1963-64 Cmnd. 2382 **Committee of Privy Council for Medical Research. Report of the Medical Research Council for the year 1962-63**

COMMITTEE OF PRIVY COUNCIL
FOR MEDICAL RESEARCH

REPORT OF THE MEDICAL RESEARCH COUNCIL FOR THE YEAR 1962-1963

Presented to Parliament by the Secretary of State for Education and Science by Command of Her Majesty July 1964

LONDON
HER MAJESTY'S STATIONERY OFFICE
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Cmnd. 2382

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The Secretary of State for Scotland
The Secretary of State for Commonwealth Relations
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R. E. Radford (*Department of Technical Co-operation*)

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REPORT OF THE COMMITTEE OF PRIVY COUNCIL FOR MEDICAL RESEARCH FOR THE YEAR 1962–1963

TO THE QUEEN'S MOST EXCELLENT MAJESTY

May it please your Majesty,

The Lords of the Committee for Medical Research of Your Majesty's Privy Council have received the Report of the Medical Research Council for the year ended 30 September 1963.

The Council's Jubilee was celebrated during this period, being the fiftieth anniversary of the establishment of the Council's direct predecessor, the Medical Research Committee. The occasion was marked by many tributes to the Council's achievements in the field of medical research; to these we wish to add our own heartfelt appreciation of the labours of the Council and their staff over fifty years.

During the financial year 1963–64, Parliament provided for the Medical Research Council a grant-in-aid of £7,033,000 (including supplementary provision of £125,000), consisting of £6,524,000 on the ordinary account, £424,000 on the non-recurrent account for buildings and £85,000 for grants for special apparatus. This grant represents an increase of nearly 20 per cent over the provision made in the preceding year.

From this grant, funds have been allocated for the National Institute for Medical Research and the Council's research units and scientific staff working independently; for grants to workers in universities, hospitals and other centres; for training awards, and for non-recurrent expenditure on buildings and special apparatus in the universities. In addition, special grants for research work were made to a number of independent institutions, including the following: the Institute of Cancer Research, London; the Royal Beatson Memorial Hospital, Glasgow; the Christie Hospital and Holt Radium Institute, Manchester; the Strangeways Research Laboratory, Cambridge, and the Royal Institution, London.

The Council now support 72 research units and 14 research groups. During the year, the Council set up an Abnormal Haemoglobin Research Unit and a Research Group on Megaloblastic Anaemias, thus extending their already wide coverage of the different aspects of blood diseases. There are now five research units and one research group almost wholly concerned with work in this field. Two other new units established were the Metabolic Reactions Research Unit, which will study metabolic reactions in living tissues, and the Psycholinguistics Research Unit, which is applying new theories to problems of speech, language and communication.

The scheme of research groups recently introduced by the Council, to provide long-term 'bridging' support for projects in university departments which it is hoped will eventually be absorbed into the university structure, has met with increasing demands and we are pleased to report that during the year five new groups (including the Research Group on Megaloblastic Anaemias) were set up. Of these, the Biomechanics Research Group will have as its main research theme the structural and mechanical properties of human tissues, the engineering principles underlying their function, and the clinical application of these principles; the Research Group on Respiration and Energy Metabolism in the Newborn will investigate physiological processes affecting the survival of newborn infants; the Research Group on Immunological Aspects of Dermatology will be concerned with the immunological mechanisms occurring in skin diseases; and the possibility that genetic factors may play a part in causing bone diseases will be investigated by the Research Group on Genetic Problems in Orthopaedic Disease.

The Council have maintained their close liaison with the Ministry of Health and the Scottish Home and Health Department, and with other departments having problems calling for new research work or for expert advice, and with the Department of Scientific and Industrial Research and the Agricultural Research Council (acting under their respective Committees of Privy Council) on matters of common interest. They have, as in the past, co-operated with the Department of Technical Co-operation, the Colonial Office and the Commonwealth Relations Office in the field of tropical medicine. They have also continued to foster scientific liaison with Commonwealth countries, the United States of America and other countries overseas, and with the World Health Organization of the United Nations.

We are glad to note also that the Council have addressed themselves to the important problem of the ethical and legal considerations which govern the conduct of clinical investigations on human subjects. The Council's statement on this subject should be widely useful.

By an Order of 10 May 1963, two new members of the Medical Research Council were appointed from 1 October 1963 (after the required consultation with the Medical Research Council and with the President of the Royal Society), as follows:

Hedley John Barnard Atkins, D.M., M.Ch., F.R.C.S. (Professor of Surgery in the University of London at Guy's Hospital Medical School) and

William Drummond Macdonald Paton, J.P., D.M., F.R.S. (Professor of Pharmacology in the University of Oxford),

in place of

Robert Milnes Walker, M.S., F.R.C.S. (Professor of Surgery in the University of Bristol) and

Alan Lloyd Hodgkin, Sc.D., F.R.S. (Royal Society Foulerton Research Professor in the University of Cambridge),

who retired in accordance with the provisions of the Charter on 30 September 1963.

By the same Order Sir Hugh Nicholas Linstead, O.B.E., LL.D., F.P.S., M.P., was reappointed as a member of the Council from 1 October 1963.

Your Majesty has been graciously pleased to confer honours on the following:

D.B.E.	Professor Honor Fell (Director, Strangeways Research Laboratory, Cambridge, and Senior Biological Adviser to Biophysics Research Unit).
Knight Bachelor	Dr. J. W. Cook (Honorary Director, Carcinogenic Substances Research Unit).
C.B.E.	Professor W. S. Feldberg (National Institute for Medical Research);
	Professor L. N. Pyrah (Honorary Director, Metabolic Disturbances in Surgery Research Unit);
	Dr. M. F. Perutz (Chairman of Board, Laboratory of Molecular Biology);
	Dr. J. C. Kendrew (Laboratory of Molecular Biology);
	Dr. F. Sanger (Laboratory of Molecular Biology);
	Professor M. H. F. Wilkins (Deputy Director, Biophysics Research Unit).
O.B.E.	Dr. R. E. Hope-Simpson (member of the Council's External Scientific Staff).

The following three members of the Council's staff were elected to the Fellowship of the Royal Society:

Dr. J. H. Humphrey (Deputy Director, National Institute for Medical Research);
Dr. J. F. Loutit (Director, Radiobiological Research Unit);
Dr. J. A. Fraser Roberts (Director, Clinical Genetics Research Unit).

On behalf of the Lords of the Committee for Medical Research of Your Majesty's Privy Council.

QUINTIN McGAREL HOGG
Secretary of State for Education and Science

HAROLD HIMSWORTH
Secretary to the Committee of Privy Council for Medical Research

9 June 1964

REPORT OF THE MEDICAL RESEARCH COUNCIL FOR THE YEAR 1962–1963

TO THE LORDS OF THE COMMITTEE OF PRIVY COUNCIL FOR MEDICAL RESEARCH

May it please Your Lordships,

The Medical Research Council beg leave to submit the following report on their proceedings during the period from 1 October 1962 to 30 September 1963. They add to their report nine short articles on selected aspects of medical research and summaries of the research projects supported during the year under review, but for a complete picture of the Council's work reference must be made to the large number of publications by members of the scientific staff and by the recipients of research grants. Lists of these publications are now too long to be included in the Annual Report but they are obtainable from the Librarian of the National Institute for Medical Research.

COUNCIL'S FIFTIETH ANNIVERSARY

In the unavoidable absence of His Royal Highness the Duke of Edinburgh, the Minister for Science was guest of honour at a dinner held by the Council at Goldsmiths' Hall on 25 November 1963 to celebrate the fiftieth anniversary of the foundation of the Medical Research Committee. This Committee, the direct predecessor of the Medical Research Council, was set up in 1913 to administer a newly created government fund for medical research. Previously a number of small grants had been made from public funds for the support of medical research, but this was the first time that the government had assumed a formal and continuing responsibility. The Committee continued in existence until 1920, when the Medical Research Council received, under Royal Charter, its present title and a constitution enabling it to pursue an independent policy for the advancement of knowledge in the medical sciences.

The broad principles of the Council's policy in supporting research in medicine and the related biological fields were established in these early days. Essentially, the Council's role was to be complementary to that of the universities, hospitals and other branches of the health services. Two years ago, in the Annual Report for 1960–61, the Council reformulated the concept of their role in the context of the developments that had occurred: 'to watch over the whole field of medical and related biological research so as to foresee, to the best of their ability, the needs and opportunities; to give support to any promising research in these fields irrespective of the agent concerned; to work in partnership with the universities and professions on the one hand and the various departments of Government on the other so that new knowledge may be made available as the need arises'.

In furtherance of these aims the Council have supported research in two main ways: by employing their own staff in their own institutes and research units and by assisting the work of staff employed by other agencies—such as universities or hospitals—by means of temporary research grants or block grants or by the setting up of research groups.

Throughout the 50 years of the Council's existence the bed-rock of the Council's research programme has been the continued and expanding support of promising work in all branches of medicine and related biology so as to assure as comprehensive a cover as possible of the field as a whole. Necessarily, however, under the pressures of need and opportunity, emphasis has changed. An account of these changes over the years is given in the articles by Sir Henry Dale and Sir Landsborough Thomson which were published in the British Medical Journal (23 November 1963) on the occasion of the Council's fiftieth anniversary.

ROCKEFELLER FOUNDATION

The Rockefeller Foundation also celebrated its fiftieth anniversary in 1963, and the Council had particular pleasure in congratulating the Foundation on its service to the advancement of knowledge and to international co-operation and understanding during the past fifty years.

The Rockefeller Foundation occupies a special place in the field of scientific and cultural endeavour. To many, it is the doyen of the foundations. Its standards have always been of the highest, its generosity has been unsparing and its influence immense in a wide variety of causes throughout the world. The Council have greatly valued the happy relationship which they have always enjoyed with the Foundation. Over the years, by many generous acts, the Foundation has contributed to the development of medical education and medical research in the United Kingdom. The Council would like to pay special tribute to one of these acts of generosity with which they have been particularly associated—the provision of Rockefeller Travelling Fellowships, with only a short intermission, from 1923 to 1963. These fellowships have long been regarded as the blue riband award for travel and study abroad and have been much sought after. Since 1923, 207 fellowships have been awarded. The holders of 67 of these have since been appointed to university chairs, 42 to consultant appointments in the National Health Service, 18 as directors or heads of departments (including directors of Council units), 12 as university readers and 11 as senior lecturers.

These fellowships are coming to an end in 1964, as a result of changes in the general policy of the Foundation. Now that many other sources of financial aid for research are available in Western Europe, its programme of aid is coming to be concentrated almost exclusively on some of the developing countries, and this reorientation is limiting what it can do in the scientifically advanced countries. Now, however, the Council are to award travelling research fellowships of their own to replace the Rockefeller awards in their scheme of travelling fellowships.

INVESTIGATIONS ON HUMAN SUBJECTS

In 1953 the Council issued a statement of the considerations which should, in their opinion, govern the conduct of scientific investigations on patients.

Since then the range and scope of technically feasible procedures have steadily increased. The Council have also been asked for their guidance on the conduct of investigations on healthy persons. They have accordingly reviewed the whole subject in consultation with their legal advisers and with the Health Departments, and have embodied the results of this review in a statement of their opinions on this matter. Their statement is given on pp. 21–25 of this Report.

COMMITTEE ON HIGHER EDUCATION

In the Report for 1960–61 it was reported that the Council had accepted an invitation to submit evidence to the Committee on Higher Education sitting under the chairmanship of Lord Robbins.

In the memorandum submitted by the Council attention was drawn to the facilities existing within their organization for the postgraduate training of young research workers and the suggestion was made that increased and more systematic use might be made of these facilities.

In the report of this Committee issued in October 1963 (Cmnd. 2154) the Council were pleased to see that recognition was given to these facilities and to the contribution which government research establishments (including those of the Research Councils) could make in the field of postgraduate study.

SIR GRAHAM WILSON

On 30 September 1963 Sir Graham Wilson retired from his post as Director of the Public Health Laboratory Service, which he had held under the Medical Research Council except during the last two years of his office, when the present statutory Board was established. He was appointed in 1941 and for two years before that had been head of the wartime regional laboratory at Oxford. When the Service was placed on a permanent footing in 1947 he relinquished his chair at the London School of Hygiene and Tropical Medicine and became full-time Director.

Over the years Sir Graham has devoted his wisdom, energy and skill to perfecting the Service as an instrument both for safeguarding the public health against epidemic disease and for the advancement of knowledge in that field. Under his guidance the Service has proved its value to the country and has won admiration abroad. His personal contribution to the achievement has been very great.

Sir Graham Wilson is also distinguished as a teacher and investigator, and as joint author of a famous text-book of bacteriology. His advisory work has been notable, and he has served on numerous official (including international) expert committees. He has received many academic honours and prizes; he was Honorary Physician to the King in 1944–46 and he was knighted in 1962.

REVIEWS OF THE SCIENTIFIC PROGRAMME

The Council, the Clinical Research Board and the Biological Research Board (formerly the Biological Research Awards Committee) each hold nine meetings yearly; the Tropical Medicine Research Board meets at quarterly intervals. Most of these meetings are preceded by ' noon sessions ' at which various fields of

research are reviewed, and experts in these fields, who may not necessarily be connected with the Council, are invited to speak. In this way, over two or three years most of the field of research is examined. The Council have been anxious to ensure that any opinions given shall be completely frank and the details of these discussions have consequently always been regarded as confidential. The following list will, however, indicate the scope of the subjects discussed during 1962–63.

COUNCIL

1962	*Speaker*	*Subject*
October	Dr. W. Hayes (Director, Microbial Genetics Research Unit)	Bacterial genetics
November	Professor E. B. Chain (Istituto Superiore di Sanità, Rome)	The chemical approach to biology
1963		
January	Dr. W. R. S. Doll (Director, Statistical Research Unit)	The uses of epidemiology in medical research
February	Sir Christopher Andrewes (formerly Head of the Division of Bacteriology and Virus Diseases, and Deputy Director of National Institute for Medical Research)	Epidemiology of virus diseases
March	Professor A. S. Parkes (Mary Marshall Professor of the Physiology of Reproduction, University of Cambridge)	The population problem
April	Professor J. N. Morris (Director, Social Medicine Research Unit)	Social medicine
May	Professor C. H. Waddington (Institute of Animal Genetics, University of Edinburgh)	Epigenetics (developmental biology)
June	Sir Keith Murray (Chairman, University Grants Committee)	Relationship between the universities and the Research Councils
October	Professor M. G. P. Stoker (Honorary Director, Experimental Virus Research Unit)	Perspectives in virology
November	Dr. M. G. Candau (Director-General, World Health Organization)	Research programme of World Health Organization

CLINICAL RESEARCH BOARD

1962		
October	Dr. J. P. Bull (Director, Industrial Injuries and Burns Research Unit)	Research on blood substitutes

1963	Speaker	Subject
January	Dr. E. T. O. Slater (Director, Psychiatric Genetics Research Unit)	Psychiatric genetics
February	Dr. J. A. Loraine (Director, Clinical Endocrinology Research Unit)	Clinical endocrinology
March	Professor M. F. A. Woodruff (Department of Surgery, University of Edinburgh)	Organ transplantation
April	Professor R. E. Tunbridge (Department of Medicine, University of Leeds)	Gerontology
May	Professor Sir Charles Illingworth (Department of Surgery, University of Glasgow)	Superoxygenation therapy in surgery
October	Dr. I. M. Roitt (Courtauld Institute of Biochemistry, Middlesex Hospital)	Auto-immunity and disease
November	Dr. D. Michie (Department of Surgical Science, University of Edinburgh)	The uses of computers in medical research

TROPICAL MEDICINE RESEARCH BOARD

1962		
December	Dr. H. Lehmann (Honorary Director, Abnormal Haemoglobin Research Unit)	Haemoglobin variants
1963		
March	Dr. R. J. W. Rees (National Institute for Medical Research)	Leprosy research
July	Dr. L. H. Collier (Honorary Director, Trachoma Research Unit)	Trachoma research

COUNCIL BOARDS

As mentioned in the last Annual Report, the Council created, in 1962, a Biological Research Awards Committee to advise them on the award of grants in the non-clinical field. This Committee has now become the Biological Research Board, complementing in the non-clinical field the responsibilities of the Clinical Research Board. Professor A. L. Hodgkin, as the senior non-clinical member of the Council, was the first chairman of this Committee; on his retirement from the Council he was succeeded by Professor Wilson Smith. The two vacancies caused by Professor W. D. M. Paton's appointment as a Council member of the Committee and by Professor Sir Brian Windeyer's retirement under the rota system were filled by Professor P. G. H. Gell and Professor D. G. Evans.

On the Clinical Research Board, Professor Hedley Atkins, already a member, succeeded Professor R. Milnes Walker as a clinical member of Council; Professor T. Crawford filled the vacancy thus created.

Following the establishment of the Department of Technical Co-operation and its assumption of the main responsibilities for medical research formerly held by the Colonial Office, amendments in the terms of reference of the Tropical Medicine Research Board became necessary. This now advises:

(*a*) the Secretary for Technical Co-operation, through the Medical Research Council, on all medical research overseas or in the United Kingdom financed from the funds of the Department of Technical Co-operation;

(*b*) the Medical Research Council on all medical research in or for tropical or subtropical countries financed from their own budget.

Professor A. C. Frazer, Sir John Boyd and Professor P. C. C. Garnham retired under the rota system from the Board, being replaced by Professor G. M. Bull and Professor D. A. Bertram.

RESEARCH ESTABLISHMENTS

Ministerial visits

During the course of the year Mr. Denzil Freeth, M.P., as Parliamentary Secretary for Science, visited the following Council establishments:

Applied Psychology Research Unit
Wernher Research Unit on Deafness
Radiological Protection Service
Unit for Research on the Epidemiology of Psychiatric Illness
Research Group on Demyelinating Diseases.

Council visits

The Council continued their series of visits to their various research establishments and during the year they saw work in progress in the following units and groups:

Hammersmith Hospital and Postgraduate Medical School	Microbial Genetics Research Unit Experimental Radiopathology Research Unit Cyclotron Unit Cardiovascular Research Group
Oxford	Population Genetics Research Unit Bone-Seeking Isotopes Research Unit Body Temperature Research Unit Blood Coagulation Research Unit Cell Metabolism Research Unit
Edinburgh	Clinical Endocrinology Research Unit Unit for Research on the Epidemiology of Psychiatric Illness Clinical Effects of Radiation Research Unit Research Group on the Organization of Central Mechanisms Subserving Vision Research Group on Experimental and Clinical Problems of Transplantation

Glasgow	Experimental Virus Research Unit Atheroma Research Unit
Sutton, Surrey	Radiological Protection Service
M.R.C. Laboratories, Carshalton	Laboratory Animals Centre Virus Research Unit Toxicology Research Unit Neuropsychiatric Research Unit.

The Council's annual visit to the National Institute for Medical Research took place in June, when the Director, Dr. P. B. Medawar, reviewed the work of the Institute.

New research units and groups

Long-term support for research is provided by the Council at the National Institute for Medical Research and through the establishment of research units. During the year the following units were set up:

The *Abnormal Haemoglobin Research Unit*, which is under the honorary direction of Dr. H. Lehmann, first established at St. Bartholomew's Hospital Medical College, London, and now moved to Cambridge, is making a chemical analysis of abnormal haemoglobins in order to determine their structure and complete their identification. Rare haemoglobins are of particular interest in genetic research.

Following Professor E. B. Chain's appointment to the Chair of Biochemistry at the Imperial College of Science and Technology, London, the Council agreed to establish a *Metabolic Reactions Research Unit* under his honorary direction. The Unit, which will not be formally established until October 1964, will investigate metabolic reactions in the tissues of higher animals and micro-organisms.

The *Psycholinguistics Research Unit*, at the Institute of Experimental Psychology, Oxford, under the honorary direction of Professor R. C. Oldfield, will study the psychological aspects of speech and language. This research is expected to have a number of applications in both medical and social work; for instance, it may help in developing a better understanding of language and speech disorders, and also in solving problems of the communication of information and in devising methods for its storage and retrieval.

Long-term support is also provided in institutions other than their own by the Council's scheme of research groups, which is intended to enable universities to develop work that is in line with the interests of particular departments. The aim is that the university will ultimately assume financial responsibility for the group if it wishes the work to be continued. During the year the Council agreed to set up the following new groups:

The *Biomechanics Research Group*, at the Department of Mechanical, Civil and Chemical Engineering, Royal College of Science and Technology, Glasgow, will undertake research in the field of 'human engineering'. Under the honorary direction of Professor R. M. Kenedi the Group are applying engineering principles to the study of physiological processes, in collaboration with hospital medical staff in the Glasgow area.

The *Research Group on Respiration and Energy Metabolism in the Newborn*, under the honorary direction of Professor K. W. Cross at the London Hospital

Medical College, will study problems of respiration and oxygen consumption in newborn infants. Respiratory failure is one of the commonest causes of death in the newborn, and it is hoped that these studies will show what are the physiological factors affecting survival.

A *Research Group on Immunological Aspects of Dermatology* has been established at the Institute of Dermatology, London, under the honorary direction of Dr. J. L. Turk in Professor C. D. Calnan's Department at the Institute. In many skin conditions, for example eczema and dermatitis, delayed hypersensitivity is encountered, which resembles the reaction of the body to a foreign protein. The study of immunological mechanisms in dermatitis arising from contact with various substances is to be the principal line of research of this group.

In the Department of Orthopaedic Surgery, University of Edinburgh, the *Research Group on Genetic Problems in Orthopaedic Disease*, under the honorary direction of Professor J. I. P. James, will investigate, by means of family surveys, the influence of genetic factors in the incidence of orthopaedic conditions, including club foot and congenital dislocation of the hip.

The *Research Group on Megaloblastic Anaemia* at the Postgraduate Medical School of London is concerned with the relationship between dietary deficiencies and anaemia. Dr. D. L. Mollin, Honorary Director of the Group, has already carried out studies in this field and his work on vitamin levels in various types of anaemia will now be expanded.

Changes in research units

During the year four units were disbanded—the Chemical Pathology of Steroids Research Unit, the Rheumatism Research Unit at Bath, the Bilharzia Research Unit and the Council's Department for Research in Industrial Medicine at the London Hospital. Responsibility for certain aspects of the work of this last unit has been assumed by the Air Pollution Research Unit at St. Bartholomew's Hospital Medical College, London.

New directors were appointed to two other units. On the retirement of Dr. L. J. Harris from the Council's staff, Dr. E. Kodicek, already a member of the staff of the unit, became Director of the Dunn Nutritional Laboratory, Cambridge; and Professor L. S. Hearnshaw took over the honorary direction of the Unit for Research on the Occupational Aspects of Ageing, following Dr. Alastair Heron's appointment as Director of the Rhodes-Livingstone Institute in the University College of Rhodesia and Nyasaland.

At the end of the year the Council's establishments consisted of the National Institute for Medical Research, 72 research units (including 4 overseas) and 14 research groups. Members of the Council's external staff continued to be attached individually to other institutions.

Institutions supported by special grants

The Council have continued to provide, by means of special grants, substantial support for a number of institutions and projects, including the following: the Institute of Cancer Research, Royal Marsden Hospital, London; the Royal Beatson Memorial Hospital, Glasgow; the Christie Hospital and Holt Radium Institute, Manchester; the Strangeways Research Laboratory, Cambridge; and the Davy Faraday Research Laboratory of the Royal Institution, London.

In meeting their obligations to advance medical research the Council recognize three broad needs; training for research, short-term support for research and sustained support over long periods. The training of young graduates in science and medicine is assisted through various scholarships and fellowships (see pp. 214–20. The long-term support of projects and of individuals is achieved by the Council in a number of ways—primarily through the employment of their own staff, working at the National Institute for Medical Research and in the various research units or individually in universities and hospitals as members of the Council's external scientific staff, by research groups or through the provision of special grants to autonomous institutions. In the field of short-term support, the Council have always attached particular importance to their scheme of research grants; these are made for a number of years—not normally more than three—as a means of providing initial support for the development of new ideas and for stimulating the growing points of research. Such grants can also provide the salaries of research workers until appropriate university or hospital appointments become available.

Over the years the number of grants awarded by the Council has grown considerably, as will be seen from the following table indicating the number of grants held at approximately ten-year intervals.

	1923–4	*1933–4*	*1939–45**	*1953–4*	*1962–3*
No. of grants held	176	205	235	271	642

The following table shows, for the past 10 years, the number of applications for grants and the percentage of these that were successful, together with the actual number of new grants awarded each year.

	1953–4	*1954–5*	*1955–6*	*1956–7*	*1957–8*	*1958–9*	*1959–60*	*1960–1*	*1961–2*	*1962–3*
No. of applications	113	128	165	142	185	201	228	274	325	351
No. of grants awarded	90	118	143	124	152	179	211	236	260	282
% of applications successful	80	92	87	87	82	89	93	86	80	80

Between 1953–4 and 1962–3 there was a four-fold increase in expenditure on grants. This has been due not only to the increasing number of grants awarded but also to the fact that the average value of each grant rose from about £600 in 1953–54 to about £1500 in 1962–63. The growing complexity of research has contributed substantially to this increase in the value of awards; for example, more and more investigations involve the use of complex equipment, radioactive isotopes and highly purified enzymes.

A complete list of grant-holders and their subjects of research, arranged according to the location of the institutions in which they have been working, is given on pp. 181–213.

* Total number of grants held during the war years, annual figures not being available.

COMMITTEES

In the different fields of their work the Council are advised by specialized committees and working parties. The Occupational Health Committee was reconstituted on a wider basis to advise and assist the Council in the promotion of research into industrial medicine, taking in the work of the Air Pollution, Toxicology and Industrial Pulmonary Diseases Committees, which were consequently disbanded. The Committee will continue to sponsor a number of panels on such specialized matters as airborne dust in relation to pneumoconiosis.

Other committees and working parties disbanded during the year were:

Climatic Physiology
Possible Carcinogenic Action of Detergents
Anterior Pituitary Hormones Standards
Sterilization of Syringes
Control of Diphtheria Toxoid

In agreement with the Nuffield Foundation, the Council also disbanded the Joint Committee on Therapeutic Trials in Chronic Rheumatic Diseases, whose work had been completed. Full details of the Council's committees are given on pp. 221–36.

OVERSEAS LIAISON

During the year there was a considerable increase in the number of visits undertaken by members of the Council's staff to countries overseas to attend international and other congresses, to lecture, and to see and take part in research work at various centres; several members of the staff were again granted leave of absence for varying periods of up to one year to work in academic centres abroad. Approximately sixty international congresses and meetings of a similar nature were attended by members of the staff.

Through the work of the Tropical Medicine Research Board and by their close liaison with the various Regional Councils the Council have continued their interest and activities, both in the United Kingdom and in territories overseas, in many aspects of medical research in the tropics. Three members of the Tropical Medicine Research Board, Professor G. Macdonald, Dr. R. Lewthwaite and Professor G. M. Bull, attended the first annual meeting of the East African Medical Research Council as delegates of the Board and visited the main research centres in East Africa. Two members of the Board, Professor M. L. Rosenheim and Dr. R. Lewthwaite, and Professor J. C. Waterlow attended, as delegates of the Board, the Annual Scientific Conference and meeting of the Standing Advisory Committee for Medical Research in the Caribbean and visited the main research centres in the Caribbean area. They were accompanied by the Secretary of the Board.

The Council continued to maintain, with support from the Department of Technical Co-operation and other sources, their Laboratories in the Gambia, the Infantile Malnutrition Research Unit in Uganda, and the Tropical Metabolism and Epidemiological Research Units in Jamaica.

Following an invitation from the New Zealand Medical Research Council, the Secretary visited New Zealand in April 1963 for the purpose of advising on the organization of medical research in that country.

In addition to the Annual Report for 1961–62 and a reprint of the articles in the Report three new Council publications appeared during the year under review. In the Special Report Series there was one new report (S.R.S. No. 302): *Tables of representative values of foods commonly used in tropical countries.* This is an extensively revised and expanded edition of S.R.S. No. 253, which was published in 1945 as a handbook for use in colonial territories. In the Monitoring Report Series two further reports (Nos. 5 and 6) were issued on levels of strontium-90 in human bone in the United Kingdom. These reports were published for the Council by H.M. Stationery Office.

Three Council committees produced reports during the year. These were: ' Treatment of acute leukaemia in adults: comparison of steroid therapy at high and low dosage in conjunction with 6-mercaptopurine ' (Working Party on the Evaluation of Different Methods of Therapy in Leukaemia—*Brit. med. J.* 1963, **1**, 7); ' A standard method of estimating 17-oxosteroids and total 17-oxogenic steroids ' (an interim recommendation by the Committee on Clinical Endocrinology—*Lancet* 1963, **2**, 1415); and ' Design and ventilation of operating-room suites for control of infection and for comfort ' (Control of Cross-Infection Committee—*Lancet* 1962, **2**, 945). A report was also published on the treatment of phenylketonuria—the findings of a conference held to discuss the practical problems of detection, early treatment and subsequent care of children suffering from the disease (*Brit. med. J.* 1963, **1**, 1961).

As has been mentioned earlier in the report, publications by workers supported by the Council are now too numerous to be listed in this volume. These publications reached a total of 4730 during the year under review and a complete list may be obtained from the Librarian at the National Institute for Medical Research, The Ridgeway, London, N.W.7.

PATENTS

All rights in the seven patent applications arising from Council-supported work during the year have been assigned to the National Research Development Corporation.

A programme of collaborative research to further the development of equipment for monitoring information from patients (for example, for the automatic recording of temperatures) has been initiated jointly by the Council, the Corporation and a commercial firm.

At the end of September 1962 a total of 177 patent applications had been assigned to the Corporation; of these 87 were on its active register.

FINANCE

The Council's detailed accounts for the year ending 31 March 1963 are shown in Appendix II (pp. 240–1). Details of the total expenditure may be

summarized as follows (the figures for the previous year being given for comparison):

	1962–63	*1961–62*
	£	£
Recurrent expenses	6,242,664	5,488,171
New buildings	417,458	713,411
Grants for special apparatus	82,879	40,130
	6,743,001	6,241,712

The proportional allocation under the main heads of expenditure for recurrent expenses was as follows:

	Per cent
Administration	5·9
Central expenses	1·1
National Institute for Medical Research	15·7
Research units and external staff	56·1
Research groups	0·9
Special grants	8·3
Temporary research grants and training awards	12·0
	100·0

The Parliamentary grant-in-aid for the year was £5,884,000, of which £5,859,000 was drawn. This was augmented by contributions for special purposes from Government departments and other official sources (£588,495), by special grants from other bodies (£140,293) and by bequests, donations etc. (£28,855). Further details of these contributions will be found in Appendices II and III (pp. 240–2).

Benefactions

Under the terms of their Charter the Council are empowered to receive and administer private funds or properties entrusted to them by grant, gift or bequest, either for the general purposes of research or for research on specific subjects. Further valuable additions to the Council's resources became available in this way during the year and for these they wish to make their grateful acknowledgement.

The sums received during the year covered by this report are acknowledged in Appendix IV (pp. 243–4).

ACCOMMODATION

Clinical Research Centre

Planning has continued for the Clinical Research Centre to be built at Northwick Park in collaboration with the North-West Metropolitan Regional Hospital Board. It is hoped to seek tenders for the work during the course of the financial year 1964–65.

Existing research establishments

Building projects completed during the year include an extension to the main building of the Radiobiological Research Unit at Harwell and a new library/

meeting room and workshop for the Rheumatism Research Unit at Taplow. Work was also completed on a laboratory at West Park Hospital, Epsom, for the clinical wing of the Neuropsychiatric Research Unit, and further extensive alterations are in progress for the conversion of accommodation at the same hospital to facilitate the unit's clinical work. Work is in progress on new buildings for the Clinical Effects of Radiation Research Unit in Edinburgh, the Toxicology Research Unit at the Council's Laboratories at Carshalton and the Pneumoconiosis Research Unit in South Wales. Plans are being prepared to provide new accommodation for certain sections of the Council's Cyclotron Unit and Experimental Radiopathology Research Unit at Hammersmith Hospital, since some of their present accommodation is due for demolition under the hospital's development proposals. Alterations are being carried out at the London School of Hygiene and Tropical Medicine in adapting laboratories for the Environmental Physiology Research Unit on its transfer from Oxford. Alterations to existing accommodation are being planned for the Clinical Endocrinology Research Unit in Edinburgh and for the Atheroma Research Unit in Glasgow.

On behalf of the Ministry of Health an extension is being made to the buildings of the Blood Products Laboratory, Elstree, and, again in conjunction with the Ministry, preliminary plans are being prepared for a new laboratory for work on low background radioactivity to be built at the Royal Marsden Hospital, Belmont, Surrey, for the Radiological Protection Service.

Agreement was reached with the Ministry of Health for the purchase of land and buildings now occupied by the Council's Laboratories at Carshalton; and buildings formerly occupied by the Betatron Research Unit (which has now been taken over by the Manchester Regional Hospital Board) have been sold to the Ministry.

Approval has been given for the building of a small extension to the existing laboratories of the Tropical Metabolism Research Unit in Jamaica. At Tanga Hospital, Tanganyika, a laboratory has been built for the Bilharzia Chemotherapy Centre, which is under the direction of Dr. A. Davis, a member of the Council's External Staff; this project is being financed from funds provided by the World Health Organization.

PERSONNEL

Obituary

The Council learned with much regret of the death of two distinguished former members of their body: Sir Wilson Jameson, G.B.E., K.C.B., Chief Medical Officer of the Ministry of Health from 1940 to 1950 and a member of Council from 1940 to 1944, who was a most valued adviser and friend and who died on 18 October 1962; and Dr. David Keilin, F.R.S., a most distinguished scientist—formerly Quick Professor of Biology in the University of Cambridge and a member of Council from 1942 to 1946—who died on 27 February 1963.

The deaths also occurred of two former members of the Council's staff, whose service had been unbroken since the days of the Medical Research Committee—Dr. Thomas Bedford, O.B.E., and Mr. H. C. Weston, O.B.E. The Council wish to pay tribute to the distinguished pioneer work they undertook in their respective fields.

The Council also noted with regret the death of Professor E. J. King, who had for long been closely concerned with the furtherance of work under their auspices, particularly in the field of industrial pulmonary diseases and toxicology.

Honours

The Council noted with much pleasure the following honours bestowed by Her Majesty the Queen during the year:

D.B.E.	Professor Honor Fell (Director, Strangeways Research Laboratory, Cambridge, and Senior Biological Adviser to Biophysics Research Unit).
Knight Bachelor ..	Dr. J. W. Cook (Honorary Director, Carcinogenic Substances Research Unit).
C.B.E.	Professor W. S. Feldberg (National Institute for Medical Research)
	Professor L. N. Pyrah (Honorary Director, Metabolic Disturbances in Surgery Research Unit)
	Dr. M. F. Perutz (Chairman of Board, Laboratory of Molecular Biology)
	Dr. J. C. Kendrew (Laboratory of Molecular Biology)
	Dr. F. Sanger (Laboratory of Molecular Biology)
	Professor M. H. F. Wilkins (Deputy Director, Biophysics Research Unit).
O.B.E.	Dr. R. E. Hope-Simpson (External Scientific Staff).

The following three members of the Council's staff were elected to the Fellowship of the Royal Society:

Dr. J. H. Humphrey (Deputy Director, National Institute for Medical Research)

Dr. J. F. Loutit (Director, Radiobiological Research Unit)

Dr. J. A. Fraser Roberts (Director, Clinical Genetics Research Unit).

The Council heard with pleasure also of the following honours gained by members of their staff: Professor W. S. Feldberg (National Institute for Medical Research), the Baly Medal of the Royal College of Physicians of London for his distinguished physiological work; Dr. I. A. McGregor (Director, Medical Research Council Laboratories, Gambia), the Chalmers Medal of the Royal Society of Tropical Medicine and Hygiene; Dr. E. A. Carmichael (Director of the former Neurological Research Unit and at present a Council grant-holder), a Medal awarded by Graz University on the centenary of its Medical Faculty; and Dr. N. A. Mitchison (National Institute for Medical Research), the Scientific Medal of the Zoological Society of London (jointly with Dr. J. W. L. Beament).

Honour was also brought to the Council by the re-election of Dr. J. O. Irwin (Statistical Research Unit) as President of the Royal Statistical Society; the election of Dr. J. S. Weiner (Director, Environmental Physiology Research Unit) as President of the Royal Anthropological Institute; and the election of Mr. W. J. Perkins (National Institute for Medical Research) as President of the International Federation of Medical Electronics.

Appointments

The new members of Council appointed from the beginning of the period under review were Professor G. M. Bull, Professor A. Neuberger, F.R.S., and Professor M. M. Swann, F.R.S.

Resignations and retirements

At the end of the year Professor A. L. Hodgkin, F.R.S., and Professor Milnes Walker retired on the completion of their term of service as Council members, being succeeded by Professor W. D. M. Paton, F.R.S., and Professor Hedley Atkins. The Council noted with much pleasure the subsequent award to Professor Hodgkin of the 1963 Nobel Prize for Medicine, jointly with Professor A. F. Huxley and Sir John Eccles, for investigations on the transmission of nerve impulses.

Sir Hugh Linstead, O.B.E., M.P., who also completed a four-year term of service on the Council, was reappointed as the House of Commons member.

Two new Assessors were appointed to the Council: Sir Keith Murray, K.C.B., was succeeded by Sir John Wolfenden, C.B.E., as the University Grants Committee Assessor, and shortly after the end of the period under review Professor Sir Lindor Brown, F.R.S., was replaced by Professor A. A. Miles, F.R.S., as the Royal Society Assessor.

The Council wish to pay special tribute on the retirement of Dr. Donald Hunter, C.B.E. Dr. Hunter has for long been closely associated with the Council's activities and since 1943 has been Director (part-time) of the Department for Research in Industrial Medicine at the London Hospital. Dr. Hunter has played a unique role in this field and the Council are happy that he is still able to make his special knowledge available to them in an honorary capacity.

The Council would also like to acknowledge, on the occasion of his retirement from the directorship of the Dunn Nutritional Laboratory, which he has held since 1927, the contribution of Dr. L. J. Harris to the study of nutrition. His own research apart, Dr. Harris has rendered yeoman service to the organization of knowledge in this field on both a national and an international scale.

Among the senior staff who left the Council's service during the year were the following: Dr. A. G. Baikie (Clinical Effects of Radiation Research Unit) on his appointment to the staff of the University of Melbourne; Dr. J. B. Brown (Clinical Endocrinology Research Unit) to a post in the Professorial Obstetric and Gynaecological Unit, University of Melbourne; Dr. Alastair Heron (Unit for Research on Occupational Aspects of Ageing) to the directorship of the Rhodes-Livingstone Institute, University College of Rhodesia and Nyasaland; Dr. I. T. T. Higgins (Epidemiological Research Unit, South Wales) to the Chair in the Epidemiology of Chronic Diseases, University of Pittsburgh, U.S.A.; Dr. K. B. Taylor (Gastroenterology Research Unit) to the directorship of the Division of Gastroenterology, Stanford University Medical School, U.S.A.; and Dr. N. P. L. Wildy (Experimental Virus Research Unit) to the Chair of Virology and Bacteriology, University of Birmingham.

Staff numbers

The number of staff employed by the Council at the end of the period covered by this report was 2931. This figure was made up of 788 scientific staff (including 45 part-time), of whom 245 were medically qualified, 1167 technical staff

(including 15 part-time), 589 administrative and clerical staff (including 60 part-time) and 387 maintenance staff (including 114 part-time). In addition, 116 locally recruited staff were employed at the Council's establishments in the Gambia and in Uganda.

ADVISERS AND ASSESSORS

The Council wish to express their gratitude to all the medical and other scientists, in addition to members of their own staff, who have assisted them with advice, whether in an individual capacity or as members of special committees.

The Secretaries of the Department of Scientific and Industrial Research and of the Agricultural Research Council, the Chief Medical Officers of the Ministry of Health and the Scottish Home and Health Department, the Chairman of the University Grants Committee and the Chairman of the Clinical Research Board are Assessors, *ex officiis*, to the Council. A further Assessor is nominated by the Royal Society on the Council's invitation. Sir George Godber (Ministry of Health), Sir Kenneth Cowan (Scottish Home and Health Department), Sir Lindor Brown (Royal Society) and Professor E. J. Wayne (Clinical Research Board) attended meetings in their capacity as Assessors. The Secretaries of the Department of Scientific and Industrial Research and of the Agricultural Research Council and the Chairman of the University Grants Committee have received papers on a reciprocal basis.

SHAWCROSS
Chairman of the Medical Research Council

HAROLD HIMSWORTH
Secretary of the Council
20 Park Crescent
London, W.1.

20 March 1964

Responsibility in Investigations on Human Subjects

STATEMENT BY THE MEDICAL RESEARCH COUNCIL

During the last fifty years, medical knowledge has advanced more rapidly than at any other period in its history. New understandings, new treatments, new diagnostic procedures and new methods of prevention have been, and are being, introduced at an ever-increasing rate; and if the benefits that are now becoming possible are to be gained, these developments must continue.

Undoubtedly the new era in medicine upon which we have now entered is largely due to the marriage of the methods of science with the traditional methods of medicine. Until the turn of the century, the advancement of clinical knowledge was in general confined to that which could be gained by observation, and means for the analysis in depth of the phenomena of health and disease were seldom available. Now, however, procedures that can safely, and conscientiously, be applied to both sick and healthy human beings are being devised in profusion, with the result that certainty and understanding in medicine are increasing apace.

Yet these innovations have brought their own problems to the clinical investigator. In the past, the introduction of new treatments or investigations was infrequent and only rarely did they go beyond a marginal variation on established practice. Today, far-ranging new procedures are commonplace and such are their potentialities that their employment is no negligible consideration. As a result, investigators are frequently faced with ethical and sometimes even legal problems of great difficulty. It is in the hope of giving some guidance in this difficult matter that the Medical Research Council issue this statement.

A distinction may legitimately be drawn between procedures undertaken as part of patient-care which are intended to contribute to the benefit of the individual patient, by treatment, prevention or assessment, and those procedures which are undertaken either on patients or on healthy subjects solely for the purpose of contributing to medical knowledge and are not themselves designed to benefit the particular individual on whom they are performed. The former fall within the ambit of patient-care and are governed by the ordinary rules of professional conduct in medicine; the latter fall within the ambit of investigations on volunteers.

Important considerations flow from this distinction.

Procedures contributing to the benefit of the individual

In the case of procedures directly connected with the management of the condition in the particular individual, the relationship is essentially that between doctor and patient. Implicit in this relationship is the willingness on the part of the subject to be guided by the judgment of his medical attendant. Provided, therefore, that the medical attendant is satisfied that there are reasonable grounds for believing that a particular new procedure will contribute to the benefit of that particular patient, either by treatment, prevention or increased understanding of his case, he may assume the patient's consent to the same

extent as he would were the procedure entirely established practice. It is axiomatic that no two patients are alike and that the medical attendant must be at liberty to vary his procedures according to his judgment of what is in his patients' best interests. The question of novelty is only relevant to the extent that in reaching a decision to use a novel procedure the doctor, being unable to fortify his judgment by previous experience, must exercise special care. That it is both considerate and prudent to obtain the patient's agreement before using a novel procedure is no more than a requirement of good medical practice.

The second important consideration that follows from this distinction is that it is clearly within the competence of a parent or guardian of a child to give permission for procedures intended to benefit that child when he is not old or intelligent enough to be able himself to give a valid consent.

A category of investigation that has occasionally raised questions in the minds of investigators is that in which a new preventive, such as a vaccine, is tried. Necessarily, preventives are given to people who are not, at the moment, suffering from the relevant illness. But the ethical and legal considerations are the same as those that govern the introduction of a new treatment. The intention is to benefit an individual by protecting him against a future hazard; and it is a matter of professional judgment whether the procedure in question offers a better chance of doing so than previously existing measures.

In general, therefore, the propriety of procedures intended to benefit the individual—whether these are directed to treatment, to prevention or to assessment—are determined by the same considerations as govern the care of patients. At the frontiers of knowledge, however, where not only are many procedures novel but their value in the particular instance may be debatable, it is wise, if any doubt exists, to obtain the opinion of experienced colleagues on the desirability of the projected procedure.

Control subjects in investigations of treatment or prevention

Over recent years, the development of treatment and prevention has been greatly advanced by the method of the controlled clinical trial. Instead of waiting, as in the past, on the slow accumulation of general experience to determine the relative advantages and disadvantages of any particular measure, it is now often possible to put the question to the test under conditions which will not only yield a speedy and more precise answer, but also limit the risk of untoward effects remaining undetected. Such trials are, however, only feasible when it is possible to compare suitable groups of patients and only permissible when there is a genuine doubt within the profession as to which of two treatments or preventive regimes is the better. In these circumstances it is justifiable to give to a proportion of the patients the novel procedure on the understanding that the remainder receive the procedure previously accepted as the best. In the case when no effective treatment has previously been devised then the situation should be fully explained to the participants and their true consent obtained.

Such controlled trials may raise ethical points which may be of some difficulty. In general, the patients participating in them should be told frankly that two different procedures are being assessed and their co-operation invited. Occasionally, however, to do so is contra-indicated. For example, to awaken patients with a possibly fatal illness to the existence of such doubts about

effective treatment may not always be in their best interest; or suspicion may have arisen as to whether a particular treatment has any effect apart from suggestion and it may be necessary to introduce a placebo into part of the trial to determine this. Because of these and similar difficulties, it is the firm opinion of the Council that controlled clinical trials should always be planned and supervised by a group of investigators and never by an individual alone. It goes without question that any doctor taking part in such a collective controlled trial is under an obligation to withdraw a patient from the trial, and to institute any treatment he considers necessary, should this, in his personal opinion, be in the better interests of his patient.

Procedures not of direct benefit to the individual

The preceding considerations cover the majority of clinical investigations. There remains, however, a large and important field of investigations on human subjects which aims to provide normal values and their variation so that abnormal values can be recognized. This involves both ill persons and ' healthy ' persons, whether the latter are entirely healthy or patients suffering from a condition that has no relevance to the investigation. In regard to persons with a particular illness, such as metabolic defect, it may be necessary to know the range of abnormality compatible with the activities of normal life or the reaction of such persons to some change in circumstances such as an alteration in diet. Similarly it may be necessary to have a clear understanding of the range of a normal function and its reaction to changes in circumstances in entirely healthy persons. The common feature of this type of investigation is that it is of no direct benefit to the particular individual and that, in consequence, if he is to submit to it he must volunteer in the full sense of the word.

It should be clearly understood that the possibility or probability that a particular investigation will be of benefit to humanity or to posterity would afford no defence in the event of legal proceedings. The individual has rights that the law protects and nobody can infringe those rights for the public good. In investigations of this type it is, therefore, always necessary to ensure that the true consent of the subject is explicitly obtained.

By true consent is meant consent freely given with proper understanding of the nature and consequences of what is proposed. Assumed consent or consent obtained by undue influence is valueless and, in this latter respect, particular care is necessary when the volunteer stands in special relationship to the investigator as in the case of a patient to his doctor, or a student to his teacher.

The need for obtaining evidence of consent in this type of investigation has been generally recognized, but there are some misunderstandings as to what constitutes such evidence. In general, the investigator should obtain the consent himself in the presence of another person. Written consent unaccompanied by other evidence that an explanation has been given, understood and accepted is of little value.

The situation in respect of minors and mentally subnormal or mentally disordered persons is of particular difficulty. In the strict view of the law parents and guardians of minors cannot give consent on their behalf to any procedures which are of no particular benefit to them and which may carry some risk of harm. Whilst English law does not fix any arbitrary age in this context,

it may safely be assumed that the Courts will not regard a child of 12 years or under (or 14 years or under for boys in Scotland) as having the capacity to consent to any procedure which may involve him in an injury. Above this age the reality of any purported consent which may have been obtained is a question of fact and as with an adult the evidence would, if necessary, have to show that irrespective of age the person concerned fully understood the implications to himself of the procedures to which he was consenting.

In the case of those who are mentally subnormal or mentally disordered the reality of the consent given will fall to be judged by similar criteria to those which apply to the making of a will, contracting a marriage or otherwise taking decisions which have legal force as well as moral and social implications. When true consent in this sense cannot be obtained, procedures which are of no direct benefit and which might carry a risk of harm to the subject should not be undertaken.

Even when true consent has been given by a minor or a mentally subnormal or mentally disordered person, considerations of ethics and prudence still require that, if possible, the assent of parents or guardians or relatives, as the case may be, should be obtained.

Investigations that are of no direct benefit to the individual require, therefore, that his true consent to them shall be explicitly obtained. After adequate explanation, the consent of an adult of sound mind and understanding can be relied upon to be true consent. In the case of children and young persons the question whether purported consent was true consent would in each case depend upon facts such as the age, intelligence, situation and character of the subject and the nature of the investigation. When the subject is below the age of 12 years, information requiring the performance of any procedure involving his body would need to be obtained incidentally to and without altering the nature of a procedure intended for his individual benefit.

Professional discipline

All who have been concerned with medical research are aware of the impossibility of formulating any detailed code of rules which will ensure that irreproachability of practice which alone will suffice where investigations on human beings are concerned. The law lays down a minimum code in matters of professional negligence and the doctrine of assault. But this is not enough. Owing to the special relationship of trust that exists between a patient and his doctor, most patients will consent to any proposal that is made. Further, the considerations involved in a novel procedure are nearly always so technical as to prevent their being adequately understood by one who is not himself an expert. It must, therefore, be frankly recognized that, for practical purposes, an inescapable moral responsibility rests with the doctor concerned for determining what investigations are, or are not, proposed to a particular patient or volunteer. Nevertheless, moral codes are formulated by man and if, in the ever-changing circumstances of medical advance, their relevance is to be maintained, it is to the profession itself that we must look, and in particular to the heads of departments, the specialized Societies and the editors of medical and scientific journals.

In the opinion of the Council, the head of a department where investigations on human subjects take place has an inescapable responsibility for ensuring that practice by those under his direction is irreproachable.

In the same way the Council feel that, as a matter of policy, bodies like themselves that support medical research should do everything in their power to ensure that the practice of all workers whom they support shall be unexceptionable and known to be so.

So specialized has medical knowledge now become that the profession in general can rarely deal adequately with individual problems. In regard to any particular type of investigation, only a small group of experienced men who have specialized in this branch of knowledge are likely to be competent to pass an opinion on the justification for undertaking any particular procedure. But in every branch of medicine specialized scientific societies exist. It is upon these that the profession in general must mainly rely for the creation and maintenance of that body of precedents which shall guide individual investigators in case of doubt, and for the critical discussion of the communications presented to them on which the formation of the necessary climate of opinion depends.

Finally, it is the Council's opinion that any account of investigations on human subjects should make clear that the appropriate requirements have been fulfilled and, further, that no paper should be accepted for publication if there are any doubts that such is the case.

The progress of medical knowledge has depended, and will continue to depend, in no small measure upon the confidence which the public has in those who carry out investigations on human subjects, be these healthy or sick. Only in so far as it is known that such investigations are submitted to the highest ethical scrutiny and self-discipline will this confidence be maintained. Mistaken, or misunderstood, investigations could do incalculable harm to medical progress. It is our collective duty as a profession to see that this does not happen and so to continue to deserve the confidence that we now enjoy.

Some Aspects of Medical Research

The subjects of these articles have been selected for review out of the large number of research studies which the Council now supports. In order to present a reasonably balanced picture of the research on a particular subject it has frequently been necessary to refer to contributions made by workers unconnected with the Council.

THE THEORETICAL BASIS OF ORGAN TRANSPLANTATION

Public interest in the surgical transplantation of various organs has been aroused as the result of some encouraging successes which have been achieved in kidney transplantation. There have also been disappointing failures and the procedure is still far from simple. In this article some of the theoretical principles involved are discussed. Transplanted organs are classified as *autotransplants*, *homotransplants* or *heterotransplants* according to whether they are obtained from the recipient himself, from another individual of the same species, or from an individual of a different species. In surgery, autotransplantation of a kidney is used occasionally as a technical manoeuvre in patients with high blood pressure resulting from narrowing of the renal artery; a few attempts have been made to transplant animal kidneys to man, but interest in organ transplantation at the present time centres on the possibility of using homotransplants obtained either from living donors or from cadavers. So far, most of the work has been concerned with homotransplantation of the kidney in selected patients with chronic renal failure, but there have been a few unsuccessful attempts to transplant the liver and the lung, and transplantation of the heart will certainly be attempted soon.

When an organ is transplanted its blood supply is re-established by connecting the artery and vein of the transplant to appropriate vessels in the recipient. This takes time, and the first necessary condition for successful transplantation is that the organ in question must be able to survive the period during which it is without a blood supply. The kidney can tolerate complete ischaemia for up to an hour, especially if it is cooled; after one to three hours function is likely to be impaired for some days or weeks, and as the period of ischaemia is increased the chances of its recovery diminish. As it is not practicable at the present time to establish nerve connections between the transplant and the recipient, the second condition of success is that the organ must be capable of functioning adequately in the absence of nervous control. Even when these conditions are fulfilled, however, homotransplants do not as a general rule survive for more than a few weeks, and they are sometimes destroyed even more rapidly.

The immunological problem

It is now clear that the destruction of a homotransplant is an immunological phenomenon. The first evidence of this came from the observation of Gibson and Medawar (1943) that when a patient received two successive homotransplants of skin from the same donor, the second was destroyed more quickly than the first, and the occurrence of this ' second-set phenomenon ' has since been confirmed by many investigators in a variety of tissues and in many different species. Secondly, it was shown by Mitchison (1954) in experiments with mice that the state of increased reactivity evoked by a homotransplant could be

transferred passively to another mouse of the same genetic constitution as the recipient by injecting it with a suspension of cells prepared from lymph nodes adjacent to the site of the graft on the first mouse. Finally, Brent, Brown and Medawar (1958) found that in one species, the guinea pig, lymphoid cells from the recipient of a homotransplant evoked an inflammatory reaction when injected into the deeper layer of the skin of the donor, and lymphoid cells from the donor (or even extracts obtained from them) evoked a similar reaction when injected into the recipient.

In one type of immunological reaction the injection of a substance (usually a protein or a polysaccharide) into an animal is followed by the appearance in the serum of a substance known as an antibody. The presence of antibody in the serum can be detected by its ability to react with material of the type injected (known as the antigen) in laboratory tests. There are, however, many immunological reactions which are mediated by cells in the absence of serological antibodies, and this kind of immunity appears to be of crucial importance in the rejection of homotransplants of normal tissues.

The particular antigens present in a homotransplant which evoke the reaction that eventually causes its rejection are determined by the genetic make-up of the donor. The antigens appear to be present in all cells that have a nucleus, and perhaps also in mature red blood cells, which in mammals have no nucleus. The chemical nature of these antigens has not been precisely determined but it is now widely believed that they are lipoproteins.

Exceptions to the rule that homotransplants are destroyed

Organ homotransplants may survive for long periods, or even permanently, as a result of compatibility of donor and recipient, or alternatively because the recipient's capacity to react immunologically against the transplant has been reduced as a result of disease or of some therapeutic procedure.

Complete compatibility occurs when there are no antigens in the transplant which are lacking in the recipient. This happens when donor and recipient are identical twins or, in experimental animals, when they are both members of a highly inbred strain which has been maintained by brother–sister mating for many generations; it may theoretically occur sometimes when the donor and recipient are drawn from a mixed population, but this must be extremely rare in the species which have been studied, including man.

Procedures which reduce the recipient's capacity for immunological response include exposure to whole-body X-irradiation and treatment with a variety of drugs. The drugs known as alkylating agents produce effects very similar to those of irradiation; other drugs, termed antimetabolites, interfere with cellular metabolism by blocking the synthesis of some essential substance and thus interfere with normal immunological processes. A further procedure, which has no direct clinical application but is of great theoretical importance, is to inject an animal during embryonic life or immediately after birth with living cells from an older animal of the same species. Under certain conditions the recipient throughout its life will retain specific tolerance of grafts from the donor of these cells and will accept such grafts permanently while having the capacity to reject grafts from other donors.

This phenomenon of specific immunological tolerance was predicted by Burnet and Fenner (1949) as a consequence of a hypothesis they put forward to account

for the fact that the immunologically active cells of an individual do not normally react against the constituents of his body. An example of naturally developing specific immunological tolerance occurs when non-identical twins interchange blood-forming tissue during foetal life and consequently go on producing red blood cells of two different kinds throughout their life. The explanation of this state of affairs, which is common in cattle and occurs very occasionally in man, was established as long ago as 1945 by Owen; the Burnet–Fenner prediction was first confirmed experimentally by Billingham, Brent and Medawar (1953, 1956).

It was at first thought that to produce tolerance the initial injection of cells had to be made during embryonic life, but it was soon found that in rats (Woodruff and Simpson, 1955) and mice (Billingham and Brent, 1956) injection shortly after birth was also effective in certain circumstances. More recently it has been found possible to induce a similar state of specific tolerance in adult animals by first exposing them to X-irradiation and then injecting cells (Michie and Woodruff, 1962) or, under certain conditions, by injecting cells or cell extracts without prior irradiation (Shapiro *et al.*, 1961; Brent and Gowland, 1962; Medawar, 1963).

A tolerant animal has lost the capacity to react to a particular set of antigens, and the maintenance of the tolerant state appears to depend on the continued presence of these antigens. Another phenomenon, which appears to be related to, but distinct from, specific immunological tolerance, is known as 'enhancement'. In this condition the survival of a homotransplant is prolonged following the injection of tissue which has been killed, for example by being frozen and then dried from the frozen state, or by chemical treatment. This material evokes the formation of serum antibody, which, somewhat paradoxically, may exert a protective effect on a subsequent transplant of living tissue, possibly by interfering with the liberation of antigenic material from the transplant. Enhancement was discovered in experiments with tumours (Kaliss, 1952), and so far attempts to produce this phenomenon in transplants of normal tissue by injection of freeze-dried material have resulted in at most a few days' increase in survival time; it remains an open question, however, whether or not 'enhancing' antibody contributes to the long survival of human kidney homotransplants which sometimes occurs (Woodruff *et al.*, 1963).

Clinical work

The possibility of avoiding the immunological barrier to organ transplantation by using an identical twin as donor was first exploited clinically by Merrill and his colleagues (1956) in the United States, and since then at least 25 patients suffering from irreversible renal failure have been treated successfully in this way. One limitation, however, apart from the comparative rarity of identical twins (1 in 300 births), is that both twins may suffer from the same disease. A further limitation arises, whether or not the donor is a twin, from the fact that if the patient is suffering from glomerulonephritis, a condition affecting the filtering organs of the kidney, this may develop subsequently in the transplant even though the donor himself is unaffected.

When an organ is transplanted from a donor other than an identical twin the usual practice at the present time is to try to promote the survival of the transplant by irradiating the recipient or by administering one of the drugs mentioned previously. These procedures are hazardous, one reason being they that reduce

the patient's resistance to infection as well as his capacity to reject a homotransplant. If proper precautions are taken, however, the danger can be appreciably reduced, and although the failure rate is high several patients are alive and well more than a year after a kidney transplantation, and one, who received a kidney from a non-identical twin, is alive and well after more than three years (Hamburger *et al.*, 1962; Küss *et al.*, 1962; Murray *et al.*, 1962; Shackman, Dempster and Wrong, 1963; Woodruff *et al.*, 1963).

Some of these patients are still receiving antimetabolite drugs in small dosage, but in others treatment has ceased. One possible explanation of the continued survival of these transplants in the absence of treatment to suppress the immunological response is that a state of specific tolerance has developed; it has been suggested alternatively that it may be due to the presence of enhancing antibody or to some form of adaptive change in the transplant itself. It is difficult to distinguish with certainty between these possibilities in man, though it should be possible to do so in experimental animals.

It appears from a study of the results of kidney transplantation in man that different patients react very differently to their transplants even when there has been little or no difference in their treatment. This can best be explained on the basis of differences in donor–recipient compatibility, and it appears that when there is a relatively high degree of compatibility it is possible even with the methods currently available to obtain quite long survival of an organ transplant. There would seem therefore to be two possible lines of future advance: the development of methods for selecting compatible donors, and an improvement in the methods used to diminish the recipient's capacity to react against his transplant.

In the absence of means of storing organs in a viable state outside the body for more than an hour or two there is often little or no choice in the matter of donor. It would nevertheless be helpful to know in advance whether or not a given donor was sufficiently compatible with the recipient to offer a reasonable prospect of his providing a long-surviving graft with the available methods of treatment: if the problem of storage is solved donor selection may become of great importance.

At present it is customary to carry out detailed blood grouping (that is, red blood cell grouping) of prospective donors and recipients prior to organ transplantation. Most authorities insist on compatibility in respect of the ABO blood group system before carrying out transplantation and, where there is a choice of donor, selection is sometimes based on compatibility in respect of the various other systems commonly investigated—Rh, MN, S, P, Kell, Duffy, Lewis and Lutheran (Woodruff *et al.*, 1963). This seems reasonable in our present state of ignorance, but the significance of red cell compatibility in relation to organ transplantation has not yet been convincingly established; it may well be quite important, but the one established fact is that compatibility of donor and recipient in respect of all the red cell systems listed above is not sufficient to ensure the survival of a homotransplant in an unrelated recipient (Woodruff and Allan, 1953).

In France, tests based on the grouping of white blood cells are also used in selecting donors for kidney transplants (Hamburger *et al.*, 1962) and there is some evidence that these are of value, though this is as yet not certain.

A test of quite a different kind has been suggested by Brent and Medawar (1963). It consists in separating the lymphocytes from a sample of the patient's blood and injecting these into the skin of all available donors. Lymphocytes are what are termed immunologically competent cells, and are able to react against the skin of the individuals into whom they are injected, causing redness and swelling. The intensity of the resulting reaction in each individual tested should in theory provide a measure of the reaction which an organ or tissue obtained from him would evoke if transplanted into the patient from whom the lymphocytes were obtained. Brent and Medawar found that in guinea pigs there is good correlation between the results of this test and the duration of survival of homotransplants of skin, though the value of the test in man is not yet established; if it proves successful it will of course be applicable only to living donors.

It would seem at first sight desirable to make a small test transplant of skin from a prospective donor before hazarding a whole organ, but this would carry the risk of immunizing the recipient against the donor and thus prejudicing the survival of a subsequent transplant. An alternative is to improve the methods used to diminish the patient's capacity to react to a homotransplant. Here the most promising approach appears to be to inject cells or cell extracts from the donor into the patient, either before or at the same time as the transplantation, under conditions designed to favour the development of specific immunological tolerance (p. 27) as against immunity. Much work along these lines is proceeding in experimental animals, but there are as yet no reports of the use of such procedures in man.

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It has been known for about 60 years that exposure to ionizing radiations can produce microscopically visible damage to chromosomes. Recognition of this fact followed the study of irradiated plant, amphibian and mammalian cells. About 40 years ago it was found that radiations produced two distinct forms of damage, one now known as the primary or physiological effect and the other as the secondary or aberration effect.

In the normal course of events the chromosomes are split longitudinally into two chromatids, which then become separated and move towards opposite poles of the cell, ultimately to constitute the chromosomes of the two daughter cells. However, cells that are irradiated during the later stages of cell division undergo temporary physico-chemical changes in the chromosomes which make them appear to be sticky. The 'stickiness' interferes with the separation of the chromatids, and then division may break down and the cell die. This is the primary effect of irradiation.

The secondary effect may occur when cells are irradiated before the commencement of division or in its early stages. In these circumstances there may be a temporary delay in the completion of the cycle in cells that have started to divide, though stickiness of the chromosomes is not seen; but whether division has started or not at the time of radiation exposure, evidence can often be found of chromosome aberrations if the cells are examined before the completion of division, or the daughter cells after the completion of division.

These aberrations are rearrangements of the material of the chromosomes, or that of their constituent chromatids, which can follow their breakage at the time of irradiation, the broken ends joining in such a way as to produce abnormal configurations. In some instances these abnormalities may be so gross as to lead to the death of the cell when it attempts to complete its division, while in others the cell may successfully divide several times before death occurs. With yet other types of rearrangement there is no theoretical reason why the ability of the cell to complete division should be impaired, but radiation-induced damage is obvious through the presence of one or more morphologically abnormal chromosomes. Much radiobiological research has been devoted to understanding the nature of chromosome rearrangements, the mechanism by which they become established, and the relationships between their numbers and the conditions of radiation exposure, particularly the total dose of radiation and its rate of administration.

Human studies

The study of chromosome damage produced in man by exposure to radiation had to await the development of suitable techniques for the examination of human chromosomes. In 1956 Tjio and Levan in Sweden, using cells from cultures of human embryonic lung tissue, showed the chromosome number of man to be 46, and gave the first accurate description of the human chromosome complement or karyotype. Their findings were confirmed in the same year by Ford and Hamerton of the Council's Radiobiological Research Unit from studies on preparations of human testicular tissue made without an intervening period of culture. A major technical advance occurred in 1960, when a method was described by workers in the United States for the culture of white cells from

human blood which allowed adequate preparations to be made for the counting and analysis of chromosomes (Moorhead *et al.*, 1960). In the same year it was reported from the Council's Clinical Effects of Radiation Research Unit in Edinburgh that, with the blood culture technique, chromosome abnormalities could be detected in patients during and after X-ray treatment (Tough *et al.*, 1960).

Two years later the results were reported of a study of eight subjects who had been accidentally exposed in 1958 to a mixed beam of gamma rays and fast neutrons at the Oak Ridge National Laboratory in the United States. The estimated doses ranged from 23 rads to 365 rads, and the investigations of Bender and Gooch (1962a) showed that chromosome damage was still present some two-and-a-half years after the accident. The persistence of this damage was confirmed by the same workers in a further study three-and-a-half years after the accident (Bender and Gooch, 1963).

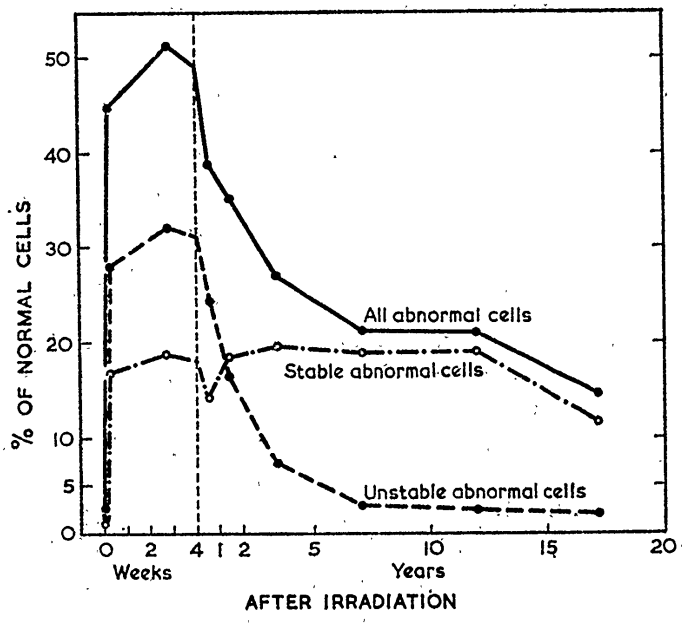

Figure 1

Changes in the proportions of abnormal cells in relation to normal cells after completion of X-ray treatment: data on 58 patients. From Buckton, Jacobs, Court Brown and Doll (1962).

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In 1962 a further report from the Clinical Effects of Radiation Research Unit provided evidence of the continued presence of detectable chromosome damage for up to 20 years after exposure (Buckton *et al.*, 1962)—see Fig. 1. This information was obtained from a study of 58 men who had had a single course of X-ray treatment to the spine for a form of spinal arthritis known as ankylosing spondylitis. An earlier investigation of subjects treated with X-rays for the disease had revealed that this form of irradiation was associated with an increased incidence of leukaemia (Court Brown and Doll, 1957).

Unstable chromosome aberrations

The chromosome aberrations that follow irradiation may be divided into two general types, those that are unstable and those that are stable. A typical example of a cell with unstable aberrations is shown in Plate I. Cells with

chromosomes showing more than one centromere (dicentric and tricentric chromosomes) or with ring chromosomes or acentric fragments, irrespective of whether other abnormalities are present, are regarded as unstable for two reasons. First, there are likely to be mechanical difficulties during division where dicentric, tricentric or ring chromosomes are involved, when the chromatids of these chromosomes come to separate. Sooner or later these difficulties are likely to lead to the breakdown of the process of division in the cell as a whole. Secondly, where there are fragments of chromosome material without a centromere, these will not become attached to the mitotic spindle, and whether or not they are incorporated in one or both daughter cells or in neither may well be a matter of chance. The loss of some or all of such material to a cell may eventually lead to its death. Observations on plant material suggest that unstable abnormalities are unlikely to persist for more than about three or four cell divisions. It is therefore of great interest to find that in man cells with unstable abnormalities may be identified in blood cultures many years after exposure to radiation. The most extensive evidence for this phenomenon so far comes from the study of patients irradiated for spondylitis, in whom unstable cells were detectable seven and more years after exposure.

Stable chromosome aberrations

A typical example of a cell with a stable type of aberration is shown in Plate II. The formation of such abnormal monocentric chromosomes is the result of the reciprocal exchange of material between chromosomes (' reciprocal translocations '), or of the inversion of the section of a chromosome between two breaks (' inversions '), or of the shifting of material from one arm of a chromosome to the other (' shifts '). Not all these abnormal chromosomes are visually detectable, and it is clear that rearrangements can produce chromosomes which mimic in their size and other features normal chromosomes of the karyotype. A clue to the presence of these chromosomes is obtained when, by analysis of the chromosome complement, it is found that there is a wrong distribution of the chromosomes between the various recognized sub-groups. From their possession of a single centromere it is assumed that abnormal monocentric chromosomes will not experience mechanical difficulties in division. This being so, there is no theoretical reason why cells possessing only stable forms of abnormality should not be perpetuated *ad infinitum* through the process of division. However, the possibility remains that at least some of these cells may be recognized as abnormal by the body and eliminated. In the patients irradiated for ankylosing spondylitis the proportion of cells with stable abnormalities found between 15 and 20 years after exposure did not significantly differ from the proportion observed in patients studied immediately after exposure; but it cannot be assumed from this that the proportion of these cells is unaffected by the lapse of time after exposure, for the patients treated in the earlier years had been exposed to higher doses than those treated more recently, and this may have concealed a tendency for the proportion of cells with stable abnormalities to fall.

Before the lines of development of this research are discussed, there are three important points to be made. First, studies have so far been made on subjects exposed to high or comparatively high doses of whole-body irradiation, as in the accident mentioned above, or on subjects who have had extensive partial-body

irradiation for therapeutic purposes. At present the work involved in chromosome counting and analysis is both tedious and time consuming, and it is not likely that the effects of low doses of radiation can be fully investigated until it becomes possible to use mechanized techniques. The second point is that at present only gross forms of chromosome damage are detectable; but it is safe to assume that the total amount of damage caused by a given dose of radiation is much greater than the amount which is at present microscopically visible. The total damage will range from such gross changes as those depicted in Plates I—III, through effects involving only small segments of chromosomes, down to effects confined to single genes. Thirdly, the cells dividing in blood cultures are lymphocytes, and damage observed in these must reflect damage inflicted on these cells or their precursors, wherever they were at the time of irradiation—in the circulation, in the lymphopoietic tissue (for example the lymphatic glands) or in any other tissue. The effect of radiation on other types of cell has yet to be properly investigated, although limited studies on bone marrow preparations have shown similar forms of damage.

Current research into radiation-induced chromosome damage in man is concerned with at least three major problems. The first is essentially practical, namely the feasibility of assessing the dose of radiation received by an individual by studying the chromosome damage. Secondly, there is a problem that is important to the rapidly expanding science of immunology—the problem of what information may be obtained on the behaviour and function of lymphocytes. Thirdly, there is the question of whether the observed damage can be related to the risks associated with radiation exposure and, in particular, to the induction of leukaemia.

Biological dosimetry

When accidents occur involving fissionable material, it is usual for there to be considerable difficulties in the physical evaluation of the radiation doses received by exposed persons. Such accidents are virtually instantaneous and totally unexpected, and these factors make the problem of dose measurement difficult. The question has been raised, therefore, of the extent to which chromosome damage may be a guide to the dose received. This topic is being studied by scientists at the Oak Ridge National Laboratory, and the inherent problems are also being considered in the Clinical Effects of Radiation Research Unit. It has been suggested that biological dosimetry may be feasible only under conditions of uniform whole-body exposure to a single dose of radiation (Bender and Gooch, 1962b). Furthermore, it is now becoming apparent that accurate dosimetry, if possible at all, can only follow a more comprehensive knowledge of how blood cells behave under conditions of tissue culture than has been so far possible. Progress is likely therefore to be slow in the study of chromosome damage as a measure of radiation dose.

The behaviour and function of lymphocytes

It has already been noted that the cells studied in blood cultures are lymphocytes, and that lymphocytes with unstable forms of damage may be identified many years after heavy exposure. It is possible through the study of the unstable forms of aberrant chromosomes to distinguish between cells that are likely to be in their first division following the original radiation damage (X_1 cells) and those that are most likely to be in at least their second division (X_2 cells). A simple example of this may be considered. The formation of a

dicentric or a ring chromosome must be accompanied by the formation of at least one acentric fragment. When a cell containing both a dicentric or ring chromosome and a fragment is seen in a blood culture, then there is a reasonable probability that this cell is in its first division since irradiation, and it may be regarded as an X_1 cell. If, however, only a dicentric or ring chromosome is present, then the cell has probably passed through at least one division for the acentric fragment to have been lost, and such a cell is regarded as an X_2 cell (see Plate III). There are certain possibilities of error in this classification, greater for X_1 than for X_2 cells; but allowing for these it may be assumed that the majority of X_1 cells are in their first division and the great majority of X_2 in at least their second division since exposure to radiation.

It has been recognized for some time that X_1 cells are found in the blood cultures of persons who have been exposed to heavy doses of radiation several years after exposure. Detailed investigations are being made of this phenomenon by the staff of the Council's Clinical Effects of Radiation and Statistical Research Units. First, it has been found that the proportion of X_1 cells in a culture is critically dependent on the time for which the cells are in culture, being very high among cells cultured for about 45 hours and falling sharply after longer periods. One obvious reason for the fall is that a proportion of unstable cells will die during division. It has also been found that if the cells are cultured for about 45 hours then no matter how long after irradiation a blood sample is taken, even if it is many years later, the majority of the unstable cells are X_1 cells. Thus although the total number of unstable cells falls with time after exposure, most of those that are recognized are probably dividing for the first time after the radiation damage was inflicted. These findings provide strong indirect evidence for the existence of a population of lymphocytes with a remarkable potential for survival in the body without division. This finding may well prove to be of considerable importance in immunology, for to the immunologist the existence of such a long-surviving lymphocyte population may provide a rational basis for the explanation of immunological ' memory '—that is, the ability of the body, having once been stimulated to make antibody against some foreign agent (for example by an infection or a prophylactic inoculation), to respond to further contact with the same agent, even many years later, by making antibody more rapidly and on a larger scale than it did in the first place.

The harmful effects of radiation exposure

It is well known that heavy doses of radiation, particularly to the whole body, can produce a severe depression of the blood-forming activity of the bone marrow (evident some two to three weeks after exposure) and also marked damage to the epithelial cells of the bowel, particularly the small intestine. It is certain that a major contributing cause of these acute effects of radiation is the death of cells shortly after exposure due to the production of severe chromosome damage at the time of irradiation.

A more difficult problem, however, is the extent to which chromosome damage might play a part in the late effects of exposure, particularly the development of cancers. Of these leukaemia has received greatest consideration, and it is now accepted that exposure to heavy doses of radiations increases the risk of leukaemia, whether the whole body or only part of it is exposed. It is also accepted, following the work of Stewart and her colleagues (1956) at Oxford and of MacMahon (1962) in the United States, that exposure of the unborn child to

low levels of radiation during the course of X-ray examination of the mother's abdomen or pelvis increases the risk of the development of leukaemia during early childhood, and also of other tumours. This risk is of course well known, and X-ray examinations are carried out only when the benefits are likely to outweigh the risk. Practically nothing is known about risks associated with low levels of radiation in postnatal life.

Several explanations may be considered for the role of radiation in the development of leukaemia. It is always possible that the production of a certain type of genetic damage in a progenitor blood cell, whether in the form of a gene mutation or of more gross changes, may be all that is necessary to initiate a malignant process. However, it is difficult at present not to consider the possibility that some, perhaps many, human leukaemias have a viral origin, as has been shown with many animal leukaemias. It may be that irradiation occasionally leads to the development of a line of cells with a genetic constitution so changed that it renders the cells liable to transformation by a suitable virus or increases their liability to such transformation, which thus initiates the leukaemic process. The study of the stable forms of chromosome damage produced by radiation exposure in man suggests that altered lines of cells are established after exposure.

The Council's Experimental Virus Research Unit has recently investigated the effect of X-irradiation on the susceptibility of hamster cells to transformation by polyoma virus and has found that the apparent frequency of transformation is increased among cells which have survived irradiation (Stoker, 1963). A satisfactory explanation for this phenomenon is not yet evident, but Stoker points out that if X-irradiation increases the susceptibility of cell populations to transformation by polyoma virus, it may also increase their sensitivity to other tumour viruses. At this time, therefore, the possibility has to be considered that radiation-induced genetic change may be an important factor in the production of human leukaemias through the agency of viral transformation. Such a suggestion raises the possibility that radiation is acting as a co-carcinogen. It could do so through the production of a cell line genetically altered in such a way as to be sensitive to viral transformation; alternatively, radiation may modify intracellular processes in some as yet unknown manner and thus alter the sensitivity of the cell to transformation.

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Early diagnosis of some genetically transmitted diseases

The brilliant work of recent years in basic genetics, including molecular biology, may to some extent have overshadowed the more slowly developing practical applications of human genetics in medicine and surgery. These are, however, substantial. First, there are a number of genetic disorders in which early recognition is important if prompt and effective treatment is to be instituted, and in which genetic knowledge can help in making the diagnosis at an early stage. A good example is provided by phenylketonuria, an inherited disorder of metabolism producing mental retardation, which can now be detected by a simple test soon after birth; a strict diet, if begun at an early age, can prevent or modify the ill effects of this disorder. Galactosaemia, a condition dependent on a recessive gene, is due to a metabolic error in which an enzyme, galactose-1-phosphate uridyl transferase, is absent or defective (Schwarz *et al.*, 1961). This enzyme is one of the essential links in the breakdown of lactose. In its absence toxic products accumulate and the results are serious. Early death is common, and even in relatively mild cases there are often profound effects, including liver damage, cataracts and mental deficiency. If the condition is recognized early enough, and if lactose is withheld from the diet, normal or almost normal development can be assured. Diagnosis is not easy, but prompt recognition and immediate treatment are possible, if not for the first, at least for subsequent children in an affected family, for it is known that there is one chance in four that any brothers and sisters of an affected child will have the disease.

In nephrogenic diabetes insipidus (which is unrelated to the far commoner diabetes mellitus) lack of an antidiuretic hormone prevents the kidney reabsorbing water. This condition may easily remain undetected, and in the absence of appropriate measures serious damage, including mental deficiency, is usual and early death not infrequent. Prompt diagnosis and the maintenance of a proper fluid and electrolyte balance may ensure relatively normal development. The abnormality is due to a recessive sex-linked gene, which is carried by an X chromosome and which will therefore exert its effect in any males to whom it is transmitted, since it will not be paired with a second and normal X chromosome as in females. Thus (barring a mutation, which may improve the chances) there is one chance in two that after the birth of an affected child any subsequent boy will also be affected. Women who are carriers can almost always be recognized by their failure to produce a normally concentrated urine (Carter and Simpkiss, 1956). Therefore the sisters of affected boys can be divided into two classes: those who have the gene, whose sons must be carefully watched, and those who have escaped and whose children are therefore not at risk.

Multiple polyposis of the colon and rectum is due to a dominant gene. It is a precancerous condition, and early examination of those at risk, namely the children of affected persons, followed by operation on those found to be similarly affected, has saved many lives (Dukes, 1952).

What promises, if confirmed, to be a remarkable example of the clinical application of genetics is due to the work of Miller and Patterson at Moorfields Eye Hospital (1962). In a family study of glaucoma simplex, a condition characterized by increased pressure within the eye, they found that only 4 out of 50 sibs of affected persons were similarly affected, and only 2 out of 75 children. But when a coefficient of the outflow of the fluid from the anterior

chamber of the eye, the Friedenwald index, was estimated it was found that just about half the sibs and half the children showed abnormal values, as against practically none of the controls. This points to a dominant gene, whose presence, moreover, can be detected down to the age of 15 years, the lowest age group studied. Only a minority of those with an abnormal coefficient will ever develop glaucoma, but if this observation is confirmed it will be well worth while to examine the close relatives of those with glaucoma simplex, and keep under observation those whose readings are abnormal.

In the majority of instances the defects are rare, though not negligible in the aggregate, for there are many of them. A much commoner condition is congenital pyloric stenosis, which occurs in about 1 in 200 boys and 1 in 1000 girls. It is the commonest reason for surgery in infancy. Treatment is highly successful and the cure permanent. But, once again, prompt diagnosis is important. The genetics are not simple, but it is known that the risk amongst relatives is high, particularly amongst the male relatives of affected females. For a woman who has had congenital pyloric stenosis there is a risk approaching 1 in 5 that any son or brother will be similarly affected (Carter, 1961).

Drug sensitivities having a genetic basis

There are somewhat similar applications of genetic principles in the field of drug-induced conditions, where sensitivities to otherwise safe and useful drugs have a genetic basis. A remarkable example comes from South Africa (Dean, 1963), where a particular variety of hereditary porphyria is common in the white and coloured populations; it is estimated that there are about 8000 affected individuals, all, remarkably enough, descended from a single couple who married in 1688. The condition is due to a dominant gene and is transmitted with perfect regularity from affected persons to half their children on the average. There is often sensitivity of the skin, particularly to sunlight, and it is easily abraded. There may also be attacks of abdominal pain and neurotic symptoms or psychotic episodes. Sometimes there are no symptoms throughout life, but porphyrin can be detected in the stools. Under natural conditions the abnormality does not do much harm, as is shown by the fantastic spread of the gene, but the administration of certain drugs may be disastrous. Of these much the most important are the barbiturates, above all a barbiturate anaesthetic, and many deaths have occurred. The bearers of the gene are offered cards warning doctors that the dangerous drugs must not be given, and it is now routine practice at some South African hospitals to test for porphyrin before giving an anaesthetic.

Brief mention may be made of one or two other examples. A sex-linked gene, very common in some populations, especially in Africa and the Middle East, is responsible for a deficiency of the enzyme glucose-6-phosphate dehydrogenase (Childs *et al.*, 1958). Under natural conditions little or no discoverable harm results, except after the eating of *Fava* beans, but certain drugs, for example the sulphonamides, may induce a haemolytic anaemia. Several recessive genes, which are probably allelic to each other, are responsible for an absence or deficiency of the enzyme pseudocholinesterase (Lehmann and Ryan, 1956), which plays a part in the conduction of nerve impulses to muscles. Again, under natural conditions no harm appears to result, but suxamethonium given as a muscle relaxant during anaesthesia to those of appropriate genetic constitution may induce a prolonged and dangerous respiratory arrest. The proportion of persons at risk is about

1 in 2000 in the British population. Already, during the course of family investigations, a number of these have been recognized and given cards warning doctors that suxamethonium must not be used.

There can be little doubt that further examples of drug-induced sensitivities with a genetic basis will occur. It is also probable that many differences in the pattern of response to drugs will be found to have a genetic basis; for instance, when isoniazid is administered in the treatment of tuberculosis it is found that human beings fall into two groups, namely, the fast inactivators of the drug and the slow inactivators. This is a simple genetic difference (Evans, Manley and McKusick, 1960). There is evidence that slow inactivators, who retain the drug for longer in their tissues, are more liable to develop peripheral neuritis during the course of treatment. Evidence is also accumulating that the difference is a fundamental one, involving the process of acetylation (Evans and White, 1964).

Some other applications of genetics

A number of other practical applications of genetics in medicine and surgery may be listed. One subject of particular importance is the genetic effects of ionizing radiations, with all the implications it carries for future human welfare. Improved techniques, improved apparatus and the avoidance of unnecessary exposure in medical and industrial practice can limit the risk of genetic damage due to radiation-induced mutation. As a result of the new techniques in cytogenetics, since 1959 abnormalities of the chromosomes have been recognized on an increasing scale in intersex states (Court Brown *et al.*, 1964) and in many other conditions. The study of Down's syndrome (mongolism) illustrates the practical importance of these techniques. The great majority of mongols have one small chromosome present in triplicate instead of in duplicate. The risk that the mother of a mongol child will have a second affected child is probably little if at all greater than for other mothers of the same age. But in a minority of instances the extra chromosome is attached to the end of a chromosome of another pair; this is known as a translocation. Outwardly normal persons can carry this double chromosome, and the risk of their having more than one affected child is quite high. Cytogenetic studies can distinguish those instances in which the risk is high (Polani *et al.*, 1960; Carter *et al.*, 1960). The effective treatment of haemolytic disease of the foetus and newborn due to maternal–foetal incompatibility of the Rhesus or other blood groups is largely an essay in applied genetics. The extremely important field of blood transfusion, and also the medico-legal applications of serology in connexion with such problems as disputed paternity and the suspected accidental interchange of babies, represent further examples of the practice of genetics.

The provision of genetic advice

There can be no doubt that the most important of the practical applications of genetics in the present state of knowledge is the provision of genetic advice for those who need it. Those who suspect from their family history that there are possible risks to children, and above all those couples who have had an abnormal child and who fear that a subsequent child might be similarly affected, are in great need of genetic advice. In practice it is found that useful advice can be given in the great majority of instances. Sometimes the inquirers have to be told that the risk is high. They may then decide not to have further children; some may adopt a child. More often, however, it transpires that the risk is relatively

small, or that it is negligible. In fact, it is probable that less harm is done by the birth of further affected children when the risk is high than by unnecessary avoidance of further children when the risks are fairly small.

Mental diseases provide many examples of conditions where genetic advice to patients is particularly important. The genetics of mental diseases, however, is a special field where psychiatric knowledge is essential in making investigations and in advising patients about genetic risks; research in this subject is being carried out by the Council's Psychiatric Genetics Research Unit at the Maudsley Hospital.

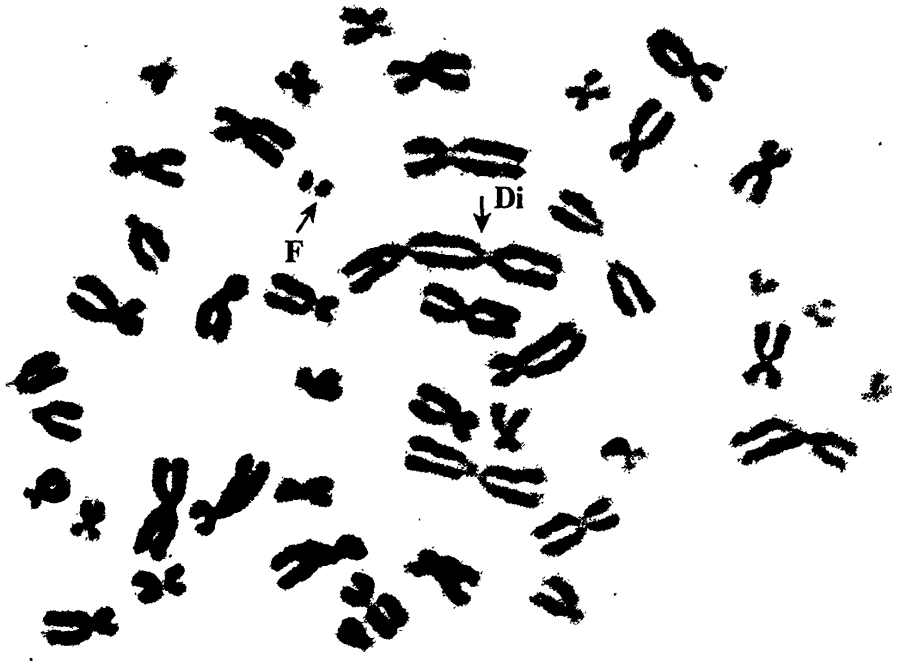
Genetics and aetiology

There is a wide field in which applications are indirect but fundamental—namely, in the assessment of the role of hereditary constitution in the causation of diseases of all kinds. Apart from the purely genetic diseases, which tend to be rare, there are very many diseases in which genetic constitution plays some part, sometimes a fairly important part, sometimes a minor part. But whenever genetic influences are involved, whatever their magnitude, it is important that their role should be assessed, otherwise no studies on causation can be complete. It is the aim of research in clinical genetics to supply the basic data for such studies, both those with immediate and direct applications and those which contribute more generally to an understanding of the causation of various diseases.

The genetics of those abnormalities which are due to single genes, whether dominant, recessive, or sex-linked, are usually not difficult to elucidate. A moderate amount of systematically collected data will give an unequivocal result, though more may be needed to make reasonably sure that complications are absent. One common complication is that what appears to be the same end-result may be due to different genes. This is notably true of hereditary deaf-mutism, for example (Stevenson and Cheeseman, 1956). Sometimes this complication is of immediate practical importance. The type of deformity known as gargoylism, a disorder of mucopolysaccharide metabolism, is usually due to a recessive gene, but in a minority of instances a sex-linked gene is responsible, and it is very important to know which is involved. If it is the recessive gene the normal sisters of an affected child run no appreciable risk of having affected children, but should it be the sex-linked gene, then on the average half the sisters will be carriers. Fortunately there is a distinction which can be observed. With recessive gargoylism opacities develop in the cornea, usually at an early age, whereas this does not happen in the sex-linked cases.

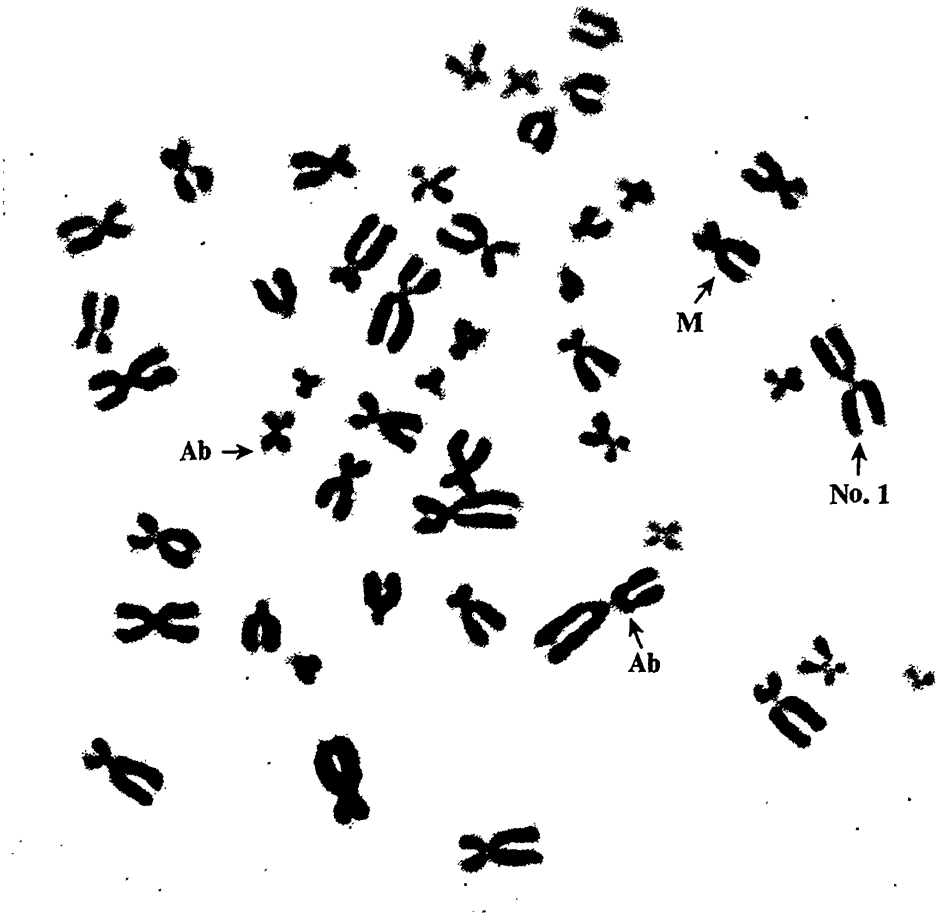
The great majority of simply inherited, or fairly simply inherited, defects are rare. This is because mutation is rare, and the processes of natural selection ensure that ordinarily the rate of manifestation of such defects is kept down to something not greatly in excess of the mutation rate. There are some exceptions, however, and naturally they are important exceptions. These are found when under particular conditions an abnormal gene confers a counterbalancing advantage. One notable example is the prevalence of ' sickling ' of the red blood cells and sickle-cell anaemia in Africa north of the Zambezi and in some other parts of the world. Two doses of the gene give sickle-cell anaemia and the sufferers rarely reproduce, but one dose simply gives sickling of the red blood cells, and this confers a considerable degree of protection against malignant

PLATE I



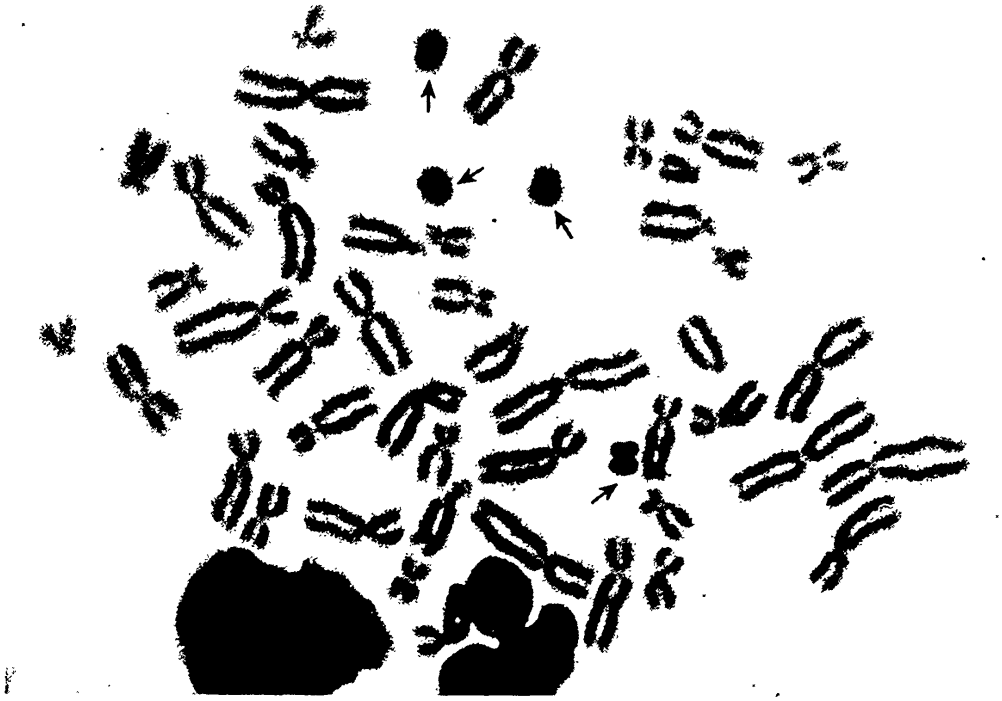
Cell from a blood culture of a male patient 5 months after treatment with X-rays for ankylosing spondylitis, showing a typical unstable chromosome aberration composed of a dicentric chromosome (Di) and an acentric fragment (F). This is scored as an X_1 cell (i.e. probably in its first division since exposure to radiation).

PLATE II



Cell from a blood culture of a male patient 4 months after treatment with X-rays for ankylosing spondylitis, showing typical stable chromosome aberrations. A chromosome of pair no. 1 and a medium-sized submetacentric chromosome have been involved in a reciprocal exchange of material, resulting in the two abnormal monocentric chromosomes marked Ab. For purposes of comparison the normal no. 1 and a medium-sized submetacentric chromosome are also marked (no. 1, M).

PLATE III



Cell from a patient 11 months after X-ray treatment for ankylosing spondylitis showing four ring chromosomes; one of these is seen end-on. This is an X_2 cell and is probably in at least its second division since radiation damage.

tertian malaria during infancy and early childhood, since the abnormal red blood cells are less easily infected by the malaria parasites. Hence the increased reproductive fitness of those with one of these genes counterbalances the loss of nearly all the homozygotes.

It is when we leave the simply inherited abnormalities, however, that practical research work in clinical genetics becomes really arduous. The common congenital malformations, such as spina bifida, anencephaly, hydrocephalus, club foot, harelip and cleft palate, and congenital dislocation of the hip, have a hereditary element in their causation, but it is not a simple one and non-genetic factors are also involved. This is equally true of many of the diseases of later life, such as diabetes, asthma, varicose veins and many mental diseases. In contrast to the relatively simple task of establishing the genetics of a condition determined by a single gene, the work involved becomes enormous. Very large numbers of patients have to be studied, and often it is necessary to examine in person many relatives, who usually have to be visited in their homes. Nor is it enough to concentrate solely on the genetic aspect; non-genetic factors must often be studied at the same time. The work is rewarding, however, and sometimes in addition to establishing, on the basis of the data on incidence, the empirical figures for the risk to relatives essential for giving genetic advice, collaborative researches may have useful consequences in regard to management and treatment.

In congenital dislocation of the hip, for example, one factor is a genetic predisposition to the development of a shallow socket to the hip joint. There is a continuous range of variation and inheritance is very probably multifactorial, being dependent on many different genes—as with stature, for example. An observation of practical importance is that in cases where only one hip is affected measurement of the width of the socket on the undislocated side gives a good indication of whether conservative treatment will be successful or not (Wilkinson and Carter, 1960). A second genetic factor is generalized laxity of the joints, which in mild form is fairly common. Joint laxity probably has a simple genetic basis. The important environmental factor is uterine posture. In a series of 200 patients, 16 per cent were breech born and a further 9 per cent underwent therapeutic version before delivery. This contrasts with a general incidence of breech presentation of only 2 per cent. In individual families it is possible to see the interaction of generalized joint laxity, a wide socket and breech presentation in producing multiple cases of congenital dislocation of the hip (Carter and Wilkinson, 1964).

The commonest congenital malformations of the central nervous system are spina bifida and anencephaly. They are due to a failure of the closure of the neural tube in the region of the spinal cord and of the head respectively as the embryo develops. It has been possible to establish on the basis of large series that a couple who have had an affected child run a risk of about 1 in 25 that any subsequent child will be similarly affected. This is an appreciable risk, it is true, but it is less than double the risk that any random pregnancy will result in the birth of a child with some serious malformation or other. But when a couple have had two affected children the risk for subsequent children rises to about 1 in 8. A word might be added about some of the non-genetic factors associated with these conditions. That these are important is shown by the fact that quite frequently only one member of a pair of identical twins is affected.

With anencephaly there is an association with social class. Its incidence varies with birth order and maternal age, and there are also variations from season to season and from year to year.

Hirschsprung's disease is a condition in which part (or, very occasionally, all) of the lower intestine is aganglionic—that is, lacks nerve cells, so that the movement of the bowel is impaired. It has been possible to establish some useful empirical figures (Bodian and Carter, 1963). In cases where the short segment (the rectum only or the rectum and sigmoid colon) is affected, the sex ratio is about seven boys for every girl; the risk to sibs is about 1 in 20 for brothers, but less than 1 in 100 for sisters. In the long segment cases, however, with the intestine affected above the sigmoid colon, the sex ratio is only two boys for every girl, and the risk to sibs of both sexes is relatively high, namely about 1 in 8. The length of aganglionic segment is usually very similar in a second affected sib to the length of the aganglionic segment in the first.

The genetic element in common diseases: multifactorial inheritance

In the case of common diseases, it is not easy to assess the risk to relatives as compared with the general population. Large samples are required, together with suitable control series. Data on incidence in the general population are needed, broken down by age and sex and other relevant groupings. The increased incidence in close relatives is usually small. A satisfying example is provided by the work of Doll and Buch (1950). They found that 8·0 per cent of the brothers of men with duodenal ulceration were also affected, compared with 3·0 per cent in a suitably matched control group. Thus the incidence in brothers is 2·7 times as great as in the general population. As in many other instances, this is not an increase of an order to cause alarm, nor does it help appreciably in the diagnosis and treatment of the individual case. But it is a basic piece of knowledge relating to the aetiology of the condition.

In order to explain the genetic element in common diseases it was usual a number of years ago to regard single genes as responsible. These were presumed to express themselves in a minority of their bearers, the action of various environmental factors being also needed before the disease became manifest. Increasingly, however, opinion is turning to multifactorial inheritance as an explanation. This depends on the combined action of many genes, each of small effect, which are additive in their action. In some conditions there is no sharp dividing line, fully developed disease shading into minor manifestations and minor manifestations into normality. Where there is continuous variation of this kind multifactorial inheritance is especially likely. The level of arterial pressure, for example, may be regarded as a continuously distributed variable, with benign essential hypertension representing one end of the range. The genetic element in essential hypertension is then seen as an aspect of the tendency for relatives to resemble each other in arterial pressure at all levels from high to low (Hamilton *et al.*, 1954). There is much evidence to support this view, though it is not universally accepted. Much of the recent work on diabetes mellitus also points to the existence of a measure of continuous variation, and to the likelihood that the genetic element in the determination of the disease is multifactorial. With diseases of an all-or-none character the same explanation often seems likely; here an underlying continuously distributed degree of susceptibility is visualized, with a 'cut-off' point beyond which disease becomes manifest. Moreover, multifactorial inheritance is emerging as a probable explanation in fields where

it has not hitherto been suspected, as for example in some of the common congenital malformations. A general review of multifactorial inheritance in relation to human disease has recently been published by Roberts (1964), director of the Council's Clinical Genetics Research Unit.

A pointer to multifactorial inheritance as the explanation of the genetic element in duodenal ulceration is provided by the greater incidence of the disease in those of blood group O than in those of groups A, B and AB and the greater incidence in those who are non-secretors of the ABO blood group substances. These are single-gene systems, and in these systems brothers tend to resemble each other to an extent which can be calculated. It is found, however, that only about 5 per cent of the resemblance between brothers in the incidence of duodenal ulceration mentioned above is accounted for by the action of these two single-gene systems; there must be many other genes contributing to that likeness, the side-effects of these two major gene systems being a small part of the total multifactorial system (Roberts, 1964).

As already mentioned, the most recent field in which a multifactorial basis for the genetic element seems to be emerging is in connexion with congenital malformations. A key piece of work has been carried out by Carter (1961), at the Council's Clinical Genetics Research Unit. Congenital pyloric stenosis is five times commoner in boys than in girls. Carter found that the risk to sibs and children of affected girls is much greater than to the sibs and children of affected boys. This finding cannot be accommodated in a single-gene hypothesis, but it is consistent with multifactorial inheritance. Affected girls are affected in spite of the protection conferred by their sex; they are therefore persons of a specially high degree of genetic susceptibility, and this is faithfully mirrored by the higher incidence of pyloric stenosis in their near relatives. There are indications that the genetic element in the causation of club foot may also be multifactorial.

There are some indications of the same kind for harelip (with or without cleft palate) and, as so often happens, there are two pieces of evidence which would be contradictory on a single-gene hypothesis. The incidence in sibs and children is the same, which points to the action of a dominant gene. But disproportionately often there are affected relatives on both sides of the family, which points equally strongly to the existence of a recessive gene. The hypothesis of multifactorial inheritance accommodates both findings.

Thus, slowly, because of the scale of the studies required, information is being built up on the magnitude of the genetic element in the causation of many malformations and diseases, and empirical risk figures are being established which can be used in giving genetic advice. In addition, the collaborative work of geneticists and other workers is helping in the understanding of the causation of diseases, and sometimes leading to improvements in diagnosis and management.

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RECENT STUDIES ON THE CONTROL OF OVARIAN FUNCTION

During the last decade great advances have been made in the development of methods for estimating levels of hormones and their metabolic products in body fluids. It is now possible to assess with reasonable accuracy the effects of a large number of naturally occurring and synthetic substances on the endocrine glands; these include potent compounds which can stimulate or inhibit the action of the ovary. Much work in this field is being carried out by members of the Council's Clinical Endocrinology Research Unit in Edinburgh.

Assessment of Pituitary Function

The anterior lobe of the pituitary gland at the base of the brain produces at least six hormones, which control reproduction, growth and the activity of the thyroid and adrenal glands. Those controlling reproduction are the *gonadotrophic hormones*, and the two most important members of this group are the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH), both of which must be present for ovulation to occur. In women the main action of FSH is to promote follicular development in the ovaries, so that each month one follicle releases an ovum; LH is responsible for the formation of a layer of hormone-producing cells, the corpus luteum, in the empty follicle after ovulation has occurred. In men these gonadotrophins stimulate the lining cells of the seminiferous tubules of the testes, which produce spermatozoa, and the interstitial cells, which liberate testicular hormones. FSH and LH are proteins and can only be assayed in body fluids by biological methods. The most widely used of such procedures is the test which provides a measurement of the activities of a mixture of the two hormones by producing an enlargement of the uterus in unmated immature mice. At the present time estimations of the levels of human pituitary gonadotrophins (HPG) in urine constitute the most satisfactory direct test of anterior pituitary activity in clinical practice, because such estimations are less laborious and more reliable than those used for other anterior pituitary hormones.

Assays carried out at the Clinical Endocrinology Research Unit have shown that in normal children of both sexes the urinary excretion of HPG is very low indeed and that it is frequently difficult to detect activity even when very sensitive bioassay methods are used. Normal men and normally menstruating women also show low values, but the readings are in general higher than those found in children. In men there is no evidence of a cyclic pattern of HPG excretion, but in a proportion of normally menstruating women a gonadotrophin peak occurs at mid-cycle and is presumably associated with ovulation (Loraine and Bell, 1963). Menopausal and postmenopausal women show much higher HPG levels than those found in women during reproductive life; such high values persist until a late age and are generally thought to result from an attempt on the part of the pituitary to stimulate unresponsive ovaries. This is one example of an alteration in the control mechanism that commonly governs the hormone secretion of the pituitary and of the various endocrine glands which it stimulates; the secretion of the peripheral (in this case ovarian) hormones normally inhibits excessive production of the stimulating pituitary hormones.

Assessment of Ovarian Function

The main hormones elaborated by this gland are the *oestrogens*, which are produced both by the developing follicle and by the corpus luteum, and *progesterone*, which is secreted by the corpus luteum following ovulation. An accurate picture of ovarian activity is provided by measuring in the same woman the urinary output of (*a*) the three 'classical' oestrogens, *oestradiol*, *oestrone* and *oestriol*; (*b*) *pregnanediol*, which is the main urinary metabolite of the parent hormone progesterone, and (*c*) *pregnanetriol*, the main precursor of which (17α-hydroxyprogesterone) is believed to be secreted by the ovary. All these substances possess the steroid ring structure and their levels are estimated in body fluids by chemical rather than by biological methods.

In women throughout reproductive life the excretion of oestrogens during the menstrual cycle shows a highly characteristic pattern (Brown, 1955). Levels are low during menstruation itself and in the early follicular phase of the cycle. They start to rise on about the seventh day of the cycle and reach a well defined maximum at mid-cycle at the time of ovulation. After the ovulatory peak, oestrogen levels in urine fall but rise again to a second peak after the corpus luteum has been formed, in the luteal phase of the cycle. Immediately prior to menstruation the oestrogen output falls rapidly and the lowest levels at any time during the cycle are found after the onset of menstrual bleeding. Levels of pregnanediol in urine are low before ovulation, rise sharply in the luteal phase and fall just prior to menstruation; the output of pregnanetriol begins to rise about mid-cycle, reaches its maximum during the luteal phase and also falls before menstruation. Figure 1, which is based on data obtained from 15 cycles in 10 women, shows the average hormone excretion at the different phases of the normal menstrual cycle.

The urinary excretion of oestrogens and pregnanediol is usually higher in women during reproductive life than in children or in women at and beyond the menopause or in normal males. In these three groups the oestrogens and pregnanediol are derived mainly from precursors secreted by the adrenal cortex, and estimation of their levels in urine provides useful information on the activity of this gland.

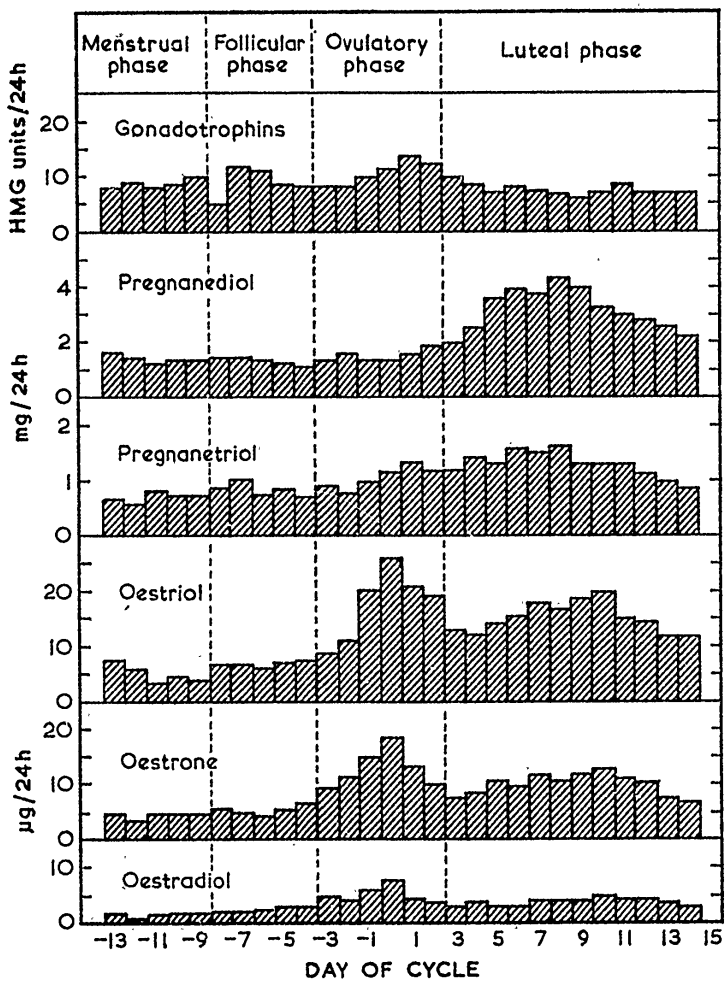

Figure 1

Mean hormone excretion during the normal menstrual cycle: data on 15 cycles in 10 women. From Loraine and Bell (1963).

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Compounds Affecting Pituitary and Ovarian Function

Substances are now available in clinical practice both for the inhibition and for the stimulation of pituitary and ovarian function. The compounds discussed in this article fall into four groups: (1) oestrogens; (2) progestational compounds; (3) dithiocarbamoylhydrazine derivatives; (4) clomiphene.

Oestrogens

The oestrogens used clinically fall into three main categories—the steroidal oestrogens such as oestradiol and oestrone which occur in the body, synthetic modifications of the natural steroidal oestrogens, such as oestradiol dibenzoate and ethinyl oestradiol, and synthetic oestrogens which are not steroids, such as stilboestrol and hexoestrol. Little reliable information is at present available on the effect of the naturally occurring oestrogens on pituitary gonadotrophic activity, but it is generally agreed that the synthetic oestrogen stilboestrol is a highly potent pituitary inhibitor as far as can be judged by urinary HPG assays

(Loraine, 1958). When this compound is administered orally to postmenopausal women in dosages as low as 1·0 mg per day a marked decrease in HPG output occurs, and if the dosage is increased to 5·0 mg per day gonadotrophins disappear from the urine; the restoration of a balanced relationship between pituitary and ovarian hormones appears to relieve the unpleasant symptoms frequently experienced at this time of life. The marked pituitary-inhibiting properties of stilboestrol have led to its use in the treatment of breast cancer and prostatic cancer, which may regress when endocrine activity—particularly that of the reproductive glands—is reduced. The compound has also been employed in disorders of childhood characterized by excessive growth.

Progestational compounds

Substances derived from progesterone have been used for some time in the treatment of certain gynaecological disorders, but in recent years they have excited great interest because of recognition of their ability to inhibit ovulation. The first extensive human trials with progestational compounds were conducted in Puerto Rico during 1956, by Pincus and his co-workers, who showed that *nor*ethynodrel given with added oestrogen in tablet form from the fifth to the twenty-fifth day of the menstrual cycle was a highly effective contraceptive agent. Although the clinical effects of such compounds have been extensively studied and are now well documented (Pincus *et al.*, 1958; Mears, 1961), little was known regarding their mode or site of action in human subjects. Recently their short-term effects on pituitary and ovarian function have been investigated in detail. Brown, Fotherby and Loraine (1962) found that *nor*ethisterone and its acetate when administered from day 5 to day 25 of the cycle inhibited ovulation, as judged by assays of oestrogens, pregnanediol and pregnanetriol in urine, without affecting HPG excretion. A typical study on a 27-year-old patient who was being treated with *nor*ethisterone acetate for severe menstrual and premenstrual pain showed that during the two menstrual cycles in which treatment was given ovulation, as judged by assays of oestrogens and pregnanediol in urine, did not occur. In the first cycle during treatment the activity of the corpus luteum was abolished, while in the second cycle neither follicular nor luteal activity was present. In the cycles immediately preceding and following those during which *nor*ethisterone was administered a normal ovulatory pattern of hormone excretion was observed. Throughout the four cycles HPG excretion remained relatively constant (Brown, Fotherby and Loraine, 1962). This suggests that the progestational compounds produce their effect by a direct action on the ovaries rather than through the pituitary. It should, however, be emphasized that the bioassay method used for HPG (the mouse uterus test) measures FSH and LH activities in combination, and for this reason the possibility of inhibition of one or other of the pituitary gonadotrophic hormones has not been definitely excluded.

A number of investigators have expressed concern about the possible long-term endocrinological effects of oral progestogens and have suggested that, when administered over months or years, such compounds may prove harmful because of their potential ability to alter hormonal interrelationships or to interfere with the endocrine environment necessary for fertilization and implantation of the ovum. In order to gain further information on this point Loraine and his colleagues (1963) conducted hormone assays both during and immediately following treatment in three women who had received this form of medication

for periods ranging from 9 to 44 calendar months. Two main findings emerged from this investigation: first that pituitary function as measured by urinary HPG assays was not suppressed by relatively long-term medication, and secondly that following withdrawal of medication the cycles immediately reverted to a normal ovulatory pattern. The results obtained in one of the subjects studied are shown in Figure 2.

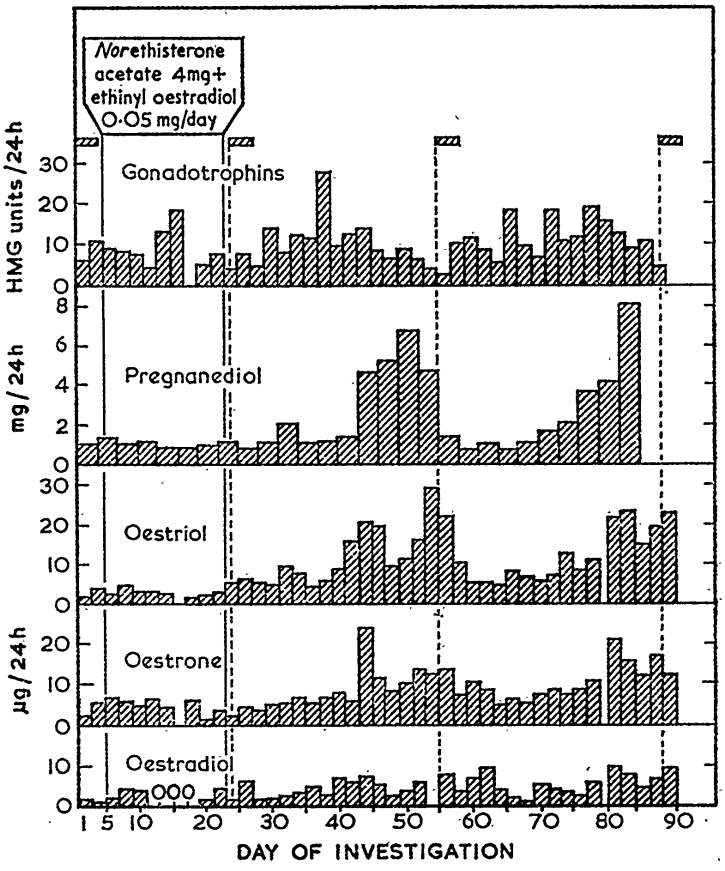

Figure 2

Effects of the administration of *nor*ethisterone with added oestrogen on hormone excretion in a normally menstruating subject. ▨ = days of menstrual bleeding. From Loraine, Bell, Harkness, Mears and Jackson (1963).

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The results obtained in these women and in a number of others investigated in a similar manner suggest that long-term therapy with oral contraceptive agents has no lasting deleterious effects on pituitary and ovarian function. Obviously further studies are required before any definite conclusions can be drawn.

In postmenopausal patients with recurrent and disseminated breast cancer, Douglas, Loraine and Strong (1960) showed that progestational agents are weak inhibitors of pituitary gonadotrophic activity. Large doses of such compounds administered over relatively long periods of time did not abolish HPG output but merely reduced it to levels found in women during reproductive life. Recent evidence suggests that this mild pituitary-inhibiting action is not a direct effect of the compounds but results from their conversion to oestrogens in the body (Brown and Blair, 1960). Such a conversion occurs both in postmenopausal women and in women during reproductive life.

Dithiocarbamoylhydrazine derivatives

In 1961 Paget, Walpole and Richardson described a series of compounds which inhibited pituitary gonadotrophic activity in rats, dogs and monkeys. These compounds were derivatives of dithiocarbamoylhydrazine and differed from the majority of previously described pituitary inhibitors in not being steroids. Bell and his colleagues (1962b) found that one of the most active of these compounds acts as a pituitary inhibitor in postmenopausal women and decreases HPG excretion during the period of its administration. The compound has no effect on adrenocortical function as judged by assays of the 17-hydroxycorticosteroids, 17-oxosteroids and oestrogens in urine.

In normally menstruating women the same compound acts in a manner analogous to that of the progestational compounds and inhibits ovulation without affecting HPG output (Bell *et al.*, 1962a). It may therefore act directly on the ovary rather than through the pituitary. A typical investigation in a woman with previously regular 30-day menstrual cycles showed that the initial cycle studied was of a normal ovulatory type as judged by steroid excretion, and that during administration of the compound, in the second cycle, ovulation was inhibited; HPG excretion, however, continued at levels comparable to those observed before treatment was started. After withdrawal of the compound the subject failed to menstruate for a further 32 days, during which time an ovulatory cycle occurred. When administered during the luteal phase of the cycle the compound had no effect on endocrine function.

Clomiphene

So far this article has dealt entirely with the effect on hormone excretion of compounds inhibiting ovarian function. Stimulation of ovarian function, notably in cases of infertility, is also of considerable importance in therapeutics, and this can now be achieved in selected patients, either by the intramuscular administration of combinations of gonadotrophic hormones as shown by Gemzell, Diczfalusy and Tillinger (1958), working in Sweden, or by the oral administration of clomiphene as shown by Greenblatt and his colleagues (1961), working in the United States.

Clomiphene is a derivative of the synthetic oestrogen chlorotrianisene. In animal studies it was found to inhibit ovulation; but in human subjects the effect was exactly opposite, and the compound was shown to be capable of restoring normal ovulatory menstrual cycles in a proportion of patients with amenorrhoea. Present evidence indicates that clomiphene is most effective in patients suffering from secondary amenorrhoea and from the Stein–Leventhal syndrome, a disease characterized by infertility and menstrual irregularities in association with bilateral ovarian enlargement. In one such patient, aged 20, who had had virtually no menstrual periods for seven years, Charles and his colleagues (1963) found that three courses of clomiphene resulted in the production of two consecutive ovulatory menstrual cycles, as judged by steroid assays in urine. This form of treatment had no marked effect on HPG excretion, and it therefore appears possible that the compound acts directly on the ovaries rather than through the pituitary. If this is indeed the case the site of action of clomiphene must be the same as that of the progestational compounds and the dithiocarbamoylhydrazine derivatives.

Potent compounds are now available for both the inhibition and the stimulation of ovarian function in human subjects and it can be confidently predicted that such compounds will become of increasing importance in human life.

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MICROBIAL DRUG RESISTANCE

The control of infective disease that has been achieved during the past 25 years by the synthesis of new drugs, the discovery of antibiotics and the development of methods of immunization represents one of the most impressive advances in medicine of recent times. It is now reasonable to say that these advances have brought some mastery over the majority of bacterial infections and of infections caused by protozoa (for example malaria and trypanosomiasis). The approach to the drug treatment of virus infections is intrinsically more difficult since the multiplication of a virus depends on the metabolic processes of the normal cell which it invades; this clearly makes the prospect of discovering a drug that will inhibit or destroy the virus without damaging the cells of the host somewhat remote. Even here, however, a glimmer of light has appeared recently in the successful use of a synthetic drug for protection against smallpox.

Encouraging as these advances are, however, it would be a mistake to regard the present situation as entirely satisfactory for two reasons. The first is that the search for new chemotherapeutic agents remains essentially empirical; there is but a dim guiding light to direct the efforts of chemists in the search for new synthetic drugs, and new naturally occurring antibiotics are only discovered by the laborious screening of many thousands of mould and bacterial products. The second reason is that in many infective diseases the initially successful treatment with a new drug may become less effective or entirely ineffective as times goes on owing to the emergence of a form of the infecting organism which is resistant to the drug. It is this phenomenon of drug resistance that is the principal continuing obstacle to successful chemotherapy.

Development of drug resistance is fortunately not invariably encountered; it has not, for example, been a problem in the treatment of cerebrospinal fever by sulphonamides or of syphilis by penicillin. The phenomenon is, however, widespread among other pathogenic organisms; it is found in infections caused by trypanosomes (among which it was first observed), and it is a serious obstacle to chemotherapy of malaria and of certain bacterial infections, particularly staphylococcal infections in hospitals, where the prevalence of forms resistant to penicillin and to other antibiotics has at times become so high as to be a real cause for anxiety. As will be seen below, this particular situation has now happily changed for the better.

In some instances drug resistance can be overcome by practical measures. Thus the resistance of the tubercle bacillus to streptomycin, which developed early and threatened to destroy the usefulness of this antibiotic in the treatment of tuberculosis, can be avoided by simultaneous administration of another antituberculous drug such as isoniazid (to which resistance also develops if it is given alone). Since resistant forms emerge when infecting organisms are exposed to low concentrations of a drug, much can be done to prevent development of drug resistance by proper therapeutic practice, avoiding ineffectively low dosage of the drug; as a corollary of this we have the discovery, at first sight paradoxical, that a good way to eliminate resistant organisms from a relatively closed area such as a hospital ward is to cease entirely to use the drug to which they have become resistant for a sufficient period. All such devices, however, are little more than makeshifts and, in the absence of any real understanding of the phenomenon of drug resistance, the measure of chemotherapeutic control of infections must depend on the balance between the speed at which chemists discover new drugs and the speed at which organisms develop resistance to them; such a situation cannot be viewed with equanimity, and it is therefore satisfactory to be able to record real progress in the understanding of at least one aspect of the problem.

Types of drug resistance

A micro-organism can become resistant to a drug in several ways. (1) It can become impermeable to the drug: it was early observed that this is what happens with trypanosomes, the resistant forms of which no longer absorb the drug, which gains ready access to the susceptible forms; (2) the vital site in the organism at which the drug exercises its lethal effect may be so altered that the drug can no longer obtain a foothold—a probable example of this will be mentioned below in connection with a rare form of penicillin resistance; (3) the resistant form of the organism may produce an enzyme that is capable of destroying the drug. It is into the third of these categories that the clinically important resistance of staphylococci to penicillin falls, since the resistant staphylococcus is resistant by virtue of its power to produce large amounts of an enzyme, penicillinase, which hydrolyses penicillin to an antibiotically inactive product; this fact has been known for a number of years, but it has only recently become possible to offer an explanation of the development of penicillin resistance as a biochemical expression of the genetic process.

Inducible enzyme production

As has been indicated above, the essential change undergone by the staphylococcus when it becomes resistant to penicillin is the acquisition of a new enzyme, or at least the capacity to produce large amounts of an enzyme that is

barely detectable in the non-resistant form; the processes leading to this change have been the subject of much discussion. Since the enzyme is a protein, the solution of the problem must depend on proper understanding of the role of the genetic material of the cell in the control of protein synthesis, and this subject has been greatly illuminated in recent years.

The process by which the structures of proteins synthesized in the cell are determined by specific genes has been fully discussed in an earlier Report (Medical Research Council, 1963). Equally important for the present discussion is the means by which the operation of the synthetic process is controlled, and much light has been thrown on this by Jacob and Monod (1961) at the Pasteur Institute in Paris; as the result mostly of studies of *Escherichia coli* these workers have arrived at the following concept.

In the process of production of a protein, two genetic elements have to be envisaged; firstly there is the structural gene already referred to which controls the course followed in the synthetic process and thus determines the chemical structure of the product; secondly, there is a control gene which regulates the rate at which the synthetic process operates. This it does by producing a specific repressor substance which is capable of inhibiting the structural gene; the efficacy of the repressor itself can in turn be affected by interaction with extrachromosomal compounds in the cell or its environment. We can now consider how this somewhat complicated control system may operate in penicillin-resistant bacteria.

For a number of years workers at the National Institute for Medical Research have been studying the penicillinases of three bacterial species, namely *Staphylococcus aureus* and the non-pathogenic organisms *B. cereus* and *B. licheniformis*. The purified penicillinases from these three species are different types of protein, each with different enzymic and chemical properties. They differ especially in the relative rates of hydrolysis of various penicillins. All, however, inactivate penicillin G and penicillin V (the natural penicillins used most commonly in clinical practice) extremely readily.

Penicillin-resistant strains of these bacterial species normally produce barely detectable amounts of penicillinase when growing in the absence of penicillin. This quantity of enzyme is insufficient to protect the bacteria against the lethal action of the antibiotic, and effective resistance to penicillin in these bacteria therefore requires a rapid production of penicillinase. All the three species that have been studied are capable of increasing their penicillinase content up to 100-fold within an hour after contact with extremely small quantities of penicillin.

The process that has just been outlined is that known as enzyme induction, and in terms of the theory of Jacob and Monod we can envisage the course of events as follows. Under normal circumstances production of penicillinase by the bacterium is not required and will be kept at a very low level by the action of the control gene which regulates the synthesis of the enzyme. When penicillin is present it will antagonize the repressor substance through which the control gene exercises its effect; in this way it will switch off the inhibition of the structural gene and so allow penicillinase production to proceed at the full rate, or at least at a greatly increased rate. There is indeed evidence that such a mechanism operates in penicillinase production by the staphylococcus and, as

with other inducible bacterial enzyme systems, the structural and control genes are very closely linked on the chromosome and function to some extent as a co-ordinated unit.

A genetic system such as that of penicillinase production is clearly liable to variation as the result of mutation of either of the genes concerned. Since most mutations lead to impairment of the function of the specific gene product, one can for instance imagine a mutation in the structural penicillinase gene which would lead to the synthesis of a defective enzyme unable to protect the bacterium by efficient destruction of penicillin. Alternatively, mutation of the control gene could lead to a defective repressor substance which failed to inhibit the structural gene and thus permitted production of penicillinase at full rate in the absence of penicillin as an inducer. In laboratory work with bacteria, variants do arise, or can be produced by the deliberate use of mutagens, that exhibit properties such as would result from mutations of the types considered; there is, however, no evidence that such variants are of particular importance in the natural situation. It seems reasonable, therefore, to believe that the closely integrated inducible enzyme-producing mechanism described above represents the actual defence mechanism against naturally occurring penicillins that has been acquired by bacteria during the course of evolution.

The new penicillins

The word 'penicillin' is, from the chemical point of view, a generic term embracing all compounds containing a certain bi-cyclic structure; individual penicillins are characterized by the sort of side-chain that is attached at a particular point on this molecule. Through its effect on the shape of the molecule, the side-chain of a particular penicillin will have an influence on the affinity of that penicillin for other molecules, particularly proteins, with which it is brought into reaction. This is a key point in the problem that we are considering since in the interaction between a penicillin and a bacterium possessing the inducible penicillinase system, the affinity of the antibiotic for a series of proteins will have decisive effects.

There is, for example, much evidence that the lethal effect of all penicillins on susceptible bacteria is exercised by interference with the system that synthesizes the bacterial cell wall (Medical Research Council, 1962); this is in all probability a penicillin–protein interaction, the extent of which may be affected by the structure of the particular penicillin involved. Similar considerations apply to the antagonization by penicillin of the repressor substance for penicillinase synthesis and finally to the affinity of penicillin for the penicillinase molecule, which will determine the rate of penicillin destruction.

The rates at which the various naturally occurring penicillins are destroyed by penicillinases produced by different organisms are all high and show no more than quantitative differences from one another; this is not surprising if we regard penicillinase production as a defence mechanism acquired during evolution. The possibility remains, however, that a penicillin containing a side-chain not found in nature might turn out to be quite different in its susceptibility to destruction by penicillinase. This possibility has, in fact, been realized through the discovery by workers in the Beecham Research Laboratories (Chain, 1962) of means of obtaining the cyclic nucleus common to all penicillins (6-amino-penicillanic acid) in quantity; it is possible by simple synthetic methods to prepare

from this compound an almost unlimited series of penicillins containing side-chains of types most unlikely to have been encountered by the staphylococcus during its evolutionary development. The more successful new penicillins obtained in this way (for example methicillin), whilst still able to induce penicillinase production, are very highly resistant to attack by the enzyme; they persist in the blood of a patient infected with penicillinase-producing staphylococci 4000 times as long as the naturally occurring penicillin G; moreover, by good fortune, they are not so far altered in structure as to have lost their lethal effect on the bacterium. By virtue of these properties they have, for the present at least, solved the serious clinical problem presented by infection with staphylococci resistant to natural penicillins.

There are two reasons for introducing a qualification into the preceding sentence. Firstly, strains of staphylococci have been isolated from hospital patients which are resistant to both the natural and the new synthetic penicillins. In these organisms production of penicillinase is quantitatively and qualitatively normal, and their resistance is ascribed to a different mechanism, probably involving an alteration in the site at which penicillin exercises its lethal effect on the bacterium. This form of resistance is so rare as to be of no practical significance at the present time; its existence, however, is a warning which should not be disregarded and which emphasizes the need for the careful therapeutic use of the new penicillins—particularly the avoidance of too low dosage.

The second reason for caution lies in the theoretical possibilities of mutational change of the penicillinase-producing system. The fact that altered penicillinases capable of destroying methicillin have not yet appeared, although methicillin has been widely used for about two years, might suggest that the mutational or genetic recombinational steps required to give the necessary properties are not possible—or at least very difficult to achieve—and that it is therefore unlikely that an enzyme hydrolysing methicillin will evolve rapidly, if at all. It is to be hoped that this is so. There are, in any case, a number of reasons for supposing that such an evolutionary change would be extremely slow—even taking into account the relatively short generation time of the bacteria concerned and a high selection pressure in its favour. The number of randomly initiated mutational steps that might be required—possibly in the correct order—and the low probability of the introduction of the necessary new genetic information in one piece would ensure that a new type of penicillinase (even if it is chemically feasible—which it may not be) must take many years to evolve. Remote as may be the possibility that such an evolution could be achieved even by the versatile staphylococcus, it is important to keep the situation under close scrutiny and to watch for any hint of the emergence of strains which are resistant to the new penicillins by virtue of their production of a modified penicillinase capable of destroying these compounds.

The fairly detailed discussion that has been given of a single type of drug resistance—albeit one that is of much clinical importance—may appear to offer a very limited approach to a subject that has wide ramifications. The restriction of treatment has, however, been deliberate; it has been imposed because in the phenomenon of penicillin resistance in staphylococci we have the first example of drug resistance for which a logical explanation and analysis can be offered in terms of biochemistry and genetics. This analysis is not only intellectually satisfying; it is a step further in the search for a rational approach to the design

of new chemotherapeutic agents, it gives new understanding of the situations in which drug resistance may arise and it offers some guidance as to how these situations can be avoided. Moreover, it should encourage similar studies of other forms of drug resistance where different mechanisms are involved; it is only through such studies that we can hope to make secure the advances in chemotherapy that have already been made and those that are still to come.

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CHEMOTHERAPY OF CANCER

The treatment of cancer by drugs would, ideally, require substances which could destroy or damage the tumour cells without causing significant harm to the normal cells of the body. It must be admitted that in this respect we have no really effective chemotherapy at present since all the substances so used are also damaging to some normal cells. Nevertheless, it is possible to give beneficial treatment with these cytotoxic drugs—which may, for example, double the survival time of children with acute leukaemia. This is because most normal tissues have a capacity for repair which enables them to recover from damage which decimates their cells. Moreover, cytotoxic drugs are not all damaging to the body as a whole; some have a fairly specific effect on certain types of cell—for instance, nitrogen mustard affects one type of white blood cell—and malignant tumours originating from that particular cell type are more likely to be affected by the drug than is the rest of the body.

There are many thousands of compounds listed in the various publications giving ' screening ' data on chemotherapeutic agents, but only about a dozen have achieved a significant clinical reputation. These fall into three groups: antimetabolites, alkylating agents, and certain natural products.

Antimetabolites

The antimetabolites represent the most ' logical ' of the anti-tumour agents, in that they are designed to interfere with specific metabolic processes. The first of these agents to be used—and still one of the most potent—was the class of compounds that interfere with the formation of folic acid, the ' folic acid antagonists ' (for example amethopterin). These compounds block metabolism by using up the enzymes needed for synthesis of folic acid. Farber and his colleagues (1948), working in the United States, have shown that these compounds produce unequivocal remissions, often lasting several months, in the leukaemias of childhood. Although nearly 50 per cent of children will respond to the drug, the leukaemias occurring in adults are hardly affected by it. A good response has been observed in cases of choriocarcinoma, a tumour developing from embryonic tissue in women, as shown by Li, Hertz and Spencer (1956), also working in the United States, though disappointing results have been obtained in the rare cases of this tumour occurring in men; the Council is supporting research

on this type of treatment at Charing Cross Hospital. Recently, favourable reports have been published on the use of folic acid antagonists in mycosis fungoides, a disease characterized by skin tumours (Wright, Gumport and Golomb, 1960). A disadvantage of such drugs is that they cause serious side-effects, primarily as a result of depression of the blood-forming tissue of the bone marrow.

A second group of antimetabolites is the class of so-called nucleic acid analogues. These are compounds designed to interfere with the metabolism of the cell's nucleic acid. They may be pyrimidine derivatives, for example 5-fluorouracil, or purine analogues such as 6-mercaptopurine: in either case they have a similar chemical structure to a constituent of nucleic acid and can be ' mistaken ' for it by the cell. 6-Mercaptopurine is used with some success in acute leukaemia in both children and adults (Burchenal *et al.*, 1953), and by combining a course of this drug with one of amethopterin it is possible to decrease the dose of the folic acid antagonist and thus reduce its toxic effect on the bone marrow.

The great difficulty in the design of antimetabolites for tumour chemotherapy is our ignorance of the metabolic processes that are specific to tumours. Both the anti-folic-acid and the anti-nucleic-acid agents will affect every cell, as is evident from the damaging effect of these compounds on the body as a whole. The fact that more frequent temporary remissions can be achieved in childhood than in adult leukaemia may well be because the normal bone marrow elements in young children have an exceptional capacity for recovery, and because the leukaemic cells have a faster growth rate—and thus a greater demand for nucleic acid synthesis—in children than in adult patients. The choriocarcinoma of women may be regarded as a ' transplanted ' tumour, originating as it does from foetal membranes, and as such it may have some immunological disadvantage in the body, as well as an unusually high requirement of folic acid like other foetal tissues.

There is no great difficulty in designing antimetabolites, whether these be antagonists or analogues to vitamins, enzymes, nucleic acids or amino acids. Many such compounds have been designed and used, but unless and until specific reactions or specific molecules can be found in tumours—molecules not present or not important in normal cells—antimetabolites will be doomed to remain cytotoxic agents which are not specific for tumours, and therefore limited to exerting a palliative effect. Many animal tumours are caused by viruses, which are composed of nucleic acid, and nucleic acid analogues can inhibit virus multiplication. Although there is no proof that human tumours are virus-induced, this possibility must be kept in mind. For this reason the anti-viral nucleic acid analogues—or indeed any other anti-viral agents—may present a new possibility for tumour chemotherapy.

Alkylating agents

By and large the limitations inherent in antimetabolites apply also to the alkylating agents. These are substances which are chemically very reactive and which react (by transferring an alkyl group) with a number of biologically important chemical groups, for example amino-, sulphydryl-, carboxyl-, hydroxyl- and phosphate groups. Although these agents have been known since 1946 to have inhibitory effects on tumours (Goodman *et al.*, 1946; Schmidt *et al.*, 1958) their mechanism of action is poorly understood. Clinically the three most important groups are: the nitrogen mustards

(HN_2, cyclophosphamide, chlorambucil), the ethyleneimines (triethylenemelamine, triethylenethiophosphoramide) and the alkyl sulphonates (Myleran). Myleran and chlorambucil were developed at the Chester Beatty Research Institute, which receives a special grant from the Council, and the possibility of developing further alkylating agents is being explored here and at the Paterson Laboratories of the Christie Hospital and Holt Radium Institute, Manchester, to which the Council also give financial support.

Because of certain similarities between the effects of alkylating agents and of ionizing radiations, these compounds have been described as 'radiomimetic' agents; but in spite of certain superficial similarities this name is misleading since in some aspects of cellular metabolism the alkylating agents are less and in others more specific than radiation.

The nitrogen mustards and ethyleneimines have a slight preference for lymphatic tissues, and they can thus be usefully employed in the malignant conditions of these tissues. HN_2 and cyclophosphamide are used in the treatment of Hodgkin's disease and some lymphosarcomas, and chlorambucil is used for the treatment of leukaemias. The alkyl sulphonate Myleran, however, has a selective effect on the granulocytic white cells of the blood (Haddow and Timmis, 1951). For this reason it has been employed in the treatment of chronic granulocytic leukaemia, and 80–90 per cent of cases show good and long-lasting remissions in response to this drug. Because of their relatively low general toxicity in therapeutic doses and their efficiency in producing remission in granulocytic and lymphocytic leukaemia, the alkylating agents are perhaps the most universally acclaimed among the chemotherapeutic agents. Nevertheless, it should be remembered that the remissions are only temporary and after two or three remissions the disease becomes refractory to further treatment.

Although the clinical usefulness of Myleran is limited to one disease, the alkyl sulphonates as a group may be exploited in a greater variety of forms than the other alkylating agents (the active group can be attached to almost any molecule) and there is at least in theory a hope of finding other compounds with a similar selective effect. However, although alkylation may eventually be made specific biochemically for a wide variety of tissues, the criticism that was used against the antimetabolites can be used against even the most tissue-specific alkylating agent: it will not provide effective chemotherapy unless it can alkylate a compound found only in the tumour. An alkylating agent that could do this would in effect be an antimetabolite for a particular tumour, inhibiting a tumour-specific biochemical reaction.

A further complication which almost inevitably arises is the development of resistance to the drug. This is achieved by cells which can develop an alternative metabolic pathway to that which is blocked by the drug and it may be that a genetic lability in malignant cells gives them a better chance of developing alternative metabolic pathways, and thus resistance to a drug, than the genetically more rigid normal cells.

Natural compounds

The third group of substances, the natural products, are results of serendipity rather than logical planning. One of these compounds, actinomycin D, is the result of a search for antibiotics derived from the soil organism *Streptomyces*. Most antibacterial agents have been tested for anti-tumour activity, but because

of basic biochemical differences between microbial and mammalian cells, there tends to be no simple relation between antibacterial and anti-tumour activity. The good palliative results shown by actinomycin D in Wilms' tumour of the kidney in children (Farber *et al.*, 1956), and its beneficial effect in some sarcomas, initiated an intensive series of investigations with compounds from various strains of *Streptomyces.* Although a number of these have anti-tumour activity in experimental systems, actinomycin D is perhaps still the most clinically useful member of this group of substances.

The plant alkaloid colchicine (from *Colchicum autumnale,* autumn crocus) has for long been known to have an inhibitory effect on cell division, and its less toxic derivative deacetylmethylcolchicine (Demecolcin) has been shown to have some effect in chronic granulocytic leukaemia. Its effect is, however, less reliable than that of the alkylating agent Myleran.

Vincaleukoblastine (Vinblastine), an alkaloid of the periwinkle (*Vinca rosea*) has been shown to have a depressant effect on the bone marrow, and its potential anti-tumour activity was investigated. It is considered to be useful in the treatment of Hodgkin's disease and also in choriocarcinoma even after this tumour becomes resistant to amethopterin (Hertz, Lipsett and Moy, 1960; Warwick, Darte and Brown, 1960). Another *Vinca* alkaloid, vincristine, shows promise in the treatment of leukaemia in children.

The last and rather special example of tumour therapy by means of natural products is the use of hormones for attempting to control the disease. Certain tissues, for example the prostate and female breast glands, require hormones for their proliferation. Tumours originating from such tissues sometimes retain some degree of dependence on the hormones; extreme cases of hormone dependence have been observed in experimental animals. In clinical practice frequent remissions can be produced with suitable types of tumour by the administration of certain sex hormones or corticosteroids (Huggins, 1956). The literature on hormone treatment of malignancy is extensive, but it is not discussed here as this treatment is in a sense not so much chemotherapy as a purposeful change in the biochemical milieu of the tumour. As tumour cells may be genetically more labile than normal cells, some of them may have a more specific requirement for a certain biochemical environment than normal cells. This same genetic lability, however, also would permit a relatively quick adaptation to new conditions, in the same way that resistance to specific metabolic inhibitors eventually develops.

The future of research in cancer chemotherapy

In this brief survey only the most universally accepted chemotherapeutic compounds for tumours have been mentioned. The total number of compounds amounts to many thousands; over 700 alkylating agents alone have been synthesized. In view of the very significant effort expended and the relatively meagre results obtained so far, the question may legitimately be asked: what is the future of cancer chemotherapy?

The crucial problem facing cancer research workers is to discover the essential nature of the malignant cell—in other words, the specific difference between this and the normal cell; for this difference could be exploited to the detriment of the malignant cell. However, the basic biochemistry of the cell is only beginning to be understood, and the sum total of the information available is still too

rudimentary to allow us to penetrate to the essential differences between normal cells and tumour cells. The development of completely ' logical ' antimetabolites or alkylating agents, therefore, will have to wait until a better understanding of the biochemistry of the cell has been achieved. In the meantime, there is every reason for a less logical approach: complicated molecules, such as certain plant alkaloids or microbial products, may still be used with some success, since the more complicated a compound is structurally, the more chance there may be that it will act specifically on one cell type and not on another. The exploration of ' combination ' treatments must also be mentioned here: different drugs may be used in combination; individual drugs may be combined with surgical techniques and perfused through the region of the tumour in order to achieve a high concentration of the drug in a circumscribed area; and radiosensitizing drugs (given either systemically or in the form of local perfusions) may be combined with radiotherapy.

Another approach to the problem might be along immunological lines, exploiting the fact that whatever is recognized as foreign to the body is rejected. It is known that many tumours are immunologically foreign and theoretically capable of evoking the body's defence reactions against them; but spontaneously occurring malignant cells do not appear to be sufficiently antigenic for the body to develop an efficient defence reaction against them, and for all that we know most spontaneous tumours may not be antigenic at all. Nevertheless, it might be possible either to accentuate existing differences in antigenicity between normal and tumour cells or even to render naturally non-antigenic tumours sufficiently antigenic to provoke an antibody reaction. Alternatively, or perhaps concurrently, the immunological sensitivity and responsiveness of the host might be stimulated. Both lines of investigation are being actively pursued by many laboratories, but are unlikely to produce quick results.

Thus research in cancer chemotherapy, for the present, must have two main approaches, the empirical and the rational. The stage has been reached when the problem has to be approached by means of many different disciplines: biology, cytology, biochemistry, physical chemistry and physics. This has been realized by almost all research institutions, and multi-disciplinary teams are making significant advances in basic biology.

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PROTEIN TURNOVER IN THE CENTRAL NERVOUS SYSTEM

In any consideration of the biochemistry of the central nervous system (that is, the brain and spinal cord), it is necessary to keep constantly in mind the principal features that distinguish this system from other organs of the body. These features are :

(1) Anatomically the brain consists of a heterogeneous and extremely complex arrangement of cells; among these are neurones, or nerve cells, with their long conducting fibres enveloped in a multi-layered membrane, the myelin sheath ; this sheath is peculiar to nerve fibres in its complexity, although its basic structure appears to be similar to that of cell membranes in general, consisting as it does of alternate layers of protein and fatty material.

(2) In gross chemical composition, the brain is characterized by a high content of lipid (fatty) material.

(3) In spite of the fact that the brain has a large blood supply, many substances of low molecular weight that are in the blood, in particular most of the amino acids, gain access to the brain only with difficulty, in contrast to the ease with which they penetrate into other tissues ; in consequence, so far as these substances are concerned, the brain is a partially isolated compartment of the body.

The nerve cells are susceptible to injury from many causes, such as attack by viruses, nutritional deficiencies and the action of chemical poisons. Such injuries frequently cause damage to the myelin sheath and when this happens, owing to the very limited capacity for repair possessed by the nerve cells, the damage tends to be progressive and to produce permanent disability. It is very probable, however, that disorders of brain function may not arise only from gross anatomical damage of this kind ; they may also result from more subtle derangements of the biochemical processes within the nerve cells. It is therefore of the first importance that these processes, as they occur in the normal nerve cell, should be thoroughly understood, and this article deals with one aspect of the problem, namely the metabolism in the nerve cell of proteins and amino acids.

Protein turnover rate

It is a general feature of the proteins of the body that they are not in a static condition but are continually undergoing processes of synthesis on the one hand and breakdown or specific utilization on the other. During the period of growth there must obviously be a net gain in synthesis, but when the adult condition is reached synthesis and breakdown are balanced so that a steady, though still dynamic, state is reached. The rate at which the total process operates is the protein turnover rate ; a measure of this can conveniently be obtained by studying the rate of incorporation of a radioactively labelled amino acid into a protein and in some cases the rate of disappearance of the protein so labelled. Turnover rates thus determined are found to vary greatly both for different organs and for individual proteins ; thus they are high for the proteins of the liver, where metabolic processes are extremely active, and low for the protein collagen, the function of which is chiefly structural.

Adult mammalian brain contains 10 per cent or more of total protein, calculated on the fresh weight of the organ. If the rate of uptake of an amino acid, for instance glycine labelled with radioactive carbon, into the total brain protein is measured, either in a homogenate of brain tissue or in the whole animal, high values are obtained, which indicate a considerable degree of metabolic activity. This result itself is of interest ; taken alone, however, it gives no more than an overall picture of protein metabolism in the brain and does not greatly help in the more subtle analysis of the process that is required. For this it is necessary to study the turnover rates of the different types of protein in the nerve cell separately.

A step towards such an analysis can be taken by utilizing the different solubility properties of the proteins of the nerve cell. Most of these proteins are soluble in water but not in organic solvents ; this water-soluble fraction, derived chiefly from the cell sap and the contents of the subcellular particles, includes the enzymes that are responsible for catalysing the biochemical reactions of the cell. By contrast, much of the protein of the myelin sheath of the nerve fibre is soluble in a mixture of chloroform and methyl alcohol but not in water ; it owes this property to the fact that, in the sheath, it is combined in a complex with fatty material. It is reasonable to regard the water-soluble proteins as being those primarily involved in active metabolic processes in the cell while the chloroform-soluble protein is presumably concerned with preservation of the integrity of the myelin sheath. By a simple procedure, therefore, it is possible to divide the proteins of the nerve cell into two groups, each with a different type of function, and to study the behaviour of each group separately.

Metabolism of brain proteins

Workers in the Council's Neuropsychiatric Research Unit were among the first to make a systematic study of the biosynthesis of water-soluble brain proteins (Gaitonde and Richter, 1953, 1956) ; by the use of methionine labelled with radioactive sulphur, they were able to demonstrate that the synthetic process followed a pattern similar to that found in other metabolically active organs of the body. These results were confirmed and extended in the United States by Lajtha and his colleagues (1957) and by Waelsch (1962) in experiments utilizing amino acids labelled with radioactive carbon as the indicator of protein synthesis. These experiments therefore indicated nothing to differentiate the mode of synthesis of water-soluble brain proteins from that prevailing for similar proteins in other tissues.

The first indication that the turnover rate of the lipoprotein of the myelin sheath was quite different from that of the water-soluble proteins was provided by the experiments of Cohn, Gaitonde and Richter (1954). In these experiments rats were injected with radioactively labelled amino acids and the rate of incorporation of these into the brain proteins was measured ; it was apparent from these results that the immediate incorporation into grey matter (that is, nerve cells not enveloped in a myelin sheath) was much greater than that into the lipoprotein of the sheath itself. Even more striking results were obtained later in long-term experiments by Davison (1961) and by Davison and Gregson (1962), in which examination of the proteins was postponed for periods of up to 324 days after administration of the radioactively labelled amino acid; at

the end of these long periods radioactivity had completely disappeared from the water-soluble proteins but still persisted in the lipoproteins of the myelin sheath. The conclusion, therefore, was quite clear that this contained protein with a turnover rate so low that it could be regarded for practical purposes as metabolically inert. It is reasonable also to conclude that this metabolic inertia of part of the protein of the myelin sheath is closely related to the restricted ability of the central nervous system to restore the myelin sheath once it has been damaged.

Another group of proteins in the nerve cell that has received special attention is that of the phosphoproteins ; these can be studied by labelling with radioactive phosphorus as shown by Rossiter (1955), and the fact that the phosphorus has a very rapid rate of turnover indicates that the phosphate group must be intimately concerned with the metabolism of the cell. Evidence was obtained by Heald (1962) that the phosphoproteins of nerve cells were probably located in the cell membrane, and he also found that the rate of turnover of phosphorus was increased by electrical stimulation ; these two observations suggest strongly that the phosphoproteins play a part in the transfer of inorganic ions across the cell membrane. It may well be that the role of phosphoproteins in ion transport across membranes is not confined to nerve cells, but the observations of Heald on the effects of electrical stimulation suggest that in these cells a transport mechanism involving phosphoproteins may be of special importance.

From what has been said so far it will be seen that, apart from the remarkable metabolic inertia of part of the protein of the myelin sheath and the possibly special significance of phosphoproteins in ion transport across the cell membrane, protein turnover is generally similar in the nerve cell to that in actively metabolizing tissues. There is, however, one major respect in which the metabolism of proteins and amino acids, particularly in its relations with carbohydrate metabolism, shows special characteristics in the nerve cell. This peculiarity of the brain is presumably due to two facts : (1) its limited ability to store carbohydrate in the form of glycogen, and (2) its relative isolation from the rest of the body owing to the difficulty with which many substances, including most amino acids, pass into it from the blood.

The brain is almost entirely dependent on glucose as a source of energy, a fact which is dramatically demonstrated by the convulsions and coma that result from deprivation of glucose in hyperinsulinism, whether spontaneous or deliberately produced in the treatment of certain types of mental illness. Direct utilization of glucose for energy production in the brain follows the course of oxidation through the tricarboxylic acid cycle, which is generally characteristic of cells, and under normal conditions this is the way in which the nerve cells derive their energy. In recent years, however, a number of workers (Winzler *et al.*, 1952; Sky-Peck, Pearson and Visser, 1956; Beloff-Chain *et al.*, 1955) have shown, by studying the fate in the nerve cell of glucose labelled with radioactive carbon, that only a relatively small part of the glucose undergoes this direct oxidation; as much as 75 per cent of the glucose carbon retained in the brain may be used for the formation of amino acids *in vivo* (Vrba, Gaitonde and Richter, 1962).

Some of these amino acids become incorporated into the cell proteins in the normal course of protein synthesis, but a large proportion remains free ; indeed the high concentration of free amino acids in the nerve cell is one of

the characteristics that differentiate this cell from those of other tissues. Moreover, it is important that the amino acids that are formed in the largest amount from glucose are glutamic and aspartic acids, because enzymic pathways exist in the nerve cell through which these amino acids can be oxidized and thus serve as a source of energy. We may therefore regard the unusually large extent of conversion of glucose into amino acids in the brain as subserving two functions: first, it ensures a readily available supply of amino acids for the synthesis of brain protein in spite of the inability of the brain to take up most amino acids from the blood ; secondly, the free amino acids in the nerve cell provide a reserve source of energy which may compensate for the limited ability of the cell to store carbohydrate in the form of glycogen.

The metabolic reactions involving glucose and amino acids that have been described as occurring in nerve cells are not specific to these cells, but there can be no doubt that they play a much larger part in the central nervous system than elsewhere ; thus the rate of conversion of glucose into amino acids is 10–20 times greater in the brain than in the liver (Roberts, Flexner and Flexner, 1959). The discovery of this difference in metabolic pattern from that characteristic of other tissues is encouraging in that it opens the way to more detailed analysis of the special features of brain metabolism ; as this analysis proceeds we may hope for a better understanding not only of the biochemical basis of normal brain function but of the deviations therefrom that may underlie disorders of the central nervous system.

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EPIDEMIOLOGICAL RESEARCH IN PSYCHIATRY

Epidemiology has been defined in several ways, perhaps most simply as the study of the distribution of disease. Epidemiologists have always been concerned with statistics; their basic research technique is to count cases of a particular disease and to calculate rates of occurrence of the disease at specific ages in defined populations. When significantly different rates are found in different populations, this prompts a search for factors that may be relevant to this difference. Subsequent surveys, prospective studies, or therapeutic investigations are then carried out to test whether such factors are of aetiological importance.

Studies of this kind were instrumental in establishing a better understanding of the causes of communicable diseases such as cholera, plague, malaria and typhoid fever and led to a large measure of control of these diseases through improved sanitation and other prophylactic measures long before potent remedies for them were available. Epidemiological studies also drew attention to the relationship between particular deficiencies in the diet and diseases such as scurvy, pellagra, beri-beri and goitre. In many cases epidemiological research enabled the source of an illness to be identified with sufficient accuracy to permit therapeutic intervention, even though the precise mode of production of the disease was only unravelled years later.

Today, the classical methods of census and survey, of calculating incidences and of seeking associated factors which may prove to be of aetiological significance are still widely used—for example, in massive field trials of anti-poliomyelitis vaccines. Because the military services have to deal with large, precisely enumerated populations whose fighting efficiency depends upon maintaining a high standard of health, epidemiology has played a major role in military medicine: it contributed to the control of tetanus and typhoid infections in the first World War, and of typhus, infective hepatitis and malaria in the second. In both wars, however, it came to be recognized, although belatedly, that psychological disorders were among the commonest causes of illness in the armed forces. In the Royal Air Force, for example, neurotic breakdown under stress was sufficiently common to require special investigation. Here epidemiological studies were able to disentangle not one but several contributory factors. Inherited predisposition was responsible for breakdown under slight stress, early in the operational tour; the existence of different degrees of strain in different occupations was illustrated by the greater incidence of breakdown among gunners and wireless operators, who had long periods of waiting and watching, than among bomber pilots and navigators, who were fully occupied throughout a long flight; while the effect of a high casualty rate among fellow airmen was found to be one of the most important contributory factors. This research which Reid (1948) carried out in the Royal Air Force showed that even in 'functional' psychiatric illness, where there is no infective agent and no organic disorder, it is possible to identify factors in the day-to-day environment of the population at risk which will contribute to the occurrence of emotional breakdown.

Prevalence of psychiatric illness

In the years between the wars surveys had already been carried out in northern Europe and in North America which gave measures of the prevalence of mental illness in defined populations. These studies were relatively crude and still leaned heavily on the criterion of admission to mental hospital as the means of identifying serious mental illness; but they represented the first attempts to draw on other sources as well as hospital records to ascertain the true prevalence of these disorders. There was a fair measure of agreement in assessments of the prevalence of serious illness (that is, of the psychoses), which was of the order of 5–10 cases per 1000 of the adult population; but with minor psychiatric disorders (neuroses) the counts varied widely, reflecting the lack of uniformity in the criteria for identifying these cases. Neurotic illness is particularly elusive of precise definition, and yet it demands investigation because it contributes largely to the total of disability in the community. This is not merely a recent finding; in the

seventeenth century Thomas Sydenham stated that one-sixth of his patients were hysterical, while in 1733 George Cheyne, in his book entitled *The English Malady*, contended that one-third of all his patients were neurotic.

During the last twenty years there has been a revival of interest in this topic. Since 1948, more than 97 per cent of the British population has been registered with National Health Service general practitioners; this provides access to representative populations on which to base estimates of the incidence and prevalence of neuroses. General practitioners, psychiatrists, epidemiologists and teachers of social medicine have severally addressed themselves to this task, and have reported widely different findings: estimates of patients suffering from neurotic illness have ranged from 5 per cent to 70 per cent of all those attending their general practitioner during a given period of observation.

Reviewing these discrepant findings, Kessel and Shepherd (1962) have pointed out that they tend to reveal more about the doctors' diagnostic habits than about the populations studied: practitioners whose interests lie in the physical manifestations of illness make a diagnosis of psychiatric illness in less than 10 per cent of their patients; those with a special interest in psychosomatic disorders find psychiatric illness in at least 20 per cent, while psychoanalytically orientated practitioners have given estimates of from 40 to 70 per cent. It is possible to reduce this wide variation in findings by introducing clearly stated definitions of psychiatric disorder for this purpose, and by requiring that the diagnoses should be based on actual observations rather than upon subjective inference; in British studies which have complied with these requirements the annual prevalence rate for psychiatric disorders has been found to vary between 6 and 12 per cent of the adult patients.

Two recent North American studies, carried out in New York City (Srole *et al.*, 1962) and in eastern Canada (D. C. Leighton *et al.*, 1963), have employed much wider definitions of psychiatric disorder and have reported correspondingly higher figures. In the first study only 18·5 per cent of 1660 subjects were judged free from psychiatric symptoms at the time of examination, while 23·4 per cent were rated as showing marked, severe or incapacitating symptoms. In the second study, 37 per cent of the population were judged to be suffering, or to have suffered at some time in the past, from a psychiatric illness severe enough to cause a significant degree of disability. If symptoms judged 'probably indicative of psychiatric disorder', such as certain forms of psychosomatic illness, were included, the number of those suffering from psychiatric disorders increased to 48 per cent of the population studied.

These are startling figures but they cannot be disregarded, because in each case they are the product of painstaking research employing carefully constructed interviews, previously validated psychological questionnaires, and tests designed to reduce the errors attributable to the subjective judgment of the psychiatrist. Like most surveys of this kind, each has employed its own methods and criteria, so that comparisons of findings are not possible; but each has provided valuable information by showing the different incidence of psychiatric disorders in different subsections of the populations studied. In New York, the lowest socio-economic group were particularly liable to mental illness; in contrast to the findings of many earlier studies it was shown that immigrants do not necessarily have a higher rate of mental disturbance—this occurs only among immigrants

who are also poor. In the study carried out by Leighton and his colleagues communities which were shown by objective sociological indices to be in a state of social disintegration were also found to have exceptionally high rates of psychiatric disorder.

In the present stage of development of epidemiological studies in psychiatry much work remains to be done on the improvement of techniques of inquiry, so that cases can be identified with greater reliability; only then will large-scale comparative studies begin to yield meaningful results. Already, however, studies carried out in relatively small defined populations have added to our knowledge. For example, a one-year survey of the incidence of psychiatric illness in a South London group practice enabled Kessel and Shepherd (1962) to demonstrate that the prevalence of neurotic illness does not reach a peak in early adult life (as studies based on the numbers of out-patients attending psychiatric clinics had previously seemed to demonstrate) but continues to manifest itself in older patients.

This was one instance where epidemiological methods have contributed to a better understanding of the natural history of a disease. Another instance can be found in the literature of research on the epidemiology of schizophrenia. A pioneer study in Chicago by Faris and Dunham (1939) suggested that schizophrenic illness occurred with exceptional frequency among people living in city slums and in members of the lowest socio-economic groups. Other research workers confirmed this finding and the argument gained ground that conditions of life in these harsh environments contributed to the aetiology of schizophrenia. More recent studies, however, carried out in Worcester, Massachussets, (Gerard and Houston, 1953) and in Bristol (Hare, 1956) suggested that the reason why a large proportion of young schizophrenics are found in the poorer parts of cities and in the less favoured occupations might be their own social and economic decline—a consequence rather than a cause of their illness. Members of the Council's Social Medicine Research Unit have now confirmed that the apparent association between schizophrenia and low social class is due to decline in the patient's status, and that their social condition is not a characteristic of their families (Goldberg and Morrison, 1963).

Cross-cultural surveys of mental illness

If it is true that factors in the social environment play an important part in the onset and outcome of mental illness, then one could hope that surveys carried out in markedly contrasting cultural settings would help to identify social factors which tend to prevent or cause such illness. While this is true in theory, there are formidable methodological difficulties to be overcome both in the identification of cultural variables and in the accurate diagnosis of psychiatric conditions. An interesting example of such surveys is provided by two investigations carried out in Formosa by Lin, who had been trained in the traditions of German psychiatry. The first was a survey of 20 000 persons in three different communities carried out in the immediate post-war years, and it revealed an incidence of 3·1 per 1000 for psychoses; this figure is well within the range found in European studies, but the survey also showed the extreme infrequency of senile psychoses and of psychopathy in this Chinese society (Lin, 1953). Fifteen years later Lin carried out a second investigation in the same areas, where the population had now more than doubled. The repeat survey showed little change

in the incidence of psychosis but a definite increase in cases of neurosis, especially marked among the expatriates from the mainland of China—a finding which has directed attention to the stresses peculiar to this group.

Quite recently A. H. Leighton and his colleagues (1963) have reported a joint United States and Nigerian enterprise in which the methods of field survey elaborated by Leighton in North America have been translated and applied to Nigerian urban and rural populations. This pioneer enterprise has served primarily as an exercise in research method; its data have been presented with many reservations but they show that West Africans have rates of neurosis and psychosomatic disorders nearly as high as those found in Canada, and that these rates are significantly higher (in women, but not apparently in men) in communities which have undergone rapid social change.

Cohort studies

A technique which has been fruitfully used in epidemiological research has been to identify a large number of cases of a condition, or of subjects at risk, and then to observe this ' cohort ' over a period of time. Perhaps the most outstanding cohort study of recent years has been the one conducted by Douglas, director of the Council's Unit for the Study of Environmental Factors in Mental and Physical Illness, who drew a random sample of some 5000 of the children born in Britain during one week in March 1946. Douglas' helpers have been periodically collecting information about these children, their parents and their environments. His publications (Douglas and Blomfield, 1958; Douglas, 1964) have so far been concerned with physical growth and health and academic progress. Already his reports have demonstrated that adverse social factors can outweigh a child's natural ability during his years of schooling. This cohort is now being used to study social and personal factors related to delinquent behaviour in adolescence.

A similar technique was used by Kidd (1963) in Edinburgh, at the Council's Unit for Research on the Epidemiology of Psychiatric Illness, in a prospective study of emotional disorders among first-year university undergraduates. He obtained data on their medical and scholastic history, their personal background and their leisure pursuits at the time of their enrolment, using a questionnaire which enabled him to test several hypotheses about factors contributing to psychiatric disorder in students. During the ensuing year he found evidence of emotional illness in 14 per cent of women and in just under 10 per cent of men students. Many of the aetiological hypotheses were not supported by the analysis of the data he obtained; but students who came from a cultural background very different from that of their colleagues, especially Afro-Asian students, showed significantly high rates of psychiatric disorder. An interesting finding was that minor degrees of psychiatric disorder did not appear to have an adverse effect upon students' performance in examinations.

Evaluation of psychiatric services

The techniques of epidemiological inquiry have been widely applied to assessment of the numbers of psychiatric patients admitted to hospital, the duration of their stay as in-patients, and the frequency of readmissions. Interest in this type of research has been quickened by the very considerable changes which have come about in psychiatric practice since 1948. The Mental Health

Acts of 1959 and 1960 have both formalized these changes and encouraged further experiments in new patterns of hospital and community care. Tooth and Brooke (1961) calculated that the decline in the numbers of in-patients in mental hospitals which had begun in 1955 might well continue until, by about 1975, only 1·8 beds per 1000 population would be needed, instead of 3·4 per 1000—the high point reached in 1954. This prediction has been used as the basis for the planning of future mental hospitals, but it has been challenged by several workers (Rehin and Martin, 1963). Brown, Parkes and Wing (1961), of the Council's Social Psychiatry Research Unit, in a study of three London mental hospitals, showed that there were marked changes in the practice regarding admission and discharge between 1951 and 1956. Far more patients were admitted in 1956 and the length of stay was shorter; however, the number of readmissions after discharge also increased markedly, especially in the case of schizophrenia, a condition occurring in a large proportion of in-patients, particularly long-stay patients, in mental hospitals. These patients can be helped by measures of rehabilitation, and Wing, Bennett and Denham (1964) have demonstrated that a small but important proportion can be resettled in the community; but members of the same Unit have also reported studies of schizophrenic patients after discharge from mental hospitals which show that, in the absence of well organized community services, there is a marked liability to relapse, and the burden on the family and community may be considerable. In the most recent study, half of the patients did not follow the course of phenothiazine medication prescribed for them, 56 per cent deteriorated during the follow-up year and 43 per cent required to be readmitted to hospital (Brown *et al.*, 1962; Wing *et al.*, 1964).

Grad and Sainsbury (1963), of the Council's Clinical Psychiatry Research Unit, compared the traditional hospital-based pattern of care in Salisbury with an alternative type of service in Chichester in which patients are frequently visited at home or treated in a day centre, and less often admitted to hospital. Even in Chichester they found that when the patient was a severe burden on the family admission to hospital was still commonly necessary, though less so than in Salisbury. In the short run, the community-based service, in spite of admitting a smaller proportion of the patients referred, appeared to give nearly as much relief to the families of patients as the hospital-based service. Further studies, however, are being undertaken to discover how lasting this relief proves to be.

Surveys of intellectual subnormality

One of the earliest, and in some respects still unsurpassed, surveys of mental subnormality was that of Lewis (1929) who screened urban and rural populations (amounting to 600 000 persons) and established an overall prevalence of 'statutory mental deficiency' of 8·6 per 1000, with a peak of 25·6 per 1000 between the ages of 10 and 14 when the demands of schooling rendered this handicap most plainly visible. Subsequent surveys in Bath, Colchester and Bristol established that severely subnormal children tend to occur in families of normal intelligence while children with higher-grade subnormality occur in families whose mean level of intelligence is lower than normal. This suggests that the more severe cases are the result either of mutations or of damage to the developing foetus, whereas the others are the product of multifactorial inheritance (Roberts, 1952). Studies on mental subnormality appeared to show an association between below-average intelligence and large family size, which led

to the conclusion that the mean I.Q. of the nation must inevitably decline in succeeding generations. However, the nation-wide screening of schoolchildren's intelligence, which was carried out by the Scottish Mental Survey in 1936 and repeated in 1947, belied this pessimistic expectation: in the 1947 survey the mean I.Q. was actually slightly higher than before. These surveys threw much light on the influence of social factors, such as quality of housing and size of family, on children's intellectual development (Scottish Council for Research in Education, 1949, 1953).

One of the most familiar conditions of mental subnormality is mongolism, or Down's syndrome, which is associated with a chromosome abnormality. This condition is discussed in the article on clinical genetics on p. 37, which also describes research on mental retardation associated with genetically determined biochemical defects. This work linking genetics and biochemistry has not only quickened interest in research into the causes of mental subnormality; it is of particular interest for the psychiatric epidemiologist, because it raises the hope that before long it may be possible to use similar techniques in order to identify subjects who have different degrees of inherited predisposition to mental diseases such as schizophrenia.

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SUMMARY OF RESEARCH

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The Ridgeway, Mill Hill, London, N.W.7

(1915)*

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The work of the Institute is generally designed to cover as wide a field as possible in basic non-clinical medical research, and investigations undertaken there are mostly of a long-term character. In some instances, such as the research on the common cold, the work verges on the clinical field; and members of the scientific staff at the Institute commonly collaborate in clinical developments arising from their discoveries. Certain major themes, such as chemotherapy, especially in its biochemical and biological aspects, and virus diseases,

are constantly under study; sometimes, as in the case of the Division of Human Physiology where the main task is to investigate the effects of extremes of temperature on human performance, a fairly closely defined field of research may be pursued; for the rest, the direction that the work takes is largely determined by the particular interests of the senior members of the staff. This principle is at present illustrated by the preoccupation of the Division of Biochemistry with problems of biosynthesis and intermediary metabolism, by the work of the Division of Physiology and Pharmacology on the access to and action on the brain of pharmacologically active substances, and by the numerous investigations into different aspects of immunology which are in progress in various laboratories throughout the Institute.

Although for administrative purposes the Institute is organized in separate Divisions, there is a large measure of collaboration in the attack on problems requiring more than one technique for their solution. Moreover, special tasks such as those relating to biological standards and the epidemiology of influenza, which the Council undertake for the World Health Organization, are interwoven with the normal research activities of appropriate Divisions throughout the Institute. For these reasons, the researches enumerated in the following summary often represent the joint work of members of more than one Division; the summary is, in fact, constructed on a scientific and not on an administrative basis.

Summary of Research

BIOCHEMISTRY

1. Protein biosynthesis:
   (*a*) Initiation of synthesis of RNA polymerase in Krebs ascites tumour cells infected by EMC virus.
   (*b*) Control of protein synthesis in cell-free systems by messenger RNA.
   (*c*) Protein synthesis by isolated reticulocyte ribosomes.
   (*d*) Mechanisms involved in release of protein chains from reticulocyte ribosomes.
   (*e*) Stimulation of protein synthesis in intact rats by thyroid hormones.
   (*f*) Protein synthesis in isolated mitochondria and in mitochondria of whole liver cells.
   (*g*) Synthesis of ferritin by cell-free preparations from rat liver.
   (*h*) Synthesis of specific γ-globulins.
2. Protein structure:
   (*a*) Characterization of the capsid protein of EMC virus.
   (*b*) Structural studies of kinins from blood plasma.
   (*c*) Chemical modification of kinins to produce kinin inhibitors.
   (*d*) Methods for end-group determination of proteins.
   (*e*) Improved micro-methods for nitrogen determination.
   (*f*) Studies on the structure of penicillinase.
3. Nucleic acids:
   (*a*) Study of secondary structure of ribosomal RNA.
   (*b*) Methods for base sequence determination on RNA.
   (*c*) Purification of reticulocyte messenger RNA.
   (*d*) Modification of RNA to induce production of interferon.
   (*e*) Inhibition of RNA synthesis by virus infection of Krebs cells.
   (*f*) Effect of interferon on RNA synthesis in chick embryo cells.
4. Hormones:
   (*a*) Biosynthesis of thyroid hormone and localization of the site of biosynthesis.
   (*b*) Mode of action of thyroid hormones at the subcellular level.
   (*c*) Purification of a neurohormone from the median eminence of the hypothalamus.

1. Metabolism of plasma proteins:
   (*a*) Rates of catabolism of iodine-labelled rat plasma proteins *in vivo* and by the perfused liver.
   (*b*) Properties of transferrins from different species.
   (*c*) Fibrinogen synthesis in induced pyrexia in rabbits.
   (*d*) Equations for calculating catabolic rates of iodine-labelled proteins from iodide data.
   (*e*) A method of measuring albumin and fibrinogen synthesis rates using ^{14}C-labelled carbonate.
   (*f*) Clinical studies of plasma protein turnover in nephrosis, rheumatoid arthritis, myeloma and macroglobulinaemia.
2. Distribution and clearance of urea in man and animals.
3. A combustion technique for measuring ^{14}C- and ^{3}H-specific activities in organic materials.
4. Properties of photographic emulsions in relation to high-resolution electron microscopy.
5. Microdensitometric studies of weight changes during staining of bacilli.
6. Microscopic localization of formazan as an indicator of intracellular sites of oxidation.
7. Euchrysine as a more effective agent for fluorescence microscopy than acridine orange.
8. Collimator localization and counting of ^{125}I.

CHEMOTHERAPY AND PARASITOLOGY

1. Filariasis:
   (*a*) Study of periodicity of microfilariae by transfusion between different hosts.
   (*b*) Incorporation of diethylcarbamazine into cooking salt, to explore the possibility of controlling human filariasis in an endemic area.
   (*c*) Cultivation *in vitro* of the microfilariae of *Wuchereria bancrofti* and of *Litomosoides carinii*.
   (*d*) Electron microscopy of microfilariae.
2. Malaria:
   (*a*) Protective immunity and serology.
   (*b*) Development of resistance to chloroquine in *Plasmodium berghei*.
3. Schistosomiasis:
   (*a*) Suitable laboratory systems for 'screening' schistosomal antigens.
   (*b*) Physico-chemical characterization of antigens.
   (*c*) Analysis of the response of immunized monkeys into cellular and humoral components.
   (*d*) Attempts to produce immunity in monkeys by X-irradiated cercariae.
   (*e*) Investigations of the antigens of *Nippostrongylus muris* and of *Dictyocaulus viviparus* and of the immune responses to these worms.
4. Spirochaetes:
   (*a*) Isolation of muramic acid.
   (*b*) Investigation of the lipid constituents by chromatography.
5. Toxoplasmosis:
   (*a*) Evaluation of direct agglutination and complement fixation tests in toxoplasmosis.
   (*b*) Investigation of mode of spread.
6. Trypanosomiasis:
   (*a*) Analysis of lipid constitution.
   (*b*) Hypersensitivity to puromycin and analogous drugs in some drug-resistant trypanosomes.
   (*c*) Nature and distribution of trypanosomal antigens.
   (*d*) Analysis of the development of drug resistance.
   (*e*) Reproduction of trypanosomes *in vivo*.
   (*f*) Cross-resistances of *T. congolense* to drugs used for cattle trypanosomiasis in Africa.
   (*g*) Kinetics of flagellar movements.
   (*h*) Electron microscopy.

1. Demonstration of antihistaminic properties of steroid glyco-alkaloids of tomatoes and other plants.
2. Search for the factor accessory to 9-oxodec-2-enoic acid in the inhibitory pheromone of the honey bee.
3. Development of methods for the synthesis of tritium-labelled vitamin D.
4. Crystallographic and chemical studies of micrococcin P.
5. Cyclization at cysteine residues in peptides in relation to biosynthesis of some sulphur-containing antibiotics.
6. Specific method for degradation of thiazole-4-carboxylic acids.
7. Ring closure of arylaminomethylene-ketones.
8. Synthesis of plasmalogens.
9. Synthesis of derivatives of muramic acid.
10. Effect of aluminium chloride on benzene.
11. Aromatic chlorination.
12. Electron capture effects of organic compounds in relation to chemical and biological properties.
13. Haemoglobin:
    (*a*) Quantitative electrophoretic analysis in starch gel of haemoglobin systems.
    (*b*) Recombination of sub-units to form new hybrid species.
    (*c*) Separation and characterization of individual globin chains.
    (*d*) Spectroscopic studies by solvent perturbation techniques.

BACTERIOLOGY, BACTERIAL PHYSIOLOGY, ANTIBIOTICS

1. Penicillinase:
    (*a*) Distribution of penicillinase in single cells of *Bacillus subtilis.*
    (*b*) Genetic analysis of penicillinase formation by *Staphylococcus aureus* and *B. subtilis.*
    (*c*) Purification and immunological analysis of penicillinase from *Staph. aureus* and *B. subtilis.*
2. Bacterial cell wall:
    (*a*) Interrelationships between teichoic acid and mucopeptide in cell wall of *Staph. aureus.*
    (*b*) Mechanism of action of penicillin.
    (*c*) Production of soluble mucopeptide by *Micrococcus lysodeikticus* protoplasts.
    (*d*) Structure of mucopeptides of *Clostridium welchii* and *M. lysodeikticus.*
3. Regulation of enzyme synthesis:
    (*a*) Induction and repression of enzyme synthesis in *Pseudomonas.*
    (*b*) Protein turnover in *Escherichia coli.*
4. Isolation and purification of flavin respiratory enzymes in *B. subtilis.*
5. Antibiotics:
    (*a*) Isolation and investigation of new antibiotics from soil bacteria.
    (*b*) Mode of action of streptomycin.
    (*c*) Inactivation of penicillin *in vivo* by plasma protein binding and metabolism.
    (*d*) Comparative evaluation of four phenoxypenicillins in man.
6. Leprosy:
    (*a*) Electron microscopy of mouse leprosy bacillus (*Mycobacterium lepraemurium*).
    (*b*) Multiplication of *M. lepraemurium* in tissue cultures.
    (*c*) Attempts to grow *M. lepraemurium* in cell-free medium.
    (*d*) Attempts to grow human leprosy bacillus (*M. leprae*) in tissue cultures.
    (*e*) Attempts to transmit *M. leprae* to experimental animals; associated histopathological changes.
    (*f*) Chemotherapy of leprosy carried out in Sungei Buloh Leprosarium, Malaysia.
7. Bacterial systematics.

1. Interferon:
   (*a*) Production of interferon in response to foreign nucleic acids.
   (*b*) Mode of action of interferon.
   (*c*) Molecular weight of chick, mouse and monkey interferons.
   (*d*) Clinical tests of interferon in common colds and in viral infections of the eye.
   (*e*) Species specificity of interferon.
   (*f*) Action of actinomycin D on enhancing the growth of some viruses while decreasing the production of interferon.
   (*g*) Ability of nucleic acids from homologous tumours to stimulate interferon production.
   (*h*) Induced tolerance of foreign nucleic acids.
2. Viruses and carcinogenesis:
   (*a*) Induction of tumours by inoculation of vacuolating virus into the cheek-pouch of adult hamsters.
   (*b*) Viral antigens appearing in tumours induced in hamsters by injection of adenovirus type 12.
3. Classification of mouse hepatitis viruses.
4. Epidemiology of ectromelia.
5. Antigenic studies of influenza viruses of man, and related viruses that infect domesticated animals.
6. Morphology and development of respiratory syncytial virus.
7. Resistance of mice to infection with lymphocytic choriomeningitis virus.
8. Antibodies to arboviruses in sera collected from Tunisia.
9. Attempt to cultivate rubella virus.
10. Common cold:
    (*a*) Preliminary tests of vaccines against common cold viruses.
    (*b*) Antigenic studies of respiratory syncytial and common cold viruses.
    (*c*) Physico-chemical properties of common cold viruses.
    (*d*) Effects of para-influenza 2 virus in human volunteers.
    (*e*) Effects of influenza A2 virus in human volunteers.
    (*f*) Antibodies to common cold and related viruses in sera collected from all six continents.
    (*g*) Manner of spread of common cold viruses.
11. Thin-section electron microscopy of respiratory viruses and of the causal agent of lymphogranuloma venereum.
12. Histological study of pathogenic and oncogenic effects of adenoviruses.
13. Pathogenesis of lymphocytic choriomeningitis.

IMMUNOLOGY

1. Fate of radioactively labelled antigens in relation to antibody production and immune paralysis.
2. Mechanisms of specific immune paralysis by simple chemicals and by purified protein antigens.
3. Development of immunological responsiveness in Rhesus monkeys during foetal life.
4. Tissue transplantation:
   (*a*) 'Typing' of homograft donors for compatibility.
   (*b*) Induction of tolerance in adult animals.
   (*c*) Chemistry of transplantation antigens.
5. Lymphoid system and lymphocytes:
   (*a*) Functions of thymus.
   (*b*) Changes in lymph nodes in delayed-type hypersensitivity and in secondary response.
   (*c*) Immunological performance of lymphocytes in diffusion chambers *in vitro*.
   (*d*) Life span of immunologically competent cells.
6. Electron microscopic studies of immune haemolysis.
7. Auto-antibody production against components of the gastro-intestinal tract.

1. Freezing and storage of tissue:
   (*a*) Pharmacology of protective agents.
   (*b*) Grafting of long-term frozen corneas.
   (*c*) Techniques for identification of grafted cells.
2. Selective exchange of serum proteins between mother and foetus in the Rhesus monkey.
3. Collection and extraction of human urinary erythropoietin.
4. Large-scale extraction of renin from rabbit kidneys.
5. Cytology of the pituitary tumours occurring in the course of toxicology experiments on rats.
6. Surface charge of tumour cells.
7. Analysis of donation and acceptance of electrons by carcinogens.
8. Erythrocyte protein variations among different monkey species.
9. Human haemoglobin variants in relation to incidence of malaria.

PHYSIOLOGY AND PHARMACOLOGY

1. Perfusion of drugs through particular compartments of the cat's cerebral ventricles.
2. Sites of action of tubocurarine for the various effects produced by its perfusion through the cerebral ventricles.
3. Relationship between the abnormal seizure discharge produced in the hippocampus by tubocurarine and by myoclonus.
4. Analysis of the hyperglycaemia produced by adrenaline perfused through the cerebral ventricles or subarachnoid space.
5. Release of adrenal medullary hormones by minute doses of bradykinin and angiotensin.
6. Functional organization in the superior colliculi.
7. Interaction of evoked potentials in the brain stem with background electrical activity—'computer averaging'.
8. Afferent connexions of the uterus to the supra-optic nucleus.
9. Parallel assays of vasopressin and oxytocin in blood on electrical stimulation of discrete points in the hypothalamus.
10. Structure–action relationships in polypeptides.
11. Analysis of the components of the preparatory cardiovascular reflex response during the defence reaction.
12. Effect of extracellular pH on excitable tissue.
13. Studies on kinins: isolation and determination of structure.
14. Formation of histamine by cat tissue.

HUMAN PHYSIOLOGY AND BIOMECHANICS

1. Heat acclimatization in man:
   (*a*) Redesign of acclimatization experiments to achieve constancy of thermal stress.
   (*b*) Changes of peripheral blood flow.
   (*c*) Physiological responses to controlled hyperthermia.
2. Analysis of the physiological results obtained on a high-altitude expedition.
3. Co-operation in physiological work in the Antarctic.
4. Diurnal rhythms in relation to shift work, with special reference to engine-drivers and miners.
5. Functional anthropometric data for the design of equipment for human operation.
6. The biomechanics of human standing and sitting postures and of locomotion.
7. The use of the force analysis platform for the study of complex movements.

1. Advisory and control work for the Ministry of Health (Therapeutic Substances Act) including revision of regulations.
2. Advisory work for the British Pharmacopoeia Commission including preparation of monographs.
3. Standards and reference preparations:
   (*a*) Preparative and assay work towards establishment of 31 international and 12 British national or research standards or reference preparations.
   (*b*) Establishment of 13 international standards or reference preparations.
   (*c*) Standardization of penicillin PAM preparations on behalf of W.H.O. anti-yaws campaign.
4. Control testing of inactivated poliomyelitis vaccine, oral poliomyelitis vaccine, influenza and smallpox vaccines.
5. National and international control of BCG vaccine.
6. Problems relating to the control of diphtheria, tetanus, pertussis and measles vaccines.
7. Collaborative assay to establish reference virus suspensions for control of neurovirulence.
8. Clinical trials of quadruple vaccine (diphtheria, tetanus, pertussis, poliomyelitis) in infants.
9. Clinical trials of response of humans to oral poliomyelitis vaccine.

INSTRUMENTATION AND BIO-ENGINEERING

1. Equipment for the estimation of alcohol in breath.
2. Self-contained devices for continuous slow injection.
3. Diffusion chamber for administering radioactive material at a slow controlled rate.
4. Determination of moisture content of freeze-dried biological standards.
5. Estimation of blood flow to the cerebral cortex.
6. Investigation of the factors influencing the stability of evoked responses.
7. Design modifications and trials on conicycle dust sampler.
8. Development of a fully-automatic patient monitoring system.
9. Work on radio aids for survivors at sea.
10. Use of temperature-sensitive radio pills in extensive field trials, and further development on pH pill.
11. Design of implantable EEG radio transmitter for small animals.
12. Development of very small recording instruments to measure simple environmental and physiological variables on ordinary members of the population.

Research Units

One of the chief means adopted by the Council for the long-term support of research has been the establishment of research units. Such units may be set up to further research into new subjects not yet appropriate for inclusion in the university curriculum or to develop subjects which require support on a scale beyond the resources of a university or hospital, or which have been hitherto neglected; but the principle underlying the establishment of a unit is that opportunity should thereby be provided for a scientist of proven ability to lead a team of investigators working, within fairly wide terms of reference, in a particular field. The majority of units are situated within or in close proximity to a university or hospital, but they are normally quite independent of the host institution both in function and administration.

DEPARTMENT OF CLINICAL RESEARCH

University College Hospital Medical School, London, W.C.1
(1919)

*Director**
E. E. Pochin, C.B.E., M.D., F.R.C.P.

Staff

C. F. Barnaby, Ph.D.
C. J. Edmonds, M.D., M.R.C.P.
D. A. W. Edwards, M.D., M.R.C.P.†
B. M. Jasani, M.Sc.
E. N. Rowlands, M.D., B.Sc., F.R.C.P. (*part-time*)†
K. Shimaoka, M.D.
B. D. Thompson, Ph.D.

The Department has clinical opportunities and laboratory facilities for the study of certain diseases and abnormalities, and for investigating methods of their diagnosis and treatment. Present work is concerned particularly with disorders of the thyroid gland and of gastrointestinal function.

Summary of Research

1. Thyroid function:
   (*a*) Hormone formation in normal and overactive glands, and the concentration of these hormones and other thyroid metabolites in the liver.
   (*b*) Compounds released from the gland during radiation.
   (*c*) Treatment of thyroid overactivity with radioactive iodine and review of possible complications of this form of therapy.
2. Thyroid cancer:
   (*a*) Evaluation of the radioiodine treatment of thyroid cancer, criteria of suitability and indications for completion of treatment.
   (*b*) Assessment of body radiation received during such treatment and of any consequent hazards.
   (*c*) Comparison of metabolites produced by cancer tissue with those from normal or overactive glands.
   (*d*) Investigation of large-area scintillation counters, liquid and solid, particularly for measurements of whole-body radioactivity.
   (*e*) Development of techniques for measurement of low-level radioactive sources, in particular radioactivity of the human body, and for use in tracer studies.

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* Salary of post partly met by permanent endowment from Rockefeller Foundation.
† Dr. Rowlands is director of the Council's Gastroenterology Research Unit at the Central Middlesex Hospital, London, of which Dr. Edwards is also a part-time member.

3. Gastroenterology:
   (*a*) Manometric and cineradiographic studies of achalasia, diffuse spasm and the hypertensive cardiac sphincter.
   (*b*) Manometric and cineradiographic studies on the applied pharmacology of the oesophagus.
   (*c*) Mechanisms concerned in the symptomatology of hiatus hernia and in gastro-oesophageal reflux, aerophagy and vomiting.
   (*d*) Measurement of gastrointestinal pH *in situ*.
   (*e*) Mechanism of anal continence.
   (*f*) Clinical and radiological studies on the effects of treatment of hiatus hernia and achalasia.

DEPARTMENT OF EXPERIMENTAL MEDICINE

Tennis Court Road
and
5, Shaftesbury Road, Cambridge
(1945)

Director
Professor R. A. McCance, C.B.E., M.D., Ph.D., F.R.C.P., F.R.S.

Assistant Director
Miss E. M. Widdowson, D.Sc.

Staff

J. W. T. Dickerson, Ph.D.
G. C. Kennedy, M.B., Ph.D.
L. Lawn, M.D. (*honorarium*)
R. D. Montgomery, M.D., M.R.C.P. (*until Oct. 1963*).
M. J. Purves, M.D., M.R.C.P.
Miss C. W. Rintoul, M.B., M.R.C.P.
D. A. T. Southgate, B.Sc.
Miss M. W. Stanier, D.Phil.
P. D. Weston, B.Sc.

Visiting and Attached Workers

Miss H. M. Bruce, B.Sc. (*M.R.C. grant-holder.*)
Mrs. P. A. Cavell, B.Sc. (*McGill University, Montreal*)
J. J. Cowley, M.Sc. (*University of Natal*)
G. Graham, M.D. (*British American Hospital, Peru*)
A. R. Hamad El Nil, M.B. (*University of Khartoum*)
Miss D. M. Nutbourne, M.B. (*M.R.C. Clinical Research Fellow*)
D. Salaman, B.Sc. (*M.R.C. Scholar*)
E. Skadhauge, M.D. (*University of Copenhagen*)
Mrs. F. Turner, Ph.D. (*University of London*)
J. M. Walshe, M.B., M.R.C.P. (*University of Cambridge*)

The Department is studying certain aspects of metabolism and nutrition, and in particular the changes which take place during growth and in states of undernutrition and disease. The work includes studies of normal infants and adults, of patients and of animals.

Summary of Research

1. The effect of development, undernutrition and rehabilitation on the composition of the body, its tissues and its cells in human beings, pigs, poultry and rats.
2. Effect of handling rats early in life on subsequent development.
3. Hypothalamic regulation of water and energy expenditure and hormone production.
4. Chemotherapy of diabetes insipidus with chlorothiazide.
5. Relation of overnutrition to growth, to diabetes and to renal disease.
6. Treatment of Paget's disease with fluorides.

7. Food, growth and homoeostasis in the neonatal period.
8. Mineral metabolism in the newborn infant.
9. Renal function of infants and animals before and after birth.
10. Development and use of an artificial placenta.
11. Acid-base regulation in the foetus.
12. Active ion transport in foetal membranes.
13. Copper metabolism in man.
14. Pathogenesis and treatment of Wilson's disease.
15. Food absorption at different ages.

RHEUMATISM RESEARCH UNIT

Canadian Red Cross Memorial Hospital, Taplow, Maidenhead
(1958)

Honorary Director
Professor E. G. L. Bywaters, M.B., F.R.C.P.

Staff

Miss B. M. Ansell, M.B., M.R.C.P. (*part-time*)
Mrs. P. C. Brown, M.D.
R. Consden. Ph.D., F.R.I.C.
L. E. Glynn, M.D., B.Sc., F.R.C.P.
E. J. Holborow, M.D.
A. Howard, B.Sc.
G. Loewi, D.M.
J. E. Scott, Ph.D.
D. J. Ward, M.B., M.R.C.P.
Senior Technical Officer: G. D. Johnson, F.I.M.L.T.

Visiting and Attached Workers

R. D. Barnes, M.B. (*Guy's Hospital Endowments Fund Fellow*)
S. K. Biswas, M.B., Ph.D., D.T.M. & H. (*Govt. of West Bengal grant-holder*)
Mrs. K. Bunsch-Welkens, M.D. (*Polish Ministry of Health Scholar*)
H. E. Jasin, M.D. (*Nuffield Foundation grant-holder*)
Mrs. E. Kaklamanis, M.D., Ph.D. (*Empire Rheumatism Council grant-holder*)
Ph. Kaklamanis, M.D. (*Council of Europe Fellow*)
J. R. Topp, M.D., F.R.C.P.Can. (*Canadian Arthritis and Rheumatism Society Fellow*)

The Unit is carrying on both clinical and laboratory investigations on the nature, course and treatment of rheumatic diseases, involving studies of both normal and abnormal connective tissue, with special emphasis on auto-immune reactions.

Summary of Research

1. Changes in connective tissue with age and disease.
2. Use of immunofluorescent methods:
   (*a*) to detect auto-antibodies in human and animal sera;
   (*b*) to study the distribution in the tissues of native and foreign antigens;
   (*c*) to study immune responses at a cellular level.
3. Experimental production of auto-antibodies and auto-immune 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. Results of treatment in rheumatic fever.

CLINICAL ENDOCRINOLOGY RESEARCH UNIT

2, Forrest Road, Edinburgh, 1

(1946)

Director

J. A. Loraine, M.B., D.Sc., F.R.C.P.E.

Staff

E. T. Bell, Ph.D.
G. P. Crean, M.B., M.R.C.P.E.
R. A. Harkness, M.B., Ph.D., M.R.C.P.E.
W. M. Hunter, B.Sc.
Miss F. James, B.Sc. (*until Oct. 1962*)
K. E. Kirkham, Ph.D.
E. Menini, Ph.D.
Miss E. J. Roy, Ph.D. (*until Aug. 1963*)
Miss H. E. C. Cargill Thompson, B.Sc.

Visiting and Attached Workers

J. L. Allen, B.Sc. (*National Women's Hospital, Auckland*)
Professor R. W. Hawker, M.D., Ph.D., F.R.A.C.P. (*University of Queensland*)
W. I. Morse, M.D. (*Dalhousie University, Nova Scotia*)
S. Mukhopadhyay, M.B., Ph.D. (*Colombo Plan Fellow*)
N. Ramaswamy, M.Sc. (*Colombo Plan Fellow*)
Å. Swahn (*Karolinska Institutet, Stockholm*)
Pachara Visutakul, M.B. (*Colombo Plan Fellow*)
G. Winkler, M.D. (*Schering Fellow*)

The main interests of the Unit continue to be the development of quantitative methods for the estimation of hormones and their metabolites in body fluids, the application of these methods to clinical problems, and the relationship of experimental and clinical endocrinology to other medical specialties.

Summary of Research

1. Assay methods for follicle-stimulating hormone (FSH) and luteinizing hormone (LH) with special reference to tests depending on ovarian cholesterol depletion and ovarian ascorbic acid depletion in rats.
2. Assay methods for human chorionic gonadotrophin with special reference to immunological procedures.
3. Effect of urea and formaldehyde on the biological activity of various gonadotrophin preparations with a view to separating FSH from LH.
4. Renal clearance of gonadotrophins in human subjects and in animals.
5. Effect of various substances on pituitary function in human subjects as judged by urinary gonadotrophin assays.
6. Content of thyroid-stimulating hormone (TSH) in human pituitary tissue and separation of pituitary TSH from LH (with Dr. Anne Stockwell-Hartree, University of Cambridge).
7. Investigation into the ' long-acting ' and ' short-acting ' TSH activity of human serum.
8. Estimations of serum TSH levels and of blood protein-bound iodine (PBI) in patients with thyroid endocrinopathies (with Dr. W. J. Irvine, Royal Infirmary, Edinburgh).
9. Tibial test for growth hormone with special reference to the effect of pituitary inhibitors.
10. Assay methods for oestrogens in body fluids with special reference to measurements in blood and to the group determination of such compounds.
11. Various clinical applications of assays of blood and urinary oestrogens, including studies on normal pregnancy, pre-eclamptic toxaemia, renal clearance in health and disease and the effect of hospital care and parturition (with Dr. M. G. Kerr, Simpson Memorial Maternity Pavilion, Edinburgh).
12. Metabolism of radioactive progesterone in human subjects.
13. Assay methods for urinary progesterone metabolites.
14. Effect of a synthetic progestogen on adrenocortical function in guinea pigs and in humans.
15. Hormonal interrelationships during the normal menstrual cycle.
16. Effect of age and parity on hormone excretion in normal pregnancy (with Dr. D. V. I. Fairweather, Royal Victoria Infirmary, Newcastle upon Tyne).
17. Effect of anti-ovulatory compounds on pituitary, ovarian and adrenal function in human subjects with special reference to the progestational compounds and the dithiocarbamoyl-hydrazine derivatives.

18. Effect of *retro*progestational compounds on hormone excretion in patients with 'incapacitating' dysmenorrhoea.
19. Hormonal interrelationships in abnormal gynaecological conditions with special reference to cystic glandular hyperplasia, endometrial carcinoma and the Stein-Leventhal syndrome (with Dr. D. V. I. Fairweather and Dr. D. G. Millar, Royal Victoria Infirmary, Newcastle upon Tyne, and Dr. D. Charles and Dr. W. Barr, Western Infirmary, Glasgow).
20. Effect of gonadal stimulators, e.g. clomiphene (MRL-41), on endocrine function in infertile patients and in male subjects (with Dr. D. Charles and Dr. W. Barr, and with Dr. G. L. Foss, Bristol General Hospital).
21. Hormonal studies in placental insufficiency and hyperemesis gravidarum (with Dr. D. V. I. Fairweather, Dr. D. Charles and Dr. W. Barr, and with Dr. Jean Ginsburg, Charing Cross Hospital Medical School, London).
22. Relationship of vaginal cytology to hormone assays in patients with threatened and habitual abortion (with Dr. Helena E. Hughes, formerly of Royal Victoria Infirmary, Newcastle upon Tyne).
23. Relationship of endocrinology to gastroenterology with special reference to:
    (*a*) Effect of hypophysectomy and hormone administration on the growth and parietal cell population of the stomach in rats.
    (*b*) Therapy of gastroenterological diseases with adrenocorticotrophic hormone and corticosteroids.
    (*c*) Effect of operative stress on endocrine function in patients subjected to gastroenterological surgery.
    (*d*) Effect of hormones on gastric secretion in human subjects.
    (*e*) Hormone excretion in patients with liver disease (in collaboration with the Gastrointestinal Unit, Western General Hospital, Edinburgh).
24. Relationship of endocrinology to nutrition with special reference to the effect of malnutrition and re-feeding on hormone excretion (with Dr. G. F. M. Russell, Maudsley Hospital, London).
25. Relationship of endocrinology to rheumatology with special reference to the treatment of patients with rheumatoid arthritis with adrenocorticotrophic hormone (in collaboration with the Rheumatic Unit, Northern General Hospital, Edinburgh).

ATHEROMA RESEARCH UNIT

Western Infirmary, Glasgow, W.1

(1962)

Director

B. Bronte-Stewart, M.D., M.R.C.P.

Staff

T. B. Begg, M.B., M.R.C.P.
C. J. W. Brooks, Ph.D.
Miss L. M. Hanaineh, B.Sc.
J. W. Kerr, M.B., M.R.C.P.
B. R. Knowles, M.B., M.R.C.P.E.
W. D. Mitchell, A.H-W.C.(Edin.), A.R.I.C.
L. E. Murchison, M.B.
R. Pirrie, M.B., M.R.C.P.E. (*part-time*)
A. S. Truswell, M.D., M.R.C.P.

The activities of this Unit are being directed towards the study of metabolic factors associated with ischaemic heart disease and other forms of occlusive vascular disease. The influence of such factors as the diet, physical exercise and other environmental variables will receive particular attention.

Summary of Research

1. Gastro-intestinal lipolytic activity in ischaemic heart disease.
2. Influence of bile acids on cholesterol and lipoprotein metabolism.
3. Abnormalities of serum lipid transport in atheroma.
4. Viscometry of blood and of related non-Newtonian fluids.
5. Interrelationships between platelet aggregation and chylomicrons, β-lipoproteins and other macromolecular substances.
6. Histamine metabolites in the urine in allergic asthma.
7. Metabolic effects of salicylate in experimental diabetes mellitus.
8. Spectroscopic studies of molecular conformation and hydrogen bonding.
9. Applications of thin-layer and gas–liquid chromatography in biochemical analysis.

BODY TEMPERATURE RESEARCH UNIT

Department of the Regius Professor of Medicine, Radcliffe Infirmary, Oxford

(1954)

Honorary Director

Professor Sir George Pickering, M.D., F.R.C.P., F.R.S.

Staff

K. E. Cooper, M.B., M.Sc.

W. R. Keatinge, M.B., Ph.D.

Attached Workers

E. Atkins, M.D. (*Yale University*)

W. I. Cranston, M.D., M.R.C.P. (*Radcliffe Infirmary*)

J. A. Downey, M.D., D.Phil. (*University of Manitoba*)

E. S. Snell, M.B., M.R.C.P. (*University of Oxford*)

The Unit is concerned with body temperature regulation, the means by which temperature regulation is altered during fever and the effects of body cooling in man.

Summary of Research

1. Site of action of bacterial and endogenous pyrogens.
2. Reaction between bacterial pyrogens and leucocytes.
3. Nature of endogenous pyrogens.
4. Location and mode of response of central temperature receptors.
5. Studies of patients with abnormalities of temperature regulation.
6. Mechanism of contraction of arterial smooth muscle.

OBSTETRIC MEDICINE RESEARCH UNIT

University of Aberdeen Medical School, Foresterhill, Aberdeen

(1955)

Honorary Director

Professor Sir Dugald Baird, M.D., D.Sc., F.R.C.O.G., D.P.H.

Honorary Deputy Director

A. M. Thomson, M.B., B.Sc., D.P.H.

Staff

W. Z. Billewicz, M.Sc.

P. S. Brown, B.M., M.R.C.P.

Mrs. A. M. Finlayson, B.A. (*part-time*)

G. W. Horobin, B.Sc.(Econ.)

F. E. Hytten, M.D., Ph.D.

R. Illsley, Ph.D.

J. C. Kincaid, B.Sc.

A. I. I. Klopper, M.B., Ph.D., M.R.C.O.G.

D. J. Oldman, B.A.

D. B. Paintin, M.B., M.R.C.O.G. (*until May 1963*)

Attached Workers

Miss J. Aitken-Swan (*M.R.C. grant-holder*)

Miss A. Anderson, M.B., D.Obst.R.C.O.G. (*M.R.C. grant-holder*)

I. Cooke, M.B., M.R.C.O.G. (*University of Sydney research grant-holder*)

K. J. Dennis, M.B., M.R.C.O.G. (*University of Aberdeen*)

T. S. Khosla, M.Sc. (*University of Aberdeen*)

Miss M. Leith, B.H.Sc. (*University of Toronto; Rotary International Fellowship*)

A. C. Turnbull, M.B., F.R.C.O.G. (*University of Aberdeen*)

The Unit collaborates with the Department of Midwifery and Gynaecology, Aberdeen University, in research on the problems of maternity and family life and of gynaecology. There are two main divisions: (*a*) epidemiology and sociology, and (*b*) clinical physiology and endocrinology.

Summary of Research

EPIDEMIOLOGICAL STUDIES

1. Causes of perinatal death.
2. Obstetrical implications of maternal height and weight and of gain in weight during pregnancy.
3. Anaemia and oedema during pregnancy.

SOCIOLOGICAL STUDIES

1. Social and obstetrical background of physically and mentally handicapped children.
2. Educational attainment, intelligence and health of school children, with reference to their birth record and the social background (with support from and in collaboration with the Association for the Aid of Crippled Children).
3. Growth and mortality in children in a rural African village (in collaboration with the Council's laboratories in the Gambia).
4. Social mobility and migration, with special reference to their effects on vital statistics.
5. Social influences in the aetiology of carcinoma of the cervix.

CLINICAL PHYSIOLOGY AND ENDOCRINOLOGY

1. Changes in body composition during pregnancy and the puerperium.
2. Volume and composition of liquor amnii.
3. Blood volume and anaemia in pregnancy.
4. Physiology and excretion of the steroid sex hormones, and levels of excretion in normal and abnormal pregnancy.
5. Renal function during pregnancy and its endocrinological background.
6. Endocrinological aspects of gynaecological abnormalities and of abortion, including the effects of treatment with hormones.
7. Bioassay of gonadotrophins.

DENTAL RESEARCH UNIT

Dental School, Lower Maudlin Street, Bristol, 1

(1961)

Honorary Director

Professor A. I. Darling, D.D.Sc., M.D.S., M.R.C.S., F.D.S.R.C.S.

Staff

R. J. Andlaw, M.S., L.D.S.R.C.S.
A. J. Gwinnett, B.D.S., L.D.S.R.C.S.
D. F. G. Poole, Ph.D.
M. V. Stack, Ph.D.

The Unit is principally concerned with the pathology of dental caries. Present work aims at determining the histological, chemical and physical properties of normal enamel, and the changes in these properties as caries develops.

Summary of Research

HISTOLOGICAL STUDIES

1. Variability of 'normal' enamel structure determined by polarized light and phase-contrast microscopy and by microradiography, and the significance of these results in the understanding of the structural changes of enamel during the earliest stages of caries.
2. Relationship between the structure and arrangement of the components of enamel, such as the packing of crystallites, and the penetration of enamel by various ions and molecules.
3. Changes in enamel structure induced artificially with acids and chelating agents compared with changes occurring in natural caries.
4. Separation and microscopic examination of living cells of the enamel organ of rats, with particular reference to the ameloblasts (with Mr. J. P. Fletcher, Department of Dental Medicine, Bristol).

CHEMICAL STUDIES

1. Initial simultaneous release of carbon dioxide and soluble organic material from enamel powder treated with acids and the significance of this in relation to caries.
2. Tryptic digestion of the organic component of enamel in different stages of development.
3. Separation and identification of acids produced by mixtures of saliva and various foodstuffs using chromatography and electrophoresis.
4. Nature of the cariostatic effects of certain ions such as fluoride and various phosphates.

PHYSICAL STUDIES

1. Crystal properties of enamel.
2. Permeability and compressibility of enamel and its mechanical functioning when subjected to stress (with Dr. D. C. Berry, Department of Dental Surgery, Bristol).

GROWTH STUDIES

1. Relationship between age and dimensions of developing permanent teeth, together with a consideration of the effects on growth of certain pathological factors.
2. Dental characteristics and tooth replacement patterns in lower vertebrates (with Mr. J. S. Cooper, Department of Dental Surgery, Bristol).

ELECTRO-PHYSIOLOGICAL STUDIES

Functional characteristics of pulpal nerves in rats (with Mr. N. R. Thomas, Department of Dental Medicine, Bristol).

TUBERCULOSIS RESEARCH UNIT

Medical Research Council Laboratories, Holly Hill, London, N.W.3

(1948)

Director

P. M. D'Arcy Hart, C.B.E., M.D., F.R.C.P.

Staff

Wallace Fox, M.D., F.R.C.P.
Miss J. F. Heffernan, M.B., D.P.H.
A. B. Miller, M.B.
Miss Christine Miller (Mrs. Manning), B.M. (*part-time*)
D. N. Mitchell, M.D. (*part-time*)

The Unit is adjusting its work to meet the present pattern of tuberculosis—in decline in Britain but still a very serious and continuing problem in many developing countries. Statistically controlled clinical trials of the value of different chemotherapeutic agents and methods have been undertaken in Britain and overseas (notably in India and East Africa, where the Council has scientific responsibility for the trials), and associated problems studied. The national trial of the value of measures of specific immunization in tuberculosis continues. The investigations of the Unit have been extended to certain methods of treatment of thoracic carcinoma, to the epidemiology of non-tuberculous mycobacterial infections in Britain, and to the aetiology of sarcoidosis. The Director also works part-time in the National Institute for Medical Research on laboratory problems of tuberculosis and leprosy. The Unit co-operates actively with the Council's Statistical Research Unit and the Unit for Research on Drug Sensitivity in Tuberculosis, and representatives of these three units visited Hong Kong to advise the Government on the establishment of a tuberculosis research group.

Summary of Research

1. Chemotherapy in tuberculosis:
   (*a*) Chemotherapy of pulmonary tuberculosis with pneumoconiosis (in collaboration with the Miners' Chest Diseases Treatment Centre, South Wales).
   (*b*) Chemotherapy of tuberculosis practicable in East Africa:
   (i) the use of thiacetazone with isoniazid;
   (ii) the use of these two drugs intensified by adding streptomycin initially.
   (*c*) Treatment of pulmonary tuberculosis in South India (in collaboration with the World Health Organization, the Indian Council of Medical Research and Madras State Government at the Tuberculosis Chemotherapy Centre, Madras), in particular:
   (i) improved prevention of isoniazid toxicity;
   (ii) effectiveness and practicability of supervised intermittent chemotherapy.
   (*d*) Possible side-effects from thiacetazone with isoniazid in various racial communities.
2. Protection afforded by BCG and vole bacillus vaccines in adolescence and early adult life in Britain.
3. Specificity of the tuberculin reaction in Britain; epidemiology of sensitivity to avian and human tuberculins.
4. Treatment of certain types of carcinoma of the bronchus by surgery compared with radiotherapy.
5. Aetiology of sarcoidosis in young adults; mechanism of the Kveim skin test.
6. Prevalence of primary drug resistance in tuberculosis in Britain (for comparison with the 1955–56 Medical Research Council survey).
7. Prevalence of drug resistance in patients applying for treatment in Hong Kong chest clinics.

UNIT FOR RESEARCH ON DRUG SENSITIVITY IN TUBERCULOSIS

Department of Bacteriology, Postgraduate Medical School of London, Ducane Road, London, W.12

(1954)

Honorary Director
D. A. Mitchison, M.B.

Staff

Miss Anna Csillag-Szekely, Ph.D.
Miss Jean M. Dickinson, L.R.C.P. & S.I.
M. J. Lefford, M.B.
J. B. Selkon, M.B. (*until Nov. 1962*)

The Unit studies the bacteriological aspects of mycobacterial infections in man. Particular attention is given to bacteriological methods in the control and epidemiology of tuberculosis, to factors such as drug resistance which influence the results of chemotherapy, and to the classification of mycobacteria. The Unit works in close association with the Council's Tuberculosis Research Unit and Statistical Research Unit.

Summary of Research

1. Centralized bacteriological services for:
   (*a*) Trial of long-term chemotherapy in the control of pulmonary tuberculosis with pneumoconiosis.
   (*b*) Trials of new methods of chemotherapy in East Africa.
   (*c*) International trial of chemotherapy regimens for pulmonary tuberculosis in 21 countries (in co-operation with the International Union against Tuberculosis).
   (*d*) National survey of the prevalence of drug resistance in tubercle bacilli from newly diagnosed patients with pulmonary tuberculosis.

2. Participation with the World Health Organization, the Indian Council of Medical Research and the Madras State Government in the work of the Tuberculosis Chemotherapy Centre, Madras :
   (*a*) Estimation of the virulence in guinea pigs of strains isolated from patients in clinical trials.
   (*b*) Estimation of the frequency with which patients and their contacts are infected with the same strains of tubercle bacilli.
3. *In vitro* and animal experiments on intermittent chemotherapy for tuberculosis.
4. Classification and life-cycle of mycobacteria.

UNIT FOR RESEARCH ON THE EXPERIMENTAL PATHOLOGY OF THE SKIN

The Medical School, University of Birmingham, Birmingham 15

(1952)

Director

C. N. D. Cruickshank, M.D., D.I.H.

Staff

M. Baxter, M.Sc.
A. O. T. Charles, Ph.D.
E. A. Fairburn, M.D., M.R.C.P. (*honorary*)
Professor P. G. H. Gell, M.B. (*honorary*)
K. R. Haye, M.B., B.Sc.
Mrs. E. A. Hell, B.A.
G. I. Horsfield, M.B.
J. H. Morris, Ph.D.
B. C. Tate, M.B.E., M.D., F.R.C.P. (*honorary*)
M. D. Trotter, Ph.D.
H. J. Yardley, Ph.D.

Senior Technical Officer: J. R. Cooper, F.I.M.L.T.

Attached Worker

Mrs. T. Webb, B.Sc. (*University of Birmingham 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 upon the study of various metabolic processes *in vitro* and upon clinical and laboratory studies of fungus infection and of allergic reactions.

Summary of Research

1. Metabolic pathways in skin (studied by various methods, including the use of radioactive isotopes), particularly the fatty acid metabolism of skin and its inhibition by plant amino acids.
2. The effects of hormonal, chemical and physical agents on the metabolism and cytology of skin *in vitro*.
3. The cytology of normal and abnormal skin in tissue culture including the behaviour of pigmented and non-pigmented dendritic cells as revealed by time-lapse cine-micrography and electron microscopy.
4. Chemical structure of the allergenic glycopeptides of the dermatophytic fungi, their cross-reactions, and the effects of modifying their chemical structure on the ' immediate ' and ' delayed ' reactions.
5. The mechanism of delayed hypersensitivity in guinea pigs: studies on delayed reactions to simple chemical groups attached to homologous (guinea pig) albumin with special reference to the specificity of their cross-reactions with related compounds.
6. Mechanism of keratin digestion by dermatophytic fungi.
7. Factors initiating regeneration of epithelium after skin injury.
8. Polysaccharides of the dermis and epidermis: a study of the effects of hormones and vitamin A upon the synthesis of mucopolysaccharides.
9. Role of the basophil and mast cell in allergic reactions.
10. Investigation of materials suspected of causing industrial skin disease.

METABOLIC DISTURBANCES IN SURGERY RESEARCH UNIT

Department of Urology, The General Infirmary, Leeds, 1

(1957)

Director

Professor L. N. Pyrah, C.B.E., Ch.M., M.Sc., F.R.C.S.

Staff

N. A. Edwards, B.Sc.
F. W. Heaton, Ph.D., A.R.I.C.
Mrs. B. A. Heppell, B.Sc.
A. Hodgkinson, Ph.D., F.R.I.C.
L. Martindale, B.Sc.
R. G. G. Russell, B.A.

The Unit is concerned with the study of metabolic disturbances in surgical conditions, particularly those in the field of urology.

Summary of Research

1. Renal lithiasis:
   (*a*) Diagnosis of primary hyperparathyroidism; assay of parathyroid hormone in urine.
   (*b*) Nature of the defect in idiopathic hypercalciuria.
   (*c*) Metabolism of oxalic acid with particular reference to oxalate stone formation.
   (*d*) Factors influencing the mineralizing propensity of urine.
2. Magnesium metabolism:
   (*a*) Effect of endocrine glands on magnesium metabolism.
   (*b*) Relationships between magnesium and other electrolytes.
   (*c*) Relation between extracellular, intracellular and skeletal magnesium.

GASTROENTEROLOGY RESEARCH UNIT

Central Middlesex Hospital, Park Royal, London, N.W.10

(1961)

Director

E. N. Rowlands, M.D., B.Sc., F.R.C.P.*

Staff

A. M. Connell, M.B., B.Sc.
D. A. W. Edwards, M.D., M.R.C.P.*
T. D. Kellock, M.D., M.R.C.P. (*honorary*)
J. J. Misiewicz, M.B., B.Sc.
T. Smith, B.Sc.
K. B. Taylor, D.M., M.R.C.P. (*until Jan. 1963*)

Attached Workers

J. Fletcher, M.B., M.A. (*Central Middlesex Hospital*)
S. F. Phillips, M.D., M.R.A.C.P. (*University of Melbourne*)
Miss M. L. Ramorino, M.D. (*University of Rome*)

The Unit is mainly concerned with the study of normal and disordered motility of the digestive tract, and with the role of immune reactions in certain gastro-intestinal diseases.

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* Dr. Rowlands and Dr. Edwards work also in the Department of Clinical Research, University College Hospital Medical School, London.

Summary of Research

1. Development of telemetering devices for measuring pressure and pH.
2. Development of systems for automatic data analysis of motility records.
3. Achalasia and oesophageal spasm.
4. Gastro-oesophageal reflux.
5. Gastric motility in anorexia nervosa.
6. Motility of small intestine in health and disease, studied with radio pills.
7. Measurement of gastro-intestinal transit using ^{51}Cr.
8. Mechanism of colonic symptoms.
9. Mechanism of anal continence.
10. Effect of diet on gastric acidity in patients with duodenal ulcer.
11. Measurement of antibodies to various antigens implicated in diseases of the intestine.
12. Auto-immune phenomena in pernicious anaemia.

EXPERIMENTAL HAEMATOLOGY RESEARCH UNIT

Wright-Fleming Institute of Microbiology, St. Mary's Hospital Medical School, London, W.2

(1946)

Director

Professor P. L. Mollison, M.D., F.R.C.P. (*part-time*)

Staff

M. Adinolfi, M.D.
S. Ardeman, B.M.
P. Barkhan, M.D., Ph.D. (*honorary*)
Miss M. Booth, D.Phil. (*until Mar. 1963*)
I. Chanarin, M.D., B.Sc., D.C.P. (*honorary*)
Miss P. E. Crome, M.B.
N. C. Hughes Jones, B.M., Ph.D.
Miss M. J. Polley, B.Sc.

Visiting Workers

A. A. Ballas, M.D. (*University of Thessaloniki*)
Miss E. Rochna Viola, M.D. (*Comision Nacional de Energia Atomica, Buenos Aires*)

The Unit's aim is to link experimental and clinical studies in the field of haematology.

Summary of Research

1. Serological differences between 7*S* and 19*S* γ-globulin antibodies.
2. Identification of complement components with specific antisera.
3. Kinetics of Rh antigen–antibody reactions *in vitro*.
4. Purification and iodination of the blood group antibody anti-A.
5. Purification and iodination of rabbit anti-human γ-globulin.
6. Nature of the 'normal incomplete cold antibody'.
7. Splenic destruction of Rh-sensitized and of heated red cells.
8. Folic acid requirements in pregnancy (in collaboration with the Obstetric Unit at St. Mary's).
9. Urinary formiminoglutamic acid excretion, serum *Lactobacillus casei* activity and liver folic acid content in tests for folic acid deficiency.
10. Chemistry of anti-haemophilic factor.
11. Separation of mitogenic and agglutinating principles of phytohaemagglutinin.
12. Clinical, haematological and biochemical investigations of abnormal haemoglobins.

BLOOD GROUP RESEARCH UNIT

Lister Institute, Chelsea Bridge Road, London, S.W.1
(1946)

Director
R. R. Race, Ph.D., F.R.C.P., F.R.S.

Staff
Miss E. J. Gavin, B.Sc.
Mrs. F. J. Greenwood, B.Sc. (*until Mar. 1963*)
J. F. Moloney, B.Sc.
Miss R. A. Sanger, Ph.D.
Miss P. A. Tippett, Ph.D.

Visiting Workers
Miss C. P. Bingham, B.S. (*Johns Hopkins Hospital, Moore Clinic Student Fellowship*)

The Unit is searching for unrecognized blood group antigens and studying the inheritance of those already known. These antigens are of importance both in the cartography of the human chromosomes and because they may be the cause of haemolytic disease of the newborn and of adverse reactions to transfusion.

Summary of Research

1. Xg system: genetics and serology of the X-linked antigen Xg^a (with Dr. T. E. Cleghorn, S. London Transfusion Centre, Sutton, and Dr. A. Cahan, Knickerbocker Biologics Inc., New York).

2. Use of Xg in attempts to improve the map of the X chromosome, by testing many families with other X-borne conditions such as glucose-6-phosphate dehydrogenase deficiency, colour blindness, haemophilia, Christmas disease, Duchenne's type of muscular dystrophy, familial hypogammaglobulinaemia, familial hypophosphataemia, ectodermal dysplasia, renal diabetes insipidus, gargoylism, angiokeratoma, keratosis follicularis, ichthyosis vulgaris, congenital deafness, spastic paraplegia and pseudoglioma. (In collaboration with Dr. A. Adam and Dr. C. Sheba, Tel-Hashomer, Israel; Professor M. Siniscalco, University of Naples; Professor J. B. Graham, University of North Carolina; Professor V. McKusick, Johns Hopkins University; Professor A. Motulsky, University of Washington; Dr. J. R. O'Brien, Portsmouth and Isle of Wight Pathological Service; Dr. Helen Blyth, University of Leeds; Dr. V. Dubowitz, University of Sheffield; Professor S. Borelli, University of Munich; Dr. L. N. Went, Academisch Ziekenhuis, Leiden; Dr. G. Fraser, Royal College of Surgeons of England; Dr. J. M. Optiz, University of Wisconsin; Dr. G. I. C. Ingram, St. Thomas' Hospital; Dr. J. Harrison, General Hospital, Birmingham; Dr. R. M. Hardisty, The Hospital for Sick Children, Great Ormond Street, London; Dr. D. Wise, Johns Hopkins University; Dr. J. H. Renwick, University of Glasgow, and many others.)

3. Use of Xg in the study of abnormalities of the X chromosome: abnormalities in number, as in Turner's and Klinefelter's syndromes, and in structure, e.g. deletions and isochromosomes. (In collaboration with the Clinical Effects of Radiation Research Unit; Professor P. Polani, Guy's Hospital; Dr. M. Fraccaro, Pavia; Dr. J. Lindsten, Stockholm; Professor McKusick, Johns Hopkins University; Dr. J. H. Edwards, University of Birmingham; Dr. A. Frøland, University of Copenhagen; Dr. M. A. Ferguson-Smith, University of Glasgow.)

4. Rh system: investigation of the 'D-like' antigen and of samples from people who have the antigen D on their red cells and anti-D in their serum.

5. Lutheran and Auberger systems: investigation of the association between the Auberger groups and a gene which inhibits the antigen Lu^b.

6. P system: investigation of the rare antigen P^k found so far only in Finnish people (with Dr. A. E. Kortekangas, Turku).

7. Examination of sera suspected of containing new blood group antibodies (sent from many parts of the world, but chiefly from the United States).

8. Investigations on twins (with Dr. E. T. O. Slater and Mr. J. Shields, Psychiatric Genetics Research Unit, and Dr. J. A. Fraser Roberts, Clinical Genetics Research Unit).

BLOOD GROUP REFERENCE LABORATORY 445

(Administered by the Council for the Ministry of Health since April 1950)

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

Director

A. E. Mourant, D.M., D.Phil., F.R.C.P., F.C.Path.

Deputy Director

K. L. G. Goldsmith, M.B., Ph.D., M.C.Path.

Staff

Miss C. M. Giles, B.Sc.
Miss E. W. Ikin, Ph.D.
Mrs. H. D. Nunn, B.Sc.

Visiting Worker

R. Narayanan, M.B. (*Safdarjang Hospital, New Delhi*)

The Laboratory issues blood grouping sera for the National Blood Transfusion Service and for hospitals in Britain and various laboratories overseas. Assistance is given to laboratories beginning transfusion work, and in particular to those which encounter difficulties arising from local conditions, and short courses of training are given to medical officers. New techniques reported in the literature are investigated and compared with established methods, with a view to their introduction, with or without modification, into routine practice. Advice is given on clinical and scientific problems and lines of research emerging from the cases concerned are followed up and investigated.

Summary of activities

1. Provision of blood grouping sera of both human and animal origin for the National Blood Transfusion Service, the Armed Forces and Colonies, and for other users in the United Kingdom and overseas.
2. Investigation of clinical and immunological problems involving blood groups referred by other laboratories, and research into matters of interest arising from these cases, in particular previously unknown or unusual blood groups.
3. Full blood grouping of staff panels from other laboratories, for use as controls.
4. Full blood grouping of donors for the National Panel of Donors, maintained for use in transfusion cases requiring blood of rare types.
5. Full Rh grouping of all recruits to the London Red Cross Blood Transfusion Service.
6. Checking of the specificity of antisera submitted by other laboratories before they are put into use as routine grouping sera; research into the properties of new and unusual antibodies found in such sera.
7. Testing of specimens received in connection with anthropological surveys.
8. Full blood grouping of foetuses in relation to marrow replacement.
9. Detailed immunological examination of proposed donors and recipients of organ and tissue grafts, including an attempt to develop compatibility tests.
10. Investigation of antibodies against human leucocytes and platelets.
11. Investigation of methods of preparing and standardizing antisera against human globulin and its components.
12. Examination of the blood group antigens of human red cells which have been rapidly frozen and then thawed.
13. Examination of maternal blood for foetal red cells.
14. Investigation of the Gm and Inv serum group systems.

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15. Attempts to produce new and improved types of haemagglutinating antisera in rabbits.

16. Investigation of the comparative immunology of primates.

17. Production of antibodies labelled with fluorescent dyes, and investigations using these antibodies.

18. Making of standard preparations of blood grouping antisera.

19. Investigation of plant haemagglutinins (lectins).

20. Service as the World Health Organization International Blood Group Reference Laboratory.

BLOOD COAGULATION RESEARCH UNIT

Churchill Hospital, Oxford
(1959)

Director

R. G. Macfarlane, C.B.E., M.D., F.R.C.P., F.R.S (*part-time*)

Staff

Mrs. E. Bidwell, Ph.D.
Miss R. Biggs, M.D., Ph.D.
B. M. Rush, M.B., M.R.A.C.P. (*part-time*)

Visiting Workers

F. Jobin, M.D. (*Canadian Rhodes Scholar*)
J. M. Matthews, M.B. (*M.R.C. Clinical Research Fellow*)
Mrs. J. Matthews, M.R.C.V.S. (*Animal Health Trust Research Training Scholar*)
Miss L. Nahas, M.D. (*British Council Bursar; grants from Research Fund of Institut Butantan, Brazil, and Campanha Nacional de Aperfeicoa Mento de Pessoal de Nivel Superior Capes*)
Mrs. S. Tuchinda, M.D. (*Siriraj Hospital, Bangkok; Thailand Government grant-holder*)

The Unit is studying the mechanism of normal coagulation and any abnormalities which may cause excessive haemorrhage or thrombosis. The object of this work is to gain knowledge which may assist in preventing the occurrence of these abnormalities and to improve the methods of treatment of patients in whom they have already occurred.

Summary of Research

1. Investigation and diagnosis of cases of abnormal bleeding due to deficiency of clotting factors or the presence of anticoagulants, and study of their aetiology, including congenital factors.

2. Production of concentrated Christmas factor in collaboration with the Blood Products Laboratory of the Lister Institute, Elstree, Herts., and its application in the treatment of Christmas disease.

3. Attempts to reduce or remove the antigenic properties ot antihaemophilic globulin derived from animal blood.

4. Purification of blood clotting factors (with Mr. J. R. P. O'Brien and Dr. M. P. Esnouf, Biochemical Department, Radcliffe Infirmary, Oxford).

5. The mechanisms of the interaction of blood clotting factors and the nature of their activity.

6. Structure of thrombi as they occur *in vivo* and the factors which favour or oppose their formation (with Professor Sir George Pickering).

ABNORMAL HAEMOGLOBIN RESEARCH UNIT*

University Department of Biochemistry,
Tennis Court Road, Cambridge

(1963)

Honorary Director
H. Lehmann, M.D., Sc.D., M.R.C.P., F.R.I.C.

Staff
D. Beale, B.Sc.
Miss D. Davies, B.Sc.

Visiting Workers
Mrs. S. Tuchinda (*Siriraj Hospital, Bangkok; Thailand Government grant-holder*)
P. K. Sukumaran (*Tata Memorial Institute, Bombay*)

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.

Summary of Research

1. Incidence of abnormal haemoglobins and abnormal pseudocholinesterase types in European populations.
2. Preservation of red cells in liquid nitrogen; storage of labile haemoglobins such as Hb-H and Hb-Bart's in liquid nitrogen.
3. Testing blood spots for abnormal haemoglobins and different pseudocholinesterase types for medico-legal purposes.
4. Treatment of sickle-cell anaemia (in collaboration with clinical departments at St. Bartholomew's Hospital).

VISION RESEARCH UNIT

Institute of Ophthalmology, Judd Street, London, W.C.1

(1962)

Director
H. J. A. Dartnall, D.Sc., F.R.I.C.

Staff
J. N. Lythgoe, Ph.D.
J. D. Moreland, Ph.D.
Mrs. P. H. Silver, Ph.D.
D. Y. Wang, Ph.D. (*until Jan. 1962*)

The Unit is concerned with the pigmentary, photochemical and photoreceptoral bases of vision in man and animals, and with all matters affecting the qualities of light incident on retinas. The visual pigments are studied both after extraction into solution and also in their native photoreceptor environment. The latter is necessary because, although the pigments are more conveniently studied in solution, their behaviour after irradiation is not necessarily the same as in the photoreceptors. Observations on the pigments in action are provided by cognate work on the visual characteristics of the relevant animals, including man. There are three main objectives in these studies: (*a*) to explore the varieties of visual pigments present in animals and to relate the findings with the light environment of the relevant animals; (*b*) to elucidate the structures and chemical reactions of these substances, and (*c*) to measure and interpret visual characteristics.

* This Unit was first established at St. Bartholomew's Hospital, London, and moved to Cambridge in February 1964.

Summary of Research

1. Visual pigments in vertebrates, and correlation with light environment (arrangements have been made in various parts of the world for specimens of retinas and eyes to be sent for examination, and a limited amount of field work is carried out using skin diving techniques to obtain fishes from known depths in the seas).
2. Effects of changing environment, e.g. influence of day length and of water salinity on visual pigments in migratory and non-migratory fish.
3. Visual pigments in rod and cone preparations.
4. Measurement of visual sensitivities with automatic apparatus.
5. Measurement of lens pigmentation.
6. Purkinje's blue arcs.
7. Relationships 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.

TRACHOMA RESEARCH UNIT

Lister Institute of Preventive Medicine, London, S.W.1 and Medical Research Council Laboratories, Gambia

(1956)

Honorary Director

L. H. Collier, M.D.

Staff

W. A. Blyth, Ph.D.
Mrs. H. M. Day, B.Sc.
Miss E. F. Fraser, B.Sc.
Miss D. M. Graham, M.Sc.
P. Reeve, Ph.D.
J. Sowa, M.Sc. (*Gambia*)
Mrs. S. C. I. Sowa, M.B., D.O. (*Gambia*)
Mrs. J. Taverne, Ph.D.

Attached Worker

Miss G. Sampson, B.Sc. (*Lister Institute, Elstree*)

At the Lister Institute, research is directed to the production and assay of experimental trachoma vaccines, the replication and serological reactions of trachoma and related micro-organisms, and the study of experimental infections in man and baboons.

In the Gambia, attention is mainly concentrated on field trials of trachoma vaccines, on the early stages of the disease in babies, and on genital tract infections of adults with trachoma/inclusion blennorrhoea agents.

Summary of Research

1. Trachoma and inclusion blennorrhoea agents:
   (*a*) Growth in chick embryos and cell cultures.
   (*b*) Serological reactions and antigenic relationships.
   (*c*) Experimental infections in man and animals.
   (*d*) Methods of purification and preservation.
2. Trachoma vaccine:
   (*a*) Methods of production and assay.
   (*b*) Field trials.
3. Field studies of trachoma:
   (*a*) Clinical aspects.
   (*b*) Epidemiology.
   (*c*) Microbiology.
   (*d*) Relation between trachoma and inclusion blennorrhoea, with special reference to genital tract infection of adults, and infection in the neonatal period.

WERNHER RESEARCH UNIT ON OPHTHALMOLOGICAL GENETICS*

Royal College of Surgeons of England, Lincoln's Inn Fields, W.C.2
(1954)

Honorary Director
Professor Arnold Sorsby, M.D., F.R.C.S.

Staff

J. P. Newhouse, B.Sc.
H. W. Reading, Ph.D.

Attached Workers

A. I. Friedmann, M.B., F.R.C.S. (*Godfrey Robinson Unit, Royal College of Surgeons*)
G. R. Fraser, M.B., Ph.D. (*Godfrey Robinson Unit, Royal College of Surgeons*)
G. A. Leary, F.S.M.C. (*Royal Eye Hospital, London*)

The Unit is studying the genetic aspects of ophthalmology, particular attention being paid to retinal dystrophy and the components of ocular refractions.

Summary of Research

1. Inherited retinal dystrophy in the rat: studies on metabolism, with particular reference to enzyme systems and protein synthesis.
2. Experimental degeneration of the retina in the rabbit, with particular reference to the significance of the role of -SH radicles.
3. Clinical studies:
   (*a*) Classification of the causes of blindness found in schools for the blind.
   (*b*) Chromatography studies on the urine of children with genetically determined affections.
4. The refraction of the eye:
   (*a*) The components of ocular refraction in man, and their genetic behaviour in the rabbit and in man with reference to their development during growth.
   (*b*) The scope of ultrasonography in the clinical measurement of the ocular components.

OTOLOGICAL RESEARCH UNIT

National Hospital for Nervous Diseases,
Queen Square, London, W.C.1
(1944)

Director
C. S. Hallpike, C.B.E., M.B., F.R.C.P., F.R.C.S., F.R.S.

Staff

S. K. Bosher, F.R.C.S.
Miss M. R. Dix, M.D., F.R.C.S.
J. D. Hood, D.Sc., F.Inst.P.

Attached Workers

J. Angell James, M.D., F.R.C.S. (*Bristol Royal Hospital; part-time, honorary*)
J. P. Moss, D.Orth., F.D.S. (*University College Hospital; part-time, honorary*)

The work of the Unit is devoted to clinical and laboratory studies of the ear and the VIII nerve system in man, including its anatomy, physiology and pathology and the clinical manifestations of disease. New methods and equipment are being developed for clinical and laboratory investigation of the auditory and vestibular apparatus.

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* Financed from Alexander Pigott Wernher Memorial Trust funds.

Summary of Research

1. Clinico-pathological investigations, including histological examination of the temporal bones and central nervous pathways in vertigo, deafness and other organic derangements of cochlear and vestibular function.
2. Clinical, anatomical and electro-acoustic investigations of the loudness recruitment phenomenon and other aspects of cochlear function in health and disease of the VIII nerve system.
3. Physiological studies of the semicircular canal system in man.
4. Experimental studies on the physiology and pathology of vertigo.
5. Biochemical studies of the labyrinthine fluids.

WERNHER RESEARCH UNIT ON DEAFNESS*

King's College Hospital Medical School,
Denmark Hill, London, S.E.5
(1949)

Director
T. S. Littler, Ph.D., F.Inst.P.

Honorary Clinical Director
T. E. Cawthorne, F.R.C.S.

Staff
J. J. Knight, Ph.D., A.Inst.P.
C. G. Rice, B.Sc.
M. Wipat, M.B., B.Sc., D.L.O., F.R.C.S.E.

Attached Workers
Professor W. Burns, M.B., D.Sc. (*Charing Cross Hospital Medical School, London*)
Surg. Cdr. R. R. A. Coles, M.B., D.L.O., R.N.

The Unit was established by the Alexander Pigott Wernher Memorial Trustees, to investigate medical and physical aspects of deafness. It collaborates with the Post Office Research Station and the Ministry of Health in research on the development of hearing aid and audiometry equipment, and is associated with the Ear, Nose and Throat Department of King's College Hospital in clinical investigations.

Summary of Research

1. Testing of hearing by bone conduction as a diagnostic procedure and the standardization of bone conduction audiometry.
2. Improvement in hearing aid equipment including the use of binaural hearing devices.
3. Special hearing aid requirements of children in schools for the deaf (in collaboration with L.C.C.).
4. Speech audiometry in children and adults.
5. Continuous recording threshold audiometry.
6. Application of pulse signal technique in audiometry and hearing aid research.
7. Audiometric surveys in industrial situations and hearing-conservation programmes (in collaboration with the National Physical Laboratory).

* The work of this unit is financed from Alexander Pigott Wernher Memorial Trust funds, with the exception of the audiometric surveys the cost of which is borne by the Ministry of Pensions and National Insurance.

RADIOBIOLOGICAL RESEARCH UNIT

Harwell, Nr. Didcot, Berks.

(1947)

Director

J. F. Loutit, C.B.E., D.M., F.R.C.P., F.R.S.

Deputy Director

R. H. Mole, B.M., F.R.C.P., M.C.Path.

Staff

D. W. H. Barnes, B.M., F.C.Path.
J. H. Barnes, M.Sc., A.R.I.C.
A. L. Batchelor, Ph.D.
G. W. Bazill, B.Sc.
B. A. Bridges, Ph.D.
Mrs. R. Brown, M.D. (*until July 1963*)
R. S. Bruce, D.Phil. (*until Aug. 1963*)
T. E. F. Carr, B.Sc.
Miss S. S. Eccles, B.Sc.
E. P. Evans, Ph.D.
H. J. Evans, Ph.D.
C. E. Ford, D.Sc.
J. Godfrey, Ph.D. (*part-time; until July 1963*)
Mrs. J. Gray, B.Sc.
Mrs. A. Harrison, Ph.C.
G. E. Harrison, D.Sc., F.Inst.P.
E. V. Hulse, M.D., M.C.Path.
Miss H. Johnstone, B.A. (*until Jan. 1963*)
J. Kahn, Ph.D.
D. R. Lucas, M.D., M.C.Path.
Miss M. F. Lyon, Ph.D.
T. W. McSheehy, B.Sc.
H. S. Micklem, D.Phil.
R. J. Munson, Ph.D.
G. J. Neary, Sc.D.
R. E. Oakey, Ph.D.
B. J. Parsons, Ph.D.
D. G. Papworth, B.Sc.
Miss R. J. S. Phillips, B.Sc.
J. St.L. Philpot, M.A., B.Sc.
C. E. Purdom, Ph.D.
J. R. K. Savage, Ph.D.
D. Scott, B.Sc.
A. G. Searle, Ph.D.
Miss J. E. Stanier, D.Phil.
S. R. Stitch, Ph.D.
L. A. Stocken, D.Phil., F.R.I.C. (*part-time*)
O. A. Trowell, M.D., F.R.S.E.
F. S. Williamson, M.A. (*until Aug. 1963*)

Senior Technical Officer: E. J. Lucas, M.B.E.

Senior Executive Officer: F. D. Bushell

Librarian: L. C. Manwaring, A.L.A.

Visiting and Attached Workers

J. Chayen, D.Sc. (*Royal College of Surgeons*)
Mrs. O. Djordjevic (*Institute of Nuclear Sciences, Yugoslavia*)
G. C. Easty, Ph.D. (*Chester Beatty Research Institute*)
Surg.-Capt. P. W. Edmondson, M.R.C.S., M.C.Path., R.N. (*Royal Naval Medical School, Alverstoke*)
R. H. Gilman, B.S. (*National Institutes of Health Fellow*)
J. E. Harris, M.D. (*Ontario Cancer Institute; E. Freyman Research Foundation Fellow*)
W. W. Kirkby, M.B.E., B.Sc., M.R.C.V.S. (*Royal College of Surgeons*)
G. G. Rhoads, B.A. (*Harvard Medical School*)
Miss S. J. Strich, D.M. (*Maudsley Hospital, London*)
Col. C. E. Stuart, M.B., B.A.O., M.C.Path., D.T.M. & H., R.A.M.C. (*Royal Army Medical College*)
Lt.-Col. J. H. Wilkins, B.Sc., M.R.C.V.S., R.A.V.C. (*War Office*)

The Unit is studying the action of ionizing radiations on living cells. Particular attention is being paid to fast neutrons and to X- and γ-radiation.

Summary of Research

PHYSICAL STUDIES

1. Detailed dose measurements for neutron and γ-ray exposures of biological specimens by means of a reactor (BEPO).
2. Neutron dosimetry with special reference to intercomparison of different techniques and calibrations between laboratories.
3. Improvements in centrifuges, homogenizers and electrophoretic separators.

CHEMICAL STUDIES

1. Alkaline earths in heparin.
2. Oxidant produced by irradiation or alarm in mice, thought to be hydroperoxide derived from unsaturated fatty acids.
3. Mechanism of inhibition of ribonuclease by α-angelica lactone and of related reactions.
4. DNA polymerase, in particular a comparison of mammalian and bacterial polymerase.
5. Search for media which will keep more than 30 per cent of extruded amoeba nuclei alive for more than six minutes.

PHYSIOLOGICAL STUDIES

1. Lenticular lesions of guinea pigs irradiated at low intensity with γ-rays or fast neutrons.
2. Dependence of relative biological effectiveness (RBE) of fast neutrons on mean neutron energy for reduction of testis weight in mice.
3. RBE of fission neutrons for whole-body irradiation of small and large mammals.
4. Availability to man of strontium in cow's milk.
5. Comparison of the specific activity of strontium in cow plasma and its ultrafiltrate.
6. Antiradiation drugs, particularly condensed phosphates and benzene polycarboxylic acids
7. Radiation chimaeras:
   (*a*) Lymphoid aplasia and secondary disease.
   (*b*) Role of thymus in lymphopoiesis.
   (*c*) Serial passage of bone marrow.
   (*d*) Amyloidosis.
8. Comparative study of iso-antigens on lymph node and thymus cells.
9. Effect of oral doses of calcium and/or phosphorus on the retention of stable strontium in man.
10. Effect of calcium status of the diet of rats on the turnover of chronically fed radioactive calcium and strontium.
11. Effect of dietary phosphorus on the metabolism of calcium and strontium in rats (with Dr. K. Kostial, Institute of Medical Research, Zagreb).
12. Factors which influence the absorption *in vitro* of calcium and strontium from the small intestine of the rat.
13. Excretion of intravenously administered calcium and strontium in the rat.
14. Effect of whole-body irradiation on the metabolism and conjugation processes of oestrogen by rat kidney, intestinal mucosa and liver.
15. Effect of high doses of radiation to the exteriorized rat ovary on oestrogen biosynthesis in the rat.
16. Oestrogen biosynthesis by the rat ovary *in vitro* (at selected stages in the oestrual cycle).
17. Capacity of human adrenal and radiation-sterilized human ovary to produce oestrogen.
18. Carcinogenic and other effects of superficial β-radiation in mice.
19. Gastric function after, and conditioning by, whole-body or localized irradiation.
20. Bile salts and changes in intestinal function after irradiation.
21. Age and sensitivity of acute and delayed responses to irradiation, including comparisons between different kinds of penetrating radiation.
22. Quantitative aspects of recovery from whole-body irradiation.
23. Development of a large multicompartmental chamber for fractionated exposures.
24. Modification of delayed effects of whole-body irradiation, especially neoplasia, with variations in parameters of exposure such as fractionation and dose rate.

1. Induction by radiation of chromosome aberrations and the modifying effect of oxygen:
   (*a*) Determination of form of dose-exposure and its dependence on oxygen and on linear energy transfer of radiation.
   (*b*) Importance of highly localized intracellular damage produced by very low energy X-rays.
   (*c*) Dependence of radiation-induced chromosome exchanges on spatial and physiological relationships in the nucleus.
   (*d*) Qualitative similarity of radiation damage produced in the presence and in the absence of oxygen.
2. Comparisons between the modes of action of maleic hydrazide, 8-ethoxycaffeine, nitrogen mustard and radiation in inducing chromosome aberrations, with special reference to the influence of DNA synthesis and cell development stage.
3. Uptake of tritiated thymidine and patterns of DNA synthesis and chromosome replication in animal and plant cells (including meiotic cells).
4. Action of pyrimidine analogues in inducing synchronous cell development, with a view to application in radiation experiments.
5. Growth requirements of pollen tubes from several species of *Tradescantia* grown on artificial media.
6. Cytological and radiation studies on mammalian cells in culture.
7. Factors influencing the radiosensitivity of lymphocytes in organ cultures of lymph nodes: oxygen, temperature, pH, dose rate etc.
8. Factors influencing the radiosensitivity of visual cells in organ cultures of retina: oxygen, temperature, pH, dose rate etc.
9. Uptake of iron and colloidal dyes by the reticulum.
10. 'Paradoxical resistance' of thymus lymphocytes to high doses of radiation, including experiments with organ cultures of thymus.
11. Effects of pH and NaCl concentration on the aerobic glycolysis of organ cultures of lymph nodes and retina.
12. Uptake of fluorescent-labelled albumin by the cells of organ cultures *in vitro* (with Dr. G. C. Easty, Chester Beatty Research Institute).
13. Early histochemical changes in organ cultures of rat liver, with particular reference to lysosomes (with Dr. J. Chayen, Royal College of Surgeons of England).
14. Cytogenetics of leukaemia in human patients.
15. Cytogenetics of spontaneous and radiation-induced neoplasms in experimental animals.
16. Cell population studies in radiation chimaeras of the mouse.

GENETIC STUDIES

1. Effect of radiation dose, intensity and quality on induction of mutations in immature germ-cells of *Drosophila melanogaster*.
2. Genetic effect of ^{14}C in *Drosophila melanogaster*.
3. Methods for detecting and measuring mutation in mice, including the use of skin-grafting and electrophoretic techniques.
4. Induction of genic and chromosomal mutations in mice by neutrons, chronic γ-irradiation and acute X-irradiation, including the effects of dose fractionation.
5. Genetic effects of radiation on fitness of mice competing in populations.
6. Gene action in the mammalian X chromosome.
7. Genetics and development of a number of mouse mutants.
8. Reversions induced by γ-radiation in a strain of *Escherichia coli* (*WP2*) requiring tryptophan.

Dr. L. A. Stocken of the Department of Biochemistry, University of Oxford, who is in receipt of a Council honorarium, is engaged on work of particular interest to the Radiobiological Research Unit.

1. Interference of phosphate transfer in irradiated thymus nuclei.
2. Loss and gain of thiols in irradiated thymic nuclei.
3. Delay in appearance of deoxycytidylic deaminase in irradiated regenerating liver.
4. Inhibition of nucleic acid metabolism in irradiated foetal, young and adult rats.

EXPERIMENTAL RADIOPATHOLOGY RESEARCH UNIT

Hammersmith Hospital, Ducane Road, London, W.12

(1953)*

Director

Miss T. Alper, M.A., M.S.(Ed.), F.Inst.P.

Staff

P. D. Cook, Ph.D. (*until Mar. 1963*)
Miss B. M. Cullen, B.Sc.
B. Dixon, B.Sc.
Mrs. J. D. Eady, B.Sc. (*part-time*)
N. T. S. Evans, Ph.D.
Mrs. S. Hornsey, B.Sc.
J. L. Moore, B.Sc.
J. A. Simmons, Ph.D.
Miss J. E. Taylor, B.Sc. (*until Sept. 1963*)
R. H. Thomlinson, M.B.

Visiting and Attached Workers

W. A. Cramer, B.Sc. (*University of Chicago*)
B. Dalos, M.D. (*F. Joliot Curie National Institute for Radiobiology, Budapest*)
C. Donninger, M.B. ('*Shell*' *Research Ltd.*)
G. Harris, M.R.C.P. (*West Middlesex Hospital*)
M. Iaccarino, M.D. (*Naples*)
R. B. Uretz, Ph.D. (*University of Chicago*)
S. Vatistas, M.D. (*University of Athens*)

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

Summary of Research

1. Modification of electron-spin resonance machine, and preliminary work on signals from amino acids.
2. Post-irradiation modification of radiation effects on micro-organisms, particularly by caffeine and basic dyes.
3. Oxygen enhancement ratios, and variations therein due to post-irradiation treatments; ratios with heavy particle irradiation for micro-organisms and mammalian cells.
4. Survival curves for mammalian cell lines cultured *in vitro* before and after irradiation; development of special techniques for irradiation in aerobic and anoxic conditions, and for exposure to heavy particle irradiation.
5. Survival curves for mouse ascites tumour cells cultured both *in vivo* and *in vitro* before and after irradiation.
6. Effects of X-rays on induction of β-D-galactosidase by *Escherichia coli*; use of this end-point to compare sensitivities of strains which differ in sensitivity to the cytocidal effect of radiation, and response to post-irradiation conditions which affect that sensitivity.
7. Changes in effectiveness of X-rays and neutrons when dose is fractionated, tested on the following systems:
   (*a*) haemopoietic tissues of mice (assay by observing deaths within 30 days);
   (*b*) small intestine of mice (assay by observing deaths within 4 days);
   (*c*) leakage from gut;
   (*d*) growing bone in mouse tails;
   (*e*) transplanted tumours.
8. Improvements in polarographic electrodes for measuring oxygen tension in tissues and in gas streams.
9. Measurements of oxygen tension in human dermis and epidermis, and observations on changes induced by alterations in inspired gas or in local application of rubifacient agents.
10. Measurement of blood flow in rat tumours, using radioactive inert gases.
11. Effects of high-pressure oxygen on tumour sensitivity to radiation, on tumours of different types (e.g. with and without necrotic areas).
12. Effects of reducing oxygen in inspired air 24 hours before irradiating transplanted tumours in rats.

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* A unit with this title was established in 1953. On the resignation of the Director in 1962, Miss Alper took charge of a new unit with the same title, consisting of some members of the existing staff.

13. Development of a technique designed to give quantitative assessment of effects of radiation on tumour bed.
14. Antibody synthesis by spleen cells *in vitro*: mechanism of stimulation by antigen of cells from immunized animals, and radiosensitivity of cells with capacity for stimulation as the end-point.

CLINICAL EFFECTS OF RADIATION RESEARCH UNIT

Western General Hospital, Edinburgh, 4

(1956)

Director

W. M. Court Brown, O.B.E., M.B., B.Sc., M.R.C.P.E., F.F.R.

Honorary Consultant Physician

J. A. Strong, M.B.E., M.B., F.R.C.P.E., F.R.C.P.

Staff

A. G. Baikie, M.B., F.R.C.P.E. (*until Feb. 1963*)
Mrs. J. A. Bond, B.Sc.
Miss K. E. Buckton, B.Sc.
T. N. Calvey, M.B., Ph.D.
D. G. Harnden, Ph.D.
Miss P. A. Jacobs, B.Sc.
D. J. Mantle, M.R.C.S.
Miss I. M. Tough, B.Sc.
E. R. D. Williamson, M.B.

The work of the Unit is particularly concerned with the delayed effects of radiation exposure on man, and with human cytogenetic studies.

Summary of Research

1. The effects of *in vivo* X-ray exposure in man on chromosome damage, and the possible relationship of this to the problem of leukaemogenesis.
2. Cytogenetic structure of human leukaemias, with particular reference to chronic myeloid leukaemia.
3. Chromosome count distribution in relation to ageing.
4. Cytogenetic studies on a random sample of the general population.
5. Viral transformation and chromosome damage.
6. Sex chromosome abnormalities.
7. Organization of a registry of abnormal human karyotypes.

BONE-SEEKING ISOTOPES RESEARCH UNIT

The Churchill Hospital, Headington, Oxford

(1959)

Honorary Director

Dame Janet Vaughan, D.B.E., D.M., F.R.C.P.

Staff

A. T. Andrews, B.A.
G. M. Herring, D.Phil.
Mrs. E. Lloyd, M.Sc.
Miss H. S. M. Macpherson, D.Phil.
Mrs. M. E. Owen, D.Phil. (*on leave at Biology Department, Brookhaven National Laboratory, U.S.A.*)
Mrs. M. C. Williamson, B.A.

Visiting Workers

S. G. Kshirsagar, Ph.D. (*Indian Atomic Energy Agency, Bombay; Colombo Plan Fellow*)
E. Muzii, Dott. (*University of Rome; British Council Scholar*)

The aim of the Unit is to study the effect of bone-seeking isotopes on the skeleton and bone marrow. Current research continues to be directed to certain fundamental physiological problems.

Summary of Research

1. Population kinetics of cells of the osteogenic connective tissue studied by means of labelled compounds, with particular reference to the fact that a proportion of the osteoblasts and preosteoblasts appear to take up tritiated thymidine but do not then divide.
2. Physical characteristics, metal binding properties, carbohydrate composition and structure of the sialoprotein isolated from cortical bone; characterization of other muco-proteins isolated (Dr. A. R. Peacocke, Biochemistry Department, Radcliffe Infirmary, is collaborating in some of these studies).
3. Histochemical and histological character of the surfaces on which plutonium and americium are concentrated.
4. Kinetics of ^{45}Ca and ^{90}Sr metabolism in the rabbit (the accepted formulae for calculating bone turnover appear to require revision).

ENVIRONMENTAL RADIATION RESEARCH UNIT

Department of Medical Physics,
University of Leeds, The General Infirmary, Leeds, 1
(1959)

Honorary Director
Professor F. W. Spiers, C.B.E., D.Sc.

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

Staff
D. Hughes, Ph.D., A.Inst.P., A.M.I.E.E.
M. Kabir, M.Sc.
M. S. Huq, M.S., M.Sc.

Attached Worker
T. R. Overton, Ph.D., A.Inst.P. (*M.R.C. grant-holder*)

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

Summary of Research

1. Potassium content of the human body in normal and pathological conditions, investigated by measuring the γ-ray emission from ^{40}K.
2. ^{137}Cs content of the human body.
3. Measurement of accidentally acquired radioisotopes in the human body.
4. Whole-body retention of γ-emitting radioisotopes.
5. External γ-radiation and cosmic radiation intensities, studied with a semi-automatic, continuously-recording apparatus at a fixed site.
6. Development of an apparatus for the assay of γ-radioactivity in soil and biological specimens.
7. Measurement of β-radioactivity in soil and other materials, and the estimation of the external β-ray dose to superficial tissues.
8. Theoretical and experimental studies on the radiation dosimetry of radioactive materials in bone.
9. Theoretical studies of the mechanism of carcinogenesis, with particular reference to radiation carcinogenesis.
10. Theoretical studies of the aetiologies of auto-immune diseases, with particular reference to the effect of radiation on ageing processes.
11. Measurement of cosmic-ray neutron dose.

RADIOLOGICAL PROTECTION SERVICE

(Jointly with the Ministry of Health)

Clifton Avenue, Belmont, Sutton, Surrey

(1953)

Director

W. Binks, C.B.E., M.Sc., F.Inst.P.

Deputy Director

E. E. Smith, B.Sc., A.Inst.P.

Staff

W. F. Bland, B.Sc., A.Inst.P.
B. L. Davies, B.Sc., A.Inst.P.
M. J. Duggan, B.Sc.
P. L. Entwistle, B.Sc.
B. E. Godfrey, M.Sc., A.Inst.P.
S. G. Goss, B.Sc.
G. Hems, Ph.D.
Mrs. G. D. Parry Howells, Ph.D.
B. E. Jones, B.Sc., A.Inst.P.
H. G. Jones, Ph.D.
T. O. Marshall, B.Sc.
Miss M. J. Minski, B.Sc.
M. C. O'Riordan, B.Sc.
Miss G. M. Pullan, B.Sc.
G. R. Stevenson, Ph.D.
J. Vennart, B.Sc., F.Inst.P.

Senior Technical Officer: S. C. Stephenson, B.Sc.

The aims of the Service are to carry out research 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. 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 for a number of radionuclides.
2. Assistance to the Medical Research 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 members of the public.
3. Assistance to the Radioactive Substances Advisory Committee and its panels and also to various governmental committees in the preparation of codes and regulations for the control of radiation hazards.
4. Participation in the work of the International Commissions on Radiological Protection and on Radiological Units and Measurements.
5. 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 employing punch card techniques for the recording, analysing and processing of the results of tests and of the cumulative totals of radiation exposure of workers.
2. Inspection of departments and sites where radiation hazards may exist, either as a result of normal operating procedures or of accidents.
3. General advisory services regarding the design of radiation departments and the reduction of hazards from new uses of radioactive isotopes, including those arising during waste disposal.
4. Measurement of amounts of various nuclides deposited in the bodies of persons exposed to unsealed radioactive materials, either during normal usages or as the result of accidents.
5. Miscellaneous measurements of environmental radioactivity, e.g. in drinking water.
6. Tests of the effectiveness of protective materials.

1. Improvement of the accuracy of techniques for measuring external radiation received by workers:
   (*a*) Development of new film holder in collaboration with the U.K.A.E.A. to provide a mutually satisfactory film technique for personnel monitoring.
   (*b*) Development of more accurate methods of monitoring all types of ionizing radiations by means of photographic methods—films or track-plates.
   (*c*) Development of equipment for measuring low-energy X-rays.
   (*d*) Response of equipment used for radiation surveys.
2. Development of new techniques for assessing the amount of radioactive material deposited in the body, including whole-body measurements, measurement of radon in breath, and chemical tests of excreta.
3. Measurement of radium body burdens of further persons formerly engaged in the luminizing industry, bringing the total so far studied to about 520 (with Dr. J. T. Boyd, Statistical Research Unit).
4. Investigation of current practice in radium luminizing to determine if there is any relationship between radium in the bodies of workers and in the working environment.
5. Relationship in humans between radium in the body and radon in breath.
6. Investigation of current practice in the use of tritium luminous compound and of mechanisms whereby tritium can enter the bodies of workers.
7. ^{40}K in humans and its relationship to obesity (with Dr. G. R. Wadsworth, Queen Elizabeth College).
8. Levels of ^{137}Cs and ^{131}I in members of the population from nuclear weapon tests.
9. Variations in local γ-ray background due to nuclear weapon tests.
10. Measurement of stable isotope concentrations in organs of the body by neutron activation and other methods, and variation of organ weights with age.
11. Distribution in different organs and retention in the body of organic compounds tagged with ^{14}C and ^{3}H, including observations on humans and experimental animals.
12. Development of solid-state devices for the absolute calibration of very low levels of radioactivity in materials and for α-ray spectrometry, and manufacture of the devices.
13. Development of electronic equipment for radiation measurements, particularly the utilization of transistors.
14. Absorption and scattering of ionizing radiations.
15. Methods of neutron shielding and neutron dosimetry.
16. Investigations on the contamination of aircraft by fall-out fission products.

CYCLOTRON UNIT

Hammersmith Hospital, Ducane Road, London, W.12

(1962)

Director

D. D. Vonberg, B.Sc.

Staff

D. K. Bewley, Ph.D.
G. Burton, B.Sc.
J. C. Clark, B.Sc.
S. B. Field, Ph.D.
A. W. Goolden, M.B., D.M.R.T. (*honorary*)
Miss C. M. E. Matthews, Ph.D.
R. L. Morgan, M.B., B.Sc., D.M.R.T., F.F.R.
C. J. Parnell, B.Sc.
J. Sharp, B.Sc.
D. J. Silvester, Ph.D.
Mrs. J. A. Silvester. B.Sc.
P. C. R. Turner, M.Sc.

Senior Technical Officer: L. C. Baker

Visiting Worker

C. J. Karzmark, Ph.D. (*Stanford University; U.S. Public Health Service Fellow*)

The Unit, which is responsible to the Council's Radiation Facilities (Hammersmith) Committee, has three main functions. These are 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.

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Summary of Research

1. Clinical use of cyclotron-produced radioactive isotopes:*
   (*a*) ^{124}I in the treatment of thyroid disease.
   (*b*) ^{15}O, ^{11}C and ^{13}N in pulmonary and circulatory studies.
   (*c*) ^{72}As, ^{74}As and ^{206}Bi for localization of brain tumours.
   (*d*) ^{18}F in dental studies (in co-operation with London Hospital Dental School) and in studies of bone metastases.
   (*e*) ^{52}Fe in studies of the distribution of erythropoietic tissue in blood disease.
   (*f*) ^{79}Kr for the study of cerebral blood flow (in co-operation with Guy's Hospital Medical School).
2. Investigations associated with the use of cyclotron-produced isotopes:
   (*a*) Effect of irradiation of lymph nodes on the homograft reaction using cyclotron-produced ^{206}Bi attached to denatured protein.
   (*b*) Development of a positron camera for *in vivo* isotope distribution studies.
   (*c*) Comparison of coincidence counting of positron-emitting isotopes and counting with focusing collimators using various isotopes for brain tumour localization.
   (*d*) Studies on the storage of CO_2 in the body using cyclotron-produced $^{11}CO_2$.
   (*e*) Use of an analogue computer in the study of distribution of isotopes in the body and other problems.
   (*f*) Development of a mathematical model to interpret the indicator dilution curve.
   (*g*) Investigation of the concentration of fibrinogen labelled with various isotopes in rat tumours.
3. Investigations associated with the production of radioisotopes by the cyclotron:
   (*a*) Development of new methods of chemical separation of the following isotopes in high specific activity: ^{13}N, ^{18}F, ^{43}K, ^{48}V, ^{52}Fe, ^{52}Mn, ^{64}Cu, ^{72}As, ^{72}Se, ^{79}Kr, ^{90}Nb and ^{110}Ag.
   (*b*) Preparation of labelled compounds with high specific activity.
   (*c*) Absolute standardization of cyclotron-produced isotopes.
4. Variation of relative biological efficiency with dose, linear energy transfer of radiation, and concentration of oxygen, using the method of survival of human kidney cells under α-rays and deuterons of various energies (in collaboration with Dr. G. W. Barendsen of the Radiological Institute, Rijswijk, Netherlands, and members of the Experimental Radiopathology Research Unit).
5. Development of fast-neutron dosimetry.
6. Experiments to determine:
   (*a*) The comparative effect of fast neutrons and 8-MeV X-rays with various fractionation schemes, using the skin of pigs.
   (*b*) The relative biological efficiency of the fast-neutron beam for various biological systems (in collaboration with the Experimental Radiopathology Research Unit).
7. Development of the radiation facilities of the cyclotron by installation and commissioning of apparatus to provide beams of fast neutrons or charged particles and to provide an additional target position for isotope production.
8. Radioactivation analysis with the cyclotron.
9. Use of 8-MeV X-ray and electron beams for radiobiological studies, particularly in relation to protection by anoxia (in collaboration with the Experimental Radiopathology Research Unit and Dr. E. A. Wright and Dr. N. A. Sharples of St. Mary's Hospital, London).

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*Except where otherwise mentioned these studies are carried out in collaboration with medical workers in Hammersmith Hospital and the Postgraduate Medical School.

CLINICAL GENETICS RESEARCH UNIT

Institute of Child Health, The Hospital for Sick Children,
Great Ormond Street, London, W.C.1

(1957)

Director

J. A. Fraser Roberts, M.D., D.Sc., F.R.C.P., F.R.S.*

Staff

C. O. Carter, B.M., M.R.C.P.
Miss M. I. Dunsdon, Ph.D.
R. M. C. Huntley, B.A., B.Ed.
Mrs. J. Slack, B.M., D.C.H. (*part-time*)

Visiting Worker

Miss H. Zoethout, M.D. (*University of Utrecht; British Council Scholar*)

The main work of the Unit falls under two headings: (*a*) the study of genetic and other factors in the causation of developmental abnormalities in man; and (*b*) investigation of the role of inheritance in the causation of common diseases, with some parallel studies on normal human variation.

Summary of Research

1. The aetiology, and especially the genetics, of the common congenital abnormalities, for example congenital pyloric stenosis, spina bifida cystica, congenital heart disease, inguinal hernia, hare-lip and cleft palate and congenital dislocation of the hip.
2. Down's syndrome (mongolism): chromosome studies in relation to family history and maternal age (in collaboration with the Department of Paediatric Research, Guy's Hospital).
3. Childhood muscular dystrophies: serum enzyme levels in known heterozygotes (in collaboration with the Department of Chemical Pathology, The Hospital for Sick Children).
4. Family studies on coronary artery disease, including estimations of serum lipoprotein lipase.
5. Quantitative human variation: physical and mental measurements on a series of twins and their relatives to obtain estimates of degrees of resemblance.
6. The role of inheritance in hypertension and diabetes mellitus.
7. Associations between blood groups and disease.

POPULATION GENETICS RESEARCH UNIT

Old Road, Headington, Oxford

(1958)

Director

A. C. Stevenson, M.D., B.Sc., D.P.H., F.R.C.P.

Staff

A. Barr, M.Sc. (*part-time*)
Miss B. C. C. Davison, M.B., D.P.H., D.Obst.R.C.O.G.
Miss S. A. Goodfellow, B.Sc.
H. A. Johnston, M.B., D.P.H.
I. B. Shine, M.B.

Visiting and Attached Workers

Mrs. Hira Doctor, Ph.D. (*Bombay; W.H.O. Fellow*)
C. B. Kerr, M.B. (*Sydney; Post-Graduate Medical Foundation grant-holder*)

The Unit is concerned primarily with work designed to illuminate the genetic structure of human populations by using 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. Four advice and referral clinics are held monthly in the hospitals of the Oxford Regional Hospital Board.

* Dr. Fraser Roberts is retiring in September 1964 and will be succeeded by Dr. Carter.

Summary of Research

1. Frequency of congenital anatomical abnormalities in different areas of the world and in different ethnic groups: parallel studies in sixteen countries organized on behalf of the World Health Organization.
2. Frequency and clinical and genetic variation of ichthyosis vulgaris in Berkshire.
3. Frequency and clinical and genetic variation of tylosis, epidermolysis bullosa, the ectodermal dystrophies, and alopecia in the Oxford Regional Hospital Board area.
4. Ascertainment of harmful sex-linked traits in the Oxford Regional Hospital Board area; the 'load' on the X chromosome in man.
5. Analysis of population data from the study of a 90 per cent sample of an island.

MUTAGENESIS RESEARCH UNIT

Institute of Animal Genetics, West Mains Road, Edinburgh, 9

(1958)

Honorary Director

Miss C. Auerbach, D.Sc., F.R.S.

Staff

B. M. Cattanach, Ph.D.
C. H. Clarke, Ph.D.
Mrs. M. E. Griffiths, B.Sc.
B. J. Kilbey, Ph.D.
C. Mathew, M.Sc.
B. M. Slizynski, Ph.D.

Visiting and Attached Workers

N. Anwar (*British Council Fellow; Ph.D. student*)
H. G. Kølmark, Ph.D. (*Copenhagen*)
N Loprieno, Dr. Agric. Sci. (*University of Pisa*)
V. J. Royes, M.Sc. (*University of Edinburgh*)

The Unit is engaged in an analysis of the process of mutation, with particular emphasis on factors modifying this process in its various stages.

Summary of Research

1. *Schizosaccharomyces:*
   (*a*) Analysis of the inhibitory action of methionine on mutation.
   (*b*) Analysis of the complex interaction between genetic site, mutagen and plating medium in the production of adenine reversions.
   (*c*) Genetic analysis of the contribution made to reversion rate by suppressor mutations for different genetic sites.
   (*d*) Analysis of the delayed action of nitrous acid by means of colour mutations.
2. *Neurospora:*
   (*a*) Analysis of mutagen specificity by means of differences between loci: in dose response to various mutagens; in response to interaction treatment; in response to temperature during irradiation; in degree of modification by differences in genetic background.
   (*b*) Comparison of various mutagens with regard to the efficiency with which they produce, on the one hand, recessive lethals and, on the other hand, reverse mutations at selected loci.
   (*c*) Analysis of the delayed action of nitrous acid by means of the recessive lethal technique.
3. *Drosophila:*
   (*a*) Delayed mutagenic action of alkylating agents.
   (*b*) Mutagenic action of DNA.
4. Cytological studies:
   (*a*) Structure and behaviour of pachytene chromosomes in male and female mice.
   (*b*) Functional changes in polytene chromosomes of *Drosophila.*
   (*c*) Chiasmata in spermatocytes of *Drosophila.*

PSYCHIATRIC GENETICS RESEARCH UNIT

Institute of Psychiatry, Maudsley Hospital, Denmark Hill, London, S.E.5

(1959)

Director

E. T. O. Slater, M.D., F.R.C.P., D.P.M. (*part-time*)

Staff

Mrs. Valerie A. Cowie, M.D., D.P.M. (*part-time*)

Miss E. J. McIver, B.Sc.

Visiting and Attached Workers

N. Parker, M.B., D.P.M. (*Brisbane*)

J. Shields, B.A.*

Ming-tso Tsuang, M.D. (*National Taiwan University Hospital, Taipei, Formosa*)

The work of this Unit deals with the effect of genetic factors in producing all types of mental ill-health (including mental deficiency, personality disorders, neurotic disturbances and the so-called organic and functional psychoses). Within this large field, problems are chosen where conditions seem propitious for some advance in knowledge—for instance, because appropriate material is available or because methodological advances have made the problems accessible. An example of such a problem is the investigation of genetic–environmental interactions in a large collection of twins whose records are available at the Institute of Psychiatry.

Summary of Research

1. Family histories and backgrounds of delinquent girls admitted to a classifying school.
2. Psychological factors in the lives of delinquent girls admitted to a classifying school and follow-up studies.
3. Follow-up study of monozygotic and same-sexed dizygotic twin pairs of which one member has been under treatment for neurosis or psychopathy.
4. Ten-year follow-up study of the social adjustment of twin schoolchildren.
5. Chromosome studies of mongols born to young mothers and mongols born to old fathers (with Dr. R. G. Chitham, M.R.C. Laboratories, Carshalton).
6. Chromosome survey of mentally subnormal children with physical abnormalities admitted to Queen Mary's Hospital for Children, Carshalton.
7. Hormonal factors in mothers of mongols (with Dr. A. Coppen, St. Ebba's Hospital, Epsom, and Dr. Margaret Stern, Chelsea Hospital for Women).
8. Incidence of miscarriage in mothers of mongols.
9. Incidence of phenylketonuria in children at approved schools.
10. Electrophoretic studies of the serum of patients with Huntington's chorea (with Dr. D. Gammack, Institute of Psychiatry).
11. A multidimensional study of mongolism in a population-based sample, with chromosomal, dermatoglyphic and general clinical investigations and a longitudinal study of neurological development beginning in the neonatal period.
12. A survey of a sample of mentally subnormal patients, taking congenital cardiac defect as the index lesion.

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* Seconded from staff of Institute of Psychiatry.

EXPERIMENTAL GENETICS RESEARCH UNIT

Department of Genetics, University College London, Gower Street, W.C.1

(1955)

Honorary Director

Professor H. Grüneberg, M.D., D.Sc., F.R.S.

Staff

M. S. Deol, Ph.D.
Mrs. L. E. Riles, M.A.
Miss G. M. Truslove, Ph.D.

Visiting and Attached Workers

G. S. Bains, Ph.D. (*Bombay*)
Mrs. Phebe Van Valen, M.Sc. (*Columbia University, New York*)
M. S. Grewal, Ph.D. (*Punjab, India*)

The Unit is concerned with the study of inherited diseases in laboratory animals, and its application to medicine. Investigations include the genetic analysis of the pathological conditions themselves, and a study of the various genetic backgrounds on which they can manifest themselves and of the pathology and development of these conditions.

Summary of Research

1. Pathology of development of skeletal mutants in the mouse.
2. Minor skeletal variation in inbred strains of mice.
3. Skeletal variation in wild populations of mice and other rodents.
4. Labyrinthine mutants in the mouse.
5. Cerebral degeneration in the mouse.
6. Genes affecting embryonic haemopoiesis.
7. A search for effects in adult life of genes ascertained through their effects in early development.
8. A search for genetic radiation effects in areas with high background radiation (Kerala, South India).

MICROBIAL GENETICS RESEARCH UNIT

Hammersmith Hospital, London, W.12

(1957)

Director

W. Hayes, M.B., D.Sc., D.P.H., F.R.C.P.I., F.R.S.

Staff

R. C. Clowes, Ph.D.
G. M. Crowley, Ph.D. (*until Jan. 1963*)
K. W. Fisher, Ph.D.
S. W. Glover, Ph.D.
J. D. Gross, Ph.D.
Miss J. L. Mitchell, B.Sc. (*until Aug. 1963*)
R. H. Pritchard, Ph.D.
Mrs. E. M. J. de Saxe, M.Sc.
J. G. Scaife, B.Sc.
K. A. Stacey, Ph.D.
N. D. Symonds, Ph.D.

Visiting and Attached Workers

J. R. Beckwith, Ph.D. (*University of Princeton*)
P. M. Broda, B.Sc. (*M.R.C. Scholar*)
M. S. Kelly, M.Sc. (*M.R.C. Scholar*)
Miss M. Monk, M.Sc. (*University of Melbourne*)
J. S. Schell, Dr.Sci. (*University of Ghent*)
S. D. Silver, Ph.D. (*Massachusetts Institute of Technology*)
G. Venema, Ph.D. (*University of Groningen*)
R. Weisberg, Ph.D. (*California Institute of Technology*)

Micro-organisms in recent years have proved to be uniquely adapted to highly refined analyses of genetic structure, organization and function. The

Unit aims at detailed study of the fine structure of genes and chromosomes, and the mechanisms of their replication and transfer to other cells (i.e. sexuality) among micro-organisms. Research is concerned primarily with the genetics of bacteria and their viruses, which are relevant to such problems as virulence, resistance to antibiotics, and host–virus relationships.

Summary of Research

1. Nature of bacterial death following deprivation of thymine, and its relationship to the induction of lysogenic bacteria.
2. Nature of chromosome mobilization and transfer by male cells of *Escherichia coli* following conjugation.
3. Genetic and physico-chemical basis of host-induced modification in bacteria and bacteriophages.
4. Structure and genetic behaviour of determinants of colicin production and other characters determined by episomal genes, in bacteria.
5. Mapping of the chromosome of *Bacillus subtilis* by transformation, and the kinetics of transformation in this organism.

HUMAN BIOCHEMICAL GENETICS RESEARCH UNIT

Department of Biochemistry, King's College, Strand, London, W.C.2
(1962)

Honorary Director
Professor H. Harris, M.D.

Staff

Mrs. K. F. Bamford, Ph.D. (*part-time*)
Miss A. M. Glen-Bott, M.B., D.Obst.R.C.O.G.
D. A. Hopkinson, M.B.
Miss E. B. Robson, Ph.D.

The aim of the Unit is to study the biochemical genetics of inherited disease and of normal variation in man.

Summary of Research

1. Qualitative and quantitative differences in human serum cholinesterases, and their relation to suxamethonium sensitivity.
2. Determination of glucose-6-phosphate dehydrogenase in individuals with sex chromosome abnormalities, with special reference to dosage phenomena (in collaboration with the Clinical Effects of Radiation Research Unit).
3. Electrophoretic studies on inherited variants of serum proteins.
4. Human red cell acid phosphatase polymorphism: its genetic and biochemical basis and possible relationship to haematological disorders.
5. Linkage studies using as markers recognizable chromosomes, serum types, red cell acid phosphatase types and red cell antigens (in collaboration with the Clinical Effects of Radiation Research Unit and Dr. T. E. Cleghorn, Deputy Medical Director, South London Blood Transfusion Centre).
6. Enzyme studies on human cells grown in tissue culture.

BIOPHYSICS RESEARCH UNIT

Department of Biophysics, University of London, King's College,
26–29 Drury Lane, London, W.C.2

(1947)

Director

Professor Sir John Randall, D.Sc., F.R.S.

Deputy Director

Professor M. H. F. Wilkins, C.B.E., Ph.D., F.R.S.

Honorary Biological Adviser

Professor Dame Honor B. Fell, D.B.E., D.Sc., F.R.S.

Staff

J. B. Alexander, B.Sc.
S. Arnott, Ph.D.
Mrs. A. V. W. Brown, Ph.D. (*part-time*)
G. L. Brown, Ph.D.
H. G. Davies, Ph.D.
G. F. Elliott, Ph.D.
W. Fuller, Ph.D.
Miss E. J. Hanson, Ph.D.
Mrs. S. Lee, Ph.D.
J. Lowy, Ph.D.
D. W. McMullen, B.Sc.
Mrs. C. A. Male, B.A.
B. M. Millman, B.Sc.
S. R. Pelc, D.Phil.
B. M. Richards, Ph.D.
M. Spencer, Ph.D.
J. Tooze, B.A.
J. R. Warr, B.Sc.
M. R. Watson, M.Sc.

Attached Workers

J. C. Draper, B.Sc. (*M.R.C. Scholar*)
M. E. J. Holwill, B.Sc. (*M.R.C. 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. Techniques such as X-ray diffraction, electron microscopy, microspectrometry, molecular fractionation and autoradiography are used.

Summary of Research

1. Isolation of soluble RNA; its characterization, chemical structure and role in protein synthesis.
2. X-ray investigation of the structures of RNA, DNA and nucleoprotein.
3. Structural, biochemical and physiological aspects of the contraction of smooth and striated muscle; associated studies of muscle proteins.
4. Fine structure in cells and tissues in relation to biological function:
   (*a*) Interrelationship of nucleus and cytoplasm.
   (*b*) Fine structure of chromosomes.
5. Development of kinetosomes and their associated cilia and flagella examined structurally and biochemically as a problem in morphogenesis and protein synthesis.

LABORATORY OF MOLECULAR BIOLOGY

University Postgraduate Medical School, Hills Road, Cambridge

(1947)

Chairman

M. F. Perutz, C.B.E., Ph.D., F.R.S.

Deputy Chairman

J. C. Kendrew, C.B.E., Sc.D., F.R.S.

Honorary Advisers

Sir Lawrence Bragg, O.B.E., M.C., F.R.S.
W. Cochran, Ph.D., F.R.S.

STRUCTURAL STUDIES

J. C. Kendrew, C.B.E., Sc.D., F.R.S. (*Head of Division*)
U. W. Arndt, Ph.D.*
D. M. Blow, Ph.D.
C. I. Bränden, *Fil.Lic.* (*until Apr. 1963*)
J. T. Finch, Ph.D.
Miss L. C. G. Goaman, Ph.D.
K. C. Holmes, Ph.D.
H. E. Huxley, M.B.E., Ph.D., F.R.S.
Miss B. A. Jeffery, B.Sc.
A. Klug, Ph.D.
R. Leberman, Ph.D.
Miss H. Muirhead, B.A.
Mrs. A. M. Ross, B.A.
M. G. Rossmann, Ph.D.
H. C. Watson, Ph.D.

Visiting and Attached Workers

A. B. Edmundson, Ph.D. (*Rockefeller Foundation, New York*)
Professor S. Krimm, Ph.D. (*University of Michigan*)
L. Mazzarella, Doct.Chem. (*University of Naples*)
E. L. McGandy, Ph.D. (*University of Boston*)
C. L. Nobbs, Ph.D. (*University of Auckland*)
E. J. O'Brien, B.A. (*Rockefeller Scholar*)
J. W. Prothero, Ph.D. (*University of Western Ontario*)
A. J. Rowe, Ph.D. (*Senior Beit Fellow*)
L. Stryer, M.D. (*Harvard University*)

MOLECULAR GENETICS

F. H. C. Crick, Ph.D., F.R.S. (*Head of Division*)
Mrs. M. L. Barnett, B.Sc.
S. Brenner, M.B., D.Phil.
R. E. Monro, Ph.D.
J. D. Smith, Ph.D.
A. O. W. Stretton, Ph.D.
R. J. Watts-Tobin, Ph.D.

Visiting and Attached Workers

H. A. Bøye, B.A. (*King's College Scholar; University of Copenhagen*)
M. S. Bretscher, B.A. (*Salters' Scholar*)
W. F. Dove, Ph.D. (*California Institute of Technology*)
R. P. Freedman, B.A. (*M.R.C. Scholar*)
P. M. Knopf, Ph.D. (*Massachusetts Institute of Technology*)
Miss H. Lamfrom, Ph.D. (*California Institute of Technology*)
H. Prell, D.Phil. (*Frankfurt University*)
A. S. Sarabhai, B.A. (*M.R.C. Scholar*)
P. L. Schell, Ph.D. (*Heidelberg University*)
Miss A. Shedlovsky, Ph.D. (*Harvard Medical School*)
E. R. Signer, Ph.D. (*Massachusetts Institute of Technology*)
A. Tissières, M.D., Ph.D. (*University of Geneva*)
R. R. Traut, Ph.D. (*Rockefeller Foundation, New York*)

PROTEIN CHEMISTRY

F. Sanger, C.B.E., Ph.D., F.R.S. (*Head of Division*)
R. P. Ambler, Ph.D.†
J. B. Clegg, B.A. (*until July 1963*)
J. I. Harris, Ph.D.
B. S. Hartley, Ph.D.
J. Hindley, Ph.D.
C. Milstein, Ph.D.
L. F. Smith, Ph.D.
J. Williams, M.B., B.Sc.

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* Working at the Royal Institution until April 1963.
† On leave of absence: working in the University of California.

Visiting and Attached Workers

J. R. Brown, Ph.D. (*University of Washington, Seattle*)
A. N. Glazer, M.Sc., Ph.D. (*Sydney*)
W. R. Gray, B.A. (*M.R.C. Scholar*)
K. Marcker, Ph.D. (*Royal Dental College, Copenhagen*)
R. E. Offord, B.A. (*M.R.C. Scholar*)
R. N. Perham, B.A. (*M.R.C. Scholar*)
D. C. Shaw, B.Sc. (*Commonwealth Scientific and Industrial Research Organization, Division of Textile Industry, Victoria*)
A. G. Weeds, B.A. (*M.R.C. Scholar*)

The aim of the Laboratory is the study of the structure, function and synthesis of large molecules of biological importance. In the divisions of structural studies and of protein chemistry, crystalline proteins (including enzymes), muscle, nucleic acids and viruses are studied by both physical and chemical methods. The division of molecular genetics is concerned with the biosynthesis of proteins and its genetic control.

Summary of Research

STRUCTURAL STUDIES

1. Refinement of atomic model of myoglobin: the resolution of the Fourier synthesis is being raised from 2·0 Å to 1·4 Å and the atomic co-ordinates are taken through successive cycles of refinement, each time the accuracy of the existing co-ordinates being increased and atoms whose positions were formerly unknown being added. Investigation by X-ray methods of the mode of attachment of ligands in myoglobin.
2. Determination by chemical methods of the sequence of amino acids in sperm whale myoglobin.
3. Development of automatic counter spectrometers for extending the three-dimensional Fourier of horse haemoglobin to a resolution of 2 Å (in collaboration with the Royal Institution).
4. X-ray study of reduced human haemoglobin and of haemoglobin H, with a view to gaining better understanding of the oxygenation process.
5. Theoretical work in protein crystallography: development of a mathematical function for finding the symmetry of protein molecules in crystals and for the determination of phases.
6. Crystal structure of chymotrypsin.
7. Use of new heavy atom derivatives in an attempt at phase determination by the method of isomorphous replacement in an X-ray study of tobacco mosaic virus.
8. X-ray photography of the rod-shaped tobacco rattle virus, with a view to finding its helical parameters and radial density distribution.
9. Investigation of heavy atom derivatives of crystalline tomato bushy stunt virus and turnip yellow virus, to determine the phases of the X-ray reflexions.
10. Electron microscope studies on the arrangement of subunits in small spherical viruses.
11. Structure of striated muscle and of the muscle proteins, with particular reference to the mechanism of contraction.
12. Development and use of techniques for the examination of nucleic-acid-containing structures in the electron microscope.
13. Determination of the structure of a crystal containing the base pair 9-ethylguanine and 3-methylcytosine.

MOLECULAR GENETICS

1. Mutants, especially of the acridine type, of the r_{II} locus of bacteriophage *T4*.
2. The mechanism of protein synthesis, and in particular the role of guanosinetriphosphate, the attachment point of the polypeptide chain, the binding of messenger RNA and the nature of polysomes.
3. Synthesis of synthetic polyribonucleotides and their effect in stimulating amino acid incorporation in the cell-free system.
4. Studies on fragments of the head protein on phage *T4* produced by certain mutants.
5. The mechanism of genetic suppression.
6. Integration and growth of temperate bacteriophage.
7. Elucidation of the mechanisms controlling replication in *Escherichia coli* (with Dr. F. Jacob of Paris).

PROTEIN CHEMISTRY

1. Use of isotopic methods for determining amino acid sequences, with special reference to the active centres of biologically active proteins.
2. Development of fluorescent techniques for amino acid analysis and sequence determination.
3. Determination of the amino acid sequence and disulphide bridges in chymotrypsinogen.
4. Structure of glyceraldehyde phosphate and other related dehydrogenases from rabbit and pig muscle and from yeast.
5. Structure of insulins from different species.
6. Chemical investigation of subunits in myosin.
7. Protein and RNA components of tobacco rattle virus.
8. Use of isotopic iodine for studying the reactivity and catalytic function of specific side chains in biologically active proteins.
9. Chemical nature of interferon and of the components of influenza virus.
10. Relative priming efficiencies of DNA–histone complexes for RNA synthesis with RNA polymerase from *E. coli.*
11. Structure and mode of action of messenger RNA.

CELL METABOLISM RESEARCH UNIT

University Department of Biochemistry,
South Parks Road, Oxford
(1945)

Honorary Director
Professor Sir Hans Krebs, M.D., D.Sc., F.R.C.P., F.R.S.

Staff

K. Burton, Ph.D.
J. T. Y. Chou, D.Phil.
G. R. Eagle, B.A.
J. A. Grunau, Ph.D.
D. E. Hughes, Ph.D.
Miss M. R. Lunt, D.Phil.
J. R. Quayle, Ph.D.
D. S. Robinson, Ph.D.

Visiting and Attached Workers

Dr. L. Adler (*Carnegie Trust Scholar*)
Dr. P. de Gasquet (*A.E.C. Société de Chimie Organique et Biologique, Paris*)
A. Gear (*M.R.C. Scholar*)
Miss P. A. Johnson (*U.S. Air Force Research Assistant*)
Dr. E. A. Newsholme (*Beit Memorial Fellow*)
Dr. J. C. Siebke (*Royal Norwegian Council for Scientific and Industrial Research Fellow*)
B. J. Smith, B.Sc. (*M.R.C. Scholar*)
M. G. Smith, M.Sc. (*1851 Scholar*)
A. H. Underwood (*Wellcome Trust Scholar*)
Dr. T. Yoshida (*National Institutes of Health Fellow*)

The Unit is concerned with the study of the mechanism and control of metabolic processes. The properties of various enzymes of special importance in this respect are also being investigated.

Summary of Research

METABOLIC STUDIES

1. Rate-controlling factors in respiration.
2. Metabolism of ketone bodies in animal tissues.
3. Gluconeogenesis.
4. Biochemistry of bacteriophages.
5. Metabolism of phosphate polymers in bacteria.
6. Microbial growth on C_1-compounds.
7. Metabolism and function of inner ear tissues.

ENZYME STUDIES

1. Oxalyl coenzyme A reductase, oxalyl coenzyme A decarboxylase, oxalyl coenzyme A thiophorase, formate dehydrogenase.
2. Carboxylation of ribulose diphosphate.
3. Bacterial polymetaphosphatase.

CHEMOTHERAPY RESEARCH UNIT
Molteno Institute, Downing Street, Cambridge
(1942)

Director
Miss A. Bishop, Sc.D., F.R.S.

Staff
Mrs. E. W. Smart, Ph.D. (*part-time*)

Attached Worker
Miss F. C. Wayland, B.Sc. (*M.R.C. Scholar*)

The Unit is studying the biology of protozoa, with special reference to drug resistance, particularly in malaria parasites, and growth requirements of *Entamoeba* in axenic culture.

Summary of Research

1. Resistance to 4, 6-diamino-1-(*p*-chlorophenyl)-1, 2-dihydro-2, 2-dimethyl-*s*-triazin pamoate in *Plasmodium gallinaceum.*
2. Effect of sexual reproduction upon the inheritance of drug resistance in *P. gallinaceum.*
3. Development of synthetic media for the maintenance of axenic cultures of *Entamoeba invadens.*
4. Cultivation and life-cycle of the flagellate *Scytomonas.*
5. Sensitivity of *Tetrahymena pyriformis* to antimalarial drugs.

EXPERIMENTAL VIRUS RESEARCH UNIT
Institute of Virology, Church Street, Glasgow, W.1
(1959)

Honorary Director
Professor M. G. P. Stoker, M.D., F.R.S.E.

Assistant Director
N. P. L. Wildy, M.B., F.R.S.E.*

Staff
L. V. Crawford, Ph.D.
I. A. Macpherson, Ph.D.
H. Subak-Sharpe, Ph.D.
M. Sussman, Ph.D.
V. Thorne, Ph.D.
D. H. Watson, Ph.D.
F. G. Wingfield Digby, Ph.D.

Visiting and Attached Workers
Mrs. D. Bourgaux M.D. (*Université Libre de Bruxelles*)
P. Bourgaux, M.D. (*Université ,Libre de Bruxelles*)
Miss L. Diamond, Ph.D. (*Sloan-Kettering Institute for Cancer Research, New York*)
Miss M. Gharpure, M.B. (*Indian Government Polio Research Unit, Bombay*)
E. Gold, M.D. (*National Institute of Allergy and Infectious Diseases, Bethesda, Md.*)
K. Habel, M.D. (*National Institute of Allergy and Infectious Diseases, Bethesda, Md.*)
I. H. Holmes, Ph.D. (*University of Melbourne*)
A. L. Kisch, M.D. (*National Institutes of Health, Bethesda, Md.*)

The Unit carries out research on virus structure and multiplication, with particular reference to latency and to tumour viruses. Special attention is devoted to virus-induced changes in the genetic structure of animal cells.

* Professor Wildy was appointed to the Chair of Bacteriology at the University of Birmingham from October 1963.

Summary of Research

1. Mechanism of neoplastic transformation by polyoma virus studied *in vitro*.
2. Characteristics of the DNA and protein components of polyoma and papilloma group viruses.
3. Characteristics of neoplastic cells compared with those of normal cells from the same clone.
4. Structure and assembly of herpes virus particles.
5. Chemical changes in herpes-infected cells.
6. Genetics of herpes virus.
7. Studies on a stable diploid cell line.

VIRUS RESEARCH UNIT

Medical Research Council Laboratories, Woodmansterne Road,
Carshalton, Surrey
(1955)

Director
F. Kingsley Sanders, D.Phil.

Staff

A. J. D. Bellett, M.Sc. (*until Mar. 1963*)
A. T. H. Burness, Ph.D., A.R.I.C.
P. Faulkner, Ph.D.
M. L. Fenwick, Ph.D. (*until Aug. 1963*)
S. M. McGee-Russell, D.Phil.
A. D. Vizoso, Ph.D.

Visiting and Attached Workers

Miss A. D. Bellamy, B.Sc. (*M.R.C. Scholar*)
J. G. Bennette, M.B. (*Middlesex Hospital*)
L. Montagnier, Dr.Med. (*Institut du Radium, Paris*)

The work of the Unit is concerned with intracellular events following infection by viruses. Suspensions of cells in simple media, where (*a*) virus growth can be initiated simultaneously in a large number of cells, and (*b*) the behaviour of the infected cells can subsequently be investigated by chemical, morphological and virological methods, are being used to elucidate the cellular mechanisms concerned in virus synthesis.

Summary of Research

1. Intracellular events during the growth of a cell-destroying virus in mouse ascites tumour cells, kept alive outside the bodies of their hosts either in liquid suspension or in agar layers, studied in order to correlate (*a*) the time sequence of different phases of virus growth and (*b*) the intracellular sites of synthesis of different virus components with biochemical and morphological alterations of infected cells.
2. Characterization of the material carrying virus properties in nucleic acid preparations made either from purified virus or from virus-infected cells at various intervals after infection, to investigate the mode of replication of viral nucleic acid within infected cells.
3. Mode of interaction between infective virus nucleic acid and cells showing the early intracellular events following invasion by virus.
4. Development of similar cell–virus systems for the study of cellular events during the growth of viruses of varying size and pathogenicity containing different sorts of nucleic acid.
5. Characterization and study of the growth in a tissue culture system of a murine non-pathogenic virus capable of destroying tumour cells *in vivo*.

HUMAN NUTRITION RESEARCH UNIT

Nutrition Building, National Institute for Medical Research,
The Ridgeway, Mill Hill, London, N.W.7

(1944)

Director

Professor B. S. Platt, C.M.G., M.B., Ph.D.

Staff

Miss I. M. Barrett, B.Sc.
L. Chin, B.Sc.
B. H. Doell, M.Sc.
C. R. C. Heard, D.Phil.
Miss A. Mittwoch, M.Sc.
D. J. Naismith, Ph.D.
P. R. Payne, B.Sc.
B. T. Squires, O.B.E., D.M.
M. R. Turner, M.Sc.

Senior Technical Officer: R. J. C. Stewart, M.Inst.Biol.

Visiting and Attached Workers

H. Al-Rabii, D.Sc. (*University of Baghdad*)
N. R. H. El-Maraghi, M.B. (*University of Assiut, Egypt*)
W. Frankul, M.Sc. (*Royal College of Medicine, Baghdad*)
Mrs. S. R. Gupta; M.B. (*Leverhulme grant-holder*)
Miss M. Jacob, M.Sc. (*Rockefeller Foundation grant-holder*)
Mrs. A. K. Lebshtein, M.B. (*University of Assiut, Egypt*)
A. Meyer, M.D. (*University of London*)
S. R. Morcos, Ph.D. (*National Research Centre, Cairo*)
R. Orraca-Tetteh, B.Sc. (*Rockefeller Foundation grant-holder*)
B. Y. Nadkarni, M.Sc. (*Rockefeller Foundation grant-holder*)
G. Pampiglione, M.D., M.R.C.P., D.Neurol. (*Hospital for Sick Children, Great Ormond Street, London*)
Mrs. W. Skilladz, M.Sc. (*F.A.O. Fellow*)
Mrs. I. Talmon, M.D. (*Hospital Melberi, Pardes-Ketz, Israel*)
Miss J. A. Wimbush, B.Sc. (*U.N.I.C.E.F. grant-holder*)

At the London School of Hygiene and Tropical Medicine

W. R. Aykroyd, C.B.E., M.D., Sc.D.
Miss R. Schwartz, Ph.D.
} *Department of Nutrition*

Miss M. E. Cameron, B.H.Sc., Dep.Diet.(N.Z.)
T. P. Eddy, C.B.E., M.R.C.S., D.P.H.
D. S. Miller, B.Sc.
Miss A. Nicholson, B.Sc.
P. L. Pellett, Ph.D., A.R.I.C.*
} *Nuffield Provincial Hospitals Trust grant-holders*

Mrs. J. Doughty, B.Sc.
D. C. Morley, M.D., D.P.H.
Miss J. A. S. Ritchie, M.Sc.
} *U.N.I.C.E.F. grant-holders; fellowship course in food science and applied nutrition*

The main study of the Unit has been the malnutrition of people in colonial territories and other tropical and sub-tropical countries; this includes the development of methods for the evaluation and quantitative expression of dietary protein requirements and of the dietary protein values of foods as eaten, and the experimental study of various forms of protein malnutrition. The work is being extended to the study of the dietary protein requirements and intake and the nutritional status of selected groups of the population of the United Kingdom, including children and hospital patients; the relevance of some of the changes produced in animals on various diets to the aetiology of certain disorders occurring in the population of the United Kingdom is also being investigated. The work of the Unit continues to be closely associated with that of the Department of Human Nutrition at the London School of Hygiene and Tropical Medicine.

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*Seconded to Massachusetts Institute of Technology.

Summary of Research

1. Study of the various forms and manifestations of malnutrition, especially of the effects in man and animals of low-protein, high-carbohydrate diets:
   (*a*) Interrelationships of dietary and endocrine factors.
   (*b*) Effects on the reproductive system, on the foetus and infant, on the development and function of the mammary gland, on the nervous system, alimentary canal and skin, and on bone growth.
   (*c*) Biochemical changes in tissues, body fluids and secretions, including milk.
   (*d*) Interrelationships of malnutrition and the effects of zymotic disease, including malaria and worm infestations.
   (*e*) Interrelationships of the metabolism of protein with that of other nutrients.
2. Protein requirements and protein value of foods:
   (*a*) Nutritional value of proteins determined by biological and chemical methods in foods, dishes, meals and dietaries.
   (*b*) Dependence of dietary protein value on other factors, including protein: calorie ratio and total caloric intake.
3. Nutritional status in relation to food processing and its effect on the nutritional value of the food:
   (*a*) Technology of food processing in relation to nutritional values of the processed product.
   (*b*) Surveys of hospital diets.
   (*c*) Surveys of nutritional status of children in institutions where dietary intake can be evaluated.

DUNN NUTRITIONAL LABORATORY

Milton Road, Cambridge

(1926)

*Director**

E. H. Kodicek, M.D., Ph.D.

Deputy Director

T. Moore, Sc.D.

Staff

Miss E. M. Cruickshank, Ph.D.
D. E. M. Lawson, Ph.D.
I. M. Sharman, Ph.D., F.R.I.C.
M. G. Stanton, B.A. (*until Aug. 1963*)
Mrs. K. J. I. Thorne, Ph.D.

Visiting and Attached Workers

Miss I. Antonowicz, M.Sc. (*Boston, U.S.A.*)
V. H. Booth, Ph.D. (*Agricultural Research Council*)
Professor A. Fidanza, Dr.Med. (*Rome*)
H. D. Stowe, Ph.D., D.V.M. (*Michigan, U.S.A.*)

The Unit is engaged in research on vitamins and other nutrients, including the physiology of their action, the effects of deficiency, and methods for their estimation in living tissues and in natural and processed products.

Summary of Research

1. Vitamin C studies in relation to: connective tissue and mucopolysaccharides; role in photosynthesis.
2. 'Bound' nicotinic acid in cereals.
3. Vitamin A: mode of action, particularly at subcellular levels; effects of deficiency; blood levels in human subjects; significance for farm animals; characterization of carotenoids.
4. Vitamin E studies in relation to: human nutrition; 'haemolysis' test; redox dyes; selenium; methods of determination; biological and antioxidative functions; kidney degeneration; cod-liver oil (pro- and anti-vitamin); enzymic destruction.
5. Vitamin D: studies of distribution in rat tissues and subcellular fractions; metabolism of ^{14}C-labelled D_2 in rats and tissues cultivated *in vitro*; effect of vitamin D and parathyroid on absorption of ^{45}Ca; mechanisms affecting calcium homeostasis.
6. Pantothenic acid: effects of deficiency in guinea pigs and rats; influence on lipid metabolism; possible interrelationships with ascorbic acid.

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* Dr. L. J. Harris was Director of the Unit until his retirement in August 1963.

7. Blood volumes: effect of age, nutritional deficiencies and other factors, in guinea pigs and rats.
8. Biosynthesis of isoprenoid compounds in bacteria.
9. Experimental calcium deficiency: influence on bone structure in the rat; balance between iron, calcium and copper.
10. Determination and identification of tocopherols, carotenoids and other vitamins in vegetables, fruits and other plants; effect of wilting, cooking, mechanical damage, viruses.

MEDICAL RESEARCH COUNCIL LABORATORIES

Fajara, Nr. Bathurst, Gambia, West Africa

(1953)

Director

I. A. McGregor, O.B.E., M.R.C.P., D.T.M. & H.

Staff

M. E. C. Giglioli, Ph.D.*
D. S. Harling, M.D., M.R.C.P., D.T.M. & H.
P. D. Marsden, M.B., M.R.C.P., D.T.M. & H.† (*until Oct. 1962*)
G. Thompson, M.B. (*until Sept. 1963*)
Miss E. Topley, M.D.
Miss G. H. Walker, M.B.
Miss H. M. Wilson, M.R.C.S., D.T.M. & H., D.C.H.

Visiting Workers

Professor Sir Dugald Baird, M.D., D.P.H., F.R.C.O.G. (*Obstetric Medicine Research Unit*)
Professor D. S. Bertram, D.Sc., F.I.Biol. (*London School of Hygiene and Tropical Medicine*)
W. Z. Billewicz, M.Sc. (*Obstetric Medicine Research Unit*)
S. Cohen, M.D., Ph.D. (*Wright-Fleming Institute, St. Mary's Hospital, London*)
Mrs. T. S. Detinova, D.Bs. (*Institute of Medical Parasitology and Tropical Medicine, Moscow*)
R. Illsley, Ph.D. (*Obstetric Medicine Research Unit*)
A. M. Thomson, M.B., B.Sc., D.P.H. (*Obstetric Medicine Research Unit*)
R. W. D. Turner, O.B.E., M.D., F.R.C.P. (*University of Edinburgh*)

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 Trachoma Research Unit has a permanent field station at the Gambia Laboratories.

Summary of Research

1. Effects of repeated parasitic infection on the health of a rural community.
2. Distribution of glucose-6-phosphate dehydrogenase deficiency in a rural population.
3. Effects of heavy and repeated malarial infections on Gambian infants and young children.
4. Mechanism of malarial immunity.
5. Antigenic specificity of *Plasmodium falciparum* in East and West Africa.
6. Metabolism of serum protein in Gambians.
7. Incidence and aetiology of anaemia in a rural African population.
8. Value of diethylcarbamazine (Hetrazan) in the field control of Bancroftian filariasis.
9. Epidemiology and importance of measles in Gambian children.
10. Pattern of illness in Gambian children.
11. Determination of the factors responsible for high rates of mortality in Gambian children.
12. Effect of socio-economic influences on growth and mortality of Gambian children.
13. Effect of schistosomiasis on the health of a rural population.
14. Incidence, importance and aetiology of seasonal oedematous states in Gambian adults.
15. Bionomics of mosquitoes of the *Anopheles gambiae* complex.
16. The female reproductive system and the gonotrophic cycle in *A. gambiae*.
17. Calcium metabolism in Gambian subjects.

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* Transferred to External Scientific Staff in September 1963, at the Department of Entomology, London School of Hygiene and Tropical Medicine.
† Seconded from the staff of the London School of Hygiene and Tropical Medicine.

TROPICAL METABOLISM RESEARCH UNIT

University of the West Indies, Mona, Jamaica
(1955)

Director

Professor J. C. Waterlow, M.D., M.R.C.P.*

Assistant Director

J. S. Garrow, M.D., Ph.D., M.R.C.P.

Staff

H. Chan, M.B.
K. Fletcher, Ph.D.
A. E. M. McLean, B.M., Ph.D. (*until July 1963*)
D. I. M. Picou, M.B., Ph.D.
Miss J. M. L. Stephen, Ph.D.*

Attached Workers

D. Halliday, B.Sc. (*M.R.C. Scholar*)
Miss P. Rodgers, M.B., M.R.C.P.E. (*Colonial Research Fellow; jointly with Department of Medicine, U.W.I.*)
M. B. Wilson, B.Sc. (*Colonial Medical Research Student*)

The Unit is investigating problems of normal and abnormal physiology associated with conditions of life in the tropics. At present it is concerned mainly with the clinical and biochemical effects of malnutrition in infants and young children, and particularly with the study of protein metabolism.

The Unit collaborates with members of the staff of the Department of Medicine, University of the West Indies, and with the Government of Jamaica in the study of practical nutritional problems.

A small branch of the Unit has been established at St. Mary's Hospital Medical School, London, W.2.

Summary of Research

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 composition: development of new methods and application of the mass spectrometer.
3. Electrolyte disturbances.
4. Protein turnover, studied with ^{35}S-and ^{15}N-labelled amino acids.
5. Activity of enzymes in liver and serum.
6. Absorption and utilization of leaf protein.

STUDIES ON ADULTS

Epidemiological, clinical and immunological characteristics of Jamaican myelopathy.

EXPERIMENTAL WORK

1. Fatty acid synthesis by liver tissue *in vitro*.
2. Distribution of protein synthesis in protein depletion.
3. Measurement of protein turnover in the rat in relation to dietary conditions.

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* Working at St. Mary's Hospital, London.

INFANTILE MALNUTRITION RESEARCH UNIT

Mulago Hospital, Kampala, Uganda

(1953)

Director

Professor R. F. A. Dean, Ph.D., F.R.C.P.

Staff

Miss S. G. Cameron, B.A.
Miss J. E. Gregory, B.Sc.
Miss K. M. MacWilliam, M.B., M.R.C.P.E., D.C.H.
Miss I. H. E. Rutishauser, B.Sc.
Mrs. C. E. Smith, B.A. (*until Jan. 1963*)
R. G. Whitehead, Ph.D.

Attached Worker

H. J. L. Burgess, M.B., D.T.M. & H. (*Ministry of Health, Uganda*)

The Unit studies individual children who have become malnourished, and the relationship of the children to their environment. The Unit is an Associated Institute of Makerere University College, and works closely with the Uganda Government's Nutrition Unit.

Summary of Research

1. The biochemical abnormalities that may be due to malnutrition.
2. Utilization of locally produced foods for the prevention and treatment of nutritional disease.
3. The home environment of the malnourished child and the after-effects of an episode of malnutrition.

SOCIAL PSYCHIATRY RESEARCH UNIT

Institute of Psychiatry, Maudsley Hospital, Denmark Hill, London, S.E.5

(1948)

Honorary Director

Professor Sir Aubrey Lewis, M.D., F.R.C.P.

Staff

G. W. Brown, Ph.D.
J. E. Cooper, B.M., M.R.C.P., D.P.M.*
Mrs. B. Hermelin, Ph.D.
J. G. Ingham, Ph.D.
R. D. King, B.A., Dip.Criminol.
J. B. Loudon, B.M., Dip.Anthrop.
Mrs. E. M. Monck, B.A. (*until Jan. 1963*)
N. O'Connor, Ph.D.
K. Rawnsley, M.B., M.R.C.P., D.P.M.
Miss N. V. Raynes, M.A.
J. O. Robinson, Ph.D.
M. L. Rutter, M.D., M.R.C.P., D.P.M.
J. Tizard, Ph.D.
P. H. Venables, Ph.D.
J. K. Wing, M.D., Ph.D., D.P.M.
W. Yule, M.A.

Visiting and Attached Workers

P. Bryant, B.A. (*M.R.C. Scholar*)
V. Lotter, B.A. (*Middlesex County Council*)
M. P. Smith, Ph.D. (*U.S. Public Health Service Fellow*)
Miss B. Spain, B.A., Dip.Psychol. (*M.R.C. Scholar*)
W. Wolfensberger, Ph.D. (*National Institutes of Health Fellow*)

The Unit studies the influence of social factors on the occurrence, continuance and outcome of mental illness and mental subnormality. Special attention is given to the measurement of social abnormalities and to deviations from normal psychological development.

* Joint appointment with the Unit for the Study of Environmental Factors in Mental and Physical Illness.

Summary of Research

1. (*a*) Psychological disabilities in autistic children.
   (*b*) Prevalence of autism and allied conditions in children aged 8–10 in Middlesex.
   (*c*) Follow-up study of autistic children seen at Maudsley Hospital.
2. Epidemiology of child maladjustment in Aberdeen (jointly with the Obstetric Medicine Research Unit).
*3. (*a*) Sociological investigation of residential institutions for children.
   (*b*) Psychological study of children and staff in residential institutions.
4. Education and management of severely subnormal children.
5. (*a*) Immediate memory and attention in imbeciles.
   (*b*) Transfer phenomena in imbeciles.
6. Measurement of family relationships and estimates of the satisfaction these afford.
7. (*a*) Social structure and value systems of a rural population.
   (*b*) Periodic enumeration of a rural and a coal-mining valley by private census (in collaboration with the Pneumoconiosis Research Unit).
   (*c*) Prevalence of psychiatric symptoms and attitudes towards them in a rural population.
8. (*a*) Impact of different types of community services on discharged schizophrenic patients.
   (*b*) In-patient surveys of mental hospitals with different types of social organization.
9. Psychological and physiological functions in normal persons and chronic schizophrenic patients.

UNIT FOR RESEARCH ON THE EPIDEMIOLOGY OF PSYCHIATRIC ILLNESS

Department of Psychological Medicine, University of Edinburgh,
2, George Square, Edinburgh, 8

(1960)

Honorary Director

Professor G. M. Carstairs, M.D., F.R.C.P.E., D.P.M.

Assistant Director

W. I. N. Kessel, M.D., M.R.C.P., D.P.M.

Staff

C. B. Kidd, M.D., Ph.D., D.P.M.
R. S. Knox, M.D. (*until June 1963*)
A. Munro, M.B., M.R.C.P.E., D.P.M.
Miss M. Whiteley, M.A.

Visiting and Attached Workers

R. Giel, M.D. (*University of Groningen; Council of Europe Fellow*)
Miss C. Hassall, Dip.Soc.Sc. (*Nuffield Provincial Hospitals Trust grant-holder*)
M. G. Jayasundera, M.B., D.P.M. (*Colombo Plan Fellow*)
B. F. Picken, M.D. (*U.S. Public Health Service Fellow*)
Miss C. A. Renton, S.R.N. (*Mental Health Research Fund grant-holder*)

The Unit studies sections of the population in which there is a high risk of contracting particular illnesses and examines clinical and social features of mental illness in order to develop aetiological hypotheses. The long-term aim in both instances is to pave the way for preventive action.

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* Supported by the U.S. Association for the Aid of Crippled Children.

Summary of Research

1. Social and medical factors contributing to psychological disturbance in students.
2. Clinical, social and ecological factors generating attempts at suicide.
3. Effect of opening a mental health centre in Plymouth upon the numbers, diagnoses and disposal of psychiatric patients there (in collaboration with the Nuffield Provincial Hospitals Trust).
4. Relationship between subsequent medication and relapse rates of discharged schizophrenic patients.
5. Status of neurotics 5 years after attending a psychiatric out-patient clinic.
6. Subsequent medical histories of neurotics identified in general practice 10 years previously.
7. Incidence of pregnancy in neurotic and normal university students.
8. Psychiatric evaluation of women with triple-X chromosomes (in collaboration with the Clinical Effects of Radiation Unit).
9. Incidence and clinical characteristics of psychopaths treated in hospital.
10. Smoking habits of university graduates and their modification as a result of the report of the Royal College of Physicians.
11. Aetiological studies in depressive illness.
12. Detection of psychiatric cases in general practice and in a general out-patient department.
13. Epidemiology of stammering.
14. Techniques for studying the epidemiology of illness in families.
15. Epidemiological studies of psychosomatic diseases.

NEUROPSYCHIATRIC RESEARCH UNIT

Medical Research Council Laboratories, Woodmansterne Road, Carshalton, Surrey

(1957)

Director

D. Richter, Ph.D., M.R.C.S.

Staff

R. Balazs, M.D., Ph.D.
A. W. Brown, B.Sc. (*until Aug. 1963*)
A. J. Coppen, M.D., D.P.M. (*part-time*)
D. R. Dahl, M.D., Ph.D.
G. B. David, D.Phil. (*until Sept. 1963*)
M. K. Gaitonde, Ph.D.
Miss T. L. Julian, M.B.E., M.Sc.
B. S. Meldrum, M.B., Ph.D.
Mrs. M. Metcalfe, Dip.Psych.App. (*part-time*)
D. M. Shaw, M.B., Ph.D., M.R.C.P.
J. D. Swales, M.B.
R. Vrba, D.Sc. (*Prague*)

Visiting Workers

H. S. Bachelard, Ph.D. (*University of Melbourne; Rockefeller Foundation grant-holder*)
F. Bilodeau, Ph.D. (*McGill University, Montreal; Canadian M.R.C. Research Fellow*)
Mrs. N. A. Dahl, Ph.D. (*University of Kansas; National Institutes of Health Fellow*)
K. A. C. Elliott, D.Sc., F.R.S.C. (*McGill University, Montreal*)
G. Feuer, Ph.D., C.Med.Sc. (*Academy of Sciences, Budapest; Mental Health Research Fund grant-holder*)
Y. Machiyama, M.B., D.Med.Sc. (*University of Tokyo; British Council Fellow*)
S. A. Marchi, M.D. (*University of Milan; N.A.T.O. Research Fellow*)
F. T. Mérei, M.D. (*University of Pecs, Hungary; International Atomic Energy Agency Fellow*)

The Unit carries out basic and clinical research on the causes and treatment of mental disorders.

Summary of Research

1. Biochemical and biophysical changes associated with mental illness.
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. Organization and function of the nerve cell.

NEUROPHARMACOLOGY RESEARCH UNIT

Department of Experimental Neuropharmacology, The Medical School, Birmingham, 15

(1958)

Honorary Director

P. B. Bradley, D.Sc.

Staff

B. J. Key, Ph.D. (*honorary*)
A. R. King, Ph.D.
M. H. T. Roberts, B.Sc.
J. H. Wolstencroft, Ph.D.

Attached Workers

B. N. Dhawan, M.D. (*University of Lucknow*)
R. I. Porter, B.Sc. (*M.R.C. Scholar*)
R. J. Stephens, B.Sc. (*M.R.C. 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. Investigations are also being carried out on 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 which may be important as neurohumoral agents.

Summary of Research

1. Effects of drugs on sensory generalization and sensory discrimination in animals.
2. Effects of drugs on the inflow and integration of sensory information in the brain.
3. Effects of stimulant and sedative drugs on the performance of animals in problem-solving situations in relation to different intensities of background noise.
4. Effect of electrical stimulation of the brain on the behaviour of animals.
5. Effects of drugs and of electrical stimulation of different parts of the brain on recent memory in primates.
6. Effects of drugs on the activity of single neurones in the brain when applied by iontophoresis.

CLINICAL PSYCHIATRY RESEARCH UNIT

Graylingwell Hospital, Chichester, Sussex

(1957)

Director

P. Sainsbury, M.D., D.P.M.

Staff

W. R. Costain, M.B., D.P.H., D.P.M.
Miss J. C. Grad, Ph.D.
J. B. Knowles, B.Sc., Dip.Psych.
N. B. Kreitman, M.D., D.P.M.
J. W. T. Redfearn, M.D., D.P.M. (*until Dec. 1962*)*
J. C. Shaw, B.Sc.

Visiting Worker

K. I. Pearce, M.D., L.M.C.C. (*University of Saskatchewan*)

The Unit is concerned with the investigation of clinical problems in psychiatry, and much of its work is carried out in conjunction with the hospital staff. Two main subjects have been selected: (*a*) factors in the social and family environment

* Transferred to External Scientific Staff (see p. 160).

of psychiatric patients associated with their breakdown and admission to hospital, and (*b*) the neurophysiological mechanisms underlying psychiatric symptoms.

CLINICAL AND SOCIAL STUDIES

1. Evaluation of a community mental health service, to assess factors determining admission to mental hospital, the effects on the family of caring for mentally ill patients, and the outcome after two years.
2. Mental illness in married couples.
3. Therapeutic trials and the problems of their design in psychiatry.

EPIDEMIOLOGY

1. Factors determining referral rates of psychiatric patients.
2. Psychological and somatic illness in a general practice.

PSYCHOSOMATIC AND NEUROPHYSIOLOGICAL STUDIES

1. A clinical study of chronic hypochondriasis.
2. Verbal and motor activity in mental illness and as personality characteristics.
3. Methods of processing psycho-physiological data.
4. Quantitative studies of EEG voltage distribution.
5. Perception, stress, and EEG alpha activity.

EXPERIMENTAL PSYCHOLOGY

1. Experimental studies of operant verbal conditioning.
2. Acquiescence and other response distortion to questionnaires.

UNIT FOR RESEARCH ON THE CHEMICAL PATHOLOGY OF MENTAL DISORDERS

Department of Physiology, The Medical School, Birmingham, 15
(1960)

Honorary Director
Professor I. E. Bush, M.B., Ph.D.

Staff

A. A. Boulton, Ph.D.
Miss M. E. P. Hele, M.B., Ph.D.
F. A. Jenner, M.B., Ph.D., D.P.M. (*part-time*)
R. J. Pollitt, Ph.D.
P. W. Ramwell, Ph.D.

Attached Workers

Miss S. A. Hunter, B.Sc. (*University of Birmingham*)
Miss J. E. Shaw, B.Sc. (*M.R.C. Scholar*)
M. Sheridan, M.B., M.R.C.P.E., D.P.M. (*Hollymoor Hospital, Birmingham*)

The aims of this Unit are to investigate possible biochemical and humoral abnormalities in patients with mental disorders, and aspects of chemical physiology which may bear on this problem.

PHARMACOLOGICAL STUDIES

1. Factors affecting the spontaneous and evoked release of non-cholinergic substances from the cerebral cortex.
2. Separation and identification of these and similar pharmacologically active substances from brain extracts.

BIOCHEMICAL STUDIES

1. Interaction of phenothiazine derivatives and imipramine with nucleic acids and other polyphosphates of biological interest.
2. Identification and study of oligonucleotides controlling the rate of *in vitro* reactions involved in protein synthesis.

CLINICAL STUDIES

1. Factors producing water retention in periodic psychosis, and the relationship between these changes and the changes in mental state.
2. Collection of urine and other body fluids from patients and normal subjects for physiological and pharmacological investigations.

STEROID METABOLISM

1. Metabolism *in vitro* of 11-oxygenated steroids, particularly those reactions affecting the biological activity of cortisone analogues.
2. Mode of action of hydrocortisone.

ANALYTICAL METHODS

1. Design and construction of apparatus for the automatic treatment and scanning of paper chromatograms for methods of quantitative estimation.
2. Physico-chemical analysis of solvent systems used for partition chromatography in order to improve the use of this method for the estimation of known substances and in the identification of unknown substances.
3. Physico-chemical properties of unknown pharmacologically active substances present in urine.

UNIT FOR THE STUDY OF ENVIRONMENTAL FACTORS IN MENTAL AND PHYSICAL ILLNESS

London School of Economics, Houghton Street, Aldwych, London, W.C.2 (1962)

Director

J. W. B. Douglas, B.M., B.Sc.

Staff

J. E. Cooper, B.M., M.R.C.P., D.P.M.* Miss J. M. Ross, B.Sc.
Miss A. R. L. Lawrence, Ph.D.

Attached Workers

D. G. Mulligan, M.A. (*Home Office grant-holder*) D. M. Nelson, M.A. (*D.S.I.R. grant-holder*)

This Unit was set up to study problems on the borderline of medicine and sociology and one of its aims is to promote the co-operation of doctors, sociologists and psychologists in joint research and in the development of new techniques. It will also offer to postgraduate students, whether trained as doctors or sociologists, an opportunity to do research in the field of social medicine.

* Joint appointment with the Social Psychiatry Research Unit.

Summary of Research

1. The National Survey of Health and Development—a longitudinal study of 5000 children who have been under observation since they were born in March 1946. The following studies are now in progress:
   (*a*) Environmental factors in secondary education (in collaboration with Rothamsted Experimental Station).
   (*b*) Effects of illness and other causes of absence from school on measured ability.
   (*c*) Air pollution and respiratory tract infections (in collaboration with the Air Pollution Research Unit).
   (*d*) Mental development of prematurely born children.
2. A study of young children who have obsessional or neurotic parents.
3. Early child-rearing patterns in different social classes.
4. Vocational training and technical education (supported by a grant from the Department of Scientific and Industrial Research).
5. Delinquency and maladjustment among the National Survey children (supported by a grant from the Home Office).

NEUROENDOCRINOLOGY RESEARCH UNIT

University Department of Human Anatomy, South Parks Road, Oxford (1962)

Honorary Director

Professor G. W. Harris, D.M., Sc.D., F.R.S.

Staff

D. J. El Kabir, M.B.
D. Exley, D.Phil.
Miss M. Reed, B.Sc.

Attached and Visiting Workers

K. Brown-Grant, M.D. (*Royal Society Locke Research Fellow*)
W. H. Florsheim, Ph.D. (*Veterans' Hospital, California; U.S.P.H.A. Fellow*)
W. N. Adams Smith, M.B. (*New Zealand; Nuffield Dominions Demonstrator*)
M. X. Zarrow, Ph.D. (*Purdue University, U.S.A.; Senior Postdoctoral Fellow, National Science Foundation*)

The Unit is concerned with investigations into the 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 in the foetus and newborn animal.
2. Chemical mediators by which the hypothalamus regulates the activities of the anterior pituitary gland.
3. Mode of action of the progestational compounds (including contraceptive steroids) on metabolism and on ovarian function.
4. Estimation of thyrotrophic hormone in blood in man and in the experimental animal.
5. Thyroid–ovarian interrelationships.
6. Neuroendocrine factors in induced ovulation in the immature rat.
7. Endocrine activity in psychiatric patients during different phases of mental illness.

APPLIED PSYCHOLOGY RESEARCH UNIT

15, Chaucer Road, Cambridge

(1944)

Director
D. E. Broadbent, M.A.

Assistant Directors
R. Conrad, Ph.D. E. C. Poulton, M.B.

Staff

A. D. Baddeley, Ph.D.
M. J. F. Blake, B.Sc.
I. D. Brown, B.Sc.
A. Carpenter, M.B.
W. P. Colquhoun, Ph.D.
D. W. J. Corcoran, Ph.D.
H. C. A. Dale, Ph.D.
P. R. Freeman, B.A.
M. Hammerton, Ph.D.
J. A. Leonard, Ph.D.
J. Morton, Ph.D.
P. M. A. Rabbitt, Ph.D.
L. H. Shaffer, Ph.D.
R. T. Wilkinson, Ph.D.
Miss M. M. Woodhead

Visiting Worker
M. Brandon, B.A. (*D.S.I.R.* (*N.A.T.O.*) *Grant*)

The purpose of the Unit is to observe and measure human behaviour with the aim of establishing general principles about healthy human performance in various environments and types of work. The intention is to find principles which are of general scientific interest, and also of practical value when applied to men working in either industry or the Services. The investigations usually consist of experimental studies of individual human activity.

Summary of Research

1. Perception:
   (*a*) Alertness during prolonged visual inspection.
   (*b*) Presentation of technical information.
   (*c*) The effect of context on sensory judgments.
   (*d*) Factors affecting the intelligibility of speech.
2. Thinking:
   (*a*) Information theory research.
   (*b*) Subjective probability estimates and location of faults in electronic and other systems.
   (*c*) Human limits in decision taking: speed and load stress in a variety of skilled performances.
   (*d*) Coding of information.
3. Moving:
   (*a*) Transfer of training between control systems.
   (*b*) Effects of orders of control, time lags, and control sensitivity in tracking.
   (*c*) Experiments on car driving performance.
   (*d*) Design of keyboards.
4. Working conditions:
   (*a*) Achievement after lack of sleep.
   (*b*) High intensity noise effects.
   (*c*) Effects of alcohol.
   (*d*) Length and arrangement of work shifts.
   (*e*) Effects of compressed air.
   (*f*) Effects of heat.
5. Learning:
   (*a*) Factors affecting immediate memory, especially in serial tasks.
   (*b*) Training of skills.
   (*c*) Factors affecting verbal learning.
6. Personality:
   (*a*) Relation of individual differences to skilled performance.
7. Methods:
   (*a*) Methods of assessing degree of confidence in experimental results.
   (*b*) Mathematical models for human performance.
   (*c*) Development of portable apparatus for assessing the deterioration of skill.
   (*d*) Automatic data reduction techniques.

INDUSTRIAL PSYCHOLOGY RESEARCH UNIT

Department of Psychology, University College London, Gower Street, W.C.1

(1918)

Honorary Director
Professor G. C. Drew, M.A.

Honorary Deputy Director
J. W. Whitfield, M.A.

Staff

L. J. Buck, B.Sc.
Mrs. G. C. de la Mare, M.A. (*part-time*)
Mrs. N. Harris, B.Sc.
Miss H. A. Long, B.Sc.
Miss D. Monnington, B.Sc.
R. Sergean, M.A.
R. D. Shepherd, B.Sc.
Miss S. B. N. Shimmin, B.Sc. (*until Aug. 1963*)
J. Walker, Ph.D.
P. C. Wason, Ph.D.*
Mrs. A. Zajaczkowska, Ph.D.

The aim of the Unit is to study occupational problems of scientific interest. Among these are some which can be studied only by field investigation and others which are amenable to laboratory experiment. Studies are also made to assess the value of the methods used in this type of research.

Summary of Research

1. Investigation of industrial motivation and behaviour: primarily field studies of individual and social factors affecting behaviour at all occupational levels.
   (*a*) Factors influencing preferred hours of work, e.g. overtime, shift cycles.
   (*b*) Individual differences in adaptation to shift work.
   (*c*) Financial and other incentives.
   (*d*) Personality, motivation and performance under stress.
   (*e*) Specific aspects of industrial behaviour, e.g. absence and attendance, labour turnover.
   (*f*) Development and refinement of methodology in field research.
2. Investigation of accidents:
   (*a*) Individual differences in accident behaviour.
   (*b*) Retrospective and prospective diagnosis of causative factors by the study of accident data and normal performance.
   (*c*) Relation between accidents and sensory information, particularly with respect to the content of sensory input and its form of presentation.
   (*d*) Evaluation of devices designed to maintain perceptual vigilance.
3. Studies on thinking and the communication of information:
   (*a*) Variables affecting:—
      (i) the comprehension of complex instructions,
      (ii) the composition of complex instructions.
   (*b*) Factors affecting the reaction time to negatively expressed sentences.
   (*c*) Transfer between conceptual systems, e.g. problems affecting the conversion to decimal coinage.
   (*d*) Information systems (types of information and the associated storage and flow arrangements) used in industry and elsewhere, showing (i) relation to success and failure in identifying and solving open problems such as production and policy problems, and also success in conceiving entirely new approaches to such problems; (ii) aspects of organization associated with the kinds of information systems provided by managements for control purposes.
   (*e*) Analysis of the flow of information within industry, and the effect of various organizational structures on such flow.
4. Analysis of skills:
   (*a*) Proprioceptive factors in muscular skill.
   (*b*) Sensory control of skilled movements, especially inter- and crossed modality problems.
   (*c*) Conceptual skills in classification tasks.
   (*d*) Effects of drugs on skills and individual differences in susceptibility.
   (*e*) Display/control problems in skill.
5. Perception studies:
   (*a*) Geometry of visual space.
   (*b*) Factors influencing efficiency of signs—e.g. road traffic signs.

* On leave of absence until August 1963 at Center for Cognitive Studies at Harvard University.

UNIT FOR THE EXPERIMENTAL INVESTIGATION OF BEHAVIOUR

Department of Psychology, University College London, Gower Street, W.C.1
(1955)

Honorary Director
Professor G. C. Drew, M.A.

Assistant Director
I. S. Russell, Ph.D.

Staff

Miss M. Khairy, Ph.D.*
N. Mrosovsky, Ph.D.
Miss C. M. Tinson, B.Sc.

Attached Workers

Mrs. L. Elliott, B.A. (*University College London*)
K. Oatley, B.A. (*M.R.C. Scholar*)
R. B. Ross, M.Sc. (*University College London*)
K. Strongman, B.A. (*D.S.I.R. Student*)
J. D. Valentine, B.A. (*M.R.C. Scholar*)

The Unit is studying the neurological correlates of behaviour. The work is concerned with analysing mechanisms of learning, conditioning and motivation.

Summary of Research

1. Use of stimulation, ablation and stereotactic lesions in the hypothalmus, limbic system and cortex to evaluate the roles of such systems in learning and motivation.
2. Use of spreading cortical depression as a technique of functional ablation combined with ' split-brain ' techniques to study the role of the cortex in learning and memory.
3. Effects of drugs, hypothermia and electroshock on conditioned behaviour.

UNIT FOR RESEARCH ON OCCUPATIONAL ASPECTS OF AGEING

Department of Psychology, University of Liverpool,
7, Abercromby Square, Liverpool, 7
(1955)

Honorary Director†
Professor L. S. Hearnshaw, M.A.

Honorary Medical Adviser
Professor A. B. Semple, V.R.D., M.D., D.P.H., Q.H.P.

Honorary Scientific Adviser
D. B. Bromley, Ph.D.

Staff

Mrs. S. M. Chown, Ph.D. (*honorarium*)
F. I. M. Craik, B.Sc.
Mrs. A. D. M. Davies, B.A.
C. K. Elliott, B.A. (*until Sept. 1963*)
R. V. J. Stevens, B.A. (*until July 1963*)
N. E. Wetherick, B.A.

The Unit is studying psychological changes with age in adult life, with particular reference to changes considered likely to be of occupational importance. Equal emphasis is being laid on laboratory and on field investigations.

Summary of Research

1. The adjustment of older workers, with special reference to the impact of unemployment and redundancy.
2. Adult learning and problems of the retraining and rehabilitation of older persons.
3. Experimental work on memory, problem solving, confidence and visual perception.
4. Evaluation of measures of ' functional age '.

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* Seconded to the Toxicology Research Unit from September 1962.
† Dr. Alastair Heron was Director of the Unit until August 1963.

SOCIAL MEDICINE RESEARCH UNIT

The London Hospital Research Laboratories, Ashfield Street, London, E.1

(1948)

Director
Professor J. N. Morris, D.Sc., F.R.C.P., D.P.H.

Assistant Director
J. A. Heady, Ph.D.

Staff

Mrs. M. Brewis, M.B.
Mrs. M. D. Crawford, M.D. (*part-time*)
P. A. Draper, M.B.
M. J. Gardner, B.Sc., Dip.Math.Stat.
Miss E. M. Goldberg, Dip.S.S. (*part-time*)
J. A. H. Lee, M.D., B.Sc., D.P.H.
L. Lipworth, M.B., B.Sc. (*until Mar. 1963*)
D. C. Pattison, M.B., D.Obst.R.C.O.G., D.P.H.
M. J. Power, Dip.S.S.
Miss E. Shoenberg, M.A., M.R.C.S., D.P.M. (*part-time*)
W. Watson, D.F.C., Ph.D. (*part-time; honorarium*)
S. Yasin, M.A.

Visiting and Attached Workers

Mrs. D. Drutman, Ph.D. (*Israel; British Council Fellow*)
Z. Hejl, Dr.Med. (*Prague; W.H.O. Fellow*)
M. Sarner, M.B., M.R.C.P. (*St. George's Hospital, London*)
J. P. Strong, M.D., B.S. (*Louisiana State University, U.S.P.H.S. Award*)

The Unit investigates the influence that social factors may have upon health and sickness, and the relation of social to other factors. Studies are made of populations and groups and of their environments, and individuals are studied in relation to these.

Summary of Research

STUDIES ON CARDIOVASCULAR DISEASE

1. Coronary artery disease and ischaemic heart disease in relation to nature of work and to other factors, including physique and obesity, blood pressure, blood lipids and family history.
2. Inheritance and environment in relation to levels of blood pressure and of blood lipids.
3. Prognosis of ischaemic heart disease in relation to diet (therapeutic trial in collaboration with several hospitals); diet and obesity in middle age; diet and blood lipids.
4. Relation of cardiovascular disease to the water supply and other local factors in British towns.
5. Epidemiology of ruptured cerebral aneurysm and subarachnoid haemorrhage (in collaboration with St. George's Hospital).

STUDIES ON MENTAL DISEASE

1. Background of young men admitted to local mental hospitals: occupational history over three generations, family structure and relationships, and the family history of admission to mental hospitals.
2. Follow-up study of the young men in the community after discharge.

SOCIAL STUDIES

1. Juvenile delinquency in East London.
2. Patterns of leisure in middle age; physical activity apart from work.

MISCELLANEOUS STUDIES

1. Mortality and major morbidity in young people.
2. Study of the observed concentration of the clinical onset of leukaemia in the summer months.

3. Cancer of the stomach in relation to the nature of local water supplies and atmospheric pollution in England and Wales.
4. Current trends in mortality and morbidity in Britain.
5. Methodological studies:
   (*a*) Use of electronic computers.
   (*b*) Development of food tables for diet surveys.

OPERATIONAL RESEARCH ON THE WORKING OF HEALTH SERVICES

1. Condition of patients, care received, and post-operative morbidity and mortality in teaching and non-teaching hospitals.
2. Local and personal variations of prescribing rates in general practice; the use by general practitioners of other health and welfare services (in collaboration with the Department of Pharmacology, London Hospital Medical College, and the Department of Statistics, Rothamsted Experimental Station).

STATISTICAL RESEARCH UNIT

University College Hospital Medical School,
115, Gower Street, London, W.C.1
(1926)

Director
W. R. S. Doll, O.B.E., M.D., D.Sc., F.R.C.P.

Staff

J. T. Boyd, M.B., D.P.H.
Miss C. M. Devine, B.Sc.
A. S. Fairbairn, M.B.
I. D. Hill, B.Sc.
J. O. Irwin, Sc.D., D.Sc.* (*adviser in biometric techniques*)
B. K. Kelly, B.A.†
Miss B. J. Kinsley, B.Sc. (*until July 1963*)
W. J. Martin, D.Sc.*
M. C. Pike, Ph.D.
I. Sutherland, D.Phil.
Miss R. Tall, B.Sc.

Visiting Worker
J. H. O. Schröder, M.D. (*Würzburg University; British Council Scholar*)

The Unit is concerned with the development and application of statistical methods in medicine and in its 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 not only the individual researches of members of the Unit's staff but also the main items of collaborative work with other Council units, the Council's committees and other scientific workers.

Summary of Research

EPIDEMIOLOGY AND AETIOLOGY OF DISEASE

1. Aetiology of cancer of the lung, with particular reference to smoking, air pollution and industry.
2. Epidemiology of cardio-respiratory diseases.
3. Atmospheric pollution and respiratory disease.
4. Long-term effects of therapeutic irradiation.
5. Effects of small amounts of absorbed radium.
6. Effects of smoking on mortality.
7. Blood groups and gastro-duodenal diseases.

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* Working at the London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1.

† Transferred to External Staff from July 1963, in charge of the Computer Services Centre at 172, Tottenham Court Road, London, W.C.1.

8. Epidemiological features of mortality from leukaemia and from cancer of bone, thyroid, stomach and cervix uteri.
9. Comparisons between human and experimental data on carcinogenesis.
10. Prevalence of infection with drug-resistant tubercle bacilli.
11. World-wide survey of measles.
12. Sources of emotional disturbance in children.

THERAPEUTIC TRIALS

1. Drugs in respiratory tuberculosis in this country and abroad.
2. Drugs in depressive illness.
3. Treatment of leukaemia and carcinoma of the bronchus.
4. Treatment of gastric ulcer.
5. Treatment of leprosy.
6. Analgesics in midwifery.

FIELD TRIALS OF PROPHYLACTIC AGENTS

1. BCG and vole bacillus vaccine in the prevention of tuberculosis in adolescents.
2. BCG vaccine in the prevention of leprosy.
3. Trachoma vaccines.
4. Influenza vaccine for chronic bronchitics and old persons, and live virus vaccines for the prevention of influenza.
5. Fluoride tooth paste for dental caries.

MISCELLANEOUS STUDIES

1. Problems of railway accidents.
2. Studies of tuberculin sensitivity.
3. Reactions to Kveim antigen in healthy subjects.
4. Studies of drug toxicity in different countries.
5. Methods of assessing alcohol in tissue fluids.
6. Analysis of survival curves of micro-organisms subject to irradiation.
7. Use of the electronic computer in epidemiological work.

INDUSTRIAL INJURIES AND BURNS RESEARCH UNIT

Birmingham Accident Hospital, Bath Row, Birmingham, 15

(1952)

Director

J. P. Bull, M.D.

Staff

Miss S. Baar, F.R.I.C.
W. J. D. Bradfield, M.B., F.R.C.S. (*until Dec. 1962*)
Mrs. G. M. Buck, B.Sc.
J. W. L. Davies, Ph.D.
Miss S. P. Farrow, B.Sc.
D. MacG. Jackson, M.D., F.R.C.S. (*part-time*)
R. J. Jones, Ph.D.
J. C. Lawrence, Ph.D.
E. J. L. Lowbury, D.M.
C. R. Ricketts, D.Sc.

Visiting Worker

G. Arturson, M.D. (*University of Uppsala*)

The work of the Unit is concerned with the causes, local and general pathology, complications and treatment of accidental injuries, including burns and scalds. The Unit works in close liaison with the staff of the Birmingham Accident Hospital.

Summary of Research

1. Types, causes and prevention of common injuries; a special study of industrial burns.
2. Studies of the shock stage following burns:
   (*a*) Comparative trial of different colloid replacement fluids, correlating changes in red cell and blood volume with clinical signs and mortality.
   (*b*) Role of oral and intravenous saline solutions in the treatment of burns.
3. Re-examination of the specification of clinical dextran; effect of different dextran preparations on plasma volume.
4. Effect of heat on haemoglobin and on certain red cell enzymes; cation exchange of heated red cells and the effect of metabolic inhibitors and stimulators on this exchange.
5. Albumin, globulin and fibrinogen metabolism following burns and other injuries, studied with ^{131}I- and ^{125}I-labelled proteins.
6. Changes in serum lipoproteins after burns and other injuries, including studies with β-lipoprotein labelled with ^{131}I.
7. Plasma protein changes and acid–base balance in burn patients not receiving intravenous fluid.
8. Sodium requirements in burns; estimation of biological half-life of ^{22}Na in burn patients.
9. Skin metabolism in relation to burns and the healing of wounds and grafts:
   (*a*) The effects of thermal damage and therapeutic materials on skin cells.
   (*b*) *In vitro* formation of collagen in skin.
   (*c*) Action of proteolytic enzymes on skin.
   (*d*) Composition, toxicity and antigenicity of extracts from burned skin.
10. Contribution of bacterial infection to the pyrexia, blood changes and other general effects of burns; formation in patients with burns of antibodies to bacteria and other possible antigens in the burn.
11. Development of methods for identification of wound flora.
12. Epidemiology of infection of burns and wounds, with special reference to the hygiene of operating theatres and to the distribution and characteristics of *Staphylococcus aureus* in different environments.
13. Controlled trials of local chemotherapy and chemoprophylaxis in burns and open wounds; studies of various methods of skin disinfection.

TOXICOLOGY RESEARCH UNIT

Medical Research Council Laboratories, Woodmansterne Road, Carshalton, Surrey

(1947)

Director

J. M. Barnes, C.B.E., M.B.

Staff

W. N. Aldridge, Ph.D.
T. W. Clarkson, Ph.D.
Miss V. M. Craddock, Ph.D.
Miss J. E. Cremer, B.Sc.
D. F. Heath, D.Phil.
M. K. Johnson, B.Sc., A.R.I.C.
P. N. Magee, M.B.
J. Matthews, Ph.D.
A. R. Mattocks, Ph.D., A.R.I.C.
V. H. Parker, B.Sc.
M. S. Rose, B.Sc.
Miss R. Schoental, D.Sc.
H. B. Stoner, M.D., B.Sc.
B. Terracini, Laurea in Med.
Miss M. Thomas, B.Sc. (*until Aug. 1963*)
C. J. Threlfall, B.Sc.

Visiting workers

Miss P. M. Fullerton, D.M., M.R.C.P. (*Institute of Neurology*)
Miss M. Khairy, Ph.D. (*Unit for the Experimental Investigation of Behaviour*)
K. Y. Lee, Ph.D. (*Division of Oncology, Chicago Medical School*)
L. Magos, M.D. (*State Institute of Occupational Health, Budapest*)

The aim of the Unit is to learn more about physiological processes by a study of the disturbances produced by both physical and chemical injury. The standard physical injury is tourniquet shock. The toxic substances being studied include: aflatoxin and ground nut meals, alkyl nitrosamines, beryllium, lead,

dichlorovinylcysteine, methyl bromide and iodide, *N*-nitroso-*N*-methylurethane, organo-tin, -lead and -mercury compounds, organophosphates and carbamates (used as insecticides), pyrrolizidine alkaloids and other plant materials.

Summary of Research

1. Metabolic responses of tissue slices and cell fractions, both poisoned *in vitro* and taken from poisoned animals.
2. Interrelationship of glucose and amino acid metabolism in rat brain.
3. Examination of the chemical, biochemical and physical properties of substances which uncouple oxidative phosphorylation.
4. Biochemical effects of trialkyltin compounds.
5. Alkylation of cell constituents by alkyl nitrosamines and other agents *in vivo* and its possible relation to cellular injury and carcinogenesis.
6. Mechanism of the toxic action of alkyl nitrosourethanes, with special reference to sulphydryl groups.
7. Substrate specificity and sensitivity to inhibitors of esterases in the central nervous system of the fowl.
8. Mechanism of toxic injury to renal tubules by dichlorovinylcysteine.
9. Toxicity-structure relations in semi-synthetic pyrrolizidine alkaloids.
10. Biochemistry of the toxic action of methyl bromide and iodide.
11. Inhibition of enzymes by beryllium.
12. Toxic and diuretic action of mercury compounds.
13. Peripheral nerve injury produced by inorganic lead.
14. Quantitative studies on the reactions of glycolysis, gluconeogenesis and the tricarboxylic acid cycle *in vivo* after physical injury.
15. Fat metabolism after physical injury.
16. Role of bacterial products from gut flora in the response to physical injury.
17. Influence of cold-acclimation on the effects of physical injury.
18. Observations on the body temperature of patients with multiple injuries.
19. Measurement of rate of heat loss after physical injury in a gradient layer calorimeter (with Dr. J. D. Pullar, Rowett Research Institute).
20. Behaviour changes in rats as an early index of poisoning.

ENVIRONMENTAL PHYSIOLOGY RESEARCH UNIT

London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1
(1948)

Director
J. S. Weiner, Ph.D., M.R.C.S.

Staff

C. R. Bell, B.A.
K. J. Collins, D.Phil.
G. W. Crockford, B.Sc.
K. G. Foster, B.Sc.
R. F. Hellon, D.Phil.

Visiting and Attached Workers
P. W. Humphreys, B.Sc. (*National Coal Board*)
A. R. Lind, D.Phil. (*National Coal Board*)

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. Effects of heavy muscular work and static effort on the peripheral circulation in different environmental conditions.
3. Relationship of raised body temperature to performance in high temperature environmental conditions.
4. Intense radiant heat in relation to the development of protective clothing.

5. Biochemistry and histochemistry of sweat gland activity in man and animals.
6. Growth and heat tolerance of animals at high temperatures.
7. Role of endocrine glands in heat adaptation.
8. Fluid and electrolyte balance during heat exposure in man.
9. Neurological basis of temperature regulation.
10. *Ad hoc* studies include:
    (*a*) Limits of work in coal mining, steel works and other industries in relation to environmental conditions.
    (*b*) Application of anthropometric data to the design of seats and other equipment in vehicles, laboratory and hospital furniture, and for the Services.

PNEUMOCONIOSIS RESEARCH UNIT
Llandough Hospital, Penarth, Glamorgan
(1945)

Director
J. C. Gilson, O.B.E., M.B., F.R.C.P.

Staff

J. D. Abernethy, M.B.
D. P. G. Bolton, B.M. (*part-time*)
W. G. Clarke, M.S.R.
G. W. Cook, M.A.
J. E. Cotes, B.M., M.R.C.P.
Mrs. M. McDermott, B.Sc.
N. Mishra, M.M.F., D.T.M. & H. (*part-time*) (*until Apr. 1963*)
C. B. McKerrow, M.D., M.R.C.P.
T. G. Morris, Ph.D., D.I.C.
P. D. Oldham, M.A.
N. Pearl, M.D., B.Sc.
I. P. Priban, Ph.D. (*until May 1963*)
C. E. Rossiter, M.A.
P. L. Storring, M.B.
V. Timbrell, Ph.D., D.I.C.
J. C. Wagner, M.D.
J. Winch, B.M. (*until Aug. 1963*)

Senior Technical Officer : F. Meade

The Unit is investigating the effects of age and of dust exposure and other environmental factors on the lung. The work includes physical studies on respirable dust. Part of the work is carried out in collaboration with the Epidemiological Research Unit (South Wales).

Summary of Research

FIELD STUDIES

1. A prospective investigation of byssinosis in the cotton industry (in collaboration with Departments of Occupational Health at London School of Hygiene and University of Manchester).
2. Relation of type of asbestos dust exposure to pulmonary malignancy.
3. Surveys of workers exposed to sisal, hemp, beryllium, hard metal, and mouldy hay dusts.
4. Acute pulmonary function changes produced by cigarette smoking in working populations (in collaboration with Postgraduate Medical School, University of London).

STUDIES ON CARDIO-PULMONARY FUNCTION

1. Physiological effects of inhaling oxygen.
2. Effects of technical factors, age, size, race, and time of day and year on pulmonary diffusing capacity.
3. Physical and physiological parameters affecting response to inhaled aerosols.
4. Methods of measuring lung elasticity and ventilation/perfusion ratios.
5. Multivariate analysis of physiological measurements on a group of miners studied at an interval of 11 years.
6. Seasonal variations in lung function.
7. Development of portable dry timed-spirometer.

PATHOLOGY

1. Relation of quantity and composition of dust in lungs to pathology and X-ray category in various types of pneumoconiosis (with Dr. D. Rivers, Coventry and Warwick Hospital, and Safety in Mines Research Establishment, Sheffield).

2. Techniques for relating lung function and morbid anatomy in chronic lung disease.
3. Immunological factors in coalworkers' pneumoconiosis (with Professor B. Pernis, Clínica del Lavoro, Milan).

EXPERIMENTAL PATHOLOGY

1. Production of mesothelial tumours of the pleura by various types of asbestos.
2. Relation of rank of coal to deposition and retention in animal lungs.
3. Chemical and biochemical analysis of normal and pathological lungs.

DUST PHYSICS

1. Performance testing of gravimetric sampling instruments designed to collect respirable fraction of the airborne dust.
2. Analysis of particle size by double-image microscopic micrometer.

RADIOGRAPHY

Standardization of chest radiographs and methods of copying films; supervision of set of films distributed by I.L.O.

TREATMENT

1. Controlled trials of chemotherapy in early chronic bronchitis and complicated pneumoconiosis of coalworkers with and without tuberculosis.
2. Inconspicuous methods of administration of oxygen.

EPIDEMIOLOGICAL RESEARCH UNIT (SOUTH WALES)

4, Richmond Road, Cardiff

(1960)

Honorary Director

Professor A. L. Cochrane, M.B.E., M.B., M.R.C.P., D.P.H.

Honorary Assistant Director

W. E. Miall, M.D.*

Staff

H. Campbell, M.B., F.S.S. (*part-time*)
I. T. T. Higgins, M.D., M.R.C.P. (*until Feb. 1963*)
F. C. Hollows, M.B., F.R.C.S.I., D.O.
J. W. Palmer, B.A., D.P.S.A.
J. Thomas, M.A. (*until Nov. 1962*)

The Unit is developing epidemiological techniques for the study of the prevalence and attack rates of common diseases with the ultimate objective of obtaining clues to aetiology and prevention. In addition, the Unit is continuing a series of longitudinal studies of the factors influencing various common diseases. The Unit works in close association with the Epidemiological Research Unit in Jamaica and the Social Psychiatry Research Unit.

Summary of Research

1. Factors influencing the prevalence, attack rate and progression rate of coalworkers' pneumoconiosis, in particular the more serious form, progressive massive fibrosis.
2. Tuberculin reaction in miners, ex-miners and children in the Rhondda Fach.
3. Prevalence of atypical tubercle bacilli in the population of the Rhondda Fach (with Dr. J. Marks, Central Tuberculosis Reference Laboratory, Cardiff).
4. Social factors associated with juvenile delinquency in the Rhondda Fach.
5. Anaemia in school children in Cardiff (with Dr. Stewart Kilpatrick, Cardiff Royal Infirmary, and Dr. W. Powell Phillips, Medical Officer of Health for Cardiff), and general studies in anaemia (with Medical Unit, Cardiff Royal Infirmary).
6. Factors influencing the prevalence of glaucoma in communities.
7. Development of techniques for keeping a census up to date in a local authority area.

* Also Director of the Epidemiological Research Unit (Jamaica).

EPIDEMIOLOGICAL RESEARCH UNIT (JAMAICA)

University of the West Indies, Mona, Jamaica
(1962)

Director
W. E. Miall, M.D.*

Staff

M. T. Ashcroft, D.M., D.P.H., D.T.M. & H.
H. G. Lovell, B.A.
H. I. McKenzie, B.Sc.
K. A. Smith, M.B.†
K. L. Standard, M.D., M.P.H. (*honorary; part-time*)

Visiting and Attached Workers

J. Fodor, M.D. (*Institute of Cardiovascular Research, Prague; W.H.O. Fellow*)
P. Ratan, M.B., M.R.C.P. (*Port of Spain General Hospital, Trinidad; Rockefeller Foundation grant-holder*)

The aim of the Unit is to conduct a series of long-term epidemiological studies of common diseases in the general population of the Caribbean. Survey techniques developed in the Council's Pneumoconiosis and Epidemiological Research Units in South Wales are being applied to provide comparable data in representative samples of West Indians and Welshmen.

Summary of Research

CARDIOVASCULAR RESEARCH

1. A longitudinal study of the influence of environmental and genetic factors on arterial pressure in rural and urban populations in Jamaica and South Wales, with a view to discovering whether differences exist between the two races in the environmental influences determining the rate of rise of arterial pressure with age, in the magnitude of the genetic factor, and in the prognosis of all ranges of arterial pressure.
2. Role of bacteriuria in the aetiology of hypertension in Jamaica and South Wales (with Dr. E. H. Kass, Harvard University Medical School).
3. Clinical and electrocardiographic studies of the prevalence and attack rates of angina pectoris, myocardial disease, intermittent claudication and cerebrovascular lesions in middle-aged adults.
4. Factors influencing the attack rate of pre-eclampsia.
5. Relationship between fibromyomata of the uterus and hypertension.
6. Influence of the nature of water supplies and other geographical features on cardiovascular mortality.
7. The roles of hypertension and treponemal infection in the aetiology of aortic disease.

STUDIES ON CHILD DEVELOPMENT AND MORTALITY

1. Factors influencing child development in a rural population in Jamaica (these studies are designed to be comparable with similar investigations carried out at the Medical Research Council Laboratories, Gambia, and the Obstetric Medicine Research Unit, Aberdeen).
2. Investigation of 10 per cent of all deaths in the island among children aged 6 months to 3 years to reveal the children at greatest risk and the socio-medical factors involved (in collaboration with the Jamaican Ministry of Health and the Tropical Metabolism Research Unit).
3. A sociological study of the influence of different types of family structure on child development and performance in a rural population.
4. Measurement of heights and weights of school children in various rural and urban areas of Jamaica to compare rate of growth with that in other countries and to correlate it, if possible, with nutritional status.

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* Also Honorary Assistant Director of the Epidemiological Research Unit (South Wales).
† Seconded from the Ministry of Health, Jamaica.

In collaboration with the Jamaican Government and the University of the West Indies, the Unit has taken over the responsibility for providing the health service for a rural population of 8000 subjects. It is hoped that this operational research may reveal, by comparisons with other areas, what a more comprehensive type of health service can be expected to achieve in terms of reduced morbidity and mortality, and at what cost, and to indicate possible ways in which the health service can be improved in rural areas in the Caribbean.

AIR POLLUTION RESEARCH UNIT

St. Bartholomew's Hospital Medical College, Charterhouse Square, London, E.C.1

(1955)

Director

P. J. Lawther, M.B., F.R.C.P.

Staff

B. T. Commins, Ph.D., A.R.I.C.
Mrs. J. Coulson, B.Sc.
J. McK. Ellison, Ph.D.
G. Kazantzis, M.B., Ph.D., F.R.C.S., M.R.C.P.
Miss W. Moulds, B.Sc. (*until Jan. 1963*)
T. Nash, B.Sc., A.R.I.C.
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.

Summary of Research

1. Physical characteristics of particulate pollution; minute structure of particles as shown by the electron microscope; chemical nature of solid, liquid and gaseous air pollutants and the reactions which occur between them, especially during temperature inversions.
2. Development of analytical techniques in determination of pollutants in the extreme dilutions occurring in urban atmospheres.
3. The 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 the clinical condition of patients with chronic bronchitis and emphysema in relation to daily changes in weather and air pollution.
8. Clinical trials of smog masks and other protective devices.
9. The health and sickness absence of Sheffield children entering school in 1956 in areas of contrasting air pollution.
10. Survey of all deaths in Sheffield in relation to air pollution.
11. Evaluation of data from National Insurance certification of incapacity ascribed to bronchitis, pneumonia and influenza in Sheffield.
12. Clinical study of workers exposed to compounds of mercury and cadmium.
13. Respiratory function in patients with occupational disease of the lungs.
14. Carcinogenic action of certain compounds of cadmium, nickel, arsenic and other metals.
15. Possible hazards associated with the manufacture and application of insecticides.

CARCINOGENIC SUBSTANCES RESEARCH UNIT

Washington Singer Laboratories, The University, Exeter

(1956)

Honorary Director

Sir James Cook, D.Sc., F.R.S.

Staff

A. Bhati, Ph.D.
W. Carruthers, Ph.D.
A. G. Douglas, B.Sc.
R. A. W. Johnstone, Ph.D.
P. M. Quan, B.Sc. (*until Aug. 1963*)
D. A. M. Watkins, Ph.D.

The Unit is investigating the chemistry of tobacco smoke and of certain high-boiling fractions of petroleum. Direct experimental evidence is being sought for the possible role of cigarette smoke in the causation of lung cancer by chemical analysis of the smoke and identification of any carcinogens which may be present. The origin of some constituents of the smoke and their mode of formation from substances present in the tobacco leaf are being studied. The work on high-boiling petroleum fractions relates to the carcinogenic activity of some of these materials, and has as its object the isolation and identification of substances responsible for the carcinogenic activity of selected oils.

Summary of Research

STUDIES ON TOBACCO SMOKE

1. Chemical investigation of cigarette smoke, and isolation and identification of pure constituents.
2. Mode of formation of certain constituents of cigarette smoke.
3. Investigation of the constituents of green and cured tobacco leaf.

STUDIES ON MINERAL OILS

1. Chemical examination of carcinogenic fractions distilled from selected crude oils, and isolation and identification of pure constituents.
2. Synthetic preparation of larger samples of these pure constituents for biological testing.

LABORATORY ANIMALS CENTRE

Medical Research Council Laboratories, Woodmansterne Road, Carshalton, Surrey

(1947)

Director

W. Lane-Petter, M.B.

Staff

J. Bleby, B.Vet.Med.
Miss A. M. Brown, Ph.D.
Miss M. J. Cook, B.Sc.
Miss M. Dinsley, Ph.D.
G. Porter
A. A. Tuffery, M.Sc.

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 on all problems concerning laboratory animals, and to maintain liaison with comparable organizations in

other countries: to this end it prepares news letters, catalogues, and other material for distribution to other laboratories, and administers an accreditation scheme for breeders of guinea pigs, mice and rabbits; (2) to maintain primary-type colonies of special strains—at present fifteen inbred strains and one non-inbred strain of mice, and one inbred and one non-inbred strain of rats; (3) to conduct relevant research, and (4) to train staff, both graduate and technical.

Summary of Research

1. Methods of large-scale production of mice and rats conforming to a given specification genetically, and to certain standards of health and nutrition.
2. Control of health in large laboratory populations of high density, especially in conditions of rigorous isolation.
3. Assessment of adequacy of compound diets, especially after sterilization.
4. Assessment of differences in response to various stimuli between different strains of mice (mostly inbred).
5. Anatomy of the mouse.

Research Groups

The scheme of research groups has been instituted by the Council to enable them to assist in the development of a research programme in a university department where they regard it as in the national interest to do so. 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 absorb it into its normal structure at the end of the agreed period of tenure, if it wishes the work to continue.

RESEARCH GROUP ON ADRENERGIC MECHANISMS

University Laboratory of Physiology, Oxford
(1960)

Honorary Director
Professor Sir Lindor Brown, C.B.E., M.B., M.Sc., F.R.C.P., F.R.S.

Staff
D. P. Dearnaley, B.A.
C. B. Ferry, B.Sc., B.Pharm.

Attached Worker
A. G. H. Blakeley, B.A. (*Theodore Williams Scholar*)

The Group is studying the factors regulating the release and inactivation of the substance transmitting the effects of adrenergic nerves.

Summary of Research

1. Uptake and release of isotopically labelled *nor*adrenaline by the isolated perfused spleen.
2. Pattern of innervation of tissues with sympathetic nerve supply.

BIOMECHANICS RESEARCH GROUP

Bio-Engineering Unit, Department of Mechanical Engineering,
The Royal College of Science and Technology, Glasgow, C.1
(1963)

Honorary Director
Professor R. M. Kenedi, Ph.D., A.R.C.S.T., A.M.I.Mech.E., A.F.R.Ae.S.

Honorary Clinical Directors
Professor R. Barnes, M.B., B.Sc., F.R.C.S.
T. Gibson, M.B., F.R.C.S.E., F.R.C.S.G.

Staff
T. C. Duggan, B.Sc., A.Inst.P.
J. P. Paul, B.Sc., A.R.C.S.T., A.M.I.Mech.E. (*part-time*)
E. R. Robertson, B.Sc., A.R.C.S.T., A.M.I.Mech.E. (*part-time*)
D. S. Ross, Ph.D., A.R.C.S.T., A.M.I.Mech.E., A.M.Prod.E., A.M.Inst.R. (*part-time*)
C. Sorbie, M.B., F.R.C.S.E. (*honorary*)
R. Zalter, M.D.

The basic aim of the Group is the investigation of the structural and mechanical properties of human tissues, the engineering principles underlying their function and any practical clinical applications which may arise from these. The Group operates under the general guidance of a medical-engineering steering committee, the engineering investigations being closely correlated with associated clinical studies.

1. Skin tensions:
   (*a*) Determination of the physical and mechanical characteristics of human skin and formulation of a theory to describe in analytical terms its mechanical behaviour.
   (*b*) Determination of the normal and blanching tension patterns in the skin of the human body, with reference to the directions and relative values of maximum and minimum tensions.
   (*c*) Analytical and experimental investigation of the phenomena of skin stretch, its correlation with changes in body dimensions, and its influence on scar formation, stitching tension and root blanching of flaps and relaxation of tension across tightly stitched wounds.
2. Dynamic forces in joints:
   (*a*) Analytical and experimental investigation of the force actions transmitted by the hip joint of the human body during activity, including evaluation of force actions exerted on the body, determination of the inertia effects of the relevant limbs, identification of the muscle groups significant in action with respect to the force transmitted by the joint-bearing surfaces, and the magnitude and line of action of the joint force itself.
   (*b*) Investigation of the force-deformation characteristics of bone and bone-implant combinations *in vivo* and *in vitro*, directed to evaluation of the mechanical characteristics most significant in the development and design of implants.
3. Characteristics of human cartilage:
   (*a*) Determination of the physical and mechanical characteristics of human cartilage and formulation of a theory to describe in analytical terms its mechanical behaviour.
   (*b*) Determination of the self-locked stress actions in human rib cartilage and its functional role in movement of the rib cage.
   (*c*) Development of techniques for the transplantation of the articular cartilage of the hip joint.

CARDIOVASCULAR RESEARCH GROUP

Postgraduate Medical School of London,
Ducane Road, London, W.12
(1961)

Director
J. P. Shillingford, M.D., F.R.C.P. (*part-time*)

Staff
I. Gabe, M.D., M.R.C.P.

Visiting and Attached Workers

O. W. Boicourt, M.D. (*National Institutes of Health Fellow*)
C. T. Dollery, M.B., M.R.C.P. (*Postgraduate Medical School of London*)
P. Gillam, M.B., M.R.C.P. (*Postgraduate Medical School of London*)
S. L. Kountz, M.D. (*National Institutes of Health Fellow*)
R. Malcrona, med. lic. (*Swedish Medical Research Council*)
C. J. Mills, B.Sc. (*The Royal Society, Paul Instrument Fund Research Fellow*)
R. E. Nagle, M.B., M.R.C.P. (*Postgraduate Medical School of London*)
B. Pentecost, M.B., M.R.C.P. (*Postgraduate Medical School of London*)
M. Thomas, M.B., M.R.C.P. (*M.R.C. Junior Research Fellow*)
J. Tuckman, M.D. (*National Institutes of Health Fellow*)

The Group is concerned with the study of the circulation in health and disease. The research programme includes the development of new methods designed to improve the early diagnosis of heart disease, the investigation of the causes of high blood pressure and studies on hypertensive and coronary heart disease. These investigations are augmented by basic laboratory studies, including research into the biophysics of the circulation.

Summary of Research

1. Study of the circulation, by indicator dilution curves:
   (*a*) Measurements of changes in cardiac output in association with other haemodynamic data in patients receiving hypotensive drugs.
   (*b*) Detection and estimation of intracardiac shunts.
   (*c*) Measurement of local venous flow and its application to the study of renal and arterial disease.
2. Direct measurement of the velocity of blood flow in man and its application to the study of resistance to blood flow in the pulmonary artery and aorta in health and disease.
3. Studies on blood pressure in man, by means of continuous peripheral recording, and assessment of drugs in hypertension.
4. Studies in association with the intensive care unit for coronary thrombosis.

RESEARCH GROUP ON DEMYELINATING DISEASES

13, Framlington Place, Newcastle upon Tyne, 2
(1961)

Honorary Director
E. J. Field, M.D., M.S., Ph.D.

Honorary Clinical Adviser
H. G. Miller, M.D., F.R.C.P., D.P.M.

Staff
E. A. Caspary, M.Sc. V. R. Cunningham, Ph.D.

The Group is continuing its study of evidence for an allergic mechanism at work in the pathogenesis of multiple sclerosis. A highly encephalitogenic factor which members of the Group have isolated from human brain (active at doses of 1 μg in 500 g guinea pigs) is being studied. It appears to be a protein of about 40 000–50 000 molecular weight and its main constituents have been determined. Antibodies to it are present not only in the blood of multiple sclerotic patients but also in the blood of those suffering from other diseases in which there is reason to believe that brain disintegration has taken place.

Summary of Research

1. Toxicity studies of disseminated sclerosis serum for glial cells and myelinated nerve fibres in tissue culture.
2. Pathogenicity for animals (especially sheep, goats and monkeys) of nervous tissue from cases of acute disseminated sclerosis.
3. Demyelination in wabbler-lethal mice, studied by both light- and electron microscopy.
4. Chemical and biological properties of a highly encephalitogenic factor isolated from human brain.
5. Factor(s) from tubercle bacillus active in Freund's adjuvant, and its possible use in the prevention of experimental 'allergic' encephalomyelitis.
6. Analysis of data from an extended survey of disseminated sclerosis in north-eastern England with special reference to familial occurrence and the role of pregnancy in the natural history of the disease.
7. Clinical trials of treatment with chloroquine and gamma globulin.

RESEARCH GROUP IN ENZYMOLOGY

Department of Chemical Pathology, St. Mary's Hospital Medical School, London, W.2

(1960)

Honorary Director
Professor A. Neuberger, M.D., Ph.D., F.R.S.

Staff

Miss M. Matthew, B.Sc.
G. H. Tait, Ph.D.
J. M. Turner, Ph.D.

The Group is continuing its work on the formation of bacteriochlorophyll and related enzymic problems. The Group is also examining the composition and formation of chromatophores in photosynthetic micro-organisms.

Summary of Research

1. Studies on an enzyme which incorporates zinc into protoporphyrin monomethyl ester but is not active with magnesium; incorporation of magnesium into protoporphyrin.
2. Studies on a variety of transamination reactions in micro-organisms.
3. Metabolism of aminomalonate and mesoxalate.

EPIGENETICS RESEARCH GROUP

Institute of Animal Genetics, The University, West Mains Road, Edinburgh 9

(1962)

Honorary Director
Professor C. H. Waddington, C.B.E., Sc.D., F.R.S.

Deputy Director
H. Kacser, Ph.D. (*part-time*)

Staff

J. A. Burns, B.Sc.
Mrs. Ruth M. Clayton, M.A. (*honorary*)
R. O. Jones, B.Sc.
A. Jurand, M.Biol.
H. Kacser, Ph.D. (*part-time*)
G. G. Selman, Ph.D. (*honorary*)
Miss S. Ullman, Ph.D.

The general aims of the Group are to study the macromolecular, ultrastructural and genetic processes by which embryonic cells develop into the different types found in the adult.

Summary of Research

1. Electron microscopical investigations of developing cells, particularly in the embryos of *Drosophila* and amphibia.
2. Nuclear–cytoplasmic interactions in *Micrasterias*.
3. Use of antisera, labelled with fluorescent dyes or electron-dense labels, on differentiating cells.
4. Integration of gene-controlled enzymatic pathways into organized networks: theoretical study with an analogue computer, experimental study on certain enzyme systems in *Neurospora*.

CLINICAL IMMUNOLOGY RESEARCH GROUP

Institute of Diseases of the Chest, Brompton Hospital, London, S.W.3
(1960)

Director
J. Pepys, M.B., M.R.C.P.

Staff
P. A. Jenkins, B.Sc.
Miss J. L. Longbottom, M.Sc.

The Group is investigating the immunological responses in man to the common pathogenic and non-pathogenic fungi, to organic vegetable dusts and to mycobacteria, in particular *Mycobacterium tuberculosis* and *Myco. leprae*, and the relationship of the immunological findings to clinical manifestations in pulmonary disorders. Controlled studies in the management of allergic disorders are to be conducted.

Summary of Research

1. Separation and identification of antigens and allergens from *Aspergillus fumigatus* and their investigation in patients suffering from broncho-pulmonary aspergillosis.
2. (*a*) Nature and development in mouldy hay of antigens responsible for Farmer's Lung, and their testing in affected subjects; antigenic composition of mouldy hays produced under laboratory conditions (with Dr. P. H. Gregory, Rothamsted Experimental Station).
   (*b*) Epidemiological and immunological aspects of Farmer's Lung.
3. (*a*) Demonstration of immunological responses to a wide variety of vegetable dusts and fungi and correlation with the clinical findings.
   (*b*) Antigenic relationships of vegetable dusts and fungi.
4. Chemical and immunological changes of the sera of patients during treatment for leprosy (with Dr. R. J. W. Rees, National Institute for Medical Research).
5. Types of hypersensitive response elicited by protein, polysaccharide and lipopolysaccharide components of *Myco. tuberculosis*.

RESEARCH GROUP ON EXPERIMENTAL AND CLINICAL PROBLEMS OF TRANSPLANTATION

Department of Surgical Science, The University, Edinburgh, 8
(1961)

Honorary Director
Professor M. F. A. Woodruff, M.D., D.Sc., M.S., F.R.C.S.

Staff
N. F. Anderson, M.B.
J. G. Howard, M.D., Ph.D. (*honorary*)
D. Michie, M.A., D.Phil. (*honorary*)
B. Nolan, M.B., F.R.C.S. (*honorary*)

Visiting and Attached Workers
H. M. Abaza, M.B., D.Ch. (*Alexandria Medical Research Institute Scholar*)
J. L. Boak, M.B., F.R.C.S.E. (*M.R.C. Junior Fellow*)
G. J. A. Clunie, M.B., F.R.C.S. (*University of Edinburgh*)
C. J. Inchley, B.Sc. (*M.R.C. Scholar*)
D. Stickel, M.D. (*Duke University, North Carolina*)

The Group is engaged in clinical and laboratory investigations on tissue transplantation immunity. These include both technical studies of transplantation procedures and fundamental research on the biological processes involved.

Summary of Research

1. Effect of heterologous antilymphocytic serum and/or a thoracic duct fistula on the survival of homografts in rats and dogs.
2. Attempts to induce specific immunological tolerance of homografts in lymphocyte-depleted adult rats and dogs by means of partially purified histocompatibility antigens.
3. Immunological modifications of autoimmune haemolytic anaemia in mice.
4. Use of a cytological analysis with the *CBA/T6* strain of mouse for investigating the significance of the Kupffer cell response in graft-versus-host reaction.
5. Attempts to initiate immune responses by the transfer of Kupffer cells isolated from mice immunized against bacteriophage.
6. Attempts to induce antibody formation *in vitro* by the addition to lymphocytes of ribonucleic acids prepared from spleens and Kupffer cells of antigen-injected mice.
7. Use of immunologically competent cells in the treatment of experimental tumours.
8. Use of skin grafting to isolate a co-isogenic sub-strain in inbred rats.
9. Clinical study of renal isografts and homografts, including the use of total-body irradiation and/or antimetabolites to promote acceptance of the graft, the development of supportive measures in the totally irradiated patient and the development of techniques for the prolonged maintenance of a sterile environment.
10. Clinical study of the treatment of advanced cancer by transplantation of foreign immunologically competent cells.
11. Comparative studies of the splenomegaly and chorio-allantoic membrane systems of immune assay in the chick embryo.
12. Attempts to increase the resistance of organs to ischaemia by the use of enzyme-inhibiting agents.

RESEARCH GROUP ON THE ORGANIZATION OF CENTRAL MECHANISMS SUBSERVING VISION

Department of Physiology, University Medical School, Teviot Place, Edinburgh, 8

(1961)

Honorary Director

Professor D. Whitteridge, D.M., F.R.S.

Honorary Staff

R. M. Gaze, D.Phil.
M. Jacobson, Ph.D.
B. P. Choudhury, M.B.
M. E. Wilson, M.B.

The aims of the Group are to use information on the mapping of the retina on receptive areas to study the mechanisms by which orderly representation develops. In the adult the main aim is to study the mode of action of the cortex in the analysis and synthesis of visual patterns.

Summary of Research

1. Normal pattern and regeneration of optic nerve fibres in the goldfish.
2. Regeneration in compound eyes.
3. Function of areas 18 and 19 in the visual cortex.
4. Behavioural studies on lamination in the lateral geniculate body.

RESEARCH GROUP ON THE RELATION OF FUNCTIONAL TO ORGANIC PSYCHIATRIC ILLNESS

Department of Psychological Medicine, 11, Framlington Place,
Newcastle upon Tyne, 2

(1962)

Honorary Director

Professor M. Roth, M.D., F.R.C.P., D.P.M.

Staff

G. Blessed, M.B., D.P.M.
C. Gurney, M.B., D.P.M.
M. A. Harper, M.B., D.P.M. (*honorary*)
D. W. K. Kay, D.M., D.P.M. (*honorary*)
B. E. Tomlinson, M.B., M.R.C.P. (*honorary*)

The Group is specially concerned with inquiries in the indeterminate territory between functional and organic forms of mental disorder. In particular it is setting out to utilize information about those forms of mental disorder which have known cerebral or organic causes to shed light on the causation of mental disorders with a similar or identical picture in which aetiological factors are obscure or unknown. In the course of this work, clinical, statistical, neuropathological and biochemical techniques are being employed.

Summary of Research

1. Assessment of thyroid function and pattern of psychiatric disorder in cases clinically diagnosed as:
   (*a*) thyrotoxicosis;
   (*b*) possible thyrotoxicosis;
   (*c*) anxiety neurosis.
2. Neuropathology of functional and organic mental disorders in old age with special reference to occlusion and stenosis of extracranial vessels.
3. Incidence and localization of organic disease in patients presenting with schizophrenic illness.
4. A computer analysis of psychiatric and social observations in patients suffering from anxiety, phobic and depressive states.
5. Psychiatric disturbance in a consecutive series of patients with cerebral tumour.
6. Physiological and biochemical studies in the phobic anxiety depersonalization syndrome.

External Scientific Staff

On occasion the Council appoint to their staff individual research workers who are based in university departments or similar institutions; they are known as members of the Council's 'External Scientific Staff'.

Birmingham

UNIVERSITY

Chemistry Department

R. G. H. B. BODDY, Ph.D.

The development of microchemical methods for the analysis of dusts causing pneumoconiosis.

Experimental Pathology Department

C. OSORIO, Dr.Med.

1. Application of the ^{131}I-tri-iodothyronine uptake test to the diagnosis of thyroid diseases.
2. Determination of free thyroxine in human plasma.
3. Effect of salicylate, diphenylhydantoin and carbon dioxide on the binding of thyroid hormones by the plasma proteins.
4. Role of the binding of thyroid hormones by the plasma proteins with reference to the excretion of thyroxine in the bile and to the biological activity of thyroxine and tri-iodothyronine.
5. Measurement of cortisol-binding protein in human plasma.

Experimental Pathology Department and General Hospital

J. D. BLAINEY, M.D., M.R.C.P. (*part-time*)
(with grant for assistance by Miss S. M. Betts, B.Sc.)

1. Separation and identification of ultraviolet-absorbing substances in urine with particular reference to purines, aromatic amino acids and phenolic acids.
2. Application of such separation and identification to the urine in mental retardation and renal failure.
3. Natural history of renal disease investigated by renal biopsy and by prolonged clinical and biochemical studies, with particular reference to the nephrotic syndrome and pyelonephritis.
4. Metabolic studies in acute and chronic renal failure.
5. The applications of haemodialysis.

School of Dental Surgery

S. L. ROWLES, D.Phil.

1. Biochemistry of saliva and dental calculus in animals and man.
2. Chemistry of certain natural and synthetic calcium phosphates.
3. *In vitro* studies on dental plaques.

Cambridge

UNIVERSITY

Biochemical Laboratory: Sub-department of Chemical Microbiology

R. DAVIES, Ph.D.

1. Stimulation of enzyme formation in yeasts by cyclic dipeptides of arginine and proline.
2. Synthesis of cyclic dipeptides.

B. A. NEWTON, Ph.D.

1. Protein and nucleic acid metabolism in trypanosomid flagellates.
2. Mode of action of trypanocidal drugs.
3. The mechanisms of drug resistance.

Chemical Laboratory

Mrs. O. KENNARD, M.A., A.Inst.P.

1. Investigation of the structure of natural products by X-ray diffraction methods.
2. Crystallographic studies on micrococcin P (in collaboration with the Organic Chemistry Division, National Institute for Medical Research).
3. Application of X-ray powder techniques to high-precision determination of the molecular weight of organic compounds.

Molteno Institute

H. W. LASER, M.D., Sc.D.
(with grant for assistance by B. E. B. Moseley, Ph.D.)

Research on the biochemical basis of the biological effects of ionizing radiation:

1. Physiological and biochemical changes in organs, yeast, bacteria and enzymic systems which occur during application of ionizing irradiation.
2. Microbiological studies comprising:
   (*a*) Radiobiological analysis of lysogenic systems.
   (*b*) Mechanism of radiation resistance in *Micrococcus radiodurans* and some of its spontaneous and X-ray-induced mutants.
   (*c*) Effect of post-irradiation treatment on the viability of radiation-resistant bacteria.

Physiological Laboratory

C. R. AUSTIN, B.V.Sc., D.Sc.

1. Investigation of sperm motility: study of the ultrastructure of spermatozoa and the distribution of enzymes and substrates in these cells.
2. Ultrastructural changes shown by rabbit spermatozoa during their 'capacitation' and during their passage through egg membranes.
3. Comparative survey of gamete morphology and physiology, and of fertilization, in a variety of non-mammalian organisms.

Psychological Laboratory

W. E. HICK, M.D.

1. Study of skill with special reference to machine (including vehicle, aircraft, etc.) control and supervision, and perceptual problems related to the interpretation of information.
2. Development of usable mathematical (including logical) methods for investigating the above and other psychological problems.
3. Alleged fatigue as a factor in the causation of accidents in aviation and other modes of transport, and of errors in general.
4. Psychotherapeutic techniques using hallucinogens such as lysergic acid diethylamide and phencyclidine.

Miss A. W. HEIM, Ph.D.

Miss K. P. WATTS

Mental tests and personality assessment:

1. The Self-judging Vocabulary, the Brook Reaction (interests) and the Word-in-context Tests.
2. Two versions of a new high-grade adult test of intelligence (AH 6, AG and SEM).
3. The Shapes Analysis Test: a test of spatial perception devised for potential engineers and architects.
4. Use of these tests in experimental inquiries into such problems as student selection and specialization.

Miss M. A. VINCE, B.A.

Mrs. A. J. WATSON, B.A. (*part-time*)

The development and early behaviour of birds:

1. Relation between physical development, behaviour and environment in nestling great tits.
2. Temperature requirements of the eggs as a factor in the species-specific behaviour patterns of nest-building and incubation.
3. Factors underlying the synchronization of hatching in bobwhite quail eggs.
4. Effects of age and experience on the learning capacity of bobwhite and painted quail.
5. The concept of fear with respect to call-notes in the great tit.
6. Manipulation of aggressiveness at different ages in bobwhite flocks.

School of Agriculture

Miss R. DEANESLY (Mrs. Parkes), D.Sc.

The sexual cycle in the female guinea pig:

1. Mode of action of progesterone:
   (*a*) in early embryonic development;
   (*b*) in synchronization of oestrus.
2. Effects of reserpine on the corpus luteum.

Cirencester

EPIDEMIOLOGICAL RESEARCH UNIT

R. E. HOPE-SIMPSON, O.B.E., M.R.C.S.

1. Elucidation of the peculiar natural history and symptomatology of the individual viruses causing the common respiratory infections in a general practice used as an unselected population.
2. Participation in a long-term co-operative study of the significance of convulsive disorders in persons under 20 years.
3. Study of Herpes zoster as an example of a latent infection.

Edinburgh

WESTERN GENERAL HOSPITAL

Gastro-Intestinal Unit

W. SIRCUS, M.D., Ph.D., M.R.C.P., F.R.C.P.E.

1. Gastric secretion in man with particular reference to histamine and insulin.
2. Effect of injection of saliva and gastric juice extracts on function and structure of gastric mucosa in dogs.
3. Detailed studies on an atypical case of Zollinger-Ellison syndrome.
4. Controlled trials of therapeutic agents for the management of aphthous ulceration.
5. Effect of obstructed gastric emptying on gastric secretion in humans and dogs.

Surgical Neurology Department

J. P. LAIDLAW, M.B., M.R.C.P.E.

1. The development of methods of detecting and measuring changes in the background rhythmic activity of the human EEG.
2. Investigation of the part played in the production of these changes by physiological and psychological factors and by disease.
3. Investigation of the possible differential effect of drugs on patients with certain conditions affecting the brain.

Elstree

LISTER INSTITUTE OF PREVENTIVE MEDICINE

Mrs. J. M. DOLBY, Ph.D.

1. Role of antibodies, complement and lysozyme in the bactericidal reaction of *Bordetella pertussis* antisera against sensitive strains of organisms.
2. The parts played by local and by general immunity in *B. pertussis* infections in the brains of immunized mice.

Miss M. E. MACKAY, Ph.D.

1. Proteolytic enzyme in human plasma.
2. Pharmacologically active substances in human plasma fractions.

Hendon, Middlesex

WEST HENDON HOSPITAL

Institute of Orthopaedics Poliomyelitis Centre

A. B. KINNIER WILSON, M.B., M.R.C.P., D.P.M.

A. H. BOTTOMLEY, M.B.

R. P. J. G. MCWILLIAM, B.A.

1. Studies in the use of an analogue computer for the analysis of:
   (*a*) Mechanics of obstructed breathing.
   (*b*) Control of powered artificial arms.
2. Development of muscle substitutes (in collaboration with the Committee for Research on Apparatus for the Disabled of the National Fund for Poliomyelitis Research):
   (*a*) Design of suitable motor units.
   (*b*) Study of control factors involved.
   (*c*) Development of a myoelectric control system.
   (*d*) Study of various types of transmission systems (splints, artificial arms, harness, etc.).

Hertford

JOHN INNES INSTITUTE

Cell Biology Department

J. NEWSOME, M.D., D.T.M. & H.

1. Stimulation of cell division in cultured tissue and blood cells.
2. Phagocytosis of particulate antigens.
3. Establishment of a line of antigen-stimulated cells.

Leeds

UNIVERSITY

Medical Physics Department

J. B. DAWSON, Ph.D.

1. Development of instruments and methods of atomic absorption spectrophotometry to extend the range of elements which may be estimated by this technique.
2. Development of a high-speed scanning spectrophotometer for the study of optical emission and absorption spectra with particular reference to the simultaneous estimation of several elements (in collaboration with the Metabolic Disturbances in Surgery Research Unit).
3. Development of a method suitable for the routine estimation of serum iodine using ^{131}I in a radioisotope exchange and dilution procedure.

London

BRITISH MUSEUM (NATURAL HISTORY)

D. J. LEWIS, Sc.D.

1. The biology of adult *Simulium damnosum* in relation to onchocerciasis (in the Cameroon Republic, with Dr. B. O. L. Duke).
2. The *Phlebotominae* and *Simuliidae* of West Pakistan, with special reference to the sandflies of the Kala-azar area in the Shyok valley (the field work was under the auspices of the Pakistan Medical Research Centre, Lahore).
3. Phlebotomine sandflies in British Honduras.
4. The sandflies of West Africa and the Congo Republic.

CENTRAL PUBLIC HEALTH LABORATORY, COLINDALE

Cross-Infection Reference Laboratory

O. M. LIDWELL, D.Phil.

D. KINGSTON, M.A.

1. The sources of bacterial contamination and their contribution to the airborne flora of an operating room, investigated under alternative ventilating regimes.
2. Air movement in subdivided hospital wards and the effect of such subdivision on the transfer of infection.
3. Methods of testing self-disinfecting surfaces, with particular reference to coatings that emit formaldehyde.
4. Causes of discomfort experienced by surgeons when operating.

GUY'S HOSPITAL MEDICAL SCHOOL

Chemical Pathology Department

B. MCARDLE, M.D., F.R.C.P., D.C.H.

Variations in the content of phosphatides and other lipids in the cerebrospinal fluid, plasma and muscle in various neuromuscular disorders.

Experimental Medicine Department

N. VEALL, B.Sc., F.Inst.P.

V. PARSONS, D.M., M.R.C.P.

1. The use of ^{47}Ca for metabolic studies in patients with bone disease.
2. The use of radioiodine-labelled compounds in the investigation of patients with renal disease.
3. Investigation of cerebral blood flow by ^{133}Xe inhalation and extracranial recording.
4. Studies on lymphatic drainage in patients with lymphoedema using the local tissue clearance of ^{131}I-labelled plasma proteins (in collaboration with the Plastic Surgery Centre, Salisbury).

INSTITUTE OF CANCER RESEARCH

Chester Beatty Research Institute

E. J. DELORME, M.D., F.R.C.S.Can.

1. Conditioning effect of urethane on the incidence of bladder tumour induced by implanted glass beads in mice.
2. Relative importance of size and shape of implanted surgical sponge (Ivalon) on its carcinogenicity in rats.
3. Induction of intracerebral tumours in rats by implantation of benzpyrene pellets and investigation of the therapeutic effect of rendering the animals' own lymphoid cells accessible to such tumours.
4. *In vivo* and *in vitro* studies of anti-tumour activity of lymphoid cells (immunocytes) obtained from animals pre-inoculated with trypsin-separated tumour cells.

INSTITUTE OF PSYCHIATRY, MAUDSLEY HOSPITAL

F. B. BYROM, M.D., F.R.C.P.

1. Production, mechanism and effects of experimental hypertension.
2. Toxic effects of angiotensin on vessels and kidney.

Miss S. J. STRICH, D.M.*

(On leave of absence for a course in biochemistry at the University of Oxford).

1. Complications of traumatic subdural haematoma.
2. Study of various strains of mice with hereditary diseases of the nervous system.

LEWISHAM HOSPITAL

P. WOLF, M.D.

1. Purification of human AHF protein.
2. Attempt to assay human AHF by an immunological method (with Dr. K. W. Walton, Department of Experimental Pathology, University of Birmingham).
3. Qualitative and quantitative studies of human fibrogen with the aid of anti-fibrinogen sera.

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* Re-imbursement of salary by block grant to Institute of Psychiatry.

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE

C. N. DAVIES, D.Sc., F.Inst.P.

1. Methods of measuring irregular shapes.
2. Errors in sampling airborne dust particles due to gravity and inertia.
3. Deposition of inhaled aerosol in man.

MIDDLESEX HOSPITAL MEDICAL SCHOOL

Institute of Clinical Research

J. COLOVER, M.D., M.R.C.P. (*part-time*)

1. A new method of concentrating small amounts of biological fluids.
2. Changes in the protein fractions in the cerebrospinal fluid in various neurological conditions as revealed by electrophoresis, using uni-dimensional and two-dimensional electrophoretic techniques.
3. Comparison of measurement of γ-globulin and other proteins in cerebrospinal fluid in various disease processes, including multiple sclerosis, by different electrophoretic and immunological methods.

NATIONAL HOSPITAL FOR NERVOUS DISEASES

J. A. V. BATES, M.B. (*part-time*)

1. Development of physiological criteria for determining the site for stereotactic operations on the human brain.
2. Effect of stereotactic lesions on tremor and rigidity.
3. Study of Parkinson syndrome by electromyography.
4. Surgical relief of epilepsy.

A. M. HALLIDAY, M.B., B.Sc.

1. Factors affecting the form of cortical evoked responses in healthy subjects.
2. Changes in cerebral evoked potentials occurring in patients with disorders of sensation or perceptual awareness and with various lesions of the central nervous system.
3. Development of more versatile methods of recording cerebral action potentials using digital computer techniques.
4. Clinical trial of the therapeutic value of unilateral electro-convulsive therapy in depression and a comparison of its effect on memory with that of conventional bilateral E.C.T.

P. W. NATHAN, M.D., M.R.C.P.

1. Spontaneous and induced movements in spasticity due to partial and complete transverse lesion of the spinal cord in man, and the adaptation of chemical rhizotomy with phenol solutions as treatment, in order to reduce spasticity without damaging purposeful movements.

Miss M. C. SMITH, M.D., B.Sc.

Anatomo-pathological studies, with special reference to nerve tract degeneration resulting from therapeutic operations, cerebrovascular catastrophes, or from trauma, and the correlation between the pathological lesion and the clinical state. The principal fields of study are:

1. The central nervous system of patients who have had stereotactic operations for the relief of tremor and rigidity, or who have small lesions of the extrapyramidal system due to other causes.
2. The central nervous system of patients who have had antero-lateral cordotomies or other pain-relieving procedures.

POSTGRADUATE MEDICAL SCHOOL OF LONDON

Department of Medicine

P. HUGH-JONES, M.D., F.R.C.P. (*part-time*)*

Mrs. M. W. MCGRATH, Ph.D.

1. Distribution of ventilation and blood-flow in different parts of the lungs in a variety of medical and surgical conditions.
   (*a*) Regional studies, without intubation of patients, by the use of radioactive gases (in collaboration with members of the staff of the Postgraduate Medical School).
   (*b*) Changes in different lobes and segments of the lungs by continuous gas analysis, using a mass spectrometer, during routine diagnostic bronchoscopy.

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* From January 1964, part-time Director of the Council's Clinical Pulmonary Physiology Research Unit at King's College Hospital Medical School, Denmark Hill, London, S.E.5.

2. Assessment of lung function (by means of new techniques) in chronic lung disease, in an attempt to define the functional change and to establish different clinical entities.
3. Regional function in emphysema, studied in order to find indications for surgery.

Pathology Department

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J. S. McKINLEY-McKEE, Ph.D.

1. Kinetic studies with liver and yeast alcohol dehydrogenase and various substrates and inhibitors.
2. Enzyme complexes, the enzymatic active centre, and possible modes of action of various drugs investigated by means of spectrophotofluorometry, fluorescence polarization, optical rotatory dispersion and nuclear magnetic resonance conformation change.
3. Denaturation, protection and role of thiol groups in alcohol dehydrogenase.
4. Mode of action of mevaldic reductase.

Cyclotron Building (Medical Research Council)

N. B. MYANT, D.M., B.Sc., M.R.C.P.

Mrs. I. GORE, Ph.D.

Miss V. J. ILIFFE, B.Sc.

B. LEWIS, M.D., Ph.D., M.R.C.P.E., A.R.I.C.

C. OSORIO, Dr.Med. (*until Jan. 1963*)

1. Influence of thyroxine on the synthesis and degradation of lipids:
   (*a*) in cell-free systems;
   (*b*) with reference to disorders of lipid metabolism in human beings.
2. Factors governing the biological effectiveness of thyroid hormone and its distribution to the tissues.
3. Effect of thyroxine on biochemical mechanisms in the central nervous system during the early stages of its development.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

Physiology Department

N. AMBACHE, M.A., M.R.C.S.
(with grant for assistance by D. W. Shapiro, B.Sc.)

Mrs. J. M. C. WHITING, B.Sc.

1. Development of a more sensitive method for the assay of some physiologically active unsaturated hydroxy-acids by the use of muscles from *Meriones libycus* and *Meriones trystiami*, and breeding of these two species of jirds.
2. Detection by this method of an active substance in the eye perfusates produced by irritation and injury.
3. The species difference in iris reaction between cats and rabbits; comparison of irin content in these two animals.
4. Vasodilator phenomena investigated by electromanometric techniques.
5. Occurrence and distribution of atropinesterase in rabbits.

THE ROYAL FREE HOSPITAL AND INSTITUTE OF NEUROLOGY

A. ELITHORN, M.D., M.R.C.P., D.P.M. (*part-time*)
(with grants for assistance by D. Jones, B.Sc., and D. Lee, B.A.)

Mrs. M. KERR, B.A. (Econ.) (*part-time*)

1. Relationship between perceptual capacity and intellectual capacity.
2. Relationship between anxiety and depression.

ROYAL HOLLOWAY COLLEGE, ENGLEFIELD GREEN

Zoology Department

W. A. GAUNT, Ph.D.

1. Distribution of chemical substances during active tooth root formation.
2. Histochemistry of typical and atypical ameloblasts.
3. Comparative study of the structure and development of the dental follicle.
4. Quantitative analyses of the growth of the teeth and jaws.
5. Vascular architecture associated with permanent and deciduous teeth.

THE TAVISTOCK CLINIC

E. J. M. BOWLBY, M.D., M.R.C.P.

Short-term effects of the temporary loss of a mother-figure.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL

Department of Medicine

A. ANTONIS, Ph.D., F.R.I.C. (with grant for assistance by Mrs. F. Weinreich, B.Sc.)

1. Influence of dietary factors on production of lipaemia and its relationship to concentration, composition and rates of clearance or turnover of serum chylomicrons and other serum and tissue lipoproteins.
2. Lipid studies in bus conductors and drivers and their sibs (with Social Medicine Research Unit).
3. Physiological and pharmacological control of release of plasma-free fatty acids.
4. Development of automated techniques in lipid analysis.

UNIVERSITY COLLEGE

Anatomy Department

J. L. de C. DOWNER, Ph.D.

Miss J. R. PARRISS, B.A.

1. Function of parastriate areas in visual learning and interhemispheric transfer.
2. Interhemispheric organization of sensori-motor skills.
3. The role of proprioceptive cues in mediating visually guided limb movements.
4. The effect of hemicerebellectomy on tactile 'crossed-placing' reactions.

Physiology Department

H. DAVSON, D.Sc.
(On leave of absence for one year from October 1963 as Visiting Professor of Ophthalmic Research at the University of Louisville, U.S.A.)

Ventriculo-cisternal perfusion.

J. W. T. REDFEARN, M.D., D.P.M.

Polarization of the cerebral cortex in the experimental animal (in collaboration with Dr. O. C. J. Lippold).

UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL

Dermatology Department

R. I. C. SPEARMAN, Ph.D. (*until May 1963*)

1. Effects of vitamin A from various sources, triamcinolone and other substances on epidermal growth and keratinization, and their relation to the treatment of psoriasis.
2. Comparative studies of different types of epidermal keratinization occurring in vertebrates and abnormal keratinization in human dermatoses.
3. Effects of the dermis on epidermal growth and keratinization in skin grafts.
4. Histochemistry of nail formation.

UNIVERSITY OF LONDON COMPUTER UNIT

Computer Services Centre, 172, Tottenham Court Road, W.C.1.

B. K. KELLY, B.A.

Assistance is being given to the research units and the external staff in the application of computers to their research problems.

Manchester

UNIVERSITY

Turner Dental School

S. A. LEACH, Ph.D. (*until July 1963*)

1. Effect of various anions on the solubility of enamel and dentine in acid.
2. Fluoride content of the dental plaque.

3. Release and breakdown of sialic acid from human salivary mucin and its role in the formation of dental plaque.
4. Infrared studies of the interaction of weak acid anions with hydroxyapatite.
5. Role of sialic acid in the biological function of human salivary mucin.
6. Development of a simple method for the determination of submicrogram amounts of fluoride.

A. S. HALLSWORTH, Ph.D.

Availability of ε-amino groups in collagen aggregation states in the calcification process.

Malaysia

SUNGEI BULOH SETTLEMENT

Research Unit

J. H. S. PETTIT, M.D., M.R.C.P.

1. Controlled clinical trials:
   (*a*) Lepromatous leprosy: a comparison of a group of patients treated with diethyl dithiolisophthalate and diaminodiphenyl sulphone and a group treated with diaminodiphenyl sulphone alone.
   (*b*) Pilot trial to assess the value of griseofulvin as an adjuvant to established anti-leprous therapy.
2. Investigation of the naturally occurring tuberculin and lepromin positivity in Chinese children and of methods for converting lepromin negativity to lepromin positivity with BCG and lepromin.
3. Studies of cases of leprosy with clinical indications of bacterial resistance to routinely expected therapy (diaminodiphenyl sulphone and diphenyl thiourea).
4. Survey of the bony changes in the maxilla and the dental changes associated with leprosy.
5. Genetic background of patients with leprosy, with special reference to blood groups, colour vision, the salivary secretin factor and glucose-6-phosphate dehydrogenase deficiency.

Oxford

THE CHURCHILL HOSPITAL

Central Workshop

F. D. STOTT, D.Phil.

1. Pulmonary circulation studies with the whole-body plethysmograph (with Dr. G. De J. Lee).
2. Improvements to instruments and methods of diagnosis in cardiac surgery.
3. Measurements of the physical properties of surfaces in contact with blood and the possible effect on coagulation (with the Blood Coagulation Research Unit).
4. Development of instruments for automatic recording of blood pressure (with Department of Regius Professor of Medicine).

Department of the Regius Professor of Medicine

L. I. WOOLF, Ph.D.
(with grant for assistance by B. Goodwin, M.A., and Miss N. Kennaway, B.Sc.).

1. Biochemical genetics, diagnosis and treatment of phenylketonuria.
2. Defects in the metabolism of tyrosine and tryptophan.
3. Chemical investigation of myelination in phenylketonuria and allied disorders.
4. Chemistry of lipidoses.
5. Metabolism of amino acids, phenolic acids and keto-acids in relation to neurological disease.

Sir William Dunn School of Pathology

J. C. F. POOLE, D.M.

1. The fine structure of experimental thrombi.
2. Factors influencing platelet agglutination.
3. The effects of hyperlipaemia on cellular changes in fabric grafts on the aorta and in experimental endarterectomy.
4. DNA synthesis in endothelial nuclei.

D. S. ROBINSON, Ph.D.*

1. Rôle of the clearing factor lipase in fat transport.
2. Control of clearing factor lipase activity.
3. Uptake and release of plasma lipoproteins in the liver with particular reference to the development of fatty livers.

A. M. WOODIN, Ph.D.

Miss A. A. WIENEKE, D.R.S. (*Utrecht*)

1. The mechanism of secretion of granule material in mammalian cells.
2. The primary cytotoxic effect of leucocidin.
3. The composition and separation of the granules of the polymorphonuclear leucocyte.

Republic of South Africa

NELSPRUIT, EASTERN TRANSVAAL

Bilharziasis Research Unit, South African Council of Scientific and Industrial Research

D. S. BROWN, Ph.D.

1. Incidence of human bilharziasis, and the distribution of intermediate hosts in north-eastern Transvaal and Natal (with Dr. R. J. Pitchford).
2. Taxonomy of intermediate hosts of *Schistosoma* in Africa.

Sheffield

NETHER EDGE HOSPITAL

Rheumatism Research Unit

H. F. WEST, M.D., M.R.C.P., D.T.M.

1. Estimation of corticosteroid hormones and their tissue metabolites in body fluids.
2. Therapeutic trials for rheumatoid arthritis.

UNIVERSITY

Virus Research Laboratory (Lodge Moor Hospital)

R. N. P. SUTTON, B.M., D.C.H.

Field studies on respiratory viruses.

Stanmore

INSTITUTE OF ORTHOPAEDICS

Clinical Research Wing

A. MCPHERSON, M.B., M.R.C.P.

L. JUHÁSZ, Ph.D.

A. ZBROŻYNA, M.B.

1. Viscero-somatic reflexes.
2. The central nervous control of the bladder.
3. Blood flow in bone.
4. The electrical measurement of fibrinolysis.

Stoke-on-Trent

CITY GENERAL HOSPITAL

Respiratory Physiology Department

M. C. S. KENNEDY, B.A., M.R.C.S. (*part-time*)

1. The natural history of the asthma–bronchitis–emphysema syndrome.
2. Interrelation of cardiac and pulmonary factors in causing dyspnoea in patients with valvular disease of the heart (in collaboration with Dr. J. P. P. Stock, Cardiologist to the Stoke-on-Trent Group).

* Transferred to the Cell Metabolism Research Unit 1 August, 1963.

Tanganyika

NACHINGWEA

Government Hospital

A. D. BERRIE, B.Sc.

1. Bionomics of the snail vectors of *Schistosoma haematobium.*
2. Seasonal variation in transmission of *S. haematobium.*
3. Survey of vector snails in the Mtwara region of Tanganyika.

W.H.O./M.R.C. BILHARZIASIS CHEMOTHERAPY CENTRE, TANGA

A. DAVIS, M.B., M.R.C.P.E., D.T.M. & H.

1. Establishment of chemotherapy centre.
2. Comparative clinical trials of antimonial drugs.

Wickford, Essex

RUNWELL HOSPITAL

J. DAWSON, M.B., M.Sc.

1. The influence of alterations in electrolyte and water metabolism on the electroencephalogram in depressive patients and normal women.
2. The effect of antidepressive drugs on sodium and potassium transport.

Institutions Supported by Special Grants

Through special (or block) grants, the Council provide support, in whole or part, for the research activities of a number of autonomous institutions. The main centres assisted in this way are listed below.

INSTITUTE OF CANCER RESEARCH: ROYAL CANCER HOSPITAL
Fulham Road, London, S.W.3

Chairman of the Committee of Management
The Rt. Hon. the Earl of Halsbury, F.R.I.C., F.Inst.P.

Secretary
N. P. Hadow, O.B.E., M.A.

CHESTER BEATTY RESEARCH INSTITUTE

Director
Professor A. Haddow, M.D., D.Sc., F.R.S.

Staff

P. Alexander, Ph.D., D.I.C., D.Sc.
E. J. Ambrose, D.Sc.
Mrs. M. Amosu, A.L.A. (*until Mar. 1963*)
Professor F. Bergel, D.Phil.Nat., D.Sc., F.R.I.C., F.R.S.
M. S. C. Birbeck, M.A.
Miss J. M. Booth, Ph.D.
Professor E. Boyland, D.Sc.
Mrs. G. Bramley, M.Sc. (*until Aug. 1963*)
R. C. Bray, Ph.D., A.R.I.C.
P. Brookes, Ph.D.
D. A. Brunning, A.L.A.
Professor J. A. V. Butler, D.Sc., F.R.I.C., F.R.S.
R. A. M. Case, M.D., Ph.D.
P. Cohn, Ph.D., F.R.I.C., M.P.S.
Miss D. I. Connell, Ph.D.
T. A. Connors, Ph.D.
A. R. Crathorn, Ph.D.
D. A. Darcy, D.Phil.
A. J. S. Davies, Ph.D.
W. Davis, Ph.D.
C. J. Dean, Ph.D.
Mrs. S. M. Doak, Ph.D. (*until Dec. 1962*)
C. E. Dukes, O.B.E., M.D., D.P.H., F.R.C.S. (*part-time*)
Mrs. D. M. Easty, Ph.D. (*part-time*)
G. C. Easty, Ph.D.
L. A. Elson, D.Sc., Ph.D., F.R.I.C.
J. L. Everett, F.R.I.C.
Mrs. M. J. Fahmy, Ph.D.
O. G. Fahmy, Ph.D.
J. A. Forrester, B.A.
L. Foulds, M.D.
W. Galbraith, M.A.
D. A. Gilbert, Ph.D.
G. N. Godson, Ph.D.
R. J. Goldacre, Ph.D.
Mrs. G. A. Grant, Ph.D.
B. Green, Ph.D., A.R.I.C.
Miss A. Greenwood, B.A.
P. L. Grover, M.Sc.
L. D. G. Hamilton, Ph.D.
Miss J. L. Harley, B.Sc.
K. R. Harrap, Ph.D.
G. C. Hartman, Dip.Tech.
J. R. B. Hastings, B.Sc.
I. Hieger, D.Sc., Ph.D.
D. T. Hughes, Ph.D.
E. W. Johns, A.R.I.C.
J. M. Johnson, B.Sc. (*until Oct. 1962*)
P. C. T. Jones, Ph.D. (*until Feb. 1963*)
R. Lumley Jones, Ph.D.
K. S. Kirby, D.Sc.
A. Knowles, Ph.D.
Professor P. C. Koller, D.Sc.
D. J. R. Laurence, Ph.D.
P. D. Lawley, Ph.D.
C. L. Leese, Ph.D., A.R.C.S., D.I.C.
J. T. Lett, Ph.D.
Miss E. Leuchars, B.A.
J. H. Lister, Ph.D., A.R.I.C.
A. Loveless, Ph.D.
D. Manson, Ph.D.
A. B. Mauger, Ph.D.
E. G. Mayhew, B.Sc.
E. H. Mercer, D.Sc. (*until Jan. 1963*)
J. F. A. P. Miller, M.B., Ph.D.
K. G. Moreman, A.R.P.S., A.I.B.P.
R. Nery, Ph.D., A.R.I.C.
J. T. Nodes, M.Sc. (*until Dec. 1962*)
Professor R. D. Passey, M.C., M.D., D.P.H.
Miss M. A. Peutherer, B.Sc.
D. M. Phillips, Ph.D.
P. D. Regan, B.A.
E. Reid, D.Sc., Ph.D.
J. M. Reid, B.A.
S. H. Revell, Ph.D.
J. J. Roberts, Ph.D.
A. B. Robins, Ph.D.
Miss E. M. F. Roe, Ph.D.
F. J. C. Roe, D.M.
D. Rosen, Ph.D.
V. M. Rosenoer, M.B., Ph.D., M.R.C.P. (*until July 1963*)
W. C. J. Ross, D.Sc., F.R.I.C.

Staff—contd.

Miss K. Shepley, B.Sc.
G. Shields, M.Sc.
K. V. Shooter, D.Sc.
P. Sims, Ph.D.
Miss P. Simson, B.Sc.
J. B. Solomon, Ph.D.
Mrs. E. Stewart, B.Sc.
J. A. Stock, Ph.D., F.R.I.C.
G. M. Timmis, D.Sc., F.R.I.C.
R. Wade, Ph.D.
Miss V. Wallis, B.Sc.
Mrs. M. A. Walters, B.Sc.
G. P. Warwick, Ph.D.
D. N. Wheatley, B.Sc.
K. Williams, Ph.D.
J. A. H. Wylie, M.D., D.Phil.
Miss M. M. Yarnell, M.Sc.

Attached Workers

A. B. El-Aaser, B.Sc. (*United Arab Republic, Ministry of Education*)
J. Z. Beer, Magister (*International Atomic Energy Agency Fellow*)
A. Bhisey, M.Sc. (*Wellcome Trust Travel grant-holder*)
Robin D. Currie, M.Sc. (*Royal Marsden Hospital Scholar*)
E. J. Delorme, M.D., F.R.C.S. (*M.R.C. External Staff*)
A. P. L. Drochmans, M.D. (*W.H.O. Fellow*)
P. Dukor, M.D. (*Swiss Academy of Medicine Fellow*)
G. J. Goldenberg, M.D. (*National Cancer Institute of Canada Fellow*)
Myrna Guest, M.D. (*Gordon Jacobs Research Fellow*)
J. S. Harington, Ph.D. (*Anna Fuller Fund grant-holder*)
G. D. F. Jackson, B.Sc. (*Wellcome Trust Research Fellow*)
Boonanake Kallapravit, M.B., Ph.D. (*Colombo Plan Fellow*)
Suad Al Kassab, M.Sc., Ph.D. (*University of Baghdad*)
E. Kelemen, M.D. (*Lady Tata Memorial Trust Scholar*)
Arnavaz Kerawalla, M.Sc. (*Royal Marsden Hospital Scholar*)
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S. Liu, M.D. (*Chinese Government grant-holder*)
G. Manolov, M.D. (*Institute of Oncology, Sofia*)
P. A. McNamara, Ph.D. (*U.S. Public Health Service Fellow*)
T. Ohnuma, M.D. (*W.H.O. Travel grant-holder*)
D. Osoba, M.D., F.R.C.P. (*McEachern Fellow, Cancer Institute of Canada*)
Marianne Pentelenyi, B.Sc. (*Gordon Jacobs Research Fellow*)
Z. Pravda, Cand.Sci. (*W.H.O. Fellow*)
R. K. Ralph, Ph.D. (*Eleanor Roosevelt International Cancer Fellow*)
A. Riad-Fahmy, Ph.D. (*Gordon Jacobs Research Fellow*)
V. M. Sivaramakrishnan, Ph.D. (*Nuffield Foundation Dominion Travelling Fellow*)
D. A. Stevens, B.A. (*U.S. Public Health Service Fellow*)
J. Sugár, M.D. (*Eleanor Roosevelt International Cancer Fellow*)
Mary Szekerke, Ph.D. (*Hungarian Academy of Sciences*)
Chitra Talukdar, M.Sc. (*West Bengal Government Scholar*)
M. K. Turner, B.A. (*Royal Marsden Hospital Scholar*)
L. W. Wattenberg, M.D., B.S. (*University of Minnesota*)
M. Whisson, M.B. (*Australian Cancer Society Fellow*)
B. R. Wilkinson, M.Agr.Sc. (*New Zealand Wool Research Organization Fellow*)
H. T. Yost, A.B., Ph.D. (*Johns Hopkins University, Baltimore*)
Evstopt Zharova, M.D. (*W.H.O. Fellow*)

PHYSICS DEPARTMENT

Director

Professor W. V. Mayneord, C.B.E., D.Sc., F.Inst.P.

Staff

Professor L. F. Lamerton, Ph.D., F.Inst.P.
W. Anderson, Ph.D.
J. P. M. Bensted, M.B.
R. E. Bentley, Ph.D.
N. M. Blackett, Ph.D.
A. B. Cairnie, Ph.D.
M. F. Cottrall, M.Sc.
Mrs. V. D. Courtenay, B.Sc.
J. O. Crookall, A.R.I.C.
I. G. F. Gilbert, Ph.D., D.I.C.
C. A. Greatorex, Ph.D.
C. R. Hill, Ph.D.
H. J. D. Ireland, B.Sc.
C. H. Jones, Ph.D.
J. C. Jones, M.A., F.Inst.P.
R. P. Parker, Ph.D.
J. M. Radley, Ph.D. (*until Jan. 1963*)
P. J. Roylance, M.B.
A. J. Stacey, B.Sc.
J. B. H. Stedeford, Ph.D.
G. G. Steel, Ph.D.
D. M. Taylor, Ph.D., F.R.I.C.
G. Threlfall, B.Sc., A.R.I.C.
N. G. Trott, Ph.D., F.Inst.P.
R. C. Turner, Ph.D.

Attached Workers

R. D. Cherry, M.Sc. (*University of Cape Town*)
D. Gvozdanovic, M.Sc. (*Institute of Occupational Health, Belgrade; International Atomic Energy Agency Fellow*)
A. R. Jones, M.Sc. (*Atomic Energy of Canada Ltd.*)
K. Tungsubutra, M.D., D.M.R.T. (*Siriraj Hospital, Bangkok*)
J. K. Malesa, M.Sc. (*Institute of Oncology, Warsaw; International Atomic Energy Agency Fellow*)
Z. J. Marzecki, M.D. (*Medical Academy, Szczecin, Poland; International Atomic Energy Agency Fellow*)

RADIOTHERAPY DEPARTMENT

Director

Professor D. W. Smithers, M.D., F.R.C.P., F.R.C.S., F.F.R.

Staff

K. B. Dawson, M.Sc.
E. O. Field, D.M., D.M.R.D.
Miss M. M. Gwyther, B.Sc.
Mrs. E. M. Ledlie, M.B., D.M.R.
H. Madoc-Jones, B.A. (*Gordon Jacobs Research Fellow*)
Miss E. M. Stanley, B.Sc.
Mrs. E. N. K. Wallace, M.B., D.M.R.

AT THE ROYAL MARSDEN HOSPITAL:

Miss J. W. Baker, M.B., D.M.R.T.
J. M. Barnes, B.A., D.M.R.T.
H. J. G. Bloom, M.D., M.R.C.P., F.F.R.
Miss V. M. Dalley, M.B., D.M.R.T.
J. N. Godlee, M.B., F.F.R.
N. V. Hawkins, M.B., D.M.R.T.
N. Howard, B.M., F.F.R.
E. D. Jones, M.B., D.M.R.T.
M. Lederman, M.B., D.M.R.E., F.F.R.
J. M. Mallett, D.O.M.S.
A. Tadros Massih, D.M.R.D., F.F.R.
J. Q. Matthias, M.D., M.R.C.P.
P. J. O'Kelly, M.B., D.M.R.T.
C. A. Poulter, M.B.
S. Demetrious Rafla, D.M.R.E., F.F.R.
Mrs. P. Rigby-Jones, M.B., F.F.R.
Mrs. M. Williams, B.A., D.M.R.T.

Visiting and Attached Workers

A. S. Glicksman, M.D. (*Memorial Hospital, New York*)
A. L. Lomas, F.R.C.S., F.R.A.C.S. (*Waikato Hospital, Hamilton*)
Miss W. M. Ross, M.Sc., M.D., C.M. (*Montreal General Hospital*)
K. Tungsubutra, M.D., D.M.R.T. (*Siriraj Hospital, Bangkok*)
G. Vassilacopoulos, M.B., Ch.B. (*National University of Athens*)

CLINICAL RESEARCH DEPARTMENT

Honorary Director

P. E. Thompson Hancock, M.B., F.R.C.P.

Staff

Miss E. A. M. Boesen, M.B., M.R.C.S.
Miss J. M. Davies, B.A., Dip.P.S.A.
D. A. G. Galton, M.D.
Mrs. S. D. Lawler, M.D.
Miss H. S. Shatwell, B.Sc.
Miss D. E. M. Speed, M.B.
M. W. Weg, B.Sc.
Miss E. Wiltshaw, M.B.

AT THE ROYAL MARSDEN HOSPITAL:

Miss R. Bell, B.Sc.
Miss A. Buck, M.A.
C. I. Cooling, F.R.C.S. (*part-time*)
O. F. Garai, M.R.C.S., M.R.C.P. (*part-time*)
J. D. Griffiths, M.S., F.R.C.S. (*part-time*)

The Council assumed the major responsibility for the Institute of Cancer Research from the beginning of the financial year 1951–52, but the Institute has continued to receive substantial support from the British Empire Cancer Campaign. The work of the Institute consists of that of the Chester Beatty Research Institute and of the research activities of the Departments of Physics, Radiotherapy and Clinical Research, which are joint Departments of the Institute of Cancer Research and the Royal Marsden Hospital. Formerly a school of the

University of London, the Institute still has a similar status through its recognition as an Institute of the British Postgraduate Medical Federation. The subjects under study at the Chester Beatty Research Institute include the mechanism of action of carcinogenic and mutagenic chemical agents, cytology and cytogenetics, control mechanisms in normal growth, the study of tumour viruses, and experimental chemotherapy. In the Physics Department (Fulham Road Branch) investigations are mainly related to the physical aspects of the clinical use of radioactive isotopes and the applications of other branches of physics to medicine; at the Sutton Branch of the Department the work is of a longer-term character and is devoted to various aspects of radiobiology, particularly carcinogenesis resulting from radiations; there is also a large-scale programme of investigations into natural and artificial radioactivity at low levels and studies of human metabolism of the radioactive materials. In the Radiotherapy Department the programme of research includes clinical studies of malignant disease and the results of treatment, the use of radioactive isotopes for therapy and investigation, and other radiobiological researches. In the Clinical Research Department the research includes a study of chemotherapy, both systemic and regional, and an intensive study of human tumours in a programme designed to characterize human cancer, together with an environmental investigation into patients whose tumours are being studied.

Summary of Research

CHESTER BEATTY RESEARCH INSTITUTE

EXPERIMENTAL CHEMOTHERAPY

1. Carrier and latency principle.
2. Exploitation of pH differences between normal and neoplastic cells.
3. Exploitation of differences in oxidation potential between normal and neoplastic cells.
4. Selective protection of normal cells against the action of alkylating agents.
5. Potential antipurines with an alkylating function.
6. Synthetic studies of actinomycin analogues.
7. Effect of certain enzymes and sodium oleate on spontaneous mammary tumours in mice.
8. Effect of carcinostatic agents on a transplantable mouse plasma cell tumour.

CLINICAL CHEMOTHERAPY

1. Assessment of the results of therapy in malignant lymphoma.
2. Chemotherapy of ovarian carcinoma.
3. Melphalan in multiple myelomatosis.

MECHANISMS OF CARCINOGENESIS

1. The carcinogenic action of metals.
2. Carcinogenic nitrosomines.
3. The carcinogenicity of cadmium sulphate.
4. Carcinogenicity of 2-naphthylamine and 2-naphthylhydroxylamine.
5. Experimental induction of tumours in mice by implantation of pellets in the bladder.
6. Carcinogenesis tests using newborn mice and newborn hamsters.
7. Induction of mammary tumours by oral administration of 7, 12-dimethylbenz[*a*]anthracene.
8. Binding of carcinogenic and related aromatic hydrocarbons to cellular constituents of mouse skin.
9. Complex formation between nucleic acid and hydrocarbons.
10. Histochemical investigations of metabolism of carcinogens.
11. Effect of length of exposure to a tumour-promoting stimulus on ultimate incidence of malignant neoplasms.
12. Azo-dye carcinogenesis, including metabolism of uridine nucleotides.

13. Acid-soluble ribonucleotides in azo-dye carcinogenesis.
14. Reaction of glutathione with β-propiolactone.
15. Interaction of alkylating carcinogens with micro-organisms.
16. Intramolecular cross-linking of DNA by difunctional alkylation.
17. Effects of cigarette smoking on growth and metabolism.

IONIZING RADIATIONS AND PHOTOBIOLOGY

1. Protective action of metal ions on inactivation of trypsin.
2. Role of hydrogen transfer in treatments which modify radiosensitivity.
3. Factors influencing the radiosensitivity of cells.
4. Increased synthesis of RNAase in lymphoid tissue following whole-body irradiation.
5. Mechanisms of shortening life-span of mice by X-rays.
6. Energy-transfer processes in flavins.

CELLULAR CONSTITUENTS

1. Isolation and fractionation of RNA and DNA from various organisms.
2. Biosynthesis of DNA and RNA in mammalian cells.
3. Biosynthesis of RNA in *Bacillus megaterium*.
4. RNA metabolism in liver and hepatoma.
5. Histones and other basic proteins.
6. Structural changes in proteins on their denaturation.
7. Xanthine oxidase and purine pool.
8. Lysosomal enzymes.
9. Guanase.
10. Pyridoxine metabolism in leukaemia.
11. Sulphydryl and disulphide levels in leukaemia.

IMMUNOLOGY AND IMMUNOGENETICS

1. Role of the thymus in lymphopoiesis and immune response.
2. Role of the thymus in neonatal life.
3. Role of the thymus in adult life.
4. Restoring thymectomized animals to normal reactivity.
5. Identification of cells with immunological potential.
6. Attempts to demonstrate the existence of a humoral thymus factor.
7. Regeneration of the liver in allogeneic radiation chimaeras.
8. Repopulation of haematopoietic sites in syngeneic chimaeras.
9. Rejection of host-type skin grafts by allogeneic chimaeras.
10. Nature of the protective effect of isogenic thoracic duct lymphocytes in the post-irradiation syndrome in the rat.
11. Actively acquired immunity to erythrocyte and transplantation antigens in the chick embryo.
12. Breakdown of the tolerant state associated with runting in chicks.
13. Attachment of antibodies to cell surfaces.

EXPERIMENTAL LEUKAEMIA

1. Virus-induced leukaemias in *AK* mice.
2. 'Accelerated' virus-induced leukaemias.
3. Primary virus-induced leukaemias in *C3H* mice.
4. Chemically-induced leukaemias.
5. Radiation-induced leukaemias.
6. Bone marrow therapy of leukaemia in thymectomized mice.

MUTAGENESIS

1. Macromolecular mutagenesis.
2. The mutagenicity of 5-iododeoxyuridine.

INVASIVENESS AND METASTASIS

1. The invasiveness of tumour cells.
2. Invasion in organ culture.
3. Invasion of chorioallantoic membrane of chick embryo by tumour cells.
4. Barriers to diffusion of solutes through certain organs.

CELLULAR PHYSIOLOGY

1. Cell physiology: an electro-osmotic theory of protoplasmic streaming.
2. Positive tropism in *Amoeba proteus*.
3. Cell transformations using polyoma virus.
4. Possible rudimentary histogenesis of cells in monolayer culture.

ENVIRONMENTAL PATHOLOGY AND MEDICAL STATISTICS

Mortality from cancer and respiratory diseases in England and Wales.

BIOLOGY AND BIOCHEMISTRY OF HUMAN CANCER

1. Pyridoxine metabolism in human leukaemia.
2. Histochemical studies of normal-appearing mucosa in patients with hereditary multiple polyposis.
3. Direct effect of human tissues on the growth of human tumour cells *in vitro*.

PHYSICS DEPARTMENT

CLINICAL APPLICATIONS OF PHYSICS

1. Radioactive isotopes:
   (*a*) Application of low-background counting techniques to human metabolic problems including studies of the retention of compounds labelled with ^{47}Ca, ^{59}Fe, ^{58}Co, ^{125}I or ^{131}I and vitamin B_{12}.
   (*b*) Digital computer methods for analysis of γ-spectral measurements of radioactivity in human subjects.
   (*c*) Applications of low-energy γ- and positron-emitting isotopes in scanning and uptake measurements on patients.
   (*d*) Development of radioactive tracer techniques including ^{125}I, ^{131}I-labelled Hippuran, ^{203}Hg-labelled Neohydrin for kidney function (in collaboration with Radiotherapy Department), and ^{133}Xe for lung function (in collaboration with Institute for Diseases of the Chest).
   (*e*) 4π β–γ proportional and scintillation counter systems for radioactive isotope standardization.
2. Beam radiation and solid-source techniques:
   (*a*) Application of scintillation spectrometry to determination of X- and γ-ray spectra for 6-meV linear accelerators, 2-meV Van de Graaff generator and ^{60}Co unit.
   (*b*) Calorimetry in measurements of output of high-energy machines and of absorbed dose in tissue-equivalent materials.
   (*c*) Radiation dose at interfaces for various elements and radiation energies.
   (*d*) Tissue-equivalent phantoms for investigation of effect of inhomogeneities, particularly due to lung and bone, on radiation distributions in the human body, and a study of the possibility of using thermoluminescent radiation-measuring systems.
   (*e*) Design and construction of thoracic phantom for radiotherapy, with applications in diagnostic radiology (in collaboration with Radiotherapy Department).
   (*f*) Technique of mammography and of radiation protection problems associated with new types of X-ray equipment (in collaboration with X-ray Diagnostic Department).
   (*g*) Digital computer techniques for treatment planning in radiation therapy.
   (*h*) Optical integrator and direct calculator to determine γ-ray dose distributions around solid sources of simple geometric shape to obtain charts indicating maximum and minimum dosage levels.
   (*i*) Development and use of high-pressure oxygen during radiotherapy (in collaboration with Radiotherapy Department).
   (*j*) Properties of cadmium sulphide radiation detectors and their use in gynaecological probes and for measurements of low dose-rates.
   (*k*) Spectroscopic methods for detection of low-energy γ-radiation in relation to clinical studies.

ENVIRONMENTAL RADIOACTIVITY (NATURAL AND ARTIFICIAL)

1. Monitoring of fission products, particularly in relation to ^{131}I and ^{137}Cs in milk.
2. Levels of natural fall-out: ^{210}Pb and ^{210}Po in foodstuffs and the extent to which these nuclides are retained by humans.
3. Levels of ^{210}Pb, ^{210}Po and ^{239}Pu in the atmosphere and examination of the extent to which the polonium and lead may be of other than natural origin.
4. Location and biochemical state of polonium in tissue, and possible analogy with selenium.
5. Human tissue distribution of heavy elements (including radium, thorium, actinium, polonium and plutonium) in normal and occupationally exposed humans.

NEUTRON DOSIMETRY OF COSMIC RADIATION

1. Measurements of the magnitude and possible variations of radiation dose to man due to neutrons of cosmic-ray origin, with particular reference to the reasons for the discrepancy between preliminary measurements made in the Department and those made elsewhere by indirect methods.
2. Experimental and theoretical studies of the attenuation of fast-neutron flux by tissue and the rate of production of additional neutrons by spallation reactions.
3. Investigation of the possible existence of hitherto undetected activation products of biological interest.
4. Fast-neutron dose-rates in the vicinity of the 6-meV linear accelerators in the new Royal Marsden Hospital at Sutton and the possibility of using γ-ray–neutron threshold reactions as a means of beam-energy calibration in such machines.

ENVIRONMENTAL AND DIETARY FACTORS IN CAUSATION OF GASTRIC CANCER

1. Investigation into the possibility that the preparation of food with waters of different constitution may lead to significant differences in the composition of certain items of the diet, with particular reference to the composition of beverages.
2. Analysis of the constituents of drinking waters sampled from various regions of the country.

SUBCELLULAR DISTRIBUTION OF METALS AND RADIOISOTOPES

1. Uptake of radioisotopes by cytoplasmic constituents with particular attention to metals possessing carcinogenic properties, and to studies with beryllium.
2. Plutonium distribution in the liver cell.
3. Development of technique applicable to metal-distribution studies for the isolation of nucleoli from mammalian tissues.
4. Mineral content of the cell nucleus as a function of the cell cycle.

METABOLISM OF RADIOACTIVE MATERIALS, PARTICULARLY TRANSURANIC ELEMENTS

1. Turnover of radioactive material in bone; retention of radionuclides in bone.
2. Biological effects of plutonium and americium.
3. Retention of radionuclides in the reproductive organs, with particular attention to the uptake, distribution and retention of a number of radionuclides, including ^{85}Sr, ^{239}Pu and other transuranic elements, in the testes and ovaries of rats.
4. Transport of transuranic elements in the body.
5. Effects of physiological factors on the retention of transuranic elements, with particular reference to the effects of pregnancy, lactation and treatment with parathyroid hormone on the retention of plutonium in bone and other tissue of the rat.
6. Uptake, distribution and retention of ^{32}P in human tumours and complementary studies on animal tumours.
7. Biochemical studies in regenerating tissues: biochemical changes resulting from radiation and other agents in the kidney during the compensatory hypertrophy occurring after unilateral nephrectomy, with special reference to DNA synthesis.

EXPERIMENTAL BIOLOGICAL AND PHYSIOLOGICAL INVESTIGATIONS

The effects of continuous γ-irradiation on the renewal of tissues of experimental animals are studied over a wide range of radiation dose-rates. These investigations include:

1. Changes in the cell population of the bone marrow of rats irradiated continuously at 50 rads/day, and at other dose-rates; an attempt to obtain labelled mitosis curves for bone marrow cells following injection of tritiated thymidine.

2. Effects of acute and continuous irradiation, using two techniques for estimating the stem cell content of erythroid and lymphoid tissue, and the response of the tissue when it is not itself damaged as, for example, in anaemia and in polycythaemia produced by red cell transfusion and stimulation of lymphocyte production.
3. Growth rate of rats under continuous irradiation.
4. Effects of continuous irradiation on the ability of the liver to regenerate following partial hepatectomy in rats and mice, to establish the extent to which liver cells store radiation injury: cell cycle times during recovery measured by techniques using tritiated thymidine.
5. Effects of continuous irradiation on the growth of two different strains of murine lymphoma cells in culture using tritiated thymidine and colchicine, with particular reference to the determination of chromosome abnormalities and the extent to which alterations in cell cycle time and change in cell death rate account for the slower rate of increase in cell numbers.
6. Nature of the physiological changes in the small intestine of the rat during development, with particular reference to changes in the pattern of cell proliferation induced by continuous irradiation and also by surgical resection.
7. Rate of vibrissal growth following acute irradiation and during continuous irradiation: investigations of the changes in cell kinetics and cell proliferation in the hair follicles using tritiated thymidine and also ^{35}S-labelled cystine.
8. Responses of transplanted tumours to continuous irradiation, including studies of the mitotic cycle of these tumours and the amount of necrosis and cell death, using tritium labelling techniques.
9. Possible effects of Thorotrast using different strains of mice, *C57BL* mice being used as controls for determining the incidence of spontaneous tumours.
10. Histogenesis of bone tumours in rats following the administration of plutonium, using different dosages of the nuclide, with particular emphasis on possible occurrence of examples of myelogenous leukaemia in these rats; effects of chelating agents on tumour incidence; studies of the serum proteins of continuously irradiated animals together with an analysis of the populations of some of the lymphoid tissues as revealed by tritium labelling techniques.
11. Compensatory processes subsequent to unilateral nephrectomy in rats and mice of various ages, with particular reference to the precise determination of chemical and histological changes and the effect of continuous irradiation.
12. Investigation of the possibility that the relatively long cell cycle time found in corneal and ear epithelium is due to the lower temperature of these tissues compared to other tissues.
13. Measurement of the bone marrow volume of experimental animals to determine whether there is any species variation.

BIOLOGICAL EFFECTS OF ULTRASOUND

1. Focussing properties of ultrasonic beams as a possible means of producing localized tissue destruction and of enhancing the effect of certain conventional methods of tumour therapy.
2. Modes of action of ultrasound in producing changes in biological systems.

INSTRUMENT DEVELOPMENT AND EVALUATION

1. New designs of transistorized clinical dosimeters and radiation monitors.
2. Provision of electronic and mechanical facilities for the new low-background laboratory at the Surrey Branch site.
3. Measurements and continuous recording of uptake of β-emitters in tumour tissue, including development of appropriate measuring apparatus.
4. Survey of techniques currently available for patient monitoring, with particular reference to their use in recovery and reverse-barrier nursing wards; methods of measuring and monitoring physiological data.
5. Development of ultrasonic scanner and attempts to solve the problem of acoustic contact.
6. Behaviour of solid-state radiation detectors, particularly with regard to their applications as counters, spectrometers and dosimeters.

RADIOTHERAPY DEPARTMENT

LONG-TERM CLINICAL STUDIES

1. Influence of treatment on prognosis in relation to pathology and natural history, and to factors predisposing to the development of tumours at different sites, with special reference to the bladder, brain, breast, eye, larynx and pharynx, lungs, oesophagus, skin, testicles, thyroid and uterus, and also to the development of leukaemia, polycythaemia, and the lymphomas.
2. Observations on detrimental long-term effects of radiation on the bone marrow and the eyes and on the induction of tumours.
3. Application of lymphangiography to the study of the lymph node drainage of tumour sites and to the radiological demonstration of deep-seated involvement of lymph nodes and their changes under treatment, particularly in patients with testicular tumours or lymphomas; possibilities of using radioactive contrast media not only for localization but also for the treatment of lymph nodes involved in neoplastic disease, particularly in relation to the lymphomas.

ISOTOPE INVESTIGATIONS

1. Renal pathology by simultaneous recording of ^{131}I-labelled Hippuran excretion by both kidneys.
2. Improvement of external scanning techniques for detecting hepatic metastases with colloidal ^{198}Au or ^{64}Cu.
3. Preliminary work on a method for delineating the haemopoietic system by positron scanning with ^{52}Fe, and investigations of various abnormalities of the haemopoietic system with ^{59}Fe and ^{51}Cr.
4. Measurements of leakage of chemotherapeutic agents during regional perfusion, using ^{51}Cr-tagged red cells, or ^{131}I.H.S.A. and external monitoring; method evolved for rapidly calculating various leakage parameters during operation in cases where complete surgical isolation cannot be achieved.
5. The use of radioisotopes for a variety of therapeutic purposes, including: systemically selective concentration (^{131}I, ^{32}P, ^{131}I.H.S.A.); intracavitary application (colloidal ^{198}Au); interstitial application (^{198}Au, ^{90}Y grains and ^{182}Ta wire as small sources); surface application (^{90}Sr plaques); beam therapy (^{137}Cs, ^{60}Co).

EXPERIMENTAL RADIOBIOLOGY

1. Tissue culture studies to determine the radiosensitivity of isolated tumour cells, and the effect of X-radiation on cell cycle kinetics in relation to dose fractionation by means of a new double isotope autoradiographic technique.
2. Investigation of the metastatic spread of tumours, the viability of tumour cells isolated from patients' blood being assessed by means of labelled nucleic acid and protein precursors.
3. Influence of irradiation on collagen synthesis *in vivo*.
4. Mechanism of the response of nervous tissue to irradiation at high dose-rate, studied in frog nerve-muscle preparations, and the implication of this response for nerve physiology in general.
5. Effects of different concentrations of CO_2 combined with pure oxygen inhalation on the radiosensitivity of whole animals (part of a long-term study into the potentialities of high-pressure oxygen in clinical radiotherapy).
6. Homologous disease in rats, with emphasis on methods for labelling lymphocytes *in vitro*.

CHARACTERIZATION OF HUMAN CANCER

Human tumours and normal tissue are subjected to a comprehensive analysis, with detailed studies of the environment of the patients.

1. Collection and registration service.
2. Tumour-cell culture and inhibitory effect of cytotoxic drugs.
3. Co-enzyme I.
4. Respiratory behaviour.
5. Trace metal content.
6. Karyotype and immunology.
7. Level of soluble thiols and disulphides in leukaemia.
8. Tissue storage.
9. Environmental pathology.
10. Correlation and assessment of results.

CHEMOTHERAPY

1. Systemic studies:
   (*a*) Chemotherapy of ovarian carcinoma: comparison of mannitol, Myleran and chlorambucil.
   (*b*) Participation in Medical Research Council's therapeutic trial of busulphan and splenic irradiation in chronic granulocytic leukaemia.
   (*c*) Clinical trial of continuous therapy with chlorambucil in malignant lymphoma.
   (*d*) Malignant disease of the alimentary tract treated with merophan (*o*-merphalan).
   (*e*) Clinical trial of melphalan in multiple myelomatosis.
2. Regional studies: perfusion and infusion techniques using different cytotoxic drugs alone or in combination.

STEROID HORMONE METABOLISM

1. Steroid hormone metabolism in those tumours amenable to perfusion techniques.
2. Effects of cancer chemotherapeutic agents on human tumour metabolism as reflected in changes of perfusion blood constituents.
3. Specific aspects of liver physiology possibly relevant to carcinogenesis or cancer chemotherapy.

KARYOTYPE AND IMMUNOLOGICAL STUDIES

1. Immunology: qualitative aspect of red cell antigens.
2. Karyotype analysis in multiple myelomatosis, macroglobulinaemia and leukaemia, with special emphasis on the Philadelphia chromosome.
3. Collaborative study of blood groups and chromosomes.

CARCINOMA OF PHARYNX

1. Clinical and detailed environmental study of patients.
2. Blood state and iron metabolism.

HODGKIN'S DISEASE: THERAPEUTIC TRIAL

Early cases of Hodgkin's disease treated by radiotherapy alone compared with those treated by radiotherapy combined with nitrogen mustard (in collaboration with several other hospitals).

CARCINOMA OF BLADDER

1. Investigation of possible carcinogens in urine.
2. Local chemotherapy of bladder tumours in dogs and in humans.

CLINICAL PATHOLOGY

1. Care of the marrow-depleted patient.
2. Properties of human lymphocytes.
3. Assessment of immunological status.

ENVIRONMENTAL PATHOLOGY

Detailed histories by specially trained interviewers from a wide range of patients with different types of cancer.

ROYAL BEATSON MEMORIAL HOSPITAL
132–138, Hill Street, Glasgow, C.3

CANCER RESEARCH DEPARTMENT

Director

P. R. Peacock, M.B., F.R.F.P.S.G.

Staff

Miss M. Broadfoot, B.Sc.
J. G. Chalmers, B.Sc., F.R.S.E.
G. S. Fell, Ph.D. (*until May 1963*)
Mrs. M. A. Head, M.D.
S. Iversen, M.D.*
W. B. McLaren, Ph.D.
J. J. Milne, B.Sc.*
Mrs. Andree Peacock, B.Sc.*
J. B. Spence, A.R.C.S.T.

The main function of the hospital is the diagnosis, treatment and investigation of cancer; the Cancer Research Department works in close association with the departments of clinical pathology, biochemistry and photography.

Summary of Research

1. Correlation of morphological and biological evidence for the presence of viruses in certain tumours and attempts to assess the value of negative evidence in normal and in some neoplastic cells.
2. Aetiological investigations of spontaneous and induced lung tumours in mice with reference to their anatomical sites, morphology and associated lesions.
3. The role of male mice (apparently normal) in transmitting mammary tumour agent (MTA) to susceptible mice of different ages, as shown by the development of mammary tumours in the females.
4. The incidence of mammary, hepatic and pulmonary tumours in MTA-free mice of *RIII$_f$* pure line, F_1 hybrids *C3H$_f$* × *RIII$_f$* and back-cross (*C3H$_f$* × *RIII$_f$*) × *RIII$_f$*, and second generation back-cross breeders; secrosterone (purified progesterone) compared with progesterone in *C3H$_f$* breeding females for possible influence on the incidence of mammary or hepatic tumours.
5. Bioassay of substances for carcinogenicity.
6. Attempts to correlate morphological and cytometric data with the biological properties of cells, with special reference to the mass and arrangement of nuclear DNA.
7. Mechanisms of energy transfer in cells and the influence of physical agencies, such as ultraviolet and ionizing radiations, on free radical production as a possible factor in carcinogenesis.
8. Metabolism of isoniazid and related compounds in rats and mice.
9. Comparative biochemical analyses of tumours in fowls, small mammals and man.

*Working under a full-time grant from the British Empire Cancer Campaign.

CHRISTIE HOSPITAL AND HOLT RADIUM INSTITUTE

Withington, Manchester, 20

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PATERSON LABORATORIES

Director

L. G. Lajtha, M.D., D.Phil.

Staff

A. J. Bateman, D.Sc.
D. Bradley, B.Sc.
A. S. Buttoo, M.B.
J. W. Byron, Ph.D.
Miss A. C. Chandley, M.Sc.
A. W. Craig, Ph.D.
J. V. Davies, Ph.D., A.R.I.C.
T. J. Davy, B.Sc. (*until Mar. 1963*)
M. Ebert, Ph.D.
B. W. Fox, Ph.D.
C. W. Gilbert, Ph.D.
Mrs. M. V. Haigh, B.Sc.
B. Hemsworth, M.Sc.
Miss A. Howard, Ph.D.
H. Jackson, M.B., Ph.D. (*M.R.C. External Staff*)
R. M. V. James, Ph.D.
J. P. Keene, Ph.D.
E. J. Land, Ph.D.
C. S. Lange, B.S.
J. Law, Ph.D.
Miss M. E. Macauley, M.B.
S. Muldal, Cand.Real.
A. H. W. Nias, M.B., D.M.R.T.
C. H. Ockey, Ph.D.
P. J. O'Connor, Ph.D.
Miss M. Partington, Ph.D.
D. J. Pillinger, B.Sc.
D. D. Porteous, B.Sc.
C. Russell, Ph.D.
R. Schofield, B.Sc.
L. G. Skinner, B.Sc.
A. J. Swallow, D.Sc.

Visiting Fellows

J. C. Buchanan, M.B., M.R.C.P.E. (*Auckland Hospital, New Zealand; Nuffield Foundation grant-holder*)
B. Cercek, Ph.D. (*Institut Josef Stefan, Yugoslavia; Institutional Fellow*)
J. Fisher, Ph.D. (*University of Tennessee, Memphis*)
Mrs. V. Polekisic-Markovic (*Institute of Nuclear Sciences, Belgrade*)
L. Morra, M.D. (*University of Genoa, International Atomic Energy Agency Fellowship; British Council Fellow*)
S. F. Ryan, M.B. (*Cornell University, New York*)
M. A. Siddiqui, M.B., D.M.R.T., F.R.C.S.E. (*Pakistan Atomic Energy Commission; Beit Memorial Fellow*)
L. Tiepolo, D.Sc. (*University of Pavia, Italy*)

The main object of the laboratories is to pursue basic research in the problems of cancer and radiation biology in the broadest sense. Special emphasis is laid on a multidisciplinary approach to all the problems by close collaboration within the various specialities.

Summary of Research

1. Flash radiolysis:
   (*a*) Development of apparatus and adaptations to shorter pulses.
   (*b*) Ferrous sulphate reaction.
   (*c*) Hydrated electron studies.
   (*d*) Microsecond pulses in biological systems.
   (*e*) Investigations of chemical reactions, e.g.: cyclohexane–benzene mixtures, methylene blue, cysteine, glycine, iodine in cyclohexane, aqueous ethylene, aromatic liquids, aqueous carbon monoxide.
   (*f*) Development of a method of analysis of absorption curves using a digital computer.
2. Radiolysis of alkyl iodides.
3. Evaluation of the health hazard arising from radiolysis products.
4. Radiolysis of cyclohexane–hydrogen chloride mixtures.
5. Effect on radiosensitivity of inert and anaesthetic gases on ascites tumour cells.
6. Survival and growth of latera[1] roots of *Vicia* after irradiation.
7. Radical production and lethality in fern spores after irradiation; comparison of effects of electron-spin resonance (ESR) with biological damage.
8. Radiosensitivity of spores of *Oedogonium* in respect of the oespore effect on survival of a green cell.

9. Correlation of radiosensitivity and ploidy using *Planaria.*
10. Quantitative aspects of radiation-induced mitotic delay in normal mouse epidermis *in vivo.*
11. Quantitative cell culture studies:
    (*a*) Chronic irradiation by β-emitters in the medium.
    (*b*) Synchronized HeLa cultures for correlation of radiosensitivity with phase of cell cycle.
    (*c*) Studies on the genetic lability of cell lines *in vitro.*
    (*d*) Attempts to establish lines of human diploid cells from blood cultures.
    (*e*) Dose–response relationship studies with alkylating agents.
12. Kinetic studies on bone marrow stem cells:
    (*a*) Residual damage of bone marrow stem cells after irradiation.
    (*b*) Stimulation of recovery of stem cell population following irradiation.
    (*c*) Theoretical study of kinetic models by computer analysis.
    (*d*) Dose–effect relationship of alkylating agents on stem-cell survival *in vivo.*
13. Metabolic processes involved in stem cell differentiation:
    (*a*) Effect of metabolic inhibitors.
    (*b*) Biochemical effects of erythropoietin administration.
    (*c*) Autoradiographic studies on stem cell differentiation into the erythron.
14. Recovery of Rhesus monkeys from 800 rads total body X-irradiation; establishment of an antibiotic regime to serve as basis of evaluating the merits of marrow grafting in primates.
15. Attempts at producing experimental auto-immune anaemia.
16. Study of possible organ-specific growth inhibitors involved in liver regeneration.
17. Alkane sulphonic esters and ethyleneimines in relation to fertility.
18. Cell population and dominant lethal studies using alkane sulphonic esters.
19. Metabolic studies with labelled alkane sulphonic esters.
20. Effects of alkylating agents on the foetal gonad.
21. Effects of alkylating agents on the gametes and on cleavage of the zygote in the sea urchin.
22. Alkylating agents and haemopoiesis.
23. Action of certain alkylating agents on the morphology and function of the thymus.
24. Morphological studies of human chromosome abnormalities.
25. Abnormal cell types: time sequence of chromosome duplication in man.
26. Variation in the duration of the DNA synthesizing phase in chimaeric stem lines.
27. Chromosome aberrations of transient and permanent type in irradiated Rhesus monkeys.
28. Autoradiographic studies of sex chromosome abnormalities.
29. Chromosome labelling in human leukaemia.
30. Comparative chromosome-labelling studies in man and the Rhesus monkey.
31. Screening for sex chromosome aberrations in small rodents.
32. DNA synthesis in human diploid cultures.
33. Radiosensitivity of oocytes and oogonia in *Drosophila* in respect of chromosome non-disjunction and stage of oogenesis.
34. Effect of tritiated thymidine incorporated into mouse oocytes.
35. Mutagenic action of MMS (methyl methanesulphonate) on male germ cells of the mouse and *Drosophila.*
36. Correlation of gonadotrophin levels with clinical response.
37. Extracorporeal irradiation of the blood: clinical trial of a ^{90}Sr radiation unit.
38. Changes in ^{32}P concentration in breast tumours.
39. Development of apparatus for rapid measurement of chromosome lengths and arm ratios, and analysis by digital computer.
40. Development of an autoradiographic grain counter.
41. Development of a cell counter for colony-size distributions in monolayer cultures.
42. Effect of NO on the ESR spectrum of polymethylmethacrylate and its response to radiation.
43. ESR studies on substances of biological interest.
44. Use of barley roots as a model biological system for radiation studies.
45. Problems of radiosensitivity in microbial systems.

STRANGEWAYS RESEARCH LABORATORY

Wort's Causeway, Cambridge

Director
Professor Dame Honor B. Fell, D.B.E., D.Sc., F.R.S.
(*Research Professor of the Royal Society*)

Deputy Director
A. Glucksmann, M.D.
(*British Empire Cancer Campaign*)

Staff

Miss J. M. Allen, B.Sc. (*M.R.C. External Staff*)
Mrs. M. L. Armstrong, B.Sc. (*M.R.C. External Staff*)
Miss C. P. Cherry, M.B. (*British Empire Cancer Campaign*)
G. D. Clarke, Ph.D. (*M.R.C. External Staff*)
Miss M. R. Daniel, M.D., B.Sc. (*British Empire Cancer Campaign*)
J. T. Dingle, B.Sc. (*M.R.C. External Staff*)
Miss A. M. Glauert (Mrs. Franks), M.Sc. (*Sir Halley Stewart Fellow*)
J. C. Heath, B.Sc. (*British Empire Cancer Campaign*)
Miss S. Fitton Jackson, Ph.D. (*M.R.C. External Staff*)
W. Jacobson, M.D., Sc.D. (*Sir Halley Stewart Fellow*)
Miss I. Lasnitzki (Mrs. Glucksmann), M.D., Ph.D. (*Sir Halley Stewart Fellow*)
J. A. Lucy, Ph.D. (*M.R.C. External Staff*)
T. R. Munro, M.A. (*British Empire Cancer Campaign*)
D. A. T. New, Ph.D. (*M.R.C. External Staff*)
F. G. Spear, M.D., F.F.R. (*M.R.C. External Staff; part-time*)
Miss S. Waite, B.A. (*M.R.C. External Staff*)
M. Webb, D.Sc. (*M.R.C. External Staff*)
L. Weiss, M.D., Ph.D. (*M.R.C. External Staff*)

Visiting and Attached Workers

O. Aasmundrud (*Technical University of Norway*)
F. T. Algard, Ph.D. (*Stanford University*)
N. B. Atkin, M.B. (*Mount Vernon Hospital*)
E. M. Brieger, M.D. (*Department of Technical Co-operation grant-holder*)
Mrs. S. Denham, B.Sc. (*British Empire Cancer Campaign*)
J. W. Dodson, B.Sc. (*M.R.C. Scholar*)
Miss L. C. Dryburgh, B.D.S. (*University of Edinburgh*)
D. A. Fischman, M.D. (*Cornell University*)
D. Franks, Ph.D. (*M.R.C. grant-holder*)
G. S. Gordan, M.D. (*University of California*)
C. E. Graham, B.Sc. (*University of Birmingham*)
Miss M. C. Hammond (*London School of Hygiene and Tropical Medicine*)
J. C. Houck, Ph.D. (*University of Georgetown, Washington*)
D. C. Mears, B.A. (*Cornell University, New York*)
D. S. O'Dell, B.Sc. (*M.R.C. Scholar*)
Miss K. F. Stein, Ph.D. (*University of Chicago*)
Miss B. Wallace, M.D. (*Trinity College, Dublin*)

Since 1917 an annual grant towards the running expenses of the Strangeways Research Laboratory has been provided by the Council and by their predecessors the Medical Research Committee; several members of the Council's External Scientific Staff work in the Laboratory. The Laboratory also receives support from a number of other sources.

The research of the Laboratory concerns cells and tissues of different types, their structure and physiology, their interactions with one another and their response to such agents as vitamins, hormones, carcinogens, radiations and antibodies.

Summary of Research

MORPHOGENESIS AND CYTOLOGY

1. Connective tissue:
   (*a*) Interaction between epithelia and connective tissue.
   (*b*) Comparison of the morphogenesis of different cartilages, and the structural nature of protein–polysaccharide complexes of high molecular weight in the developing chick.
   (*c*) Comparison of mineralization processes in developing cartilage and bone.
   (*d*) Synthetic balance between the components of intercellular material.
2. Morphogenesis, including fine structure, of developing avian skin *in vivo* and in culture.
3. Development of techniques for growing post-implantation mouse and rat embryos *in vitro*.
4. Fine structure of monolayer cultures of Chinese hamster and rat fibroblasts.

CELL PHYSIOLOGY

1. Cell surface:
   (*a*) Physical surface-properties of tumour cells from a common pool, grown in different sites in mice (with Dr. G. V. F. Seaman and Dr. G. M. W. Cook, University of Cambridge).
   (*b*) Mechano–chemical analysis of surfaces of intact cells.
   (*c*) Cellular locomotive thrust in relation to cell contacts.
   (*d*) Cell separation in relation to metastasis.
2. Action of saponin on cell membranes.
3. Artificial membranes:
   (*a*) Analysis of the structure of artificial complexes of lecithin, cholesterol and saponin in terms of the constituent molecules.
   (*b*) Fine structure of myelin forms composed of lecithin and cholesterol.
   (*c*) Development of a micellar model for the lipids of cell membranes.
4. Lysosomes:
   (*a*) Demonstration of lysosomes in living cells.
   (*b*) Effects on lysosomes of cytoplasmic and nuclear damage caused by microdissection.
   (*c*) Lysosomal stability in the developing chick.

THE ACTION OF VITAMINS

1. Vitamin A:
   (*a*) Behaviour of vitamin A derivatives in aqueous medium.
   (*b*) Penetration of lecithin–cholesterol monolayer by vitamin A (with Dr. A. D. Bangham, A.R.C. Institute of Animal Physiology, Babraham, Cambridge).
   (*c*) The effect of vitamin A on mitochondrial swelling.
   (*d*) Release by vitamin A of hydrolytic enzymes from partially purified lysosomal fractions from rat liver.
   (*e*) Action of low doses of vitamin A on lysosomal and mitochondrial stability.
   (*f*) Inhibition of hypotonic haemolysis by low concentrations of vitamin A.
   (*g*) Action of vitamin A on fibroblasts in culture.
   (*h*) Lysosomal enzymes of foetal membrane bone and their release by vitamin A from lysosomes isolated from bone.
   (*i*) Fine structure of bone in culture during resorption produced by vitamin A.
   (*j*) Biochemistry of bone resorption induced by vitamin A.
   (*k*) Lysosomal stability in relation to excess and deficiency of vitamin A in the rat (with Dr. I. M. Sharman and Dr. T. Moore, Dunn Nutritional Laboratory).
   (*l*) Effects of excess vitamin A on the embryonic chick.
   (*m*) Effects of excess vitamin A on cultures of skin from the tail and pads of rat embryos, and from the trunk, tail and pads of rabbit embryos.
   (*n*) Effects of ribonuclease on cultures of embryonic chick skin compared with the effects of vitamin A.
   (*o*) Metaplastic action of excess vitamin A on the rat oesophagus in organ culture.
2. Effect of vitamin E deficiency on the stability of rat kidney lysosomes.

THE ACTION OF PROTEINS ON THE RESORPTION OF BONE AND CARTILAGE MATRIX

1. Histology and biochemistry of bone and cartilage resorption induced by certain plasma proteins added to a chemically defined medium.
2. Inhibition of this resorption by hydrocortisone.

IMMUNOLOGY

1. Effects of antisera on cells and tissues in culture:
   (*a*) Release of lysosomal enzymes from cells *in vitro* by cytotoxic antisera.
   (*b*) Inhibition of this release by hydrocortisone.
   (*c*) Severe resorption of bone and cartilage, and necrotic changes produced by cytotoxic antiserum.
   (*d*) Inhibition of these effects by hydrocortisone.
2. Factors involved in the acquisition and loss of membrane antigens by cells *in vitro* (with members of the Department of Pathology, University of Cambridge).

1. Leukaemia:
   (*a*) Microbiological assays of folic and folinic acid and their antagonists in leukaemic cells of children and of mice after exposure to precursor compounds.
   (*b*) Cortisone–hydrocortisone equilibrium in leukaemic cells and other tissues.
   (*c*) Analysis of effects of vincristine on leukaemic and normal tissues.
2. Carcinogenic action of metals:
   (*a*) Toxic action of cobalt on myoblasts and on differentiated muscle fibres in culture, studied by time-lapse cine-photomicrography, and modification of this toxicity by zinc.
   (*b*) Implantation into rat muscle of cobalt spheres to determine the rate of dissolution of the metal in relation to the appearance of tumours.
   (*c*) Action of cell-free fractions, including nucleic acid preparations, from metal-induced and related tumours on short-term cultures of myoblasts and fibroblasts.
   (*d*) Physico–chemical investigations of the structures of chelates of dihydrolipoic acid and dihydrolipoamide with divalent cations.
   (*e*) Mechanisms of inhibition of ketoglutarate dehydrogenase by various divalent cations.
   (*f*) Significance of cation–dihydrolipoic acid interactions in relation to the inhibition of cellular oxidative metabolism by metallic ions.
3. Metabolism and cytology of cultured cells derived from tumours induced by the implantation of cobalt-tolerant and other strains of dermal fibroblasts.
4. Alterations in metabolism, cytology and malignant potential of embryonic rat cells after prolonged cultivation *in vitro* under conditions of either oxygen or glucose deficiency.
5. Effect of chemical carcinogens on organ cultures:
   (*a*) Effect of chemical carcinogens on respiration and glycolysis in the rat prostate.
   (*b*) Effect of hydrocortisone, testosterone, oestrogens and insulin on the growth pattern of the rat prostate *in vitro*.
   (*c*) Influence of hydrocortisone, testosterone and oestrogens on the effect of chemical carcinogens in the rat prostate.
   (*d*) Interaction of hydrocortisone with testosterone, oestrogens and insulin on the rat prostate.
   (*e*) Implantation of organ cultures of skin and prostates treated with carcinogens *in vitro* into suitable hosts.
6. Influence of hormonal factors on chemically induced carcinogenesis in intact and castrate rats:
   (*a*) Effects of thyroxine, thiouracil, oestrogens, androgens and a combination of oestrogens and androgens on the induction of tumours in salivary glands.
   (*b*) Effects of hyper- and hypoglycaemia, testosterone, and testosterone combined with stilboestrol on the induction of cervico–vaginal tumours.
   (*c*) Effect of stilboestrol combined with thyroxine or thiouracil on the induction of cervico–vaginal tumours.
   (*d*) Effect of thyroxine and thiouracil on the induction of skin tumours in female rats.
7. Radiobiology:
   (*a*) Effect of fractionated localized radiation and additional treatment with thyroxine and thiouracil on the induction of skin tumours in rats.
   (*b*) Effect of radiation and of radiomimetic drugs on the eye of the suckling rat.
   (*c*) Effect of radiation on the uptake of tritiated thymidine in the eye of the suckling rat.
   (*d*) α-irradiation of single cells.
   (*e*) Attempt to correlate the results of cancer radiotherapy with experiments on the radiation of cells in culture (theoretical study).
8. Clinico–pathological studies of human cancers:
   (*a*) Radiation dosage and cure rate in cancer of the uterine cervix in relation to tumour type and host factors.
   (*b*) Histogenesis of microcarcinoma of the uterine cervix.
   (*c*) Radiation dosage and cure rate of oral-cavity cancers in relation to tumour type and host factors.
   (*d*) Relation of tumour type to sensitivity reaction in cervical cancers at different centres.
   (*e*) Value to the radiotherapist of routine pathological reports on serial biopsies taken from individual cancers of the uterine cervix during radiation treatment.

1. Pathway of leucine biosynthesis in *Aerobacter aerogenes.*
2. Fine structure of the radiation-resistant coccus, *Micrococcus radiodurans* (with Dr. M. J. Thornley, Low Temperature Research Station, Cambridge).
3. Cellular response to mycobacterial infection:
   (*a*) Interpretation of the fine structure of *Mycobacterium leprae* in tissue sections by comparison with that of *M. lepraemurium.*
   (*b*) Acid phosphatase activity shown by electron microscopy in the peribacillary areas of cells in mice infected with *M. lepraemurium* (with Dr. R. J. W. Rees, National Institute for Medical Research, and Dr. A. Gautier, Centre de Microscopie Electronique, Lausanne).
   (*c*) Lysosome-like bodies in leprosy cells and their association with leprosy bacilli in various stages of degeneration.

THE ROYAL INSTITUTION

21, Albemarle Street, London, W.1

DAVY FARADAY RESEARCH LABORATORY

Director
Sir Lawrence Bragg, O.B.E., F.R.S.

Assistant Director
Professor Ronald King, Ph.D.

Staff employed by Medical Research Council

D. W. Green, Ph.D., A.Inst.P.
A. C. T. North, Ph.D., A.Inst.P.
D. C. Phillips, Ph.D., F.Inst.P.

For some years certain members of the Council's External Scientific Staff have been working in the Davy Faraday Research Laboratory of the Royal Institution on the structure of protein molecules, in close collaboration with the Council's Laboratory of Molecular Biology in Cambridge. In April 1960 the Council agreed to provide further support for these researches by making an annual grant to the Institution. The work on molecular structure also receives financial support from the United States National Institutes of Health.

Summary of Research

1. Development of high-speed recording apparatus for measuring crystal diffraction.
2. Chemical study of methods of attaching heavy atoms to protein molecules.
3. Programming of electronic computer for analysis of results.
4. Structure analysis of the proteins lactoglobulin and lysozyme.
5. Damage suffered by the protein crystal when exposed for prolonged periods to X-rays.
6. Comparison of the structures of whale and seal myoglobin.

Research Work Aided by Grants

The Council have always attached considerable importance to their scheme of research grants. These are awarded to workers who are not members of their own staff, normally for a three-year period, in aid of individual research projects carried out at universities and other centres. Such grants may be for the personal remuneration of individual research workers, for the provision of scientific and technical assistance to senior workers or for special research expenses.

Aberdeen

UNIVERSITY

Anatomy Department

McKENZIE, Dr. J.—assistance by Miss J. E. C. Sinclair: effect of antimycin A and other materials on the developing chick embryo. (1)

Biological Chemistry Department

BURKE, Dr. D. C.—expenses: interferon. (2)

GRANT, Dr. P. T.—expenses: comparative biochemistry of mammalian trypanosomes. (3)

PORTEOUS, Dr. J. W.—assistance by Dr. B. Clark, and expenses: biochemical activities of subcellular components of intestinal mucosal cells. (4)

ROBERTSON, Dr. H. A.—expenses: ^{131}I content of human thyroid glands. (5)

SIMKIN, Dr. J. L.—assistance by Dr. E. R. Skinner, and expenses: role of the microsome material in protein biosynthesis in mammalian cells. (6)

Chemical Pathology Department

HENDRY, Mr. N. G. C.—assistance by Miss P. Alexander, and expenses: relationship of glycosidases to abnormalities of connective tissue. (7)

Materia Medica and Therapeutics Department

STOWERS, Dr. J. M.—assistance by Mrs. Janet Stein, and expenses: metabolic defects in diabetes mellitus with particular reference to fat metabolism. (8)

Midwifery and Gynaecology Department

BAIRD, Professor Sir Dugald—assistance by Miss J. Aitken-Swan, and expenses: social aetiology of carcinoma of the cervix uteri. (9)

TURNBULL, Dr. A. C.—assistance by Dr. Anne Anderson, and expenses: uterine activity with special reference to prolonged pregnancy and labour. (10)

Pathology Department

CURRIE, Professor A. R.—expenses (from special funds for the purchase of costly apparatus): relationship between deoxyribonucleic acid, ribonucleic acid and specific cytoplasmic protein (enzyme or hormone) production. (11)

NAIRN, Dr. R. C.—expenses: immunopathological investigation of (i) organ specificity; (ii) auto-immune disease. (12)

Physiology Department

MALCOLM, Professor J. L.—(1) assistance by Dr. A. Bruce, and expenses: mode of action of substances that alter cerebral electrical activity; (2) expenses: an investigation of the sera of schizophrenic patients. (13)

SCOTT, Dr. Mary J.—assistance by Dr. R. D. M. Macleod, and expenses: cardiovascular responses to chemoreceptor stimulation in the cat. (14)

Surgery Department

CLARK, Mr. C. G.—assistance by Dr. R. Buchan, and expenses: absorption from intestine following procedures which alter gastric secretion. (15)

DUDLEY, Mr. H. A. F.—assistance by Mr. J. P. Masterton, and expenses: (i) body water, skin thickness and tube feeds in surgical patients; (ii) sleep patterns of patients and surgeons. (16)

Barton-on-Humber

PUBLIC HEALTH DEPARTMENT

ROBERTSON, Dr. J. S.—personal and expenses: toxoplasmosis as a cause of stillbirth, infant deaths and morbidity in children. (17)

Bath

ROYAL NATIONAL HOSPITAL

KERSLEY, Dr. G. D. and COSH, Dr. J. A.—expenses: neuropathy and myopathy in the connective tissue diseases. (18)

Beckenham

BETHLEM ROYAL HOSPITAL

HARE, Dr. E. H.—expenses: epidemiological study of mental health in two areas of Croydon. (19)

REES, Dr. W. Linford—assistance by Dr. Irene Martin, and expenses: psychological relationships in depressive illness. (20)

Belfast

CITY HOSPITAL

HUTH, Dr. Mary C.—expenses: blood group survey of the population of Northern Ireland. (21)

THE QUEEN'S UNIVERSITY

Biochemistry Department

LESLIE, Dr. I.—assistance by Mr. S. J. Martin, and expenses: coupling of energy metabolism and synthetic reactions occurring in tissue cultures of normal and malignant human cells. (22)

Microbiology Department

MACKENZIE, Dr. D. W. R.—expenses: mycological diseases. (23)

Therapeutics and Pharmacology Department

WADE, Professor O. L.—(1) assistance by Mrs. P. Busby, and expenses: experimental bronchitis and emphysema; (2) expenses: chronic pulmonary disease in rats. (24)

Birmingham

BIRMINGHAM GENERAL HOSPITAL

COOKE, Dr. W. T.—expenses: jejunal biopsies. (25)

BIRMINGHAM AND MIDLAND HOSPITAL FOR WOMEN

Clinical Endocrinology Department

CROOKE, Dr. A. C.—(1) assistance by Dr. Anneliese Wolf, and expenses: immunological investigations on pituitary trophic hormones; (2) assistance by Mr. D. Whyman, and expenses: action of certain oral contraceptives. (26)

QUEEN ELIZABETH HOSPITAL

Department of Neurosurgery

HUGHES, Professor E. B. C.—assistance by Dr. H. G. Clark, and expenses: production of focal lesions in the central nervous system. (27)

Department of Surgery

BROOKE, Mr. B. N.—assistance by Dr. Phillida A. Sampson, and expenses: steroid therapy in ulcerative colitis. (28)

TURNER, Mr. E. A.—assistance by Mr. B. N. Williams: arrest of cerebral circulation during brain surgery. (29)

Department of Surgery

WATTS, Mr. G. T.—personal, and expenses: mechanisms affecting the deposition of collagen and changes in the ground substance and its components. (30)

UNIVERSITY

Anatomy Department

ZUCKERMAN, Professor Sir Solly—(1) assistance by Dr. Heather M. Beaumont, and expenses: response of foetal tissues to X-irradiation; (2) expenses: gametogenesis; (3) expenses: (i) posture; (ii) dimensions and growth of the craniomandibular apparatus; (4) assistance by Dr. J. A. Hickman, and expenses: the structure and function of the hypothalamo-hypophysial tract in the ferret. (31)

Bacteriology Department

BISSET, Dr. K. A.—assistance by Mr. B. C. Cole and Mr. B. J. Harrington, and expenses: bacteriology of dental caries. (32)

Biochemistry Department

PERRY, Professor S. V.—(1) assistance by Mr. S. C. Bondy, and expenses: nitrogen metabolism of brain; (2) assistance by Miss J. Cotterill, and expenses: biological activity and sub-unit structure of myosin. (33)

KLEMPERER, Dr. H. G.—expenses: enzymes concerned in ribonucleic acid synthesis and their relationship to protein synthesis. (34)

WALKER, Dr. D. G.—assistance by Mrs. S. Rao, and expenses: development and control of enzyme systems within the developing mammalian foetus and newborn animal. (35)

Chemistry Department

STACEY, Professor M.—assistance by Mr. G. A. Powers, Mr. A. B. Clayton and Mr. T. Rimmington, and expenses: preparation of a range of fluorocarbon compounds for test as anaesthetic agents. (36)

BELCHER, Professor R.—expenses: submicro-methods for the analysis of organic compounds. (37)

BARKER, Dr. S. A.—assistance by Mrs. G. I. Pardoe, and expenses: structure and function of mucoproteins in chronic bronchitis. (38)

Department of Medicine

ARNOTT, Professor W. M.—assistance by Dr. Josephine A. Gloster, and expenses: (i) metabolic effects of exercise; (ii) studies of human plasma lipids. (39)

Medical Biochemistry and Pharmacology Department

FRAZER, Professor A. C.—(1) expenses: problems of fat absorption and other metabolic studies; (2) assistance by Mrs. M. Hayward, and expenses: folic acid metabolism; (3) assistance by Mr. K. Burdett: absorption of lipid-soluble materials from small intestine of the rat. (40)

DILS, Dr. R. R. A. and POVER, Dr. W. F. R.—expenses: biosynthesis of fatty acids. (41)

Experimental Neuropharmacology Department

ANSELL, Dr. G. B.—assistance by Miss E. F. Marshall, and expenses: relative importance of different pathways of phospholipid synthesis in the various anatomical areas of the brain. (42)

Experimental Pathology Department

SQUIRE, Professor J. R.—expenses: hypogammaglobulinaemia. (43)

GELL, Professor P. G. H.—(1) assistance by Dr. A. Kelus: immunological and genetic investigation on human and animal globulins; (2) expenses: genetically labelled serum proteins (allotypes). (44)

BLAINEY, Dr. J. D.—assistance by Miss S. M. Betts, and expenses: biochemical studies on cases of mental handicap of unknown aetiology. (45)

CREWS, Mr. S. J.—personal: the vitreous body of the eye. (46)

DYKES, Dr. P. W.—assistance by Dr. B. N. Sharma, and expenses: (i) irradiation of the reticulo-endothelial system; (ii) effects of radiation on regional blood flow. (47)

HARDWICKE, Dr. J.—assistance by Dr. A. R. Boyns, and expenses: physical and biological properties of antigen-antibody complexes. (48)

Paediatrics and Child Health Department

WOLFF, Dr. O. H.—assistance by Miss A. S. Fosbrooke: disturbances of lipid metabolism in childhood. (49)

Pathology Department, Cancer Research Laboratories

WOODHOUSE, Dr. D. L.—expenses: work on behalf of the Committee on the Carcinogenic Action of Mineral Oils. (50)

Physics Department

FREMLIN, Dr. J. H.—assistance by Mr. J. N. Kudahl, and expenses: (i) structure of mature enamel; (ii) fluoride content of the dental plaque. (51)

Physiology Department

HARRIES, Dr. E. H. L.—expenses: relationship between gastric blood flow and secretion. (52)

JENNER, Dr. F. A.—assistance by Mr. J. C. Goodwin, and expenses: diuresis and anti-diuresis in periodic psychotics. (53)

ROWE, Dr. C. E.—expenses: lipid metabolism in brain tissue. (54)

SINGER, Dr. Bertha—assistance by Dr. A. K. Wahid, and expenses: regulation of aldosterone secretion in normal and pathological conditions. (55)

WHITFIELD, Dr. I. C.—assistance by Miss P. E. Stopp, and expenses: neural mechanisms of hearing. (56)

School of Dental Surgery

MACGREGOR, Professor A. B.—expenses: bacteriology of the dental plaque studied by means of the ' artificial mouth ' technique. (57)

Social Study Department

LAFITTE, Professor F.—assistance by Mrs. Barbara J. Gray, and expenses: investigation of domestic accidents to elderly persons. (58)

Bracknell

HEATING AND VENTILATING RESEARCH ASSOCIATION'S LABORATORIES

BILLINGTON, Mr. N. S.—assistance by Mr. L. R. Groves, and expenses: ventilation and air conditioning of hospital operating theatres. (59)

Bradford

INSTITUTE OF TECHNOLOGY

SHAW, Dr. G.—assistance by Mr. M. Franks and Mr. C. P. Green, and expenses: nucleic acid synthesis. (60)

Bristol

COLLEGE OF SCIENCE AND TECHNOLOGY

TAYLOR, Dr. N. F.—expenses: synthesis of potential inhibitors of carbohydrate and nucleic acid metabolism. (61)

ROYAL HOSPITAL

FREUNDLICH, Mr. H. F. and JAMES, Mr. J. A.—assistance by Mr. P. N. T. Wells, and expenses: clinical and physical aspects of ultrasonics for the surgical treatment of Ménière's disease. (62)

TUDWAY, Dr. R. C.—expenses: malignant tumour activity assessed by radiophosphorus uptake. (63)

ROYAL INFIRMARY

CAPPER, Mr. W. M. and BUTLER, Mr. T. J.—assistance by Mr. K. Buckler, and expenses: pH of the mucosa of the stomach. (Also at Frenchay and Southmeads Hospitals.) (64)

Medical Physics and Radiodiagnosis Department

FREUNDLICH, Mr. H. F. and BULLEN, Mr. M. A.—assistance by Mr. P. N. T. Wells, and expenses: use of ultrasonics in medical diagnosis. (65)

Pathology Department

GILLESPIE, Dr. W. A.—assistance by Dr. R. B. Linton: hospital cross-infection. (66)

Bacteriology Department

COOPER, Professor K. E.—assistance by Mr. L. B. Quesnel: early phases of growth of a bacterial inoculum in continuous microculture, and the effect of low concentrations of streptomycin sulphate. (67)

Chemistry Department

HOUGH, Dr. L.—assistance by Dr. J. M. Williams, and expenses: biosynthesis of antibiotic amino sugars. (68)

Pharmacology Department

HELLER, Professor H.—assistance by Dr. B. O. Amure: renal excretion of histamine. (69)

GINSBURG, Dr. M.—assistance by Mr. M. P. Ireland: protein and peptide metabolism in the hypothalamo-neurohypophysial system. (70)

Physiology Department

BROCKLEHURST, Professor R. J.—assistance by Miss M. Luscombe: purification and characterization of the enzyme responsible for the degradation of chondromucoprotein. (71)

HALLETT, Dr. C. P.—expenses: gastrin extraction and animal assay. (72)

WILLIAMS, Dr. T. D.—(1) expenses: the nerve inputs to the globus pallidus and neighbouring structures of the basal ganglia; (2) assistance by Dr. E. M. Sedgewick, and expenses: the role of the sensory nervous system in the physiology of the caudate nucleus. (73)

Psychology Department

HALL, Professor K. R. L.—assistance by Miss M. J. Goswell and Mr. R. C. Boelkins, and expenses: factors affecting avoidance behaviour and fear responses in monkeys. (74)

GARTLAN, Mr. J. S.—expenses: early learning in monkeys. (75)

GRIEW, Dr. S.—assistance by Dr. D. R. Davies, and expenses: vigilance performance and cardiac activity. (76)

Surgery Department

PEACOCK, Mr. J. H.—assistance by Dr. Christine Tyler, and expenses: the role of the catecholamines in the maintenance and production of portal hypertension. (77)

Zoology Department

HINTON, Dr. H. E.—expenses: biology and physiology of the *Simuliidae*. (78)

Bromley

BROMLEY HOSPITAL

TYLDEN, Dr. Elizabeth—personal, and expenses: significance of mental illness in pregnancy and the puerperium. (79)

Cambridge

ADDENBROOKE'S HOSPITAL

WITHYCOMBE, Mr. J. F. R.—assistance by Dr. H. Alice Orgel, and expenses: vesico-ureteric reflux investigated by cystometry and cine-radiology. (80)

A.R.C. INSTITUTE OF ANIMAL PHYSIOLOGY, BABRAHAM

KRNJEVIC, Dr. K.—assistance by Dr. D. W. Straughan, and expenses: neuronal inhibition and distribution of choline acetylase in the cerebral cortex. (81)

STRANGEWAYS RESEARCH LABORATORY

BRIEGER, Dr. E. M.—personal: host-parasite relationship in leprosy. (82)

UNIVERSITY

Student Expeditions (from private funds at the Council's disposal)

BOWEN-SIMPKINS, Mr. P.—expenses: survey of some genetic characters in two Eritrean tribes, the Kunama and the Barya (Cambridge Expedition to Eritrea). (83)

PATTERSON, Dr. M. C.—expenses: distribution of blood groups and secretor gene, and an estimate of the long-term effects of radiation in tribes in India (Cambridge University Expedition to Eastern Ghats and Kerala). (84)

Anatomy School

HORN, Dr. G.—assistance by Mrs. S. H. Traut, and expenses: experimental neurological studies of attention. (85)

HUGHES, Dr. A. F. W.—assistance by Mr. M. Prestige; neuroembryological studies. (86)

SHUTE, Dr. C. C. D. and LEWIS, Dr. P. R.—expenses: histochemical investigation of the central nervous system following lesions involving fibre tracts in the rat. (87)

Sir William Dunn School of Biochemistry

YOUNG, Professor F. G.—(1) assistance by Miss A. F. M. d'Arcy, and expenses: metabolism of orally administered sugars; (2) assistance by Dr. Anne S. Hartree, and expenses: purification of hormones from human pituitary glands. (88)

CHAPPELL, Dr. J. B.—assistance by Mr. A. R. Crofts, and expenses: relationship between the spatial localization of enzymes in isolated mitochondria and their function. (89)

DIXON, Dr. H. B. F.—expenses: chemistry of corticotrophin and the melanophore-stimulating hormone. (90)

IVERSEN, Mr. L. L.—expenses: kinetics of inactivation of unmetabolized catecholamine by intracellular binding mechanisms. (91)

KORNER, Dr. A.—expenses: hormone control of protein biosynthesis. (92)

NEWTON, Mrs. A. A.—expenses: nature of the virus-cell complex. (93)

RANDLE, Dr. P. J.—assistance by Mr. R. M. Denton: control and interactions of glucose and glyceride metabolism in mammalian tissues. (94)

TUBBS, Dr. P. K.—expenses: study at the enzyme level of the inhibition of fatty acid biosynthesis by fatty acids. (95)

Cavendish Laboratory

COSSLETT, Dr. V. E.—assistance by Dr. T. A. Hall: microanalysis of biological material by X-ray spectrometry. (96)

Colloid Science Department

HAYDON, Dr. D. A.—expenses: cell membrane structure and behaviour. (97)

Department of Experimental Medicine

BRUCE, Miss H. M.—personal: reproductive physiology and behaviour. (98)

Department of Medicine

GAIRDNER, Dr. D. M. T.—assistance by Dr. Mary Webb, and expenses: respiratory failure in the newborn. (99)

Pathology Department

COOMBS, Dr. R. R. A.—assistance by Mr. W. E. Parish, and expenses: hypersensitivity to milk in relation to cot death in infants. (100)

FRANKS, Dr. D.—personal and expenses: serological tests for species of origin and antigenic structure of cell strains in culture (in association with the Strangeways Research Laboratory). (101)

WATERSON, Dr. A. P.—expenses: detailed structure of virus particles, especially of the influenza-mumps group (myxoviruses). (102)

Pharmacology Department

BURGEN, Professor A. S. V.—expenses: micro-electrode study of chromaffin cells. (103)

Physiology Laboratory

ADRIAN, Dr. R. H.—expenses: cation movements and their relation to the initiation of contraction in striated muscle. (104)

BRINDLEY, Dr. G. S.—expenses: the functions of the cerebellum. (105)

Psychological Laboratory

ZANGWILL, Professor O. L.—(1) assistance by Dr. B. R. Gomulicki, and expenses: experimental studies of tactual perception; (2) assistance by Mrs. S. Naidoo, and expenses: handedness in children. (106)

GREGORY, Mr. R. L.—(1) assistance by Miss C. Shopland, and expenses: distance perception and its limitation by 'neural noise'; (2) expenses: nerve deafness. (107)

WATSON, Mr. A. J.—assistance by Mr. A. W. Still: factors controlling complex learning in the rat. (108)

WEISKRANTZ, Dr. L.—(1) assistance by Dr. J. Steiner, and expenses: memory and temporal lobe function; (2) assistance by Miss R. Mingay: cerebral mechanisms of memory in the monkey. (109)

Radiotherapeutics Department

MITCHELL, Professor J. S.—(1) expenses: clinical and laboratory studies, using the linear accelerator, on the therapeutic applications of 15-MeV X-rays; (2) assistance by Mr. G. M. W. Cook: surface structure of tissue cells; (3) assistance by Mrs. B. Chipperfield: distribution and possible localization in tumour tissue of tritium-labelled drugs with a view to their possible use as a form of treatment for cancer; (4) expenses: radioactive drugs for selective internal therapeutic irradiation; (5) assistance by Mr. R. A. Pope: measurement of total body radioactivity in health and disease. (110)

SIMON-REUSS, Mrs. I.—personal: the effects of ionizing radiations and chemical agents on malignant cells. (111)

Zoology Department

HINDE, Dr. R. A.—assistance by Miss H. Y. Spencer-Booth, and expenses: primate behaviour. (112)

Cardiff

UNIVERSITY COLLEGE OF SOUTH WALES AND MONMOUTHSHIRE

Anatomy Department

BECK, Dr. F.—assistance by Mr. J. B. Lloyd, and expenses: biochemical and embryological nature of experimental teratogenesis. (113)

Biochemistry Department

DODGSON, Dr. K. S.—assistance by Mr. G. Jones, and expenses: biochemistry of naturally occurring sulphate esters. (114)

DODGSON, Dr. K. S. and LLOYD, Dr. A. G.—assistance by Mr. P. J. Large, and expenses: bacterial degradation of algal heteropolysaccharides and their monomers. (115)

Physiology Institute

STONE, Dr. S. L.—assistance by Mr. V. Zakian: measurement of the effective moment of inertia of the eye, the viscous damping of the eye in its socket and the passive elasticity of the extra-ocular muscles. (116)

WELSH COLLEGE OF ADVANCED TECHNOLOGY

NICHOLLS, Dr. P. J.—assistance by Miss G. R. Lloyd: nature of biologically active material present in cotton dust and its relation to byssinosis. (117)

WELSH NATIONAL SCHOOL OF MEDICINE

Surgical Unit

FORREST, Professor A. P. M.—(1) assistance by Dr. J. W. McIntosh, and expenses: effect of an adrenal inhibitor on gastric secretion in experimental animals and man; (2) assistance by Mr. J. H. Lawrie, and expenses: gastric hypothermia in man and experimental animals. (118)

Coventry

COVENTRY AND WARWICKSHIRE HOSPITAL LABORATORY

RIVERS, Dr. D.—personal, and expenses: relation of X-ray category to content and composition of dust in the lungs and to pathology in simple pneumoconiosis of coal workers. (119)

Dartford

BEXLEY HOSPITAL

BANNISTER, Dr. D.—personal, and expenses: conceptual relationships in schizophrenic patients. (120)

Dumfries

CRICHTON ROYAL HOSPITAL

MCADAM, Dr. W.—assistance by Mr. B. G. Blake: alcoholism in relation to conditioning and conditioned aversion therapy. (121)

Dundee

QUEEN'S COLLEGE, UNIVERSITY OF ST. ANDREWS

Biochemistry Department

DUTTON, Dr. G. J.—assistance by Mr. S. Myles, and expenses: mechanism and significance of extrahepatic glucuronide synthesis. (122)

STANSFIELD, Dr. D. A.—expenses: mode of action of gonadotrophins on the corpus luteum and of the function of ascorbic acid in the corpus luteum. (123)

TIBBS, Dr. J.—(1) expenses: biochemical changes responsible for and accompanying motility in micro-organisms; (2) assistance by Miss J. M. Bennett: biological and structural changes associated with loss of motility and encystment in *Colpoda steinii*. (124)

Pharmacology Department

HUNTER, Professor R. B.—expenses: adrenal inhibitors. (125)

MARSHALL, Dr. P. B.—assistance by Miss J. D. Reid, and expenses: relationship of histidine decarboxylase to other amino-acid decarboxylases. (126)

Physiology Department

HEMINGWAY, Dr. J. T.—expenses: action of ascorbic acid on corticosteroid control of mitosis. (127)

Psychiatry Department

MCGHIE, Dr. A.—assistance by Mr. J. S. Lawson: clinical and experimental study of disturbances of attention and perception in schizophrenia. (128)

Edinburgh

NORTHERN GENERAL HOSPITAL

Rheumatic Diseases Unit

DUTHIE, Dr. J. J. R.—assistance by Miss I. Bett, and expenses: pathogenesis of rheumatoid arthritis. (129)

ROYAL EDINBURGH HOSPITAL

ROBERTSON, Dr. Elizabeth E. and ASHCROFT, Dr. G. W.—assistance by Miss J. W. Dobson: metabolic aspects of mental illness. (130)

ROYAL INFIRMARY

Therapeutics Department

IRVINE, Dr. W. J.—expenses: the cytotoxic factor in thyroid disease. (131)

UNIVERSITY

Student Expedition

HUDSON, Mr. R. C. L.—expenses: expedition to Madagascar (from private funds at the Council's disposal). (132)

Bacteriology Department

CRUICKSHANK, Professor R., and WILKINSON, Dr. J. F.—expenses: (i) chemical and physical fractionation and antigenic analysis of bacterial pathogens; (ii) development and mode of action of antigen adjuvants. (133)

WILKINSON, Dr. J. F.—assistance by Mr. A. L. S. Munro: continuous culture of bacteria. (134)

Biochemistry Department

JOCELYN, Dr. P. C.—expenses: inhibitory effect of vitamin B_{12} on the oxidation of glutathione in human erythrocytes and the role of serum copper on this oxidation. (135)

OTTAWAY, Dr. J. H.—expenses: control of metabolism in muscle. (136)

Child Health Department

INGRAM, Dr. T. T. S.—assistance by Miss A. W. Mason and Miss J. A. Williamson, and expenses: retarded speech development in children. (137)

Department of Medicine

DONALD, Professor K. W.—assistance by Dr. D. C. Flenley: blood gas tensions in respiratory insufficiency, and the use of oxygen as treatment. (138)

DOIG, Dr. A.—assistance by Dr. I. M. L. Donaldson, and expenses: unilateral renal disease. (139)

Institute of Animal Genetics

BEALE, Professor G. H.—assistance by Dr. I. G. Jones and Mrs. M. Mott, and expenses: genetic and biochemical studies of the antigens of *Paramecium.* (140)

BISHOP, Dr. J. O.—expenses: gene-controlled specificity of protein synthesis. (141)

FALCONER, Dr. D. S.—assistance by Dr. J. L. Bloom, and expenses: genetics of susceptibility of mice to induced pulmonary tumours. (142)

Medical Physics Department

GREENING, Dr. J. R.—assistance by Dr. A. F. Bedford, and expenses: an investigation of chemiluminescence. (143)

Pathology Department

MONTGOMERY, Professor G. L.—expenses: coronary arterial disease. (144)

Pharmacology Department

PERRY, Professor W. L. M.—assistance by Dr. D. Eccleston, and expenses: amino-acid and amine metabolism in relation to mental illness. (145)

GINSBORG, Dr. B. L.—expenses: effects on synaptic transmission of the various ganglion-blocking agents. (146)

Psychological Medicine Department

OSWALD, Dr. I.—assistance by Mr. R. Berger, and expenses: studies of sleep and of allied spontaneous and induced alterations of consciousness. (147)

Respiratory Diseases and Tuberculosis Department

CROFTON, Professor J. W.—assistance by Dr. G. Crompton: transmural bronchial pressure. (148)

School of Dental Surgery

BEAGRIE, Mr. G. S.—expenses: periodontal disease in the mouse. (149)

Surgical Science Department

WOODRUFF, Professor M. F. A.—assistance by Dr. M. O. Symes: effect of transplanting homologous immunologically competent cells in animals bearing spontaneous or transplanted tumours. (150)

Therapeutics Department

GIRDWOOD, Professor R. H.—expenses: mucosal changes in intestinal malabsorption. (151)

HARRIS, Dr. E. A.—assistance by Dr. K. B. Slawson: chemical control of respiration. (152)

Zoology Department

WALKER, Dr. P. M. B.—assistance by Dr. T. Okada: microspectrophotometric study of RNA and DNA fractions at different stages of the growth and differentiation of single cells. (153)

WESTERN GENERAL HOSPITAL

Gastro-Intestinal Unit

WHITTERIDGE, Professor F. W., and CARD, Dr. W. I.—assistance by Dr. P. W. C. Harvey, and expenses: the vascular reflexes arising from the alimentary tract in man. (154)

CARD, Dr. W. I.—(1) assistance by Dr. S. K. Lai, and expenses: development of an assay method for gastrin, and the measurement of the gastrin content of human stomachs; (2) assistance by Dr. A. Makhlouf, and expenses: action of gastrin on human gastric secretion. (155)

Pathology Department

MACLEAN, Dr. N.—expenses: chromosomal anomalies in normal and mentally retarded subjects. (156)

Elstree

LISTER INSTITUTE OF PREVENTIVE MEDICINE

STANDFAST, Dr. A. F. B.—assistance by Dr. M. A. Vincent: identification of the two immunizing antigens of *Bordetella pertussis.* (157)

Exeter

UNIVERSITY

Washington Singer Laboratories

SCHOFIELD, Dr. K.—assistance by Mr. J. D. Hardstone: chemical synthesis and biological properties of bi- and tri-cyclic tropolones analogous to colchicine. (158)

Glasgow

ROYAL INFIRMARY

Surgery Department

MACKEY, Professor W. A.—assistance by Dr. A. M. Harper, and expenses: physiology of cerebral blood in relation to metabolism. (159)

ROYAL MENTAL HOSPITAL

FREEMAN, Dr. T.—assistance by Mr. C. E. Gathercole, and expenses: clinical and psychological investigation of psychotic reactions. (160)

UNIVERSITY

Biochemistry Department

LEAF, Dr. G.—assistance by Mr. W. B. McLaren, and expenses: chemical structure of cytochrome *c*. (161)

Genetics Department

RENWICK, Dr. J. H.—assistance by Miss M. M. Izatt, and expenses: arrangement of some of the known gene loci in man into linkage groups, each group consisting of loci on the same chromosome pair. (162)

Department of Medicine

DOUGLAS, Dr. A. S.—assistance by Dr. G. P. McNicol, and expenses: thrombolytic therapy and fibrinolytic states. (163)

Pathology Department

SYMINGTON, Professor T.—assistance by Dr. W. C. Chan, and expenses: densitometric and election microscope appearances of tissue cultures of the adrenal. (164)

Institute of Physiology

DURNIN, Dr. J. V. G. A.—assistance by Miss W. J. McLees, and expenses: investigation of the diets of pre-school children in the Glasgow area. (165)

GILLESPIE, Dr. J. S.—assistance by Dr. S. M. Kirpekar: possible re-incorporation of adrenergic transmitter into postganglionic nerve endings. (166)

Regional Physics Department

LENIHAN, Dr. J. M. A.—assistance by Dr. Hamilton Smith and Mr. G. D. Paxton, and expenses: trace elements in human disease. (167)

Surgery Department

ILLINGWORTH, Professor Sir Charles—assistance by Dr. J. N. Norman: carbon monoxide poisoning. (168)

Wellcome Laboratory Veterinary Hospital

MACKEY, Professor W. A.—assistance by Dr. G. Bell, and expenses: autoregulation of the flow of blood in the skin and renal cortex investigated by methods depending on the rate of clearance of radioactive 'inert' gases. (169)

WESTERN INFIRMARY

Department of Medicine

WAYNE, Professor E. J.—assistance by Dr. R. McGlashan Harden: iodine metabolism in health and disease. (170)

NORDIN, Dr. B. E. C.—assistance by Dr. J. MacGregor: investigation of the solubility of bone salts and extension of techniques employed to the study of the physical chemistry of renal stones. (171)

INDUSTRIAL HEALTH CENTRE

TAYLOR, Lord—expenses: (i) health of higher executives; (ii) mental health in Harlow. (172)

Hull

UNIVERSITY

Biochemistry Department

DAWES, Professor E. A.—assistance by Mr. B. T. Hamlin, and expenses: diauxic growth effect in *Pseudomonas aeruginosa.* (173)

CROSBIE, Dr. G. W.—expenses: pyrimidine biosynthesis investigated by means of radioactive compounds. (174)

Psychology Department

HOWARTH, Dr. C. I.—expenses: temporal characteristics of the visual system. (175)

Ibadan, Western Nigeria

UNIVERSITY COLLEGE

Chemical Pathology Department

EDOZIEN, Dr. J. C.—assistance by Mr. M. E. Obasi, and expenses: biochemical studies in kwashiorkor. (176)

Children's Department

HENDRICKSE, Professor R. G.—expenses: a therapeutic trial of treatment of malarial nephrosis in children. (177)

Physiology Department

GRAYSON, Professor J.—expenses: the use of internal colorimetry in the determination of blood flow in solid organs. (178)

Jamaica

UNIVERSITY OF THE WEST INDIES

HUGHES, Dr. A. F. W.—expenses: experimental embryology of *Eleutherodactylus.* (179)

UNIVERSITY HOSPITAL

RODGERS, Dr. Pamela E. B.—personal, and expenses: electrophoretic studies on Jamaican patients with neuropathy. (180)

Kampala, Uganda

MAKERERE COLLEGE

Pharmacology Department

LOCK, Mr. J. A.—expenses: isolation, characterization and pharmacology of materials from *Bersama Abyssinica* var. *paullinoides.* (181)

Physiology Department

LUCK, Professor C. P.—expenses: development of the lemur eye. (182)

WRIGHT, Dr. P. G.—expenses: peripheral circulation in the monkey. (183)

Keele

UNIVERSITY

Department of Communication

MACKAY, Professor D. M.—(1) assistance by Dr. M. E. Wilson, and expenses: brain lesions in relation to anomalous visual responses (in association with Dr. Eliot Slater, National Hospital for Nervous Diseases, Queen Square, London); (2) assistance by Dr. N. de M. Rudolf, and expenses: mechanisms of motion perception in the human visual and cutaneous nervous systems. (184)

Electronics Department

INGRAM, Professor D. J. E.—assistance by Mr. G. A. Helcké: different haemoglobin derivatives investigated by electron resonance. (185)

Kumi, Uganda

KUMI LEPROSY CENTRE

BROWN, Dr. J. A. Kinnear—personal, and expenses: trial of BCG in leprosy. (186)

Leeds

GENERAL INFIRMARY

Department of Medicine

HALL, Dr. D. A.—assistance by Mrs. J. E. Wilkinson, and expenses: purification and characterization of an activator in elastic tissue for pancreatic lipoprotein lipase. (187)

Thoracic Surgery Department

WOOLER, Mr. G. H.—expenses: (i) combination of hypothermia with extracorporeal circulation for open cardiac surgery; (ii) measurement of coronary blood flow. (188)

Department of Urology

FOX, Mr. M.—personal, and expenses: some basic immunological and cellular problems of homotransplantation. (189)

UNIVERSITY

Bacteriology Department

OAKLEY, Professor C. L.—assistance by Miss A. Mostratos: attempt to type *Clostridium welchii* by diffusion methods. (190)

Biochemistry Department

HAPPOLD, Professor F. C.—assistance by Mr. H. M. Henderson: enzymology of the transamination reaction. (191)

DODD, Professor J. M.—assistance by Dr. Margaret H. I. Dodd, and expenses: (i) comparative studies on goitrogenesis; (ii) bioassay of TSH and thyroid hormones in micro amounts of body fluids and pituitary fractions. (192)

CHATTAWAY, Dr. F. W.—assistance by Mr. J. S. Best, and expenses: mode of inhibition of growth of fungi by certain steroids. (193)

DAGLEY, Dr. S.—assistance by Mrs. A. E. White: effect of antibiotics on bacterial cell constituents. (194)

Department of Medicine

ROSE, Dr. G. A.—assistance by Dr. A. Causton, and expenses: metabolic bone diseases. (195)

Medical Physics Department

SPIERS, Professor F. W.—(1) assistance by Mr. J. C. Duggleby, and expenses: development of a differential high-pressure ionization chamber apparatus for continuous recording of background radiation; (2) assistance by Mr. C. B. Oxby: development of physical techniques for the measurement of stable iodine in biological media. (196)

REED, Mr. G. W.—assistance by Dr. P. J. Atkinson, and expenses: quantitative histology of cortical bone. (197)

Pathology Department

LUMSDEN, Professor C. E.—assistance by Dr. T. E. Blecher, and expenses: immunological studies in experimental allergic encephalitis and in human multiple sclerosis. (198)

Experimental Pathology and Cancer Research Department

GREEN, Professor H. N.—assistance by Dr. M. R. Anderson, and expenses: work on behalf of the Committee on the Carcinogenic Action of Mineral Oils. (199)

LAWS, Dr. J. O.—expenses: action of chemical carcinogens on organ cultures of human foetal lung. (200)

Pharmacology Department

MACKAY, Dr. D.—expenses: mechanism of action of drugs using micro-electrode techniques. (201)

Physiology Department

O'CONNOR, Dr. W. J.—expenses: urinary excretion of sodium, potassium and bicarbonate. (202)

School of Dentistry

WEIDMANN, Dr. S. M.—assistance by Mr. J. R. Auty, and expenses: the mechanism of calcification. (203)

Leicester

UNIVERSITY

Biochemistry Department

KORNBERG, Professor H. L.—assistance by Dr. M. Kelly: metabolism of simple carbon compounds in micro-organisms. (204)

Zoology Department

GUTHRIE, Dr. D. M.—expenses: physiology of regenerating nerve fibres in insects. (205)

Lincoln

ST. GEORGE'S HOSPITAL

Biochemical Laboratory

NATFALIN, Dr. L.—(1) expenses: early post-operative metabolic changes; (2) expenses: changes in amino-aciduria after therapeutic irradiation. (206)

Liverpool

UNIVERSITY

Anatomy Department

BOWSHER, Dr. D. R.—expenses: secondary sensory neurones in primates. (207)

Biochemistry Department

GLOVER, Dr. J.—expenses: metabolism of ubiquinone. (208)

Department of Medicine

COHEN OF BIRKENHEAD, Lord—expenses (from special funds for the purchase of costly apparatus): intracellular metabolic polymorphisms in man. (209)

Obstetrics and Gynaecology and Physiology Departments

TINDALL, Dr. V. R.—assistance by Dr. J. M. Beazley, and expenses: liver function and blood flow at different stages of normal and abnormal pregnancy, and at various stages in the menstrual cycle of non-pregnant women. (210)

Organic Chemistry Department

BATTERSBY, Professor A. L.—assistance by Dr. R. S. Kapil: structure of the alkaloids of *Strychnostoxifera.* (211)

Pharmacology Department

WILSON, Professor A.—assistance by Mr. B. H. Thomas, and expenses: metabolism and excretion of neostigmine. (212)

School of Dental Surgery

HARTLES, Dr. R. L.—expenses: minor cations of teeth and bones. (213)

School of Tropical Medicine

MAEGRAITH, Professor B. G.—(1) assistance by Mr. M. G. N. Angus, and expenses: electron microscopy of liver lesions in experimental malaria; (2) expenses (from special funds for the purchase of costly apparatus): changes in cell structure initiated by the serum factor and by malaria. (214)

KERSHAW, Professor W. E.—assistance by Mr. D. J. Brewster and Mrs. G. Hearnshaw, and expenses: the effect of parasitism on animal intelligence. (215)

WALTON HOSPITAL

Laryngology Department

TUMARKIN, Mr. A.—expenses: speech transmission systems (from Alexander Pigott Wernher Memorial Trust Funds). (216)

BEDFORD COLLEGE

Physiology Department

WIDDAS, Professor W. F.—(1) assistance by Miss J. Howard: hexose permeability; (2) expenses (from special funds for the purchase of costly apparatus): transfer of sugars across placental membrane. (217)

BIRKBECK COLLEGE

Crystallography Laboratory

BERNAL, Professor J. D.—assistance by Mr. A. W. Longley, and expenses: X-ray diffraction studies on turnip yellow mosaic virus and heavy-atom derivatives. (218)

BRITISH GELATINE AND GLUE RESEARCH ASSOCIATION

SUTTON, Dr. D. A.—assistance by Mr. J. J. Harding, and expenses: structure and behaviour of collagen. (219)

CENTRAL MIDDLESEX HOSPITAL

Departments of Cardiology and Thoracic Surgery

BALL, Dr. K. P.—assistance by Dr. D. E. Sharland, and expenses: clinical trial of diet in coronary thrombosis (with Professor J. N. Morris). (220)

BALL, Dr. K. P., and JOULES, Dr. H.—assistance by Dr. M. W. McNicol, and expenses: management of respiratory failure in chest and other diseases. (221)

Gastroenterology Department

JONES, Dr. F. Avery—assistance by Miss B. White: peptic ulceration. (222)

SHINER, Dr. Margot—personal: development of the technique of small intestine biopsy. (223)

CHARING CROSS HOSPITAL MEDICAL SCHOOL

Anatomy Department

GLENISTER, Dr. T. W.—assistance by Miss J. Everett, and expenses: biology of implanting mammalian blastocysts (also at West London Hospital Electron Microscope Unit). (224)

Chemical Pathology Department

SPENCER-PEET, Dr. J.—expenses: relationship between deficiency of glycogen synthetase and the occurrence of hypoglycaemia in man. (225)

Department of Medicine

DE WARDENER, Professor H. E.—assistance by Dr. W. L. Ashton, and expenses: presence of synalbumin antagonism in the relatives of diabetics and others (grant formerly held by Dr. J. Vallance-Owen). (226)

Pharmacology Department

BAKER, Dr. J. B. E.—assistance by Dr. R. G. Penn, and expenses: influence of drugs on the isolated myocardium subjected to varying degrees of asphyxia. (227)

CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY

Chemistry Department

JAMES, Dr. A. M.—assistance by Dr. M. J. Hill, and expenses: ionizable surface groups and their relationship to known antigens in various types of streptococci. (228)

EVERED, Dr. D. F.—assistance by Mr. P. B. Nunn, and expenses: amino acid uptake in various animal tissues. (229)

GUY'S HOSPITAL

WHITTY, Dr. H. P. B.—expenses: observer errors in assessing skin hues. (230)

Anaesthetics Department

HALL, Dr. J. M.—personal: development of non-explosive anaesthetic agents (in collaboration with Dr. T. H. S. Burns). (231)

Student Expedition

RAYNES, Mr. A. E.—expenses (from private funds at the Council's disposal): Guy's Hospital Medical School Physical Anthropological Expedition to the Aeolian Isles, 1963. (232)

Anatomy Department

BROOKES, Dr. M.—expenses: vascularization of bone. (233)

Bacteriology Department

KNOX, Professor R.—expenses: work on steam pressure sterilizers on behalf of the Council's Working Party on Steam Pressure Sterilizers. (234)

GORRILL, Dr. R. H.—assistance by Miss K. M. Suckling: experimental bacillary pyelonephritis. (235)

Biochemistry Department

DAVISON, Dr. A. N.—assistance by Mrs. L. M. Cuzner and Miss E. Graham-Wolfaard, and expenses: lipid and protein metabolism in disseminated sclerosis. (236)

Chemical Pathology Department

THOMPSON, Professor R. H. S.—assistance by Dr. L. Rathbone, and expenses: action of lysolecithin and phospholipase A on the nervous system. (237)

Department of Medicine

ACHESON, Dr. R. M.—assistance by Miss G. B. Fowler, and expenses: effect of environment on human growth. (238)

Experimental Medicine Department

BUTTERFIELD, Professor W. J. H.—assistance by Dr. Winifred L. Stafford, and expenses: tissue respiration in diabetes mellitus. (239)

GRANT, Dr. R. T.—personal, and expenses: anti-insulin serum in the investigation of carbohydrate metabolism and insulin secretion. (240)

Pathology Department

BLAU, Dr. J. N.—personal, and expenses: (i) blood thymus barrier to radioactive-labelled proteins, vital dyes and antigens; (ii) relationship of lymphocytes and germinal centres. (241)

CAVANAGH, Dr. J. B.—assistance by Dr. L. Illis, and expenses: pathological processes leading to peripheral nerve and spinal tract degeneration. (242)

MACDERMOT, Dr. Violet—personal: anatomy and pathology of human intramuscular nerve fibres. (243)

Pharmacology Department

ROBSON, Professor J. M.—assistance by Mr. M. J. Neal, and expenses: analgesic properties of anaesthetic agents. (244)

NISSIM, Dr. J. A.—assistance by Mr. S. L. Hart, and expenses: pharmalogical inhibition and stimulation of intestinal absorption. (245)

Physics Department

ALLSOP, Professor C. B.—assistance by Miss A. E. Bowley: production of low temperatures by semi-conductor thermoelectric methods, with particular reference to their applications to surgery. (246)

Surgery Department

ELLIS, Dr. F. G.—expenses: bladder motility. (247)

HAMMERSMITH HOSPITAL

MORTIMER, Dr. Patricia E.—personal: family study of coeliac disease (also at the Queen Elizabeth Hospital for Children, Hackney). (248)

Physics Department

MALLARD, Dr. J. R.—assistance by Mr. M. J. Myers, and expenses: development of improved quantitative scanning techniques for radioisotope localization. (249)

MORRISON, Dr. R., and MALLARD, Dr. J. R.—expenses: *in vivo* technique for studying hormone dependence of tumour growth. (250)

MORRISON, Dr. R.—expenses: analysis of the results of treatment of malignant disease by the Council's 8-MeV linear accelerator. (251)

THE HOSPITAL FOR SICK CHILDREN

PAMPIGLIONE, Dr. G.—expenses: electroencephalograms of children before and after measles. (252)

Morbid Anatomy Department

BODIAN, Dr. M.—expenses: chromosome studies in neoplastic and other conditions. (253)

Haematology Department

HARDISTY, Dr. R. M.—expenses: blood coagulation. (254)

IMPERIAL CANCER RESEARCH FUND

Division of Experimental Biology

MARRIAN, Dr. G. F.—assistance by Mr. J. N. Wilson: differences in biological properties of avian tumour viruses. (255)

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

Electrical Engineering Department

CHERRY, Professor C.—assistance by Mr. H. Levitt: determination of the parameters of a sound which separate it from several others occurring simultaneously. (256)

Technical Optics Department

WRIGHT, Professor W. D.—assistance by Mr. K. H. Ruddock: relation between colour vision and age. (257)

INSTITUTE OF CANCER RESEARCH

KOLLER, Professor P. C.—assistance by Miss E. Leuchars and Miss V. J. Wallis, and expenses: role of chromosomes in carcinogenesis. (258)

ALEXANDER, Dr. P.—assistance by Mr. C. J. Dean, and expenses: susceptibility of cells to ionizing radiations (also at Botany Department, Imperial College). (259)

KIRBY, Dr. K. S.—assistance by Mr. J. R. B. Hastings: methods of separating DNA and RNA from the same tissue. (260)

ROE, Dr. F. J. C.—assistance by Mrs. G. A. Grant, and expenses: carcinogenicity of combinations of cigarette smoke condensate and air pollutants and related problems, including the effects of thymectomy. (261)

INSTITUTE OF CHILD HEALTH

WILKINSON, Professor A. W.—assistance by Dr. D. A. Toms: metabolic response to the injury of operation on the newborn infant. (262)

TANNER, Dr. J. M.—expenses: steroid excretion and physique in adults and children. (263)

INSTITUTE OF DENTAL SURGERY

Pathology Department

KRAMER, Professor I. R. H.—expenses: behaviour of osteoclasts and other forms of multinucleate giant cells. (264)

INSTITUTE OF DERMATOLOGY

CALNAN, Professor C. D., and SCHILLING, Professor R. S. F.—assistance by Dr. M. L. Newhouse, and expenses: incidence of skin disease in industry, and assessment of causative factors. (265)

MAGNUS, Dr. I. A.—(1) assistance by Dr. Jennifer Lloyd, and expenses: photosensitivity of skin; (2) expenses: phosphate esters in psoriatic skin. (266)

RYAN, Dr. Elizabeth A.—personal, and expenses: degenerative changes in human skin. (267)

SARKANY, Dr. I.—personal, and expenses: effect of griseofulvin on the pathogenesis of dermatophytoses. (268)

SHUSTER, Dr. S.—expenses: factors influencing senile purpura and corticosteroid purpura. (269)

REID, Dr. Lynne M.—expenses: certain aspects of mucus secretion in the bronchial tree. (270)

Biochemistry Department

LONGMUIR, Dr. I. S.—assistance by Mr. M. G. P. McCabe, and expenses: transport of oxygen in the tissues. (271)

INSTITUTE OF LARYNGOLOGY AND OTOLOGY

HINCHCLIFFE, Dr. R.—expenses: (i) clinical investigation of vertigo; (ii) bioelectric potentials in the cochlea of the cat. (272)

INSTITUTE OF NEUROLOGY

CUMINGS, Professor J. N.—expenses: collection of post-mortem material from cases of chronic neurological disease. (273)

GILLIATT, Professor R. W.—assistance by Dr. Pamela M. Fullerton, and expenses: neurological disorders produced experimentally in animals by toxic substances. (274)

MCMENEMEY, Dr. W. H.—(1) assistance by Dr. M. Kidd, and expenses: presenile dementias; (2) assistance by Madame K. Gavrilescu, and expenses: comparison between the protein fractions of the cerebrospinal fluid with those in the blood. (275)

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY

BROWNE, Professor J. C. McClure—assistance by Miss O. L. Abrahams, and expenses: oxytocic lipids in human amniotic fluid. (276)

PINKERTON, Professor J. H. M.—assistance by Dr. Eleanora P. Giorgi: normal and abnormal ovarian function in the human. (277)

BOOTH, Dr. R. T.—expenses: identification of malignant cells by fluorescence microscopy. (278)

HURLEY, Dr. Rosalinde—expenses: pathogenicity of commensal species of the genus *Candida*, their role in infection of the vagina in the human, and certain methods of treatment of vaginal moniliasis. (279)

MACGREGOR, Mr. W. G.—assistance by Dr. W. A. W. Walters: cardiac output in pregnancy. (280)

SANDLER, Dr. M.—(1) assistance by Dr. S. Contractor: investigation of 5-hydroxyindole metabolism in the laboratory animal; (2) expenses: urinary excretion of biologically active amines in pregnancy. (281)

INSTITUTE OF OPHTHALMOLOGY

DUKE-ELDER, Sir Stewart—expenses: analysis of records derived from research clinics. (282)

Physiological Optics Department

WEALE, Dr. R. A.—assistance by Mr. J. Mellerio: connection between accommodation in man and pupillary miosis. (283)

INSTITUTE OF ORTHOPAEDICS

SEDDON, Sir Herbert—expenses: evaluation of treatment of osteogenic sarcoma of the femur and tibia (on behalf of the Council's Working Party on Bone Sarcoma). (284)

INSTITUTE OF PSYCHIATRY

Biochemistry Department

MCILWAIN, Professor H.—assistance by Dr. I. M. Gibson, and expenses: chemical contributions to electrical studies of the mammalian brain. (285)

GAMMACK, Dr. D. B.—assistance by Mr. H. F. Bradford, and expenses: chemical investigation of cerebral constituents. (286)

Experimental Neurology Department

DAWSON, Professor G. D.—(1) assistance by Dr. A. Angel: control of transmission in the sensory pathways through the thalamus; (2) assistance by Dr. O. Holmes: alterations of functional and anatomical organization in the cerebral cortex associated with epileptogenic lesions; (3) expenses: cerebral electrical activity in animals. (287)

Neuropathology Department

BRIERLEY, Dr. J. B.—expenses: (i) histology of human brains after death following open cardiac surgery; (ii) neuropathology of animals subjected to various experimentally induced conditions. (288)

DUCHEN, Dr. L. W.—personal, and expenses: changes in the pituitary gland after pituitary stalk section. (289)

Physiology Department

CAMPBELL, Dr. H. J.—expenses: determination of the extrahypothalamic regions of the central nervous system involved in anterior pituitary responses to emotional stress. (290)

Psychiatry Department

MARLEY, Dr. E.—assistance by Mrs. G. Prout, and expenses: release of sympathins by stimulation of the peripheral and central nervous system and their effect on the central nervous system. (291)

MICHAEL, Dr. R. P.—(1) expenses: action of hormones on the activity of the brain; (2) assistance by Dr. J. Herbert: investigation of the mechanisms underlying the expression of sexual behaviour in the female primate. (292)

Psychology Department

EYSENCK, Professor H. J.—assistance by Mr. O. White, and expenses: structure of mental ability. (293)

GRANGER, Dr. G. W.—expenses: effect of alcohol on human visual thresholds. (294)

SHAPIRO, Dr. M. B.—assistance by Miss I. L. Neufeld and Mrs. B. Fox, and expenses: measurements and investigation of fluctuations in the clinically relevant aspects of depressive illness. (295)

SLATER, Dr. P.—assistance by Mr. I. A. Syed, and expenses: standardization and revalidation of the Sutton Booklet and the Selective Vocabulary Test. (296)

KING'S COLLEGE

Physiology Department

BULLER, Dr. A. J.—(1) expenses: influence of motor innervation on the contractile properties of striated muscle fibres; (2) expenses: functional significance of differences between mammalian fast and slow skeletal muscle. (297)

HILTON, Dr. Gerta—personal, and expenses: role of the motoneurone in the determination of functional properties of skeletal muscle. (298)

Zoology Department

DAWES, Professor B.—assistance by Mr. T. Ghosh: relationships between species and strains of *Entamoeba.* (299)

BARNARD, Dr. E. A.—(1) assistance by Dr. K. Ostrowski, and expenses: isotopic labelling of specific reagents and antibodies as a quantitative cytochemical method; (2) assistance by Dr. S. Shall, and expenses: structure and function of deoxyribonucleoprotein and the roles of particular amino acid groups therein. (300)

KING'S COLLEGE HOSPITAL

Wernher Research Institute on Deafness

CAWTHORNE, Mr. T.—assistance by Dr. T. D. H. Wilson: temporal bone histology and neuro-otology. (301)

KING'S COLLEGE HOSPITAL MEDICAL SCHOOL

Bacteriology Department

PARTRIDGE, Miss B. M.—personal, and expenses: *in vivo* studies of pathogenic fungi. (302)

Chemical Pathology Department

GRAY, Professor C. H.—(1) expenses: metabolism of cortisol; (2) assistance by Miss J. Butler: metabolism of steroids in disease; (3) assistance by Mrs. A. Kulczycka: bile pigment metabolism; (4) assistance by Mr. M. Waterfield, and expenses: biochemical abnormality in acute intermittent porphyria. (303)

SMITH, Dr. M. J. H.—assistance by Mr. W. J. W. Hines, and expenses: effects of salicylate on the incorporation of ^{14}C-labelled substrates into the metabolic intermediates of preparations of animal tissues. (304)

Clinical Pathology Department

DAVIDSON, Professor W. M.—assistance by Miss J. C. Bradley and expenses: nuclear sex and human chromosomal abnormalities and their relation to various developmental abnormalities. (305)

Medical Unit

ANDERSON, Dr. J.—expenses: sodium transport. (306)

Medicine and Diabetic Unit

TAYLOR, Dr. K. W.—personal, and expenses: insulin synthesis and secretion in normal and diabetic human serum. (307)

Pathology Department

KROLL, Dr. Una M.—expenses: aetiology and recurrence rate of cervical erosion and its relationship to carcinoma. (308)

Surgical Unit

MURRAY, Mr. J. G.—(1) assistance by Dr. A. K. Armitage, and expenses: distribution of pharmacologically active substances in the walls of the stomach of man and animals, and their relation to gastric function; (2) assistance by Mr. A. Dean, and expenses: behaviour of the upper gastro-intestinal tract; (3) assistance by Dr. B. P. Whitney, and expenses: stomach emptying after pyloroplasty. (309)

LEWISHAM GENERAL HOSPITAL

STAFFURTH, Dr. J. S.—personal, and expenses: plasma volume and total body water in various conditions. (310)

LISTER INSTITUTE OF PREVENTIVE MEDICINE

MORGAN, Professor W. T. J.—(1) assistance by Dr. J. T. Painter and Mrs. V. Rege, and expenses: chemical basis of blood group specificity in man; (2) assistance by Mr. A. Pusztai, and expenses: structure of the amino-acid-containing moiety in mucopolysaccharides. (311)

CREETH, Dr. J. M.—assistance by Mr. G. C. Knight: physico-chemical studies of blood group substances and their derivatives. (312)

STOCKER, Dr. B. A. D.—assistance by Mr. T. V. Subbaiah: genetics of virulence in *Salmonella*. (313)

WATKINS, Dr. Winifred M.—assistance by Dr. Sheila Gompertz, and expenses: enzymic decomposition of blood group specific substances. (314)

WHELAN, Dr. W. J.—(1) assistance by Mrs. P. M. Taylor, and expenses: action of certain rabbit muscle enzymes and the synthesis of haptens and inhibitors in the dextran–antidextran system; (2) assistance by Dr. Mukhtar Abdullah, and expenses: the glycogen-debranching enzyme system in rabbit muscle. (315)

LONDON HOSPITAL

PENINGTON, Dr. D. G.—personal, and expenses: methods for preparation of erythropoietin and studies of the factors governing its secretion in animals and in man. (316)

Physiology Department

PARKS, Mr. A. G.—assistance by Dr. D. J. Fishlock: *in vitro* study of the physiology and pharmacology of the human colon. (317)

LONDON HOSPITAL MEDICAL COLLEGE

Bacteriology Department

BARWELL, Professor C. F.—assistance by Miss M. J. Davey: antigenic differences between various strains of trachoma virus. (318)

CUMMINS, Dr. C. S.—expenses: cell wall polysaccharide antigens in gram-positive bacteria. (319)

Bernhard Baron Institute of Pathology

WEINBREN, Dr. H. K.—assistance by Dr. A. Taghizadeh: chemical mechanisms in regeneration of the liver. (320)

Dental School

SLACK, Professor G. L.—(1) expenses: bacteriology of dental disease; (2) assistance by Mr. R. A. D. Williams, and expenses: metabolism of oral filamentous organisms. (321)

Dental Pathology Department

MILES, Professor A. E. W.—assistance by Mr. J. C. Elliott, and expenses: ultrastructure of human amelogenesis and early enamel lesions. (322)

HOLLOWAY, Dr. P. J.—assistance by Mr. R. A. D. Williams, and expenses: effects of nutritional factors in the development and maintenance of oral tissues. (323)

Physiology Department

ROBERTS, Dr. K. B.—expenses: studies on human leucocytes. (324)

SPEIRS, Dr. R. L.—expenses: relation between the chemical composition of teeth and resistance to caries. (325)

LONDON SCHOOL OF ECONOMICS AND POLITICAL SCIENCE

Psychology Department

HIMMELWEIT, Dr. Hilde T.—assistance by Mr. D. G. Harper, and expenses: anxieties and tensions in children. (326)

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE

BERTRAM, Professor D. S. and ORMEROD, Dr. W. E.—expenses: toxoplasma infections of humans. (327)

GARNHAM, Professor P. C. C. and SMITH, Dr. C. E. G.—assistance by Mr. I. F. Keymer: collection of material for the evaluation of African mammals as reservoirs of zoonoses. (328)

PLATT, Professor B. S.—assistance by Dr. D. C. Morley, and expenses: statistical analysis of the principal causes of morbidity and mortality among young children in African villages. (329)

Applied Physiology Department

THOMSON, Dr. M. L.—assistance by Mr. F. F. Cinkotai, and expenses: human lung function in the home and in industry. (330)

Bacteriology and Immunology Department

MURRAY, Dr. I. G.—assistance by Miss V. Van Niekerk, and expenses: mycetoma. (331)

Medical Statistics and Epidemiology Department

ARMITAGE, Professor P.—assistance by Miss W. R. Grant, and expenses: statistical analysis of the results of clinical trials with gamma globulin conducted by the Council's Working Party on Hypogammaglobulinaemia. (332)

ROSE, Dr. G. A.—expenses: the use of steroids in the nephrotic syndrome in adults. (333)

Occupational Health Unit

SCHILLING, Professor R. S. F.—assistance by Mr. M. K. B. Molyneux, and expenses: prospective clinical, physiological and environmental survey of cotton mill workers for the study of byssinosis. (334)

MAUDSLEY HOSPITAL

Children's Department

TIZARD, Dr. Barbara—personal, and expenses: personality of epileptic children. (335)

MIDDLESEX HOSPITAL

LOGUE, Mr. V.—assistance by Mrs. D. Asso: mental functions of the human optic thalamus (also at the Maida Vale Hospital for Nervous Diseases). (336)

Academic Unit of Psychiatry

HINTON, Dr. J. M. and MEYER, Dr. V.—assistance by Miss E. A. Withers, and expenses (from private funds at the Council's disposal): clinical tests of the sensorium in psychiatric patients. (337)

MIDDLESEX HOSPITAL MEDICAL SCHOOL

Anatomy Department

BEARN, Dr. J. G.—expenses: (i) foetal endocrinology; (ii) biological activity of DNA. (338)

Barnato Joel Laboratories

ROBERTS, Professor J. E.—(1) assistance by Mr. W. Tampion, and expenses: circulating thyroid hormones; (2) expenses (from special funds for the purchase of costly apparatus): clinical studies, with radioactive isotopes, using autogamma counter. (339)

Courtauld Institute of Biochemistry

ROITT, Dr. I. M.—(1) assistance by Mr. N. R. Ling: biochemical aspects of thyroid autoimmunity; (2) assistance by Dr. A. B. Acton and expenses: hypersensitivity in human autoimmune disease. (340)

Institute of Nuclear Medicine

O'RIORDAN, Dr. J. L. H.—(1) personal: role of glucagon in man; (2) expenses: immunoassay of glucagon. (341)

Psychological Medicine Department

MEYER, Dr. V.—assistance by Mr. J. M. M. Mair: auditory and long-term retention functions in temporal lobectomy cases. (342)

Surgical Studies Department

PATEY, Mr. D. H.—assistance by Mr. J. A. Fleming: tumour cells in the blood. (343)

NATIONAL HOSPITAL FOR NERVOUS DISEASES

Psychology Department

WARRINGTON, Dr. E. K.—assistance by Miss M. James: experimental analysis of perceptual disorders. (344)

NATIONAL INSTITUTE FOR MEDICAL RESEARCH

Biochemistry Division

FREEMAN, Dr. K.—personal: mitochondria. (345)

Physiology and Pharmacology Division

CARMICHAEL, Dr. E. A.—personal: pathways of absorption between the blood, cerebrospinal fluid and brain substance. (346)

Human Physiology Division

BLACK, Dr. S.—personal: mechanisms involved in the inhibition, by direct suggestion under hypnosis, of allergic skin reactions. (347)

NATIONAL PHYSICAL LABORATORY

PRIBAN, Dr. I. P.—personal, assistance by Mr. W. F. Fincham, and expenses: control of breathing using control systems theory and an analogue computer. (348)

NEW END HOSPITAL

SHALOM, Dr. E. S.—personal, and expenses: iodine constituents in the blood and urine. (349)

POSTGRADUATE MEDICAL SCHOOL OF LONDON AND HAMMERSMITH HOSPITAL

Anaesthetics Department

SYKES, Dr. M. K.—expenses: respiratory function after heart, lung and abdominal surgery. (350)

Bacteriology Department

BARBER, Professor Mary—expenses: laboratory and clinical studies of new antibiotics, with special reference to new penicillins. (351)

Cardiovascular Research Group

SHILLINGFORD, Dr. J. P.—expenses: acute myocardial infarction. (352)

Haematology Department

DACIE, Professor J. V.—assistance by Dr. A. J. Grimes: carbohydrate metabolism of erythrocytes in hereditary haemolytic anaemias. (353)

MOLLIN, Dr. D. L.—(1) expenses: metabolism of vitamin B_{12}, studied by a method of microbiological assay with *Euglena gracilis*; (2) assistance by Dr. Eileen B. Harris: refractory sideroblastic anaemias. (354)

Department of Medicine

FRASER, Professor T. Russell—(1) assistance by Miss D. N. Reid, and expenses: establishment of assay procedures for growth hormone in plasma, and their application to problems of clinical endocrinology; (2) expenses: clinical trials of human growth hormone (on behalf of the Council's Clinical Endocrinology Committee); (3) assistance by Miss D. Gooch: assay of growth hormone in serum; (4) assistance by Dr. N. Samaan, and expenses: nature of serum 'atypical' insulin-like activity. (355)

MCMICHAEL, Professor J.—(1) assistance by Mr. D. W. Hill, and expenses: pathology of retinitis in hypertension and diabetes; (2) assistance by Dr. J. B. West, and expenses: lung function in health and disease. (356)

CAMPBELL, Dr. E. J. M.—(1) assistance by Dr. A. S. E. Fowle: changes in body 'CO_2 space'; (2) assistance by Dr. D. C. F. Muir: particle deposition in the lungs. (357)

COPE, Dr. C. L.—expenses: aldosterone metabolism in human disease. (358)

FLETCHER, Dr. C. M.—assistance by Dr. C. M. Tinker, Dr. J. Angel and Mrs. J. R. Diamond, and expenses: preclinical stages of chronic bronchitis. (359)

Medical Physics Department

FOWLER, Professor J. F.—expenses: effect of fractionated irradiation of normal tissue and tumours in animals. (360)

Neurology and Rheumatology Department

BYWATERS, Professor E. G. L. and PALLIS, Dr. C.—assistance by Dr. Elaine M. Allen: neuromuscular complications of rheumatoid arthritis and related diseases. (361)

Chemical Pathology Department

KING, the late Professor E. J.—assistance by Miss W. Trevella: experimental pneumoconiosis. (362)

WOOTTON, Professor I. D. P.—assistance by Miss P. Ross, and expenses: toxic factors in acute renal failure. (363)

MACINTYRE, Dr. I.—assistance by Miss S. Boss: experimental magnesium deficiency in the rat. (364)

Pathology Department

BELCHER, Dr. E. H.—expenses: radioactive tracer studies of the fate of injected and inhaled dust particles in the lung. (Grant previously held by the late Professor E. J. King). (365)

DAVIES, Dr. J. N. P.—expenses: (i) comparative cancer studies; (ii) analysis of histopathological changes in endomyocardial fibrosis and rheumatism in African patients. (366)

Experimental Surgery Department

DEMPSTER, Mr. W. J.—assistance by Mr. M. A. Williams and Mr. H. M. Tyler, and expenses: rejection mechanism of tissues exchanged between two individuals of the same species. (367)

STRUTHERS, Mr. N. W.—expenses: hydrodynamics of the upper urinary tract, and evaluation of a plastic ureteric prosthesis. (368)

PUBLIC HEALTH LABORATORY SERVICE

PUBLIC HEALTH LABORATORY SERVICE BOARD—(1) expenses: co-ordinated studies of the pattern of infection in acute respiratory virus infections; (2) assistance by Miss A. M. Field and Dr. N. S. Galbraith, and expenses: incidence of all types of enteroviruses, including those of poliomyelitis; (3) expenses: neurological sequelae of measles. (369)

Enteric Reference Laboratory

ANDERSON, Dr. E. S.—assistance by Mr. A. H. Rogers, and expenses: constitution of the cell in *Salmonella paratyphi B* and related organisms. (370)

Cross-Infection Reference Laboratory

WILLIAMS, Professor R. E. O. and LIDWELL, Dr. O. M.—assistance by Mr. D. P. Wyon, and expenses: comfort conditions in operating theatres. (371)

Epidemiological Research Laboratory

MCDONALD, Dr. J. C.—assistance by Dr. Catherine Peckham, and expenses: evaluation of gamma globulin in prevention of congenital malformations due to rubella and undefined infections in early pregnancy. (372)

Nutrition Department

YUDKIN, Professor J.—(1) assistance by Dr. M. Tietz, and expenses: interrelationship between dietary phytate, other dietary factors, calcification and intestinal phytase; (2) assistance by Mr. D. S. Millar, and expenses: dietary composition and the efficiency of food utilization. (373)

Physiology Department

KNOX, Professor J. A. C.—expenses (from special funds for the purchase of costly apparatus): provision of automatic scintillation counter for investigations of the Departments of Physiology and Biology. (374)

WHALER, Dr. B. C.—assistance by Mr. D. A. Westwood, and expenses: ionic movements at the nerve endings of normal and botulinum-poisoned nerve-muscle preparations. (375)

ROYAL COLLEGE OF SURGEONS OF ENGLAND

Anaesthesia Department

MUSHIN, Professor W. W.—assistance by Dr. I. R. Verner: interaction of pethidine and myoneural blocking agents in anaesthetized patients. (376)

WOOLMER, Professor R.—assistance by Dr. Fiona Acheson: residual paralysis persisting after the use of muscle relaxants in surgical anaesthesia. (377)

Biochemistry Department

LONG, Dr. C.—assistance by Dr. R. Odavic, and expenses: brain lipids. (378)

Dental Science Department

COHEN, Professor B.—assistance by Mr. C. J. Smith: (i) reaction of bone cells to the presence of secondary carcinomatous deposits; (ii) comparison of the normal processes of keratinization in the mouth epithelium with those observed in cancerous and precancerous lesions. (379)

Pathology Department

CUNNINGHAM, Professor G. J.—assistance by Dr. Lucille Bitensky, and expenses: cytochemical studies on early cell damage, particularly in the liver. (380)

Pharmacology Department

BORN, Professor G. V. R.—(1) assistance by Dr. M. J. Cross, and expenses: biochemical changes occurring in blood platelets and plasma during clotting; (2) assistance by Miss Sonia A. Fitch: blood platelet aggregation. (381)

Physiology Department

GREENFIELD, Mr. B. E.—personal: activity of muscles of mastication in children with normal and abnormal occlusion. (382)

ROYAL EYE HOSPITAL

SORSBY, Professor A.—expenses (from Alexander Pigott Wernher Memorial Trust Funds): variations in the components of refraction during growth. (383)

ROYAL FREE HOSPITAL SCHOOL OF MEDICINE

Anatomy Department

DAVIS, Dr. P. R.—assistance by Dr. J. D. G. Troup, and expenses: effects of material handling methods on respiratory and trunk mechanics. (384)

MACKINNON, Dr. Pamela C. B.—assistance by Dr. Gillian Greenberg: relationship between the suprarenal cortex and palmar sweating and the correlation of the latter with various mental states. (385)

Bacteriology Department

CROWLEY, Dr. Nuala F. T.—assistance by Miss C. M. Notley: role of starch synthesized by *Streptococcus pyogenes* in the pathogenesis of acute rheumatic fever. (386)

Biochemistry Department

WIGGINS, Dr. H. S.—personal, and expenses: absorption of triglyceride in the small intestine. (387)

Department of Medicine

SHERLOCK, Professor Sheila—(1) assistance by Dr. Ellis Samols: carbohydrate metabolism in liver disease; (2) assistance by Dr. A. I. Rae: renal changes in jaundiced patients; (3) assistance by Dr. H. K. Ibbertson: the metabolism of thyroid hormones in liver disease. (388)

BILLING, Dr. Barbara H.—assistance by Miss M. Cartter: bile pigment metabolism in jaundice. (389)

DAWSON, Dr. A. M.—expenses: the effect of bile salts on the esterification of fatty acids by the small gut mucosa. (390)

Haematology Department

PITCHER, Dr. C. S.—expenses: iron metabolism in haemachromatosis. (391)

Medical Physics Department

SIMONS, Dr. H. A. B.—assistance by Dr. Elizabeth M. Davis, and expenses: possible protective action against ionizing radiations of a series of compounds incorporating the thioureido and guanidino structures. (392)

Morbid Anatomy Department

SCOTT, Dr. G. B. D.—expenses: thrombotic sequelae of the generalized Schwartzman reaction. (393)

Pharmacology Department

ZAIMIS, Professor Eleanor J.—assistance by Mr. P. G. Withrington: mode of action of reserpine. (394)

HODGES, Dr. J. R.—assistance by Dr. M. T. Jones: mechanisms controlling the release of adrenocorticotrophic hormone from the adenohypophysis. (395)

Physiology Department

DOWNMAN, Professor C. B. B.—assistance by Dr. B. J. Prout, and expenses: functional topography of the brain stem reticular formation in small mammals. (396)

COLERIDGE, Dr. J. C. G.—assistance by Dr. Hazel M. Coleridge, and expenses: reflexogenic receptors in the pulmonary circulation. (397)

MOORE, Dr. R. E.—assistance by Mr. M. A. Simmonds, and expenses: control of heat production in the newborn. (398)

ROYAL HOLLOWAY COLLEGE

Zoology Department

TWIGG, Dr. G. I.—assistance by Miss C. M. Summers, and expenses: *Leptospira* in rodent populations. (399)

ROYAL MARSDEN HOSPITAL

Clinical Pathology Department

KAY, Dr. H. E. M.—assistance by Dr. J. H. L. Playfair, Dr. P. K. Hopper and Dr. M. E. Peppercorn, and expenses: collection and preservation of foetal tissues. (400)

ST. BARTHOLOMEW'S HOSPITAL MEDICAL COLLEGE

Biochemistry Department

FRANCIS, Dr. G. E.—assistance by Miss E. A. Willman, and expenses: chemistry of natural products of British Guiana of medicinal importance. (401)

Pathology Department

SPECTOR, Professor W. G.—(1) expenses: mechanics of increased capillary permeability; (2) expenses: pathogenesis of experimental renal tubular necrosis. (402)

LEHMANN, Dr. H.—expenses: abnormal haemoglobins. (403)

Pharmacology Department

QUILLIAM, Professor J. P.—assistance by Mr. R. C. Elliot: spinal neuropharmacology. (404)

Physics and Physiology Departments

ROTBLAT, Professor J.—assistance by Mr. B. W. G. Morgan, and expenses: long-term effects of radiation, with particular reference to their relation to age at the time of irradiation. (405)

Physiology Department

DALY, Professor M. de Burgh—(1) expenses: mechanisms underlying the control of the circulation by chemoreceptors; (2) assistance by Mr. R. W. Wilmott: control of heart rate by chemoreceptors in the lungs. (406)

DAVIES, Dr. B. N.—expenses: synthesis and release of *nor*adrenaline at postganglionic nerve endings. (407)

Zoology and Comparative Anatomy Department

LACY, Dr. D.—expenses: mammalian spermatogenesis. (408)

ST. GEORGE'S HOSPITAL

Cardiac Department

LEATHAM, Dr. A. G.—assistance by Dr. V. J. Redding: coronary artery disease. (409)

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL

Bacteriology Department

LAMBERT, Dr. H. P.—expenses: Eaton agent in chronic respiratory disease. (410)

Haematology Department

STAFFORD, Dr. J. L.—assistance by Dr. Margaret B. Howell, and expenses: comparative study of blood coagulation and fibrinolysis in West African and English males (in association with University College, Ibadan). (411)

Department of Medicine

DORNHORST, Professor A. C.—expenses: clinical trial of diet in coronary thrombosis (with Professor J. N. Morris). (412)

Chemical Pathology Department

MARTIN, Professor N. H.—assistance by Mr. J. C. Gregory: significance of organic ions of low molecular weight in the complexing of metals with proteins. (413)

Pathology Department

CRAWFORD, Professor T.—expenses: comparative study of arterial pathology and histochemistry in autopsied patients from London and Glasgow. (414)

ST. MARK'S HOSPITAL

YOUNG, Dr. A. C.—assistance by Dr. J. Halls: (i) radiographic study of the normal physiology and anatomy of the colon; (ii) functional changes in disease. (415)

ST. MARY'S HOSPITAL MEDICAL SCHOOL

Anatomy Department

BREATHNACH, Dr. A. S.—expenses: electron microscopy of human skin. (416)

Bacteriology Department

WILLIAMS, Professor R. E. O.—assistance by Mr. G. Colman, and expenses: classification of non-haemolytic streptococci. (417)

Biology Department

ALLANSON, Dr. Marjorie—personal, and expenses: cytological and histochemical study of the mammalian adenohypophysis (also at Zoology Department, King's College). (418)

Chemical Pathology Department

BARNES, Dr. H. D.—personal, and expenses: porphyrin metabolism. (419)

JAMES, Dr. V. H. T.—assistance by Miss B. C. Hood: adrenocortical secretion in man, with particular reference to the adrenal androgens. (420)

Immunology Department

COHEN, Dr. S.—(1) expenses: mechanism of malarial immunity in Gambian adults; (2) expenses: relationship of gamma globulin to malarial immunity. (421)

Metabolic Unit

WYNN, Dr. V.—assistance by Dr. J. Landon: (i) methods and principles in metabolic medicine; (ii) steroid chemistry, with special reference to androgens. (422)

Pathology and Bacteriology Department

PORTER, Dr. K. A.—expenses: immunological study of X-irradiated animals with marrow transplants. (423)

Pharmacology Department

NASMYTH, Dr. P. A.—assistance by Dr. J. M. Telford, and expenses: relationship of adenosine 3′, 5′-phosphate to the activity of sympathomimetic amines. (424)

Physiology Department

HUGGETT, Professor A. St. G.—expenses: the placental role in foetal nutrition. (425)

CREESE, Dr. R.—(1) expenses: sodium exchange in isolated muscle; (2) expenses; labelled end-plate drugs in muscle. (426)

HOLTON, Dr. Pamela M.—expenses: chemical transmitters at nerve endings. (427)

Surgical Unit

KENYON, Mr. J. R.—expenses: deep hypothermia with exsanguination and total circulatory arrest, and its application to human patients for certain surgical procedures. (428)

Wright-Fleming Institute of Microbiology

MOLLISON, Professor P. L.—expenses: production of anti-globulin reagents. (429)

PORTER, Professor R. R.—(1) assistance by Mr. P. C. Y. Chan: antibodies to horse serum allergens; (2) assistance by Mr. P. J. Piggott: chemical structure of gamma globulin. (430)

ST. THOMAS'S HOSPITAL

Anaesthetics Department

BURNS, Dr. T. H. S.—personal: development of non-explosive anaesthetic agents (in collaboration with Dr. J. M. Hall). (431)

CHURCHILL-DAVIDSON, Dr. H. C.—expenses: neuromuscular transmission in man. (432)

Radiography Department

CHURCHILL-DAVIDSON, Dr. I.—assistance by Dr. C. A. Foster and Dr. D. B. L. Skeggs: use of high-pressure oxygen in the radiotherapy of malignant tumours. (433)

WIERNIK, Dr. G.—personal, and expenses: effect of ionizing radiation in tissues. (434)

ST. THOMAS'S HOSPITAL MEDICAL SCHOOL

Medical Unit

MILLS, Dr. I. H.—expenses: mechanisms controlling the excretion of sodium by the kidney. (435)

Pathology Department

CURRAN, Professor R. C. and HALE, Dr. A. J.—assistance by Dr. V. R. Switsur: development of a scanning X-ray microanalyser for quantitative cytochemistry. (436)

Sherrington School of Physiology

EVANS, Dr. M. H.—expenses: possible sites of action and effects of those animal toxins that affect the nervous system. (437)

UNIVERSITY COLLEGE LONDON

Anatomy and Embryology Departments

YOUNG, Professor J. Z.—assistance by Dr. Eileen M. Evans: synaptic structure in the autonomic nervous system. (438)

Anthropology Department

BARNICOT, Professor N. A.—assistance by Mrs. P. J. A. Travers: the human karyotype in various populations. (439)

Biochemistry Department

BALDWIN, Professor E. H. F.—expenses (from special funds for the purchase of costly apparatus): analysis of peptides. (440)

CLARKE, Mrs. P. H.—(1) assistance by Miss J. A. Waltho: permeability of *Pseudomonas aeruginosa* to organic acids; (2) assistance by Mr. D. S. Turner: structure and mode of synthesis of cell walls of *Pseudomonas* spp. (441)

ELLARD, Mr. G. A.—personal, and expenses: potentially antileprotic diphenylthioureas in laboratory animals and in man and their effects on the metabolism of certain non-pathogenic mycobacteria and on *Mycobacterium leprae*. (442)

KERLY, Dr. L. M.—assistance by Miss J. E. L. Spruyt, and expenses: amino-acid metabolism in the perfused rat liver. (443)

RABIN, Dr. B. R.—assistance by Mr. E. P. Whitehead, and expenses: mechanism of action of dehydrogenase. (444)

Chemistry Department

WASSERMANN, Dr. A.—assistance by Dr. J. Upadhyay, and expenses: molecular size and shape of muscle proteins in dilute solution. (445)

Eugenics, Biometry and Genetics Department

PENROSE, Professor L. S.—assistance by Mrs. J. D. A. Delhanty: chromosomal translocations. (446)

Pharmacology Laboratory

SCHILD, Professor H. O.—assistance by Dr. Barbara Boughton: delayed allergic reactions, with special reference to the role of cell-bound antibodies in autosensitization. (447)

Physiology Department

GRAY, Professor J. A. B.—assistance by Mr. D. R. G. Fuller, and expenses: transmission of information about external stimuli in primary and second-order receptor neurones. (448)

HUXLEY, Professor A. F.—assistance by Dr. B. S. Meldrum and expenses: action of phospholipases on the resting and action potentials of nerve and on muscle neuromuscular transmission. (449)

BANKS, Dr. Barbara E. C.—(1) personal: mode of action of the glutamic aspartic transaminase of pig heart muscle; (2) expenses: purification of γ-aminobutyric acid transaminase from brain, and other enzyme studies. (450)

DAVSON, Dr. H.—assistance by Dr. M. W. Bradbury: mechanism of formation and drainage of the cerebrospinal fluid. (451)

PASCOE, Mr. J. E.—(1) expenses: central control of muscle spindles; (2) assistance by Mr. M. E. Rosenberg, and expenses: relative importance of alpha and gamma activation in muscle reflexes. (452)

SCHACHTER, Dr. M.—assistance by Dr. L. H. Smage: possible physiological significance of kinins and of the enzymes which release them. (453)

WILKIE, Dr. D. R.—assistance by Dr. B. R. Jewell: muscle physiology. (454)

Psychology Department

DREW, Professor G. C.—assistance by Dr. Sheila Jones, and expenses: inductive and deductive thinking. (455)

KEIR, Miss G. H.—expenses: psychological study of the children of school age in the Tristan da Cunha settlement. (456)

Student Health Service Department

LUCAS, Dr. C. J.—assistance by Mr. A. B. Ojha, and expenses: prevalence of mental ill-health in a population of university students. (457)

UNIVERSITY COLLEGE HOSPITAL

Obstetrics Department

GUNTHER, Dr. Mavis—personal, and expenses: development of immune responses to cows' milk in infants during the first weeks of life. (458)

UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL

Bacteriology Department

BELYAVIN, Professor G.—assistance by Dr. S. Roy: antibody response to poliovirus immunization. (459)

Chemical Pathology Department

HEATH, Dr. H.—expenses: metabolism of the retina and other ocular tissues in alloxan-produced diabetes. (460)

REES, Dr. K. R.—assistance by Miss V. L. Shotlander, and expenses: role of permeability changes in cell and mitochondrial membranes in liver injury. (461)

Medical Unit

DENT, Professor C. E.—assistance by Dr. M. Friedman: osteoporosis in young people. (462)

DICKINSON, Dr. C. J.—expenses: (i) renal pulse pressure in relation to the rate of urine secretion; (ii) cerebral vascular resistance in the control of blood pressure. (463)

WESTALL, Mr. R. G.—expenses: inherited diseases which exhibit disorders of amino-acid metabolism. (464)

Morbid Anatomy Department

CAMERON, Sir Roy—assistance by Dr. N. C. Ganguli and Dr. K. K. Bhattacharya, and expenses: investigation into liver disturbances due to schistosomal infection. (465)

SMITH, Dr. J. F.—expenses: rate of reabsorption of protein from the cerebrospinal fluid. (466)

Pharmacology Department

STRANG, Dr. L. B.—assistance by Mr. P. W. Humphreys, and expenses: pathogenesis of hyaline membrane disease. (467)

UNIVERSITY OF LONDON COMPUTER UNIT

BUCKINGHAM, Dr. R. A. and ELITHORN, Dr. A.—assistance by Mr. D. N. Lee: factors which determine failures in problem solving by human subjects. (468)

WESTFIELD COLLEGE

KLYNE, Professor W.—assistance by Mr. J.C. Danilewicz, Mr. C. B. Thornton and Miss C. M. Peach, and expenses: preparation of compounds for the Steroid Reference Collection. (469)

WEST MIDDLESEX HOSPITAL

COGHILL, Dr. N. F.—(1) assistance by Dr. K. N. Jeejeebhoy: (i) protein metabolism in various forms of enteropathy; (ii) fat metabolism in steatorrhoea; (2) assistance by Dr. D. N. Croft: aspirin-induced exfoliation of gastric epithelial cells. (470)

MCALLEN, Dr. P. M.—assistance by Dr. Edda Hanington, and expenses: clinical trial of diet in coronary thrombosis (with Professor J. N. Morris). (471)

WESTMINSTER HOSPITAL

WILKINSON, Dr. J. H.—assistance by Miss W. Withycombe, and expenses: specificity of serum enzyme tests. (472)

WESTMINSTER MEDICAL SCHOOL

ALTMANN, Mr. B.—expenses: serological test for transplantation antibody (also at Royal Veterinary College and Queen Victoria Hospital, East Grinstead). (473)

Chemical Pathology Department

MACLAGAN, Professor N. F.—(1) expenses: origin and absorption of blood phospholipids; (2) assistance by Dr. E. M. Jepson, and expenses: familial hypercholesterolaemic xanthomatosis. (474)

WHITTINGTON HOSPITAL

JOEKES, Dr. A. M.—assistance by Dr. T. Sherwood, and expenses: abnormalities of renal function in man (also at St. Philip's Hospital). (475)

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MELLANBY, Lady—expenses: the structure of teeth. (476)

FAULKNER, Dr. Joan—expenses: investigation into convulsive disorders, for the Committee for Research in General Practice. (477)

MILES, Professor A. A. (Lister Institute of Preventive Medicine), KING, Mr. Ambrose J. (London Hospital) and JEFFERISS, Dr. F. J. G. (St. Mary's Hospital)—assistance and expenses (from funds provided by the United States Public Health Service): aetiology and treatment of non-specific urethritis, on behalf of the Working Party on Non-specific Urethritis. (478)

RYLE, Dr. A.—personal, and expenses: neuroticism and family relationships of 14-year-old children. (479)

CAWLEY, Dr. R. H.—assistance by Mrs. B. Grant, and expenses: clinical trial of anti-depressant drugs, for the Clinical Psychiatry Committee. (480)

Manchester

ROYAL INFIRMARY

Haematology Department

WILKINSON, Dr. J. F.—expenses: purification and assay of animal anti-haemophilic globulin. (481)

Chemistry Department

BARKER, Dr. G. R.—assistance by Dr. M. D. Montague: nucleotide analogues and bacterial growth. (482)

JEVONS, Dr. F. R.—assistance by Mr. J. C. Caygill, and expenses: mode of action of enzymes acting on the carbohydrate moities of mucoproteins. (483)

Clinical Sciences Department

JENNETT, Mr. W. B.—expenses: experimental cerebral compression. (484)

Department of Education of the Deaf

EWING, Sir Alexander—assistance by Miss R. M. Oliver, and expenses (from the Alexander Pigott Wernher Memorial Trust Funds): the problems of parents of deaf children. (485)

Pathology Department

GOWENLOCK, Dr. A. H.—assistance by Miss A. Shaw: determination of vitamin D in serum. (486)

Preventive Dentistry Department

HARDWICK, Professor J. L.—assistance by Miss C. J. Martin, and expenses: fluoride content of the dental plaque. (487)

Psychiatry Department

ANDERSON, Professor E. W.—assistance by Mr. J. L. Stott and Dr. B. A. Lowe, and expenses: psychiatric disorder in an English town. (488)

Social and Preventive Medicine Department

SUSSER, Dr. M. W.—assistance by Mr. D. Y. Downham, and expenses: programming medical and survey data for analysis by Atlas computer. (489)

STEIN, Dr. Zena A.—personal, and expenses: (i) mental illness in Salford and analyses by electronic computer; (ii) school health studies in Leigh (also at the Computing Laboratory and the Salford City Mental Health Department). (490)

Mickley-on-Tyne

CLEMO, Professor G. R.—expenses: chemical constituents of cigarette smoke. (491)

Newcastle upon Tyne

UNIVERSITY

Anatomy Department

SCOTHORNE, Professor R. J.—expenses (from special funds for the purchase of costly apparatus): ultrastructural studies. (492)

GRAY, Dr. J. E.—assistance by Mr. D. A. Ogden, and expenses: sex chromatin studies and chromosome analysis in the newborn and in cases of intersex and infertility. (493)

SNELL, Dr. R. S.—expenses: melanin pigmentation in the skin. (494)

TONGE, Dr. C. H.—(1) expenses: histological studies of the developing tooth and its supporting structures; (2) expenses: examination of the teeth and jaws in undernourished pigs. (495)

Chemistry Department

WEISS, Professor J.—assistance by Mr. A. Appleby, and expenses: mechanism of the chemical action of ionizing radiations on nucleic acids, nucleoproteins and related compounds. (496)

Clinical Chemistry Department

LATNER, Professor A. L.—assistance by Dr. A. W. Skillen, and expenses: studies of iso-enzymes by starch-gel electrophoresis. (497)

Physiology Department

HARPER, Professor A. A.—expenses: hormonal and nervous effect on gastric and pancreatic secretion. (498)

JENKINS, Mr. G. N.—assistance by Mr. D. B. Ferguson, and expenses: the proteins and mucopolysaccharides of the dental plaque. (499)

TAYLOR, Dr. W.—assistance by Mr. L. G. S. Rao, and expenses: *in vitro* and *in vivo* metabolism of progesterone. (500)

KING'S COLLEGE MEDICAL SCHOOL

Surgery Department

SCOTT, Mr. J. E. S.—expenses: the dynamic and histological effects on the ureter of the dog of prolonged vesicoureteral reflux. (501)

WALDER, Dr. D. N.—(1) expenses: decompression sickness, with special reference to bone damage and pulmonary pathology, in Blackwall Tunnel workers; (2) expenses: decompression sickness in Tyne Tunnel workers; (3) expenses: decompression sickness in Clyde Tunnel workers. (On behalf of Decompression Sickness Panel.) (502)

PRINCESS MARY MATERNITY HOSPITAL

Midwifery and Gynaecology Department

RUSSELL, Professor J. K.—assistance by Dr. Patricia A. Toothill, and expenses: Newcastle upon Tyne Maternity Survey. (503)

ROYAL VICTORIA INFIRMARY

Midwifery and Gynaecology Department

FAIRWEATHER, Dr. D. V. I.—expenses: effect of age and parity on the urinary excretion of sex hormones in normal pregnancy. (504)

Newmarket

GENERAL HOSPITAL

WILLIAMS, Dr. I. P.—expenses: relation of the structure of the muscular wall of the colon to the formation of diverticula. (505)

Northampton

PUBLIC HEALTH LABORATORY

HOYLE, Dr. L.—expenses: the physical and chemical structure of the influenza virus. (506)

Nottingham

MAPPERLEY HOSPITAL

MACMILLAN, Dr. D.—assistance by Miss M. R. Phillips and Miss C. E. Davies, and expenses: subsequent history of schizophrenic patients admitted in 1956 to the Mapperley, Netherne and Severalls Hospitals. (507)

UNIVERSITY

Pharmacy Department

EVANS, Dr. W. C.—assistance by Mr. J. C. Woolley, and expenses: formation of the ditigloyl esters of tropine in the roots of various species of *Datura*. (508)

Oxford

CHURCHILL HOSPITAL

OLIVER, Mr. R.—expenses: effect of irradiation by internally deposited radioisotopes on the reproductive integrity of cells. (509)

LITTLEMORE HOSPITAL

WILLIAMS, Dr. Moyra—assistance by Mr. G. Rochford, and expenses: speech disturbances in neurological and psychiatric disorders. (510)

NUFFIELD INSTITUTE FOR MEDICAL RESEARCH

DAWES, Dr. G. S.—expenses: physiology of foetal lung. (511)

Neurology Department

POOLE, Dr. E. W.—expenses: time relationship between EEG phenomena, internal bodily events and external stimuli. (512)

RUSSELL, Dr. W. Ritchie—expenses: war wounds of the brain. (513)

Nuffield Department of Clinical Biochemistry

PEACOCKE, Dr. A. R.—assistance by Dr. J. E. Leveson, and expenses: complexes of non-basic proteins and histones with DNA. (514)

Nuffield Department of Clinical Medicine

ACHESON, Dr. E. D.—(1) expenses: epidemiological study of ulcerative colitis; (2) expenses: multiple sclerosis in immigrants. (515)

TRUELOVE, Dr. S. C.—(1) assistance by Dr. R. Wright: aetiology of ulcerative colitis, with special reference to immunological aspects; (2) assistance by Dr. O. Manousos: motor activity of the bowel, with special reference to diverticulosis coli. (516)

Nuffield Department of Surgery

ALLISON, Professor P. R.—expenses: venous thrombosis and the fate and results of pulmonary emboli. (517)

GUNNING, Mr. A. J.—expenses: the use of homologous aortic valve transplants in the surgical treatment of aortic incompetence. (518)

UNIVERSITY

Student Expeditions (from private funds at the Council's disposal)

EMPEDOCLES, Mr. P. B.—expenses: collection of blood samples, assessment of infant mortality, and anthropometric measurement, University Expedition to Afghanistan, 1963. (519)

HORROBIN, Mr. D. F.—expenses: Oxford University Expedition to Nepal. (520)

Biochemistry Department

WOODS, Professor D. D.—expenses: cellular functions of vitamin B_{12} and folic acid in micro-organisms. (521)

BARTLEY, Dr. W.—assistance by Dr. A. R. Hands: chemical identification of long-chain fatty acids. (522)

STOCKEN, Dr. L. A.—assistance by Mr. A. Beattie: metabolic routes by which DNA precursors are formed. (523)

Dyson Perrins Laboratory

YOUNG, Dr. G. T.—assistance by Dr. R. Purkayastha, and expenses: synthesis of arginine–vasopressin. (524)

Human Anatomy Department

POWELL, Mr. T. P. S. and COWAN, Dr. W. M.—expenses: connections of the nuclei of the thalamus and corpus striatum. (525)

DICK, Dr. D. A. T.—expenses: ion fluxes in single cells. (526)

WEDDELL, Dr. A. G. M.—assistance by Dr. Elizabeth Palmer: structural changes in skin and sensory nerve trunks associated with leprosy and psoriasis. (527)

Institute of Experimental Psychology

OLDFIELD, Professor R. C.—(1) assistance by Mrs. A. M. Treisman, and expenses: processes involved in selective listening to speech messages; (2) assistance by Mr. A. Wingfield, and expenses: language functions, word finding and word comprehension in normal and brain-injured individuals. (528)

ARGYLE, Mr. J. M.—assistance by Mr. P. S. Delin: personality tests in adolescent school children and delinquents. (529)

CROSSMAN, Dr. E. R. F. W.—expenses: analysis of human motor control mechanisms. (530)

Pharmacology Department

PATON, Professor W. D. M.—(1) assistance by Dr. J. A. Parsons: mode of action and individual character of anaesthetics; (2) expenses (from special funds for the purchase of costly apparatus): electron microscopy of neuro-effector systems, subcellular structures, and chemical receptor areas. (531)

BULBRING, Dr. Edith—assistance by Mr. R. N. Speden: electrophysiology of mammalian vascular smooth muscle. (532)

WARDELL, Mr. W. M.—expenses: electrical properties of neuroglial cells, with reference to their possible effects on neuronal function. (533)

Physiology Department

GORDON, Dr. G.—(1) assistance by Dr. M. G. M. Jukes: excitatory and inhibitory influences on cells in primary tactile nuclei in the cat; (2) expenses: functional organization of sensory nuclei. (534)

MATTHEWS, Dr. P. B. C.—assistance by Dr. A. Crowe: responses of muscle spindle receptors to controlled mechanical stimuli. (535)

NOBLE, Dr. D.—expenses: electrical activity of cardiac muscle. (536)

WIDDICOMBE, Dr. J. G.—expenses: central nervous and reflex control of the calibre of the trachea and bronchi. (537)

Sir William Dunn School of Pathology

GOWANS, Professor J. L.—(1) assistance by Mrs. D. Cowen: (i) life history of the mammalian lymphocyte; (ii) immunological activities of lymphocytes; (2) expenses: immunological activities of lymphocytes. (538)

ABRAHAM, Dr. E. P.—(1) assistance by Dr. H. J. Rogers, and expenses: isolation, structure and mode of action of peptide-like substance produced by *B. subtilis*; (2) expenses: biosynthesis and mode of action of microbial products with biological activity. (539)

LEVENE, Dr. C. I.—personal: mechanism of action of lathyrogenic agents. (540)

VAN HEYNINGEN, Dr. W. E.—assistance by Mrs. B. Smith: isolation of a toxin of *Clostridium septicum* and *C. sordellii* and determination of its mode of action. (541)

Social Medicine Department

STEWART, Dr. Alice—(1) assistance by Dr. Winifred Pennybacker: survey of leukaemia in adults; (2) assistance by Dr. Margaret Houghton and Mr. P. S. Spiers, and expenses: malignant diseases in childhood. (542)

Peaslake

WATSON, Dr. G. I.—personal, and expenses: infectious diseases in a rural community. (543)

Penzance

WILLIS, Professor R. A.—personal, and expenses: embryological aspects of pathology and related problems. (544)

Plymouth

TECHNICAL COLLEGE

BONEY, Dr. A. D.—expenses: effects of carcinogens and fluorescent substances on the growth and viability of marine algae (in association with the Plymouth Laboratory of the Marine Biological Association of the United Kingdom). (545)

TONGE, Dr. B. L.—assistance by Mr. G. J. Bonker, and expenses: reaction of tobacco smoke condensate with cysteine and its simple derivatives. (546)

Redcar

HODGKIN, Dr. G. K. H.—expenses: records of age, diagnosis and morbidity in a general practice. (547)

St. Andrews

UNIVERSITY

The Gatty Marine Laboratory

HORRIDGE, Dr. G. A.—assistance by Mr. J. M. Armson, and expenses: effects of neuropharmacologically active substances on selected ganglia of certain invertebrates. (548)

MATTY, Dr. A. J.—(1) expenses: role of thyroid and pituitary hormones in the tissue metabolism of lower vertebrates; (2) assistance by Mr. H. MacAskill, and expenses: effect of hormones on the permeability and transport activity of isolated membranes. (549)

NETHER EDGE HOSPITAL

WEST, Dr. H. F.—assistance by Mr. D. Murphy, and expenses: excretion of corticosteroid hormones in urine and saliva. (550)

ROYAL HOSPITAL

Department of Medicine

COX, Dr. J. R.—personal, and expenses: control of aldosterone secretion. (551)

UNIVERSITY

Biochemistry Department

DALZIEL, Dr. K.—expenses: biological kinetics. (552)

HARRISON, Mrs. P. M.—personal: structure and function of ferritin. (553)

Child Health Department

HOLT, Dr. K. S.—assistance by Miss J. Reynell, and expenses: assessment of treatment in cerebral palsy. (554)

Genetics Department

BLANK, Dr. C. E.—assistance by Mrs. A. M. Bishop and Miss M. Leese: distribution and causes of chromosomal abnormality in man. (555)

Human Biology and Anatomy Department

HARRIS, Dr. P. F.—expenses: isolation and study of cell fractions from bone marrow following irradiation. (556)

Pharmacology and Therapeutics Department

WILSON, Professor G. M. and KNOWELDEN, Professor J.—expenses: pathogenesis of non-toxic goitre. (557)

WILSON, Professor G. M.—expenses (from special funds for the purchase of costly apparatus): (i) pathogenesis of thyrotoxicosis and of non-toxic goitre; (ii) pituitary control of ovarian function. (558)

Physiology Department

SMYTH, Professor D. H.—assistance by Mr. E. M. Wright: intestinal absorption. (559)

Preventive Medicine Department

KNOWELDEN, Professor J.—assistance by Miss L. W. Thomas, and expenses: iodine consumption in goitrous and non-goitrous patients. (560)

Psychology Department

KAY, Professor H.—assistance by Miss H. Oldfield-Box and expenses: discrimination-reversal learning in old and young animals. (561)

MORAY, Dr. N. P.—assistance by Mr. K. J. Connolly and Mr. P. Arnold, and expenses: mechanisms of learning and inheritance of behaviour. (562)

Surgery Department

KAY, Professor A. W.—(1) assistance by Mr. B. Ross, and expenses: duodenal ulceration, gastric blood flow and alimentary bleeding; (2) expenses: gastric hypothermia. (563)

Watford

BUILDING RESEARCH STATION

NE'EMAN, Mr. E.—personal: problems concerned with fluorescent lighting in hospitals. (564)

Wickford

RUNWELL HOSPITAL

Neuropathological Laboratory

CORSELLIS, Dr. J. A. N.—expenses: correlation of the neuropathological with the clinical and EEG findings in epilepsy, with particular reference to the temporal lobes. (565)

Psychology Department

FOULDS, Dr. G. A.—assistance by Miss A. Adams, Mrs. P. Dixon and Mr. K. Hope, and expenses: classification of mental patients. (566)

Research Fellowships and Scholarships

FELLOWSHIPS

ROCKEFELLER TRAVELLING FELLOWSHIPS IN MEDICINE

The Rockefeller Foundation have continued to make generous provision for the award of medical travelling fellowships by the Council. These fellowships are intended for medical or scientific graduates resident in this country who have had some training in research work in clinical medicine, surgery, or medical science, and who would benefit from a year's work at a centre abroad, before taking up higher teaching or research appointments in the United Kingdom.

The following appointments were made by the Council for the academic year 1962–63:

Dr. K. W. Fisher (M.R.C. Microbial Genetics Research Unit, Hammersmith Hospital, London)—to continue investigations in the field of microbial genetics with special reference to the physiology of conjugation in *Escherichia coli K*12, at Princeton University, New Jersey (under the direction of Professor A. B. Pardee).

Dr. T. D. R. Hockaday (Nuffield Foundation for the Advancement of Medicine, Radcliffe Infirmary, Oxford)—to determine the mode of action of the glucocorticoid hormones, and to study pyruvate metabolism in humans with nutritional deficiency (especially alcoholic) and peripheral neuropathy, at the Massuchusetts General Hospital, Boston (Professor W. Bauer and Dr. L. Smith).

Dr. E. R. Huehns (Department of Biochemistry, University College London)—to investigate the possible existence of intermediary iron-carrying proteins in the human red cell, at the Department of Medicine, University of Washington, Seatle (Professor C. A. Finch).

Mr. C. Shaldon (Carey Coombs Research Fellow and Tutor in Surgery, Royal Infirmary, Bristol)—to continue investigations on abnormalities of the neurotransmitter hormones and to investigate in detail the factors which regulate the flow of blood through the splanchnic circulation, with particular regard to the activity of the sympathetic nervous system, at the Mayo Clinic, Rochester, Minnesota (Dr. G. Hallenbeck).

Mr. R. T. Tym (Department of Neurosurgery, Royal Infirmary, Manchester)—to study the production of discrete stereotactic lesions in the diencephalon of animals by heavy-particle bombardment (proton beam) and to study the effects of these lesions on the functions of the nuclei and on induced epileptic discharge, at the Massachusetts General Hospital, Boston (Dr. William Sweet).

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 Rockefeller 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 1962–63:

Dr. C. A. Hopkins (Department of Zoology, University of Glasgow)—to study the procedures used for maintaining *Hymenolepis diminuta* and to attempt to substantiate recent claims that it can be grown *in vitro*, at the Rice Institute, Houston, Texas (Professor Clark Read).

Dr. C. Kidd (Department of Physiology, University of Leeds)—to study the activity from cardiovascular neurones in the brain stem, at the Johns Hopkins University, Baltimore, Maryland (Dr. V. B. Mountcastle).

Dr. M. J. Purves (M.R.C. Department of Experimental Medicine, Cambridge)—to continue studies of the foetal circulation using an extracorporeal perfusion apparatus, and of the effects on the cardiovascular and respiratory systems of bilateral cervical vagotomy in the newborn, at the Cardiovascular Research Institute, San Francisco, California (Dr. J. H. Comroe, jun.).

Dr. D. A. R. Simmons (Department of Bacteriology, University of St. Andrews)—to continue the study of the *Shigella flexneri polysaccharides*, at the Max-Planck Institute for Immunological Research, Freiburg, West Germany.

LEDERLE TRAVELLING FELLOWSHIP IN MEDICINE

The Lederle Laboratories Division of the American Cyanamid Company again placed a travelling fellowship at the Council's disposal, and the following appointment was made for the academic year 1962–63:

Dr. J. H. Briggs (Charing Cross Hospital, London)—to continue investigations into carbohydrate metabolism with particular reference to glycogen deposition in cardiac muscle and the effect it has on function, at the University of California, San Francisco, California (Dr. P. Forsham).

LILLY FOREIGN EDUCATIONAL FELLOWSHIPS

After nomination by the Council the following appointments were made by Eli Lilly and Company, Indianapolis, U.S.A., to Lilly Foreign Educational Fellowships for the academic year 1962–63:

Dr. C. P. Aber (Thoracic Surgical Centre, Broadgreen Hospital, Liverpool)—to investigate the factors responsible for cardio-respiratory failure following pneumonectomy in varying age groups and to study the adaptations and abnormalities of the pulmonary circulation and pulmonary function in pregnancy, at the Cardiovascular Research Institute, San Francisco, California (Dr. J. H. Comroe, jun.).

Dr. G. H. Hall (Bristol Royal Hospitals, Bristol)—to investigate the vasodilator substances in mixed venous blood and their detoxication in the lung, at the Pulmonary Physiology Laboratory, University of Pennsylvania, Philadelphia (Dr. R. E. Forster).

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 completed 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 1962–63:

Dr. A. T. H. Burness (M.R.C. Virus Research Unit, Carshalton, Surrey)—to attempt to relate the nucleotide composition, and subsequently nucleotide sequences, in the nucleic acid to amino acid sequences in the protein of different strains of the same virus, at the Virus Laboratory, University of California, Berkeley, California (Dr. H. Fraenkel-Conrat).

Dr. B. M. Cattanach (M.R.C. Mutagenesis Research Unit, Edinburgh)—to study the effect of oxygen and of respiratory inhibitors on radiation mutagenesis in mice and the effect of chemical mutagens on mice, at the Biology Division, Oak Ridge National Laboratory, Tennessee (Dr. W. L. Russell).

Dr. E. D. Williams (Bernhard Baron Institute, London Hospital)—to study the control of growth of the thyroid gland in the goitrogen-treated rat, at the Massachusetts General Hospital, Boston, Massachusetts (Dr. B. Castleman).

ALEXANDER PIGOTT WERNHER MEMORIAL TRUST
TRAVELLING 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 '. Reference is made elsewhere (pp. 99, 100, 203) to the provision made by the trustees for the support of research in ophthalmology and otology under the Council's auspices at centres in the United Kingdom.

The following appointments were made for the academic year 1962–63:

Mr. H. A. Beagley (Mater Misericordiae Hospital, Auckland, New Zealand)—to employ electro-acoustic and electroneurological techniques and histochemical methods in the investigation of the physiology of the inner ear and its connections, at the Central Institute for the Deaf, St. Louis, Missouri (Professor T. Walsh and Professor C. Smith).

Mr. J. D. Abrams (Middlesex Hospital, London)—to study ultrasonographic techniques as applied to the eye, for a period of six weeks at the Bronx Veterans Hospital, New York (Dr. G. Baum).

This fellowship is provided from an endowment by the late Mr. and Mrs. Eugen M. Schlesinger, in memory of their daughter, and is intended for research in the field of neuropathology. On the advice of the Fellowship Advisory Committee, preference has been given in recent years to candidates preparing to investigate mechanisms underlying degenerative processes affecting the brain.

No award was made for the academic year 1962–63.

MAPOTHER BEQUEST RESEARCH FELLOWSHIP

This fellowship is provided from a benefaction by the late Dr. and Mrs. Edward Mapother for research in psychiatry.

The following appointment was made for the academic year 1962–63:

Miss Barbara C. Stevens—to undertake an investigation concerned with the previous fertility of women who have reached the age of 50 years and who have had a psychotic illness not attributable to physical disease, at the Institute of Pyschiatry, Maudsley Hospital, London (Professor Sir Aubrey Lewis and Professor D. V. Glass).

NATHAN TRUST RESEARCH FELLOWSHIP

In 1960 the Trustees of the Nathan Bequest for Cancer Research generously agreed to make funds available to the Council for the award of a fellowship to a British medical graduate who would undertake an investigation of bone sarcoma. The award is held at present by Mr. D. R. Sweetnam (The Middlesex Hospital) for a study of the prognosis in sarcoma of the lower limb, under the auspices of the Working Party on Bone Sarcoma (Committee on Evaluation of Different Methods of Cancer Therapy).

CLINICAL RESEARCH FELLOWSHIPS

These fellowships 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, and that his training should preferably be given in departments other than his own.

The following appointments were made for the academic year 1962–63:

Fourth Year Fellow

Dr. Doreen M. Nutbourne (St. Thomas's Hospital, London)—to the M.R.C. Department of Experimental Medicine, Cambridge (Professor R. A. McCance).

Third Year Fellow

Dr. M. E. Abrams (Queen Elizabeth Hospital, Birmingham)—to the Department of Experimental Medicine, Guy's Hospital Medical School, London (Professor J. W. H. Butterfield).

Second Year Fellows

Dr. M. G. Gelder (Maudsley Hospital, London)—to the Department of Psychology, Birkbeck College, London (Professor A. Summerfield).

Dr. R. N. Herrington (Department of Psychological Medicine, University of Glasgow)—to the Department of Physiology, University of Aberdeen (Professor J. L. Malcolm).

Dr. J. H. Jones (Metabolic Research Unit, Little Bromwich General Hospital, Birmingham)—to the Department of Experimental Pathology, University of Birmingham (Professor J. R. Squire).

Dr. R. D. Lowe (Medical Unit, University College Hospital Medical School, London)—to the Department of Medicine, St. George's Hospital Medical School, London (Professor A. C. Dornhorst).

Dr. J. K. Luffingham (Orthodontic Department, King's College Hospital, London)—to the Dental Department, Guy's Hospital Medical School, London (Dr. W. J. Tulley).

Dr. J. Wilson (National Hospital for Nervous Diseases, London)—to the Department of Chemical Pathology, Guy's Hospital Medical School, London (Professor R. H. S. Thompson).

First Year Fellows

Dr. J. H. Clark (Fountain Hospital, Tooting Grove, London)—to the Burden Neurological Institute, Bristol (Dr. W. Grey Walter).

Dr. E. P. Langworth (Department of Medicine, University of Leeds)—to the Department of Physiology and Pharmacology, National Institute for Medical Research, London (Dr. V. Abrahams).

Dr. J. M. Matthews (Churchill Hospital, Oxford)—to the M.R.C. Blood Coagulation Research Unit, Oxford (Dr. R. G. Macfarlane).

Dr. I. D. Melville (Royal Infirmary, Glasgow)—to the Department of Clinical Neurology, National Hospital for Nervous Diseases, London (Professor R. W. Gilliatt).

JUNIOR RESEARCH FELLOWSHIPS

During the period under review a new scheme of Junior Research Fellowships was introduced by the Council.

These fellowships are intended primarily for medical graduates who have completed their pre-registration 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 1962–63:

Dr. A. P. Fletcher—to the Department of Chemical Pathology, St. Mary's Hospital Medical School, London (Professor A. Neuberger).

Dr. A. Gorchein—to the Department of Chemical Pathology, St. Mary's Hospital Medical School, London (Professor A. Neuberger).

Dr. R. S. Harris—to the Department of Radiodiagnosis, University of Bristol (Dr. J. H. Middlemiss).

Dr. R. F. Macadam—to the Laboratory of Cytopathology, National Institute for Medical Research, London (Dr. J. S. F. Niven).

Dr. T. R. Overton—to the M.R.C. Environmental Radiation Research Unit, Leeds (Professor F. W. Spiers).

SCHOLARSHIPS

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 undermentioned French Scholars were nominated by the C.N.R.S. for awards to be held in Great Britain during the academic year 1962–63:

Dr. R. S. Saddi (Laboratoire de Recherches de Biochimie Médicale, l'Hôpital des Enfants Malades, Paris)—to the Division of Biochemistry, National Institute for Medical Research, London (Dr. T. S. Work).

Mme. N. B. Glynn (Institut Pasteur, Paris)—to the Wright-Fleming Institute of Microbiology, St. Mary's Hospital Medical School, London (Professor R. R. Porter), the Department of Chemical Pathology, St. George's Hospital Medical School, London (Professor N. H. Martin), and the Chester Beatty Research Institute, London (Professor J. A. V. Butler).

The following Scholar was nominated by the Council for an award to be held in France during the academic year 1962–63:

Dr. J. J. C. St. Laurent (Royal Victoria Hospital, Montreal)—to the Laboratoire de Neurophysiologie Comparée, Faculté des Sciences, Université de Paris (Professor Pierre Buser).

SCHOLARSHIPS FOR TRAINING IN RESEARCH METHODS AND AWARDS FOR FURTHER EDUCATION IN THE MEDICAL SCIENCES

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 are also made to enable graduates with a medical 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.

Ninety-four new scholarships and awards were made for the academic year 1962–63 and the total number of persons under instruction during that academic year was 230. The numbers of awards according to subject studied were: biochemistry, 67; physiology, 31; psychology, 20; pharmacology, 18; microbiology, 15; radiation, 15; psychiatry, 10; biophysics, 8; anatomy, 7; genetics, 5; immunology, 5; zoology, 5; pathology, 4; social and environmental health, 4; cancer, 3; chemistry, 3; dental, 3; internal medicine, 2; tropical, 2; special senses, 1; unclassified, 2.

Scholarships and awards for further education were held at the following centres:

Aberdeen University	6
Bangor: University College of North Wales	2
Belfast: Queen's University	4
Birmingham University	20
Bristol University	4
Cambridge: University	31
Laboratory of Molecular Biology	6
Strangeways Research Laboratory	2
Cardiff: University College of South Wales and Monmouthshire	3
Edinburgh University	9
Glasgow University	9
Leeds University	5
Leicester University	2
Liverpool University	5
London: University	
Bedford College	1
Birkbeck College	3
Chelsea College of Science and Technology	2
Guy's Hospital Medical School	2
Imperial College of Science and Technology	2
King's College	3
Lister Institute of Preventive Medicine	1
London Hospital Medical College	2
London School of Economics and Political Science	2
London School of Hygiene and Tropical Medicine	1
Middlesex Hospital Medical School	2
Royal Free Hospital School of Medicine	2
Royal Holloway College	1
St. Mary's Hospital Medical School	2
School of Pharmacy	5
University College	22
Westfield College	1
British Postgraduate Medical Federation	
Institute of Psychiatry	9
Postgraduate Medical School	1
Microbial Genetics Research Unit	2
National Institute for Medical Research	2
Virus Research Unit	1
Manchester University	2
Nottingham University	4
Oxford University	38
Reading University	1
St. Andrews University: Queen's College, Dundee	2
Sheffield University	4
Southampton University	2

MEMBERS OF THE COUNCIL'S PRINCIPAL COMMITTEES

At date of Report

Non-explosive Anaesthetic Agents

Professor W. D. M. Paton, D.M., F.R.S. (*Chairman*)
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G. S. W. Organe, M.D., D.A., F.F.A.R.C.S.
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Professor G. Stead, D.Sc.
J. D. Robertson, M.D., F.R.C.P.E. (*Secretary*)

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D. Hill, B.Sc.
Professor J. C. McClure Browne, M.B., F.R.C.S.E., F.R.C.O.G.
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W. N. Rollason, M.B., F.F.A.R.C.S. (*Secretary*)

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W. Binks, C.B.E., M.Sc., F.Inst.P. (*Secretary*)

Subcommittees:

Permissible Levels
Radiobiology

Possible Hazards to Human Health from ' Microwave ' Radiations

Professor G. Payling Wright, D.M., F.R.C.P.* (*Chairman*)
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W. J. Bray, M.Sc.
H. F. Cook, Ph.D.
Sir Stewart Duke-Elder, G.C.V.O., M.D., D.Sc., F.R.C.P., F.R.C.S., F.A.C.S., F.R.S.
R. E. Glover, D.Sc., F.R.C.V.S.
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A. E. Hawkins, Ph.D., A.R.C.S.
H. G. Hopkins, Ph.D.
J. E. Lovelock, D.Sc.
Professor Sir John Randall, D.Sc., F.R.S.
R. A. Weale, D.Sc. (*Secretary*)

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Sir Charles Harington, K.B.E., Sc.D., F.R.S. (*Chairman*)
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Professor J. McMichael, M.D., F.R.C.P., F.R.S.
E. E. Pochin, C.B.E., M.D., F.R.C.P.
D. D. Vonberg, B.Sc.
Professor Sir Brian Windeyer, M.B., F.R.C.P., F.R.C.S., D.R.M.E., F.F.R.
R. C. Norton, M.B., D.Obst.R.C.O.G. (*Secretary*)

Evaluation of Different Methods of Cancer Therapy

Professor Sir Brian Windeyer, M.B., F.R.C.P., F.R.C.S., D.M.R.E., F.F.R. (*Chairman*)
Professor H. J. B. Atkins, D.M., F.R.C.S.
Professor Sir Austin Bradford Hill, C.B.E., D.Sc., F.R.S.
Professor R. B. Hunter, M.B.E., M.B., F.R.C.P.E., F.R.C.P.
Professor R. W. Scarff, C.B.E., M.B., R.F.C.S., F.R.S.E.
Professor L. J. Witts, C.B.E., D.M., F.R.C.P.
Margaret Gorrill, B.A., M.B. (*Secretary*)

Working Parties:

Carcinoma of the Bronchus
Leukaemia
Bone Sarcoma
High Tension Oxygen and Radiotherapy

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* Died 4 April 1964.

Aetiology of Lung Cancer

Professor Sir Austin Bradford Hill, C.B.E., D.Sc., F.R.S. (*Chairman*)
J. M. Barnes, C.B.E., M.B.
Professor J. W. S. Blacklock, M.D., F.R.C.P.G.
Sir James Cook, D.Sc., F.R.S.
T. D. Day, M.D.
W. R. S. Doll, O.B.E., M.D., D.Sc., F.R.C.P.
Professor A. Haddow, M.D., D.Sc., F.R.S.
P. Hugh-Jones, M.D., F.R.C.P.
A. J. Lindsey, Ph.D., F.R.I.C.
G. F. Marrian, D.Sc., F.R.I.C., F.R.S.
P. R. Peacock, M.B., F.R.C.P.G.
D. L. Woodhouse, Ph.D., F.R.I.C.
M. P. W. Godfrey, M.B., M.R.C.P. (*Secretary*)

Carcinogenic Action of Mineral Oils

Professor T. Ferguson, C.B.E., M.D., D.Sc., F.R.C.P.E., D.P.H. (*Chairman*)
W. Carruthers, Ph.D. (*also Scientific Secretary*)
Sir James Cook, D.Sc., F.R.I.C., F.R.S.
Professor H. N. Green, M.D., M.Sc.
I. Hieger, D.Sc.
J. O. Irwin, Sc.D., D.Sc.
P. J. King, Ph.D.
Professor F. Morton, D.Sc., F.R.I.C.
Professor R. D. Passey, M.C., M.B., D.P.H
Professor J. R. Squire, M.D., F.R.C.P.
D. L. Woodhouse, Ph.D., F.R.I.C.
P. J. Chapman, M.B. (*Secretary*)

Working Party on Typing of Leukaemia

Professor L. J. Witts, C.B.E., D.M., F.R.C.P. (*Chairman*)
R. Bodley-Scott, D.M., F.R.C.P.
Sheila T. E. Callender, M.D., M.R.C.P.
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Anti-depressant Drugs in General Practice

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Measurement and Composition of Dust
Biological Activity of Dust
Epidemiology
Decompression Sickness

Research on the Toxicity Testing of Drugs

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Joint Medical Research Council/Atomic Energy Authority Co-ordinating Committee for Radiobiological Research

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R. C. Norton, M.B., D.Obst.R.C.O.G. *(Acting Secretary)*

APPENDICES

Headquarters Staff

At date of Report

20, Park Crescent, London, W.1.

SECRETARY

Sir Harold Himsworth, K.C.B., M.D., F.R.C.P., F.R.S.

DEPUTY SECRETARY

C. Y. Carstairs, C.M.G.

PRINCIPAL MEDICAL OFFICERS

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B. S. Lush, M.D., F.R.C.P.

SENIOR MEDICAL OFFICERS

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R. C. Norton, M.A., M.B., D.Obst.R.C.O.G.

MEDICAL OFFICERS

M. J. T. Adams, M.B., D.M.R.T.

H. W. Bunjé, M.D., M.R.C.P.

P. J. Chapman, M.B.

E. M. B. Clements, M.B.

M. P. W. Godfrey, M.B., M.R.C.P.

Margaret Gorrill, B.A., M.B.

B. E. C. Hopwood, M.R.C.S., D.P.H., D.I.H.

Sheila M. Howarth, M.B.

PRINCIPAL ADMINISTRATIVE OFFICER

J. G. Duncan, M.A., LL.B.

ASSISTANT SECRETARIES

C. A. Kirkman, M.A.

J. D. Whittaker, M.B.E.

ADMINISTRATIVE OFFICERS

D. J. Cawthron, M.A.

A. M. Gerrard, O.B.E., M.A. (seconded to M.R.C. Laboratories, Carshalton)

J. C. R. Hudson, M.A.

F. Rushton

R. F. Smart

A. E. Turner

CHIEF EXECUTIVE OFFICER

J. M. Jeffs, A.A.C.C.A.

CONSULTANT ADVISER

Sir Charles Harington, K.B.E., Sc.D., F.R.S.

SPECIAL DUTIES

Sir Landsborough Thomson, C.B., O.B.E., D.Sc. (*part-time*)

F. E. E. Smith, M.B.E.

Accounts of receipts and payments

RECURRENT

1961–62 £	Receipts	£	£
7,477	Balance 1 April 1962		23,427
4,861,950	Parliamentary grant-in-aid		5,501,000
	Contributions from Government Departments		
(263,799)	Ministry of Health	296,493	
(74,527)	Department of Technical Co-operation	105,722	
(30,000)	War Office	35,000	
(19,350)	Admiralty	19,100	
(4,364)	Other departments	11,614	
392,040			467,929
	Contributions from public bodies		
(51,336)	Regional health boards	38,787	
(4,505)	National Coal Board	3,407	
(2,197)	Others	9,747	
58,038			51,941
	Contributions from special grants		
(33,334)	World Health Organization	32,575	
(35,297)	Other grants	77,781	
68,631			110,356
27,826	Contributions from bequests, donations etc.		28,855
95,636	Miscellaneous receipts		88,186
£5,511,598			£6,271,694

NON-RECURRENT

1961–62 £	Receipts	£	£
32,673	Balance 1 April 1962		44,879
710,000	Parliamentary grant-in-aid		358,000
	Repayments for new buildings		
(5,824)	Ministry of Health	68,625	
(9,822)	Colonial Office	—	
15,646			68,625
40,101	Contributions from special grants		29,937
—	Sale of property		3,566
£798,420			£505,007

for the year ended 31 March 1963

EXPENSES ACCOUNT

1961–62 £	*Payments*	£	£
	Administration		
(245,130)	Salaries and wages	248,255	
(123,422)	Other expenses	118,298	
368,552			366,553
	Central expenses		
(10,560)	Pensions, honoraria etc.	23,790	
(44,877)	Other expenses	47,513	
55,437			71,303
	National Institute for Medical Research		
(607,465)	Salaries and wages	694,625	
(197,243)	Other expenses	285,327	
804,708			979,952
	Research units and external scientific staff		
(2,335,795)	Salaries and wages	2,432,138	
(867,953)	Other expenses	1,068,717	
3,203,748			3,500,855
4,432,445	Total direct expenditure		4,918,663
607,006	Temporary research grants and training awards		746,410
40,531	Grants to universities for research groups		55,872
408,189	Special grants to institutions		521,719
5,488,171	Total expenditure		6,242,664
23,427	Balance 31 March 1963		29,030
£5,511,598			£6,271,694

EXPENSES ACCOUNT

1961–62 £	*Payments*	£
713,411	New buildings	417,458
40,130	Grants to university departments for special apparatus ..	82,879
44,879	Balance 31 March 1963	4,670
£798,420		£505,007

APPENDIX III

Major contributions received from government departments and other sources in the year ended 31 March 1963

Source	*Purpose*
Ministry of Health ..	Division of Immunological Products Control, National Institute for Medical Research, for therapeutic testing; Radiological Protection Service (part cost); Blood Group Reference Laboratory; Blood Products Laboratory.
Department of Technical Co-operation	Contributions towards the cost of: M.R.C. Laboratories, Gambia; Tropical Metabolism Research Unit, Jamaica; Trachoma Research Unit, London and the Gambia; Epidemiological Research Unit, Jamaica; Abnormal Haemoglobin Research Unit, and other research in tropical medicine.
Admiralty	Investigations proposed by Council's Royal Naval Personnel Research Committee.
War Office	Investigations proposed by Council's Army Personnel Research Committee.
World Health Organization	International Laboratory for Biological Standards; World Influenza Centre; International Blood Group Reference Laboratory; International Reference Centre for Respiratory Virus Diseases; trial of chemotherapeutic agents against tuberculosis (India); contributions for special investigations at several Council establishments.
Wellcome Trust	Contributions towards the cost of: Laboratory of Molecular Biology; Epidemiological Research Unit, Jamaica; Tropical Metabolism Research Unit, Jamaica; Trachoma Research Unit.
Alexander Pigott Wernher Memorial Trust	Contributions towards the cost of: Wernher Research Unit on Deafness and Wernher Research Unit on Ophthalmological Genetics.

Benefactions

During the period covered in this Report, the Council have gratefully received the following funds from private sources:

	GRANTS	
Rockefeller Foundation, New York	$45,000	Travelling fellowships
	£1,252	Research in X-ray crystallography of proteins
Department of Health Education and Welfare (Public Health Service, National Institutes of Health), U.S.A.	£11,614	Biophysics Research Unit
The Wellcome Trust	£10,000	Travelling fellowships
Association for the Aid of Crippled Children	£4,581	Investigation of effect of institutional life on normal children
	PAYMENTS ON ACCOUNT OF BEQUESTS	
The late Miss D. defreitas West (final payment)	£4,025	General purposes of medical research
The late Mrs. L. E. Taylor	£1,646	
The late C. E. W. V. Reynolds (further payment)	£1,411	
The late Mrs. E. E. L. Clark	£1,100	
The late Mrs. H. E. Norris	£200	
The late Miss E. M. Beer	£500	Research in cancer
The late Miss A. E. Hodkinson	£253	Research in rheumatism
The late Miss I. Riley	£30	Research in poliomyelitis
The late H. L. Wild (further payment)	£15	Research in bronchitis and asthma
The late J. Herring Smith (further payment)	£6	Research in asthma
	DONATIONS	
Knickerbocker Foundation, Inc.	$10,000	Blood Group Research Unit
Amounts under £50		
Anonymous; D. M. Elliott; Mrs. Evelyn Finn, Rickmansworth; Order of Amaranth, Inc., Perth; Mr. S. Tolson, Leeds; Winchester County High School for Girls		General purposes of Medical Research
(*In memory of J. D. Blyth*) Hull, York and East Riding Voluntary Health Contributory Scheme		
(*In memory of Mrs. Mary Geraldine Camm*) "All at Martins", Newick; A. N. Baldwin, Newick; J. P. Barling, Newick; D. C. Beer, Newick; Mrs. G. Byron, Uckfield; M. K. Cannon, Newick; J. M. S. Chamberlain, Newick; Violet Chrestien, Piltdown; Mrs. G. F. J. Cumberledge, Birch Grove; G. E. Davis, Newick; Mrs. F. G. Dimble, North Chailey; Mrs. E. M. Hawkes, Haywards Heath; Mr. and Mrs. W. S. Hick, Lewes; N. B. Jackson, Newick; Mrs. G. Jones, Newick; Canon and Mrs. C. B. H. Knight, North Chailey; Marie Lear, Newick; Sonia Mackay, Chailey; Marjorie E. Mann, Uckfield;		

Mr. and Mrs. J. Manning, Newick; Mr. and Mrs. J. W. R. Meyers, Newick; Lt.-Col. and Mrs. F. H. Moore, Piltdown; Mr. and Mrs. E. M. Neynoe, Newick; Major and Mrs. Peckitt, Lewes; Mrs. I. C. V. Playne, Newick; E. B. Renwick, Haywards Heath; B. E. Russell, Steyning; Mr. and Mrs. Sclater, Newick; Mr. and Mrs. G. E. Sclater and Family, Newick; Mrs. A. W. Sclater, Newick; Mr. and Mrs. J. N. Sharp, Newick; Marjorie Vaughan and Judy, Newick; D. W. and D. J. W. Wilkins, Lewes	
(*In memory of Mr. Collier*) Mrs. F. Collier, Ashbourne	
(*In memory of Dr. J. A. K. Griffiths*) J. L. Griffiths, Ramsey	
(*In memory of Mr. Howarth*) Mrs. E. Howarth, Mr. and Mrs. Cheetham	
(*In memory of Evan Francis Jones*) Relatives and friends	
(*In memory of Mr. Langley*) Mr. John Craig, Thornton Heath	
(*In memory of P. W. Milroy*) Mrs. J. Wookey	
(*In memory of Isobel Taylor*) Major and Mrs. Peckitt, Lewes	
(*In memory of M. R. Parry*) Relatives and friends	Research in cancer
(*In memory of Dr. Ann Gladstow*) British Rorschach Forum	
T. W. Parry, Gloucester; Form 1a, Tiffin Girls' School, Kingston-upon-Thames	
The Crossley and Porter Boys' School Relief Club	Research in common cold
(*In memory of George Twigge*) Mr. J. W. Colwell, Ashbourne; Mrs. C. Twigge, Ashbourne	Research in coronary thrombosis
Over 60's Club, Sheffield	Research in heart and chest disease
Radford Congregational Church Young People's Fellowship; Form 1a, Tiffin Girls' School, Kingston-upon-Thames	Research in kidney disease
Edward Arnold Ltd., further royalties on book by Professor R. F. A. Dean	Research in kwashiorkor
G. J. N. Tait	Research in molecular biology
Townswomen's Guild, Stevenage (further donation)	Research in mongolism (Richard Harrison Memorial Fund)
Mr. E. J. Proctor, London; Mr. J. D. Proctor, Crowthorne; Mrs. C. A. Proctor, London; Miss M. D. Proctor, London; (further donations)	Research in psychiatry
Mrs. A. J. Dods, Tunbridge Wells; (further donation)	Research in rheumatism
Mrs. Phyllis Prior, Upminster	Research in spondylitis
D. W. Turner, Mapperley	Research in virus diseases
(*In memory of C. S. Harrison*) P. J. F. Giffard	For the work of the Department of Clinical Research
Form 5a, King's Warren School, Plumstead; Reigate County School for Girls, Science Sixth; Mrs. R. Vickery, Cuckfield	For the work of the National Institute for Medical Research

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