to ascertain the common causes of death of laboratory animals.
4. Formulation, compounding and assessment of diets for laboratory animals, and methods of sterilizing food.
5. Observations on the effects of housing SPF animals under conventional conditions and the effects of environment on reproduction.
6. Preparation of index of laboratory animals maintained by laboratories and breeders throughout the world.
7. Breeding and maintenance of germ-free and gnotobiotic (i.e. with defined bacterial flora) animals.
8. Internal and external parasites of laboratory animals and their control.
9. Determination of optimum environmental husbandry and the development of barrier maintenance.

External Scientific Staff

The Council appoints to its staff a small number of individual research workers, who are based for the most part in university departments.

Birmingham

GENERAL HOSPITAL

Department of Surgery

J. A. WILLIAMS, CH M, FRCS (*part-time*)

1. Comparison of haematological and metabolic status of patients after partial gastrectomy and after vagotomy and pyloroplasty.
2. Data recording in gastrointestinal disease: computer storage of clinical data and automation of follow-up procedure.
3. Natural history and aetiology of postvagotomy diarrhoea.

UNIVERSITY

Experimental Pathology Department

P. WOLF, MD

A. HOWARD, B SC*

Immunochemical characterization of human plasminogen.

Renal Research Laboratory, Queen Elizabeth Hospital

J. D. BLAINEY, MD, FRCP (*part-time*)

J. B. WHITFIELD, M SC

1. Biochemistry of the organic acids of the citric acid cycle, with particular reference to renal failure and effects of dialysis.
2. Significance of small-molecular-weight protein and enzymes in urine.
3. Natural history of glomerulonephritis: long-term clinical, biochemical and histological studies.
4. Specific antibody proteins in human and animal urine in nephritis.

Cambridge

STRANGEWAYS RESEARCH LABORATORY†

Miss J. M. ALLEN, B SC

1. Mechanism of attachment and ingestion of bacteria by macrophages (with Dr G. M. W. Cook).
2. Phagocytosis and digestion of particles and bacteria by macrophages: effect of drugs on these processes.

G. M. W. COOK, PH D (see also under Miss J. M. ALLEN)

1. Plasma membranes and their glycoproteins.
2. Electrophoretic and biochemical properties of cell surfaces.

J. T. DINGLE, PH D

P. E. N. MARTIN

1. Lysosomes: storage of dyes and carcinogens; synthesis, secretion and antigenicity of enzymes; roles in reproductive physiology (with ARC Unit of Reproductive Physiology and Biochemistry).
2. Mode of action of calcitonin.
3. Extracellular and intracellular digestion of skeletal matrix (with Dame Honor Fell).

* Seconded from the MRC Rheumatism Unit.

† The Strangeways Research Laboratory receives a block grant from the Council and further information about its work is given on p. 181. Many of the investigations listed above were carried out in collaboration with staff of the Laboratory.

Dame HONOR FELL, DBE, D SC, FRS (*honorarium*; see also under Dr J. T. Dingle)
Effects of antibodies on bone, cartilage and thyroid in culture (with Dr J. T. Dingle and with Professor R. R. A. Coombs, University of Cambridge).

Miss S. FITTON JACKSON, PH D
1. Morphogenesis: stages in formation of collagen, protein polysaccharides and keratin.
2. Regulation of the synthetic balance in skeletal tissue.
3. Interaction between intercellular macromolecules and cell surfaces in connective tissues.

M. WEBB, D SC
Mrs K. M. SMITH, BA
1. Magnesium and zinc metabolism in mammalian cells; metalloprotein synthesis in the prostate.
2. Biochemistry of metal carcinogenesis.
3. Biochemical aspects of vitamin-A-induced mucous metaplasia in embryonic chicken epidermis.

D. J. WIGGLESWORTH, FDS
Role of vitamins in the development of teeth in culture.

UNIVERSITY

Department of Biochemistry: Subdepartment of Chemical Microbiology
R. DAVIES, PH D
1. Stimulation of enzyme formation in yeasts by cyclic dipeptides of arginine and proline.
2. Action of sulphydryl compounds on yeast cell-wall structures.
3. Synthesis of cyclic dipeptides.

Chemical Laboratory
Mrs O. KENNARD, MA, F INST P (with Mr D. Chenery and members of the Crystallography Group, University Chemical Laboratory)
1. Analysis of the structure of organic phosphates, including the sodium salt of ATP, as part of an X-ray investigation of the high-energy phosphate bond.
2. Structure of medium-sized molecules (steroids, natural products) of biological interest.
3. Compilation of a computerized library of organic structures to correlate common features.

Psychological Laboratory
Miss A. W. HEIM, PH D, FB PS S
Miss K. P. WATTS
E. G. CHAMBERS, MA (*honorarium*)
1. Development of psychological tests: self-judging vocabulary, shapes analysis, word-in-context and two versions of a high-grade intelligence test.
2. Brook reaction: a test to assess interests and personal adjustment.
3. Use of these tests in experimental inquiries into such problems as student selection and specialization and for psychiatric diagnosis.

Miss M. A. VINCE, BA
R. E. ADKINS, B SC
Mrs D. LEWITTER, MA (*part-time, technical staff; until Jan. 1969*)
1. Signals produced by embryo quails that can accelerate or retard their siblings' time of hatching; developmental stages associated with these signals and the mechanism of synchronization.
2. Effects of pre-hatching stimulation on later physique and behaviour.
3. Effects of stimulation on the establishment of lung ventilation.

Federal Cameroon Republic

CENTRE MEDICAL DE RECHERCHES, KUMBA

Helminthiasis Research Unit
B. O. L. DUKE, OBE, MD, MRCP, DTM & H
R. H. L. DISNEY, BA
1. Trials of drugs against *Onchocerca volvulus*
2. Bionomics of *Simulium damnosum;* transmission and control of onchocerciasis.
3. Control of urinary schistosomiasis in isolated foci by combined attack with drugs and molluscicides.

Cirencester

PUBLIC HEALTH LABORATORY SERVICE

Epidemiological Research Unit

R. E. HOPE-SIMPSON, OBE, MRCS (*part-time*)

1. Natural history of influenza viruses and of other viruses causing common respiratory infections in a general practice.
2. Latent infection.
3. Convulsive disorders in young persons: long-term cooperative study.

Dartford Heath, Kent

BEXLEY HOSPITAL

D. BANNISTER, PH D, DIP PSYCH (*part-time; with grant for assistance*)

J. R. ADAMS-WEBBER, PH D

W. I. PENN, M PHIL

A. R. RADLEY, B TECH

1. Assessment and experimental modification of schizophrenic thought disorder.
2. Development of repertory grid methods of conceptual analysis.
3. Application of personal construct theory concepts to psychiatric problems.

Edinburgh

WESTERN GENERAL HOSPITAL

Gastrointestinal Unit and Department of Medicine

W. SIRCUS, MD, PH D, FRCP, FRCPE (*part-time*)

1. Diseases of small and large bowel.
2. Peptide-secreting adenomas.
3. Gastric secretion.

London

BRITISH MUSEUM (NATURAL HISTORY)

D. S. BROWN, PH D

1. South African freshwater snails, with special reference to schistosomiasis (with Professor J. A. Van Eeden, University of Potchefstroom, Transvaal).
2. Ethiopian freshwater snails in relation to schistosomiasis (with Dr C. A. Wright, British Museum, and Dr A. Lemma, Haile Selassie I University, Addis Ababa).

D. J. LEWIS, SC D

1. Phlebotaminae (sandflies), with special reference to vectors of leishmaniasis and to species from the oriental zoogeographical region and Aldabra, Cameroons, Egypt, Kenya, Nigeria, South Africa, Sudan, Trinidad, Tunisia and Uganda.
2. Simuliidae (blackflies), with special reference to vectors of onchocerciasis and to species from the Cameroons, Ivory Coast and Upper Volta.

CENTRAL PUBLIC HEALTH LABORATORY, COLINDALE

Cross-Infection Reference Laboratory

O. M. LIDWELL, D PHIL

N. FOORD, B SC

D. KINGSTON, MA*

R. SPEERS, PH D

1. Cross-infection in hospitals: effect of ventilation, ward subdivision and other environmental conditions.
2. Protective isolation of highly susceptible hospital patients: assessment of various constructions and nursing procedures.

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* Seconded to the MRC Rheumatism Unit.

GUY'S HOSPITAL MEDICAL SCHOOL

Anatomy Department

W. A. GAUNT, PH D

1. Quantitative analyses of the growth of teeth and jaws.
2. The dental follicle.
3. Innervation and vascularity of teeth and associated tissues.

Chemical Pathology Department

B. MCARDLE, MD, FRCP, DCH

Miss H. PELS, AIST (*technical staff*)

Levels of RNA, DNA and certain glycolytic and other enzymes of muscle in various neuromuscular disorders and, in rats, during growth and regeneration.

Radioisotopes Laboratory

Miss M. L. KEMBALL, MB, MRCP

Assistance to Mr N. Veall, head of the Radiochemistry Section being built up for the Clinical Research Centre (see p. 110):

1. Radioimmunoassay of insulin and growth hormone in newborn infants.
2. Development of radioimmunoassay technique for calcitonin.

HAMMERSMITH HOSPITAL

Medical Research Council Cyclotron Building

N. B. MYANT, DM, B SC, MRCP

Miss V. J. ILIFFE, B SC

K. A. MITROPOULOS, PH D

C. D. MOUTAFIS, DR MED

1. Regulation of the metabolism of fatty acids and cholesterol, including bile acid metabolism, using cell-free mammalian preparations.
2. Disorders of lipid metabolism in humans.
3. Role of brown fat in the regulation of body temperature in newborn animals.

INSTITUTE OF CANCER RESEARCH*

Chester Beatty Research Institute

E. J. DELORME, MD, FRCS(CAN)

Cell-mediated immunity, with special reference to tumour-specific antigens and host responses.

INSTITUTE OF NEUROLOGY

J. A. V. BATES, MB, MRCP (*part-time*)

1. Development of physiological criteria for determining the site for stereotactic operations on the human brain.
2. Preparation of free text for computer processing.
3. Effect of stereotactic lesions on tremor and rigidity.
4. Surgical relief of epilepsy.

A. M. HALLIDAY, MB, B SC (*part-time*)

W. N. FLOYD, MD

W. F. MICHAEL, BM, MRCP

J. R. PITMAN (*technical staff*)

1. Factors affecting the form of cortical evoked repsonses in healthy subjects: changes in cerebral evoked potentials produced by various lesions of the nervous system.
2. Clinical trial of the therapeutic effect of unilateral electroconvulsive therapy in depression and a comparison of its effect on memory with that of conventional bilateral ECT.
3. Recording of spontaneous and evoked activity in the human thalamus as a means of better localization during stereotactic thalamotomies.

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* The Institute of Cancer Research receives a block grant from the Council: see p. 177.

J. D. HOOD, D SC, F INST P

G. DANTA, B SC, MB, MRACP (*attached worker*)

Miss M. R. DIX, MD, FRCS

E. TRINDER, MIEE (*technical staff*)

G. FRIEDMAN, MD (*attached worker*)

1. Clinical and experimental investigations of vertigo, deafness and other organic derangements of cochlear and vestibular function resulting from lesions of the end-organ and central pathways.
2. Electronystagmographic investigations of induced vestibular nystagmus, optokinetic nystagmus, spontaneous nystagmus and disordered eye movements.
3. Clinical, anatomical and psychoacoustic investigations of the loudness recruitment phenomenon and other aspects of cochlear function in health and disease of the VIII nerve system.
4. Studies of semicircular canal and otolith function in the normal subject, including the habituation phenomenon, with particular reference to its clinical significance.

P. W. NATHAN, MD, FRCP

1. Tracts of the spinal cord in relation to anterolateral cordotomy, rhizotomy and other pain-relieving operations.
2. Physiology of the human spinal cord, with particular reference to the mechanisms and treatment of spasticity.

Miss M. C. SMITH, MD, B SC, MRCP, FC PATH (*part-time*)

1. Correlation between post-mortem findings and the clinical effects of stereotactic operations.
2. Functional anatomy of the human central nervous system, studied by means of investigations of neurological conditions.

Department of Neurosurgery

L. SYMON, MB, FRCS, FRCSE (*part-time; with grant for assistance*)

1. Changes in cortical metabolism in experimental cerebral vascular occlusion.
2. Long-term adaptation of the cerebral circulation to reduction in afferent flow.
3. Prolonged recording of intracranial pressure *in vivo*.

MRC SOCIAL PSYCHIATRY UNIT (p. 153)

Mrs L. G. WING, MD, DPM

The Camberwell Register: compilation of a cumulative psychiatric disease register to provide epidemiological information and a sampling frame for intensive studies of specific problems.

LISTER INSTITUTE OF PREVENTIVE MEDICINE

Chelsea Bridge Road

D. G. GODFREY, OBE, PH D

1. Interspecific and intraspecific differences in the surface charge of trypanosomes.
2. Effect of enzymes and surface-active agents on the permeability of trypanosomes.
3. Ultrastructure of the trypanosome surface.

Elstree

Miss M. E. MACKAY, PH D

1. Proteolytic enzyme in human plasma.
2. Pharmacologically active substances in human blood and plasma fractions.

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE

C. N. DAVIES, D SC, F INST P

1. Air flow in human lungs.
2. Human inhalation of aerosol.
3. Aerosol sampling.

NATIONAL INSTITUTE OF INDUSTRIAL PSYCHOLOGY

P. BRANTON, BA (*until Feb. 1969*)

1. Development of field research methods to measure skill variability in industrial tasks in relation to accidents at the place of work.
2. Observational study of the mental work load of industrial executives and supervisors.

L. CURRIE, BA, C ENG, MI PROD E

1. Perception of danger by the individual in various hazardous occupations.
2. Development of safety margins adopted by the individual when performing certain tasks.
3. Risk and personality: personal constructs of probability, pay-off and anxiety related to hazard and safety in the work situation.

R. SERGEAN, MA

1. Operator performance under different shift arrangements.
2. Use and effects of shifts of long duration.
3. Factors influencing the acceptance of change in working hours.

P. A. WERR, BA

Sleeping habits of shift workers in a variety of shift systems.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

Pharmacology Department

Mrs H. M. PAYLING WRIGHT, PH D, LMSSA

1. Histology and reactions of small blood vessels.
2. Effect of vitamin C deficiency on platelet behaviour.
3. Platelet behaviour in multiple sclerosis and certain other clinical conditions.
4. Measurement of arterial endothelial regeneration using tritiated thymidine.

Physiology Department

N. AMBACHE, MA, MRCS

Mrs M. A. FREEMAN, PH D

M. ABOO ZAR, MB, D PHIL

1. Release by electrical stimulation of atropine-resistant myenteric spasmogen from Auerbach's plexus; extraction, separation and characterization of this substance.
2. Myenteric localization of 'true' and 'pseudo' cholinesterases (with Professor F. Hobbiger, Middlesex Hospital Medical School).
3. Mode of action of various neurotoxins and their application to physiological problems.

ROYAL FREE HOSPITAL AND INSTITUTE OF NEUROLOGY

A. ELITHORN, MD, MRCP, DPM (*part-time*)

T. J. BARNETT, BA (*until Mar. 1969*)

J. O. PICKLES, BA

J. A. WEINMAN, BA

1. Relationship between perceptual capacity and intellectual capacity.
2. Relationship between anxiety and depression.
3. Computer simulation of human problem solving.

ST BARTHOLOMEW'S HOSPITAL

Serological Population Genetics Laboratory

Serological Section

A. E. MOURANT, DM, D PHIL, FRCP, FC PATH, FRS

Mrs M. J. GODBER, B SC

Full determination of the blood groups (erythrocyte antigens) and haemoglobins, and a large range of genetically determined plasma protein and red-cell isoenzyme groups, in blood samples collected on a population basis, especially by expeditions sponsored by the International Biological Programme.

Statistical Section

Mrs A. C. KOPEĆ, D ES SC

1. Collection, tabulation and statistical treatment of all available data, published and unpublished, showing the incidence of genetically determined serological and biochemical characters in human populations.
2. Operation as the world information centre for such data.

TAVISTOCK INSTITUTE OF HUMAN RELATIONS

E. J. M. BOWLBY, MD, FRCP (*part-time*)

Short-term effects of the temporary loss of the mother figure.

UNIVERSITY COLLEGE LONDON

Department of Pharmacology

M. H. LADER, MD, PH D, DPM (*also at the Institute of Psychiatry; with grant for assistance*)

D. L. JULIER, MB, MRCP

1. Action of psychotropic drugs on evoked potentials in man.
2. Autonomic measures as predictors of treatment response in depressives.

Physiology Department

H. DAVSON, D SC (*with grant for assistance*)

C. PURVIS (*technical staff*)

1. Exchange of material between blood, cerebrospinal fluid and brain and cord.
2. Effects of various pharmacological agents on rate of secretion of cerebrospinal fluid and turnover of ^{22}Na in brain.
3. Measurement of intracranial resistance to flow of cerebrospinal fluid.

Psychology Department

Mrs A. ZAJACZKOWSKA, PH D

1. Functional relationships between visual space and kinaesthetic space.
2. Role of muscle spindles in visual perception of distances.
3. Improvement of visual judgment of distances as an effect of kinaesthetic activation.

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172 Tottenham Court Road

D. P. BURKITT, MD, FRCSE

Detailed geographical distribution of cancer and some non-neoplastic conditions in eastern Africa: relation of distribution to environment (with Miss P. J. Cook, MRC Statistical Unit).

Malaysia

SUNGEI BULOH LEPROSARIUM

Research Unit

M. F. R. WATERS, MB, MRCP

J. M. H. PEARSON, BM, MRCP*

1. Clinical drug trials in leprosy, with particular reference to the treatment of erythema nodosum leprosum and of sulphone-resistant leprosy.
2. Immunological studies in erythema nodosum leprosum.
3. Correlation of neurohistology of peripheral nerves (at the level of both the light and the electron microscope) with clinical findings.

SEMONGOK AGRICULTURAL RESEARCH CENTRE

P. J. E. BENDELL, PH D

O. H. U. HEATHCOTE, B SC, DAP & E

M. N. HILL, B TECH†

1. Ecology and behaviour of the mosquito vectors of Japanese encephalitis.
2. Determination of the incidence of Japanese encephalitis virus in mosquito vectors.
3. Immunology of Japanese encephalitis.

(In collaboration with the Institute for Medical Research, Kuala Lumpur.)

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* Seconded from the Virology and Bacteriology Division of the National Institute for Medical Research (see p. 101).

† Seconded from the Microbial Research Establishment, Porton.

Manchester

PATERSON LABORATORIES, CHRISTIE HOSPITAL AND HOLT RADIUM INSTITUTE*

Experimental Chemotherapy Department

H. JACKSON, MB, D SC

1. Effects of sulphonic esters and related compounds on mammalian spermatogenesis: relationship between activity and structure.
2. Possible correlation between antispermatogenic effects, mutagenicity and antitumour activity.
3. Cumulative toxic actions of certain alkylating chemicals.

Nottingham

UNIVERSITY

Psychology Department

J. A. LEONARD, PH D (*with grant for assistance; until May 1969*)

1. Mobility of blind people: field observations, on familiar and on new routes; assessment of levels of mobility performance; relationship between intensity of stimulation of artificial or natural signals and walking speeds; measurement of stress in various modes of travel.
2. Development of keyboard skills.

Oxford

THE CHURCHILL HOSPITAL

Mrs M. E. OWEN, D PHIL

B. A. ASHTON, B SC

G. M. HERRING, D PHIL

Mrs H. WILLIAMSON, B SC (*part-time*)

1. Synthesis of nucleic acids, proteins and mucoproteins by the cells of the osteogenic connective tissue; effects of different metabolic inhibitors and hormones on these processes.
2. Isolation and characterization of glycosaminoglycans and glycoproteins from calcified tissues; separation and analysis of these constituents from small samples of bone.

J. St. L. PHILPOT, MA, B SC (*with grant for assistance*)

D. A. STOCK (*technical staff*)

Rapid continuous-flow electrophoresis.

Central Workshop

F. D. STOTT, D PHIL

1. Pulmonary and systemic blood flow and pressure measurements in man (with Dr G. de J. Lee, Radcliffe Infirmary).
2. Long-term continuous recording of blood pressure in ambulant patients (with the Department of the Regius Professor of Medicine).
3. Thrombus formation: assistance to Professor R. G. Macfarlane.

Oxford Haemophilia Centre, Research Laboratory

Miss R. BIGGS, MD, PH D (*Director, Oxford Haemophilia Centre; part-time MRC appointment*)

K. W. E. DENSON, D PHIL, FIMLT

1. Clinical studies on abnormal bleeding due to deficiency of clotting factors or to the presence of anticoagulants; aetiology of clotting defects; assay and purification of clotting factors and their inhibitors.
2. Problems arising from the widespread use of cryoprecipitate in the Haemophilia Centres of the United Kingdom.
3. Coagulant activity of normal and abnormal platelets (with Professor R. G. Macfarlane and Dr J. E. French, Sir William Dunn School of Pathology, Oxford, and the Renal Dialysis Unit, Churchill Hospital, Oxford).

UNIVERSITY

Department of Biochemistry

K. G. H. DYKE, PH D

1. Evolution of resistance to penicillins.
2. Regulation of synthesis of penicillinase in *Staphylococcus aureus*.

* The Paterson Laboratories receive a block grant from the Council (see p. 180).

D. S. ROBINSON, PH D

1. Role of tissue clearing-factor lipase in determining plasma triglyceride level.
2. Hormonal factors regulating clearing-factor lipase activity in adipose tissue.
3. Release of triglycerides from the liver in different physiological states.

Nuffield Department of Clinical Medicine

Miss P. LUND, B SC

D. H. WILLIAMSON, D PHIL

L. V. EGGLESTON, B SC (*technical staff*)

R. HEMS (*technical staff*)

(working under the supervision of Sir Hans Krebs)

1. Regulation of metabolic processes, with special reference to gluconeogenesis and ketogenesis.
2. Metabolic characteristics of kidney cortex.

Sir William Dunn School of Pathology

Professor R. G. MACFARLANE, CBE, MD, FRCP, FRS

1. Normal microcirculation in the vessels of the hamster cheek-pouch, studied by high-speed cinematography, and the responses to physical or chemical injury, in particular platelet aggregation.
2. Construction of artificial systems simulating the microcirculation, and study of the behaviour of platelets and other small particles flowing through such systems under different mechanical and electrical conditions.
3. Effect of pharmacological agents supposed to modify platelet behaviour, studied by means of the natural and artificial systems used in (1) and (2).

J. C. F. POOLE, DM

1. Electron microscope studies of natural and artificial thrombi.
2. Cellular mechanisms in experimental atherosclerosis.

A. M. WOODIN, PH D

Miss A. A. WIENEKE, DRS

1. Interaction of leucocidin with lipids.
2. Properties of leucocyte cell membranes.
3. Sulphydryl reagents in protein secretion and granule movement.

Penarth, Glamorgan

LLANDOUGH HOSPITAL

Department of Psychological Medicine, Welsh National School of Medicine

J. G. INGHAM, PH D

D. J. L. HUGHES, MB, DPM

M. M. WOOD, B SC

C. A. FLETCHER, BA (*MRC Scholar*)

V. J. SHACKLETON, BA (*MRC Scholar*)

1. Comparative studies of the distribution of psychiatric disorders in a mining area and an agricultural area.
2. Development of scales for the assessment of subjective symptoms.
3. Investigation of individual differences in the parameters of stimulus detection.
4. Application of statistical detection theory to the detection of physiological changes.

Porton, Wilts.

MICROBIOLOGICAL RESEARCH ESTABLISHMENT

A. D. VIZOSO, PH D

1. Natural history of *Herpes simiae* (B virus); mode of transmission, especially the possibilities during the latent phase; comparison with *Herpes simplex* and other viruses of the group.
2. Characterization of agents obtained from wild squirrels that are apparently capable of inducing cell transformation *in vitro*.

St Lucia

CASTRIES

Research and Control Department

P. JORDAN, MD, DTM & H

1. Epidemiology of *Schistosoma mansoni* infection prior to application of control measures.
2. Factors involved in the development and natural history of hepatosplenic schistosomiasis.

Sheffield

NETHER EDGE HOSPITAL

Rheumatism Research Unit

H. F. WEST, MD, FRCP, DTM (*part-time; with grant for assistance*)

1. Metabolism of cortisol and its analogues and the disposition of these hormones and their metabolites in the body fluids of patients and controls.
2. Application of gas chromatography and mass spectrometry to chemical pathology.

Southampton

UNIVERSITY

Department of Physiology and Biochemistry

J. A. WILKINSON, MB, M CH. B SC, FRCS (*part-time*)

1. Neonatal surveys for othopaedic congenital anomalies.
2. Cineradiographic studies of cervical spine movements in normal and abnormal conditions, and the relation to clinical syndromes.

Tanzania

TANGA

WHO/MRC Tanzania Bilharziasis Chemotherapy Centre

A. DAVIS, MD, MRCPE, DTM & H

D. R. BAILEY, MB, DTM & H, D OBST RCOG

1. Methodology of clinical trials in schistosomiasis.
2. Evaluation of organophosphorus compounds as schistosomicides.
3. Investigation of chemotherapeutic control of bancroftian filariasis in a closed community.

West Indies

UNIVERSITY OF THE WEST INDIES

Trinidad Regional Virus Laboratory

J. B. DAVIES, M SC

1. Biology and ecology of *Culex* (*Melanoconion*) *portesi*, main vector of arboviruses in Trinidad.
2. Study of *Culicoides* and *Simulium* spp.

C. O. R. EVERARD, B SC

1. Ecology and parasites of small mammals associated with arboviruses in Trinidad.
2. Ecology of the mongoose/rabies complex on the Island of Grenada.

Institutions assisted by block grants

The Council is also able to assist the progress of research through its scheme of block grants. These grants are used to support, in whole or in part, the research activities of a number of autonomous institutions. In addition, individual members of the Council's staff are working in most of these institutions: further details will be found under the appropriate entry in the section 'External Scientific Staff' (p.167).

INSTITUTE OF CANCER RESEARCH: ROYAL CANCER HOSPITAL

Fulham Road, London S.W.3

(01–584 9112)

Chairman of the Committee of Management

The Rt Hon. the Earl of Halsbury, FRIC, F INST P

Secretary

N. P. Hadow, OBE, MA

The Institute was recognized in 1927 as a school of the University of London; since 1951 it has had similar status as an Institute of the British Postgraduate Medical Federation. The work of the Institute is carried out in the Chester Beatty Research Institute and in the research activities of the Departments of Physics, Biophysics, Radiotherapy and Clinical Research, which are joint departments of the Institute of Cancer Research and of the Royal Marsden Hospital. Since 1951 the Council has made an annual block grant to the Institute; substantial support is also received from the British Empire Cancer Campaign for Research. Detailed accounts of the Institute's scientific work are available in the Annual Reports of the British Empire Cancer Campaign for Research, and only a brief survey will be given here.

Research programme

CHESTER BEATTY RESEARCH INSTITUTE

(01–352 8133)

Director

Professor Sir Alexander Haddow, MD, D SC, FRS

The programme of work of the Institute is centred on the study of basic mechanisms of carcinogenesis and of the nature of the neoplastic change. At present one of the main interests in basic research is the study of the chemistry of the control of cell division and cell differentiation. Ideas and knowledge stemming from these basic studies find application in attempts to develop new ways of treating patients with cancer by drugs, ionizing radiation, surgery or immunotherapy, or combinations of these.

Epidemiological studies sometimes lead to the experimental investigation of environmental factors that may be involved in the aetiology of human cancers. Alternatively laboratory demonstration of carcinogenicity may prompt epidemiological surveys. In both cases the eventual aim is to find new ways of preventing cancers.

PHYSICS DEPARTMENT

(01–642 9471)

Professor J. W. Boag, D SC, F INST P, FIEE

During the year a digital computer provided by the Department of Health and Social Security to speed up and improve radiotherapy planning has been installed, and the associated apparatus and programmes are nearly complete. Gamma camera and isotope scanning methods of tumour location have made further progress and are now an indispensable aid in clinical diagnosis. The department is collaborating with the Department of Health and with Government laboratories in the development of a novel type of gamma camera employing semiconducting strips of special form as the detecting element. The results so far are promising. Thermographic scans of breast skin temperatures have been made on about 1200 subjects, some normal and others with malignant lesions, and it has been possible to classify the normal patterns into a few groups, thus assisting the recognition of abnormal patterns.

The method of pulse radiolysis has been used to study the kinetics of radiation damage to pyrimidine bases, the phosphorescence spectra from irradiated DNA and from the component bases, and the mode of action of selenourea as a protective agent against radiation damage to living systems. The reactions of excited states of the pyrimidines have also been studied by flash photolysis.

Ultrasound studies on DNA and on cells in culture have continued and clinical work with ultrasound as an aid to tumour location has begun. The careful measurement of low values of oxygen tension has revealed grave inadequacies in certain techniques commonly used for experiments on anoxia in radiobiology and has indicated how these can be overcome.

BIOPHYSICS DEPARTMENT

(01–642 9471)

Professor L. F. Lamerton, D SC, F INST P

Work has continued on problems of cell proliferation in various types of malignant and norma tissues. Experimental studies with tumours have been concentrated on slowly growing tumours that have growth rates within the range of human tumours. The problems of relationship between cell proliferation and vascularity in tumours have been investigated, radioisotope methods being used for the study of blood flow and stasis. Work with an *in vitro* system under continuous irradiation is providing interesting information on the development of resistant cell types during radiation exposure.

The studies previously made on the cell population kinetics of the red cell system in the rat and mouse have provided an experimental model for comparing the response to radiation and various cytotoxic drugs of cells of different proliferation characteristics, and this is now being exploited. Work on the cell population kinetics of the granulocyte system has been started. The responses of skin to radiation and of the bronchial epithelium to tobacco smoke are being studied by means of techniques suited to slowly dividing tissues, and the capacity of the kidney for compensatory growth is being investigated at the biochemical level.

In the field of radiation carcinogenesis, a study is being made of the interaction of plutonium and other actinide elements with protein and other components of bone and soft tissue.

RADIOTHERAPY DEPARTMENT

(01–352 8171)

Director

Professor D. W. Smithers, MD, FRCP, FRCS, FFR

The research programme falls into four sections: (1) clinical studies of tumours: (2) investigations on human and experimental lymphomas; (3) *in vitro* studies on the drug-sensitivity and radiosensitivity of cells, and (4) clinical investigations with radioactive isotopes.

Long-term clinical studies have continued on tumours at various sites, their mode of spread, growth rate and response to treatment. A small closed international symposium on Hodgkin's disease was held under the auspices of the Institute of Cancer Research.

The evaluation of predisposing factors in the aetiology of Hodgkin's disease and of the lymphomas in general has proceeded. Increasing emphasis has been given to studies on leucocyte kinetics in the lymphomas. These have included isotope labelling procedures and analyses of chromosome aberrations induced in lymphocytes in patients undergoing treatment by extracorporeal irradiation of the blood. Cytophotometric studies on lymph node populations have also been extended so that the various proliferating cell compartments can be identified with more precision. The possibility of a viral aetiology has been explored in the induction of tumours that arise as a late consequence of graft-versus-host disease in rats.

An automated apparatus for continuous monitoring and sampling of cell cultures has been constructed for studying the response of mammalian cells to combinations of cytotoxic agents and radiation and to different fractionation procedures. The direct effect of radiations on the permeability of the cell membrane to ions has been investigated both with cultured cells and with isolated nerves.

The clinical isotopes investigations are concerned with tumour detection and localization, rectilinear scanning and the gamma camera being used in conjunction with ultrasonic scanning. Metabolic studies have been continued on the influence of temperature on the incorporation of radiophosphorus by tumour and normal tissues and on extrapituitary sources of thyroid-stimulating hormones in various types of thyroid disease.

CLINICAL RESEARCH DEPARTMENT

(01–352 8171)

Director

P. E. Thompson Hancock, MB, FRCP

The clinical research programme is divided into two main sections: (1) investigation of patients' defence mechanisms, their environmental background and the characteristics of their tumours, and (2) studies of new methods of treatment. In all these projects clinical research is closely integrated with the fundamental research carried out at the Institute.

The investigatory work is mostly incorporated in a project known as the ' Characterization of Human Cancer ', in which a series of biochemical, cytogenetic, immunological and other investigations is carried out by small teams. There is a collection, registration and distribution service that supplies specimens for all purposes. The environmental pathology of the patients from whom the tumours have been removed is also investigated.

Special groups are kept under observation, including (1) individuals known to have been exposed to a carcinogen, for example rubber and cable workers; (2) women who, at routine cervical smear screening, have shown some abnormal enzyme content (with or without cytological changes); and (3) gas and tar workers. Normal women and women with breast tumours are being studied to see if thermographic scanning is a useful adjunct to physical examination in the detection of early breast tumours.

Clinical trials of systemic chemotherapy, including a trial of asparaginase in acute leukaemia, continue, some of them in collaboration with the Council's Committee on the Evaluation of Different Methods of Cancer Therapy. Hormone therapy for inoperable carcinoma of the kidney and local application of cytotoxic drugs for skin tumours are being evaluated, and intensive chemotherapy in sterile wards and specific immunotherapy are being attempted in selected cases. Research on regional chemotherapy by arterial infusion continues. A series of investigations has begun in which the IBM cell separator is used for the separation of blood into plasma, platelet-rich plasma, granulocytes, lymphocytes, blast cells and red cells as a continuous process.

BEATSON INSTITUTE FOR CANCER RESEARCH

Royal Beatson Memorial Hospital
132–138 Hill Street, Glasgow C.3
(041–332 0286)

Director
John Paul, MB, PH.D, MRCPE, MRCPG, MC PATH, FRSE

The Beatson Institute for Cancer Research has received a block grant from the Council since 1957. It also receives financial support from the British Empire Cancer Campaign for Research. The ordinary maintenance costs of the Institute are met by the Western Regional Hospital Board and a Research Endowments Fund administered by the Western and Gartnavel Hospitals Board of Management.

Research programme

The Institute's research is concerned with the hypothesis that the essential lesion in carcinogenesis is faulty cell differentiation. The main lines of inquiry are therefore directed towards studying the molecular biology of differentiation and comparing the mechanisms in normal and tumour cells.

For studying the molecular biology of differentiation tissue culture systems have been developed in which the maturation of red blood cells can be initiated by the addition of erythropoietin. The proteins and nucleic acids synthesized in differentiating erythropoietic tissue are being studied.

Investigations have provided strong evidence in support of the theory that a major factor in cell differentiation is the masking of some genes by proteins so that only a restricted set can be expressed in each kind of cell. The mechanism of this masking is being studied and direct comparisons of the patterns of gene masking in normal and cancer cells are being made. Methods whereby the regulation of a single gene or group of genes can be investigated are being evolved. The effects of carcinogens and carcinogenesis on gene masking are also under investigation.

CHRISTIE HOSPITAL AND HOLT RADIUM INSTITUTE

Withington, Manchester 20
(061–445 8123)

PATERSON LABORATORIES

Director
L. G. Lajtha, MD, D PHIL

The Laboratories are under the immediate control of a Cancer Research Executive Committee, and administrative services are provided by the South Manchester Hospital Management Committee.

Research programme

The research interest of the Laboratories is strongly slanted towards radiotherapy and the chemotherapy of malignancy. The understanding of malignant disease and, eventually, its rational treatment must depend on the furtherance of chemical and biological knowledge of fundamental cellular processes and the effects of radiation and specific drugs on them. To this end the radiation chemistry group is vigorously pursuing the study of the immediate effects of radiation on chemical systems of biological interest, and the biochemistry group is analysing the mechanism of action of specific alkylating agents. The cytogenetics group is studying the chromosome duplication pattern and behaviour of various mammalian cells, including human cells originating from malignant and other pathological tissue, and genetic studies on the effects of radiation are continuing in mice and *Drosophila*. Studies on cell killing by radiation and alkylating agents are being carried out on dormant and dry cells as well as on mammalian tissues *in vivo* and *in vitro*. The regulation and control of growing and steady-state cell populations is investigated in a variety of experimental systems.

On the clinical side, the problems confronting the radiotherapist in his attempt to achieve the maximum effect on the tumour while sparing adjacent normal tissue underlie much of the effort that is being made to measure the sensitivity of tissues to radiation and to study various factors controlling this sensitivity.

STRANGEWAYS RESEARCH LABORATORY

Wort's Causeway, Cambridge

(0223 47583)

Director

Professor Dame Honor Fell, DBE, D SC, LL D, FRS (*Research Professor of the Royal Society*)

Deputy Director

A. Glücksmann, MD (*Senior Gibb Fellow, British Empire Cancer Campaign for Research*)

The Laboratory is an independent institution devoted to the study of cell biology. It is loosely subdivided into biological, pathological, biochemical and biophysical sections.

Research programme

The policy of the Laboratory is to develop as far as possible a multilateral attack on individual problems by the combined application of morphological, biochemical and biophysical methods. The *in vitro* techniques of organ culture and cell culture are used extensively, often in conjunction with animal experiments.

The normal biosynthetic processes of skeletal tissue and the direct effect of various biologically active agents are being investigated in organ cultures of bone and cartilage. The structure and physiology of biological membranes of various types have received much attention, particularly in connection with endocytotic phenomena, the invasiveness of different strains of mouse leukaemic cells and lysosomal activity *in vivo* and *in vitro*. The action of various carcinogenic agents on cells and tissues both in culture and in animals, the influence of hormonal and other environmental factors on the carcinogenic process and (in collaboration with various hospitals) the effects of radiation on human tumours are being studied.

McINDOE MEMORIAL RESEARCH UNIT

Blond Laboratories, Queen Victoria Hospital, East Grinstead, Sussex

(0342 2411)

Director

Richard Batchelor, MD (*Honorary Professor, Royal College of Surgeons*)

The Unit, which is administered by the East Grinstead Research Trust, receives financial support from several sources, including the Leverhulme Trust as well as the Council.

Research programme

The work is centred on the study of biological problems of tissue transplantation and is chiefly concerned with the serological and chemical characterization of human transplantation antigens of the HL-A system. The serological definition of HL-A antigens and their influence on the survival of skin and kidney grafts is under investigation. Chemical studies are aimed at identifying the structures responsible for HL-A serological specificity. A radioimmunoassay for soluble HL-A substances, which should facilitate further analysis, is being developed.

STEROID REFERENCE COLLECTION

Chemistry Department, Westfield College, London N.W.3
(01–435 7601)

Honorary Curator
Professor W. Klyne, D SC

Honorary Deputy Curator
D. N. Kirk, PH D

The Collection was set up in 1954 and now includes about 750 compounds. It provides reference samples of steroids for use as standards in chromatography, spectroscopy and other chemical and physical techniques, particularly for work related to the metabolism of steroid hormones. The Council's block grant to the Collection is supplemented by assistance from the US National Institutes of Health, and the Collection has received many gifts of materials from the pharmaceutical industry at home and abroad.

Research programme

The staff are engaged in developing better methods for the preparation of hormone metabolites (including 'tetrahydro' derivatives, 3α-hydroxy-5α-steroids, 6-hydroxy-4-en-3-ones and 20α-hydroxypregnanes). Extensive work on the preparation of steroid conjugates (sulphates and glucuronides) has recently been started.

Research Groups

The scheme of research groups was instituted by the Council to enable it to assist in the development of a research programme in a university department where this seems desirable in the interests of the national coverage of biomedical research. Research groups are established for an agreed period, normally related to the current or next University Grants Committee quinquennium, and are financed by means of a block grant to the university concerned; staff working in research groups are employed by the university. The main prerequisite for the establishment of a group is that the university should undertake to integrate it into its normal structure at the end of the agreed period of tenure.

University of Birmingham

RESEARCH GROUP ON MECHANISMS OF MICROBIAL PATHOGENICITY

Department of Microbiology, The University,
Birmingham 15
(021–472 1301)

Director
Professor H. Smith, D SC

1. Nutritional basis of growth of *Vibrio fetus* in bovine foetal tissue.
2. Factors influencing the localization of trachoma in conjunctival tissue of primates.
3. Factors influencing the localization of influenza in respiratory epithelium.
4. Comparative study of intracellular survival and virulence components of staphylococci grown *in vitro* and *in vivo*.
5. Virulence attributes of organisms isolated from infected animals.

University of Bristol

RESEARCH GROUP ON METABOLISM CONTROL

Department of Biochemistry, The Medical School, Bristol BS8 1TD
(0272 24161)

Director
Professor P. J. Randle, MD, PH D, MRCP

1. Control of insulin release: carbohydrate metabolism of separated islets of Langerhans; influence of hormones on islet cell metabolism.
2. Interactions of glucose and glyceride metabolism: control of lipogenesis in adipose tissue; influence of fatty acid oxidation on glycoprotein biosynthesis; control of pyruvate kinase and PEP carboxykinase.
3. Mitochondrial permeases: delineation of mitochondrial permeases for dicarboxylic and tricarboxylic acids and amino acids; nature of hydrogen transfer from reduced coenzymes across mitochondrial membrane; permeability of artificial phospholipid membranes.
4. Organization of lipid metabolism; properties of the electron-transferring pathways from fatty acid oxidizing enzymes to the respiratory chain; biosynthesis of intracellular membranes in yeasts; biosynthesis of energy conservation sites in yeast mitochondria.

RESEARCH GROUP ON NEUROSECRETION

Department of Pharmacology, The Medical School, Bristol BS8 1TD

(0272 24161)

Director

Professor H. Heller, MD, PH D, MRCP

1. Pharmacological and chemical characteristics of the neurohypophysial hormones of elasmobranchs.
2. Subcellular distribution of vasopressin, oxytocin and acetylcholine in the mammalian neurohypophysis.
3. Effect of neurohypophysial hormones on the oviduct of lower vertebrates.
4. Chemical structure of the protein carriers of neurohypophysial hormones.
5. Neurosecretory substances in the cerebrospinal fluid.
6. Biosynthesis of neurohypophysial hormones.

University of Edinburgh

RESEARCH GROUP ON BACTERIAL ENZYME VARIATION

University Department of Molecular Biology, Mayfield Road, Edinburgh 9

(031–667 1011)

Director

Professor M. R. Pollock, MB, FRS

1. Genetic and enviromental control of enzyme function and biosynthesis *in vivo* and *in vitro*.
2. Determination of amino acid sequence, structure and function in homologous series of proteins.
3. Analysis of structural organization at a subcellular level.
4. Identification of codons operative *in vivo*.

EPIGENETICS RESEARCH GROUP

Institute of Animal Genetics, West Mains Road, Edinburgh 9

(031–667 1011)

Director

Professor C. H. Waddington, CBE, SC D, FRS

1. Electron microscope investigations of developing cells, particularly in the embryos of *Drosophila* and amphibia.
2. Nucleolar changes in frog kidney cells infected with Lucké sarcoma virus.
3. Molecular structure of lens proteins, mainly of amphibia and birds; changes during regeneration and metaplasia; gene effects; immunology.
4. Synthesis of ribosomal RNA in normal and anucleolar embryos of *Xenopus* and determination of the number of DNA cistrons coding for ribosomal RNA.
5. Sedimentation constants of the RNA's synthesized in different tissues at various stages of early embryonic development in newt and chick embryos.
6. Preparation of RNA *in vitro* from native or deproteinized DNA obtained from various tissues, and comparisons of these RNA's by molecular hybridization.
7. Availability of DNA to prime RNA synthesis in different tissues.

RESEARCH GROUP ON MAPPING THE MAMMALIAN GENOME

Department of Zoology, West Mains Road, Edinburgh 9

(031–667 1011)

Director

Professor P. M. B. Walker, PH D

1. Sequence homologies between DNA's isolated from different animals.
2. Isolation and characterization of mouse satellite DNA and other special DNA fractions from chromosomes.
3. Separation and characterization of DNA complementary to the RNA present in different tissues and cell types.
4. Regularities in the oligonucleotides prepared from satellite DNA (preparation for study of the base sequence).

University of Glasgow

RESEARCH GROUP IN ADRENAL AND ENDOCRINE PATHOLOGY

University Department of Pathology, Royal Infirmary, Glasgow C.4

(041–552 3535)

Director

Professor T. Symington, MD, B SC, FRIC, FRCPG, FC PATH, FRSE

1. Investigation of vascular anatomy, physiology and pathology of adrenal glands, particularly of muscular veins.
2. *In vitro* studies on adrenal gland: (*a*) androgen formation, particularly C-7-oxygenated steroids; (*b*) kinetic and substrate characteristics of the corticosteroid- and androgen-synthesizing enzyme systems of normal and abnormal adrenal glands; (*c*) intermediates in aldosterone biosynthesis in Conn's syndrome adenomas.
3. Preparation of ACTH with high specific activity, for autoradiographic and electron microscope investigation of the site of ACTH action in the adrenal.
4. Electron microscope investigation of the structure of cell organelles in normal and abnormal human adrenal glands.
5. Plasma binding of adrenal steroids; mechanism of potentiation by corticosteroids of catecholamine action on vascular smooth muscle; pathogenesis of tubular degeneration of adrenal gland.

RESEARCH GROUP ON IRON AND PORPHYRIN METABOLISM

University Department of Medicine, Gardiner Institute, Western Infirmary, Glasgow W.1

(041–339 8822)

Director

Professor A. Goldberg, MD, D SC, FRCP

1. Mechanisms involved in the absorption of iron and its handling by the reticuloendothelial system.
2. Clinical and experimental studies on iron storage disease, with particular reference to the use of iron chelators.
3. Measurement of haem enzymes in various anaemias occurring in man and experimentally induced in animals.
4. Incidence, natural history, pathogenesis and treatment of the porphyria group of diseases.
5. Lead intoxication, with particular reference to the effect of lead on the nervous system.

University of Keele

NEUROPHYSIOLOGY RESEARCH GROUP

Department of Communication,
University of Keele, Keele, Staffs.

(0782–71 371)

Director
Professor D. M. MacKay, PH D, F INST P

1. Identification of neural elements responsible for the effects of space- and time-varying visual stimuli observed perceptually and by EEG recording in human subjects.
2. Investigation of neural processes underlying the perception of pitch and the analysis of complex sounds.
3. Investigation of information processing in the cerebellum.

University of Kent at Canterbury

RESEARCH GROUP ON BIOLOGICAL INORGANIC CHEMISTRY

University Chemical Laboratories, The University of Kent, Canterbury, Kent
(0227 66822)

Director
R. D. Gillard, PH D, DIC

1. Stereoselectivity in reactions of metal complexes of biological molecules.
2. Cotton effect studies of non-haem iron proteins.
3. Metal ions and complexes as probes of biopolymer structure.
4. Stereospecificity of metal complex formation with peptides.
5. Model systems, including studies of absolute configuration and interactions of asymmetric molecules.

University of Leicester

RESEARCH GROUP ON THE PHYSIOLOGY OF MEMBRANE TRANSPORT AND SECRETION

Department of Physiology, University of Leicester,
University Road, Leicester LE1 7RH

(0533 50000)

Director
Professor R. Whittam, PH D

1. Mechanism of active transport of ions across cell membranes, with particular reference to the energetics of the process.
2. Interdependence of metabolism and active transport in intact cells.
3. Method for the determination of adenosine triphosphatase activity by potentiometric recording of the liberation of protons.
4. Influence of inorganic phosphate on the hydrolysis and synthesis of ATP.
5. Relationship between the electrochemical potential gradient across the erythrocyte membrane and the associated reactions of adenine nucleotides.

University of Liverpool

RESEARCH GROUP ON THE CHEMOTHERAPY OF PROTOZOAL DISEASES AND DRUG RESISTANCE

Department of Parasitology, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool L3 5QA

(051–709 7611)

Director
Professor W. Peters, MD, MRCS, DTM & H

1. Development of drug-resistant strains of rodent malaria parasites.
2. Evaluation of old and new antimalarial drugs in sensitive and resistant strains.
3. Ultrastructure and cytochemistry of malaria parasites.
4. Interaction of antimalarial drugs with plasmodial nucleic acids.
5. Genetics and dynamics of drug resistance in malaria.
6. Hybridization and characterization of clone-derived strains.

University of London

RESEARCH GROUP ON CONTROL OF PROTEIN BIOSYNTHESIS IN ANIMAL CELLS

Department of Biochemistry, King's College, Strand, London W.C.2

(01–836 5454)

Director
Professor H. R. V. Arnstein, D SC

1. Control of chain initiation in protein biosynthesis.
2. Isolation, fractionation and biosynthesis of haemoglobin messenger RNA.
3. Translation of homologous and heterologous messenger RNA.
4. Biosynthesis of nuclear RNA.
5. Fractionation of valyl transfer RNA.

RESEARCH GROUP ON THE BIOLOGY OF AGEING

Department of Zoology, University College London, Gower Street, W.C.1

(01–387 7050)

Director
A. Comfort, MB, D SC

1. Ageing patterns in captive fish populations; culture and senescence of annual fish.
2. Analysis of mammalian age records.
3. Ageing processes and causes of death in fixed postmitotic cells: (*a*) nature and histology of the senile changes in striped muscle; (*b*) survival of *Drosophila* imagos and the temperature coefficient of imaginal longevity; (*c*) protein turnover and marker incorporation in *Drosophila* imago protein; (*d*) effect of various agents on longevity of *Calliphora*.
4. Descriptive pathology of age processes in *Lebistes* spp. (with Dr A. Woodhead and Mrs S. Ellett, Ministry of Agriculture, Fisheries and Food, Fisheries Laboratory, Lowestoft).
5. Effects of antioxidants on the growth and survival of mice.
6. Irradiation studies in *Drosophila* (with Dr M. J. Lamb, Birkbeck College).
7. Organization of library and information service on ageing.

CEREBRAL FUNCTIONS RESEARCH GROUP

Department of Anatomy, University College London, Gower Street, W.C.1 (01–387 7050)

Director
Professor P. D. Wall, DM

1. Single-unit studies on various stages of sensory transmission pathways from skin, muscles and viscera.
2. Behavioural studies on the role of various cortical areas and of pathways to the higher centres in the analysis and retention of stimuli.
3. Collaborative clinical investigation of certain hypotheses about pain mechanisms arising from the physiological studies outlined in (1) above.

RESEARCH GROUP IN MEMBRANE BIOLOGY

Department of Biochemistry, Charing Cross Hospital Medical School, Chandos Place, London W.C.2 (01–836 7788)

Director
Professor A. N. Davison, B PHARM, D SC, FPS

1. Changes in the chemical composition of myelin and subcellular membranes in the brain during development and in desease.
2. Identification of a metabolically active fraction in adult myelin.
3. Biochemical studies on phenylketonuria.
4. Effects of undernutrition and stress on the biochemistry of the developing brain.

RESEARCH GROUP ON RENAL INFECTION

Department of Medicine, Charing Cross Hospital Medical School, Fulham Hospital, London W.6 (01–748 2050)

Director
Professor H. E. de Wardener, MBE, MD, FRCP

1. Use of macroangiological techniques in the diagnosis of pyelonephritis in life.
2. Bactericidal action of serum in patients with pyelonephritis.
3. Controlled trial of long-term and short-term administration of antibiotics in acute and chronic pyelonephritis.
4. Incidence of bacteriuria in the newborn.
5. Controlled trial of treatment in recurrent lower urinary infections.

RESEARCH GROUP ON THE METABOLISM AND HAEMODYNAMICS OF LIVER DISEASE

Department of Medicine, King's College Hospital, Denmark Hill, London S.E.5 (01–274 6222)

Director
R. Williams, MD, MRCP

1. Effect of phenobarbitone and other hepatic enzyme-inducing agents on bilirubin metabolism: animal and human trials.
2. Differential diagnosis of jaundice in man: a computer-based approach.
3. Mechanism of enlarged plasma volume in cirrhosis, blood dyscrasia and other conditions associated with splenomegaly.
4. Factors causing increased iron absorption and regulation of iron stores in haemochromatosis.
5. Hepatic transplantation in man: diagnosis of the rejection process and its control.

RESEARCH GROUP IN HAEMOLYTIC ANAEMIA

Department of Clinical Haematology,
University College Hospital Medical School, Gower Street, London W.C.1
(01–387 5861)

Director
Professor T. A. J. Prankerd, MD, FRCP

1. Haemoglobin synthesis in normal and thalassaemic red cell precursors.
2. Determination of the molecular abnormality in various abnormal haemoglobins.
3. Dissociation of haemoglobin.
4. Transport of iron to the foetus and into body stores.
5. Methods of detecting organ pooling of red cells in man and the relevance of pooling to red cell survival and dilution anaemia.
6. Metabolic changes in human red cells during *in vitro* incubation and in haemolytic anaemias.

RESEARCH GROUP IN EXPERIMENTAL PATHOLOGY

University College Hospital Medical School,
University Street, London W.C.1
(01–387 5861)

Director
Professor J. D. Judah, BM, MRCP

1. Mechanism of ion transport in cells and mitochondria, with special reference to K–H exchange and Ca transport.
2. Role of the phosphoprotein adenosine triphosphatase in ion transport in normal and injured cells.
3. Role of diet and microsomal enzymes in metabolism of hepatotoxins to their active forms.

RESEARCH GROUP ON HAEMOLYTIC MECHANISMS

Department of Haematology, Royal Postgraduate Medical School, Ducane Road,
London W.12
(01–743 2030)

Director
Professor J. V. Dacie, MD, FRCP, FC PATH, FRS

1. Relationship between intravascular coagulation and haemolysis.
2. Clinical study of patients with the haemolytic-uraemic syndrome, with particular reference to the value of heparin in treatment.
3. Red cell metabolism in hereditary haemolytic anaemias.
4. Synthesis of unstable haemoglobins in hereditary Heinz-body anaemias.
5. Characterization of the autoantibodies in autoimmune haemolytic anaemias and response of patients to immunosuppressive drugs.

RESEARCH GROUP IN CLINICAL PHARMACOLOGY

Department of Medicine, Royal Postgraduate Medical School,
Ducane Road, London W.12
(01–743 2030)

Director
Professor C. T. Dollery, MB, B SC, FRCP

1. Clinical pharmacology of β-adrenergic blocking drugs, with special reference to their hypotensive action.
2. Pharmacological action and metabolic fate of isoprenaline and other β-stimulant drugs used in the treatment of asthma.

3. Evaluation of the diabetogenic effects of chronically administered benzothiadiazine diuretics and their relationship to abnormalities of glucose metabolism in patients with vascular disease.
4. Relationship of a positive antiglobulin test and antinuclear factor test in patients treated with methyldopa to plasma and red cell binding and to the metabolism of the drug.
5. Interactions between drugs caused by enzyme induction or alterations in protein binding.
6. Long-term follow-up study of 1000 hypertensive patients receiving prolonged treatment to evaluate the influence of known risk factors in hypertensive cardiovascular disease and the effects of treatment.

INTESTINAL MALABSORPTION RESEARCH GROUP

Department of Medicine, Royal Postgraduate Medical School, Ducane Road, London W.12

(01–743 2030)

Director

Professor C. C. Booth, MD, FRCP

1. Absorption and intracellular digestion of protein.
2. Aetiology of coeliac disease.
3. Compensatory mechanisms in the small intestine, such as those that develop after intestinal resection or in various types of dietary stress.
4. Absorption of bile salts.
5. Bacterial flora of the small intestine in disease and its effects on metabolism.

RESEARCH GROUP ON THROMBOSIS

Department of Pharmacology, Royal College of Surgeons of England, Lincoln's Inn Fields, London W.C.2

(01–405 3474)

Director

Professor G. V. R. Born, MB, D PHIL

1. Mechanisms that cause blood platelets to adhere to vascular endothelium and to each other to form aggregates *in vivo* and *in vitro*.
2. Metabolism of adenosine derivatives in blood, with special reference to those that cause platelet aggregation and its inhibition.
3. Effects of hormones and vitamins on the properties of platelets and endothelium.
4. Experimental production of thrombosis in animals and its inhibition by chemical substances.
5. Effects on the microcirculation of drugs and other active substances applied by iontophoresis.

RESEARCH GROUP IN IMMUNOLOGY

Institute of Child Health, 30 Guilford Street, London W.C.1

(01–242 9789)

Director

Professor J. F. Soothill, MB, MRCP

1. Collection of quantitative control data on humoral and cellular immune response for characterization of partial immunity deficiency states.
2. Characterization of functionally deficient immunoglobulins in the antibody deficiency syndrome.
3. Effect of large doses of antigens on immunological mechanisms, both specific and non-specific, in newborn animals (with reference to the association of acquired congenital hypogammaglobulinaemia with congenital rubella).

4. Separation of antigen excess soluble complex in serum of patients with glomerulonephritis particularly the *Plasmodium malariae* nephrotic syndrome, with a view to antigen analysis and possibly hyposensitization.
5. Role of complement-dependent mechanisms, and specifically of antigen excess soluble complex, in milk allergy.
6. Mechanism of destruction of target cells by sensitized lymphocytes and effects of immunosuppressive agents on this, with particular reference to transplantation immunity and autoimmune disease.
7. Methods for increasing the therapeutic efficiency of immunosuppressive regimens by combined use of immunosuppressive and protective agents and by modification of therapeutic schedules.
8. Immunity to tumours in experimental animals and man.
9. Modes of action of the immunosuppressive sulphonic acid esters.
10. Characterization of the Fc fragment of IgG (with the Department of Experimental Pathology, Birmingham, and Department of Biochemistry, Uppsala).
11. Genetic characterization of subfragments of human IgG (with the Research Institute of Rheumatology, Oslo).

RESEARCH GROUP IN APPLIED NEUROBIOLOGY

Institute of Neurology, Queen Square, London W.C.1
(01–837 3611)

Director
Professor J. B. Cavanagh, MD, MRCP

1. Fine structure and chemical environment of the Ranvier's nodes.
2. Fine structure of the muscle spindle.
3. Protein synthesis in relation to myelination.
4. Metabolic lesion in organophosphorus and other experimental neuropathies.
5. Quantitative cell relationships around a brain wound.
6. Cell replacement mechanisms in normal brain.

University of Newcastle upon Tyne

RESEARCH GROUP ON THE BIOSYNTHESIS OF MACROMOLECULES

Department of Biochemistry, University of Newcastle upon Tyne NE1 7RU
(0632 28511)

Director
Professor K. Burton, PH D

1. Structure and function in amino acid transfer RNA.
2. Control of ribosomal RNA synthesis in bacteria.
3. Chemical structure of bacterial ribosomal RNA.
4. Effects of polyoma infection on the light satellite band of mouse cells; effects of bromodeoxyuridine on infection.

University of Oxford

RESEARCH GROUP IN MOLECULAR BIOPHYSICS

Laboratory of Molecular Biophysics,
Department of Zoology, Parks Road, Oxford
(0092 55278)

Director
Professor D. C. Phillips, PH D, F INST P, FRS

1. Atomic structures of globular proteins and their complexes, including lysozymes, myoglobins, glycolytic enzymes, immunoglobulins, α-lactalbumin and insulin.

2. Genesis of tertiary structure in proteins.
3. Primary structures of nucleic acids and proteins.
4. Structure of muscle.
5. Development of apparatus and methods for structural analysis.

University of Sheffield

RESEARCH GROUP ON INTESTINAL ABSORPTION

University Department of Physiology,
Western Bank, Sheffield S10 2TN
(0742 78555)

Director
Professor D. H. Smyth, MD, FRS

1. Location in the intestinal epithelial cells of the mechanism for transfer processes.
2. Electrical changes in the epithelial cell in relation to transfer.
3. The sources of energy for transfer processes and the competition between different systems for this energy.

University College of South Wales and Monmouthshire

RESEARCH GROUP ON THE STRUCTURE AND FUNCTIONS OF MICROORGANISMS

Microbiology Department, University College of South Wales and Monmouthshire, Cathays Park, Cardiff CF1 3NR
(0222 23590)

Director
Professor D. E. Hughes, D SC, F INST BIOL

1. Regulation of bacterial metabolism of O_2 and eH.
2. Differentiation in eukaryotic microorganisms.
3. Mitochondria of colourless algae and protozoa.
4. Microbial metabolism of fatty acids.
5. Biological effects and medical hazards of ultrasound.

University of Southampton

RESEARCH GROUP IN TISSUE TRANSPLANTATION IMMUNOLOGY

University Department of Zoology, Southampton
(0703 56331)

Director
Professor L. Brent, PH D

1. Mechanism of the normal lymphocyte transfer reaction.
2. Separation of small and large cells from antigen-stimulated lymphocytes and their immunological responsiveness.
3. Analysis of allogeneic inhibition.
4. Induction of tolerance with tissue extracts and antilymphocytic serum.
5. Strain specificity of antilymphocytic serum in mice.

University of Sussex

RESEARCH GROUP FOR GENETIC AND BIOCHEMICAL STUDIES ON BACTERIA AND BACTERIAL VIRUSES

School of Biological Sciences, University of Sussex, Falmer, Brighton

(0273 66755)

Director

Professor N. Symonds, PH D

Studies on the metabolism of DNA in bacteria, with particular reference to repair and recombination:

1. Behaviour of bacterial and bacteriophage mutants unable to complete successfully the process of genetic recombination.
2. Effects of ultraviolet irradiation on bacterial conjugation.
3. Thymine metabolism in *Escherichia coli* and the physicochemical basis of death following deprivation of thymine.

RESEARCH GROUP ON THE MECHANISMS OF BIOSYNTHESIS OF PROTEINS AND NUCLEIC ACIDS IN MAMMALIAN TISSUES

School of Biological Sciences, University of Sussex, Falmer, Brighton

(0273 66755)

Director

A. Korner, MA, PH D

1. Effect of hormones on protein synthetic activity of ribosomes.
2. Effect of hormones and amino acids on RNA and DNA synthesis in liver.
3. Antibody synthesis *in vitro*.

Research work aided by grants

The Council has always attached much importance to its scheme of grants. These are awarded, normally for a three-year period, for particular research projects to be carried out at universities and other centres by workers who are not members of its own staff. Such grants may be for the personal remuneration of individual workers, for the provision of scientific and technical assistance or for special research expenses. Grants are also given in a limited number of cases to universities for the purchase of costly equipment that will advance the work of one or more departments. The cost of grants is mostly met from the Council's grant-in-aid, and where this is not the case the source is indicated. Information about the number of grants awarded by the Council will be found on p. 273. The following list includes grants held or awarded between January and December 1968. Separate grants held by a single worker are indicated by (1), (2) etc., while (a), (b) etc. indicate separate projects supported by a single grant.

Aberdeen

ROWETT RESEARCH INSTITUTE

Enzymology Department

Dr G. A. LEVVY—glycosidases, with particular reference to the structure of glycoproteins. (1)

UNIVERSITY

Biological Chemistry Department

Dr D. C. BURKE—production of interferon. (2)

Professor H. M. KEIR—enzymes concerned in the biosynthesis of DNA in normal and virus-infected cells. (3)

Dr J. R. SARGENT—biosynthesis of proteins of the electron transfer pathway in rat liver microsomes. (4)

Genetics Department

Professor H. J. EVANS—actions of ultraviolet radiation and of chemical mutagens in producing chromo some damage in human cells *in vitro*. (5)

Chemical Pathology Department

Professor S. C. FRAZER and Mr W. MICHIE—thyroidectomy and parathyroid dysfunction (*also at Aberdeen Royal Infirmary and the Rowett Research Institute*). (6)

Chemistry Department

Dr R. A. CHALMERS—determination of tracers of alkaloids in fluorimetry. (7)

Dr A. B. TURNER—steroid conjugates. (8)

Materia Medica and Therapeutics Department

Dr J. CROOKS—mechanisms regulating thyroid function in physiological and pathological states. (9)

Medical Physics Department

Professor J. R. MALLARD—(1) development of improved quantitative scanning techniques for radioisotope localization; (2) electron-spin resonance measurements on body tissues and development of techniques for *in vivo* studies. (10)

Obstetrics and Gynaecology Department

Dr A. I. KLOPPER—functions of steroid hormones in pregnancy. (11)

Pathology Department

Dr A. L. STALKER—high-speed cinephotomicrography of the microcirculation in red cell aggregation and experimental defibrination. (12)

Physiology Department

Dr T. J. CROW—function of an ascending system of noradrenergic neurones in the brain. (13)

Psychology Department

Dr D. A. ALLPORT—coding of signals in the human visual system: temporal features of pattern recognition. (14)

Dr R. M. GILBERT—stimulus functions in sequential behaviour. (15)

Statistics Department

Dr A. W. F. EDWARDS—computer study of some aspects of human population. (16)

Aldershot

BROMPTON HOSPITAL, FRIMLEY

Dr A. F. FOSTER-CARTER—survey to investigate a possible connection between isoniazid and carcinoma. (17)

Aylesbury

STOKE MANDEVILLE HOSPITAL

Pathology Laboratory

Dr C. L. GREENBURY—role of antibody in the inhibition of the primary immune response to erythrocytes. (18)

Babraham

AGRICULTURAL RESEARCH COUNCIL INSTITUTE OF ANIMAL PHYSIOLOGY

Dr Ruth DEANESLY—reproductive physiology of the guinea pig, (19)

Dr Shirley GLASSTONE—development of teeth in tissue culture. (20)

Dr Marthe VOGT—(1) effect of drugs on brain monoamines and their metabolites; (2) identification and release of monoamines from neurones in the brain and modification by drugs of concentration, metabolism and activity of brain amines. (21)

Belfast

THE QUEEN'S UNIVERSITY

Anaesthetics Department

Professor J. W. DUNDEE—survey of side-effects and efficacy of standard and new analgesic drugs. (22)

Biochemistry Department

Dr D. T. ELMORE—proteolytic enzymes. (23)

Botany Department

Dr D. PARK and Dr P. M. ROBINSON—effects of ageing on fungal cultures. (24)

Child Health Department

Professor I. J. CARRÉ and Dr D. W. NEILL—inborn errors of metabolism in handicapped children. (25)

School of Dentistry

Mr C. P. ADAMS—dental growth and development in children. (26)

Department of Medicine

Professor J. VALLANCE-OWEN—free sulphydryl groups and synalbumin-insulin antagonism. (27)

Mental Health Department

Professor J. G. GIBSON—physiological responsiveness in psychiatric and normal subjects. (28)

Microbiology Department

Professor K. B. FRASER—farmer's lung: epidemiological and laboratory studies. (29)

Therapeutics and Pharmacology Department

Professor O. L. WADE—actions of the autonomic system on thyroid function. (30)

Birmingham

UNIVERSITY OF ASTON

Applied Psychology Department

Professor W. T. SINGLETON—skills analysis for outdoor work involving mobile powered tools. (31)

Biological Sciences Department

Professor A. J. MATTY—absorption of folic acid compounds and analogues through the intestine of the rat. (32)

Metallurgy Department

Dr D. J. ARROWSMITH—development of surgical implant alloys resistant to chloride ion attack. (33)

Pharmacology Department

Dr M. D. DAY—role of the sympathetic nervous system in arterial hypertension and its interaction with angiotensin. (34)

BIRMINGHAM ACCIDENT HOSPITAL

Dr J. P. BULL—work related to the Council's Monitron trial. (35)

DUDLEY ROAD AND ST CHAD'S HOSPITALS

Department of Medicine

Dr R. F. FLETCHER—work related to the Council's trial of potassium, glucose and insulin therapy in acute myocardial infarction. (36)

UNITED BIRMINGHAM HOSPITALS

BIRMINGHAM AND MIDLAND HOSPITAL FOR WOMEN

Clinical Endocrinology Department

Dr A. C. CROOKE—gynaecological endocrinology. (37)

CHILDREN'S HOSPITAL

Pathology Department

Dr A. H. CAMERON—abnormalities of conception: chromosome studies on oocytes and aborted foetuses and morphological studies on foetuses and placentas. (38)

GENERAL HOSPITAL

Nutritional and Gastrointestinal Unit

Dr W. T. COOKE—pH changes in the duodenum and jejunum of man in normal and pathological states. (39)

UNIVERSITY

Anatomy Department

Dr J. HERBERT—neuroendocrine basis of sexual and social behaviour of primates. (40)

Dr D. B. THOMAS—transplantation of foetal lymphomyeloid cells. (41)

Dr G. H. THOMAS—identification of acid metabolites of progesterone. (42)

Professor Sir Solly ZUCKERMAN—analysis of reaction of ferret ovaries to measured intensities of light and different light regimes. (43)

Biochemistry Department

Dr H. G. KLEMPERER— (1) enzymes in virus-infected cells; (2) regulation of RNA synthesis of chromatin. (44)

Professor S. V. PERRY—muscle biochemistry, including enzymic adaptation to contractile activity. (45)

Dr D. G. WALKER—development and control of enzyme systems within the developing mammalian foetus and newborn animal. (46)

Chemistry Department

Mr S. J. CREWS—polysaccharides in the human eye. (47)

Dr A. S. JONES—(1) relationship between chemical structure and biological function of nucleic acids; (2) synthesis and biological activity of analogues of oligonucleotides. (48)

Professor M. STACEY—preparation of a range of fluorocarbon compounds for test as anaesthetic agents. (49)

Institute of Child Health

Professor D. V. HUBBLE—growth hormone assays and observation of the biochemical effects of administration of growth hormone in the differential diagnosis of short stature in children. (50)

Dental Health Department

Professor P. M. C. JAMES—epidemiological study of dental and oral disease and related conditions in 5-year-old children resident in different areas of the West Midlands. (51)

Experimental Neuropharmacology Department

Dr G. B. ANSELL—relative importance of different pathways of phospholipid synthesis in the various anatomical areas of the brain. (52)

Experimental Pathology Department

Dr M. J. CHAMBERLAIN—insulin metabolism after myocardial infarction and during surgical operations, with particular reference to cardiac surgery. (53)

Dr P. W. DYKES—(1) use of isotopically labelled substances in clinical research problems, studied by means of the whole-body counter; (2) metabolism of the elements selenium, magnesium, manganese, copper, zinc and cobalt, studied with radioactive isotopes and the whole-body counter; (3) membrane digestion in the small intestine. (54)

Professor P. G. H. GELL—(1) occurrence of allotypic 'deletion' and 'disproportion' in antibodies; (2) hypogammaglobulinaemia; (3) production of specific antisera to human immunoglobulins; (4) biological studies of macrophages, with special reference to their origin and role in the immune response in the rabbit. (55)

Dr A. S. KELUS—genetic markers of immunoglobulins of experimental animals. (56)

Dr N. R. LING—lymphocyte transformation studies. (57)

Dr D. R. STANWORTH—(1) role of structurally altered IgG in the formation of rheumatoid factor; (2) characterization of immunoglobulins and their association and dissociation products; (3) isolation and characterization of biologically active fragments of immunoglobulins. (58)

Dr K. W. WALTON—(1) physicochemical and biological characterization of a new immunoglobulin (IgD); (2) application of isoelectric focusing in pH gradients for separation of subclasses, isotopes and allotypes of serum proteins; (3) immunochemical investigation of structure of human β-lipoprotein allotypes. (59)

Medical Biochemistry and Pharmacology Department

Dr R. COLEMAN—lipid metabolism related to structure in animal cell surface membranes. (60)

Dr G. H. A. HÜBSCHER—(1) carbohydrate metabolism and the electron transfer system in the mucosal cell of the small intestine; (2) lipid metabolism in the mucosa of the small intestine. (61)

Dr W. F. R. POVER—(1) measurement of body radioactivity, with special reference to self-absorption and neutron activation; (2) metabolism of the intestinal mucosa, using suspensions of intact epithelial cells. (62)

Department of Medicine

Professor J. M. BISHOP—respiratory gas exchange in chronic bronchitis and emphysema. (63)

Dr C. W. CRANE—protein metabolism in patients suffering from malnutrition. (64)

Dr G. CUMMING—time course of gas mixing in lung and gas exchange with the blood. (65)

Dr R. F. FLETCHER—lipid metabolism. (66)

Neurocommunications Research Unit

Dr Phyllis E. STOPP—source of the cochlear afterpotential. (67)

Paediatrics and Child Health Department

Dr R. H. R. WHITE—investigation of urinary cell excretion in children, in health and in renal disease. (68)

Physiology Department

Dr Gerta HILTON—role of the motoneurone in the determination of functional properties of skeletal muscle. (69)

Dr Bertha SINGER—regulation of aldosterone secretion in normal and pathological conditions. (70)

Dr J. H. WOLSTENCROFT—chemical transmission and function in the reticular formation. (71)

Surgery Department

Mr R. M. BADDELEY—investigation of gastric mucus in cirrhosis of the liver, aspirin therapy and some metabolic derangements associated with surgical stress. (72)

Mr A. D. BARNES—immunogenetics of homograft rejection. (73)

Mr C. W. O. WINDSOR—gastric hypersecretion following resection of the small bowel. (74)

Transportation and Environmental Planning Department

Dr G. M. MACKAY—traffic injury, vehicle damage and the environment. (75)

Virology and Bacteriology Department

Professor M. P. L. WILDY—structural proteins in the virus particle of herpes simplex. (76)

Blackburn

THE ROYAL INFIRMARY

Dr I. W. DELAMORE—effect of iron deficiency on gastric function. (77)

Bradford

UNIVERSITY

Biological Sciences Department

Mr T. CROSS—actinomycete taxonomy and the thermophilic actinomycetes in relation to farmer's lung. (78)

Pharmacy Department

Dr J. M. FOY—factors affecting water transport in the gastrointestinal tract. (79)

Textile Technology Department

Mr C. H. PEARSON—neutral sugars and glycopeptides of the human intervertebral disc. (80)

Brighton

UNIVERSITY OF SUSSEX

Biological Sciences Department

Dr R. J. ANDREW and Mr F. A. MILES—neurophysiological and behavioural study of vision in the chick. (81)

Dr R. COLE—(1) factors influencing cytodifferentiation during mammalian development *in vivo* and *in vitro* and their relevance to carcinogenic and other disease transformations; (2) cell population kinetics in foetal and mutant erythroid tissue of mice and rats. (82)

Dr A. FEINSTEIN—structure and function of immunoglobulins. (83)

Dr M. T. GILLIES—mosquito behaviour. (84)

Dr B. C. GOODWIN—intercellular communication and the timing of biosynthetic events during the bacterial cell cycle. (85)

Professor A. KORNER—(1) biosynthesis, nature and biological action of macromolecules; (2) mechanism and control of protein and nucleic acid biosynthesis in mammalian tissues. (86)

Professor J. MAYNARD SMITH—protein synthesis and ageing in *Drosophila*. (87)

Dr S. SHALL—(1) synthesis of heavy-atom derivatives of bovine pancreatic ribonuclease; (2) chemical synthesis of heavy-atom derivatives of insulin. (88)

Dr D. SCHULSTER—role of the adrenocorticotrophic hormone in stimulating steroidogenesis in the adrenal gland of the rat. (89)

Professor N. SYMONDS—work with the Council's Research Group for Genetic and Biochemical Studies on Bacteria and Bacterial Viruses. (90)

Dr K. W. TAYLOR—synthesis and secretion of glucagon. (91)

Dr M. WALLIS—structure of pituitary growth hormone and prolactin. (92)

Dr P. A. WHITTAKER—electron transport mechanisms and respiratory deficiency. (93)

Experimental Psychology Laboratory

Dr A. D. BADDELEY—long-term and short-term memory. (94)

Mr M. S. HALLIDAY—(1) reinforcing properties of warning signals; (2) acquisition of free-operant avoidance behaviour. (95)

Dr E. M. MACPHAIL—functional analysis of avian forebrain structures involved in learning. (96)

Dr W. H. A. MUNTZ—physiological mechanisms underlying perception. (97)

Dr K. OATLEY—thirst and the control of water intake. (98)

Professor N. S. SUTHERLAND—(1) sensory motor adaptation; (2) biochemically differentiated mechanisms in systems mediating hunger. (99)

University Health Service

Dr A. RYLE—personality, psychiatric illness and psychiatric treatment in relation to the university careers of students. (100)

Bristol

BATH UNIVERSITY OF TECHNOLOGY

Pharmacy School

Dr M. R. W. BROWN—effect of Tween 80 on the resistance of *Pseudomonas aeruginosa* to chemical inactivation. (101)

FRENCHAY HOSPITAL

Neurological Surgery Department

Mr A. HULME and Dr R. COOPER—intracranial pressure in man (*also at Burden Neurological Institute*). (102)

SOUTHMEAD HOSPITAL

Pathology Department

Dr J. B. HOLTON—(1) dietary treatment, inheritance and pathogenesis of histidinaemia; (2) assessment of an automated fluorometric method of measuring blood phenylalanine as a screening test for phenylketonuria. (103)

UNITED BRISTOL HOSPITALS

ROYAL HOSPITAL FOR SICK CHILDREN

Dr D. BURMAN—iron deficiency anaemia in infancy. (104)

ROYAL INFIRMARY

Dr R. P. WARIN—aspects of urticaria and dermatographism. (105)

UNIVERSITY

Bacteriology Department

Professor W. A. GILLESPIE—significance of L-forms of bacteria in chronic pyelonephritis. (106)

Dr D. B. PEACOCK—respiratory syncytial virus. (107)

Biochemistry Department

Professor P. B. GARLAND—mitochondrial organization. (108)

Professor P. J. RANDLE—enzyme regulator sites and the genetic basis of metabolic disease. (109)

Department of Medicine

Dr J. R. CLAMP and Professor L. HOUGH—structure of immunoglobulins and related glycopeptides produced in various diseases (*also at Department of Chemistry, Queen Elizabeth College, London*). (110)

Dr M. I. V. JAYSON—rheumatic diseases. (111)

Oral Biology Department

Professor D. J. ANDERSON—sensory mechanisms in the teeth and their supporting structures. (112)

Pharmacology Department

Professor H. HELLER—uptake and release of hormones from neurohypophysial subcellular granules. (113)

H. H. Wills Physics Laboratory

Professor C. F. POWELL—use of ultrasonics in medical diagnosis. (114)

Physiology Department

Professor A. J. BULLER—projection from the cerebral cortex on to the cerebellar cortex by way of the inferior olive. (115)

Dr R. J. HARVEY—electrophysiological investigation of the inferior olive. (116)

Dr D. M. LEWIS—central control of muscle spindle sensitivity. (117)

Dr P. F. MILLINGTON—(1) effects of hormones on the development of phosphatase activity in the small intestine; (2) cell morphology and histochemistry in developing cell systems and effects of hormones on development of cells. (118)

Dr I. A. OLSON—investigation of the site of mitotic activity in the thymus of the guinea pig using combined autoradiography and mitotic arrest. (119)

Dr M. J. PURVES—respiratory and cardiovascular physiology. (120)

Dr A. F. ROGERS—prostaglandins and changes in the foetal circulation. (121)

Dr T. D. WILLIAMS—connections between the thalamus and the caudate nucleus and the part they play in the rhythmic response of the caudate nucleus to sensory stimuli. (122)

Psychology Department

Dr J. H. CROOK—field and laboratory study of the behaviour of the Sykes monkey. (123)

Radiodiagnosis Department

Professor J. H. MIDDLEMISS—cranio-cervical region in children and a study of normal and abnormal findings at the occipito-cervical junction from birth to adolescence. (124)

Surgery Department

Professor A. G. RIDDELL, Mr J. H. PEACOCK and Dr M. O. SYMES—homotransplantation of the pig liver. (125)

Veterinary Surgery Department

Dr S. J. BACH—the carcinostatic behaviour of certain enzymes, with special reference to asparaginase. (126)

Zoology Department

Dr P. C. CALDWELL—turnover of radioactively labelled compounds after injection into single muscle fibres. (127)

Professor G. M. HUGHES—(1) development of limb innervation; (2) ontogeny of cutaneous innervation in anural amphibians; (3) degeneration and regeneration of molluscan nervous systems. (128)

Cambridge

DUNN NUTRITIONAL LABORATORY

Dr Anne LLOYD—tuberculin sensitivity in undernourished and malnourished guinea pigs. (129)

FULBOURN HOSPITAL

Dr K. MYERS—therapeutic community treatment of chronically disturbed patients (*also at St Audry's Hospital, Woodbridge, Suffolk*). (130)

STRANGEWAYS RESEARCH LABORATORY

Dr T. MOORE—mode of action of vitamins A and E. (131)

UNIVERSITY

Anatomy Department

Dr M. A. MESSAGE—growth and development of mammalian skeletal muscle fibres.

Dr P. A. G. MONRO—microcirculation in man and animals. (133)

Dr R. PRESLEY—ultrastructure of early mammalian embryos. (134)

Animal Pathology Department

Professor W. I. B. BEVERIDGE—development of transplantable and transmissible tumours in the dog and cat. (135)

Sir William Dunn School of Biochemistry

Dr Anne STOCKELL HARTREE—purification of hormones from human pituitary glands. (136)

Professor H. LEHMANN—irregularities in amino acid sequences in normal protein. (137)

Dr A. J. MUNRO—biosynthesis of immunoglobulins. (138)

Dr P. K. TUBBS—study at the enzyme level of the inhibition of fatty acid biosynthesis by fatty acids. (139)

Dr P. K. TUBBS, Dr J. F. A. CHASE and Dr B. MIDDLETON—metabolism of coenzyme A and carnitine, with particular reference to the organization of fatty acid oxidation and the synthesis of ketone bodies and acetylcholine. (140)

Dr V. P. WHITTAKER—biochemical and morphological studies on presynaptic nerve endings and synaptic vesicles isolated from the central nervous system. (141)

Professor F. G. YOUNG—hormonal control of the activity of the pancreatic islets. (142)

Botany Department

Dr H. L. K. WHITEHOUSE—genetic investigation of the mechanism of crossing-over by means of spore colour mutants in *Sordaria brevicollis*. (143)

Colloid Science Department

Dr D. A. HAYDON—cell membrane structure and behaviour. (144)

Experimental Medicine Department

Professor R. A. McCance—(1) salt and water requirements in hot climates (*also at the University of Khartoum*); (2) writing of papers on renal function studies and experiments on salt and water requirements in hot climates. (145)

Genetics Department

Professor J. M. Thoday—genetic variation and endocrine function. (146)

Human Ecology Department

Dr R. G. Carpenter—application of numerical taxonomy to leucocyte typing and general medical problems. (147)

Investigative Medicine Department

Miss H. M. Bruce—reproductive physiology and behaviour of mice. (148)

Professor I. H. Mills—(1) effect of human pituitary fractions on adrenal steroid synthesis; (2) studies in women with secondary amenorrhoea (MRC trial of human gonadotrophins); (3) the artificial placenta; (4) control of androgen production in humans; (5) radioimmunoassay of luteinizing hormone; (6) intermittent corticosteroid therapy. (149)

Dr J. M. Walshe and Dr S. B. Osborn—normal and abnormal copper transport (*also in the Medical Physics Department, King's College Hospital, London*). (150)

Medical Applications of Psychology Research Unit

Dr P. C. Barrington—application of numerical taxonomy to clinical neurology. (151)

Dr J. L. Gedye—fundamental psychological problems relating to development of automated guidance systems for use in the industrial rehabilitation of patients with brain damage. (152)

Department of Medicine

Dr D. M. T. Gairdner—respiratory failure in the newborn (*also at Cambridge Maternity Hospital*). (153)

Professor J. S. Mitchell—techniques of short-term culture of haemic cells and the use of cytochemical and autoradiographic methods in the analysis of cell behaviour in normal and certain pathological states. (154)

Molteno Institute

Dr. P. Tate—encystation and excystation of *Entamoeba*. (155)

Organic Chemistry Department

Dr D. M. Brown—chemical mutagenesis. (156)

Pathology Department

Dr R. D. Barry—nucleic acids produced in cells infected with influenza viruses. (157)

Professor H. R. Carne—pathogenic corynebacteria related to *C. diphtheriae and C. ovis*. (158)

Professor R. R. A. Coombs—(1) chemical coupling of red cell antibodies with protein allergens; (2) standardization of class and subclass specific antiglobulin reagents for antiglobulin tests. (159)

Professor R. R. A. Coombs and Dr D. G. Chalmers—leucocyte typing. (160)

Dr D. Franks—marker antigens on cultured cells. (161)

Dr P. J. Lachmann—preparation of purified complement components and monospecific antisera to them. (162)

Dr B. W. J. Mahy—replication of influenza virus RNA. (163)

Pharmacology Department

Dr B. A. Callingham—effect of antidepressant drugs on uptake of catecholamines in the central nervous system. (164)

Dr E. K. Matthews—biophysical properties of endocrine and exocrine cells in relation to function. (165)

Dr J. F. Mitchell—release of transmitter substances from central synapses. (166)

Physiological Laboratory

Professor C. R. AUSTIN—problems of fertilization and embryonic development. (167)

Dr G. S. BRINDLEY—functions of the cerebellum. (168)

Dr F. W. CAMPBELL and Dr C. B. BLAKEMORE—transmission and transformation of spatial signals in the visual system. (169)

Dr J. G. ROBSON and Dr G. F. COOPER—sensory transformations in a primate retina. (170)

UNIVERSITY OF CAMBRIDGE (Dr D. A. T. NEW)—embryological studies, with special reference to *in vitro* techniques. (171)

Psychological Laboratory

Mr G. C. GRINDLEY—role of attention in visual perception. (172)

Dr P. WHITTLE—adaptation and contrast in brightness and colour perception. (173)

Professor O. L. ZANGWILL—the cerebral cortex in the learning processes of lower primates, with special reference to temporal lobe function. (174)

Surgery Department

Professor R. Y. CALNE—(1) renal transplantation; (2) liver transplantation. (175)

Veterinary Clinical Studies Department

Dr L. W. HALL—evaluation of new non-explosive anaesthetic agents. (176)

Dr R. V. SHORT—effect of the uterus on growth of tumours and other tissues. (177)

Zoology Department (Animal Behaviour Laboratory)

Professor R. A. HINDE—(1) mother-infant interaction in rhesus monkeys; (2) longitudinal study of behavioural development in mongol children. (178)

Mrs C. F. SCHOENBERG—contractile mechanism of vertebral smooth muscle. (179)

Student Expeditions

Mr D. G. ASHTON—importance of rodents in the transmission of schistosomiasis in East Africa: Cambridge Expedition to East Africa. (180)

Mr D. R. T. GUNDRY—atherosclerosis in squirrel monkeys in their natural habitat: Cambridge Medical Expedition to Colombia. (181)

Canterbury

UNIVERSITY OF KENT

Chemical Laboratory

Dr S. T. REID—design and synthesis of benz(*c*,*d*)indole derivatives related to 5-hydroxytryptamine. (182)

Dr A. WILLIAMS—mechanism of action of bacterial alkaline phosphatase. (183)

Cardiff

PUBLIC HEALTH LABORATORY

Institute of Preventive Medicine

Dr R. W. S. HARVEST—initiation and sources of salmonellosis in man in South Wales. (184)

VELINDRE HOSPITAL

South Wales Radiotherapy Centre

Dr P. B. KUNKLER—randomized controlled trial of radiotherapy under high-tension oxygen. (185)

UNIVERSITY COLLEGE OF SOUTH WALES AND MONMOUTHSHIRE

Anatomy Department

Dr J. C. BROWN—central nervous control of salivation. (186)

Professor J. D. LEVER—catecholamines in adrenergic neurones. (187)

Mr D. B. MOFFAT—morphology and functions of the medulla of the kidney. (188)

Chemistry Department

Professor L. CROMBIE—synthesis in the prostaglandin group of hormones. (189)

Department of Diseases of the Skin

Professor A. L. COCHRANE—analysis of data on a Gambian community. (190)

Microbiology Department

Professor D. E. HUGHES—biological effects of ultrasound in relation to possible medical hazards. (191)

UNIVERSITY COLLEGE (Dr A. CHARLES)—electron microscope location of enzymes in a metabolic chain by means of ferritin-labelled antibodies. (192)

Mining Engineering Department

Professor J. PLATT—recognition of industrial and other pollution and pathogenic particles. (193)

Psychology Department

Dr J. O. ROBINSON—personality characteristics and symptoms of individuals with high blood pressure who consult general medical practitioners. (194)

WELSH COLLEGE OF ADVANCED TECHNOLOGY

Chemistry and Biology Department

Dr R. E. HUGHES—passage of ascorbic acid across biological membranes. (195)

School of Pharmacy

Dr P. J. NICHOLLS—pharmacological properties of cotton dust and other vegetable fibre dusts in relation to the acute symptoms of byssinosis. (196)

WELSH NATIONAL SCHOOL OF MEDICINE

Anaesthetics Department

Dr W. W. MAPLESON—uptake and distribution of inhaled anaesthetic agents. (197)

Bacteriology Department

Dr T. D. BROGAN—mucous ground-substance of sputum in chronic bronchitis. (198)

Obstetrics and Gynaecology Department

Professor A. C. TURNBULL—(1) uterine activity, with special reference to prolonged pregnancy and labour; (2) induction of labour in pregnancy. (199)

Surgery Department

Professor A. P. M. FORREST—effect of the synthetic gastrin-like pentapeptide ICI 50,123, and of meals of varying buffering capacity on gastric secretion in dogs. (200)

Mr R. SHIELDS—(1) measurement of the rate of gastric emptying in man; (2) absorption of glucose, water, sodium and potassium by the intestine of conscious man and dog. (201)

Caterham

ST LAWRENCE'S HOSPITAL

Dr R. G. WESTHALL—metabolic studies in mental retardation. (202)

Cirencester

EPIDEMIOLOGICAL RESEARCH UNIT

Virus Laboratory

Dr P. G. HIGGINS—application of organ cultures to the diagnosis and epidemiology of virus infections in the general community. (203)

Dagenham

BARKING REGIONAL COLLEGE OF TECHNOLOGY

Dr D. H. EYRE—synthesis of bisquaternary salts of potential value in the chemotherapy of cancer. (204)

Dartford Heath

JOYCE GREEN HOSPITAL

Dr H. G. CLOSE—incidence of XXX females in the general population. (205)

Dundee

UNIVERSITY

Anatomy Department

Professor D. A. T. DICK—role of intracellular membranes in cellular ion and water fluxes. (206)

Bacteriology Department

Dr D. M. GREEN—enteroviruses in the urine of patients with aseptic meningitis and the effects of Coxsackie virus B5 on the renal tissue of experimentally infected mice. (207)

Biochemistry Department

Dr G. C. BARR—(1) primary effects of mutagens in the causation of errors of replication during DNA and RNA biosynthesis *in vitro*; (2) genetic crossing-over in bacterial transformation and the influence of mutagens and carcinogens on the process. (208)

Mr R. BOOTH—mechanism of sterol absorption. (209)

Dr G. J. DUTTON—stimulation of glucuronide synthesis and associated enzymes in the chick embryo liver. (210)

Dr J. C. KERNOHAN—carbonic anhydrase reactions studied by spectrophotometric stopped-flow apparatus. (211)

Dr D. A. STANSFIELD—gonadotrophins and the function of ascorbic acid in the corpus luteum. (212)

Chemistry Department

Mrs Margaret R. WRIGHT—(*a*) some aspects of enzyme kinetics related to haemolysis; (*b*) equilibria and kinetics of hydrolysis of some compounds of biological importance. (213)

Child Health Department

Professor J. L. HENDERSON—adrenal function in newborn infants and children. (214)

Gynaecology and Midwifery Department

Professor J. WALKER—steroid studies in pregnancy. (215)

Physics Department

Dr H. R. WILSON—virus structure. (216)

Dr D. M. SHEPHERD—histidine decarboxylase, with particular reference to its role in gastric secretion. (217)

Social and Occupational Medicine Department

Professor A. MAIR—epidemiology of asbestosis and mesothelioma in Scotland. (218)

Dr J. SIMPSON—significance of anaemia among women factory workers. (219)

Dr W. TAYLOR—(1) social disability from noise-induced hearing loss; (2) measurement of hearing levels and possible correlating factors on the Island of Westray, Orkney. (220)

Durham

UNIVERSITY

Psychology Department

Dr G. W. GRANGER—effect of drugs on visual thresholds. (221)

Mr A. W. STILL—variability in the choice behaviour of rats, with particular reference to the memory mechanisms involved. (222)

Zoology Department

Professor D. BARKER—innervation of skeletal muscle. (223)

Edinburgh

CITY HOSPITAL

Professor J. W. CROFTON—physiology of the bronchus. (224)

HERIOT-WATT UNIVERSITY

Chemistry Department

Professor D. J. MANNERS—structure and metabolism of glycogen, with special reference to glycogen storage diseases. (225)

MOREDUN INSTITUTE

Professor A. St G. HUGGETT—location of fructose in the sheep foetus. (226)

UNIVERSITY

Institute of Animal Genetics

Professor G. H. BEALE—genetics of malaria parasites. (227)

Bacteriology Department

Professor R. CRUICKSHANK—(*a*) possible role of mycoplasmas in human infection; (*b*) antibiotic levels in respiratory infection. (228)

Dr D. M. WEIR—immune deviation in rats, with respect to naturally occurring antitissue antibodies, and effect of the physical state of antigen and lymphoreticular cell stimulation on the induction of the primary immune response to a simple protein antigen. (229)

Biochemistry Department

Dr P. C. JOCELYN—reduction of cystine in rat tissues. (230)

Dr J. S. M. MCKEE—mechanism of enzyme and coenzyme action and structure of the alcohol dehydrogenases. (231)

Dr J. H. OTTAWAY—kinetics of biological systems in intermediary metabolism. (232)

Dr A. P. RYLE—structure and activity of pepsin C and pepsinogen C. (233)

Child Life and Health Department

Dr T. T. S. INGRAM—retarded speech development in children. (234)

Clinical Chemistry Department

Dr F. L. MITCHELL—metabolism of C-19 and C-21 steroids in the foetus and newborn infant. (235)

Dr D. W. MOSS—comparison of alkaline phosphatase from different animal tissues. (236)

Professor L. G. WHITBY—enzymological studies, with particular reference to the development of diagnostically useful procedures. (237)

Dentistry Department

Dr J. A. HARGREAVES—survey of the dental health of children living in the Isle of Lewis. (238)

Forensic Medicine Department

Dr H. V. STREET—development of a rapid method of toxicological analysis. (239)

General Microbiology Department

Dr J. F. WILKINSON—repair of ultraviolet and ionizing radiation damage in the bacterium *Micrococcus radiodurans.* (240)

Machine Intelligence and Perception Department

Professor R. L. GREGORY—(1) visual illusions in stationary and in moving observers; (2) neurophysiological studies. (241)

Professor C. LONGUET-HIGGINS—computer simulation of linguistic skills. (242)

Professor D. MICHIE—(1) quantitative study of problem-solving behaviour; (2) biomedical computing on an 'open-shop' basis. (243)

Department of Medicine

Professor K. W. DONALD—efficacy of the Monitron apparatus in acute clinical situations. (244)

Natural Philosophy Department

Dr D. W. GREEN—determination of X-ray crystallographic structure of β-lactoglobulin and other proteins. (245)

Dr Mary MACDONALD—electron microscopy of human and experimental renal disease. (246)

Obstetrics and Gynaecology Department

Dr D. T. BAIRD—production, secretion and interconversion of oestrogen in the human and in the ewe. (247)

Dr M. G. KERR—cytogenetic study of female subfertility. (248)

Orthopaedic Surgery Department

Mr D. L. HAMBLEN—effect of hyperbaric oxygen on mouse cartilage and bone rudiments in tissue culture. (249)

Pathology Department

Dr B. E. HEARD—clinicopathological investigation of patients with irreversible airways obstruction; (2) quantitation of muscle in the trachea and bronchi in chronic bronchitis, emphysema and asthma. (250)

Pharmacology Department

Dr W. SIRCUS—relation between bradykinin-like polypeptides and pathological conditions of the gastrointestinal tract, with particular reference to surgical procedures. (251)

Physiology Department

Dr G. H. HAGGIS—high-resolution electron microscope study of proteins and lipoproteins. (252)

Dr W. E. WATSON—(1) factors influencing the metabolism of neurones and glial cells of the mammalian central nervous system; (2) application of quantitative microchemical techniques to a study of the response of the nerve cell to alteration of its functional state. (253)

Psychiatry Department

Dr R. C. B. AITKEN—psychophysiological study of anxiety in asthma. (254)

Professor G. M. CARSTAIRS—epidemiological study of the psychiatric and allied factors contributing to student wastage at the university. (255)

Dr D. W. STRAUGHAN—chemical transmission in the limbic system. (256)

Surgery Department

Professor Sir Michael WOODRUFF—immunological aspects of cancer. (257)

Surgical Neurology Department

Professor F. J. GILLINGHAM—investigation of the physiopathological mechanisms of Parkinsonism and the other dyskinesias. (258)

Therapeutics Department

Dr Joyce D. BAIRD—clinical and laboratory study of the relationship between growth hormone and diabetes mellitus. (259)

Dr M. A. EASTWOOD—bile salt metabolism. (260)

Professor R. H. GIRDWOOD—(1) interrelationships of iron deficiency anaemia, pernicious anaemia and gastric carcinoma; (2) structure and function of the gastric mucosa in iron deficiency and chronic gastric atrophy due to other causes. (261)

Veterinary Physiology Department

Dr A. L. HAIGH—relationship of circulatory changes to secretory activity in the mammalian stomach. (262)

Ashworth Laboratory of Zoology

Mrs K. M. G. ADAM—DNA-mediated transformation of free-living amoebae. (263)

Dr J. G. HOWARD—immunological aspects of reticuloendothelial cells. (264)

Dr A. H. MADDY—role of proteins in plasma membrane structure. (265)

Dr H. S. MICKLEM—(1) ageing in haematopoietic cell populations: (2) cells forming allo-antibody after tissue allografting. (266)

Dr P. A. G. WILSON—economy of free-living stages of parasites. (267)

WESTERN GENERAL HOSPITAL

Regional Neurophysiology Centre

Dr H. R. A. TOWNSEND—statistics and quantification in clinical neurophysiology. (268)

Entebbe, Uganda

EAST AFRICA VIRUS RESEARCH INSTITUTE

Dr G. W. KAFUKO—Burkitt's tumour and other cancers in the West Nile District (*from private funds at the Council's disposal*). (269)

Epsom

Dr E. J. C. KENDALL—acute respiratory infections occurring in a general practice population. (270)

Exeter

UNIVERSITY

Chemistry Department

Professor H. N. RYDON—synthesis of peptide models of esterase-active centres. (271)

Physics Department

Mr K. P. S. CALDWELL and Dr F. C. FLACK—control of rectal and urinary incontinence (*also at Royal Devon and Exeter Hospital*). (272)

Psychology Department

Professor R. L. REID—associative shifting. (273)

Dr D. K. STRONGMAN—effects of stress on discrimination learning. (274)

Fajara, The Gambia

MEDICAL RESEARCH COUNCIL LABORATORIES

Mrs M. E. WILSON—incidence of malaria. (275)

Glasgow

ROYAL BEATSON MEMORIAL HOSPITAL

Pathology Department

Dr H. Morag MCCALLUM—glutamylaminoacetonitrile and its analogues as tools in the study of mucopolysaccharide synthesis and as possible therapeutic agents. (276)

ROYAL INFIRMARY

Biochemistry Department

Sir David CUTHBERTSON—metabolic response to physical injury, with particular reference to the effects of diet and temperature and to injuries induced by various types of radiation. (277)

Department of Medicine

Professor A. S. DOUGLAS—nature and action of prothrombin converting principle. (278)

Professor E. M. MCGIRR and Dr J. A. THOMSON—thyroglobulin biosynthesis (*under scheme for provision of costly equipment*). (279)

Orthopaedic Surgery Department

Mr J. WHITE—a comparison of free and pedicled bone grafts in dogs. (280)

Surgery Department

Mr J. M. ANDERSON—homograft rejection. (281)

Professor W. A. MACKEY—cerebral blood flow. (282)

UNIVERSITY

Bacteriology Department

Dr D. A. R. SIMMONS—immunochemistry of lipopolysaccharides from *Shigella flexneri*. (283)

Professor R. G. WHITE—mechanism of activity of mycobacteria and other bacteria as immunological adjuvants. (284)

Professor R. G. WHITE and Dr D. M. V. PARROTT—cytoarchitecture of the immunological system. (285)

Biochemistry Department

Dr J. G. BEELEY—structure and mechanism of biosynthesis of glycoproteins. (286)

Dr W. H. HOLMS and Dr C. A. FEWSON—bacterial permeation. (287)

Dr D. G. LEAF—release of amino acids from isolated insect nerve muscle preparations: biochemical aspects. (288)

Professor R. M. S. SMELLIE—nucleic acids and proteins in chromosomes and viruses (*under scheme for provision of costly equipment*). (289)

Chemistry Department

Dr C. J. W. BROOKS—(1) gas chromatography of corticosteroids and other biological materials; (2) application of combined gas chromatography and mass spectrometry to the study of steroids of clinical interest; (3) analytical characterization of steroid drugs and their metabolites. (290)

Dr C. J. W. BROOKS and Dr W. A. HARLAND—arterial tissues in atherosclerosis (*also in Pathology Department*). (291)

Dr. B. CAPON—intramolecular catalysts in glycoside hydrolysis. (292)

Dr A. WALTON—^{14}C in the environment and its importance in the assessment of radiation hazards. (293)

Wellcome Laboratory for Experimental Parasitology

Dr C. A. HOPKINS—(1) electron microscope study of the structure of tapeworm cuticle; (2) nutrition and *in vitro* cultivation of tapeworms. (294)

Genetics Department

Dr M. A. FERGUSON-SMITH—possible factors leading to chromosomal non-disjunction in man. (295)

Professor J. H. RENWICK—mapping of gene loci in man. (296)

Geriatric Medicine Department

Professor W. FERGUSON ANDERSON—recording of cardiac signs in the elderly. (297)

Infectious Diseases Department

Professor N. R. GRIST—virological study of sudden death in infancy. (298)

Department of Medicine in Relation to Mathematics and Computing

Professor W. I. CARD—construction and testing of models of medical diagnosis. (299)

Department of Medicine

Dr A. GOLDBERG—release of iron from the reticuloendothelial cells in rats. (300)

Professor G. M. WILSON—effect of thyroid disease and treatment of thyrotoxicosis by ^{131}I on bone density. (301)

Microbiology Department

Dr E. M. HARPER—electron microscope study of the effects of bacterial toxins on cell membranes, artificial membranes and cell organelles. (302)

Ophthalmology Department

Professor W. S. FOULDS—toxic optic neuropathies, with particular reference to aetiology and treatment. (303)

Department of Orthopaedic Surgery

Professor Roland BARNES—prospective survey of intracapsular fractures of the neck of the femur. (304)

Pathological Biochemistry Department

Dr A. FLECK—plasma albumin metabolism in disease states and following injury. (305)

Institute of Physiology

Dr I. A. BOYD—(*a*) muscle spindle as a transducer; (*b*) release of acetylcholine in skeletal muscle (*also at the Boyd Medical Research Institute*). (306)

Dr J. S. GILLESPIE—storage and release of catecholamines in adrenergic nerves. (307)

Steroid Biochemistry Department

Dr J. K. GRANT—biosynthesis of steroids and its abnormalities, with particular reference to the gonads in man. (308)

Surgery Department

Professor A. W. KAY—potential clinical applications of hyperbaric oxygenation. (309)

Zoology Department

Mr S. A. BARNETT—effects of breeding mice in a cold environment. (310)

Dr P. N. R. USHERWOOD—release of amino acids from isolated insect nerve muscle preparations. (311)

UNIVERSITY OF STRATHCLYDE

Applied Microbiology and Biology Department

Dr W. W. HUTCHISON—transmission of *Toxoplasma gondii*. (312)

Biochemistry Department

Professor P. J. HEALD—biochemistry of reproduction. (313)

Pharmacy Department

Professor W. C. BOWMAN—mechanism of action of adrenaline on muscle. (314)

Dr Mary DAWSON—antibacterial substances of animal origin. (315)

Dr F. FISH and Dr B. CADDY—application of capillary column gas chromatography to problems of drug analysis in humans. (316)

Dr R. T. PARFITT—chemical and physicochemical properties of the 6,7-benzomorphan analgesics and their pharmacological activity. (317)

Dr J. R. PARRATT—(*a*) mechanism of regulation of coronary blood flow; (*b*) coronary vasoconstrictor reflexes; (*c*) mode of action of antianginal drugs. (318)

Dr N. G. WATON—histamine formation in mammals. (319)

Radiation Laboratory

Dr A. WARD—classification of cells and chromosomes by pattern recognition. (320)

VICTORIA INFIRMARY

Pathology Department

Dr J. E. CRAIK—microarchitecture of skin and its behaviour under stress. (321)

WESTERN INFIRMARY

Pathology Department

Mr R. TYM—growth rate kinetics and radiation sensitivity in human and experimental malignant cerebral tumours. (322)

WESTERN REGIONAL HOSPITAL BOARD

Regional Physics Department

Dr F. C. GILLESPIE—measurement of diffusion coefficients of ^{133}Xe and ^{85}Kr in body tissues. (323)

Dr J. M. A. LENIHAN—strontium content of human tissue. (324)

Dr J. M. A. LENIHAN and Dr S. ALEXANDER—bladder electrode studies. (325)

Royal and Western Infirmaries

Dr C. BAINBRIDGE—feasibility and pilot studies for the establishment of blood pressure clinics. (326)

Hull

UNIVERSITY

Biochemistry Department

Dr Eileen RAMSDEN—kinetics and mechanism of enzymic hydrolysis of adenosine-3′,5′-phosphate. (327)

Chemistry Department

Dr G. W. GRAY—sensitivity of Gram-negative bacteria to ethylenediaminetetraacetic acid. (328)

Neurosurgery Department

Mr A. N. GUTHKELCH—three-dimensional analysis in the angiographic diagnosis of brain tumour. (329)

Dr G. W. GRAY and Dr S. G. WILKINSON—the cell wall of Gram-negative bacteria. (330)

Psychology Department

Professor A. D. B. CLARKE—varieties of lateral asymmetry. (331)

Dr H. C. A. DALE—coding in human memory. (322)

Inveresk

ARTHUR D. LITTLE RESEARCH INSTITUTE

Biochemistry Department

Dr A. K. SIM—activation of the fibrinolytic system. (333)

Kampala, Uganda

MAKERERE UNIVERSITY COLLEGE

Department of Medicine

Dr A. G. SHAPER—pattern of fibrinolysis and blood coagulation in different racial groups, with particular reference to intravascular thrombosis. (334)

Pharmacology and Therapeutics Department

Dr S. M. M. KARIM—effect of prostaglandins on the human umbilical blood vessels at different stages of pregnancy. (335)

Zoology Department

Dr Thelma E. ROWELL—social behaviour of monkeys in relation to the menstrual cycle. (336)

MRC CHILD NUTRITION UNIT

Professor R. A. MCCANCE—(1) direction of the Unit (*until February 1969*); (2) capacity of various ethnic groups to sweat in response to pilocarpine stimulus. (337)

MULAGO HOSPITAL

Dr T. HALL—infantile malnutrition. (338)

Keele

UNIVERSITY

Communication Department

Professor D. M. MACKAY—electrophysiological steady-state responses to periodic stimuli (see also p. 186). (339)

Kettering

GENERAL HOSPITAL

Department of Medicine

Dr G. S. CROCKETT—assessment of Monitron (patient-monitoring system). (340)

Kew

COMMONWEALTH MYCOLOGICAL INSTITUTE

Dr Phyllis M. STOCKDALE—taxonomy of dermatophytes. (341)

Khartoum, Sudan

UNIVERSITY

Dr J. R. KUSEL—carbohydrate metabolism of cercariae of *Schistosoma mansoni.* (342)

Kingston, Jamaica

UNIVERSITY OF THE WEST INDIES

Haematology Department

Dr P. F. MILNER—influence of specific nutritional deficiencies on the genetic expression of anaemia (*also at the MRC Tropical Metabolism Research Unit*). (343)

Pathology Department

Professor G. BRAS—chromosomal abnormalities in Jamaica. (344)

Physiology Department

Professor B. SCHOFIELD—intramural nerve plexuses in the control of gastric secretion. (345)

Kumi, Uganda

KUMI LEPROSY CENTRE

Dr J. A. KINNEAR BROWN—trial of BCG for leprosy. (346)

Leeds

UNITED LEEDS HOSPITALS

GENERAL INFIRMARY

Medical Physics Department

Dr J. B. DAWSON—development of new instruments and techniques for increasing the sensitivity and speed of emission and absorption flame photometry. (347)

Renal Research Unit

Mr P. B. CLARK—long-term storage of the kidney (*also in the University Chemical Pathology Department*). (348)

UNIVERSITY

Anaesthesia Department

Professor D. G. MCDOWALL—assessment of the effects of anaesthetic drugs on intracranial pressure, especially in patients with intracranial space-occupying lesions. (349)

Dr S. J. S. WEBB—work related to the Council's Monitron (patient-monitoring equipment) trial. (350)

Anatomy Department

Dr Julia M. FOURMAN—role of enzymes in sodium transport. (351)

Bacteriology Department

Dr J. G. SHOESMITH—effects of heat and radiation on tetanus spores. (352)

Biochemistry Department

Professor P. N. CAMPBELL—protein synthesis by animal cell components. (353)

Dr F. W. CHATTAWAY and Dr A. J. E. BARLOW—pathogenicity of *Candida albicans* (*also at the Royal Infirmary, Huddersfield*). (354)

Biophysics Department

Dr P. F. KNOWLES—electron-transfer processes in systems of biological importance. (355)

Chemical Pathology Department

Dr D. B. MORGAN—(1) metabolism *in vitro* of bone from cases of osteomalacia; (2) metabolism of organic phosphorus compounds and the effect of vitamin D on cell metabolism of phosphorus. (356)

Professor G. H. LATHE—(1) mechanisms of bile secretion; (2) green plasma in women taking contraceptive pills; (3) biochemical effects of high concentrations of dimethylsulphoxide on kidney at low temperatures; (4) pathways of bile secretion in relation to cholestatic jaundice. (357)

Dr R. E. OAKEY—mechanism of action of gonadotrophins on steroid biosynthesis by the follicle. (358)

Dr C. TOOTHILL—haem biosynthesis in human blood and bone marrow. (359)

Dental School

Dr J. A. WEATHERELL—microchemical investigation of dental enamel and dentine. (360)

Professor S. M. WEIDMANN—(1) biological activity of enamel and bone; (2) nature and composition of enamel protein in fully developed human teeth. (361)

Dermatology Department

Dr N. R. ROWELL—immunological studies in pemphigus, pemphigoid and dermatitis herpetiformis. (362)

Earth Sciences Department

Dr G. HORNUNG—mechanism of renal stone formation, studied with various biophysical techniques. (363)

Experimental Pathology and Cancer Research Department

Professor E. H. COOPER—biological testing of mineral oil fractions. (364)

Procter Department of Food and Leather Science

Dr H. E. NURSTEN—interaction between elastin and simple acid dyestuffs. (365)

Genetics Department

Dr M. d'A. CRAWFORD—control of gene action and human cells in culture. (366)

Professor J. R. S. FINCHAM—(1) genetic control of recombination in *Neurospora crassa*; (2) structure of wild type and mutant forms of *Neurospora* glutamate dehydrogenase. (367)

Medical Physics Department

Mr G. W. REED—*in vivo* measurement of the calcium content of bone by a radiation absorption method. (368)

Professor F. W. SPIERS—measurement of fallout fission products by computer analysis of γ-ray spectra. (369)

Department of Medicine

Dr M. S. LOSOWSKY—assay of plasma fibrin stabilizing factor activity in patients with congenital and acquired deficiencies. (370)

Dr M. S. LOSOWSKY and Mr J. KELLEHER—factors relating to vitamin E deficiency in man. (371)

Physiology Department

Dr R. HAINSWORTH—effects of stimulating left atrial receptors on blood flow in peripheral vascular beds. (372)

Professor G. R. HERVEY—regulation of energy balance and body fat content in the rat. (373)

Dr C. KIDD—central connections of cardiovascular afferent fibres. (374)

Dr R. J. LINDEN—(1) effect of hypoxia on pulmonary veins and of the stimulation of left atrial receptors on resistance to flow in the pulmonary circulation; (2) basic physiology of the cardiovascular system; (3*a*) effect of distension of the pulmonary vein on ventricular contractility; (3*b*) effect of distension of a pouch of the right atrium on the heart rate. (375)

Dr P. P. NEWMAN—properties of visceral afferent units in the cerebellum and cerebral cortex. (376)

Dr W. J. O'CONNOR—water and sodium balance in dogs. (377)

Surgery Department

Professor J. C. GOLIGHER—gastric secretion in patients with peptic ulcer. (378)

Zoology Department

Professor J. M. DODD—endocrine studies on the larvae of *Xenopus laevis*. (379)

Leicester

UNIVERSITY

Biochemistry Department

Dr A. J. ROWE—characterization of conformation changes in myosin. (380)

Genetics Department

Dr I. B. HOLLAND—nature and activity of enzymes concerned with recombination and repair of bacterial DNA, and mode of action of the antibacterial agent colicin, which appears to affect the activity of some of these enzymes. (381)

Laboratory of General Physiology

Dr O. HOLMES—(1) electrical activity of cells in the cerebral cortex of experimental animals and abnormalities in cortical activity in animals experiencing experimentally induced seizures; (2) cerebral activity in convulsive states and around epileptogenic lesions of the cerebral cortex. (382)

Leigh (Lancashire)

LEIGH INFIRMARY

Dr M. C. STONE—very-low-density lipoprotein levels and their relation to sex, age and body weight in a randomly selected group of 1000 subjects. (383)

Liverpool

ALDER HEY CHILDREN'S HOSPITAL

Dr E. P. HUDSON—organization of a phenylketonuria register (*on behalf of the Council's Phenylketonuria Working Party*). (384)

UNIVERSITY

Bacteriology Department

Professor K. MCCARTHY—varicella and other herpes group viruses in primates. (385)

Biochemistry Department

Dr J. M. TURNER—role of aminoacetone and 1-aminopropan-2-ol in the biosynthesis of vitamin B_{12}, and the possible antimicrobial activity of aminopropanol analogues and derivatives. (386)

Computer Laboratory

Professor A. YOUNG—computer studies of extraction processes in the liver. (387)

Dental Science Department

Professor R. L. HARTLES—the dental plaque. (388)

Obstetrics and Gynaecology Department

Professor T. N. A. JEFFCOATE—aetiology of defective folate metabolism in pregnancy. (389)

Organic Chemistry Department

Dr R. A. W. JOHNSTONE—composition of cigarette smoke. (390)

Pharmacology and General Therapeutics Department

Professor A. WILSON—metabolism and excretion of neostigmine. (391)

Physiology Department

Dr G. L. KIDD—(1) electrophysiological study of the intrafusal fibres of the mammalian muscle spindle; (2) response of muscle receptors to combinations of mechanical, thermal and chemical stimulation. (392)

Psychiatry Department

Professor C. A. CLARKE—clinical investigation of acute schizophrenia. (393)

School of Tropical Medicine

Professor S. G. COWPER—cultivation of adult schistosomes *in vitro* in a continuous-flow apparatus. (394)

Dr W. W. MACDONALD—physiology of filarial parasites and their mosquito hosts. (395)

Professor B. G. MAEGRAITH—(1) electron microscopy of liver lesions in experimental malaria; (2) effect of malarial and other protozoal infections on enzymes, including those of mitochondria. (396)

Dr G. PRINGLE—development of cell-mediated immunity in the pleural exudate of rodents experimentally infected with a filarial parasite. (397)

Professor H. L. SHEEHAN—pathology of eclampsia. (398)

Veterinary Anatomy Department

Dr T. D. GLOVER—neurovascular control of the production of spermatozoa. (399)

London

BATTERSEA: UNIVERSITY OF SURREY

Biochemistry Department

Professor D. V. PARKE—factors affecting the metabolism of drugs. (400)

Dr E. REID—control of nucleic acid metabolism in normal and cancerous liver. (401)

Metallurgy and Materials Technology Department

Professor M. B. WALDRON—wear and corrosion of surgical implants. (402)

BEDFORD COLLEGE

Physiology and Biochemistry Department

Dr J. R. LAGNADO—amine oxidases in developing brain tissue. (403)

Professor W. F. WIDDAS—lipid-soluble glucose complexes extractable from red cell ghosts. (404)

Psychology Department

Dr Monica LAWLOR—activity patterns in the golden hamster. (405)

Sociology Department

Dr G. W. BROWN—measurement and significance of crises in psychiatric and normal populations. (406)

Zoology Department

Dr E. G. HEALEY—visual discrimination of pattern and its relation to the pattern on the skin of certain fishes. (407)

BIRKBECK COLLEGE

Psychology Department

Professor P. H. VENABLES—psychophysiological and behavioural investigations of subclasses of chronic schizophrenics (*also at Netherne and Springfield Hospitals*). (408)

Zoology Department

Dr Marian J. LAMB—radiation-induced life shortening and ageing in *Drosophila*. (409)

BOROUGH POLYTECHNIC

Physics Department

Mr J. S. BEVAN—microscopic distribution of radiation dose and linear energy transfer. (410)

BROMPTON HOSPITAL

see Institute of Diseases of the Chest

CENTRAL MIDDLESEX HOSPITAL

Cardiothoracic Department

Dr K. P. BALL and Dr M. W. MCNICOL—haemodynamic and respiratory changes in acute myocardial infarction. (411)

Gastroenterology Department

Dr F. AVERY JONES—peptic ulceration. (412)

CHARING CROSS HOSPITAL MEDICAL SCHOOL

Bacteriology Department

Professor H. I. WINNER—antigenicity of *Candida albicans* and the associated allergy. (413)

Haematology Department

Dr G. D. PEGRUM—cytotoxicity of recipient lymphocytes following renal allografts. (414)

Department of Medicine

Professor H. E. de WARDENER—(1) bacteriological work connected with the Council's Research Group on Renal Infection; (2) control of salt and water excretion. (415)

Dr A. GUZ—afferent vagal discharge from the lungs of man and animals. (416)

Dr M. I. M. NOBLE—mechanical properties of isolated cardiac muscle. (417)

Dr Doreen M. NUTBOURNE—control of renal excretion of sodium and water by hormones other than aldosterone and vasopressin. (418)

Dr E. K. M. SMITH—cation transport across red cell membranes in health and disease. (419)

Mr J. STUBBS—production of a completely denervated heart in a dog. (420)

Obstetrics and Gynaecology Department

Mr P. CURZEN—value of heat-stable alkaline phosphatase in the serum of pregnant women as an index of placental function. (421)

Professor N. F. MORRIS—human placental metabolism in normal and abnormal pregnancies. (422)

Pharmacology Department

Professor J. B. E. BAKER—effect of drugs on coronary flow. (423)

Physiology Department

Dr J. LEE—(*a*) vasopressin-like substances in carcinomas; (*b*) methods for assay of vasopressin; (*c*) renal clearance of vasopressin in the dog. (424)

CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY

Biophysics Department

Dr D. ROSEN—electrical properties of phospholipids and proteins in model systems. (425)

Pharmacology Department

Professor M. GINSBURG—neurohypophysial hormones and reproductive function in males. (426)

Professor M. GINSBURG and Dr P. J. THOMAS—proteins that bind the hormones of the neurohypophysis. (427)

Pharmacy Department

Professor A. H. BECKETT—biochemical and metabolic aspects of narcotic drug addiction. (428)

Physics Department

Dr H. G. LEVENTHALL—infrasonic noise in industrial and city environments. (429)

Physiology Department

Professor S. E. DICKER—nature of the protein carrier neurophysin in newborn mammals. (430)

Dr A. HOWE—integration of responses of the respiratory and cardiovascular systems. (431)

Dr D. T. PLUMMER—enzymes present in serum and urine. (432)

FULHAM HOSPITAL

Edgar and Tenovus Laboratories

Dr K. D. BAGSHAWE—acute leukaemia in children. (433)

GUY'S HOSPITAL

Anaesthetics Department

Dr J. M. HALL—development of non-explosive anaesthetic agents (*in collaboration with Dr T. H. S. Burns, St Thomas's Hospital*). (434)

Handicapped Children's Centre, Newcomen House

Dr Mary D. H. SHERIDAN—developmental tests for infants and young children, with special reference to visual and language disorders. (435)

GUY'S HOSPITAL MEDICAL SCHOOL

Anatomy Department

Professor J. JOSEPH—control and mechanisms of tissue regeneration in the adult mammal.

Professor R. WARWICK—(1) biological effects of ultrasound; (2) temperature-dependent properties and dimensional characteristics of cytomembranes and their subunits. (437)

Bacteriology Department

Professor R. KNOX—characterization of chromosomal and episomal penicillinases in Gram-negative bacteria. (438)

Biochemistry and Chemistry Department

Dr D. B. GOWER—(1) biosynthesis of androst-16-en-3α-ol and other 3-hydroxy-Δ^{16} steroids; (2) metabolism of androst-16-enes in diseases of the adrenals, ovaries and testes. (439)

Professor G. A. D. HASLEWOOD—(1) changes in mitochondrial components that occur in perinatal life in relation to intolerance to anoxia; (2) small intestinal metabolism and absorption of bile salts in man. (440)

Dr D. C. WATTS—role of protein synthesis in hereditary muscular dystrophy. (441)

Chemical Pathology Department

Professor S. COHEN, Professor P. C. C. GARNHAM and Dr J. D. FULTON—isolation of protective malarial antigens (*also at the London School of Hygiene and Tropical Medicine*). (442)

Dr B. MCARDLE—human and experimental (plasmocid) myopathy (see also p. 170). (443)

Department of Medicine

Dr M. E. ABRAMS—biochemical studies of the surface-active lipoprotein isolated from mammalian lung. (444)

Professor W. J. H. BUTTERFIELD—(1) metabolism of isolated mammalian islets of Langerhans; (2) spontaneous diabetes in the spiny mouse; (3) patterns of protein excretion in early diabetic nephropathy and the effect of *p*-aminosalicylic acid on these patterns. (445)

Paediatric Research Unit

Dr M. ADOLFI—ontogenesis of human lysozyme. (446)

Professor P. E. POLANI—(1) Xm serum system in man and its genetics; (2) rates of cell division in aneuploid cells. (447)

Professor P. E. POLANI and Dr J. A. FRASER ROBERTS—(1) autosomal anomalies and some hereditary defects in a population sample; (2) parental irradiation and chromosome aberrations in the offspring. (448)

Dr Mary J. SELLAR—phenotype modifications in experimental chimeras in mice. (449)

Pathology Department

Dr J. N. BLAU—behaviour of the thymus in normal and pathological conditions, with special reference to Hassall's corpuscles. (450)

Pharmacology Department

Dr B. V. ROBINSON—anti-inflammatory factor found at inflammatory sites. (451)

Professor J. M. ROBSON—(1) effect of drugs on pregnancy; (2) mechanism of intestinal absorption. (452)

Physics Department

Professor C. B. ALLSOPP—development of an ultrasonic flowmeter for investigation of blood flow. (453)

Physiology Department

Dr T. J. H. CLARK—relationship between control of breathing and alveolar ventilation in patients with pulmonary disease (*also in the Department of Medicine*). (454)

Dr Betty COLES—clinical significance of serum isoamylases and some factors that influence their concentration. (455)

Dr J. N. CROSSLEY—dietary carbohydrate absorption and its influence on lipid metabolism. (456)

Professor I. MACDONALD—comparison of the metabolism of various carbohydrates after intravenous and oral administration. (457)

Surgery Department

Professor Sir Hedley ATKINS—Monitron (patient-monitoring) trial. (458)

Mr F. G. ELLIS—(1) bladder motility; (2) correlation of function of kidneys during extra-corporeal perfusion with subsequent function after reimplantation. (459)

HAMMERSMITH HOSPITAL

see Royal Postgraduate Medical School

HESTON: BOROUGH OF HOUNSLOW HEARING CLINIC

Dr L. FISCH—(*a*) new type of screen test for early detection of congenital deafness; (*b*) relation of parental age and parity to congenital deafness. (460)

HOSPITAL FOR SICK CHILDREN

see Institute of Child Health

HOSPITAL FOR TROPICAL DISEASES

Dr D. S. RIDLEY—histology of leprosy. (461)

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

Aeronautics Department

Dr C. G. CARO—(1) mechanics of small blood vessels and microcirculatory networks; (2) pattern of flow and flow properties in large arteries. (462)

Biochemistry Department

Professor E. B. CHAIN and Dr F. HIMMELWEIT—non-specific immunity. (463)

Chemistry Department

Dr J. A. BARRIE—diffusion in the mechanism of inert gas anaesthesia. (464)

Electrical Engineering Department

Professor J. C. ANDERSON—electrical properties of wet bone. (465)

Electrical Engineering Applied to Medicine Department

Professor B. McA. SAYERS—computer analysis of biological signals. (466)

Mechanical Engineering Department

Mr M. A. R. FREEMAN, Dr S. A. V. SWANSON, Dr P. G. BULLOUGH and Dr Helen MUIR—lubrication and load carriage in human synovial joints (*also at the Kennedy Institute of Rheumatology, London, and Nuffield Department of Orthopaedic Surgery, Oxford*). (467)

Physics Department

Dr B. H. CRAWFORD—colour discrimination in photocells and its relation to the solid-state theory of human colour vision. (468)

Department of Zoology and Applied Entomology

Dr Elizabeth U. CANNING—(1) sexual differentiation in sporozoa, with particular reference to coccidia and malarial parasites; (2) life cycle of new strains of murine malaria parasites and their cyclical transmission in the laboratory (*both at Ascot Field Station*). (469)

INSTITUTE OF BASIC MEDICAL SCIENCES,
ROYAL COLLEGE OF SURGEONS OF ENGLAND

Anaesthetics Department

Professor J. P. PAYNE—(1) circulatory, respiratory and metabolic responses to high concentrations of carbon dioxide during anaesthesia; (2) application of computer techniques to problems of anaesthesia. (470)

Biochemistry Department

Professor C. LONG—(1) structure of the erythrocyte membrane; (2) pathogenesis of hereditary retinal dystrophy in the rat. (471)

Dental Surgery Department

Professor B. COHEN—nutritional value of milk subjected to the ion-exchange process. (472)

Ophthalmology Department

Dr H. IKEDA—single-fibre optic nerve discharge properties, especially in relation to amblyopia. (473)

Pathology Department

Dr A. J. M. REESE and Dr M. S. ISRAEL—(1) role of the thymus in the development of the immune response; (2) formation of neoplasms of the thyroid following thyroid hyperplasia in neonatally thymectomized mice. (474)

Pharmacology Department

Professor G. V. R. BORN—(1) physicochemical factors involved in the action of glycosides on ion transport; (2) attempts to modify the surfaces of leucocytes, particularly lymphocytes; (3) mechanism and inhibition of platelet aggregation; (4) microiontophoresis of small blood vessels; (5) uptake and function of catecholamines in blood platelets. (475)

Professor J. R. VANE—(1) pharmacology of renin, angiotensin, catecholamines and gastrin; (2) circulating hormones. (476)

INSTITUTE OF CANCER RESEARCH AND ROYAL MARSDEN HOSPITAL

Biophysics Department

Dr N. M. BLACKETT—proliferation of transplanted bone marrow cells (*at the Surrey Branch of Royal Marsden Hospital*). (477)

Chester Beatty Research Institute

Professor P. ALEXANDER—mechanism of action by which immune lymphocytes prevent the growth of tumour cells *in vitro* and *in vivo*. (478)

Professor E. BOYLAND—enzyme-catalysed conjugations of glutathione with unsaturated compounds. (479)

Dr R. C. BRAY—(1) temperature-jump electron-spin resonance studies of enzyme mechanisms; (2) magnetic susceptibility measurements on paramagnetic metalloproteins down to helium temperatures (*also at Inorganic Chemistry Department, Imperial College of Science and Technology*). (480)

Dr P. BROOKES—(1) isolation and fractionation of nucleic acids and nucleoproteins; (2) mechanism of action of polycyclic aromatic hydrocarbon carcinogens; (3) metabolic activation of aromatic hydrocarbons by rodent embryo cells in culture (*all at Pollards Wood Research Station*). (481)

Dr A. R. CRATHORN—processes associated with DNA synthesis in synchronously dividing mammalian cells (*at Pollards Wood Research Station*). (482)

Professor L. A. ELSON—mechanism of acquired resistance of tumours to chemotherapeutic alkylating agents. (483)

Dr J. A. FORRESTER—isolation of growth control factors from normal and tumour cells. (484)

Professor A. B. FOSTER—(1) synthesis and evaluation of antitumour and other biological activity of fluorinated carbohydrates; (2) metabolism of aniline mustard and related compounds. (485)

Dr K. R. HARRAP—control of sulphur metabolism and the mechanism of action of alkylating drugs. (486)

Professor P. C. KOLLER—(1) role of chromosomes in carcinogenesis; (2) influence of environmental factors on karyotype stability. (487)

Dr F. J. C. ROE—(1) response to thymectomy and exposure to chemical carcinogens of mice maintained under germ-free conditions; (2) asbestos migration and carcinogenesis. (488)

Professor W. C. J. ROSS—substituted nicotinamide adenine dinucleotides that may act as stereospecific inhibitors of glycolysis and selectively inhibit tumour growth. (489)

Dr G. P. WARWICK—mechanism of action of liver carcinogens. (490)

Clinical Pathology Department

Dr H. E. M. KAY—collection and preservation of foetal tissues. (491)

Cytogenetics and Experimental Pathology Departments

Dr A. J. S. DAVIES and Dr R. L. CARTER—effect of malignant cell populations on the immunological processes. (492)

Physics Department

Dr C. R. HILL—biological action of ultrasound. (493)

Radiotherapy Department

Dr E. O. FIELD—immunological and haemopoietic disturbances in Hodgkin's disease (*at the Surrey branch of the Royal Marsden Hospital*). (494)

INSTITUTE OF CARDIOLOGY

Professor P. HARRIS—microsomal adenosine triphosphatase activity in the human myocardium. (495)

INSTITUTE OF CHILD HEALTH AND HOSPITAL FOR SICK CHILDREN

Mr H. H. NIXON—mechanism of the anal sphincter and its abnormalities. (496)

Chemical Pathology Department

Dr Barbara E. CLAYTON and Professor J. M. TANNER—growth hormone in children. (497)

Child Health Department

Dr D. HULL—metabolism of brown adipose tissue *in vivo*. (498)

Professor O. H. WOLFF—(1) metabolic effects of a medium-chain triglyceride diet in children; (2) lipoprotein abnormalities in the familial hyperlipoproteinaemias in childhood, and the effect of treatment. (499)

Growth and Development Department

Professor J. M. TANNER—(1) development of adrenal function in children; (2) growth and development of children (Harpenden growth survey). (500)

Haematology Department

Dr R. M. HARDISTY—(1) acute leukaemia in children; (2) interrelationships of platelet function and ultrastructure in health and disease. (501)

Microbiology Department

Dr J. A. DUDGEON—(1) congenital abnormalities, with particular reference to the effects of rubella in pregnancy; (2) rubella vaccine trials (*on behalf of the Council's Subcommittee on Rubella*); (3) bacteriology of wound and other infections following major surgery in infancy and childhood. (502)

Neonatal Department (at Hammersmith Hospital)

Professor J. P. M. TIZARD—metabolism of brown adipose tissue in newborn animals. (503)

Dr J. S. WIGGLESWORTH—functional and structural studies on the lungs of premature babies and rabbits. (504)

Paediatric Pathology Department

Dr J. S. WIGGLESWORTH—experimental studies on growth retardation in the foetal rat. (505)

INSTITUTE OF DENTAL SURGERY

Children's Dentistry Department

Professor G. B. WINTER—(*a*) changes in periodontal membrane and bone subsequent to experimental pulpal injury in deciduous molar teeth of primates; (*b*) effects of a devitalizing and mummifying paste on the deciduous pulp after experimental pulpotomy in primates (*also at Buckston-Browne Surgical Research Farm, Downe, Kent*). (506)

INSTITUTE OF DERMATOLOGY

Bacteriology Department

Dr W. C. NOBLE—precise bacterial flora of skin lesions, with special reference to any patterns of infection during therapy and healing. (507)

Biochemistry Department

Dr P. D. MIER—acid mucopolysaccharides and the inflammatory reaction in the skin. (508)

Histochemistry Laboratory

Dr Elizabeth A. RYAN—degenerative conditions of human skin. (509)

Immunology Department

Dr J. L. TURK—(1) cytochemistry of sensitization; (2) identification of the allergen causing 'Dogger Bank itch'; (3) relevance of lymphocyte transformation *in vitro* to cutaneous contact sensitivity; (4) skin reactions induced by products of cell-antigen interaction *in vitro* and characterization of soluble mediators. (510)

Photobiology Department

Dr I. A. MAGNUS—(1) identification of DNP-hapten-protein complexes in skin; (2) ultraviolet radiation and the ageing of skin; (3*a*) liver function in skin photosensitization; (3*b*) lysosomes and photodynamic action; (4) porphyrin metabolism and sulphanilamide photosensitivity of the skin. (511)

INSTITUTE OF DISEASES OF THE CHEST AND BROMPTON HOSPITAL

Clinical Immunology Department

Professor J. PEPYS—immunochemical analysis of fungal and other glycopeptides. (512)

Experimental Pathology Department

Professor Lynne M. REID—(1) certain aspects of mucus secretion in the bronchial tree; (2) intracellular changes associated with mucus secretion; (3) bronchial mucus hypersecretion. (513)

Department of Medicine

Dr Margaret E. H. TURNER-WARWICK—immunological aspects of (*a*) interstitial pulmonary fibrosis and (*b*) intrinsic and extrinsic asthma. (514)

Pathology Department

Dr K. F. W. HINSON—standardization of Kveim test suspension. (515)

INSTITUTE OF EDUCATION

Professor J. TIZARD—(1) cytogenetic and psychiatric aspects of mongolism in Surrey; (2) advantages and disadvantages of different types of resident care for the mentally subnormal in Wessex (*with Wessex Regional Hospital Board at Winchester*). (516)

INSTITUTE OF LARYNGOLOGY AND OTOLOGY

Mr H. A. BEAGLEY—properties of the auditory evoked cortical potential as applied to audiometric testing. (517)

Oto-rhino-laryngology Department

Professor D. F. N. HARRISON—(1) normal and malignant larynges studied by serial section; (2) changes in the inner ear during administration of ototoxic and cytotoxic drugs. (518)

INSTITUTE OF NEUROLOGY AND NATIONAL HOSPITAL FOR NERVOUS DISEASES

Dr E. H. REYNOLDS—(*a*) electrolyte distribution in epilepsy; (*b*) anticonvulsant therapy and folic acid metabolism (*also at the MRC Neuropsychiatry Unit and West Park Hospital, Epsom*). (519)

Dr R. W. Ross RUSSELL—experimental cerebral embolism in the rabbit. (520)

Chemical Pathology Department

Dr G. CURZON—(1) aromatic amine metabolism in the brain; (2) biochemical studies on caeruloplasmin. (521)

Clinical Neurology Department

Professor R. W. GILLIATT—(1) toxic neuropathy in the baboon; (2) regeneration and remyelination of peripheral nerves in the baboon. (522)

Dr L. J. HERBERG—(1) neurological basis of motivation; (2) experimental epilepsy in the rat; (3) hypothalamic regulation of secondary drive. (523)

Dr W. I. MCDONALD—mechanism of recovery from the effects of acute demyelination. (524)

Electron Microscope Laboratory

Dr P. K. THOMAS—electron microscope study of experimental allergic neuritis. (525)

Neuropathology Department

Professor W. BLACKWOOD—microanatomical localization in the cerebellar cortex. (526)

Neurophysiology Department

Dr T. A. SEARS—centrifugal control of afferent transmission from receptors excited by the movements of breathing. (527)

Neurosurgical Department

Mr V. LOGUE—analysis of disorders of motor skill in patients with cerebral lesions. (528)

Pathological Department

Professor W. H. MCMENEMEY—(1) presenile dementias; (2) comparison between the protein fractions of the cerebrospinal fluid and those in the blood. (529)

Psychology Department

Dr Elizabeth K. WARRINGTON—(1) behavioural changes consequent on cerebral disease; (2) memory and perception in patients with cerebral lesions. (530)

Professor O. L. ZANGWILL—constructional apraxia. (531)

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY AND QUEEN CHARLOTTE'S MATERNITY HOSPITAL

Bacteriology Department

Dr Rosalinde HURLEY—pathogenesis of candidiasis. (532)

Chemical Pathology Department

Dr M. SANDLER—(1) catecholamine and 5-hydroxyindole metabolism and immunosympathectomized rats; (2) endometrial monoamine metabolism during the menstrual cycle; (3) isoenzymes of soluble monoamine oxidase. (533)

Obstetrics and Gynaecology Department (Hammersmith Hospital)

Professor J. C. MCCLURE BROWNE—(1) placental localization and estimation of chorio-decidual blood flow by means of ^{133}Xe inhalation; (2) maturational changes in the prostate of the human foetus, neonate and infant. (534)

Mr W. G. MACGREGOR—measurement of peripheral blood flows in normal pregnancy and the puerperium. (535)

INSTITUTE OF OPHTHALMOLOGY

Experimental Ophthalmology Department

Dr G. B. ARDEN—analysis of retinal activity. (536)

Pathology Department

Professor N. ASHTON—pathology of the vascular retinopathies. (537)

Physiological Optics Department

Dr R. A. WEALE—(1) ageing of the crystalline lens; (2) effect of movement on visual resolution; (3) laser and physiological properties of the eye. (538)

INSTITUTE OF ORTHOPAEDICS

Biomechanics and Surgical Materials Department (Stanmore)

Mr D. J. D. PERRINS—hyperbaric oxygen in the limitation of tissue destruction in burns of porcine skin. (539)

Burns Unit (Mount Vernon Hospital)

Dr J. T. SCALES—extended feasibility trial of levitation in the treatment of burns. (540)

Orthopaedics Department

Mr H. B. S. KEMP—electrical induction of bone formation in animals. (541)

Morbid Anatomy Department

Dr H. A. SISSONS—(1) bone structure and osteoporosis; (2) evaluation of treatment of osteogenic sarcoma of the femur and tibia. (542)

INSTITUTE OF PSYCHIATRY

Biochemistry Department

Dr H. S. BACHELARD—membrane proteins from mammalian brain. (543)

Professor H. MCILWAIN—electrical and chemical responses in isolated tissues from the mammalian brain to stimuli specifically patterned in time and locality. (544)

Dr C. D. RICHARDS—*in vitro* studies of synaptic transmission in the mammalian brain. (545)

Experimental Neurology Department

Dr G. ETTLINGER—(1) effects of damage to the cerebral cortex on the ability to make sensory discrimination; (2) identification of the brain structures concerned with cross-model transfer of training in the monkey. (546)

Professor Sir Denis HILL—(1) effect of epileptogenic lesions and ablations of the brain on complex behaviour in the monkey; (2) orienting reaction; (3) recording and analysis of data from studies on central nervous function (*under the scheme for provision of costly equipment*). (547)

Forensic Psychiatry Department

Professor T. C. N. GIBBENS—violence in prisoners. (548)

Neuroendocrinology Department

Dr W. A. LISHMAN—mechanisms underlying the association of sensory and senorimotor components in conditioned avoidance learning. (549)

Neuropathology Department

Professor P. M. DANIEL—distribution of insulin in body fluids and some factors regulating its secretion. (550)

Dr J. R. HENDERSON—metabolism of insulin, with special reference to the liver. (551)

Dr O. E. PRATT—effects of abnormal metabolism of amino acids on the brain. (552)

Psychiatry Department

Dr G. ETTLINGER—behavioural changes associated with (1) removal of frontal cortex in the monkey and (2) agenesis of the corpus callosum; (3) independence of the secondary focus in experimental epilepsy, and the properties of cortical units in such a focus. (553)

Dr G. W. FENTON—computer analysis of the EEG in schizophrenia. (554)

Dr T. C. N. GIBBENS—survey of epileptic offenders. (555)

Dr I. M. MARKS—comparative trial of conditioning treatment of neuroses. (556)

Dr E. MARLEY—(1) central effects of sympathomimetic and allied amines, with particular reference to temperature regulation; (2) action of sympathomimetic amines on the central nervous system; (3) effects of sympathomimetic amines on hypothalamic function. (557)

Dr R. P. MICHAEL—brain mechanisms underlying sexual and agonistic behaviour in primates. (558)

Dr S. RACHMAN and Dr I. MARTIN—psychophysiological and behavioural examination of desensitization procedures. (559)

Dr G. F. M. RUSSELL—psychiatric disorder and the prognosis in anorexia nervosa (*also at the Maudsley Hospital*). (560)

Professor M. SHEPHERD—clinical trial of maintenance therapy in depressive illness. (561)

Psychology Department

Dr P. SLATER—development of a service for analysing repertory grids by computer. (562)

INSTITUTE OF UROLOGY

Mr J. D. FERGUSSON—possible relationships between 'endemic' (primary) bladder stones and malnutrition. (563)

Dr George A. ROSE—(1) parathyroid hormone in urine; (2) effect of bendrofluazide on glomerular filtration rate. (564)

KENNEDY INSTITUTE OF RHEUMATOLOGY

Dr D. C. DUMONDE—role of the macrophage in delayed hypersensitivity (*also at the Immunology Department, Wright-Fleming Institute, St. Mary's Hospital Medical School*). (565)

Biochemistry Division

Dr Helen MUIR—connective tissue protein polysaccharides and their metabolic interrelation. (566)

Cellular Biology Division

Dr J. CHAYEN and Dr Lucille BITENSKY—function of lysosomes of the synovial cells in rheumatoid arthritis. (567)

KING'S COLLEGE

Anatomy Department

Professor Sir Francis KNOWLES—neuroendocrine control. (568)

Biochemistry Department

Dr M. CANNON—interaction of transfer RNA with ribosomal subunits. (569)

Dr A. DARBRE—phenolic compounds in urine. (570)

Dr Mary WHITTAKER—genetic and clinical studies of cholinesterase isoenzymes of tissues in various species, including man, with special reference to the central nervous system. (571)

Dr G. W. OFFER—structural and enzymic properties of myosin. (572)

Physiology Department

Dr A. TAYLOR—feedback control of voluntary muscle contraction in normal animals. (573)

KING'S COLLEGE HOSPITAL

Dr Ellen L. RHODES—deposition of a neutral glycoprotein in diabetic vascular lesions and pancreas and in diabetic and prediabetic skin lesions. (574)

KING'S COLLEGE HOSPITAL MEDICAL SCHOOL

Chemical Pathology Department

Professor C. H. GRAY—(1) enzymic degradation of haem proteins to bile pigments; (2) isomeric types of bile pigments; (3) protein and RNA metabolism in experimental porphyria; (4) metabolism in porphyria. (575)

Clinical Research Wing

Dr R. S. WILLIAMS—iron metabolism in liver disease. (576)

Dental School

Dr J. R. GARRETT—effects of duct ligation on salivary glands. (577)

Medical Unit

Dr V. PARSONS—collagen metabolism during healing of phosphate depletion rickets, studied with ^{14}C-labelled proline. (578)

Department of Medicine

Professor J. ANDERSON—(1) distribution of intracellular sodium and potassium in normal human tissues and in states of abnormal sodium metabolism; (2) development of an agreed medical terminology. (579)

Professor M. J. H. SMITH and Dr K. W. TAYLOR—(*a*) regulatory mechanism for insulin release in isolated islets of Langerhans; (*b*) measurement of anti-inflammatory drug concentrations and of their effects on some aspects of metabolism in animal tissue preparations. (580)

Obstetrics and Gynaecology Department

Dr P. F. DIXON—protein binding of steroids in plasma. (581)

Dr P. F. DIXON and Mr J. P. NEWTON—mode of action of clomiphene, studied by radioimmunosorbant assay, and its clinical application. (582)

Pathology Department

Dr Una M. KROLL—aetiology and recurrence rate of cervical erosion and its relationship to carcinoma (*also in Dr Kroll's general practice at St Paul's Cray, Kent*). (583)

Surgery Department

Professor J. G. MURRAY—(*a*) the vagal nerve in relation to treatment of duodenal ulcer; (*b*) interrelationship of pancreatic activity and gastric hypersecretion; (*c*) mode of action of gastrin. (584)

LISTER INSTITUTE OF PREVENTIVE MEDICINE

Biochemistry Department

Dr G. M. GRAY—(1) lipid components of the cytoplasm membranes of mammalian cells; (2) ceramide-containing glycolipids in mammalian tissues, with special reference to their biosynthesis. (585)

Professor W. T. J. MORGAN—(1) chemical basis of blood group specificity in man; (2) multiple blood-group-specific serological characters associated with simple glycoprotein molecules. (586)

Dr Winifred M. WATKINS—biosynthesis of blood-group-specific glycoproteins and red cell antigens. (587)

Biophysics Department

Dr J. M. CREETH—characterization of protein by the ultracentrifugal steady-state method. (588)

Dr R. A. KEKWICK—(1) macroglobulins of normal human plasma; (2) structure of IgM. (589)

Experimental Pathology Department

Dr W. E. PARISH—tissue-sensitizing antibodies in sera from cases of cot-death and milk sensitivity. (590)

Microbiology Department

Mrs J. M. DOLBY—immunology of *Bordetella pertussis* (*at Elstree*). (591)

Dr Ruth M. LEMCKE—antigenic structure of *Mycoplasma hominis*. (592)

Dr Elinor MEYNELL—genetics of drug resistance factors and other bacterial plasmids. (593)

Mr A. F. B. STANDFAST—(1) distribution of serotypes of *Bordetella pertussis*; (2) separation and characterization of the antigenic components of *Bordetella pertussis* (*at Elstree*). (594)

Dr A. B. STONE—regulation of DNA synthesis in microorganisms. (595)

Virology Department

Dr J. ALWEN—(*a*) role of adenovirus in the aetiology of infectious hepatitis; (*b*) hypersensitivity to smallpox vaccine. (596)

LONDON HOSPITAL

Dr L. FRY—(*a*) action of drugs in psoriasis; (*b*) follow-up of patients with dermatitis herpetiformis. (597)

Medical Unit

Dr F. B. BYROM—experimental hypertension. (598)

Professor C. WILSON—growth hormone clearance from the blood in man. (599)

Physiology Department

Mr A. G. PARKS—*in vitro* study of the physiology and pharmacology of human intestinal muscle (*also at the Research Department, St Mark's Hospital*). (600)

LONDON HOSPITAL MEDICAL COLLEGE

Bacteriology Department

Dr G. L. ASHERSON—(1) cytotoxic action of immune cells *in vitro*; (2) mechanism of immune deviation and the passive transfer of delayed hypersensitivity; (3) role of different cells in the induction of cellular immunity. (601)

Dr D. R. BAINBRIDGE and Dr G. GOWLAND—(1) kinetics of transplantation immunity; (2) role of bacterial antigens in transplantation immunity. (602)

Professor C. F. BARWELL—cytophilic antibody and the fate of intracellular organisms. (603)

Dental Anatomy Department

Mr R. W. FEARNHEAD—X-ray probe microanalysis of tooth channel. (604)

Endocrinological Medical Unit

Dr A. S. MASON—trial of human growth hormone therapy (*on behalf of the Council's Subcommittee on Human Pituitary Hormones*). (605)

Oral Medicine and Oral Pathology Department

Dr R. DUCKWORTH—diffusion of ions into sound and carious dental enamel. (606)

Dr N. W. JOHNSON—dental plaque and the pathogenesis of enamel caries and periodontal disease. (607)

Pharmacology Department

Dr F. B. GIBBERD—effect of decamethonium and other muscle relaxants on the neuromuscular block on potassium uptake and efflux of the isolated perfused rat diaphragm. (608)

Dr C. R. B. JOYCE—effectiveness of various therapeutic procedures. (609)

Physiology Department

Professor K. W. CROSS—pattern of oxygen uptake in the resuscitated newborn animal compared with that in the adult animal. (610)

Bacteriology and Immunology Department

Professor D. G. EVANS—antibacterial and antifungal activity of Vitricin. (611)

Dr A. J. ZUCKERMAN—(1) attempts to isolate the hepatitis virus; (2) action of mycotoxins and other hepatotoxins on human liver cell cultures. (612)

Department of Clinical Tropical Medicine

Professor A. W. WOODRUFF—toxocariasis in man. (613)

Electron Microscope Unit

Dr R. G. BIRD—electron microscope studies of the causal agents of tropical diseases and studies of the vector host tissues. (614)

Entomology Department

Dr B. R. LAURENCE—histology and histochemistry of mosquitoes and larval filarial worms. (615)

Dr M. G. R. VARMA—culture of tissues from arthropods and cold-blooded vertebrates for infection with arboviruses. (616)

Medical Statistics and Epidemiology Department

Professor P. ARMITAGE—(1) sequential significance tests; (2) mathematical epidemiology of disease with intermediate hosts. (617)

Dr Geoffrey A. ROSE—use of steroids in the nephrotic syndrome in adults. (618)

Mycological Reference Laboratory

Dr I. G. MURRAY—serology in the classification of fungi and in the diagnosis of mycoses. (619)

Occupational Health and Applied Physiology Department

Professor R. S. F. SCHILLING—(*a*) mortality of cohorts of workers at Cape Asbestos Factory, Barking; (*b*) asbestos exposure of patients diagnosed as suffering from mesothelioma. (620)

Dr M. L. THOMSON—(1) prospective study of asbestosis (*also at Cape Asbestos Factory, Barking*); (2) measurement of mucociliary efficiency in the normal and diseased lung (*also at the Institute of Nuclear Medicine, Middlesex Hospital Medical School*). (621)

Parasitology Department

Dr J. D. FULTON—(*a*) development of new tests for antibodies to *Toxoplasma*; (*b*) isolation of malaria antigens with a view to developing a vaccine for monkey malaria. (622)

Dr W. E. ORMEROD—protein metabolism of the malaria parasite. (623)

Mr G. WEBBE—comparative study of different strains of *Schistosoma haematobium* in both intermediate and definitive hosts (*at Winches Farm Field Station*). (624)

Ross Institute of Tropical Hygiene

Dr B. B. WADDY—biology and genetics of anopheline mosquitoes. (625)

Social Medicine Department

Dr J. H. RENWICK—search for various types of clustering of loci on human chromosomes. (626)

Virology Department

Professor F. FULTON—(*a*) immune adherence to tissue culture; (*b*) transmission of arboviruses by arthropods. (627)

MAIDA VALE HOSPITAL FOR NERVOUS DISEASES

see Institute of Neurology

MAUDSLEY HOSPITAL

see Institute of Psychiatry

MIDDLESEX HOSPITAL

Myerstein Institute of Radiotherapy

Dr A. M. JELLIFFE—extracorporeal irradiation of blood. (628)

MIDDLESEX HOSPITAL MEDICAL SCHOOL

Anatomy Department

Professor P. H. S. SILVER—heteroplastic and homoplastic combinations of primary optic vesicles and competent ectoderm in chick and duck. (629)

Courtauld Institute of Biochemistry

Dr J. B. JEPSON—metabolism of aromatic amino acids, with special reference to problems associated with mental health and neurological disorders. (630)

Dr A. E. KELLIE—(1) plasma levels of progestational steroids; (2) application of the principle of ' saturation analysis ' to steroids. (631)

Professor P. N. MAGEE—molecular mechanisms of carcinogenesis. (632)

Dr K. J. ZILKHA—fatty acid metabolism in multiple sclerosis. (633)

Department of Biology as Applied to Medicine

Dr N. E. GILLIES—restoration of bacterial cells exposed to ionizing or ultraviolet radiation. (634)

Mr R. F. J. WITHERS—action of lactones and related compounds on human chromosomes. (635)

Professor L. WOLPERT—(1) the motile components of amoeboid cells; (2) the cell surface membrane in cellular communication and cellular responses. (636)

Chemistry Department

Dr S. J. HOLT—effect of trypsin inhibitors on protein synthesis in the pancreas. (637)

Institute of Clinical Research

Dr J. D. N. NABARRO—(*a*) idiopathic hirsutism; (*b*) adrenocortical and metabolic response to acute medical stress. (638)

Ear, Nose and Throat Department

Mr W. S. LUND—motor nerve supply of the larynx and the mechanism and treatment of vocal cord paralysis. (639)

Experimental Pathology Department

Dr M. A. EPSTEIN—role of unknown herpes-like virus in cultured Burkitt lymphoblasts. (640)

Medical Unit

Dr J. L. H. O'RIORDAN—radioimmunoassay of human parathyroid hormone. (641)

Institute of Nuclear Medicine

Dr W. S. REITH—iodotyrosines and thyroid hormones in various states of thyroid function. (642)

Ferens Institute of Otology

Dr C. S. HALLPIKE—(*a*) histological studies of temporal bone; (*b*) biology of the inner ear fluids. (643)

Pharmacology Department

Professor C. A. KEELE—(1) bradykinin and related peptides; (2) isolation and mode of action of pain-producing substances. (644)

Rheumatology Research Department

Dr I. M. ROITT—(1*a*) hypersensitivity in human autoimmune disease; (1*b*) autoimmunity in thyrotoxicoses; (2) electron microscope investigations of autoimmune disease; (3) connective tissue diseases. (645)

MOORFIELDS EYE HOSPITAL

Mr D. AINSLIE—refractive keratoplasty. (646)

MOUNT VERNON HOSPITAL

Dr S. DISCHE—use of high-pressure oxygen chamber in radiotherapy. (647)

Mr I. F. K. MUIR—blood flow of pedicle and flap grafts used in plastic and reconstructive surgery. (648)

NATIONAL HOSPITAL

see Institute of Neurology

NATIONAL INSTITUTE FOR MEDICAL RESEARCH

Miss S. L. NEHLSEN—work in the Institute's programme (*from private funds at the Council's disposal*). (649)

Human Physiology Division

Miss Margaret A. CHAMBERS—dietary survey of Tristan da Cunha islanders. (650)

Physiology and Pharmacology Division

Professor W. FELDBERG—physiology and pharmacology of the brain, with particular reference to temperature regulation and convulsive activity (*see also p. 101*). (651)

Virology and Bacteriology Division

Dr P. M. D'ARCY HART—(*a*) mechanism of the antituberculous effect of macrocyclon; (*b*) growth of leprosy bacilli in cell-free media. (652)

Mr W. D. WINTERS—adenovirus (*from private funds at the Council's disposal*). (653)

NATIONAL PHYSICAL LABORATORY

Dr I. P. PRIBAN—control of breathing, studied by means of control systems theory and an analogue computer. (654)

NUFFIELD INSTITUTE OF COMPARATIVE MEDICINE

Dr P. A. J. BALL—immunity to *Necator americanus*. (655)

Dr L. G. GOODWIN—(1) immunofluorescence techniques in the study of malaria and helminth infections of man and animals; (2) investigation in animals and birds of normal serum components that interfere with serological tests for arboviruses; (3) atherosclerosis and food lipid structure. (656)

Dr Christine M. HAWKEY—(1) fibrinolysis; (2) isolation and characterization of active substances in saliva of the vampire bat *Desmodus rotundus*. (657)

PADDINGTON GENERAL HOSPITAL

Pathology Department

Dr J. FIELDING—iron metabolism, with special reference to chelation. (658)

PADDINGTON GREEN CHILDREN'S HOSPITAL

Pathology Department

Dr S. B. ROSALKI—composition and function of lactate dehydrogenase isoenzymes in normal and diseased muscle. (659)

PUBLIC HEALTH LABORATORY SERVICE

PUBLIC HEALTH LABORATORY SERVICE BOARD—coordinated studies of the pattern of infection in acute respiratory virus infections. (660)

Central Public Health Laboratory, Colindale

Dr S. P. LAPAGE—analysis of the genetic material of the bacterial cell. (661)

QUEEN CHARLOTTE'S MATERNITY HOSPITAL

see Institute of Obstetrics and Gynaecology

QUEEN ELIZABETH COLLEGE

Biochemistry Department

Dr D. ROBINSON—intracellular location and role of β-glycosidases in the kidney. (662)

Chemistry Department

Professor L. HOUGH and Dr J. R. CLAMP—structure of immunoglobulins and related glycopeptides produced in various diseases (*also at Department of Medicine, University of Bristol*). (663)

Professor L. HOUGH—synthesis of new glycopeptide derivatives for the study of their chemical and biological properties. (664)

Microbiology Department

Dr G. E. MATHISON—biochemical basis for the pathogenicity of dermatophytes. (665)

Professor S. J. PIRT and Dr. G. E. MATHISON—dynamics of interferon production by suspended cell cultures. (666)

Nutrition Department

Dr D. S. MILLER—protein-calorie interrelationships. (667)

Professor J. YUDKIN—sugar intake and arterial disease. (668)

Physics Department

Dr M. E. V. HOLWILL—mechanisms of wave propagation in flagella. (669)

QUEEN MARY COLLEGE

Botany Department

Professor E. A. BEVAN—genetic effects of ultrasound. (670)

Chemistry Department

Dr E. W. RANDALL—hydrogen bonding, structure and tautomerism in molecules of biological importance. (671)

ROYAL DENTAL HOSPITAL

School of Dental Surgery

Dr W. G. ARMSTRONG—significance of phospholipids in the calcification mechanism. (672)

Professor H. J. J. BLACKWOOD—jaw opening, jaw closing and swallowing reflexes. (673)

Dr J. D. MANSON—bone morphology and activity in the jaws. (674)

ROYAL FREE HOSPITAL

Chemical Pathology Department

Professor D. N. BARON—(1) computer studies on the correlation between signs and symptoms and laboratory findings in liver disease (*also at University of London Institute of Computer Science*); (2) purification, properties and distribution of isoenzymes of NADP-specific isocitrate dehydrogenase. (675)

Dr Joyce BELL—isocitrate dehydrogenase and malate dehydrogenase in the investigation of placental disease. (676)

Dermatology Department

Dr I. SARKANY—organ culture of human skin, with particular reference to drug-induced stimulation of peripheral lymphocytes *in vitro*. (677)

Department of Medicine

Dr I. A. D. BOUCHIER—(1) changes in the bile and biliary tree during experimental cholelithiasis; (2) glycoproteins in the bile of patients with cholelithiasis. (678)

Dr Ten FEIZI—cold agglutinins caused by *Mycoplasma pneumoniae* infection. (679)

Dr N. MCINTYRE—control of intestinal and hepatic sterol biosynthesis. (680)

Professor Sheila SHERLOCK—(1) rate of albumin synthesis *in vitro* in normal and diseased states; (2) enzymatic control of bilirubin homeostasis in jaundice. (681)

Pathology Department

Dr Katherine M. DORMANDY—problems of children with coagulation disorders (*at North Western Branch, Lawn Road*). (682)

Renal Unit

Dr J. F. MOORHEAD—DNA synthesis in human peripheral blood lymphocytes *in vitro* (*at North Western Branch, Lawn Road*). (683)

ROYAL FREE HOSPITAL SCHOOL OF MEDICINE

Biochemistry Department

Dr H. BAUM—ultrastructural aspects of glycogen metabolism in health and disease. (684)

Dr A. T. DIPLOCK—role of vitamin E in relation to selenium and non-haem iron proteins. (685)

Professor J. A. LUCY—(1) chemical properties of vitamin A in relation to its biochemical mechanisms of action; (2) role of vitamin A in the biosynthesis and secretion of corticosteroids. (686)

Dr Brenda E. RYMAN—glycogen metabolism, with particular reference to the glycogen storage diseases. (687)

Biology Department

Dr R. J. BERRY—seasonal changes in a wild mouse population, with particular reference to climatic adaptation and survival. (688)

Medical Physics Department

Dr N. F. KEMBER—(1) cell proliferation kinetics of growth cartilage; (2) effects of radiation on cartilage cells in organ and tissue culture; (3) dosimetry and microdistribution of ^{239}Pu in rat bone. (689)

Department of Medicine

Dr Barbara H. BILLING—bile acid metabolism in liver disease. (690)

Dr E. SAMOLS—interrelationships between hormones and metabolites in health and disease. (691)

Pathology Unit

Professor K. R. HILL—changes in liver blood flow after poisoning with pyrrolizidine alkaloids and dimethylnitrosamine. (692)

Pharmacology Department

Professor Eleanor J. ZAIMIS—(1) drug-induced myocardial abnormalities; (2) biochemical abnormalities in drug-induced cardiomyopathies; (3) histochemical investigations in drug-induced cardiomyopathies. (693)

Physiology Department

Dr W. H. H. ANDREWS—abdominal afferent nerves, with special reference to osmoreceptors in the liver. (694)

Professor C. B. B. DOWNHAM—(1) supraspinal control of visceral activity; (2*a*) causative factors in the formation of urinary calculi; (2*b*) effects of radioprotective compounds on mammalian cells grown *in vitro*. (695)

ROYAL HOLLOWAY COLLEGE

Chemistry Department

Professor E. J. BOURNE and Dr J. B. PRIDHAM—hydrolytic enzymes involved in glycogen metabolism, with particular reference to hereditary disorders (*also in Biochemistry Department*). (696)

Dr A. FINCH—oxidizing properties of nitrogen fluorides and their degradation products, with special reference to methaemoglobinaemia. (697)

Zoology Department

Dr G. I. TWIGG—*Leptospira* in rodent populations. (698)

ROYAL INSTITUTION

Davy Faraday Research Laboratory

Dr C. W. BUNN—structure of the protein rennin. (699)

ROYAL MARSDEN HOSPITAL

see Institute of Cancer Research

ROYAL POSTGRADUATE MEDICAL SCHOOL OF LONDON AND HAMMERSMITH HOSPITAL

Anaesthesia Department

Dr J. NORMAN—effect of anaesthetic drugs and changes in respiration on the nervous control of the heart. (700)

Professor J. G. ROBSON—effect of anaesthetic drugs on the central nervous system. (701)

Dr M. K. SYKES—(1) effect of applied pressure waveforms on differences in alveolar arterial gas pressure and pulmonary blood flow during mechanical ventilation in the dog; (2) effects of anaesthetic drugs on pulmonary circulation. (702)

Bacteriology Department

Dr Naomi DATTA—transmissible drug resistance in Enterobacteriaceae. (703)

Biophysics Department

Dr D. K. HILL—optical changes in skeletal muscle resulting from length changes and from stimulation. (704)

Chemical Pathology Department

Dr K. FOTHERBY—metabolism of ovulation-suppressing agents. (705)

Professor I. MACINTYRE—isolation, structure and physiological effects of calcitonin. (706)

Professor I. D. P. WOOTTON and Dr J. R. HOBBS—protein studies for the Council's therapeutic trial in myelomatosis. (707)

Professor I. D. P. WOOTTON and Dr B. LEWIS—disorders of bile acid metabolism. (708)

Diagnostic Radiology Department

Dr F. H. DOYLE and Dr G. V. FOSTER—effects of chronic calcitonin administration on bone. (709)

Haematology Department

Professor J. V. DACIE—biochemistry of abnormal red cell metabolism in atypical congenital haemolytic anaemia. (710)

Dr S. M. LEWIS—pathogenesis of red cell defects in paroxysmal nocturnal haemoglobinuria and aplastic anaemia. (711)

Medical Microbiology Department

Professor A. P. WATERSON—structure of certain viruses and non-viral microorganisms and structure and action of antibodies. (712)

Medical Physics Department

Professor J. F. FOWLER—(1) improved radioisotope localization techniques for clinical diagnosis and for studies of turnover *in vivo*; (2) changes in the proportion of hypoxic cells in tumours as a function of time. (713)

Department of Medicine

Dr E. J. M. CAMPBELL—(1) proprioceptive mechanisms in the control of breathing and in the sensation of dyspnoea; (2) clinical value of physiological studies during exercise, and development of equipment for their performance. (714)

Dr C. T. DOLLERY—retinal circulation. (715)

Dr C. M. FLETCHER—preclinical stages of chronic bronchitis. (716)

Professor T. RUSSELL FRASER—(1) clinical trials of human growth hormone (*on behalf of the Council's Clinical Endocrinology Committee*); (2) nature of serum 'atypical' insulin-like activity; (3) radioimmunoassay of protein hormones and study of electrolyte kinetics in endocrine and metabolic disorders; (4) protein binding by gel filtration, with special reference to cortisol; (5) immunoassay of vasopressin in blood and urine; (6) stimuli affecting human pituitary function; (7) development of immunoassays for parathormone and calcitonin. (717)

Dr D. J. GALTON—regulation of biosynthesis and breakdown of triglycerides in man. (718)

Dr G. NEALE—absorption and metabolism of vitamin E in man and experimental animals. (719)

Dr J. B. WEST—blood flow, ventilation and gas exchange in the lung. (720)

Dr O. M. WRONG—reutilization of urea nitrogen for protein synthesis in man. (721)

MRC Microbial Genetics Unit (before transfer to Edinburgh)

Dr Elinor W. MEYNELL—resistance transfer factors in bacteria. (722)

Pathology Department

Professor C. V. HARRISON—human and experimental pulmonary hypertension. (723)

Professor A. G. E. PEARSE—elucidation of the sites of the effect and mechanism of the activity of calcitonin and localization of its source. (724)

Pharmacology and Therapeutics Department

Professor D. S. MUNRO—long-acting thyroid stimulator of thyrotoxicosis. (725)

Radiodiagnostic Department

Professor R. E. STEINER—lung densitometry for the study of pulmonary ventilation and pulmonary circulation. (726)

Radiology Department

Dr J. P. LAVENDER—comparison of gamma camera with non-isotope diagnostic techniques. (727)

Radiotherapy Department

Professor J. F. FOWLER and Dr R. MORRISON—technique for *in vivo* studies of hormone dependence of tumour growth. (728)

Surgery Department

Mr G. D. CHISHOLM—quantitation of renal blood flow and glomerular filtration rate by external counting methods (*with Gamma Camera Team*). (729)

Mr H. DAINTREE JOHNSON—mechanisms of gastric emptying, with special reference to the effects of surgery. (730)

Professor R. B. WELBOURN—insufficiency of the small bowel. (731)

Urology Department

Mr M. A. E. KULATILAKE—isolated kidney perfusion with whole blood. (732)

Professor R. SHACKMAN—acid excretions in the isolated kidney. (733)

ROYAL VETERINARY COLLEGE

Mr A. C. TALBOT—pathological survey of the warthog in the Queen Elizabeth Park, Uganda: Royal Veterinary College East Africa Research Expedition (*from private funds at the Council's disposal*). (734)

Dr P. A. MAYES—factors directly controlling the production of lipoproteins by the liver. (735)

ST BARTHOLOMEW'S HOSPITAL

Isotope Department

Mr L. N. HAWKINS—radiation dose to bone from ^{22}Na. (736)

Psychological Medicine Department

Dr C. M. B. PARE—differentiation of two genetically specific types of depression by the response to antidepressant drugs. (737)

ST BARTHOLOMEW'S HOSPITAL MEDICAL COLLEGE

Anatomy Department

Dr J. A. CLARKE—ultrastructure of normal and otosclerotic stapes. (738)

Biochemistry and Chemistry Department

Dr A. M. DAWSON—absorption of water, electrolytes and sugars from the small intestine in man. (739)

Haematology Department

Professor D. L. MOLLIN—vitamin B_{12} metabolism in subcellular components of animal tissues. (740)

Pathology Department

Professor W. G. SPECTOR—(*a*) lymphoid cell factors as mediators of local hypersensitivity reactions; (*b*) origin and fate of mononuclear cells in inflammatory exudates. (741)

Pharmacology Department

Professor J. P. QUILLIAM—(1) relation of electron microscope structure of ganglion cells to pharmacological action; (2) isolation and study of the active principles of *Clibadium sylvestre* and *Cissampelos ovalifolia;* (3) psychopharmacological assessment of effects of centrally active drugs in man. (742)

Physics Department

Professor J. ROTBLAT—age factor in radiation sensitivity of mammals. (743)

Physiology Department

Professor M. DE BURGH DALY and Dr N. JOELS—mechanisms concerned in the integration of responses of the respiratory and cardiovascular systems. (744)

Dr B. N. DAVIES—blood flow through the spleen and release and content of the sympathetic transmitter. (745)

Dr N. JOELS—integration of chemoreceptor reflexes with brain stem activity. (746)

Dr Elizabeth ULLMANN—mechanism of hydrogen ion secretion in the mammalian kidney. (747)

Skin Department

Dr T. W. E. ROBINSON—defence mechanisms in herpes simplex virus infection. (748)

Zoology and Comparative Anatomy Department

Dr M. J. HOLLINGSWORTH—the ageing process in *Drosophila.* (749)

ST GEORGE'S HOSPITAL

Dr J. S. JENKINS—hypothalamic-pituitary-adrenal function in man. (750)

ST GEORGE'S HOSPITAL MEDICAL SCHOOL

Chemical Pathology Department

Professor N. H. MARTIN—specific metal binding of transferrin and caeruloplasmin and the effects of environment on the ' active ' centres and the relationship of these to the biological function of the molecules. (751)

Medical Microbiology Department

Dr L. O. BUTLER—(1*a*) DNA synthesis and the transforming activity of the indigenous DNA of the pneumococcus at different stages of the replication cycle; (1*b*) mechanisms involved in the integration of introduced DNA; (2) mapping of the chromosome of the pneumococcus. (752)

Department of Medicine

Dr T. R. E. PILKINGTON—lipoprotein metabolism and its regulation and the control of ketosis in man. (753)

Pathology Department

Dr W. B. ROBERTSON—ultrastructure of the placental bed in normal and abnormal pregnancies. (754)

Dr N. WOOLF—malignant hyperpyrexia during general anaesthesia in the pig. (755)

Psychiatry Department

Dr A. H. CRISP—relationship between nutritional status and psychiatric morbidity. (756)

Mr H. GWYNNE JONES—visual perceptual functioning in patients with localized cerebral lesions. (757)

Surgical Department

Professor B. BROOKE—total water loss in clinical conditions in relation to changes in the skin. (758)

ST MARK'S HOSPITAL

Dr B. C. MORSON—genetic studies in inflammatory and neoplastic bowel disease. (759)

ST MARY'S HOSPITAL

Paediatric Unit

Dr D. BARLTROP—influence of maturation and of vitamin D on the metabolism of lead. (760)

ST MARY'S HOSPITAL MEDICAL SCHOOL

Anatomy Department

Dr A. S. BREATHNACH—electron microscopy of human skin. (761)

Bacteriology Department

Dr G. W. CSONKA—aetiology of non-gonococcal genital infections (*also at Central Middlesex Hospital and Twyford Virus Laboratory*). (762)

Dr A. A. GLYNN—nature of the actions of complement, antibody and lysozyme on bacteria, and factors affecting the susceptibility of strains of enterobacteria to the bactericidal activity of serum. (763)

Professor R. E. O. WILLIAMS—(1) classification of non-haemolytic streptococci; (2) chemical investigation of staphylococci and their extracellular products during the early stages of subcutaneous injection. (764)

Professor R. E. O. WILLIAMS and Dr Margot SHINER—intestinal bacterial flora in healthy humans. (765)

Chemical Pathology Department

Dr A. P. FLETCHER—biosynthesis of glycoprotein in isolated renal tubules. (766)

Dr V. H. T. JAMES—control of adrenal secretion. (767)

Professor A. NEUBERGER—interaction of lysozyme with substrates and inhibitors. (768)

Immunology Department

Dr D. C. DUMONDE—role of the macrophage in delayed hypersensitivity. (769)

Applied Immunology Department

Dr L. B. HOLT—assay of potency of antigens in combined vaccines. (770)

Department of Medicine

Dr V. F. ACKROYD—immunological basis of drug hypersensitivity. (771)

Dr J. F. MOWBRAY—action of ribonucleases as immunosuppressive agents. (772)

Professor W. S. PEART—physiological and pathological role of the renin-angiotensin system. (773)

Microbiology Department

Professor K. DUMBELL—role of arginine and carbon dioxide in the growth of DNA viruses. (774)

Paediatric Department

Dr D. BARLTROP—binding of lead by tissues, with special reference to its subcellular distribution and effect on the stability of the lysosomal membrane. (775)

Pathology Department

Professor K. A. PORTER—glomerular and vascular complications in long-surviving renal allografts. (776)

Pharmacology Department

Dr Marta WEINSTOCK—the mechanism by which analgesic drugs produce lenticular opacities. (777)

Physics Department

Dr J. A. SIRS—flow of red cell suspensions through artificial capillary beds. (778)

Physiology Department

Dr D. P. ALEXANDER, Dr H. G. BRITTON and Dr D. A. NIXON—hormones and metabolism in foetal life. (779)

Physiology Department

Dr R. CREESE—labelled depolarized drugs in striated muscle. (780)

Professor A. D. M. GREENFIELD—effects of acute and chronic changes in the viscosity of blood on the reactivity of blood vessels responsible for peripheral resistance. (781)

Dr Pamela M. HOLTON—(1) secretion, vascular resistance and oxygen consumption in the stomach of the anaesthetized dog; (2) measurement of gastric mucosal blood flow and secretion in conscious dogs. (782)

Surgical Department

Mr J. L. BOAK—inhibition of circulating lymphocyte activity by antilymphocytic serum. (783)

ST THOMAS'S HOSPITAL

Anaesthetics Department

Dr T. H. S. BURNS—development of non-explosive anaesthetic agents (*with Dr J. M. Hall, Guy's Hospital*). (784)

Gastrointestinal Laboratory

Dr B. CREAMER—electron microscope study of iron in the mucosa of the small intestine. (785)

Haematology Department

Dr R. G. HUNTSMAN—survey of samples of cord blood for foetal haemoglobin variants (*also at Lambeth Hospital*). (786)

ST THOMAS'S HOSPITAL MEDICAL SCHOOL

Chemical Pathology Department

Professor F. T. G. PRUNTY—measurement of steroid hormones in peripheral blood. (787)

Gynaecology Department

Dr M. G. BRUSH and Mr R. W. TAYLOR—uptake and intracellular distribution of oestradiol and progesterone by carcinoma of the endometrium and hyperplastic endometrium. (788)

Dr Maureen YOUNG—(1) placental transfer of amino acids; (2) regional blood flow changes during a reduction in systemic pulse pressure and during asphyxia in young animals. (789)

Medical Microbiology Department

Dr J. E. BANATVALA—diagnosis and nature of rubella. (790)

Department of Medicine

Dr R. D. LOWE—(1) mechanical assistance to the failing heart by synchronous assistance of ventricular ejection; (2) some circulatory effects of low-pressure baroceptor reflexes. (791)

Physiology Department

Dr M. W. B. BRADBURY—electrolyte distribution and exchange in the blood-brain-cerebrospinal fluid system. (792)

Dr F. J. IMMS—nature of the 'permissive' action of corticosteroids. (793)

Dr M. T. JONES—regulation of pituitary adrenocorticotrophic activity. (794)

Surgery Department

Mr N. L. BROWSE—factors involved in the aetiology, treatment and prophylaxis of deep vein thrombosis. (795)

Professor J. B. KINMONTH—(*a*) endolymphatic therapy of transplantable tumours; (*b*) lymphangiography. (796)

Professor E. W. HORTON—role of prostaglandins in relation to brain function. (797)

Dr A. S. MILTON—release of pharmacologically active substances present in the central nervous system. (798)

UNIVERSITY COLLEGE LONDON

Anatomy Department

Dr A. BOYDE—development and structure of hard tissue, physiological resorption and pathological destruction. (799)

Dr D. H. L. EVANS—quantitative method for detecting the presence of aggressive factors in lymphocytes and serum in experimental autoimmune conditions. (800)

Professor E. G. GRAY—(1) electron microscopy of excitatory and inhibitory synapses; (2) transmitter substances in octopus brain. (801)

Biochemistry Department

Dr Patricia H. CLARKE—comparison of wild-type and mutant amidase proteins from *Pseudomonas aeruginosa.* (802)

Dr K. L. MANCHESTER—hormones and protein synthesis in muscle. (803)

Dr Pauline M. MEADOW—cell envelopes of *Pseudomonas aeruginosa* and their relationship to its antibiotic and antiseptic resistance. (804)

Dr B. R. RABIN—mechanism of action of glutamic dehydrogenase. (805)

Biophysics Department

Dr P. FATT—(1) mechanism of visual excitation; (2) photoconductive charges in rod outer segments. (806)

Dr E. J. HARRIS—relations between ions and metabolism. (807)

Professor B. KATZ—subcellular localization of acetylcholine in cholinergic nerve terminals. (808)

Dr R. NIEDERGERKE—calcium fluxes in the frog heart. (809)

Botany Department

Dr D. WILKIE—biogenesis of mitochondria. (810)

Dr D. WILKIE and Dr D. V. BANTHORPE—genetics and chemistry of actidione action in yeast (*also in Chemistry Department*). (811)

Chemistry Department

Professor Dame Kathleen LONSDALE—crystallographic studies of urinary calculi. (812)

Dr P. J. PAULING—structure of molecules active in cholinergic systems. (813)

Professor C. A. VERNON—structure and biological activity of the wasp venom kinins. (814)

Professor C. A. VERNON and Dr S. DOONAN—structure and mode of action of phospholipase A from bee venom. (815)

Dr A. WASSERMANN—molecular size and shape of muscle proteins in dilute solution. (816)

Human Genetics and Biometry Department

Dr J. O. IRWIN—theory of discrete distributions and its application to biometry. (817)

Professor H. KALMUS—genetic variation of colour vision, taste and smell. (818)

Professor C. A. B. SMITH—statistical study of factors associated with spontaneous abortion. (819)

Mechanical Engineering Department

Dr S. R. MONTGOMERY—portable energy supplies for powered prostheses. (820)

Medical Sciences Department

Professor S. P. DATTA—data processing for neurophysiology (*under scheme for provision of costly equipment*). (821)

Pharmacology Department

Dr D. COLQUHOUN—mechanisms of passive sensitization in the guinea pig and of drug hypersensitivity in man. (822)

Dr M. Maureen DALE—the process of recovery from desensitization in smooth muscle after the anaphylactic reaction. (823)

Dr D. H. JENKINSON—effects of catecholamines on the membrane potential and ionic permeability of hepatic cells. (824)

Professor J. L. MONGAR—(1) comparison of the biochemical and morphological changes occurring in isolated cells during anaphylaxis; (2) changes in the cell surface accompanying the secretion of histamine from isolated mast cells and leucocytes. (825)

Professor H. O. SCHILD and Dr C. A. VERNON—isolation and identification of urogastrone. (826)

Professor H. O. SCHILD—action of psychotropic drugs. (827)

Professor H. O. SCHILD and Professor J. Z. YOUNG—transmitters in the central nervous system (*also in Anatomy Department*). (828)

Dr Hannah STEINBERG—analysis of drug dependence in rats. (829)

Physiology Department

Dr J. DIAMOND—(1) histochemical and autoradiographic studies of the location of enzymes and substrates in the vertebrate central nervous system; (2) physiological investigation of adaptive changes in the central nervous system. (830)

Dr P. H. ELLAWAY—control of sustained regular discharges of fusimotor neurones to hind limb muscles of the mammal. (831)

Dr R. D. HARKNESS—nature of mechanical linkages in connective tissue frameworks. (832)

Professor A. F. HUXLEY—various programmes of research in the Physiology Department (*under scheme for provision of costly equipment*). (833)

Dr O. C. J. LIPPOLD—origin of the alpha rhythm as tremor of the extraocular muscles. (834)

Mr J. E. PASCOE—central control of muscle spindles. (835)

Professor D. R. WILKIE—(1) muscle physiology (*also at Plymouth Laboratory of the Marine Biological Association*); (2) time course of chemical change during muscular contraction. (836)

Dr R. C. WOLEDGE—comparative physiology of muscular energetics. (837)

Psychology Department

Professor R. J. AUDLEY—relation between the latency and probability of a response in a situation involving choice. (838)

Dr P. N. JOHNSON-LAIRD and Dr P. C. WASON—effect of linguistic variables on cognitive performance (*also in Phonetics Department*). (839)

Dr P. C. WASON and Mrs S. JONES—departmental projects in psychology. (840)

Zoology Department

Professor M. ABERCROMBIE—cell locomotion, cell metabolism and the cell surface. (841)

Dr C. A. KING—adsorption of protein on to tissue, with particular reference to the adsorption of immunoglobulin in immunological processes. (842)

UNIVERSITY COLLEGE HOSPITAL

Dr J. E. LENNARD-JONES—mechanism, control and neutralization of gastric hypersecretion in patients with duodenal ulcer. (843)

Clinical Pathology Department

Dr F. V. FLYNN—proteinuria accompanying generalized renal tubular malfunction. (844)

UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL

Biophysics Department

Professor J. D. JUDAH—calcium shifts in red cells. (845)

Chemical Pathology Department

Dr H. HEATH—metabolism of the retina and other ocular tissues in alloxan-produced diabetes. (846)

Dr P. A. RILEY—*in vitro* effects of ring-substituted anisoles on isolated melanocytes in culture. (847)

Dr T. F. SLATER—biochemical mechanisms concerned in the primary stages of experimentally produced liver injury. (848)

Clinical Haematology Department

Professor T. A. J. PRANKERD—methaemoglobin reductase activity in red cells. (849)

Dermatology Department

Dr A. JARRETT—quantitative histochemistry of the skin. (850)

Dr R. I. C. SPEARMAN—epidermal growth and keratinization. (851)

Experimental Pathology Department

Dr A. E. M. MCLEAN—effect of chronic liver damage on induction of synthesis of detoxicating enzymes. (852)

Medical Unit

Professor C. E. DENT—disorders of calcium and phosphorus metabolism. (853)

Professor C. E. DENT and Professor H. HARRIS—totally synthetic diets in the investigation and treatment of human disease (*also in Human Genetics Department, University College London*). (854)

Paediatrics Department

Professor L. B. STRANG—pathogenesis of hyaline membrane disease. (855)

Surgery Department

Mr J. H. WYLLIE—prostaglandins in clinical practice. (856)

WELLCOME INSTITUTE OF COMPARATIVE MEDICINE

Dr Barbara J. WEIR—comparative reproductive physiology of hystricomorph rodents. (857)

WESTMINSTER HOSPITAL

Cardiology Department

Dr V. J. REDDING—(*a*) myocardial blood flow; (*b*) effects of drugs of potential value in coronary disease. (858)

Ophthalmic Department

Mr P. D. TREVOR-ROPER—long-term preservation of the human cornea (*also at Moorfields Eye Hospital and Royal Veterinary College, London*). (859)

WESTMINSTER MEDICAL SCHOOL

Anaesthetics Department

Professor Sir Geoffrey ORGANE—haemodynamic changes and alterations in the subdivisions of tidal volume associated with induced controlled hypotension. (860)

Chemical Pathology Department

Dr J. D. BILLIMORIA—chemical synthesis of radioactive phospholipids doubly labelled with ^{32}P and ^{14}C and their use in studies of blood coagulation and lipid metabolism. (861)

Professor N. F. MACLAGAN—projects to be carried out in the Department of Chemical Pathology: (*a*) radioisotope displacement methods for estimation of thyroid function (by Professor Maclagan); (*b*) forms of vitamin B_{12} in blood and tissues and the interrelationships between cyanide and vitamin B_{12} metabolism (by Dr D. M. Matthews); (*c*) Dr Billimoria's project (see above) (*under scheme for provision of costly equipment*). (862)

WILLESDEN GENERAL HOSPITAL

Radiology Department

Dr G. A. DOUGLAS—ultrasonic methods of diagnosis for the heart and lungs. (863)

Loughborough

UNIVERSITY OF TECHNOLOGY

Ergonomics and Cybernetics Department

Professor W. F. FLOYD and Dr E. EDWARDS—response to unexpected signals in relation to accidents during the performance of repetitive operations. (864)

Professor W. F. FLOYD and Dr E. J. HAMLEY—self-generated vibration and impulses. (865)

Mr P. T. STONE—relationship between discomfort glare and age. (866)

Manchester

Dr C. R. KAY—oral contraception (*on behalf of Royal College of General Practitioners*). (867)

ROYAL INFIRMARY

Dr J. B. L. HOWELL—neurological factors affecting breathing in normal subjects and in those with pulmonary disease. (868)

Dr K. G. WORMSLEY—gastric and duodenal function in health and in cases of peptic ulceration. (869)

ROYAL MANCHESTER CHILDREN'S HOSPITAL

Mr N. R. E. ROBERTSON and Mr A. JOLLEYS—long-term growth study of children with major facial deformities (*also in University Department of Orthodontics*). (870)

Mental Retardation Research Unit

Dr G. M. KOMROWER—long-term follow-up study of galactosaemia. (871)

Pathology Department

Dr D. K. EVANS—treatment of leukaemia. (872)

UNIVERSITY

Department of Audiology and Education of the Deaf

Professor I. G. TAYLOR—temporal factors affecting perception of sensory stimuli, with special reference to hearing and speech. (873)

Bacteriology Department

Professor P. J. COLLARD—mixed continuous cultures of bacteria as a model of the ecology of the bowel. (874)

DR N. W. PRESTON—serological investigation of the effectiveness of vaccines in the prevention of whooping cough. (875)

Dr G. TAYLOR—byssinosis antigen (*also in Immunology Department, Royal Infirmary*). (876)

Chemistry Department

Professor G. R. BARKER—requirements for transforming activity in DNA from *Bacillus subtilis*. (877)

Dr S. HUNT and Dr A. G. LOWE—adenosine triphosphatases activated by sodium and potassium. (878)

Dr W. D. STEIN—(1) isolation and characterization of the glucose carrier from the human erythrocyte membrane; (2) isolation of the glucose transport system from muscle cell membranes, and study of the interaction of insulin with this system in a broken cell preparation. (879)

Dr W. D. STEIN and Dr C. H. WYNN—configurational changes in the anticompetitive inhibition of arylsulphatases of *Alcaligenes metalcaligenes*. (880)

Child Health Department

Dr J. DOBBING—vulnerable periods in the developing brain. (881)

Department of Medicine

Professor S. W. STANBURY—vitamin D metabolism in man. (882)

Obstetrics and Gynaecology Department

Dr F. A. LANGLEY—abnormalities of the epithelium of the cervix uteri investigated by tissue culture methods. (883)

Dr W. M. O. MOORE—*in vitro* permeability of placental membrane. (884)

Orthopaedic Surgery Department

Dr D. L. GRIFFITHS—tuberculosis of the spine in the tropics. (885)

Pharmacology Department

Dr B. ROBINSON—synthesis of *d*-physostigmine and comparison of its antiacetylcholinesterase activity with that of *l*-physostigmine, *l*-physovenine, *l*-eseramine, *l*-geneserine and *l*-*N*(*a*)-norphysostigmine. (886)

Physiology Department

Dr D. H. PAUL—analysis of the activity of neurones in the cat's cerebellum that receive afferent impulses originating in the skin. (887)

Rheumatism Research Centre

Professor J. H. KELLGREN and Dr J. A. CHAPMAN—mechanism of collagen fibrogenesis. (888)

Institute of Science and Technology

Professor F. MORTON—isolation of aromatic hydrocarbons from petroleum. (889)

Professor H. H. ROSENBROCK—controlled haemodialysis. (890)

Social and Preventive Medicine Department

Professor A. SMITH—computer program for analysis of surveys. (891)

WITHINGTON HOSPITAL

Public Health Laboratory

Dr J. O'H. TOBIN—cytomegalovirus infection in the Manchester area. (892)

Menston, Ilkley

HIGH ROYDS HOSPITAL

Dr R. P. HULLIN and Dr R. MCDONALD—changes in body water and electrolytes in manic-depressive psychosis and depressive illness. (893)

Middlesbrough

GENERAL HOSPITAL

Public Health Laboratory

Dr E. BLOWERS—biochemical factors controlling nose and skin carriage of *Staphylococcus aureus*. (894)

Midhurst

KING EDWARD VII HOSPITAL

Sir Geoffrey TODD—investigation of the possible carcinogenicity of isoniazid. (895)

Newcastle upon Tyne

UNITED NEWCASTLE HOSPITALS

ROYAL INFIRMARY

Dr H. A. DEWAR—activators and inhibitors of fibrinolysis in regional veins. (896)

Dermatology Department

Dr G. HOLTI—the microcirculation in the clinically unaffected skin of psoriatic patients and their relatives. (897)

UNIVERSITY

Anatomy Department

Professor R. J. SCOTHORNE—correlated studies of structure and function in the developing parathyroid and salt glands. (898)

Biochemistry Department

Dr A. ALLEN—effects of viral transformation on the macromolecular carbohydrate components in mammalian cell lines (*under scheme for provision of costly equipment*). (899)

Professor K. BURTON—structure, function and biosynthesis of macromolecules. (900)

Chemistry Department

Dr G. SCHOLES—pulse radiolysis of aqueous solutions of nucleoproteins, nucleic acids and related substances. (901)

Child Health Department

Professor S. D. M. COURT and Dr P. S. GARDNER—acute respiratory infection in children, with special reference to respiratory syncytial virus (*also in Virology Department*). (902)

Dr W. WALKER—role of toxaemia of pregnancy in Rh-isoimmunization. (903)

Clinical Biochemistry Department

Professor A. L. LATNER—isoenzyme studies. (904)

Sutherland Dental School

Professor G. N. JENKINS—metabolic studies of intact dental plaque by gas chromatography. (905)

Professor C. H. TONGE—histological studies of the developing tooth and its supporting structures, including the teeth and jaws of undernourished pigs. (906)

Dermatology Department

Dr M. W. GREAVES—zinc metabolism in psoriasis and other dermatoses. (907)

Professor S. SHUSTER—enteropathies of skin disease and the systemic effects of erythroderma. (908)

Human Genetics Department

Dr D. F. B. ROBERTS—quantitative genetics and human disease. (909)

Nuffield Department of Industrial Health

Dr R. I. McCALLUM—measurement of *in vivo* antimony content of the human lung by differential absorption of X-rays. (910)

Professor D. N. WALDER—decompression sickness (*on behalf of the Council's Decompression Sickness Panel*). (911)

Neurology Department

Professor J. N. WALTON—clinical, genetic and histopathological studies in muscular dystrophy and other muscle diseases. (912)

Pathology Department

Professor A. G. HEPPLESTON—influence of duration and intensity of exposure on the elimination of high- and low-rank coal dusts. (913)

Physical Chemistry Department

Dr P. JONES and Dr R. H. PAIN—formation, nature and reactivity of catalase subunit species (*also in Biochemistry Department*). (914)

Physiology Department

Professor A. A. HARPER—hormonal and nervous effects on gastric and pancreatic secretion. (915)

Dr H. J. LAKE—hormones of the gastrointestinal tract. (916)

Dr A. J. McCOMAS—neuronal control of cells in the dorsal column nuclei. (917)

Dr W. TAYLOR—*in vitro* and *in vivo* metabolism of progesterone. (918)

Psychological Medicine Department

Professor M. ROTH—classification of schizophrenic illness and its hereditary and environmental aspects. (919)

Psychology Department

Dr G. H. FISHER—locus of organization of illusions and figural after-effects. (920)

Surgery Department

Professor D. N. WALDER—(1) decompression sickness in Tyne Tunnel workers; (2) bone necrosis in compressed air workers: radiographic surveys; (3) detection of bubbles in decompression sickness by ultrasound (*on behalf of the Council's Decompression Sickness Panel*). (921)

Zoology Department

Professor L. C. BEADLE—salt and water regulation during the development of planorbid snails. (922)

Norwich

UNIVERSITY OF EAST ANGLIA

School of Biological Sciences

Dr M. BALLS—the transmissible lymphosarcoma of *Xenopus laevis*. (923)

Dr C. H. CLARKE—influence of repair systems on ultraviolet and chemical mutagenesis in microorganisms. (924)

Professor J. DAINTY—relations between structure and properties of cell membranes, with special reference to artificial phospholipid membranes. (925)

Dr I. GIBSON—(1) gene action in *Paramecium*; (2) regulation of gene action in protozoa. (926)

School of Chemical Sciences

Professor S. F. MASON—structure and bonding of the complexes formed by proteins and DNA with aromatic hydrocarbons, dyes and nucleotides. (927)

Nottingham

UNIVERSITY

Human Morphology Department

Professor R. E. COUPLAND—(*a*) catecholamine synthesis and storage by chromaffin cells; (*b*) effects of corticosteroids on methylation. (928)

Pathology Department

Professor K. WEINBREN—biochemical mechanisms in the control of restoration of the liver. (929)

Pharmacology Laboratories

Dr J. CROSSLAND—nature and behaviour of chemical transmitter substances in the central nervous system. (930)

Psychology Department

Dr D. E. BLACKMAN—behavioural effects of prenatal stress in rats. (931)

Professor C. I. HOWARTH—(1*a*) mobility of blind people; (1*b*) development of keyboard skills; (2) integration of information from different sense organs in the control of simple motor acts. (932)

Oswestry

THE ROBERT JONES AND AGNES HUNT ORTHOPAEDIC HOSPITAL

Mr N. W. NISBET—experimental problems of transplantation. (933)

Oxford

UNITED OXFORD HOSPITALS: CHURCHILL HOSPITAL

Neurology Department

Dr J. M. OXBURY—neuropsychological defects associated with focal epilepsy. (934)

Dr E. W. POOLE—time relationship between EEG phenomena, internal bodily events and external stimuli. (935)

Radiotherapy Department

Dr F. ELLIS—modification of radiation effects by physical and pharmacological means. (936)

Radiation Physics Department

Mr R. OLIVER—(1) dosimetry and measurement of beam characteristics in relation to the use of lasers in biological and medical research; (2) biological effects of ultrasonic irradiation in relation to the physical parameters of the radiation field. (937)

COWLEY ROAD HOSPITAL

Geriatric Medicine Department

Dr L. WOLLNER—abnormalities of temperature regulation and vasomotor control in the elderly. (938)

NUFFIELD ORTHOPAEDIC CENTRE

Pathology Department

Dr C. G. WOODS—histological study of bone in rheumatoid arthritis. (939)

RADCLIFFE INFIRMARY

Cardiac Department

Dr G. de J. LEE and Dr D. L. SCHULTZ—mechanics of pulsatile blood flow in the pulmonary circulation of man (*also in University Department of Medicine and Engineering Science Department*). (940)

Dr P. SLEIGHT—baroreceptor reflex sensitivity in man. (941)

Clinical Medicine Department

Dr G. H. SPRAY—some aspects of vitamin B_{12} deficiency. (942)

Neurology Department

Dr C. W. M. WHITTY—pathophysiology of migraine. (943)

Otolarnygology Department

Mr B. H. COLMAN—temporal bone microtomy: animal studies and human otopathological investigations. (944)

Pathology Department

Dr M. S. DUNNILL—quantitative morphological investigation of chronic non-specific lung disease. (945)

Agricultural Department

Dr J. M. BARRY—increases *in vitro* of enzyme activities in mouse mammary tissue. (946)

Nuffield Department of Anaesthetics

Professor A. CRAMPTON SMITH—sympathetic nervous system activity in tetanus and during anaesthesia. (947)

Biochemistry Department

Dr H. BLASCHKO—uptake and metabolism of amino acids related to phenylalanine. (948)

Dr K. DALZIEL—kinetics and mechanisms of pyridine nucleotide-linked dehydrogenases, with special reference to isocitric dehydrogenases and malic enzyme. (949)

Dr C. J. FIELDING—analysis of blood and adipose tissue glycolipids and investigation of their role in triglyceride metabolism. (950)

Dr L. A. STOCKEN—biochemical effects of ionizing radiation on mammalian systems. (951)

Nuffield Department of Clinical Biochemistry

Dr M. P. ESNOUF—amino acids, at the active centre of activated factor X, concerned in the conversion of prothrombin to thrombin. (952)

Dr A. PEACOCKE—physical chemistry of biological macromolecules in solution. (953)

Botany School

Dr B. S. COX—(1) ultraviolet-sensitive mutants and recombination in yeast; (2) biochemical and radiobiological characterization of sensitive mutants. (954)

Dyson Perrins Laboratory

Dr B. R. BROWN—enzyme-catalysed oxidation of phenols and amines with concurrent synthesis of sulphones. (955)

Dr J. R. KNOWLES—enzyme and antibody specificity. (956)

Dr G. LOWE—structure and mechanism of action of the proteolytic enzyme papain. (957)

Dr G. T. YOUNG—synthesis of peptides. (958)

Department of Engineering Science

Dr D. L. SCHULTZ, Mr A. J. GUNNING and Dr B. J. BELLHOUSE—development of a laminar-flow aortic valve prosthesis and left-ventricle bypass (*also in Nuffield Department of Surgery*). (959)

Engineering Department

Mr D. C. WITT—feasibility study on automatically controlled powered lower-limb prostheses. (960)

Institute of Experimental Psychology

Dr J. A. GRAY—(1) effect of reproductive hormones on the behavioural responses to stress in the rat; (2) functional similarities between fear and frustration. (961)

Dr M. KINSBOURNE—short-term and long-term memory processes and their impairment in organic cerebral disease (*also at Littlemore Hospital*). (962)

Dr P. M. RABBITT—choice reaction time as an index of complexity in information coding and retrieval. (963)

Dr Anne M. TREISMAN—(1) interrelation of selective attention, short-term memory and verbal recognition in auditory and visual perception; (2) applications of coding theory and decision theory to the study of language and language users. (964)

Professor L. WEISKRANTZ—(1) cerebral mechanisms in visual discrimination and memory; (2) grant awarded to the university for work on (1); (3) applications of a Linc-8 computer to experimental psychology (*under scheme for provision of costly equipment*). (965)

Human Anatomy Department

Mr I. W. BAYMAN—feedback effects and site of action of the ovarian steroids in the control of ovulation in the rat. (966)

Dr K. BROWN-GRANT—experimental analysis of the thyroid–ovary interrelationship. (967)

Dr H. M. CHARLTON—control of gonadal activity in the vole, with special reference to the roles played by the pineal gland, pituitary gland and hypothalamus. (968)

Dr F. NAFTOLIN—(*a*) establishment and use of radioimmunoassay for gonadotrophin measurement in humans; (*b*) effects of environmental changes on the endocrinology of the primate. (969)

Dr T. P. S. POWELL—cerebral connections of certain sensory systems. (970)

Dr K. B. RUF—experimental studies on releasing factors of anterior pituitary hormones in hypophysial portal vein blood in rats. (971)

Dr A. G. M. WEDDELL—(1) structural changes in skin and sensory nerve trunks associated with leprosy and psoriasis; (2) transmission and growth of *Mycobacterium leprae* in experimental animals and man; (3) effect on *Myco. leprae* of alterations in the basement membranes around nerve and muscle fibres. (972)

Inorganic Chemistry Department

Dr L. M. VENANZI—metal-containing histochemical stains. (973)

Dr R. J. P. WILLIAMS—metalloprotein complexes, especially in relation to enzymes. (974)

Nuffield Department of Clinical Medicine

Professor P. B. BEESON—mechanisms of eosinophilia. (975)

Dr Sheila T. E. CALLENDER—importance of iron deficiency, autoimmunity and other factors in the Plummer-Vinson syndrome. (976)

Sir Hans KREBS—(1) regulation of metabolic processes, with special reference to gluconeogenesis and ketogenesis; (2) metabolic characteristics of kidney cortex. (977)

Dr S. C. TRUELOVE and Dr G. M. ARDRAN—motility of human colon in health and disease. (978)

Nuffield Institute for Medical Research

Dr G. S. DAWES—distribution of uterine flow in pregnant animals and cardiac output in the newborn (*under scheme for provision of costly equipment*). (979)

Department of the Regius Professor of Medicine

Professor Sir George PICKERING—(1) clinical aspects of genetically determined errors of amino acid metabolism; (2) arterial occlusion. (980)

Neurology Department

Professor W. RITCHIE RUSSELL—selective deficit in relation to focal cerebral lesions and its implications for theories of hemispheric asymmetry of function. (981)

Nuffield Laboratory of Ophthalmology

Mrs Antoinette PIRIE—(1) metabolism of the lens in relation to cataract formation; (2) investigation of the conditions under which proteins precipitate within the lens, together with chemical and physical analysis of the precipitated proteins. (982)

Dr S. G. WALEY—the lens protein γ-crystallin. (983)

Nuffield Department of Orthopaedic Surgery

Professor R. B. DUTHIE—interrelation between pyrophosphatases, polyphosphatases and alkaline phosphatases. (984)

Sir William Dunn School of Pathology

Professor E. P. ABRAHAM—biosynthesis, structure and function of some microbial products. (985)

Dr J. E. FRENCH—composition, structure and properties of blood platelets, with particular reference to their surface membranes. (986)

Dr C. F. GRAHAM—cell fusion in early mammalian embryos. (987)

Professor H. HARRIS—(1) RNA synthesis in normal and virus-infected cells; (2) investigation of the structure of blood vessels, particularly of endothelium. (988)

Pharmacology Department

Sir Lindor BROWN—adrenergic mechanisms. (989)

Professor Edith BÜLBRING—physiology and pharmacology of smooth muscle. (990)

Dr E. W. GILL—polypeptide models of drug receptors. (991)

Dr D. B. HOPE—(1) biochemical pharmacology of neurophysin, oxytocin and vasopressin; (2) biosynthesis of the hormones of the pituitary posterior lobe. (992)

Professor W. D. M. PATON—the renin-angiotensin system. (993)

Dr H. P. RANG—acetylcholine receptors. (994)

Dr A. D. SMITH—molecular mechanisms in the storage and secretion of catecholamines. (995)

Dr V. E. M. WILLIAMS—effects of cholera toxin in infant rabbits. (996)

Physiology Laboratory

Dr R. Jean BANISTER—analysis of membrane currents in amphibian myocardial fibres. (997)

Dr D. H. BERGEL—*in vivo* studies of arterial elasticity, with special reference to the baroreceptor areas. (998)

Dr Marianne FILLENZ—chemical transmission at synapses. (999)

Dr G. GORDON—functional organization of somatosensory nuclei in the mammalian nervous system and their control by the higher parts of the brain. (1000)

Mr D. J. A. JENKINS—fasting levels of plasma free fatty acid, ketone bodies and cortisol, and their relationship to fasting insulin levels and levels of other blood metabolites in patients who have had myocardial infarction. (1001)

Mr B. B. LLOYD—chemical and other factors in the regulation of respiration. (1002)

Dr D. NOBLE—actions of calcium, adrenaline and other drugs on electrical activity in cardiac cells. (1003)

Professor I. C. G. PHILLIPS—motor systems in primates. (1004)

Dr P. SLEIGHT—cardiovascular afferent fibres in animals and in man. (1005)

Professor D. WHITTERIDGE—cellular basis of colour vision. (1006)

Social Medicine Department

Dr Alice STEWART—survey of childhood cancers. (1007)

Nuffield Department of Surgery

Mr A. J. GUNNING—(*a*) long-term fate of transplanted heterologous heart valves; (*b*) immunological study of these valves. (1008)

Zoology Department

Dr J. B. GURDON—(1) changes in the function of living cell nuclei on exposure to different cytoplasmic environments; (2) control of nucleic acid synthesis during early animal development. (1009)

Dr D. R. S. KIRBY—(1) physiology of mouse trophoblast and the effect of extrauterine pregnancy on the oestrous cycle; (2) role of uterine lysosomal enzymes in the decidual transformations occurring during pregnancy in the rat. (1110)

Professor D. C. PHILLIPS—research programme of the Council's Research Group in Molecular Biophysics (see p. 191). (1011)

Peaslake

Dr G. I. WATSON—infectious diseases in a rural community. (1012)

Port-of-Spain, Trinidad

UNIVERSITY OF THE WEST INDIES

Regional Virus Laboratory

Dr A. JONKERS—streptococcal nephritic disease in Trinidad. (1013)

Porton

MICROBIOLOGICAL RESEARCH ESTABLISHMENT

Dr C. E. SMITH—transmission of flea-borne infections from adult fleas directly to their progeny (*also at Liverpool School of Tropical Medicine*). (1014)

Portsmouth

ST MARY'S HOSPITAL

Radiotherapy Department

Dr J. B. MCEWEN—clinical trials of megavoltage radiotherapy and high-pressure oxygen. (1015)

Reading

UNIVERSITY

Chemistry Department

Dr J. E. PRUE—specific interaction in aqueous solutions of cations and oxyanions of biological importance. (1016)

Physics Department

Professor R. W. DITCHBURN—eye movements in relation to visual perception. (1017)

Psychology Department

Professor M. TREISMAN—(1) hierarchical mechanisms in visual and auditory perception; (2) interference and interaction in visual and auditory perception. (1018)

Redcar

Dr G. K. H. HODGKIN—ulcer-type dyspepsia and its relation to peptic ulcer. (1019)

St Andrews

UNIVERSITY

Biochemistry Department

Dr J. C. GILBERT—effects of anticonvulsant drugs on the permeability of brain cells to sugars. (1020)

Professor G. R. TRISTRAM and Dr G. A. J. GOODLAD—(*a*) separation of normal and tumour cells; (*b*) separation of the protein components of tissue, particularly collagen; (*c*) fractionation of enzymes. (1021)

Pharmacology Department (Gatty Marine Laboratory)

Dr G. A. COTTRELL—subcellular localization of biologically active amines in nervous tissue of certain invertebrate species. (1022)

Zoology Department (Gatty Marine Laboratory)

Dr G. A. HORRIDGE—(1) memory as a factor in movement perception in the crab: electrophysiological experiments; (2) establishment of neuron pathways and synapses. (1023)

Dr G. A. T. TARGETT—(1) serology and protective immunology in experimental animals infected with or immunized against malaria; (2) immunoglobulin changes in human malarial infections. (1024)

Salford

UNIVERSITY

Biology Department

Dr N. V. WILLIAMS—relation of water chemistry to the ecology of snail vectors of schistosomiasis and to their ability to act as vectors. (1025)

Electrical Engineering Department

Dr M. E. BRYAN—(1) middle ear reflex; (2*a*) evaluation of the Bekesy audiometer for the diagnosis of hearing disorders; (2*b*) variation in the threshold of hearing in normal subjects. (1026)

Dr W. TEMPEST—effect of low-frequency sound on the static and dynamic labyrinths. (1027)

Sheffield

THE JESSOP HOSPITAL FOR WOMEN

Endocrine Investigation Centre

Dr G. W. PENNINGTON—source of polar steroids and their excretion in biological fluids, including changes in excretion in both normal and pathological pregnancy. (1028)

NETHER EDGE HOSPITAL

Dr H. F. WEST—excretion of corticosteroid hormones in urine and saliva. (1029)

UNIVERSITY

Anaesthetics Department

Dr J. A. THORNTON—the ultralight methohexitone intravenous technique in conservative dentistry. (1030)

Biochemistry Department

Dr P. BANKS—protein and nucleic acid synthesis by stimulated superior cervical ganglia *in vitro*. (1031)

Dr G. COLEMAN—cell-free protein synthesis in *Bacillus subtilis*. (1032)

Mrs P. M. HARRISON—structure and function of ferritin. (1033)

Dr R. E. S. PROUT—role of lipids in prevention of dental caries. (1034)

Chemistry Department

Dr G. M. BLACKBURN—interaction of benzopyrene and related carcinogens with DNA and RNA and their components. (1035)

Child Health Department

Dr V. DUBOWITZ—fibre types in normal and diseased human and animal muscle. (1036)

Dermatology Department

Dr I. B. SNEDDON—protein fractions in serum and blister fluid in bullous diseases. (1037)

Genetics Department

Professor J. A. ROPER—genetic instability. (1038)

Human Biology and Anatomy Department

Professor R. BARER—(1) development and application of histochemical methods in electron microscope studies; (2) development of electromagnetic flowmeters. (1039)

Dr I. A. CARR—cellular basis of reticuloendothelial stimulation. (1040)

Dr E. J. CLEGG—(1) effects of exposure to lowered atmospheric pressures on the reproductive system of laboratory animals; (2) responses of experimental animals to reduced atmospheric pressures. (1041)

Microbiology Department

Dr B. A. FRY—structure and morphogenesis of temperate bacteriophage. (1042)

Pharmacology and Therapeutics Department

Dr K. J. DORRINGTON—structure of immunoglobulins. (1043)

Professor R. KILPATRICK—stimulation of ovarian steroid biosynthesis *in vivo* and *in vitro* in response to luteinizing hormone. (1044)

Professor D. S. MUNRO—(1) nature and significance of the long-acting thyroid stimulator associated with (1) hyperthyroidism and (2) thyrotoxicosis. (1045)

Professor G. M. WILSON—effects of drugs on tissue transport mechanisms and subcellular localization of drug action. (1046)

Physiology Department

Dr A. ANGEL—action of anaesthetics and convulsants on the central nervous system. (1047)

Psychology Department

Mr K. J. CONNOLLY—development of perceptual processing in the newborn (*also at the Jessop Hospital for Women*). (1048)

Department of Medicine

Professor C. H. STUART-HARRIS—immunoglobulins in nasal secretion and resistance to virus infections. (1049)

Professor C. H. STUART-HARRIS and Dr Gwen BARER—airways and pulmonary vascular resistances. (1050)

Surgery Department

Professor H. L. DUTHIE—effect of vagotomy on the digestion and absorption of fat. (1051)

Dr K. G. WORMSLEY—gastric, pancreatic and duodenal function in health and peptic ulceration. (1052)

Shenley

HARPERBURY HOSPITAL

Dr J. M. BERG—(1) genetic aspects of mental subnormality; (2) clinical and genetic investigation of mental subnormality. (1053)

Professor L. S. PENROSE—genetic aspects of mental subnormality. (1054)

Shrewsbury

SHELTON HOSPITAL

Dr R. WEST—pharmacological actions and therapeutic potentialities of diaboline and related *Strychnos* alkaloids (*also at National Institute for Medical Research*). (1055)

Shrivenham

ROYAL MILITARY COLLEGE OF SCIENCE

Physics Department

Professor A. CHARLESBY—basic radiobiological mechanisms investigated by electron-spin resonance spectroscopy. (1056)

Smethwick

SMETHWICK HOSPITAL

Midland Centre for Neurosurgery

Dr M. V. SALMON—morphological and cytochemical changes in the central nervous system. (1057)

Dr A. L. WOOLF—innervation and metabolism of muscle. (1058)

Southampton

GENERAL HOSPITAL

Endocrine Laboratory

Dr R. M. BUCKLE—hormonal control of calcium metabolism. (1059)

UNIVERSITY

Physiology and Biochemistry Department

Dr M. AKHTAR—enzymatic aspects of the biosynthesis of steroid hormones. (1060)

Professor G. A. KERKUT and Dr E. M. SEDGWICK—the basal ganglia of the cat. (1061)

Institute of Sound and Vibration Research

Professor B. L. CLARKSON—clinical and acoustic studies. (1062)

Zoology Department

Dr F. S. BILLETT—effect of nucleic acid antimetabolites on the early development of avian embryos. (1063)

Dr M. MACLEAN—genetic control mechanisms governing the synthesis of haemoglobin. (1064)

Stock (Essex)

ANIMAL HEALTH TRUST FARM LIVESTOCK RESEARCH CENTRE

Dr L. F. TAFFS—fluorescent-antibody staining in the serodiagnosis and immunology of helminth parasites in man and animals. (1065)

Sunderland

TECHNICAL COLLEGE

School of Pharmacy

Dr E. G. BEVERIDGE—stability of pharmaceutical preservatives in relation to microbial attack. (1066)

Teheran

UNIVERSITY

Immunology Department

Dr H. MIRDAMADI—structure of abnormal haemoglobins. (1067)

Valletta

ROYAL UNIVERSITY OF MALTA

Physiology Department

Professor W. M. BANNISTER—subcellular distribution of cytochrome *c* in gastric mucosa (*from private funds at the Council's disposal*). (1068)

Wickford

RUNWELL HOSPITAL

Neuropathology Department

Dr J. A. N. CORSELLIS—anatomy and pathology of the limbic areas in man. (1069)

Wigan

ROYAL ALBERT EDWARD INFIRMARY

Dr J. SCHRAGER—carbohydrate and amino acid components of the gastric mucopolysaccharides. (1070)

Mr J. S. S. STEWART—chimerism in man. (1071)

York

UNIVERSITY

Biology Department

Professor J. R. BRONK—physiological and structural characteristics of rat intestinal mucosa. (1072)

Physics Department

Dr D. W. GOODWIN—development of a multipurpose laser operating in the infrared, visible and ultraviolet regions of the spectrum and its applications to medicine. (1073)

Professor M. M. WOOLFSON—factors governing threshold vision. (1074)

YORK GROUP OF HOSPITALS

Dr C. N. PULVERTAFT—gastroduodenal ulceration. (1075)

Zaria (Nigeria)

AHMADU BELLO UNIVERSITY

Dr G. OSUIDE—neuropharmacological studies on the domestic fowl. (1076)

Fellowships and scholarships

Various forms of assistance are provided by the Medical Research Council for suitably qualified medical, dental and scientific graduates who wish to prepare themselves for careers in research. These awards are ordinarily restricted to British subjects resident in the United Kingdom.

MEDICAL RESEARCH COUNCIL TRAVELLING FELLOWSHIPS

These fellowships are intended for medical or scientific graduates of registrar or lecturer status, resident in the United Kingdom, who have undertaken some training in research in clinical medicine, surgery or some other branch of medical science and who are likely to profit by a period of work at a recognized centre abroad before taking up appointments in higher teaching or research in the United Kingdom.

The following appointments were made by the Council for the academic year 1968–69:

Dr G. P. CLEIN (*Medical Unit, Royal Victoria Infirmary, Newcastle upon Tyne*): Department of Haematology, University of Utah.

Dr J. FLETCHER (*Research Group in Haemolytic Anaemia, University College Hospital, London*): Thorndyke Memorial Laboratory, Harvard Medical School.

Dr J. A. GRAY (*Department of Psychology, University of Oxford*): Department of Psychology, Rockefeller University, New York.

Mr J. HERMON-TAYLOR (*Surgical Professorial Unit, London Hospital*): Mayo Clinic, Rochester, Minnesota.

Dr C. H. O'NEILL (*MRC Virology Unit, Glasgow*): Biochemical Laboratory, Massachusetts General Hospital.

Dr D. N. WHEATLEY (*Department of Pathology, University of Aberdeen*): McArdle Memorial Laboratory, University of Wisconsin Medical School.

SIR HENRY WELLCOME TRAVELLING FELLOWSHIPS IN MEDICINE

These fellowships, which have been made available through the generosity of the Wellcome Trustees, are of similar standing to the Medical Research Council Travelling Fellowships. They are open to medical and scientific graduates with research experience in any field of medical science, although—in accordance with the wishes of the Trustees—the subjects of physiology, biochemistry, pharmacology and tropical medicine are given preference.

The following appointments were made by the Council for the academic year 1968–69:

Mr P. R. F. BELL (*Department of Surgery, University of Glasgow*): Department of Surgery, University of Colorado.

Dr R. McG. HARDEN (*Department of Medicine, University of Glasgow*): Department of Medicine, Royal Victoria Hospital, Montreal.

Dr J. B. LLOYD (*Department of Biochemistry, University College, Cardiff*): Department of Biochemistry, Miami University.

Dr T. C. MUIR (*Division of Experimental Pharmacology, University of Glasgow*): Department of Physiology, University of Monash, Australia.

Dr J. R. WALTON (*London School of Hygiene and Tropical Medicine*): Department of Medical Microbiology, Stanford University, California.

LILLY FOREIGN EDUCATIONAL FELLOWSHIP

After nomination by the Council the following appointment was made by Eli Lilly and Company, Indianapolis, USA, to a Lilly Foreign Educational Fellowship for the academic year 1968–69:

Dr Ten Feizi (*Department of Medicine, Royal Free Hospital, London*): Rockefeller University, New York.

UNITED STATES PUBLIC HEALTH SERVICE FELLOWSHIPS

In 1958 the National Institutes of Health of the United States Public Health Service inaugurated a programme of research fellowships for European scientists and invited the Council to nominate candidates from the United Kingdom. The fellowships are open to medical or scientific graduates, and preference is given to candidates who have obtained a doctoral degree in one of the medical sciences and have shown outstanding research ability. After nomination by the Council, the following candidates were elected by the United States Public Health Service to fellowships for 1968–69:

Dr G. M. Besser (*Medical Professorial Unit, St Bartholomew's Hospital Medical College, London*): Division of Endocrinology, School of Medicine, Vanderbilt University, Nashville, Tennessee.

Dr I. R. Cameron (*Department of Medicine, St Thomas's Hospital Medical School, London*): Cedars-Sinai Medical Center, Los Angeles.

Dr M. J. Davies (*Department of Pathology, St George's Hospital, London*): North Western University Medical School, Chicago.

Dr B. D. Gomperts (*University College Hospital Medical School, London*): Johnson Foundation, University of Pennsylvania.

Dr J. R. Muir (*National Heart Hospital, London*): Department of Biochemistry, St Louis University School of Medicine.

ALEXANDER PIGOTT WERNHER MEMORIAL TRUST FELLOWSHIPS IN OPHTHALMOLOGY AND OTOLOGY

These awards are provided from a special fund placed at the disposal of the Council by the Trustees of the late Lady Ludlow under the terms of a bequest in memory of her son, to be used ' towards the prevention and cure of blindness and deafness in the United Kingdom and the British Empire, and, in particular, research in connection therewith by financing medical men and students within the Empire to study methods and practices in all countries of the world '.

The following appointments were made for the academic year 1968–69:

Mr R. B. Bradshaw (*Department of Otolaryngology, Radcliffe Infirmary, Oxford*): Department of Otolaryngology, University of Toronto.

Dr Eva M. Kohner (*Department of Medicine, Royal Postgraduate Medical School, London*): Moorfields Eye Hospital, London, and New York University School of Medicine.

DOROTHY TEMPLE CROSS RESEARCH FELLOWSHIPS

These fellowships, provided from an endowment by the late Mrs Odo Cross, are awarded to suitably qualified British graduates who are devoting themselves to the advancement by teaching or research of the curative or preventive treatment of tuberculosis in any of its forms, or to increasing knowledge of other diseases of the lung.

The following appointment was made for the academic year 1968–69:

Dr J. M. B. HUGHES (*Royal Postgraduate Medical School, London*): Department of Physiology, Harvard School of Public Health.

MAPOTHER BEQUEST RESEARCH FELLOWSHIP

This fellowship is provided from a benefaction by the late Dr and Mrs Edward Mapother for research in psychiatry.

No award was made by the Council for the academic year 1968–69.

CLINICAL RESEARCH FELLOWSHIPS

These fellowships, which are normally tenable for up to three years, are offered to suitably qualified medical graduates who wish to prepare for careers in clinical research. It is intended that each fellow appointed should have the opportunity, as part of his training, of studying methods of research in the basic subjects most relevant to his particular clinical interest, his training preferably being given in departments other than his own.

The following appointments were made for the academic year 1968–69:

Dr Judith M. CHESSELLS (*Department of Child Health, Hammersmith Hospital, London*): Departments of Haematology and Child Health, Hammersmith Hospital, and Royal Postgraduate Medical School, London.

Dr R. B. L. EWART (*Department of Medicine, Western General Hospital, Edinburgh*): Department of Biochemistry, University of Sussex.

Dr A. GUNN (*Professorial Surgical Unit, Dundee Royal Infirmary*): Division of Experimental Biology, National Institute for Medical Research, London.

Dr B. W. LASSERS (*Department of Cardiology, Royal Infirmary, Edinburgh*): Departments of Biochemistry and Medicine, Animal Laboratories, University of Edinburgh.

Dr T. S. MATTHEWS (*Hospital for Sick Children, Gt Ormond Street, London*): Department of Immunology, Institute of Child Health, London.

Dr P. A. REDFERN (*Department of Anaesthesia, University of Liverpool*): Department of Physiology, University of Liverpool.

Dr D. RUBENSTEIN (*Medical Unit, Middlesex Hospital, London*): Clinical Research Centre Laboratories, National Institute for Medical Research, London.

Dr E. N. WARDLE (*Department of Medicine, Royal Victoria Infirmary, Newcastle upon Tyne*): Department of Medicine, Royal Victoria Infirmary, Newcastle upon Tyne.

JUNIOR RESEARCH FELLOWSHIPS

These fellowships, which are normally tenable for up to three years, are intended primarily for medical graduates who have completed their preregistration hospital appointments, or for young dental graduates of similar standing: the awards are also open to science graduates with postgraduate degrees who wish to have a further period of specialized research experience. The fellowships are tenable in the departments in which the candidates are already working or at other suitable centres.

The following appointments were made for the academic year 1968–69 (the departments listed being those where the fellowships were held):

Dr G. M. ADDISON: Department of Biochemistry, University of Cambridge.

Dr R. E. BARRY: Department of Medicine, University of Bristol.

Dr P. C. L. BEVERLEY: Division of Experimental Biology, National Institute for Medical Research, London.

Dr B. A. de B. BRADLEY: Department of Experimental Pathology, University of Birmingham.

Dr G. W. BRADLEY: Department of Physiology, University of Bristol.

Dr M. J. CONNOCK: Department of Medical Biochemistry and Pharmacology, University of Birmingham.

Dr R. J. H. DAVIES: Department of Chemistry, University of Kent at Canterbury.

Dr A. G. DAWSON: Laboratory of General Physiology, University of Leicester.

Miss Wendy FARRANT: Department of Audiology and Education of the Deaf, University of Manchester.

Dr Margaret H. GLADDEN: Physiology Department, University of Liverpool.

Dr P. J. HUBNER: MRC Cardiovascular Unit, Royal Postgraduate Medical School, London.

Dr M. D. JOY: Medical Unit, St Thomas's Hospital Medical School, London.

Mr P. A. KIRKWOOD: Department of Physiology, University College London.

Dr A. J. KNELL: School of Molecular Sciences, University of Warwick.

Dr M. F. LEE: Surgical Unit, University College Hospital Medical School, London.

Dr Eileen D. MCDONNELL: Department of Biochemistry, University of Cambridge.

Dr R. T. D. OLIVER: Department of Bacteriology, London Hospital Medical College.

Mr M. C. PERRY: Department of Biochemistry, Royal Free Hospital School of Medicine, London.

Dr J. A. RUSSELL: Department of Physiology, University of Edinburgh.

Dr D. G. SHAW: Department of Virology, The Medical School, Birmingham.

Miss Ruth L. STEPHENS: MRC Virology Unit, Glasgow.

Dr P. L. STORRING: Department of Biochemistry, University of Cambridge.

Mr A. TATEVOSSIAN: Department of Oral Physiology, University of Newcastle upon Tyne.

Dr R. M. WATT: Department of Physiology, University of Edinburgh.

Dr R. J. WILKS: Department of Medical Physics, University of Aberdeen.

FRENCH EXCHANGE SCHOLARSHIPS IN MEDICAL SCIENCE

These awards are made in collaboration with the Centre National de la Recherche Scientifique and allow for the annual exchange of two workers from each country for a full academic year.

The following scholar was nominated by the Centre National de la Recherche Scientifique for an award to be held in Great Britain during the academic year 1968–69:

Mademoiselle C. MERLET (*Institut National de la Santé et de la Recherche Médicale*): Nuffield Institute for Medical Research, Oxford.

The following scholars were nominated by the Council for awards to be held in France during the academic year 1968–69:

Mr T. B. GREENLAND (*Unité des recherches sur les relations virus-cancer, Lyons*): Unité des recherches sur les relations virus-cancer, Lyons.

Dr J. S. LOMAS (*Laboratoire de chimie organique physique, University of Paris*): Laboratoire de chimie organique physique, University of Paris.

These awards are made in collaboration with the Institut National de la Santé et de la Recherche Médicale. Four scholarships are available annually to enable two British and two French workers to undertake clinical research in France and Great Britain respectively.

The following scholars were nominated by the Council for awards to be held in France during the academic year 1968–69:

Dr D. M. CATHRO: INSERM, Unité des recherches, Hôpital Debrousse, Lyons.

Dr G. B. SCOTT (*Department of Pathology, University of Aberdeen*): Institut des recherches scientifiques sur le cancer, Villejuif (extension of 1967–68 award).

No scholars were nominated by the Institut National de la Santé et de la Recherche Médicale for awards to be held in the United Kingdom during the academic year 1968–69.

SCHOLARSHIPS FOR TRAINING IN RESEARCH METHODS AWARDS FOR FURTHER EDUCATION IN THE MEDICAL SCIENCES AWARDS TO MEDICAL AND DENTAL STUDENTS FOR INTERCALATED COURSES IN A BIOLOGICAL SCIENCE

Scholarships are awarded to recent medical, dental or scientific graduates of special promise who wish to be trained in research techniques in order to pursue a career in medical research.

Awards for Further Education in the Medical Sciences are made to enable graduates with a medical or dental qualification or a first degree in science to receive approved postgraduate instruction—as distinct from training in research methods—in a subject ancillary to their main research interest in the field of the biological or medical sciences.

Two hundred and seventy new Scholarships and Awards for Further Education were given for the academic year 1968–69 and the total number of awards held during this academic year was 638.

The Scholarships for Training in Research Methods and Awards for Further Education held during the academic year 1968–69 were as follows:

Subject studied	*No. of awards*	*Subject studied*	*No. of awards*
Anatomy	8	Pathology	12
Bacteriology	2	Pharmacology	59
Biochemistry	186	Physiology	80
Biophysics	30	Psychiatry	10
Cancer studies	12	Psychology	70
Chemistry	13	Radiation studies	15
Dentistry	1	Social and environmental health	2
Endocrinology	3	Special senses	2
Genetics	31	Tropical medicine	11
Immunology	9	Virology	1
Microbiology	42	Zoology	24
Nutrition studies	2	Unclassified	11
Ophthalmology	1	Total	638
Paediatrics	1		

Scholarships and Awards for Further Education were held at the following centres:

Aberdeen University	6
ARC Institute of Animal Physiology	1
Aston University	5
Bath University	4
Belfast: Queen's University	5
Birmingham University	38
Bradford University	4
Bristol University	26
Cambridge University	55
Dublin University	2
Dundee University	4
Durham University	2
East Anglia, University of	4
Edinburgh University	45
Essex, University of	1
Glasgow: University	13
University of Strathclyde	4
Hull University	5
Kent, University of	1
Leeds University	17
Leicester University	6
Liverpool University	9
London: University	
Bedford College	1
Chelsea College of Science and Technology	8
Imperial College of Science and Technology	14
King's College	19
Queen Mary College	1
School of Pharmacy	6
University College	46
Guy's Hospital Medical School	1
London Hospital Medical College	1
Middlesex Hospital Medical School	1
St Bartholomew's Hospital Medical College	3
St Mary's Hospital Medical School	3
St Thomas's Hospital Medical School	1
London University—*contd*	
University College Hospital Medical School	1
British Postgraduate Medical Federation	
Royal Postgraduate Medical School	1
Institute of Cancer Research	16
Institute of Dermatology	1
Institute of Neurology	1
Institute of Psychiatry	16
London School of Hygiene and Tropical Medicine	10
Brunel University	1
City University	1
MRC Developmental Psychology Unit	2
MRC Neuropsychiatry Unit	1
National Institute for Medical Research	4
Royal College of Surgeons of England	1
Royal Institution of Great Britain	1
Manchester: Christie Hospital and Holt Radium Institute	1
University	20
Newcastle upon Tyne University	10
Nottingham University	8
Oxford University	99
Reading University	1
St Andrews University	3
Salford University	4
Sheffield University	24
Southampton University	17
Surrey, University of	2
Sussex, University of	9
Uganda: MRC Child Nutrition Unit	1
Wales, University of:	
University College of North Wales, Bangor	1
University College of South Wales and Monmouthshire, Cardiff	11
Welsh National School of Medicine	4
York University	1

Awards to medical and dental students for intercalated courses in a biological science are made to enable selected undergraduates who have completed their second MB or BDS examinations to extend their studies by intercalating a course in a biological science leading to a first degree. Two hundred and sixty-six awards were made for the academic year 1968–69.

Advisory committees of the Council

The Medical Research Council has for long greatly depended on a series of advisory committees and working parties for assistance in the promotion of research on special subjects within the broad field of medical science and in dealing with other questions calling for expert knowledge. Some of these are standing committees keeping a particular field of research under review and giving advice from time to time; others are temporary committees concerned with particular investigations; others again are committees appointed jointly by the Council and other organizations to consider questions of common interest. All members serve in an honorary capacity. Membership of the Council's principal committees and working parties is as follows:

Nitrous Oxide/Oxygen Analgesia in Midwifery

Professor Sir Dugald Baird (*Chairman*)
Dr Josephine Barnes
Professor J. C. McClure Browne
Dr Roma N. Chamberlain (*Observer: Department of Health and Social Security*)
Professor W. R. S. Doll, OBE, FRS
Dr A. G. Doughty
Mr I. D. Hill
Professor W. W. Mushin
Professor Sir Geoffrey Organe
Dr E. E. Philipp
Professor J. D. Robertson
Professor J. P. M. Tizard
Dr W. N. Rollason (*Secretary*)

Subcommittee

Specifications of Apparatus

Protection against Ionizing Radiations

Dr J. F. Loutit, CBE, FRS (*Chairman*)
Professor P. Alexander
Professor W. R. S. Doll, OBE, FRS
Professor H. J. Evans
Professor L. F. Lamerton
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Professor F. W. Spiers, CBE
Professor Sir Brian Windeyer
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Subcommittees

Permissible Levels
Radiobiology
Genetics Panel

Working Party

Doses for Volunteers and Patients

Coordinating Committee for Radiobiological Research

(*jointly with the Atomic Energy Authority*)

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(*jointly with the Agricultural Research Council*)

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Dr R. Scott Russell
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Panel

Radiobiological Research

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Working Parties

Carcinoma of the Bronchus
Clinical Trials of Radiotherapy and High Tension Oxygen
Bone Sarcoma
High-tension Oxygen and Radiotherapy
Asparaginase in the Treatment of Melanoma
Endolymphatic Therapy in Malignant Melanoma

Leukaemia

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Dr R. M. Hardisty
Dr F. G. J. Hayhoe
Dr J. H. Humphrey, FRS
Professor J. H. Hutchison
Dr L. G. Lajtha
Dr D. R. Laurence
Professor P. L. Mollison, FRS
Dr D. M. Pendreigh (*Observer: Scottish Home and Health Department*)
Dr C. E. G. Smith
Dr N. R. W. Taylor (*Observer: Department of Health and Social Security*)
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Paediatric Leukaemia
Adult Leukaemia

Subcommittee

Leukaemia Pilot Trials

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Live Influenza Vaccine

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Rubella

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Subcommittees

Human Pituitary Hormones
Polypeptide Hormones
Steroid Reference Collection
Tests of Adrenal Cortical Function

Steroid Sex Hormones

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Dr A. C. Crooke
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Supply of Drugs Giving Rise to Dependence

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Evaluation of Aspirin in the Prevention of Thrombosis

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Professor T. Ferguson Rodger, CMG
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Dr J. D. Fulton
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Dr J. L. Turk
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Working Party on Viral Epidemiology Overseas

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Professor N. R. Grist
Dr W. W. Macdonald
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Professor D. G. Evans, FRS
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Professor A. D. Hitchin
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Professor A. E. W. Miles
Professor A. G. Everson Pearse
Professor G. L. Slack, OBE
Professor A. M. Thomson
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Professor R. S. F. Schilling
Professor T. S. Scott
Dr W. H. Walton
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Professor J. S. Weiner
Dr P. J. Chapman (*Secretary*)

Panels

Measurement and Composition of Dust
Biological Activity of Dust
Ergonomics and Physical Environment
Decompression Sickness

Army Personnel Research

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Professor W. J. H. Butterfield, OBE
Professor G. C. Drew
Dr O. G. Edholm
Dr E. R. R. Holmberg
Professor H. Kay
Dr P. L. Krohn, FRS
Maj.-Gen. H. L. E. C. Leask, CB, DSO, OBE
Gen. Sir Charles Richardson, GCB, CBE, DSO, ADC
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Surgeon Vice-Admiral E. D. Caldwell, CB
Professor K. W. Donald, DSC
Professor G. C. Drew
Dr O. G. Edholm
Surgeon Captain F. P. Ellis, OBE
Surgeon Captain J. Glass, OBE
Mr B. W. Lythall, CB
Professor R. A. McCance, CBE, FRS
Vice-Admiral M. P. Pollock, CB, MVO
Mr A. W. Ross, OBE
Dr N. A. B. Wilson, OBE
Dr P. J. Chapman (*Secretary*)
Mr F. E. E. Smith, MBE (*Assistant Secretary*)

Joint Services Personnel Research

Secretary, Medical Research Council (*Chairman*)
Chairman, Army Personnel Research Committee
Chairman, Royal Naval Personnel Research Committee
Chairman, Flying Personnel Research Committee (Ministry of Defence)
Dr P. J. Chapman (*Secretary*)

Computer Advisory Committee

Dr J. A. B. Gray (*Chairman*)
Professor P. Armitage
Professor Sir Hedley Atkins, KBE
Dr D. M. Blow
Professor R. A. Buckingham
Professor G. M. Bull
Sir Edward Collingwood, CBE, FRS
Professor G. D. Dawson
Professor W. R. S. Doll, OBE, FRS
Dr A. J. Eley (*Observer: Department of Health and Social Security*)
Dr J. Howlett, CBE
Mr B. K. Kelly
Professor D. Michie
Dr C. C. Spicer
Professor I. D. P. Wootton
Mr M. J. R. Healy (*Secretary*)

Working Party

Application of Computer Techniques in the Field of Anaesthetics

Working Party on the Treatment of Parkinson's Disease with L-DOPA

Professor J. N. Walton (*Chairman*)
Professor D. R. Laurence
Dr J. T. Boyd
Dr J. A. V. Bates
Professor R. W. Gilliatt
Dr C. Mawdsley
Professor J. A. Simpson
Dr G. M. Stern (*Secretary*)

Headquarters office and other Council establishments

HEADQUARTERS OFFICE

(at date of report)

20 Park Crescent, London W1N 4AL
(01-636 5422)

SECRETARY

J. A. B. Gray, MB, SC D, F INST BIOL, QHP
Private secretary: Miss Valerie Potts, MA

SECOND SECRETARY
S. G. Owen, MD, FRCP

ADMINISTRATIVE SECRETARY
J. G. Duncan, MA, LLB

MEDICAL DIVISION A

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Section A I: General clinical medicine

SENIOR MEDICAL OFFICER
M. P. W. Godfrey, MB, MRCP

MEDICAL OFFICER
Hannah Jacoby, MB, MRCOG

Section A II: Cellular disorders

SENIOR MEDICAL OFFICER
R. C. Norton, MB, D OBST RCOG

MEDICAL OFFICERS
Elizabeth Neale, BM, MRCP
D. M. G. Murphy, MB

MEDICAL DIVISION B

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Section B I: Infectious and immune diseases and haematology

SENIOR MEDICAL OFFICER
H. W. Bunjé, MD, FRCP

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Barbara Rashbass, MB, DCH, DPH*

Section B II: Environmental and industrial medicine, applied psychology and Services research

SENIOR MEDICAL OFFICER
P. J. Chapman, MB

MEDICAL OFFICER
A. M. Baker, MRCS, DPH, DTM & H†

Other senior staff
F. E. E. Smith, MBE
L. D. Hamlyn, OBE
Daphne Self, PH D‡

*Also working in Section B II.
† Also responsible for work on tropical medicine research.
‡ Also working in Section C II.

MEDICAL DIVISION C

PRINCIPAL MEDICAL OFFICER
Joan Faulkner, MB, MRCP, DPH

Section C I: Epidemiology and social medicine, human genetics and computers

SENIOR MEDICAL OFFICER
M. Ashley-Miller, BM, D OBST RCOG, DPH

MEDICAL OFFICER
Katherine Lévy, MB

Section C II: Psychiatry, neurology and endocrinology

SENIOR MEDICAL OFFICER
Sheila Howarth, MB, MRCP

MEDICAL OFFICER
J. S. Gordon, MB, B SC, DCP

Assistants in Medical Divisions

Miss Margaret Grieve, MA
(*Executive Secretary of Clinical Research Board*)

Miss Stephanie Jones, MA
(*Executive Secretary of Biological Research Board*)

ADMINISTRATIVE DIVISION

HEAD OF DIVISION
C. A. Kirkman, MA

Establishment, organization and training

ADMINISTRATIVE OFFICER
D. Noble, BA

Other senior staff
Miss Elizabeth MacKenzie, MA
Mrs Ann de Peyer, BA

Personnel and travel

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A. E. Turner

ADMINISTRATIVE OFFICER
D. Noble, BA

CHIEF EXECUTIVE OFFICER
Miss Edna Pickavance

Other senior staff
J. A. Brown
Miss Robin Morton Smith, BA
Miss Patricia Cross
Mrs Jean Evens
T. F. Moore

Accommodation

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G. M. Levack, OBE, MA

ADMINISTRATIVE OFFICER
J. E. A. Hay, MA

CHIEF EXECUTIVE OFFICER
D. F. Green

Other senior staff
A. E. White
D. Cox, ACIS
C. A. Mackay

Grants, training awards, and supplies

ASSISTANT SECRETARY
R. Wakefield, BA

CHIEF EXECUTIVE OFFICER
D. B. H. Clark

Grants and training awards
L. J. Hale, MIPM
T. J. Gamble
Mrs Jean Gilliland, B COM

Supplies
C. R. Russell

Finance and accounts

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J. M. Jeffs, AACCA

CHIEF EXECUTIVE OFFICER
P. J. L. Farrow AAIA (*Accountant*)

Accounts
Miss Marjorie Biedermann
J. Rickards
Miss Joan Ashton
Miss Joan Beresford
G. M. Cozens

Automatic Data Processing
Miss Betty Maxwell

GENERAL DEPARTMENT

HEAD OF DEPARTMENT
D. J. Cawthron, MA

Publications
Miss Daphne Gloag, MA

Press and information
Mrs Anne Sanderson

Library and Council secretariat
Mrs Norma Morris, MA

CENTRAL STORE, COLINDALE

Colindale Avenue, Colindale, London N.W.9
(01–205 0071)

Head of Store
A. Waltho

The Central Store provides from stock a wide range of materials, equipment and services (including a printing service) for the Council's research establishments in this country and overseas. On a repayment basis it provides a similar service for the Public Health Laboratory Service and the Agricultural Research Council.

MEDICAL RESEARCH COUNCIL LABORATORIES, CARSHALTON

Woodmansterne Road, Carshalton, Surrey
(01–643 4461)

Administrative Officer
A. W. M. Cooke

Senior staff
W. E. Barker (*Project Engineer*)
S. W. Holland (*Chief Engineer*)
T. Battersby, FIMLT

The Laboratories house the MRC Toxicology Unit (p. 160), the MRC Neuropsychiatric Unit (p. 151) and the MRC Laboratory Animals Centre (p. 166), and provide administrative and other services for these establishments.

COMPUTER SERVICES CENTRE

Derbyshire House, St Chad's Street, London W.C.1

(01–278 2925)

Head of Centre

B. K. Kelly, MA

Scientific staff

Miss C. M. Devine, B SC
D. A. Franklin, M SC
T. J. Scott
Mrs C. N. Taylor, B SC

The Centre provides assistance to research units and external staff in the application of computers to their research problems by carrying out programming, arranging for data preparation and running calculations on the computer. It has access to the London University Atlas Computer and the Chilton Atlas Computer at Harwell. A program library is also being set up, which aims to keep copies of all programs likely to be of use to Council workers.

Appendices

I–III FINANCE

IV THE COUNCIL'S ACTIVITIES: FACTS AND FIGURES

V ACCOMMODATION FOR COUNCIL ESTABLISHMENTS

VI PAMPHLETS PRODUCED BY THE COUNCIL

Grants-in-aid account for

1967–68	*Receipts*	£	£
£			
81 522	Balance 1 April 1968		180 844
	Parliamentary Grants-in-aid:		
(13 700 000)	General expenses	15 167 655	
(58 004)	International subscription	62 836	
13 758 004			15 230 491
	Contributions from Government Departments:		
(628 408)	Department of Health and Social Security	702 072	
(170 676)	Ministry of Overseas Development	215 832	
(71 333)	Ministry of Defence	63 000	
(46 170)	Others	44 330	
916 587			1 025 234
	Contributions and grants from other bodies:		
(43 203)	Regional Hospital Boards and Boards of Governors	66 573	
(38 252)	World Health Organization	35 167	
(110 441)	Others	134 021	
191 896			235 761
5 136	Contributions from bequests, donations etc.		5 297
128 384	Miscellaneous receipts		160 016
15 081 529			16 837 643

* Subject to audit.

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the year ended 31 March 1969 *

1967–68 £	*Payments*	£	£
	Administration:		
(421 848)	Salaries and wages	488 922	
(154 065)	Recurrent expenses	157 611	
(1 336)	Capital equipment	—	
—	New building	—	
577 249			646 533
	Central expenses:		
(33 665)	Pensions, honoraria etc.	39 622	
(67 679)	Other expenses	84 776	
101 344			124 398
	National Institute for Medical Research:		
(1 116 634)	Salaries and wages	1 237 772	
(364 366)	Recurrent expenses	434 733	
(125 900)	Capital equipment	88 182	
(206 531)	New building	407 795	
1 813 431			2 168 482
	Clinical Research Centre:		
(149 388)	Salaries and wages	293 193	
(82 157)	Recurrent expenses	113 059	
(54 873)	Capital equipment	66 453	
(533 994)	New building	1 028 463	
820 412			1 501 168
	Research units and external scientific staff:		
(4 189 178)	Salaries and wages	4 525 579	
(1 661 774)	Recurrent expenses	1 794 081	
(782 298)	Capital equipment	645 106	
(583 433)	New building	460 778	
7 216 683			7 425 544
10 529 119	Total direct expenditure		11 866 125
(801 955)	Special grants to institutions	788 914	
(481 349)	Grants to universities for research groups	467 879	
(2 393 244)	Short-term research grants	2 732 381	
(637 014)	Training awards and fellowships	742 117	
(58 004)	Subscription to the International Agency for Research on Cancer	62 836	
4 371 566			4 794 127
14 900 685	Total expenditure		16 660 252
180 844	Balance 31 March 1969		177 391
15 081 529			16 837 643

Grants-in-aid account: summary of receipts

	1964–65	*1965–66*	*1966–67*	*1967–68*	*1968–69*
	£000's	£000's	£000's	£000's	£000's
Parliamentary grants-in-aid ..	8 753	10 088	11 825	13 758	15 231
Other income	874	958	1 016	1 242	1 426
	9 627	11 046	12 841	15 000	16 657
Recurrent expenditure on:					
Administration	472	517	556	577	646
Central expenses	111	119	100	101	124
National Institute for Medical Research	1 244	1 314	1 504	1 607	1 761
Clinical Research Centre.. ..	17	44	48	287	473
Research units and external scientific staff..	4 732	5 348	5 956	6 634	6 965
Total direct recurrent expenditure	6 576	7 342	8 164	9 206	9 969
Special grants	671	681	704	802	789
Research groups	255	407	503	481	468
Short-term research grants ..	1 358	1 787	2 197	2 393	2 732
Training awards	309	413	520	637	742
International subscription ..		54	54	58	63
Total recurrent expenditure ..	9 169	10 684	12 142	13 577	14 763
Expenditure on new building ..	460	373	637	1 324	1 897
Total expenditure	9 629	11 057	12 779	14 901	16 660

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and payments from 1964–65 to 1968–69

Percentage increases on previous year					*Proportional allocation (%)*				
1964–65	*1965–66*	*1966–67*	*1967–68*	*1968–69*	*1964–65*	*1965–66*	*1966–67*	*1967–68*	*1968–69*
24.5	15.3	17.2	16.3	10.7	90.9	91.3	92.1	91.7	91.4
					9.1	8.7	7.9	8.3	8.6
21.2	14.7	16.3	16.8	11.1	100.0	100.0	100.0	100.0	100.0
20.4	9.5	7.5	3.8	11.9	5.1	4.8	4.6	4.3	4.3
					1.2	1.1	0.8	0.7	0.9
16.6	5.6	14.5	6.8	9.6	13.6	12.3	12.4	11.8	11.7
					0.2	0.4	0.4	2.1	3.2
15.5	13.0	11.4	11.4	5.0	51.6	50.1	49.0	48.9	47.4
15.7	11.6	11.2	12.8	8.3	71.7	68.7	67.2	67.8	67·5
16.3	1.5	3.4	13.9	—	7.3	6.4	5.8	5.9	5.4
61.9	36.0	23.1	6.4	11.3	17.6	20.5	22.2	21.2	21.7
47.1	33.7	25.9	22.5	16.5	3.4	3.9	4.3	4.7	5.0
						0.5	0.5	0.4	0.4
22.8	16.5	13.6	11.8	8.7	100.0	100.0	100.0	100.0	100.0
21.2	14.8	15.6	16.6	11.8					

Appendix III

Other sources of support in the year ended 31 March 1969

SUBVENTIONS FROM GOVERNMENT DEPARTMENTS

Source	£	*Purpose*
Department of Health and Social Security (formerly Ministry of Health), Scottish Home and Health Department, and Welsh Board of Health	743 532	Division of Immunological Products Control (National Institute for Medical Research) for control testing of therapeutic substances; Blood Group Reference Laboratory; Blood Products Laboratory; part of the cost of the Radiological Protection Service; special surveys
Ministry of Overseas Development	215 832	Subvention towards the cost of: MRC Laboratories, Gambia; MRC Tropical Metabolism Research Unit, Jamaica; MRC Trachoma Unit, London and Gambia; MRC Epidemiology Unit, Jamaica; MRC Child Nutrition Unit, Uganda; other research in tropical medicine
Ministry of Defence	64 449	Investigations proposed by Council's Royal Naval Personnel Research Committee and Army Personnel Research Committee
Department of Health and Social Security (formerly Ministry of Social Security)	4 687	Audiometric surveys in industrial environments
Post Office	6 000	Study of code design and the design of keyboards

GRANTS FROM OTHER BODIES

World Health Organization	35 167	International Laboratory for Biological Standards; World Influenza Centre; International Blood Group Reference Laboratory; International Reference Centre for Respiratory Virus Diseases; International Reference Centre, MRC Toxicology Unit; International Reference Centre on Air Pollution; International Reference Centre, MRC Experimental Haematology Unit; International Reference Centre for Abnormal Haemoglobins; trial of chemotherapeutic agents against tuberculosis (India); contributions for special investigations at several Council establishments
Wellcome Trust	20 000	Fellowship awards
Alexander Pigott Wernher Memorial Trust	5 100	Fellowship awards and research on blindness and deafness
East African Tuberculosis Investigation Centre	9 100	East African tuberculosis chemotherapy trial
United States Public Health Service	6 818	Steroid Reference Collection
International Atomic Energy Agency	1 202	Research into the measurement of total body potassium in malnourished Jamaican infants by whole-body counting of natural potassium
International Agency for Research on Cancer	11 459	Study of asbestos cancers

Appendix IV

The Council's activities: facts and figures

GRANTS-IN-AID FOR 1968–69 .. .. £15 230 655

Contributions from Government departments £1 046 000

MRC ESTABLISHMENTS AND STAFF (at 1 January 1969)

Number of Council research establishments 79
(including the National Institute for Medical Research and Clinical Research Centre)

Number of staff employed by the Council (at 1 January 1969)

Scientific staff	1 004*
Technical staff	1 569
Administrative and clerical staff	798
Maintenance staff	459
Locally appointed staff overseas	146
Total	3 976

MRC GRANT-SUPPORTED WORK

Research groups (at 1 January 1969) 33

Research grants

Total number of grants in being 1 238

The following figures show how this form of support has grown over the years:

1953–4	*1963–4*	*1964–5*	*1965–6*	*1966–7*	*1967–8*	*1968–9*
271	388	857	1 035	1 083	1 210	1 238

TRAINING AWARDS

New awards for the academic year 1968–69 (total awards held are shown in brackets when the period of tenure exceeds one year)

Travelling fellowships	26
Clinical research fellowships	8 (15)
Junior research fellowships	25 (54)
Scholarships for training in research methods and awards for further education	270 (638)
Awards for intercalated courses	266

PATENTS

Number of applications filed arising out of research supported by the Council (April 1968–March 1969) ..	9
Number of patents and patent applications on the active register of the National Research Development Corporation	102

* Of these 294 are medically qualified.

Appendix V

Accommodation for Council establishments

Clinical Research Centre

The building of Phases I and II has progressed at a satisfactory rate during the year and if this is maintained there is every prospect that the handover and commissioning of Phase I of the contract will take place in the first half of 1970. Phase II should be ready for handover and commissioning by the end of August 1970.

Existing research establishments

The following building projects were completed during the year:

National Institute for Medical Research	Installation of a radiation source (cobalt-60) with an activity of more than 1500 curies. Erection of new laboratories and offices for the Animal Division and provision of further improved animal accommodation, including space for germ-free isolators for breeding gnotobiotic animals.
MRC Demyelinating Diseases Unit	New accommodation
MRC Child Nutrition Unit, Uganda	New houses and flats for staff
MRC Laboratory of Molecular Biology	Major extension, part of which is occupied by the University

Work is in progress on the following projects:

National Institute for Medical Research	Remainder of major redevelopment scheme involving (*i*) new block containing canteen and offices, (*ii*) major building for breeding SPF animals and (*iii*) conversion of old canteen to provide new laboratories for research on genetics and developmental biology
MRC Biochemical Parasitology Unit	Conversions at the Molteno Institute (in association with the University of Cambridge)
MRC Clinical and Population Cytogenetics Unit	Planning of new extension (in association with the University of Edinburgh)
MRC Child Nutrition Unit, Uganda	New laboratories and improvements to ward
MRC Unit for Physical Aids for the Disabled	New accommodation (in association with Scottish South-East Regional Hospital Board)

Minor alterations and extensions are also in progress in various other units.

Appendix VI

Pamphlets produced by the Medical Research Council

Charter of the Medical Research Council
Medical Research Council: constitution and functions
What is the MRC? (leaflet)—also in French
Benefactions for medical research by gift or bequest

ESTABLISHMENTS
National Institute for Medical Research
Northwick Park Hospital and Clinical Research Centre

CAREERS
Careers in medical research
Technical careers in the Medical Research Council
Careers and opportunities for graduates with the Medical Research Council
Conditions of service on the Council's staff

SUPPORT FOR RESEARCH
Long-term support for research
Research grants
Fellowships and scholarships awarded by the Medical Research Council

REPRINTS
The role of a research council (from the Report of the Medical Research Council for 1960–61)
Responsibility in investigations on human subjects (from the Report of the Medical Research Council for 1962–63)
Tobacco smoking and cancer of the lung (statement by the Medical Research Council, 1957).

All these pamphlets may be obtained from the Medical Research Council, 20 Park Crescent, London W.1. A catalogue entitled *Government publications: sectional list No. 12* (obtainable from the Medical Research Council or from Her Majesty's Stationery Office) gives details of all the reports published for the Council by HMSO.

Indexes

Personal names index

Index to establishments and committees

Subject index *

The italic numbers in brackets indicate individual grant-holders

* See also pp. 302–4 for research covered by committees and working parties.

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