MEDICAL RESEARCH COUNCIL ANNUAL REPORT

April 1965—March 1966

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The Medical Research Council is the main governmental agency in the United Kingdom for the promotion of medical research. Originally set up in 1913 to administer funds provided for medical research under the terms of the National Insurance Act of 1911, it was incorporated under its present title by Royal Charter in 1920. It is financed mainly by an annual grant-in-aid from Parliament, but it has executive control of its funds and full liberty to pursue an independent policy.

It is the function of the MRC to promote the balanced development of medical and related biological research in this country, and it aims to provide support for new and promising lines of investigation, particularly at the growing points of knowledge. The Council employs its own research staff and also provides grants for other institutions and for individuals who are not members of its own staff, thus complementing the resources of the universities and hospitals. In addition the Council advises Government on matters relating to medical research and co-operates with Government departments and with other organizations in this country and overseas.

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REPORT OF THE MEDICAL RESEARCH COUNCIL 1 APRIL 1965—31 MARCH 1966

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To the Secretary of State for Education and Science

The Medical Research Council submit the following report on their activities during the period from 1 April 1965 to 31 March 1966.

Appended to the report are a series of articles on selected aspects of medical research and summaries of the work of the Council's research establishments and of other projects for which they have provided support. A more complete picture of the Council's research programme may be obtained from the large number of publications in the medical and scientific journals by members of the scientific staff and by the staff of other institutions who have received support from the Council. These are too numerous to list in this report but information about papers published by members of the Council's own staff is available from the Librarian of the National Institute for Medical Research.

RETIREMENT OF LORD SHAWCROSS

On 30 September 1965, with the expiry of his term of office, Lord Shawcross retired from the chairmanship of the Council. During the period of his tenure changes took place in the governmental organization for supporting research that were greater than any that had occurred since the Research Councils were created. As a consequence of the adoption by the Government of the recommendations of the Committee on the Organization of Civil Science under the chairmanship of Sir Burke Trend, important changes took place in the financing of the Research Councils and in their relationship to the central machinery of government. Within the Council's own province of research these raised many special considerations, and the Council will always be indebted to Lord Shawcross for his expert knowledge and the skill with which he guided them in dealing with questions that were of such importance to the future of medical research in this country. At the same time the Council's own work was expanding rapidly. Internal reorganization was essential and under the guidance of Lord Shawcross this was carried through. The Council wish therefore to place on record not only their thanks to him for having presided over their business but also their indebtedness for all the particular contributions that he made to the solution of the many new problems with which they were faced.

CLINICAL RESEARCH CENTRE

Northwick Park Project

The year saw building work begin on the unique project for a combined district hospital and clinical research centre at Northwick Park in north-west London (see plate I). It therefore seems fitting to recall in this report the general aims of this major development and to give a short account of the present plans.

During the period 1957–59 the Council conducted an exhaustive review of the ways in which they were supporting clinical research. This served to emphasize that further progress would depend increasingly on such a degree of collaboration between different disciplines as can be brought about only by a deliberate concentration of clinical and para-clinical workers in one centre. In the non-clinical field the Council's National Institute for Medical Research and a wide range of research units have for long provided scope for the multi-disciplinary approach; on the clinical side, however, while the Council have supported an increasing number of units, there has been no centre comparable to the National Institute.

The Council therefore decided to set up such a centre. Shortly after this decision was announced, it became known that the North West Metropolitan Regional Hospital Board were planning to construct a large new hospital, mainly to meet the needs of the then Boroughs of Harrow and Wembley. For this a large, conveniently placed site at Northwick Park was reserved. Out of this coincidence a happy partnership between the Council and the Regional Hospital Board came into being and, with the close cooperation of the Ministry of Health, planning began in 1961 on the basis of an entirely new idea—the complete integration of clinical and research facilities in one complex of buildings.

There are obvious advantages in combining a research centre and a hospital. In particular, the hospital patients will benefit from the latest advances in medical science and from the special facilities for diagnosis and treatment available in the research centre. The research workers for their part will be in direct contact with everyday clinical problems, from which they can draw inspiration and ideas for their own research.

A brief description of the facilities to be included in the centre follows, but mention must first be made of the outstanding debt owed to one man—the late Professor John Squire, the Centre's first Director-designate, who was intimately concerned with both the general and the detailed planning. His sudden death on 6 January 1966 was a grievous blow, but he had brought the scheme into being and under the leadership of his successors it is assured of coming to fruition. Fuller tribute is paid to Professor Squire on page 28.

The Research Centre

The main research centre buildings will consist of a research institute, library, lecture hall and accommodation for patients. The research institute, with a floor area of approximately 100 000 square feet, will contain most of the centre's laboratory accommodation. Like the rest of the building complex, the laboratories have been specially designed to be as adaptable as possible so that the function of the rooms can be altered relatively easily to meet the constantly changing needs of research. The institute, which will also include accommodation for central services such as workshops and stores, is mainly intended to provide laboratory space for research teams working in association with colleagues engaged directly in the study of clinical problems. Close to the research institute an animal house will be built, where the laboratory animals essential for various types of medical research will be cared for under veterinary supervision.

One wing of the hospital ward block has been designed specifically for the needs of clinical research and will contain 140 beds, other clinical research

facilities being integrated with particular hospital departments, such as those of obstetrics and psychiatry. Accommodation for patients is mainly in two- and four-bed rooms, with clinical research laboratories nearby. In these laboratories detailed assessment of patients can be undertaken, special facilities being provided for metabolic studies.

The library, which will house a large collection of medical and scientific books and journals, will be open to local doctors as well as to the hospital and research centre staff. A lecture hall, with seating for 500 people, will be used for formal and informal lectures and discussions between staff and local doctors, meetings of medical societies and, perhaps, international conferences. An additional small lecture theatre is also to be provided, where clinical lectures and demonstrations will be held.

The guiding principle of the scheme is that the interest of the patient should be paramount at all times and the Council and the hospital authorities will cooperate to the full to ensure that this is so. It is hoped that the first patients will be admitted in 1970, when building of the first stage of the project will be complete.

Director-designate and Deputy Director-designate

After the death of Professor John Squire the Council appointed Professor G. M. Bull as Director-designate of the centre and Dr Richard Doll FRS as Deputy Director-designate.

Professor Bull qualified at the University of Cape Town in 1939, coming to this country in 1947 to work at the Postgraduate Medical School of London; in 1952 he was elected to the Chair of Medicine at Queen's University, Belfast. Since 1962 he has been a member of the Medical Research Council; he is also a member of the Clinical and Tropical Medicine Research Boards. Professor Bull's research interests cover a wide field, but he is particularly interested in renal and tropical diseases and in the study of body water and electrolyte balance.

Dr Doll has been a member of the Council's staff since 1946 and from 1948 has worked in their Statistical Research Unit, being appointed its Deputy Director in 1959 and Director in 1961. Dr Doll's main research interests are the aetiology of cancers—particularly lung cancer and leukaemia—and the treatment of peptic ulcer. In 1964 he was awarded a United Nations prize for his contribution to cancer research and this year he was elected to the Fellowship of the Royal Society.

REVIEWS OF THE COUNCIL'S FIELD OF RESPONSIBILITY

The Council set aside one full meeting a year for a general review of the scale of effort in their own research establishments and by their external scientific staff, and also of the support given by way of research groups, block grants to other institutions and short-term grants. It is their custom also to consider at the 'noon session' of their monthly meetings a particular aspect of medical or biological research or of research policy or administration on the basis of a talk by an outside speaker; the three Research Boards do the same.

In addition, progress reports from Council units, groups and members of the external scientific staff are considered at approximately three-year intervals by the Council and by one or other of the Research Boards, and there is a regular

programme of visits to see work in progress. In the case of the National Institute for Medical Research, the Director's report and the Council's visit are made annually.

NOON SESSIONS

During 1965–66 the fields reviewed were as follows:

Council

1965		
April:	Perspectives in psychiatric research	Professor Denis Hill (*Department of Psychiatry, Middlesex Hospital Medical School*)
November:	Industrial health research	Dr T. A. Lloyd-Davies (*Senior Medical Inspector, Medical Branch, Ministry of Labour*)
1966		
January:	The work of the Council for Scientific Policy	Sir Harrie Massey (*Chairman, Council for Scientific Policy*)
February:	Safety of drugs	Sir Derrick Dunlop (*Chairman, Committee on the Safety of Drugs*)
March:	The Universities and the Research Councils	Sir John Wolfenden (*Chairman, University Grants Committee*)

Clinical Research Board

1965		
April:	Neuropsychiatric Research Unit	Dr D. Richter (*Director*)
October:	Dental Research Unit	Professor A. I. Darling (*Honorary Director*)
November:	Unit for the Study of Environmental Factors in Mental and Physical Illness	Dr J. W. B. Douglas (*Director*)
1966		
January:	Clinical Immunology Research Group	Dr J. Pepys (*Director*)
February:	Applications of engineering to clinical problems	Mr H. S. Wolff (*National Institute for Medical Research*)
March:	Epidemiological Research Unit (South Wales)	Professor A. L. Cochrane (*Honorary Director*)

Biological Research Board

1965		
April:	The large radiation machines in the Cyclotron Unit	Mr D. D. Vonberg (*Director*)
May:	Mutagenesis research	Dr Charlotte Auerbach, FRS (*Honorary Director, Mutagenesis Research Unit*)
June:	Research on accidents	Dr J. P. Bull (*Director, Industrial Injuries and Burns Research Unit*)
July:	Vision Research Unit	Dr H. J. A. Dartnall (*Director*)
1966		
January:	Clinical Effects of Radiation Research Unit	Dr W. M. Court Brown (*Director*)
February:	Some molecular controls in biology	Dr M. F. Perutz, FRS (*Chairman, Laboratory of Molecular Biology*)
March:	Platelets and thrombosis	Professor G. V. R. Born, FRS (*Director, Research Group on Thrombosis*)

1965		
July:	Tropical medicine research as seen by a visiting worker	Professor G. M. Bull (*Department of Medicine, Queen's University of Belfast*)
September:	Virus research in the tropics	Dr C. E. Gordon Smith (*Microbiological Research Establishment, Porton*)
December:	Anaemia in the tropics	Professor A. W. Woodruff (*London School of Hygiene and Tropical Medicine*)
1966		
March:	Anaemia in the tropics: pathogenesis of tropical megaloblastic anaemia and its relation to tropical sprue	Dr D. L. Mollin (*Postgraduate Medical School of London*)

COUNCIL VISITS

In the course of their programme of visits to Council establishments during 1965–66 the Council saw work in progress at:

Bristol	Dental Research Unit Research Group in Neurosecretion
Chichester	Clinical Psychiatry Research Unit
Liverpool	Occupational Aspects of Ageing Research Unit
London	National Institute for Medical Research Human Nutrition Research Unit Gastroenterology Research Unit Human Biochemical Genetics Research Unit Department of Clinical Research Experimental Haematology Research Unit Statistical Research Unit Social Medicine Research Unit Research Group on Respiration and Energy Metabolism in the Newborn

RECENT WORK IN COUNCIL UNITS

It has been decided to continue the practice introduced last year of including in the report brief accounts of work being carried out in certain of the Council's research establishments—those that have reported during the year to the Council or to one of the Research Boards.

Laboratory of Molecular Biology (Chairman of Board: Dr M. F. Perutz FRS)

Many of the basic discoveries made by members of the Laboratory have thrown light on the structure and replication of nucleic acids (which form the genetic material of cells and most of the apparatus for translating the genetic message into protein structure) and on the general nature of the genetic message. Other discoveries have been concerned with the structure and function of proteins.

New methods of determining the sequence of nucleotides in fairly long nucleic acid chains are being developed in the Laboratory and are being applied to the study of transfer RNA; it is this that ' reads ' the genetic message transmitted from the DNA in the cell nucleus and inserts the amino acids in the correct positions along the protein chain.

Now that most of the genetic code is known, the emphasis of molecular genetics has shifted to the factors that control the activity of genes and the

synthesis or activity of specific proteins. Once the mechanism of starting and stopping protein synthesis is known, the signals that control the operation of the genes may be easier to find. Great interest has therefore been aroused by the discovery of a possible biochemical mechanism for initiation of the synthesis of a protein chain and by the finding that certain ' code words ' among the triplets of nucleotides bring synthesis to a halt. Surprisingly, one of the code words for the ' full stop ' is ' misunderstood ' by certain mutant bacteria, which take it to mean the continuation of synthesis instead.

On the physical side a great part of the Laboratory's effort goes into the improvement of methods for the X-ray study of muscle, viruses and crystalline proteins. This includes the development of better X-ray tubes and cameras, rapid automatic methods of recording X-ray diffraction patterns and computer programs for processing them. In the study of muscle, the technical advances have been so great that it is now possible to take X-ray diffraction photographs during a series of active contractions. Earlier work had shown that the contraction of muscle is brought about by the relative movement of two kinds of filaments—myosin and actin. In resting muscle a set of regularly arranged protein cross-bridges can be seen protruding from the myosin filaments. The new X-ray photographs suggest that in actively contracting muscle the cross-bridges move or oscillate like ratchets, attaching themselves to the actin filaments and displacing them lengthways so that they slide past the myosin filaments.

Mutagenesis Research Unit (Honorary Director: Dr Charlotte Auerbach FRS)

Mutation is a process by which a cell and its descendants acquire a new hereditary property, for example loss of an enzyme or resistance to an antibiotic. Experimentally, this process can be started by external agents such as X-rays or alkylating agents. In this Unit mutation is studied in a variety of organisms, from bacteria to mice, the choice of organism being determined by the nature of the individual problem. The first and indispensable step in mutagenesis is a chemical change in DNA, the genetic material in the cell nucleus. This step is being studied in many laboratories. It is, however, often forgotten that mutation is a *biological* process, modifiable by cellular and environmental conditions and, in turn, modifying the metabolic pattern of the cell. The main interest of this Unit is directed towards an analysis of the secondary steps that take place between the change in DNA and the emergence of a mutant clone of cells or a mutant organism. This approach should not only lead to a better understanding of the conditions of mutagenesis but also be of value for the solution of practical problems, such as cancer therapy or the production, by mutation, of new strains of microorganisms or agricultural plants with desirable properties.

In the field of cancer therapy, evidence has been obtained that the great superiority of polyfunctional over monofunctional alkylating agents may be due to the fact that in chromosomes treated with the former, but not with the latter type of agent, large numbers of breaks continue to occur for many days after cessation of treatment.

For ' mutation breeding ' it would be highly desirable if conditions could be found which preferentially increase the frequencies of certain types of mutation. It may be possible to achieve this in a certain measure by manipulating the secondary steps in the mutation process. The Unit has obtained evidence supporting this idea. It has been found that the type of mutation produced in

fission yeast depends on the medium on which the mutagenically treated cells are plated, and that in the mould *Neurospora* the relative proportions of two types of mutation induced by ultraviolet radiation can be changed drastically by certain types of treatment before or after the irradiation.

Other lines of the Unit's work concern (*a*) analysis of the delayed mutations which occur in cells that have not themselves been chemically treated but are descended from treated cells; (*b*) tests of the possibility that food sterilized by heavy X-ray doses may be mutagenic; and (*c*) the use of mice for testing the effects of certain widely used chemicals, such as caffeine and nicotine, on mammalian chromosomes.

Clinical Effects of Radiation Research Unit (Director: Dr W. M. Court Brown)
The central theme of this Unit's research is the study of radiation-induced tumours in man. In earlier years the Unit's main line of investigation consisted of surveys of groups of irradiated human beings, particularly men treated with X-rays for ankylosing spondylitis. With the growing realization that there are limits to the information that can be obtained by epidemiological methods on the nature of the mechanisms of tumour induction, other techniques have been adopted to widen the scope of the inquiry.

Since 1958 the Unit has played a leading role in the development of human cytogenetics and has investigated the chromosome constitution of cancer cells—especially from leukaemia patients—and chromosome aberrations in people who have been irradiated. A considerable amount of work has also been done on the nature, frequency and effects of sex chromosome and autosome aberrations in general; these include abnormalities both of the number and of the structure of chromosomes. The study of these abnormalities opens up new approaches to the investigation of congenital malformations, mental subnormality, subfertility and possibly some aspects of behaviour. For example, a striking recent observation has been the finding of two Y chromosomes in about 1 in 25 of the patients in an institution for men with dangerous, violent or criminal propensities (and in about 1 in 3 of those of the patients who were over 6 ft tall). This frequency is very significantly greater than that of XYY males in the newborn population or in the ordinary population of adult males. Another aspect of the cytogenetic studies has been the discovery that lymphocytes carrying unstable radiation-produced chromosome aberrations can give information about the length of time that lymphocytes survive in man. The evidence suggesting that they may survive for many years—much longer than had been thought possible—has important implications for understanding of the mechanism of the immune process.

Another current interest of the Unit is the use of computer-aided pattern recognition for the automation of chromosome counting and analysis. It is quite clear that the future development of cytogenetics depends on the possibility of counting and analysing very large numbers of cells, whether for the examination of large numbers of the population or for the study of the effects of either low doses of radiation or suspected chemical mutagens.

Recently the Unit has extended its activities into the field of experimental virology. This development stems from a renewal of interest in the hypothesis that cancer in man may have a viral aetiology; support for the hypothesis comes from the strong evidence for the existence of cancer viruses in animals and also from many observations linking virus action and chromosome damage.

Cyclotron Unit (Director: Mr D. D. Vonberg)

The Unit provides special radioisotopes and radiation beams for medical research and carries out research projects on their applications, often in collaboration with medical teams at Hammersmith Hospital and elsewhere.

The radioisotopes are all produced with the cyclotron, which is the only machine of its kind sited in a hospital and devoted entirely to medical work. Isotopes from a cyclotron are generally different in physical characteristics from those usually available from a nuclear reactor and may be preferred to the reactor product for certain applications, for example where a short half-life is important.

Comparison of the efficacy of different isotopes for the detection of brain tumours presents a complex problem requiring, among other things, knowledge of the relative concentrations of isotope in the brain and in the tumour, and of the efficiency of the detecting system. A method has now been devised (using animal experiments and mathematical analysis) for estimating an overall ' figure of merit ' for different isotopes and detectors. From this work it has become clear that no isotope or labelled compound so far examined has the best possible combination of characteristics for the detection of brain tumours. The search for the ideal substance continues.

Radioisotopes from the cyclotron have also been used in studies of the respiratory and circulatory systems. Here an analogue computer is proving to be a powerful tool for interpreting the data and guiding the design of experiments.

Radiation from the cyclotron is emitted as beams of fast neutrons, deuterons or alpha particles. Workers within the Unit and from several other laboratories use these beams, and also the X-rays and electrons from the linear accelerator, for radiobiological studies. The fast neutron beam from the cyclotron has been specially developed for an examination of the value of fast neutrons for radiotherapy. There is evidence that fast neutrons should be more effective than are X-rays in destroying the anoxic cells that many tumours contain. On the other hand, in the course of a preliminary series of tests on the skin of pigs, it has been found that when the radiation dose is administered in small fractions over a period of time, there is less recovery between doses from the radiation damage to normal tissue with fast neutrons than with X-rays. Whether fast neutron therapy has a net advantage depends on which of these two factors is the more important, and an attempt is being made to assess their relative importance in studies on rat tumours.

Epidemiological Research Unit (South Wales) (Honorary Director: Professor A. L. Cochrane)

The work of the Unit is primarily concerned with the development of techniques for calculating the attack, progression and prevalence rates of a number of conditions in a defined population. Some of these techniques were originally developed for investigations into pulmonary disease, in particular pneumoconiosis. More recently, the Unit has applied these techniques to the study of other diseases, and has been particularly successful in the fields of haematology and ophthalmology.

The Unit is at present undertaking a number of haematological studies: preliminary investigations of defined populations have confirmed that iron deficiency anaemia is prevalent in women aged over 15 years and in men aged over 60, and at present two studies aimed at the prevention of this condition are being carried out. In the first the effect of various daily supplementary doses of elemental iron is being investigated in a group of 750 Cardiff schoolgirls; it is hoped that it will eventually be possible to determine the amount of supplementary iron that is required to prevent the development of iron deficiency anaemia in adolescent girls. In the second scheme the Unit is investigating the absorption of iron from the small quantities normally added to the white flour in bread.

The Unit has also investigated the correlation between the amount of haemoglobin in the blood and clinical symptoms. Both in a prevalence study and in a controlled therapeutic study no correlation was found between haemoglobin level or changes in level and symptoms.

Recently the Unit has become interested in the application of epidemiological techniques to ophthalmology; in particular the epidemiology of glaucoma has been investigated in a defined population. In addition a method has been devised for recording the details of lens opacities and a survey has been completed of the prevalence of cataract in a defined population.

The Unit is collaborating with a number of other bodies in a detailed study of various aspects of screening for carcinoma of the cervix. It is hoped that this work will provide information about the incidence of the condition and its aetiology and also eventually make possible an assessment of the effect of screening on mortality from the disease.

Unit for the Study of Environmental Factors in Mental and Physical Illness
(Director: Dr J. W. B. Douglas)

The growth and development of children and adolescents is the main interest of this Unit. Current investigations include a continuing study of 5000 young people born in March 1946 (the National Survey of Health and Development) and a number of smaller studies on the relation between early childhood experiences and later mental, emotional and social development. The National Survey has so far included studies on the educational progress of children from different home backgrounds through their primary schools and onwards up to the sixth forms of secondary schools. The educational problems of particular groups of pupils, such as those who are maladjusted or delinquent or who have experienced an unusually heavy load of illness, have been of special interest.

The wide variation in the ages at which boys and girls reach sexual maturity leads to many educational problems, some of which are being examined by this Unit. The early maturing children are, on the average, of superior ability to those who mature late and they do especially well in tests of school attainments such as reading or mathematics; they also stay on longer at school and are more successful in 'O' Level examinations. This superiority is not the result of a pre-pubertal spurt in intelligence accompanying the pre-pubertal spurt in growth. At eight years of age, well before even the most advanced of these children show any sign of puberty, their ability is as much above that of the late maturing children as it is at fifteen, when almost all the children are adolescent. Much,

if not all, of this difference can be explained as the effect of a complex of factors such as family size which are associated both with the rate of sexual maturation and with the level of ability.

The Unit's work on the early years of childhood has been chiefly concerned with the development of quantitative measures of the amount of stimulation of different kinds that children receive in their social environment. A satisfactory technique has been developed for recording details of the care given both inside and outside the home to boys and girls at different ages and in different social classes. This technique has been applied to the study of pre-school-age children of middle and manual working class families and detailed information has been obtained about the time they spend in sleep, play and activities of various types. It has also been applied to the study of the children of women who are excessively houseproud or obsessional, and similar studies of other types of families of psychiatric interest are projected in order to see how far abnormal patterns of behaviour are passed on from parents to children.

Unit for Research on Occupational Aspects of Ageing (Honorary Director: Professor L. S. Hearnshaw)

The work of the Unit is concerned with the psychological changes in performance, capacity and attitude that take place during the second half of the span of working life, between the ages of 40 and 65. Two factors have made the study of this period of special importance today: first, the growing proportion of the work force in the upper age groups and, second, the increasing rate of technological change, which poses major problems of readjustment and retraining. The Unit's investigations are carried out both in the laboratory and in industrial environments. To assist the laboratory investigations the Unit has a panel of some 600 volunteers, ranging in age from 20 to 80.

It has been known for some time that there is a decline in the speed and power of response in many functions with increasing age, at least from the age of 40 onwards. This decline is much more marked in some functions than in others, and there are often quite large differences between individuals. Research findings support the view that the decline of intellect with age is less marked in the higher socio-occupational classes and in people who make constant use of their intellectual abilities at work than in the lower occupational classes and those whose work is not intellectually demanding. Creativity and fertility of invention show a fairly marked decline with age. Older persons appear to find special difficulty in dealing with negative ideas in reasoning problems, and the amount of information they can hold in mind while working on a problem is smaller than it is in younger persons (which may help to account for the older person's intellectual rigidity and liability to prejudice).

It has been suggested that older people might be assisted in learning new skills and acquiring new information by techniques of programmed instruction. Results of experiments in this field suggest, however, that programmed material confuses older people, and that even with younger adults it does not always prove successful, the more intelligent tending to benefit most.

In the complex situations of real life there are often compensatory factors that obscure or even reverse the findings of such laboratory investigations. As workers get older they may leave or change jobs within the firm, and in industry there is a constant process of shifting and readjustment in the work force. Among the findings from the Unit's investigations into internal labour

mobility was the tendency of older people to move from jobs in teams to solitary jobs, even when this involved inferior working conditions. When the frequency and length of absence among different age groups was compared at a given moment of time, the younger groups frequently showed a higher rate of absence than the older workers. In a longitudinal study carried out in three firms, however, there were systematic increases with age in both length and frequency of absence.

Neuropsychiatric Research Unit (Director: Dr D. Richter)

In this Unit the clinical investigation of patients is combined with basic research. Besides extending knowledge of the causes of mental illness, such research has proved of value in suggesting new lines of treatment, and frequently also in revealing in a patient the presence of a condition not previously diagnosed.

From studies on the distribution of water and electrolytes in the tissues it would appear that some people who are subject to severe depression may differ constitutionally from normal individuals in their distribution of sodium and potassium. Lithium salts, which are used in the treatment of mania to reduce excitability and euphoria, have been found to produce a change in the sodium distribution similar to that observed in depression. They also produce a measurable change in the evoked electrical responses of the brain.

A controlled clinical trial has shown that the efficacy of monoamine oxidase inhibitors (widely used for the treatment of depression) is greatly increased by simultaneous administration of the naturally occurring amino acid tryptophan. It may be that the course of a depressive illness can be influenced by amines derived from tryptophan. The search for biochemical abnormalities in schizophrenia—for instance, defective transport of amino acids across the ' blood-brain barrier '—has not hitherto met with much success, but work on this important aspect is continuing. Studies are now proceeding on the pattern of distribution of androgenic steroids in schizophrenics and in other categories of mental patients.

Studies concerned with mental disorders in children have included an investigation of the long-term effects of meningo-encephalitis. Evidence of brain damage was assessed by electroencephalographic examination, performance in psychological tests, behaviour at home and progress at school. In a series of 102 cases of meningo-encephalitis in the London area the outcome was generally good—a finding that contrasts with the results reported in other countries—but the incidence of serious consequences was higher in cases in which the start of treatment was delayed. Investigations relating to the causation of mental subnormality have included studies of homocystinuria and the effects of thyroid hormones on the development of the brain. The nature of the brain damage caused by anoxia and by circulatory defects is being studied by neuropathological techniques and also experimentally in the rhesus monkey.

In studies on animals it has been found that the start of functional activity in the developing brain is associated with considerable changes in the metabolism of amino acids and in the activity of certain enzyme systems. A better understanding of the basic biochemical and biophysical mechanisms in the brain may well improve our understanding of the causes of mental disorders and indicate methods of prevention.

Vision Research Unit (Director: Dr H. J. A. Dartnall)

Light acts on the retina through the mediation of the visual pigments, which are present in the photoreceptor cells. All known visual pigments are proteins that carry an attached group (based on either vitamin A_1 or A_2), the shape of which corresponds to a niche in the protein. When the attached group absorbs a quantum of light its shape is changed so that it no longer fits. The resulting electrical disturbance probably triggers off the receptor response. Thus the visual pigments occupy a key place in vision and their light-absorbing properties determine which parts of the electromagnetic spectrum are visible.

The work of the Unit has three main objectives: to explore the distribution of the visual pigments in the animal kingdom in relation to environment, to elucidate the photochemistry of the pigments and relate their molecular structure to the visual process, and to measure and interpret the visual characteristics of man and animals.

A species may have one visual pigment or, if it has colour vision, more than one. The visual pigments of different species have been found to vary widely, being adapted to the different light environments. The spectral locations of pigments from many different species from terrestrial, marine and freshwater environments have been measured to ascertain whether the pigments are distributed continuously or non-continuously in the spectrum. The results show that the distribution is non-continuous—that is, that the pigments are distributed over the spectrum in clusters. Thus there is a limited number of different pigments, which suggests that the variability is based on discrete structural differences in the molecule.

Fishes have the most widely varying pigments. In studies on adaptation to environment, collections of pigments have been made from fishes inhabiting various waters—from clear oceanic waters where the light is blue to turbid coastal waters and certain fresh waters where the fishes live in a permanent ' fog ' and yet apparently make full use of their well developed eyes. Deep-sea fishes, which inhabit a nearly monochromatic and very dim environment, have visual pigments with a spectral location corresponding to that of the ambient light, for these give the maximum sensitivity. Contrary to previous belief, however, it was discovered that fishes in shallower waters have visual pigments ' offset ' from the wavelength of the ambient light. This enables the fish to have an improved contrast perception at some expense to sensitivity (which can be afforded in well lit environments).

Dental Research Unit (Honorary Director: Professor A. I. Darling)

The work of the Unit is principally directed towards the solution of a number of outstanding problems concerning the process of carious decay in dental enamel. These include the nature of the destructive agent, the pattern of breakdown within the enamel, the nature of relatively resistant and relatively susceptible structures within the enamel and the sequence of the stages of breakdown in any given region of the enamel.

The nature of the attacking agent is not known but the most generally accepted view is that it is an acid or acids (such as lactic acid) resulting from the fermentation of foodstuffs by oral microorganisms. Changes in the enamel structure appear to take place much more rapidly when they are induced

artificially with simple acid solutions than when natural caries occurs; but when enamel is exposed to acidified gels the artificial breakdown closely simulates the natural, though the precise effect of the gel is unknown.

In both artificial and natural caries certain parts of the enamel resist breakdown more readily than others. For example, the surface layer of enamel remains intact even when considerable destruction has occurred below the surface. This effect may be due to the higher concentrations of fluorine and other elements at the surface or, perhaps, to some function of the size, packing and arrangement of the crystallites. However, other structures within the enamel appear to resist attack also, which poses the question whether all differences in resistance have the same cause.

The pattern of the carious attack in enamel is now clearly established. It begins with the formation of a translucent zone which, according to its behaviour under the microscope, is characterized by the appearance of large pores at the periphery of the subunits of the enamel. This is succeeded by the formation of a dark zone, characterized by the gradual development of small pores within the subunits; this is in turn followed by a further translucent area, known as the body of the lesion, when the pores become enlarged beyond a critical limit. The changes in the last two stages are associated with loss of mineral; the mechanism of the first stage is not yet clear, though the changes could be due to alteration or loss of some of the enamel's small protein content. In theory it should be possible to increase the resistance of enamel to carious attack by modifying its structure, either during development or after eruption of the teeth. Such modification might need to affect the mineral component, the organic component or, possibly, both.

Unit for Research on the Experimental Pathology of the Skin (Director: Dr C. N. D. Cruickshank)

The aim of the Unit is to achieve a better understanding of the structure and functions of the skin in health and disease. Two aspects of the Unit's work are described here.

In the production of the hair, the vibrissa (or whisker) and the feather it has been generally agreed that the dermal papilla is of prime importance. This onion-shaped aggregation of connective tissue cells enclosed by the growing end or root of the hair induces the production of the fibrous shaft and affects its manner of growth. It has been assumed that the dermal papilla is a discrete and permanent structure; but a recent study by workers in the Unit (in association with the Department of Zoology of the University of Birmingham) has shown that when dermal papillae are removed from rat whisker follicles new dermal papillae are formed and that subsequent whisker growth is normal. Even when the lower part (up to one-third) of the follicle is removed, whiskers continue to grow, though they may be shorter than normal.

Histological investigations have shown that in these circumstances the new papilla originates primarily from the mesenchymal layer (which is equivalent to the dermal sheath in hair follicles). This has been confirmed by transplanting isolated lengths of follicle under the skin of the ear, where as a result ectopic whiskers have been produced.

If, as seems likely, these observations are applicable to human hair, they must affect our view of some forms of baldness. A defect in the dermal papillae alone cannot be the cause of hair loss because the papillae can be regenerated

It may be rather that the cause is some irregularity in the dermo-epidermal relationship. It is also interesting to reflect that electrolysis operations designed to destroy the dermal papilla, and thus to prevent unwanted hair growth, are only likely to be successful if the bottom third of the follicle, as well as the dermal papilla, is destroyed.

A second example of the work of the Unit is concerned with the study of the sulphated mucopolysaccharides. This group of substances is known to be associated with the formation of collagen (a protein that occurs in bone, cartilage and connective tissue) and perhaps keratin (a major component of hair, nails and feathers). Until recently methods of isolating individual members of the group were not satisfactory; but now the Unit (in association with the Department of Chemistry of the University of Birmingham) has developed a method, using radioisotopes and tissue culture techniques, by which individual sulphated mucopolysaccharides can be isolated from the skin and other tissues even on a very small scale. This new technique is likely to have wide applications in biological science.

Wernher Research Unit on Deafness (Director: Dr T. S. Littler)

Much of the Unit's recent work has been concerned with developing and improving transistorized hearing aids. Of particular interest are the investigations carried out with the collaboration of the Greater London Council into the special requirements of some seriously deaf children. These children had much better hearing for low than for high frequencies and were not helped by standard hearing-aids (which give emphasis to the high frequencies) except at sound levels almost dangerously high. From the Unit's studies, in which a portable high-fidelity hearing-aid was used, it was concluded that for these children a special low-powered hearing-aid with good low-frequency amplification was needed.

Over the last few years the Unit has been studying the possible advantages of binaural over monaural hearing-aids. Tests were made to compare the effectiveness of two separate hearing-aids (one for each ear) with that of one aid, connected to both ears by a double lead. The conclusions reached were that although the use of two separate devices was thought to produce strikingly realistic effects there was no real advantage in this system over the use of one aid with a double lead unless hearing loss was noticeably different in the two ears. It was clear, however, that either of the binaural systems was preferable to a system using only one ear, since a satisfactory effect could be achieved with a lower intensity of sound.

In collaboration with the National Physical Laboratory the Unit has participated in the planning and operation of a survey (carried out on behalf of the Ministry of Pensions and National Insurance) of the effects on hearing of noise in industry. So far the hearing of people known to have been exposed to noise has been studied by means of automatic self-recording audiometers over a period of about three years, but the more important aspects of the work are the prospective studies. The data obtained may well also help in the development of protective measures for the conservation of hearing. Special attention has been given to possible methods of detecting those employees who are particularly susceptible to the ill effects of exposure to noise.

Shortly before the end of the period covered by this report the Unit was disbanded on the retirement of the Director, but arrangements are being made for the occupational study to continue.

Blood Coagulation Research Unit (Director: Professor R. G. Macfarlane FRS)

The study of haemophilia and other coagulation disorders is the main interest of the Unit. At present so little is known about the chemistry of the blood clotting factors that hypotheses about the theory of clotting and the validity of quantitative tests can ultimately be assessed only by observing the response of patients to treatment. The Unit aims to maintain a balance between academic experiments, which will benefit the patient in the future, and the development of practical applications of existing knowledge.

About a dozen different factors in the blood and tissues combine in a complex sequence to bring about the clotting of blood. In order that results from different centres can be compared, reliable methods for assaying these factors must be developed, which in turn depend on the existence of standard preparations against which activity can be measured. To this end the Unit is collaborating with the Division of Biological Standards at the National Institute for Medical Research in a study of assay procedures and materials. The treatment of patients is dependent on the provision of concentrates of clotting factors derived from human blood, and at present the amounts available are inadequate. A large increase in supply can be envisaged only if a way is found of using all of the blood constituents, including the red cells. A study on a small scale (in collaboration with the Lister Institute for Preventive Medicine and the Oxford Regional Blood Transfusion Service) is in progress to investigate the best method by which this could be achieved. The Unit is also carrying out investigations on the complex interaction of clotting factors and to help this work antibodies to individual clotting factors have been prepared.

The defect in haemophilic blood may be due to the absence of an essential clotting factor or to the presence of a modified and inactive protein. Work on haemoglobin has established that abnormal pigments have an abnormal electrophoretic mobility and it was hoped that it might be possible to detect the antihaemophilic factor by a similar technique, using normal plasma and the plasma of patients mildly affected with haemophilia. So far results have been disappointing but the experiments were useful nevertheless because they have shown that the antihaemophilic factor can be separated from other components, such as fibrinogen, without any great loss of potency.

At the Unit 595 patients (a substantial proportion of all those in the British Isles) with haemophilia or the closely related Christmas disease are registered for treatment or advice. In addition, the Unit is much involved in planning for the establishment of treatment and rehabilitation centres and special schools and for the provision of increased amounts of suitable therapeutic materials in the future.

COUNCIL ESTABLISHMENTS

NATIONAL INSTITUTE FOR MEDICAL RESEARCH

During the course of the year it was announced that Professor B. Delisle Burns (McGill University, Montreal) had accepted the Council's invitation to succeed

Professor W. Feldberg FRS as Head of the Division of Physiology and Pharmacology at the National Institute for Medical Research. Professor Delisle Burns will join the Council's staff in September 1966.

The Council approved proposals by the Director, Sir Peter Medawar FRS, for the creation of a new division at the Institute, with the title of Biomedical Engineering, under Mr H. S. Wolff, and for certain changes in the titles of a number of existing divisions at Mill Hill.

RESEARCH UNITS

New units

During the period under review the Council set up three new research units. Two of these are to carry on certain aspects of the work initiated in the Council's Obstetric Medicine Research Unit at Aberdeen, which was disbanded in September 1965 on the retirement of Professor Sir Dugald Baird as Honorary Director of the Unit. The *Reproduction and Growth Research Unit* is at the Princess Mary Maternity Hospital, Newcastle upon Tyne, in association with the University Departments of Midwifery and Gynaecology and of Child Health, and is under the direction of Dr Angus Thomson, who was Honorary Deputy Director of the Aberdeen Unit. This new Unit is extending the work on human reproduction and growth with which Dr Thomson and his colleagues were concerned at Aberdeen.

The *Medical Sociology Research Unit* was established in the Department of Sociology in the University of Aberdeen, with Professor Raymond Illsley as Honorary Director. Until his appointment to the recently created Chair of Sociology, Professor Illsley was a senior member of the Council's scientific staff in the Obstetric Medicine Research Unit, and the sociological studies with which he was concerned are being expanded in the new Unit. This Unit will be particularly concerned with the interactions between medical and social factors in reproduction and child development and will work in collaboration with other university departments in Aberdeen with interests in this field.

The Council's Cardiovascular Research Group at the Postgraduate Medical School of London, Hammersmith Hospital, was reconstituted during the year as the *Cardiovascular Research Unit;* this will expand the investigations into diseases of the heart and circulation previously undertaken by the research group. Special emphasis is being placed on research into the intensive care of patients after coronary thrombosis, the haemodynamic changes that take place in cardiovascular disease and methods of improving diagnosis and treatment. This work continues to be under the direction of Dr J. P. Shillingford.

Changes in units

The *Industrial Psychology Research Unit* was transferred from University College London to the National Institute for Industrial Psychology, Dr C. B. Frisby succeeding Professor G. C. Drew as Honorary Director.

Other changes in the directorship of research units which took place during the year were as follows. Professor R. A. McCance FRS agreed to act as Director of the *Infantile Malnutrition Research Unit* in Uganda, while continuing to direct the work of the Council's Department of Experimental Medicine in Cambridge. Dr Wallace Fox succeeded Dr P. M. D'Arcy Hart as Director of

the Tuberculosis Research Unit, the title of which has been expanded to *Tuberculosis and Chest Diseases Research Unit.* Dr J. K. Wing succeeded Professor Sir Aubrey Lewis as Director of the *Social Psychiatry Research Unit.* When Dr C. S. Hallpike FRS retired from the Council's staff Sir Terence Cawthorne agreed to supervise, in an honorary capacity, the work of the *Otological Research Unit.*

Dr K. L. G. Goldsmith succeeded Dr A. E. Mourant FRS as Director of the *Blood Group Reference Laboratory,* which is administered by the Council on behalf of the Ministry of Health. The Laboratory continues to deal with all aspects of work on blood groups apart from anthropological and population surveys; these surveys remain the responsibility of Dr Mourant, who has transferred to the Council's External Scientific Staff to take charge of a serological population genetics laboratory at St. Bartholomew's Hospital. Mr John Bleby succeeded Dr W. Lane-Petter as Director of the Council's *Laboratory Animals Centre* at the MRC Laboratories, Carshalton.

The *Wernher Research Unit on Deafness* at King's College Hospital Medical School was disbanded on the retirement of the Director, Dr T. S. Littler.

HEADQUARTERS OFFICE

Dr J. A. B. Gray took up an appointment with the Council in May 1966 as their Second Secretary and as such is the immediate deputy and alternate to the Secretary. Dr Gray was a member of the Council's scientific staff at the National Institute for Medical Research from 1946 to 1952. He then joined the Department of Physiology at University College London and since 1959 has held one of the Chairs of Physiology there, latterly serving as Dean of the Faculty of Science in the University.

The Council wish to take this opportunity not only of welcoming Dr Gray's appointment but also of expressing their great indebtedness to Sir Charles Harington FRS for holding this post in an acting capacity over the past two years. On his retirement from the directorship of the National Institute for Medical Research in 1962, Sir Charles joined the headquarters office as a consultant adviser to the Secretary and his knowledge, experience and wisdom have been of invaluable assistance. The Council are happy that Sir Charles continues to serve them in an advisory capacity.

COUNCIL ESTABLISHMENTS AND STAFF NUMBERS

At the end of the period under review the Council's own establishments consisted of the National Institute for Medical Research and 79 research units (including 4 overseas); members of their External Scientific Staff continued to be attached individually to other institutions. A full list of the Council's research establishments, with staff lists and summaries of their research programmes, is given on pp. 89–186. Financial information is on p. 24.

The number of staff employed by the Council on 1 January 1966 was 3410. This figure was made up of 890 scientific staff (including 62 part-time), of whom 277 were medically qualified, 1402 technical staff (including 35 part-time), 689 administrative and clerical staff (including 80 part-time), and 429 maintenance staff (including 137 part-time). In addition, 105 locally recruited staff were employed in the Gambia and in Uganda.

SUPPORT OF OTHER RESEARCH PROJECTS

RESEARCH GROUPS

The Council agreed during the year to provide support, under their Research Groups scheme, for the following projects being undertaken in university departments:

University	*Department*	*Research Group*
Birmingham	Microbiology (*Professor H. Smith*)	Mechanisms of Microbial Pathogenicity
Bristol	Biochemistry (*Professor P. J. Randle*)	Metabolism Control
Glasgow	Pathology (*Professor T. Symington*)	Adrenal and Endocrine Pathology
Leicester	Zoology (*Dr R. Whittam*)	Physiology of Membrane Transport and Secretion
London		
Institute of Child Health	Immunology (*Dr J. F. Soothill*)	Immunology
King's College	Biochemistry (*Professor H. R. V. Arnstein*)	Control of Protein Biosynthesis in Animal Cells
University College	Zoology (*Dr A. Comfort*)	Biology of Ageing
Newcastle upon Tyne	Biochemistry (*Professor K. Burton*)	Structure, Function and Biosynthesis of Macromolecules
Oxford	Zoology (*Dr D. C. Phillips*)	Molecular Biophysics
Sheffield	Physiology (*Professor D. H. Smyth*)	Intestinal Absorption
Southampton	Zoology (*Professor L. Brent*)	Tissue Immunology
Sussex	Microbiology (*Professor N. D. Symonds*)	Genetic and Biochemical Studies on Bacteria and Bacterial Viruses

At the end of the year under review the Council were providing support for 39 research groups. A full list of the groups currently receiving support and summaries of the work on which they are engaged is given on pp. 197–213.

RESEARCH GRANTS

The Council have continued to make a number of block grants to institutions and shorter-term research grants to individual workers in aid of an extensive range of clinical and laboratory investigations. Over the years the number of grants awarded to individuals by the Council has grown considerably, as will be seen from the following table:

	1923–4	*1933–4*	*1939–45*	*1953–4*	*1964–5*	*1965–66*
No. of grants held	176	205	235	271	857	1035

A complete list of grant-holders is given on pp. 214–257.

FELLOWSHIPS AND TRAINING AWARDS

The Council have maintained their various schemes of training awards during the year and detailed information about these is given on pp. 258–265.

Eighteen travelling fellowships were given for the academic year 1965–66, and 7 new clinical research fellowships were awarded. In addition, there

were 18 new junior research fellowships and 281 new training awards (including scholarships for training in research methods, awards for further education in the medical sciences and awards for intercalated courses).

The Council would like to make grateful acknowledgement of the endowment originated in 1935 by the late Mr and Mrs Eugen M. Schlesinger in memory of their daughter. This endowment, which has now expired, has made funds available for the award of the Kathleen Schlesinger Research Fellowship for work in the field of neuropathology, with special reference to the investigation of the mechanisms underlying degenerative processes affecting the brain.

OTHER ASPECTS OF THE COUNCIL'S ACTIVITIES

STATEMENTS AND EVIDENCE GIVEN BY THE COUNCIL

Alcohol and road driving

At the request of the Home Office, the Council commented on the association between the consumption of alcohol and impairment of skill in driving a motor vehicle. In the light of all the evidence from both experiments and real life situations, and from what is known about the pharmacological and anaesthetic effects of alcohol, they concluded that in an average population of motor drivers, the consumption of alcohol in amounts sufficient to cause a blood alcohol concentration of 50 or more mg per 100 ml would impair the ability to drive in an appreciable proportion of those on the road at any one time. When the amount of alcohol consumed results in a concentration in the blood of 80 or more mg per 100 ml, then the ability to drive would be impaired in the great majority of those in charge of motor vehicles.

Chronic bronchitis and occupation

In response to a request from the Minister of Pensions and National Insurance an expert committee was called together by the Council to consider the role of occupation in the aetiology of chronic bronchitis and, with the approval of the Minister, their report was published in the *British Medical Journal* on 8 January 1966. The report concluded that it was important that the research being carried out into the aetiology of this disease should continue to be vigorously pursued but that there would be little point in conducting a new inquiry that was exclusively concerned with the occupational factor. Available evidence showed how difficult it would be to determine the degree to which occupational as distinct from other environmental causes were responsible for the onset of bronchitis.

Committee on Death Certification and Coroners

During the summer of 1965 the Council were invited to submit evidence to an interdepartmental committee, under the chairmanship of Mr Norman Brodrick QC, which had been appointed by the Home Secretary to look into the law and practice relating to death certification and coroners. An *ad hoc* committee, called together under the auspices of the Council's Occupational Health Committee, considered this question and on the basis of their advice written evidence was submitted to the interdepartmental committee.

Committee on the Pharmaceutical Industry

During the period under review the Council accepted an invitation to submit evidence to the committee set up by the Health Departments under the

chairmanship of Lord Sainsbury to examine the relationship of the pharmaceutical industry in Great Britain with the National Health Service.

COMMITTEES

After the Government's acceptance of the recommendations of the official working party set up by the Council for Scientific Policy and the University Grants Committee, under the chairmanship of Professor B. H. Flowers FRS, to consider national requirements in the field of computers, the Council appointed a *Computer Advisory Committee*, with Dr J. A. B. Gray as chairman. The function of this committee is to advise on problems associated with the use of computers in medical and biological research, including the provision of equipment and the coordination of program development. The Council also appointed a steering committee, with Professor Hedley Atkins as chairman, to watch over the progress of a project for research into the clinical applications of Monitron (patient monitoring) equipment, which is to be undertaken in collaboration with the Ministry of Health.

In response to a request from the Ministry of Health for views on the possibility that a health hazard might be associated with the use of oral contraceptives, the Council set up a subcommittee under the chairmanship of Sir Robert Platt to examine the matter. The subcommittee has made a preliminary report to the Council that no definite cause for concern exists but it is continuing to keep the question under review.

The Ministry also approached the Council about policy in relation to work on vaccines and, in the light of the recommendations of a meeting convened to discuss the matter, the Council have set up a committee, jointly with the Health Departments and the Public Health Laboratory Service, to advise on research on vaccines and immunization procedures. Professor D. G. Evans FRS is Chairman of this Committee.

The Council also set up a *Working Party on the Treatment of Malignant Exophthalmos*, under the chairmanship of Sir Edward Wayne, to evaluate methods of treating this condition, with particular reference to the suppression of thyroid activity by large doses of radio-iodine.

The Committee on the Aetiology of Chronic Bronchitis was reconstituted, under the chairmanship of Professor C. H. Stuart-Harris, as the *Committee for Research into Chronic Bronchitis*. After the death of Sir John Gaddum FRS, chairman of the *Clinical Endocrinology Committee*, this committee was reconstituted with Professor F. G. Young FRS as chairman.

The *Rheumatic Fever Working Party* (Joint US : UK Study of Rheumatic Fever) was disbanded after the publication of its report. The *Working Party on Fractures in the Elderly* was also disbanded after its final report had been published.

The *Joint Committee on Biological (Non-Medical) Problems of Nuclear Physics*, appointed jointly by the Council, the Agricultural Research Council and the Development Commission (now integrated with the Natural Environment Research Council), was, with the agreement of all bodies concerned, also disbanded. Its *Monitoring Subcommittee* continues in being under the title of *Committee on the Monitoring of Radioactivity from Fallout*.

CONFERENCES

During the past year the Council continued their policy of holding a series of one-day or half-day conferences to review research in particular fields. As a

sequel to the two conferences on hyperbaric oxygen therapy reported last year, a third meeting was held in June 1965, under the chairmanship of Professor W. D. M. Paton FRS, to discuss possible dangers associated with work in hyperbaric chambers. On the advice of the Clinical Research Board, the Council have since established a standing committee to keep the field of hyperbaric oxygen therapy under review.

Three conferences were sponsored by the Council after discussions with the Ministry of Health. In April 1965 a meeting was held, under the chairmanship of Professor G. M. Bull, to review the present state of knowledge on osteoporosis, with a view to determining fruitful lines of research; and in June 1965 a conference on cot deaths took place, with Professor (now Sir Ashley) Miles FRS in the chair, to consider the hypothesis that hypersensitivity to cow's milk might cause fatal anaphylactic shock in infants. In the light of the interest aroused by recent reports on the intensive treatment of acute leukaemia in the United States, a conference was called in March 1966, under the chairmanship of Sir Robert Platt, to take stock of the present situation as regards the therapeutic methods used in this country and to consider whether further action is required.

PUBLICATIONS

A symposium entitled *Mathematics and Computer Science in Biology and Medicine* was published in September 1965. This records the proceedings of a conference held in Oxford in 1964 by the Council in association with the Health Departments. The twenty-seven papers provide a conspectus of the applications of computer techniques and mathematical methods in the biomedical sciences and an insight into the concepts and ways of thought inherent in these approaches. A new monograph was published in the Special Report Series: *Trachoma and Allied Infections in a Gambian Village* (SRS 308, 1965), by Shiona Sowa, J. Sowa, L. H. Collier and W. Blyth; this is an account of a series of clinical, epidemiological and microbiological investigations carried out by the Council's Trachoma Research Unit. A further publication in the Memorandum Series—*Spectral Requirements of Light Sources for Clinical Purposes* (Memo. 43, 1965), by the Joint Committee on Lighting and Vision of the Medical Research Council and the Building Research Station—describes a series of colour observation experiments conducted at the Sheffield Royal Infirmary. A detailed specification is proposed in this report for a fluorescent lamp that will not give rise to distortions of colour. In the Monitoring Report Series—*Assay of Strontium-90 in Human Bone in the United Kingdom*—two further reports (Nos. 10 and 11) appeared, dealing with strontium-90 levels during 1964. Finally, in addition to the Report to Parliament for October 1963–March 1965, the scientific review articles in the report were as usual reprinted under the title *Current Medical Research.* All these reports were published for the Council by Her Majesty's Stationery Office.

The following reports were produced by Council committees during the period under review:

Clinical Psychiatry Committee: Clinical trial of the treatment of depressive illness. *Brit. med. J.* (1965) **1,** 881.

Committee on the Aetiology of Chronic Bronchitis: Definition and classification of chronic bronchitis for clinical and epidemiological purposes. *Lancet* (1965) **1,** 755.

Working Party on Human Antihaemophilic Globulin: Further experience in the use of human antihaemophilic globulin (H.A.H.G.) for the control of bleeding after dental extraction in haemophilic patients. *Lancet* (1965) **1,** 969.

Working Party on Acute Respiratory Virus Infections: A collaborative study of the aetiology of acute respiratory infections in Britain 1961–4. *Brit. med. J.* (1965) **2,** 319.

Rheumatic Fever Working Party of the Medical Research Council and the Subcommittee of Principal Investigators of the American Council on Rheumatic Fever and Congenital Heart Disease, American Heart Association, Joint Report: Natural history of rheumatic fever and rheumatic heart disease; ten-year report of a co-operative clinical trial of ACTH, cortisone, and aspirin. *Brit. med. J.* (1965) **2,** 607.

Measles Vaccines Committee: Vaccination against measles—a clinical trial of live measles vaccine given alone and live vaccine preceded by killed vaccine. *Brit. med. J.* (1966) **1,** 441.

The majority of papers published by members of the staff and other research workers supported by the Council appear in the medical and scientific journals, and references to these publications may be obtained from the Librarian at the National Institute for Medical Research.

SCIENTIFIC EXHIBITIONS

The Council took part in the Government exhibition organized in conjunction with the 1965 Annual General Meeting of the Association for Science Education, held in Cambridge in December 1965. The theme of the exhibition was ' Innovations in Technology ', and the following exhibits developed by Council workers were on show:

Monitron equipment (*Division of Biomedical Engineering, National Institute for Medical Research*)

Stimulus and response timing apparatus (*Applied Psychology Research Unit*)

Therapeutic engineering (external staff working at the *Centre for Muscle Substitutes, West Hendon Hospital*)

The Council's participation in this exhibition enabled them not only to demonstrate the link between fundamental research and its practical applications but also to make known to science teachers the opportunities existing for both scientific and technical careers in the Council's research establishments.

The Council also had a stand at the Physics Exhibition held at Alexandra Palace, London, from 29 to 31 March 1966. The following exhibits from the Council's establishments were shown:

Variable delivery flexible rotor pump (*Engineering Division, National Institute for Medical Research*)

Construction of molecular models in plastic (*Engineering Division, National Institute for Medical Research*)

Socially acceptable instruments and electrochemical recording methods (*Division of Biochemical Engineering, National Institute for Medical Research*)

A correlator for EEG signals (*Clinical Psychiatry Research Unit*)

An automatic system for the complete analysis of fluorescent zones in paper strips (*Unit for Research on the Chemical Pathology of Mental Disorders*)

VISITS TO COUNCIL ESTABLISHMENTS BY MEDICAL AND SCIENCE CORRESPONDENTS

As part of the series of visits arranged for medical and science correspondents, to enable them to see some of the work being undertaken by the Council, the following establishments were visited during the year:

Edinburgh	Clinical Effects of Radiation Research Unit
London	National Institute for Medical Research
	Air Pollution Research Unit
Salisbury	Common Cold Research Unit

During the period under review members of the Council's staff continued to visit 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 granted leave of absence for varying periods to work in academic centres abroad. Approximately 110 international congresses and similar meetings were attended by members of staff.

Through the work of the Tropical Medicine Research Board and by their close liaison with the various overseas regional Medical Research Councils and Committees, the Council have continued to take an active interest, both in the United Kingdom and in territories overseas, in many aspects of research in tropical medicine. Dr E. T. C. Spooner (a member of the Board), Dr R. Lewthwaite (assessor), Dr B. S. Lush (secretary) and Professor M. D. Milne (who was nominated by the Board as their representative) attended the annual scientific conference and meeting of the Standing Advisory Committee for Medical Research in the Caribbean. Two members of the Board, Professor G. M. Bull and Dr L. G. Goodwin, with Dr Lewthwaite, visited East Africa to attend the annual meeting and scientific conference of the East African Medical Research Council and to see work in progress in some of the main research centres in the region. The chairman of the Tropical Medicine Research Board paid a visit to the Gambia during the year.

The Council continued to maintain, with support from the Ministry of Overseas Development 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.

International Agency for Research on Cancer

In 1963 proposals were made by the French Government for the establishment of an international cancer research organization to be financed by governmental grants. After discussions through diplomatic channels, negotiations were continued by scientific representatives from the participating nations, and a scheme for the establishment of a central agency linked with the World Health Organization was agreed at the 18th World Health Assembly in May 1965. As at present envisaged, the Centre, which is to be sited in Lyons, will concentrate on epidemiological problems and the exchange of information in the general field of cancer. Professor John Higginson, of the University of Kansas Medical Center, has recently been appointed its Director.

The Agency is at present being supported by seven countries—the United States, the USSR, France, West Germany, Italy, Australia and the United Kingdom. Each of the member countries has agreed to make an initial payment of $75 000 for the year ended 31 December 1965 and subsequently to contribute $150 000 annually for the permanent activities of the Agency. The Medical Research Council is responsible for providing, out of their grant-in-aid, the United Kingdom's contribution.

The Council's Secretary, Sir Harold Himsworth FRS, has been appointed by the Secretary of State for Education and Science to represent the United Kingdom on the Governing Council of the Agency. Dr Richard Doll FRS is currently chairman of the Agency's Scientific Council.

ADMINISTRATION

FINANCE

The Parliamentary grant-in-aid to the Council for the year ended 31 March 1966 was £10 280 000, including special provision of £54 000 for a subscription to the International Agency for Research on Cancer (see above); £10 087 536 of the Parliamentary grant was drawn. This provision was augmented by subventions from Government departments and other public bodies and contributions from other sources (see Appendix II). The total income on the grant-in-aid account was as follows (the figures for 1964–65 are given for comparison):

	1964–65	*1965–66*
	£	£
Parliamentary grant-in-aid	8 753 000	10 087 536
Funds from Government departments and public bodies	686 755	770 288
Special grants from other bodies	76 069	70 198
Drawings on bequests, donations etc.	4 542	5 330
Miscellaneous sales and services	106 856	112 637

The Council's detailed account for the financial year 1965–66 is shown in Appendix I (pp. 286–7). In summary, the total expenditure for the year was allocated as follows:

	1964–65	*1965–66*
	£	£
Recurrent expenses	9 019 306	10 597 580
New buildings	460 121	373 227
Grants for special apparatus	149 707	86 842
	£9 629 134	11 057 649

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

	1964–65	*1965–66*
	%	%
Administration	5·2	4·9
Central expenses	1·2	1·1
National Institute for Medical Research	13·8	12·4
Research units and external scientific staff	52·7	50·9
Research groups	2·8	3·8
Special grants	7·5	6·4
Short-term research grants and training awards	16·8	20·0
International subscription	—	0·5
	100·0	100·0

Benefactions

Under the terms of their Charter the Council can receive and administer private funds or properties entrusted to them by grant, gift or bequest, either for the general purposes of medical research or for research on specific subjects. A number of valuable additions to their resources became available in this way during the period covered by this report and for these the Council wish to make grateful acknowledgement.

Bequests and donations received during the year totalled £57 044. This includes £37 648 from a residuary bequest by the late Miss A. M. Cory to set up the Cory Fellowship Fund, £3234 as a share of the residuary estate of the

late Dr O. Spatz for research on breast cancer and coronary heart disease, £2000 as an initial payment from a share of the residuary estate of the late Miss B. S. Forni for research on diseases of the eye, and £1000 as a further donation from Mr and Mrs A. Ehrman for poliomyelitis research.

A revised version of the Council's pamphlet *Benefactions for Medical Research* was issued during the year and is available on request. In addition to advising on the allocation of benefactions within their own organization, the Council are glad to give advice generally about benefactions to be made to other bodies for the purposes of medical research.

ACCOMMODATION

Clinical Research Centre, Northwick Park

Recent progress has already been described on pp. 1–3.

Existing research establishments

The following major building projects were completed during the year:

Cyclotron Unit and Experimental Radiopathology Research Unit, Hammersmith Hospital	Extension
MRC Laboratories, Carshalton	Conversion of old library into laboratories
Human Biochemical Genetics Research Unit, University College London	Alterations at Galton Laboratories
Clinical Endocrinology Research Unit, Edinburgh	Further modernization of laboratories

Work is in progress on the following projects:

National Institute for Medical Research	Small mouse-breeding unit; additional laboratories for Division of Biological Standards
Reproduction and Growth Research Unit, Newcastle upon Tyne	Building at Princess Mary Maternity Hospital

Considerable progress has also been made with plans for alterations to the main building at the National Institute for Medical Research designed to provide more laboratory space there, and for the erection of new buildings for laboratories, ancillary services and animal accommodation; the first stage of these major developments will be started in 1966–67. Planning of a major extension for the Laboratory of Molecular Biology is nearing completion; this will include an area for use by the University of Cambridge.

Plans are also in hand for the provision of new or additional accommodation for the following establishments:

Cellular Immunology Research Unit (in association with Oxford University)	New accommodation
Tuberculosis and Chest Diseases Research Unit	Building at Institute of Diseases of the Chest, Brompton Hospital
Dunn Nutritional Laboratory	Alterations and extension
Radiological Protection Service (in association with Ministry of Health)	Low background laboratory

PATENTS

Nine patent applications, arising out of research supported by the Council, have been filed during the course of the period under review and the rights in these have been or are being assigned to the National Research Development Corporation. By the end of September 1965, 108 patents and patent applications, the rights of which had been assigned to the Corporation, were on its active register. Many of the patented inventions assigned to the Corporation have proved to be very profitable.

PERSONNEL

SIR HENRY DALE'S 90TH BIRTHDAY

Sir Henry Dale OM FRS, the first Director of the National Institute for Medical Research, celebrated his 90th birthday on 9 June 1965. He was in the vanguard of the full-time research workers appointed by the Council's predecessor, the Medical Research Committee, joining the staff as Head of the Division of Physiology and Pharmacology of the new National Institute in 1914. He was formally appointed Director of the Institute in 1928, holding this post until his retirement from the Council's service in 1942.

Sir Henry's work on anaphylaxis and the role of histamine in the body, and his later studies on the chemical transmission of nervous impulses for which he shared the Nobel Prize for Medicine in 1936, are amongst the major achievements of medical science. His influence was no less notable in matters of organization; an outstanding example of this was his leadership in developing the concept of biological standardization. His exceptional qualities and judgment as a scientist were widely recognized; after serving as Biological Secretary of the Royal Society he was elected its President during the second World War and in that capacity became Chairman of the Scientific Advisory Committee of the War Cabinet.

After the war Sir Henry was appointed Chairman of the Wellcome Trustees and the Trust paid tribute to his long and distinguished career in an exhibition to celebrate his 90th birthday. The Council were glad on this occasion to express their own appreciation of his unique contributions to their work and to the advancement of medical science in general.

MEMBERSHIP OF COUNCIL AND RESEARCH BOARDS

Council

As recorded above, Lord Shawcross retired from the Council in September 1965 on the completion of his period of service. He was succeeded as Chairman by Viscount Amory, who had served previously as the Council's Chairman for a short period before his appointment in 1961 as High Commissioner for the United Kingdom in Canada.

Professor Melville Arnott, Professor D. G. Evans FRS and Professor J. L. Gowans FRS were appointed members of Council from 1 October 1965. They succeeded Professor M. M. Swann FRS, who had earlier resigned on his appointment as a member of the Council for Scientific Policy, the late Professor Wilson Smith FRS and Professor M. L. Rosenheim, who retired on the completion of his term of membership on 30 September 1965.

Biological Research Board

Professor R. A. Gregory FRS was appointed a member of the Biological Research Board and Professor D. G. Evans FRS and Professor J. L. Gowans FRS became *ex officiis* members of the Board on their appointment to the Council.

Clinical Research Board

On his appointment to the Council Professor Melville Arnott became a member of the Clinical Research Board. The other new members appointed to the Board from 1 October 1965 were Professor A. S. Duncan and Professor T. Cecil Gray, who succeeded Professor T. N. A. Jeffcoate and Dr F. Avery Jones.

Tropical Medicine Research Board

Professor D. V. Hubble became a member of the Tropical Medicine Research Board as a Council nominee, and Professor P. C. C. Garnham as a nominee of the Ministry of Overseas Development. The following members of the Board retired on the completion of their period of service on 30 September 1965: Professor B. G. Maegraith, Professor B. S. Platt and Professor M. L. Rosenheim.

Assessors to Council and Boards

Through the scheme of assessorships other cognate organizations are enabled to be informed of developments in the Council's activities.

The Chief Medical Officers of the Ministry of Health and the Scottish Home and Health Department, the Chairman of the University Grants Committee, the Chairman of the Science Research Council, the Secretary of the Agricultural Research Council and the Chairman of the Clinical Research Board are *ex officiis* assessors to the Council; a further assessor is nominated by the Royal Society on the Council's invitation. Sir George Godber (Ministry of Health), Dr J. H. F. Brotherston (Scottish Home and Health Department), Sir Robert Platt (Clinical Research Board) and Professor Sir Ashley Miles FRS (Royal Society) attended meetings in their capacity as assessors. The Chairman of the Science Research Council and the Secretary of the Agricultural Research Council received papers on a reciprocal basis.

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

OBITUARY

Professor Wilson Smith

The Council learned with deep regret of the death on 10 July 1965 of Professor Wilson Smith FRS, who had long been associated with their work. His great contributions to microbiology, and in particular to virology, were widely recognized and he was instrumental in laying the foundations of research on the influenza virus.

Professor Wilson Smith was for a time a member of the scientific staff of the Council and later served on a number of their scientific committees, in some cases as chairman; at the time of his death he was about to complete his four-year term as a Council member. During the last year and a half of his life he had suffered progressive ill-health. Nevertheless he continued his work with

unassuming courage and, in spite of the physical effort that it cost him, he maintained its quality to the end. He will long be remembered for his personal qualities, for his outstanding achievements in medical research, and for his public-spirited service in encouraging the practical application of scientific knowledge and in guiding research policy.

Sir John Gaddum

Sir John Gaddum FRS, who died on 30 June 1965, was one of the leading figures associated with the development of research in physiology and pharmacology over the past forty years. He qualified in medicine at University College London in 1925 and was a member of the Council's staff at the National Institute for Medical Research from 1927 to 1934. His research interests were wide; his pioneer work on the principles of bioassay paved the way for the modern approach to biological standardization, while his contributions to neuropharmacology and the physiology of the sympathetic nervous system have been of far-reaching importance. Sir John served as a member of Council from 1948 to 1951 and at the time of his death was chairman of the Clinical Endocrinology Committee.

Professor J. R. Squire

Professor John Squire's untimely death on 6 January 1966 was a great loss to British medicine generally and, in particular, to the Council's own organization. Professor Squire's association with the Council began in 1946, when he was appointed Director of their Industrial Medicine Research Unit. He subsequently directed this Unit, and later the Unit for Research on the Experimental Pathology of the Skin, in an honorary capacity after his appointment to the Chair of Experimental Pathology in the University of Birmingham. He served on a number of the Council's committees and was chairman of the Army Personnel Research Committee and the Working Party on Hypogammaglobulinaemia.

When the Council decided to establish the Clinical Research Centre at Northwick Park (see p. 1) Professor Squire was designated Director. His breadth of knowledge and drive, added to his personal charm, made him singularly fitted for this position. While remaining fully committed to his professorial work in Birmingham, he worked continuously to create a clinical centre which would attract some of the best research workers in the country and make a major contribution to medical science. He gave his attention to the detailed planning of the scheme as well as to overall policy, and the foresight, enthusiasm and energy that he brought to the task inspired all those working with him. The Clinical Research Centre cannot fail to bear the stamp of John Squire and will assuredly prove a lively memorial to him.

Dr B. Bronte-Stewart

The death of Dr Brian Bronte-Stewart at the early age of 42 on 9 July 1965 was a sad loss to the Council and to the field of research in cardiovascular disease, to which he had made valuable contributions. He had been Director of the Atheroma Research Unit since 1962, having already established a distinguished reputation for his work on occlusive vascular diseases. His death has deprived the Council of one of the most eminent of their younger research workers.

On his retirement as Head of the Division of Physiology and Pharmacology at the National Institute for Medical Research, the Council wish to acknowledge the invaluable contributions to research made by Professor W. S. Feldberg FRS, who joined their staff in 1949. Professor Feldberg's work on the physiology and pharmacology of the brain has been widely recognized to be of particular distinction. He is continuing his work with the support of a research grant from the Council, who are gratified that he is continuing, in an honorary capacity, to guide the work of the Division of Physiology and Pharmacology until his successor, Professor B. Delisle Burns, takes up his appointment.

Dr R. K. Callow FRS, another distinguished member of the staff at the National Institute for Medical Research (Division of Organic Chemistry), also retired during the year, and the Council wish to express their appreciation of his long and valued services. He joined the Council's staff in 1929 as a member of a team at the National Institute which successfully isolated vitamin D and later he was for some years engaged on studies initiated at the request of the Council's Hormones Committee on the excretion pattern of steroid hormones. After the war Dr Callow carried out further notable work on the synthesis of cortisone, while more recently he has been investigating the isotopic labelling of vitamin D with a view to studying its metabolism. Another important achievement was his identification and synthesis of the pheromone of the queen honey bee.

The Council wish also to pay special tribute to three Unit directors who have retired after many years' distinguished service: Dr P. M. D'Arcy Hart (Tuberculosis Research Unit); Dr C. S. Hallpike FRS (Otological Research Unit); and Dr T. S. Littler (Wernher Research Unit on Deafness).

After previous service on the Council's staff Dr D'Arcy Hart was appointed Director of the Tuberculosis Research Unit in 1948, and in this capacity he has been instrumental in bringing about important advances in the chemotherapy and epidemiology of tuberculosis, both in this country and overseas. The part he played in organizing the early clinical trials of streptomycin was especially notable. The Council are glad that Dr D'Arcy Hart is continuing to work under their auspices with the support of a research grant.

In its special field the work of the Otological Research Unit under Dr Hallpike has been of high distinction and his personal contribution has been recognized by a number of honours and awards in this country and abroad. Dr Hallpike will continue his histological studies of temporal bone and the biology of inner ear fluids with the support of a research grant from the Council.

The Wernher Research Unit on Deafness was established under Dr Littler's direction in 1949 and it has played a significant part in the field of electro-acoustics, particularly in the development of hearing aids to physiological specifications. In collaboration with the National Physical Laboratory, the Unit has more recently been engaged upon a long-term survey of occupational deafness at the request of the Ministry of Pensions and National Insurance. The Council wish to express their appreciation of Dr Littler's contribution to their work over many years; his services are being retained in an honorary capacity.

The Council are no less indebted to two honorary directors who have retired during the year—Professor Sir Aubrey Lewis (Social Psychiatry Research Unit)

and Professor Sir Dugald Baird (Obstetric Medicine Research Unit). Sir Aubrey and the Council unit of which he was director have made a notable contribution to psychiatric research. In obstetrics, Sir Dugald Baird's contribution has been similarly outstanding, his Unit having in particular demonstrated the special importance of social and epidemiological studies in this field.

Among the other members of the scientific staff who left the Council's service during this period on appointment to senior university or hospital posts were:

Dr H. R. V. Arnstein (*National Institute for Medical Research*)	Professor of Biochemistry, King's College, London
Dr L. Brent (*National Institute for Medical Research*)	Professor of Zoology, University of Southampton
Dr R. C. Clowes (*Microbial Genetics Research Unit*)	Professor of Genetics, South-West Center for Advanced Studies, Dallas, Texas
Dr J. Dawson (*External Scientific Staff*)	Consultant Pathologist at the Runwell Hospital and the Tilbury and South-East Essex Group of Hospitals
Dr W. I. N. Kessel (*Unit for Research on the Epidemiology of Psychiatric Illness*)	Professor of Psychiatry, University of Manchester
Dr A. I. Klopper (*Obstetric Medicine Research Unit*)	Senior Lecturer in Gynaecology and Obstetrics, University of Aberdeen
Dr M. R. Pollock FRS (*National Institute for Medical Research*)	Professor of Biology, University of Edinburgh
Dr N. D. Symonds (*Microbial Genetics Research Unit*)	Professor of Microbial Genetics, University of Sussex

HONOURS

The Council noted with much pleasure the following honours awarded by Her Majesty the Queen during the period under review:

Order of Merit:	Lord Florey (*lately President of the Royal Society and a former member of Council*)
Knight Batchelor:	Dr P. B. Medawar (*Director, National Institute for Medical Research*)
	Professor A. A. Miles (*Director, Lister Institute; Royal Society Assessor to the Council and a former member of Council and of their staff*)
CBE:	Dr J. A. Fraser Roberts (*lately Director, Clinical Genetics Research Unit*)
	Professor G. W. Harris (*Honorary Director, Neuro-endocrinology Research Unit*)
	Dr F. Avery Jones (*former member of the Clinical Research Board*)
	Professor A. B. Semple (*Honorary Medical Adviser, Occupational Aspects of Ageing Research Unit*)
MBE:	Mr A. K. Rahman (*Technician, MRC Laboratories, Gambia*)

The Council also learned with pleasure that the Royal Society had awarded the Copley Medal to Professor A. L. Hodgkin (until recently a member of their body) and the Royal Medal to Dr J. C. Kendrew (Laboratory of Molecular Biology), and that the following had been made Fellows of the Royal Society:

Dr Richard Doll (*Director, Statistical Research Unit*)

Professor H. Harris (*Honorary Director, Human Biochemical Genetics Research Unit*)

Dr Alick Isaacs (*National Institute for Medical Research*)

Dr A. E. Mourant (*External staff; lately Director, Blood Group Reference Laboratory*)

The Council were glad to note the following other honours:

Sir Peter Medawar (*Director, National Institute for Medical Research*): elected as foreign associate of the US National Academy of Sciences and invited by Cornell University to become one of six 'professors-at-large' for an initial term of six years; Professor Dame Honor Fell (*Director, Strangeways Research Laboratory, Cambridge*): the Charles-Leopold Meyer Prize awarded by the Académie des Sciences de l'Institut de France; Dr J. R. Tata (*National Institute for Medical Research*): the Colworth Medal of the Biochemical Society; and Dr H. E. Huxley (*Laboratory of Molecular Biology*): the William Bute Hardy Prize of the Cambridge Philosophical Society.

In submitting this report covering their activities over the period 1 April 1965–31 March 1966, the Council wish, in conclusion, to express their gratitude to all those, including the members of their own staff, who have given them their help and advice, whether in an individual capacity or as members of special committees. This help has been of the greatest assistance to the Council in furthering their programme of research.

AMORY

Chairman of the Medical Research Council

HAROLD HIMSWORTH

Secretary of the Council
20 Park Crescent
London W.1

27 April 1966

SOME ASPECTS OF MEDICAL RESEARCH

The following articles review advances that have been made over recent years in some of the subjects with which the Council are concerned. It should be noted, however, that in order to give a balanced picture of the progress made in these fields the scope of the reviews is not confined to work sponsored by the Council.

SOME RECENT STUDIES ON THE STRUCTURE OF VIRUSES

Almost all that is now known about the detailed structure of viruses has been discovered in the last 10 years. Though this work has not yet led to any immediate prospect of a cure for virus diseases some principles have come to light, interesting in themselves, which also have a more general relevance in molecular biology. Virus structure is one of the areas where a start has been made in understanding how assemblies of inert molecules can acquire properties associated with life.

The nature of a virus

No obvious differences in clinical symptoms distinguish virus diseases and those caused by bacteria; bacteria and viruses both lead to cell death and destruction. But there is a fundamental distinction which goes beyond the simple observation that viruses are some thousand times smaller in volume than bacteria. On any definition a bacterium, though only a single cell, is a living organism. But an isolated virus has only some of the requirements for life. Though it carries all the genetic information necessary to reproduce its kind, it lacks the chemical machinery by which living things obtain energy. An isolated virus is unable to initiate its own replication and is lifeless. Only after access has been gained to a susceptible living cell does a virus become active. The cell's own metabolic processes are then usurped and redirected towards producing immense numbers of progeny virus, each an exact copy of the infecting one. A virus can thus be regarded as a simple structure built by a cell in response to the introduction of new genetic material from the invading virus. The cell is usually destroyed in the process.

When submitted to chemical analysis, all viruses are found to contain two essential constituents—nucleic acid and protein. A molecule of nucleic acid is now known to be necessarily present in every infectious virus particle, for it is the only type of molecule that can carry a genetic message. The protein surrounds the nucleic acid and has a dual role. It protects the long chain-like nucleic acid molecule from being broken and it helps the virus to enter susceptible cells.

Symmetry: a theoretical prediction

Nearly all the viruses that infect man and animals are approximately spherical in shape. Many consist simply of a core of nucleic acid surrounded by a protein shell. In 1956 Crick and Watson made some predictions about the structure of the protein shell, now known as the capsid. They argued that a virus could not carry a large amount of genetic information, so the capsid was unlikely to be a complex structure containing many different types of protein molecules. In a simple virus the ' bricks ' of which the surface is built could all be the same: a certain number of molecules of the same type might pack around the nucleic acid core to form the roughly spherical shell. The molecules in this capsid would be held together by some kind of attractive force; and if identical units are linked together in a stable way with the same forces acting on each unit, they must form a symmetrical arrangement so that nothing distinguishes one unit from any of the others. There are surprisingly stringent geometric limitations on the symmetrical packing of identical units to form a spherical surface. This can be illustrated by asking how identical postage

stamps can be stuck at points on a large sphere to give a symmetrical arrangement. (The obvious plan of spacing them equally around an equator is not counted since an equator is just a straight line and the arrangement would therefore not be three-dimensional.) Complete symmetry can only be achieved with 12, 24 or 60 stamps; with any other number, some stamps would have to be placed in different positions with respect to their neighbours and identical forces could not act on units in such an arrangement. For this reason Crick and Watson predicted that the capsid of a virus might well consist of 12, 24 or 60 identical subunits.

Electron microscopy

Most viruses are too small to be seen at all with ordinary microscopes and it is not possible to distinguish the details of their structure by ordinary optical means. At present there are two main techniques that can give information about virus structure. One is the indirect method of X-ray crystallography. Some viruses when produced in sufficient amounts can actually be made to crystallize and it may then be possible to learn something about the virus from the way the crystals diffract a beam of X-rays. However, most of our present knowledge about virus structure has come more directly from electron microscopy. Modern electron microscopes are very powerful and capable of distinguishing even individual atoms. Unfortunately there are difficulties in realizing this high resolution with biological specimens and it is only recently that techniques have made detail at the molecular level visible.

The first electron microscope pictures that clearly showed the molecular arrangement in a virus capsid were obtained at the Cavendish Laboratory, Cambridge (Horne *et al.*, 1959). A now classical picture of the adenovirus, a cause of feverish sore throats in man, showed that it has the shape of an icosahedron, a regular solid with 20 equilateral triangles as faces. (A similar electron micrograph of the adenovirus is reproduced in plate II (*a*).) The surface is composed of 252 units. Since this is not one of the numbers predicted by Crick and Watson, it must be that the units are not all symmetrically placed. Some form the edges of the icosahedron, some the vertices and some the centres of its faces. In particular, the units at the 12 vertices, each of which is surrounded by a ring of 5 neighbours, can be distinguished from the remaining 240 units, all with 6 units around them. This led Caspar and Klug (1962) to propose a modification of the original suggestion made by Crick and Watson. It is known that the direction of chemical bonds may be varied by up to 5° and the new theory is based on the idea that the demand for exact symmetry can be slightly relaxed to take account of this. Caspar and Klug fully explored the theoretical consequences and gave a mathematical classification of the possible numbers and arrangements of identical structural units that could make up approximately spherical shells. The theory demands a multiple of 60 structural units in each virus capsid, but this need not be the number of units seen by electron microscopy: the morphological units seen in the electron microscope pictures may be formed by clusters of structural units.

Further information about the molecular structure of virus surfaces has been given in recent publications by workers in two of the Council's laboratories. In both cases progress has resulted from improved techniques for viewing biological material in the electron microscope.

Adenovirus: an icosahedron with antennae

Work at the National Institute for Medical Research (Valentine and Pereira, 1965) has provided more information about the surface structure of the adenovirus. The proteins that form the adenovirus capsid were studied by observing their reactions with antiserum and were shown to be of quite distinct kinds. They have been purified and examined by electron microscopy. The units of one of the capsid proteins studied in this way, known as antigen A, appear to be more or less spherical and of similar diameter (about 80 Å) to the units seen by electron microscopy on the adenovirus surface. A second, antigenically quite different, protein was also found in the adenovirus. This is antigen B and when seen in the electron microscope it was found to have units of an unexpected shape. A head, similar to the units of antigen A, carries an antenna-like projection, on the end of which a knob can be seen. Units of both antigens are shown in plate II (*b*).

The problem of how the two types of molecule fit together to form the capsid also seems to have been solved. It was observed that when the adenovirus was broken by treatment with dilute alkali or with detergent, about 20 times as many units of antigen A were released as of antigen B. This suggested that perhaps antigen B formed the 12 vertices of the capsid and antigen A occupied the 240 other positions. Support for this idea came when it was noticed that in partly broken virus, units of antigen A were often surrounded by six similar units but that the units with antennae, antigen B, were either isolated or surrounded by five units of antigen A. To have five neighbours is the unique property of the units at each vertex. Finally pictures were obtained in which the antennae were clearly seen projecting from the vertices of the adenovirus (plate III). A model built to show the arrangement of the two proteins in the adenovirus capsid is illustrated in plate IV (*a*).

The function of the various remarkable features of the adenovirus, in particular of its twelve antennae, is still partly a matter for speculation. The very stable icosahedral shell is clearly well designed for its role of protecting the nucleic acid molecule which is folded up inside it. The antennae of the corner units are believed to have a role in the attachment of the virus to the cell it will infect. They may also play some part in the penetration of the virus into the cell, which is a necessary preliminary to the infection process. The corner units are less stable than the others. It could perhaps be the breakdown of these units inside the cell which releases the nucleic acid to start the replication of new virus.

Wart viruses: right- and left-handedness

The structure of the capsid of viruses of the papilloma–polyoma group has been under investigation at the Council's Laboratory of Molecular Biology at Cambridge (Klug and Finch, 1965; Finch and Klug, 1965). The human papilloma virus is the cause of warts in man. These growths are benign but the somewhat similar polyoma virus produces malignant tumours in experimental animals. The arrangement of the units in the capsid is harder to distinguish in these viruses than in the adenovirus. This has previously led to some confusion about the number of units in the capsid. The work at Cambridge involved the analysis of the arrangement of units on variously oriented virus particles and made use of the technique of stereo electron microscopy to gain a three-dimensional impression of the virus. It now seems established that the wart

viruses have 72 units in the capsids. Twelve of these are arranged in the same way as the units with antennae in the adenovirus, one at each vertex of an icosahedron. The other 60 form symmetrical rings of five about each vertex. The rings neatly interlock and it is here that an interesting point arises. As plate IV (*b*) shows, there are two distinct ways in which the rings of five units can be linked; the virus can have a ' right-handed ' or a ' left-handed ' form. In arrangement D, the rings of five units are interlocked so that a path through the units from the centre of one ring to the centre of any neighbouring one involves two moves forward and one diagonally to the right. This is defined arbitrarily as the ' right-handed ' (*dextro*) form. Arrangement L (two moves forward and one diagonally left) is defined as ' left-handed ' (*laevo*). Although the right- and left-handed models are unambiguously so when viewed directly, right and left can be interchanged in the formation of a photographic image. This reversal may occur at a number of stages in the production of an electron microscope picture. When these considerations were taken into account, it was found that the human wart virus is right-handed and the rabbit wart virus left-handed.

General principles of virus structure

In the adenovirus and papilloma viruses, the 12 units on the vertices of the icosahedron are each surrounded by a ring of five neighbouring units so that there are 60 such units symmetrically disposed over the surface of the virus. It is this that inevitably gives the viruses built in this way their icosahedral symmetry. This may be a common plan to which all the approximately spherical viruses are built. In the adenovirus, the 12 corner units are an entirely different protein from the other units. It is not yet known if this is true of all similarly shaped viruses.

Crick and Watson suggested that the virus surface might be composed of 60 identical molecules. It now seems that its structure is more complex, since in the adenovirus at least there are two distinct proteins in the capsid. But the number 60 may still, in a slightly different way, be the basis of the geometrical structure of viruses.

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ABNORMAL HAEMOGLOBINS

Haemoglobin, the oxygen-carrying pigment of the blood, is one of the more complex proteins, with a molecular weight of about 68 000. More than a hundred years ago it was realized that man has at least two different haemoglobins. One forms the major component at birth and is called foetal haemoglobin (Hb F); it disappears fairly early in infancy, to be replaced by adult

haemoglobin (Hb A). By more refined techniques it was discovered that adult man possesses not only Hb A but also a minor second component, Hb A_2, which amounts to about 2 per cent of the total. It is now known that each of these three haemoglobins contains four polypeptide chains, two of one type and two of another. The different types of chain are designated α, β, γ and δ, Hb A having the composition $\alpha_2\beta_2$, Hb F $\alpha_2\gamma_2$ and Hb A_2 $\alpha_2\delta_2$. It is possible that there is present in very early embryos yet another haemoglobin, $\alpha_2\epsilon_2$ (Huehns *et al.*, 1964), though no traces of the ϵ-chains are found at birth. Thus all haemoglobins have the α-chains in common but they differ in the other half of the molecule.

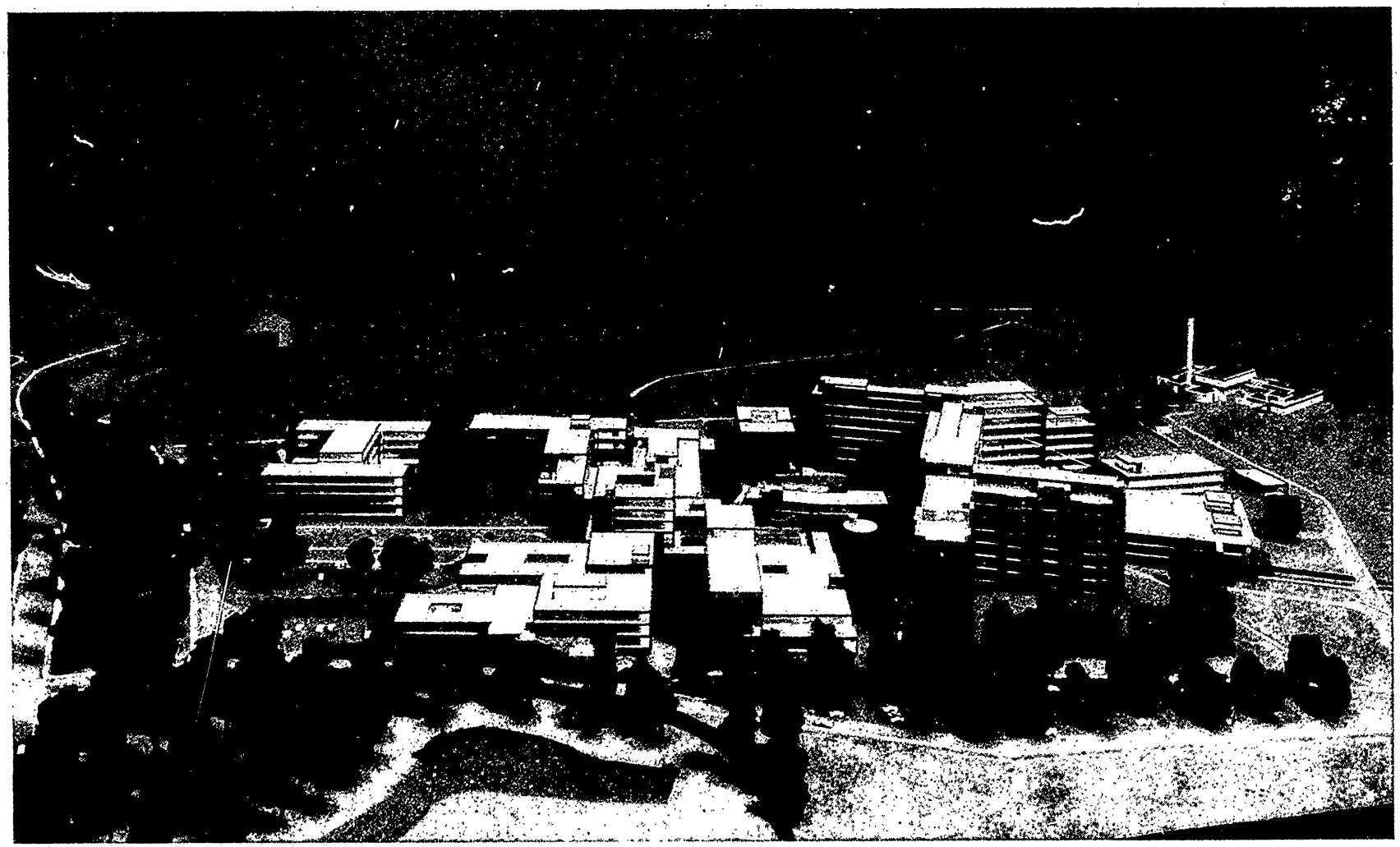
The structure of haemoglobins

In 1949 Pauling investigated the haemoglobin derived from patients with sickle-cell anaemia (a usually fatal disease found chiefly in Negro populations). He used electrophoresis, a technique that depends on the movement of charged protein molecules to either the positive or the negative electrode, and by this method he was able to demonstrate that in patients with sickle-cell anaemia the haemoglobin (Hb S) was different from that of normal adults (plate V). This discovery led to the development of the concept of ' molecular diseases '—that is, diseases arising from abnormalities of chemical structure in molecules essential to physiological function. Other haemoglobin variants were discovered by this means, and until a few years ago they were classified according to their electrophoretic properties. The simple technique of electrophoresis is still important for surveys of patients in hospital and for anthropological investigation, but it is not able to reveal the detailed chemical structure of haemoglobins. Sanger (1952), then a member of the Council's external scientific staff, inaugurated the structural study of proteins with his pioneering studies on the relatively simple insulin molecule; and his approach was extended by Ingram (1956), also working for the Council, to the more complex haemoglobin molecule.

Ingram's method consisted of breaking down the haemoglobin molecule to a mixture of small peptides under standard conditions. The mixture was separated into its components by electrophoresis followed by chromatography on paper, the resulting chromatogram forming a pattern (' fingerprint ') characteristic of the original protein. Application of this technique to normal haemoglobin and to sickle-cell haemoglobin revealed that one peptide in the former was replaced by a different one in the latter; by complete analysis of these two peptides the difference between the two haemoglobins was identified as the substitution of glutamic acid in normal haemoglobin by valine in Hb S, in position 6 of the 146 amino acid residues in the two β-chains. The complete amino acid sequences of the α-, β- and γ-chains, and most of the sequence of the δ-chain, were later worked out at laboratories in Münich (Braunitzer *et al.*, 1961), New York (Konigsberg, Guidotti and Hill, 1961), Pasadena (Schroeder *et al.*, 1963) and Cambridge, Massachusetts (Ingram and Stretton, 1962).

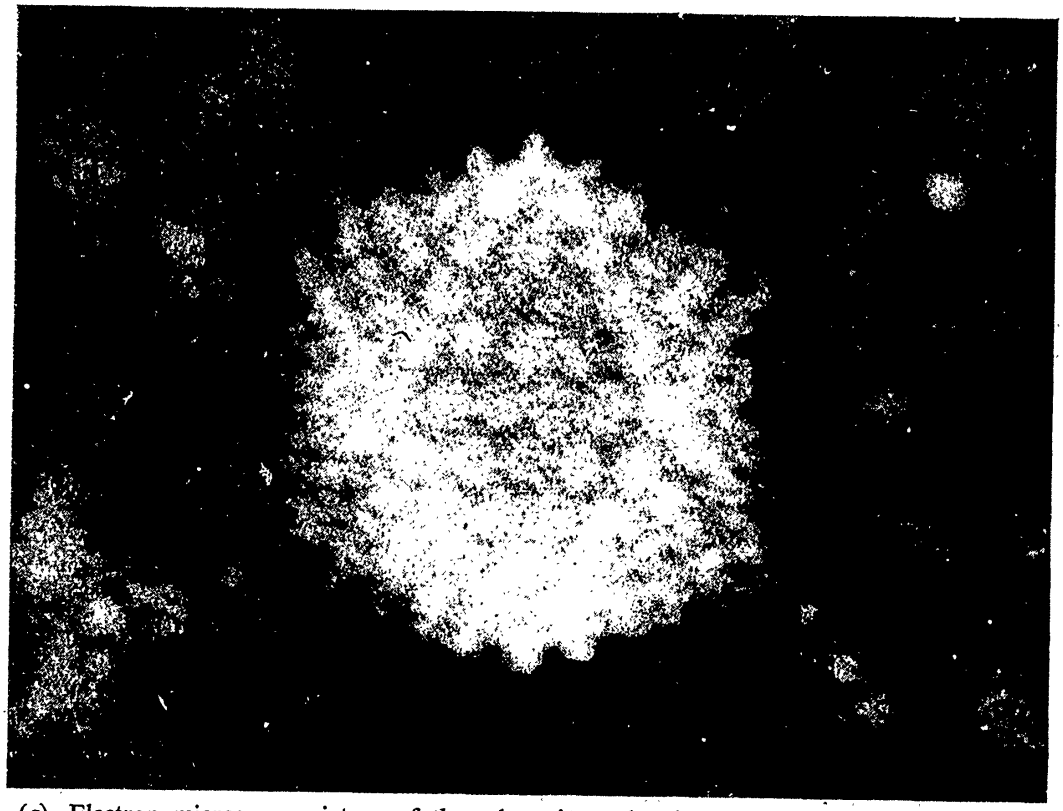
Meanwhile the three-dimensional or tertiary structure of various proteins, which results from the folding of the polypeptide chains, was being intensively investigated by the physical method of X-ray crystallography at the Council's Laboratory of Molecular Biology and elsewhere. Kendrew, working with myoglobin (the oxygen-carrying haem-protein of muscle, which consists of only one polypeptide chain) from the sperm whale, and Perutz, working with horse haemoglobin, were for the first time able to build models showing the fine structure of protein molecules. The tertiary structures of the α- and the β-chains

PLATE I

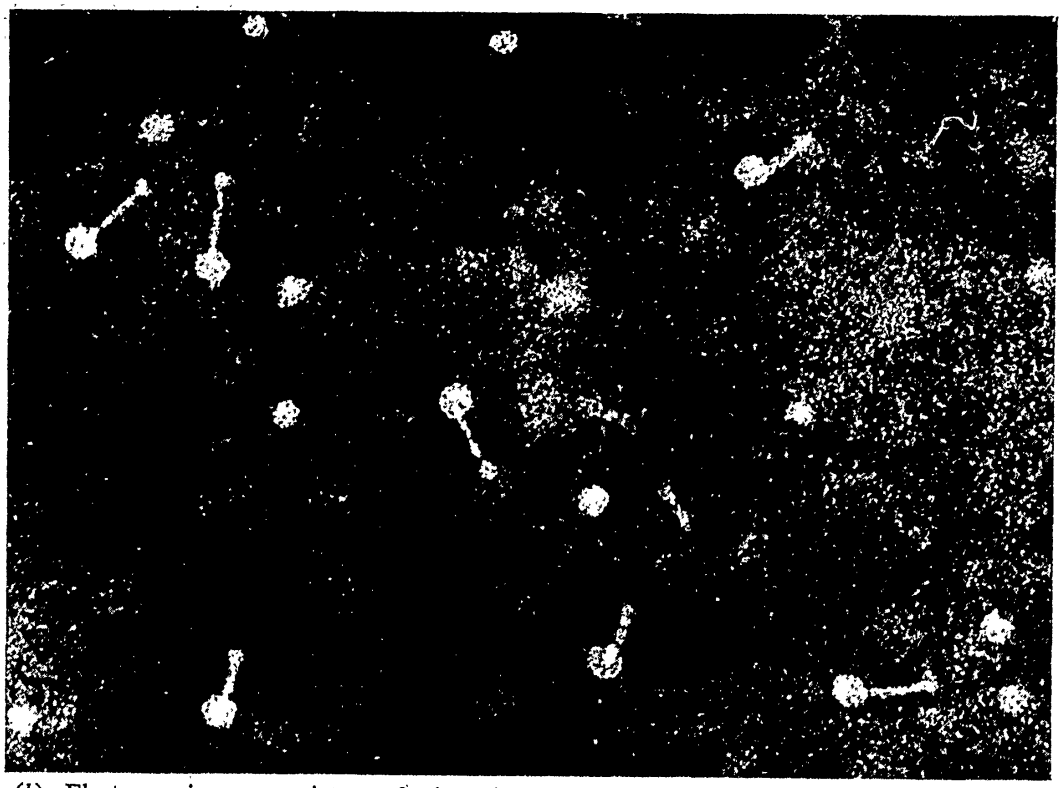


Northwick Park project: photograph of model

PLATE II



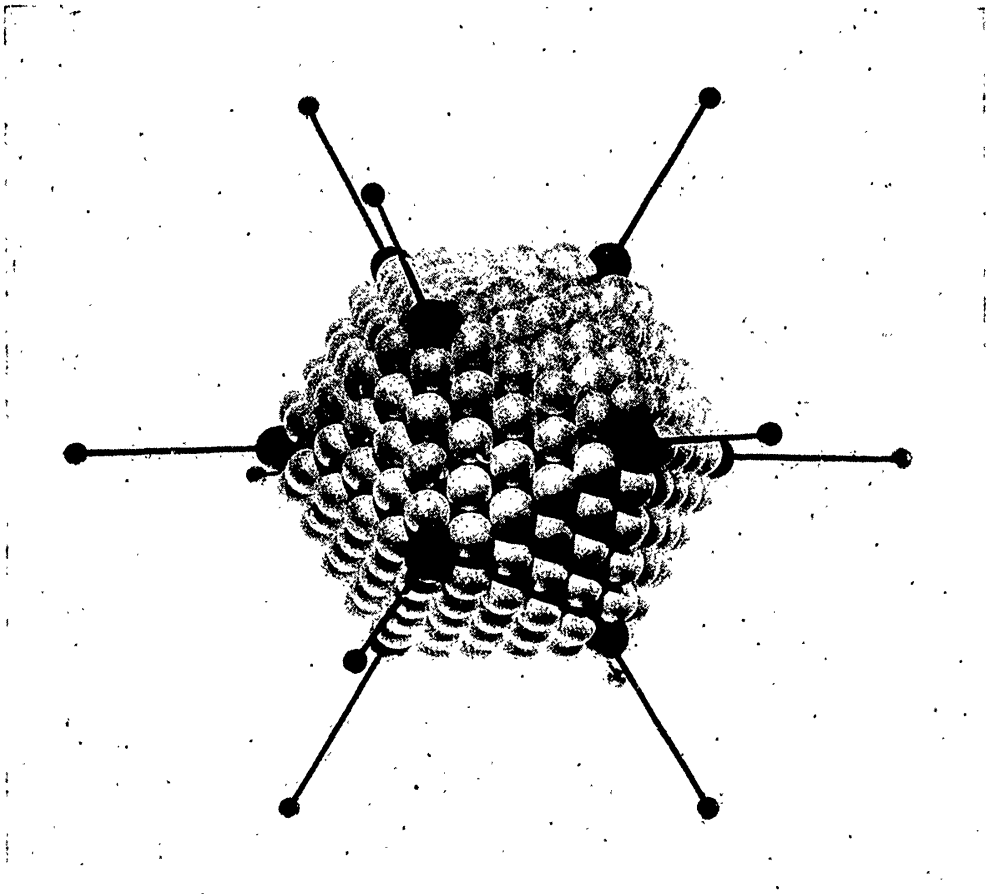
(*a*) Electron microscope picture of the adenovirus, showing the icosahedral arrangement of surface units (× 750 000).



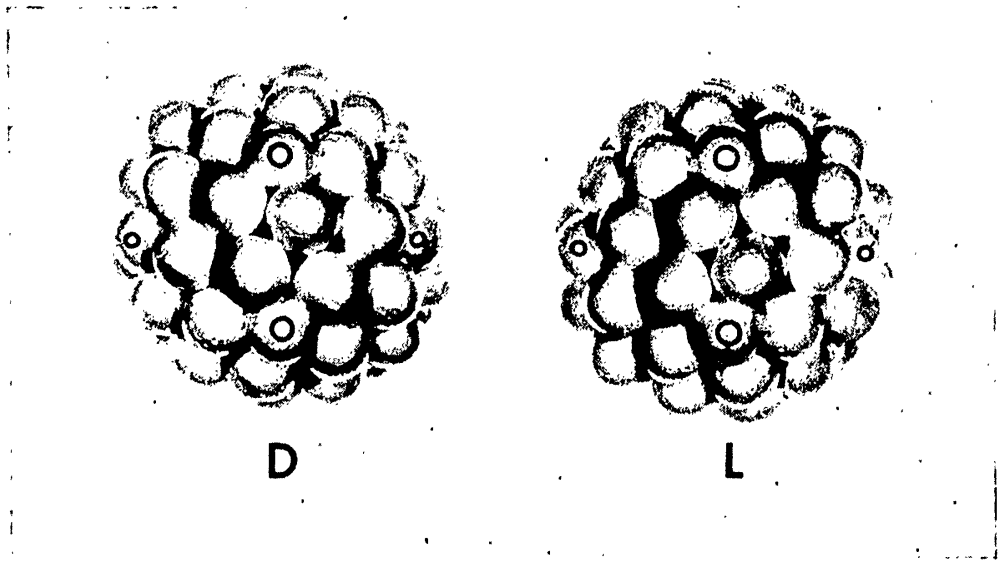
(*b*) Electron microscope picture of adenovirus surface units, showing the two quite distinct kinds, one approximately spherical and the other carrying a projection with a terminal knob (× 500 000).

Adenovirus particles; the projections associated with the vertices can be seen (× 300 000).

PLATE IV

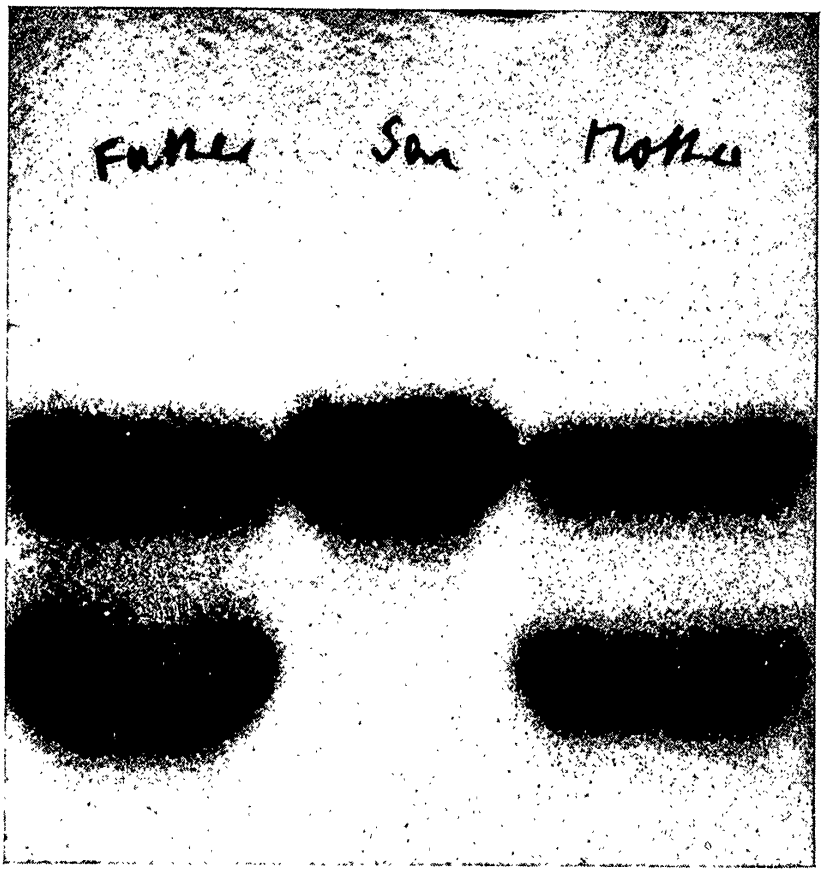


(*a*) A model of the adenovirus, built to show the arrangement of the two types of surface unit.



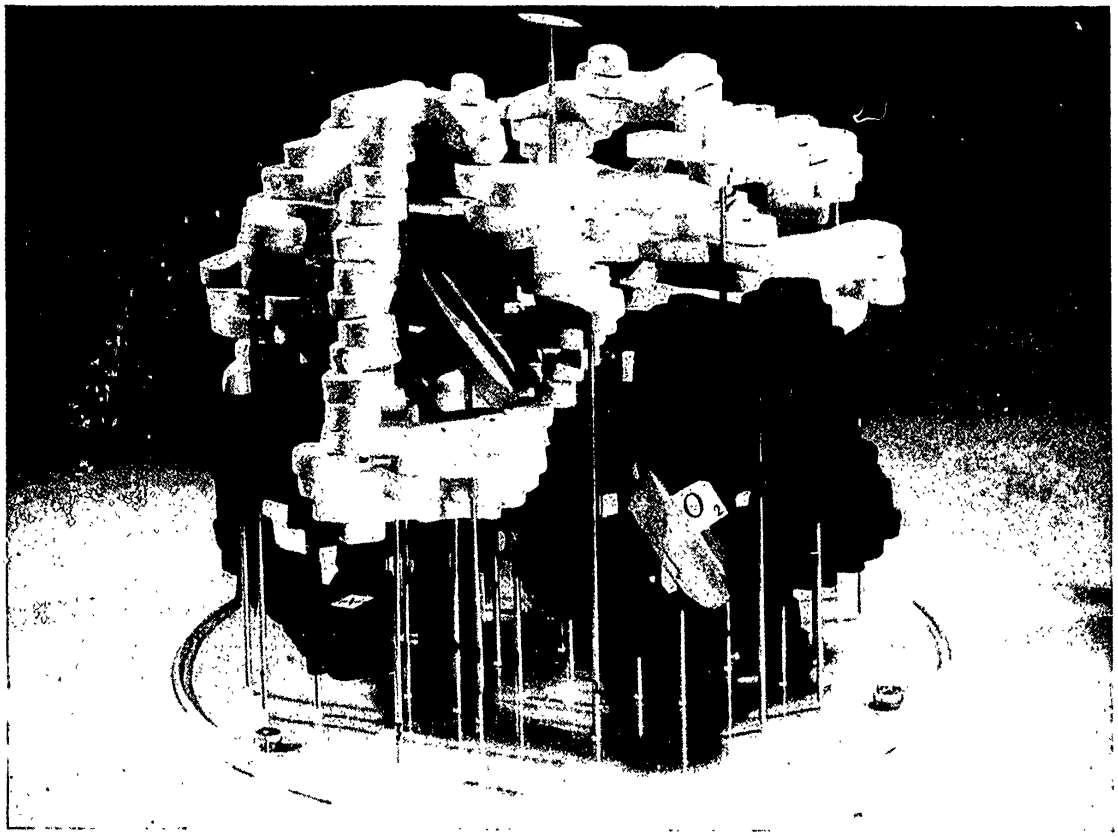
(*b*) The arrangement of surface units in the wart viruses. The twelve units that have five neighbours lie on the vertices of an icosahedron; four of these are shown marked with an O. In the right-handed form (D), found in the human wart virus, the path from one vertex through the units to any neighbouring vertex goes two steps forward and one diagonally to the right. In the left-handed form (L), found in the rabbit wart virus, the path goes two forward and one to the left.

PLATE V



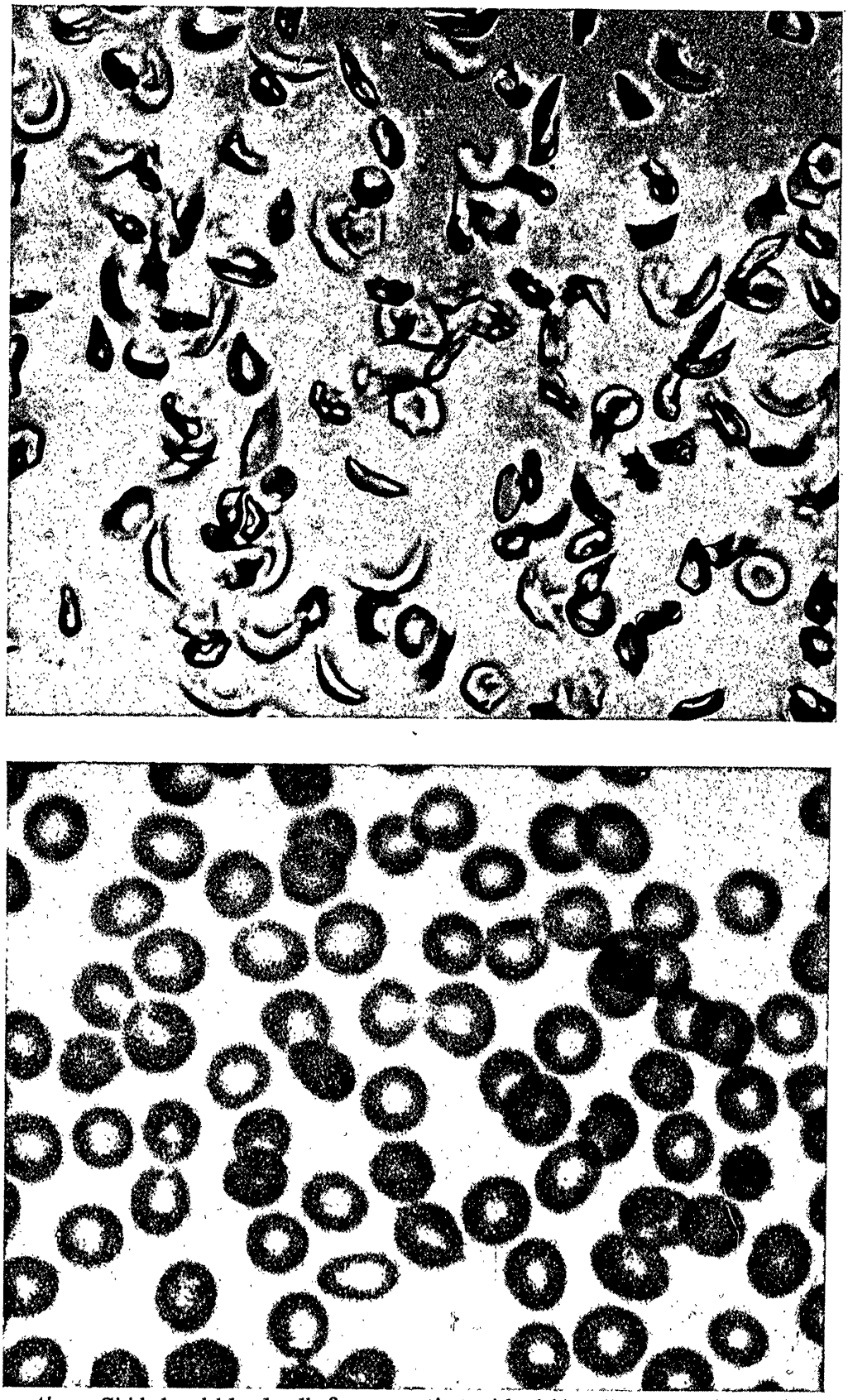
Electrophoresis of haemoglobin illustrating the inheritance of sickle-cell anaemia: the parents are both heterozygous for the sickle-cell gene and have both normal and sickle-cell haemoglobin, shown here after separation by electrophoresis; the son, having inherited the abnormal gene from both his parents, has only sickle-cell haemoglobin and suffers from sickle-cell anaemia.

PLATE VI



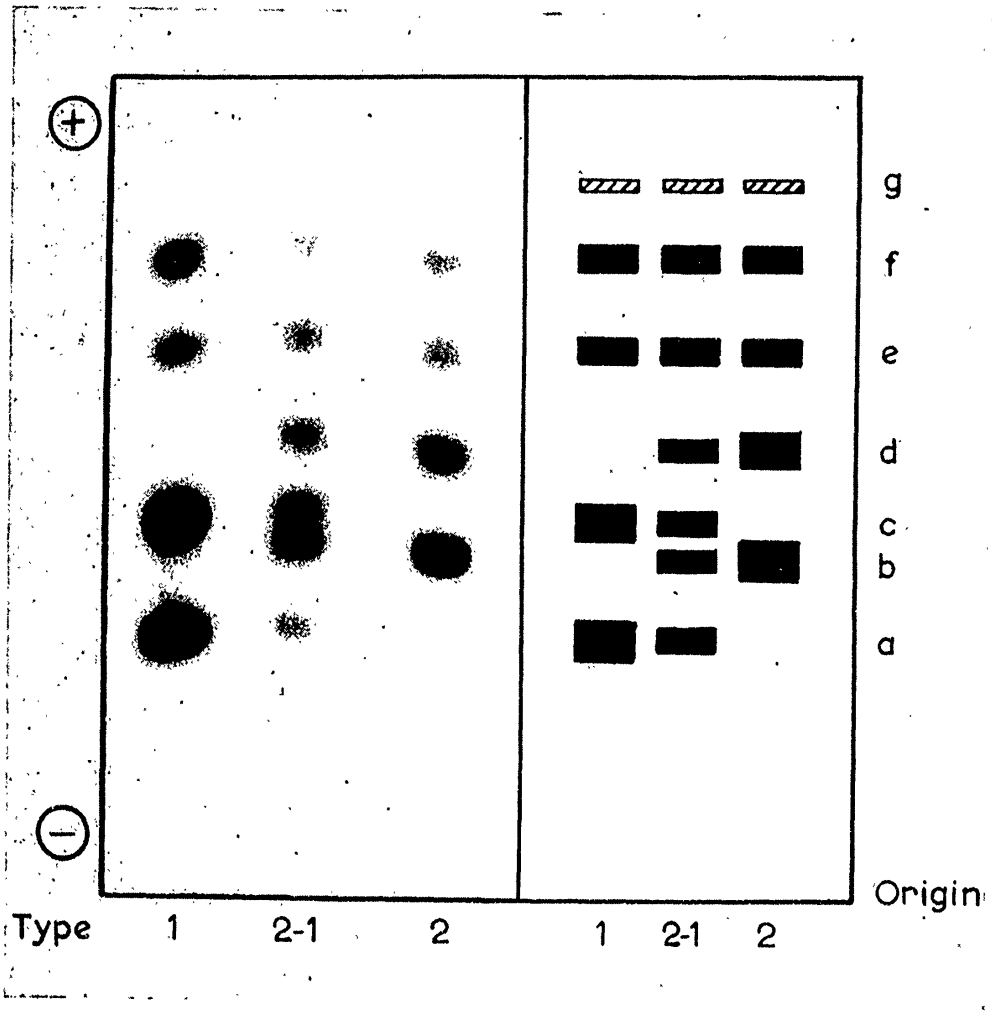
Model of haemoglobin molecule. The two α-chains are represented in black and the two β-chains in white; the discs represent the haems.

Reproduced by courtesy of Dr M. F. Perutz, Laboratory of Molecular Biology



Above: Sickled red blood cells from a patient with sickle-cell anaemia (× 1000).
Below: Normal cells (× 1000).

PLATE VIII



Photograph and diagram of phosphoglucomutase isoenzyme patterns obtained by starch gel electrophoresis at pH 7·4.

Reproduced by courtesy of the Royal Society

of human haemoglobin, even though they have less than half of their amino acid sequences in common, are strikingly similar, and these in turn have a very similar structure to that of horse haemoglobin. Moreover, the single polypeptide chain of sperm whale myoglobin (which has less than 5 per cent of its amino acid sequence in common with the α- and β-chains of human haemoglobin) is remarkably similar in structure to that of human and horse haemoglobins.

The tertiary structure of the haemoglobin molecule (see plate VI) is extremely complex. It is, moreover, very adaptable, for the chains move apart when oxygen is lacking and move together when the molecule becomes oxygenated. It would thus appear that it is this peculiar structural association of the four chains that enables haemoglobin to absorb oxygen at high tension and release it as the tension falls and also to respond to a rise in carbon dioxide in the body by releasing oxygen more readily.

The abnormal haemoglobins

After years of intensive survey work—much of which has been carried out by the Council's Abnormal Haemoglobin Research Unit under the honorary direction of Dr H. Lehmann—some three dozen variants of the haemoglobin molecule have been discovered. While all these variants have interest for the molecular biologist and the geneticist, only four, which affect many millions of the world's population, occur sufficiently commonly to present a major clinical problem (see figure 1 for a map of their distribution). The diseases arising from these four abnormal haemoglobins present a significant problem of public health. In Great Britain there is much concern about the lymphoblastic leukaemia of childhood, which affects about three in every 100 000 children born; yet in Nigeria about 1000 of every 100 000 children born will suffer from sickle-cell anaemia, and the great majority of them will die. The magnitude of the problem has not yet been properly assessed.

Sickle-cell haemoglobin is unique because it is peculiarly insoluble in the reduced state, and is liable to crystallize within the red cell and so distort the cell envelope (plate VII). Such distorted cells increase the viscosity of the blood, blocking nutrient vessels and causing death of tissue (infarction) in the organs which they supply. Such infarctions occur especially in the bones, spleen and lungs.

Sickle-cell anaemia is an inheritable disease. The many millions of heterozygote carriers of the sickle-cell trait, who have inherited the abnormal gene from only one parent, are little affected because they have sufficient normal haemoglobin in each cell for sickling not to occur in ordinary conditions. However, the children of two such carriers have a one in four chance of being homozygous, having inherited the gene from both parents. The resulting sickle-cell anaemia leads to certain death in childhood, at least where the full resources of modern medicine are not to hand; where these are available the children may on occasion survive into adult life but they are constantly subject to bouts of illness and anaemia. Yet in spite of the fact that homozygotes seldom reproduce, in parts of Africa about 20 per cent of the population (and in certain places as many as 40 per cent) carry the gene. Clearly the carrier state must confer some advantage over the normal in certain environments and there is in fact strong evidence that carriers are more resistant than others to malignant tertian malaria; it appears that their abnormal red blood cells are less suitable for survival of the malaria parasite (Allison, 1957). Certainly the geographical distribution of the

sickle-cell trait follows the distribution of endemic malaria, occurring as it does not only in Africa but also sporadically in the Middle East and in aboriginal tribes of India. It is also found among Negroes in America; but there, in a non-malarious environment, the frequency has dropped to 8 or 9 per cent.

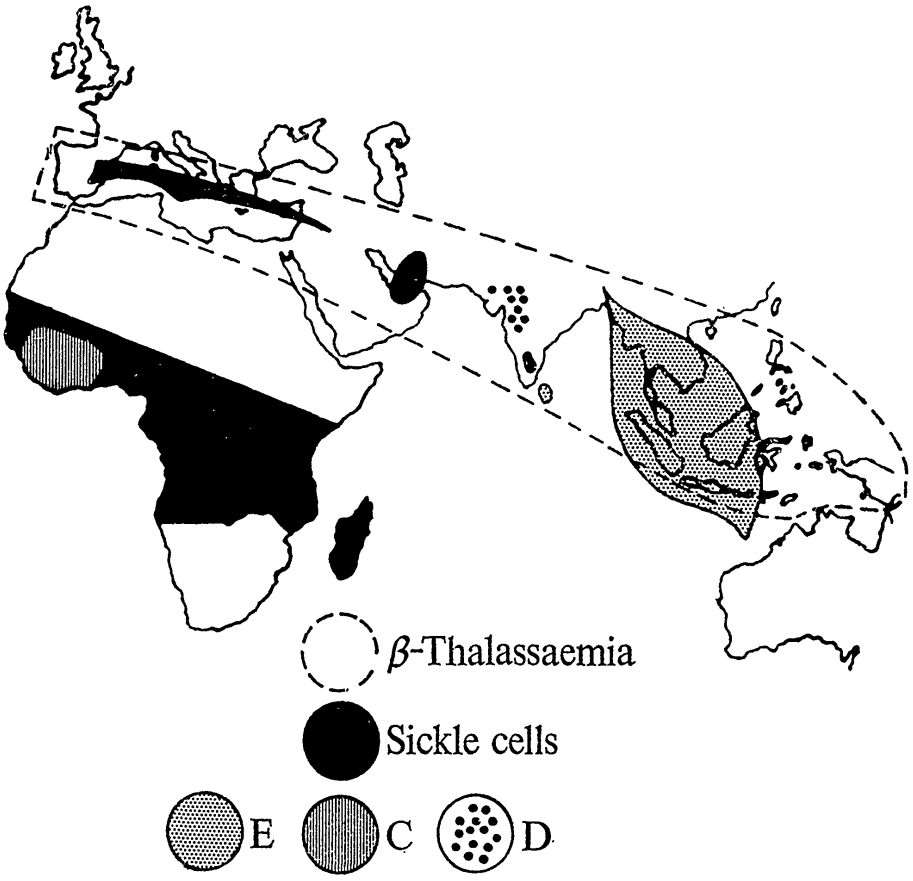


FIGURE 1

World distribution of the major haemoglobin abnormalities. (From Lehmann, Huntsman and Ager, 1965.)

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The other three common haemoglobin variants are Hb C, D and E. These haemoglobins are characterized by the substitution of different amino acids in the β-chain, the genes responsible for their inheritance being allelic to the Hb S gene. Although they are not so severely affected as are patients with sickle-cell anaemia, individuals who are homozygous for these variants are liable to some anaemia and react poorly to any extra demands on their blood-forming tissues, such as are presented by pregnancy or infection. It is possible that these haemoglobins also protect against malaria. However, selection against the homozygotes is less rigorous in these cases than against sickle-cell homozygotes, and it is therefore more difficult to obtain unambiguous evidence for the protective effect of the abnormality. There are many millions of carriers; Hb C is found mainly in West Africa (in 27 per cent of the population in some parts), Hb D in the Punjab (in 3 per cent of the population) and Hb E in the Far East

(particularly Thailand and Burma, where the prevalence is 14 per cent). Hb D also occurs occasionally in Europe and the United States—a finding that raises intriguing anthropological questions: is it the result of the close ties between Europe and India during the last 200 years or did the Mongols bring the gene both to the Punjab and to Europe?

Beta-thalassaemia or Mediterranean anaemia affects many millions of people in a wide belt stretching from the Mediterranean to China and New Guinea, the frequency reaching 30 per cent in the Po valley in Italy; the distribution appears to follow that of malaria (at least before eradication programmes were undertaken). In contrast to the diseases described above, the disorder is not due to the substitution of a different amino acid in the molecule of haemoglobin but is the outcome of defective synthesis of the normal polypeptide chains of the haemoglobin molecule. β-Thalassaemia affects only the β-chains of Hb A, and the production of the other chains—α, γ and δ—is not inhibited. Hence the synthesis of Hb F and A_2 may be increased in compensation, and a raised proportion of Hb A_2 to Hb A is a clue to diagnosis in the heterozygotes. A compensatory increase in Hb F is particularly pronounced in the homozygotes, and also occurs to a lesser extent in many heterozygotes. The heterozygote carrier state results usually in only mild anaemia, but the homozygotes almost invariably die in childhood. These children may be kept alive for some years by multiple transfusions but may then die from an excess of iron, derived from the breakdown of the transfused blood. Treatment with iron chelating agents, which combine with iron and remove it from the body, is now being attempted, but this has not yet been developed into an effective form of therapy because those chemicals used so far do not remove enough iron to have any clinical effect. In the less common α-thalassaemia (which in its most severe form results in stillbirth) the synthesis of the α-chains is defective. In certain types of α-thalassaemia, the β-, γ- and δ-chains combine to form unstable tetramers. Examples are Hb H, which consists of four β-chains (β_4), and Hb Bart's, which consists of four γ-chains (γ_4).

The recognition of carriers of both the sickle-cell trait and of β-thalassaemia is a matter of some practical importance since they constitute a significant proportion of the population in some parts of the world. Large-scale screening could provide a basis for genetic counselling.

The rare haemoglobins

About 25 less common variants have now been discovered as a result of extensive surveys. Some of these appear to be common in restricted regions of the world; for instance Hb G-Chinese has been found solely in the Chinese (see Lehmann and Huntsman, 1966).

Amino acid substitutions can occur not only in the β- but also in the α-, γ- and δ-chains; an alteration in the α-chain will obviously give rise to abnormalities in all three haemoglobins—A, A_2 and F—and alterations in the γ- and δ-chains to abnormality of Hb F and Hb A_2 respectively. A small number of mutations that cause changes in the structure of the molecule near the iron atom to which the oxygen is attached result in instability of the haemoglobin and consequently in anaemia. These mutations are rare but of considerable theoretical interest. An example is Hb Zürich. In this haemoglobin one of the two histidine residues of the β-chain to which the haem group is linked is replaced by an arginine

residue. The haemoglobin functions normally, but is much less stable than Hb A. If carriers of Hb Zürich receive a single dose of sulphonamide the haemoglobin is oxidized to methaemoglobin and loses its oxygen-carrying capacity and this results in cyanosis (in normal individuals this only happens after prolonged sulphonamide therapy). In addition the haemoglobin will precipitate inside the cells and form inclusion (Heinz) bodies. A rapid elimination of these cells in the spleen will then give rise to a haemolytic crisis. The response of such patients to sulphonamide is a typical example of a genetically determined drug sensitivity. Other genetically determined changes occurring in this region of the polypeptide chain similarly cause oxidation of the ferrous atom of the haemoglobin to the ferric state and thus make the molecule unable to carry oxygen. These haemoglobins are called Hb M (M for methaemoglobin) and the condition in which they are found and of which cyanosis is the predominant sign has been named haemoglobin M disease. There are various forms of these haemoglobins —for example Hb M Boston and Hb M Iwate, in each of which one of the haem-orientated histidines of the α-chain is replaced by tyrosine. Hb M Iwate was found to be the cause of the ' black blood disease ' or hereditary nigraemia observed in some families in Japan.

Other variants of haemoglobin have been found only in single families and appear to result from harmless mutations. Such variants are almost always found whenever large surveys are undertaken, and indeed four have been found in native English families. Although of no clinical importance they have added to knowledge of the amino acid substitutions that may occur in the polypeptide chains and are helping to clarify the relation between amino acid composition and the function of the haemoglobin molecule.

Haemoglobin variants and mutation

Each of the haemoglobin variants so far discovered results from a single mutation*. This has long been apparent from the pattern of inheritance of the variants, and the finding that the abnormality consists in each case in only a single amino acid substitution provides additional confirmation.

The sequence of incorporation of amino acids into a protein is determined by the nucleotide sequence of the DNA in the nucleus, and one amino acid change in a protein results from one nucleotide change in the DNA. The genetic code, by which certain nucleotide triplets in DNA specify one amino acid in the protein, has been worked out with bacteria and viruses. Human haemoglobins are an ideal test material on which to check whether this code applies to the synthesis of mammalian proteins. Each of the amino acid substitutions found in the human haemoglobin variants has proved to be compatible with a single change in a triplet of the genetic code as worked out by Nirenberg and his colleagues (1965). There appeared at first to be one exception, since it had been reported that in Hb I aspartic acid was substituted for lysine. It will be seen from table 1 that according to the genetic code this change cannot occur through a single mutation, since the nucleotide code for lysine is AAA or AAG and the code for aspartic acid GAU or GAC. However, on re-examination of this haemoglobin

*A variant of sickle-cell haemoglobin carrying a second amino acid substitution in the β-chain, and thus involving two mutations, has just been described. In this haemoglobin (which has been named Hb Harlem) glutamic acid is replaced by valine in the sixth position on the β-chain, as in Hb S, and in position 73 aspartic acid is replaced by asparagine (Bookchin *et al.*, 1966).

it was found that in fact glutamic acid (code GAA or GAG) was substituted for lysine—a change which is fully compatible with the genetic code. (Beale and Lehmann, 1965.)

TABLE 1

Messenger ribonucleic acid codons for amino acids involved in substitutions in human haemoglobin (surmised bases in italic)*

(Of the 20 amino acids known to occur in proteins no substitutions have yet been discovered involving cysteine, tryptophan, phenylalanine or isoleucine)

Lysine	AAA AAG	Methionine	AU*A* AUG	Glutamic acid	GAA GAG
Asparagine	AAC AAU	Glutamine	CAA CAG	Aspartic acid	GAC GAU
Threonine	ACA ACG ACC ACU	Histidine	CAC CAU	Alanine	GC*A* GCG GC*C* GCU
Arginine	AGA AG*G* CGA CG*G* CGC CG*U*	Proline	CCA CC*G* CCC CCU	Glycine	GG*A* GGG GG*C* GGU
Serine	AGC AGU UC*A* UCG UCC UCU	Leucine	CU*A* CUG CUC CUU UU*A* UUG	Valine	GU*A* GUG GU*C* GUU
				Tyrosine	UAC UAU

*A, adenine; C, cystosine; G, guanine; U, uracil.

Electrophoresis, the method by which haemoglobin variants are discovered, separates one haemoglobin from another carrying a different charge in an electrical field. To alter the charge the mutation has to involve the replacement of a neutral by an acidic or a basic amino acid (that is, either by glutamic or aspartic acid or by lysine or arginine), or the replacement of a basic or an acidic amino acid by a neutral one or, lastly, a change from an acidic to a basic amino acid or vice versa (that is, a change from lysine to glutamic acid or from glutamic acid to lysine—the only double charge change permitted by the genetic code in a single mutation). If isoleucine (which occurs in Hb F only) is included there are 20 amino acids, for which there are as many as 96 possible mutations that would not alter the charge of the haemoglobin molecule (and 50 that would). For example serine can mutate in a single step to any of twelve different amino acids. Eleven of them are neutral and only one, arginine, carries a different charge from serine. We may therefore expect that there are still a large number of haemoglobin variants to be discovered that cannot be demonstrated by electrophoresis.

The investigation of human haemoglobins has demonstrated at the molecular level the immense number of variations permitted by man's genetic endowment,

and it may be predicted with confidence that similar pathological, biochemical, genetic and anthropological studies will be carried out on many other human and animal proteins in the future.

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ENZYME DIVERSITY IN HUMAN POPULATIONS

It is now generally believed that genes exert their effects by directing the synthesis of enzymes and other proteins. There are of course a very large number of different enzymes in the human organism, and if current theory is correct one must suppose that the molecular structure of each of these is determined by at least one gene, and that there are probably other genes primarily concerned with regulating the rate of synthesis of particular enzymes or groups of enzymes. Many loci on the chromosomes can be occupied by two or more different forms (alleles) of the gene concerned, and this is the basis of genetical diversity. Thus one would anticipate that genetical diversity in a population should to a large extent be reflected in enzyme diversity, that is to say in differences between individuals either in the qualitative characteristics of the enzymes they synthesize or in the rates of synthesis. It is a matter of some interest therefore to inquire how extensive such enzyme differences between people may be.

Enzyme deficiencies

It has of course been recognized for quite a long time that certain rare metabolic disorders, the so-called ' inborn errors of metabolism ', are due to genetically determined deficiencies of specific enzymes. A considerable number of these conditions are now known (Harris, 1963), and judging from the increasing rate at which new examples have been described in recent years it seems likely that many more remain to be identified. These conditions have in general been attributed to mutant genes that result either in the synthesis of an abnormal enzyme protein with defective catalytic properties or in a severe curtailment of the normal rate of synthesis of the enzyme protein.

Homozygotes, individuals inheriting such a gene from both parents, show a gross reduction and sometimes an apparently complete absence of activity of the particular enzyme concerned, and this may result in quite striking and often serious metabolic and clinical consequences. Well known examples of such disorders are phenylketonuria, galactosaemia and maple syrup urine disease (all of which involve mental subnormality—see Medical Research Council, 1963) and pyruvic kinase deficiency, which causes haemolytic anaemia. Heterozygotes, individuals who have inherited the mutant gene from only one parent, frequently exhibit a partial deficiency of the enzyme, the level of activity often being only about half that normally present. However, such heterozygotes are usually quite healthy, presumably because the remaining activity is still adequate for normal metabolic functioning.

Most of these mutant genes appear to be relatively uncommon, occurring in between about 1 in 50 and 1 in 500 of the population (i.e. their frequencies are between about 0·01 and 0·001). Nevertheless, one may expect that in aggregate they will account for an appreciable degree of enzyme variation among apparently normal individuals, because many people will be heterozygous for one or other of them. About 1 per cent of the European population are heterozygous for the gene determining phenylketonuria and have a partial deficiency of the enzyme phenylalanine hydroxylase. This of course is only one example out of many. Specific enzyme deficiencies are also known that occur quite commonly in certain populations. The most extensively studied example is glucose-6-phosphate dehydrogenase deficiency, which is prevalent in Mediterranean countries and in parts of Africa, and is the cause of favism (a severe haemolytic anaemia precipitated mainly by eating broad beans) and also of anaemia in people treated with certain drugs. The relatively high incidence of this enzyme deficiency in these populations is thought to be due to the fact it may confer resistance to malaria; this would give it a selective advantage in parts of the world where endemic malaria is an important factor in natural selection (Motulsky, 1964).

Until very recently most of our knowledge of genetically determined enzyme variation in human populations was derived from the study of enzyme deficiencies, many of which, at least in homozygotes, are frankly deleterious and in consequence have generally been regarded as pathological abnormalities. Since, however, virtually all these conditions were identified in the first instance because of some more or less striking clinical or metabolic disturbance they represent a highly selected group of mutants; thus they cannot themselves be expected to provide us with any clear picture of how extensively genetically determined enzyme variation that does not result in overt pathological manifestations may occur in the general population. Nor do they provide us with any

certain indication of what the nature of such ' concealed ' variation might be—whether, for example, it is mainly a matter of minor quantitative differences in rates of synthesis, or whether qualitative differences involving enzyme structure are an important feature.

Enzyme polymorphism

Recent work indicates that such concealed variation is a much commoner phenomenon in human populations than had previously been thought likely. In particular, several examples of genetically determined enzyme variations—so-called polymorphisms—have now been discovered and it seems very probable that many more exist. Each of these polymorphisms serves to differentiate apparently normal and healthy individuals into distinct classes according to the chemical characteristics of a particular enzyme protein. It is not yet known whether such enzyme variants differ functionally; but if, as seems possible, they do result in one way or another in metabolic or other differences, then a great deal of human variation may be attributable to this kind of phenomenon.

It would be of obvious interest to know what fraction of the very large number of enzymes that occur in the human organism exhibit such polymorphism, and to discover what their biochemical and genetical significance might be. A project designed to throw light on this very general and somewhat daunting problem has been started by the Council's Human Biochemical Genetics Research Unit (Harris, 1966). The idea is to see whether, if a series of arbitrarily chosen enzymes are studied in sufficient detail in apparently normal and healthy individuals, genetically determined differences will be found, and if so whether such differences are rare or common and whether they are peculiar to one sort of enzyme rather than another.

At the outset it was clear that some restriction on the choice of enzymes to be studied was inevitable. Because it would be necessary to examine the selected enzymes in a fairly large number of different people, and because any enzyme differences that turned up would require the investigation of whole families, it appeared necessary in the first instance to study mainly enzymes present in blood. Some decision had also to be made about the kind of techniques to be used in looking for such differences. A wide variety of methods suitable for examining the many different properties of enzyme proteins are available, and it would have been impractical to attempt to use more than a few of these. In practice it was decided to rely initially on the technique of starch gel electrophoresis. This is known to be capable, in the right conditions, of detecting quite subtle differences in molecular charge and molecular size. It is not, however, designed to pick up other sorts of molecular difference, and it is also not very sensitive for the detection of small quantitative differences between individuals. Thus at the best one could expect to detect only a rather small proportion of all possible forms of enzyme variation.

So far ten arbitrarily chosen enzymes have been examined in this way, in none of which there was an *a priori* reason to expect any variation. Not all of them have as yet been examined in great detail, or by perhaps the most suitable methods; nevertheless three quite striking examples of enzyme polymorphism have been discovered. Two of these, those involving phosphoglucomutase and red cell acid phosphatase, are discussed below. The third involves the enzyme adenylate kinase (Fildes and Harris, 1966).

The following examples will illustrate the kind of enzyme differences that have so far been found and the relative frequencies with which they occur in the general population.

Phosphoglucomutase

Phosphoglucomutase is a phosphotransferase, which catalyses the transfer of a phosphate group between the 1 and 6 positions of the glucose molecule. It is widely distributed in mammalian tissues and has an important role in carbohydrate metabolism. Spencer, Hopkinson and Harris (1964a) found that at least seven distinct components (isoenzymes) of human phosphoglucomutase could be distinguished by starch gel electrophoresis (plate VIII). They also demonstrated that there were clear-cut differences between individuals in the pattern of the isoenzyme components present. Although mainly studied in red cells because of the ease with which these may be obtained, the characteristic isoenzyme patterns have also been demonstrated in a variety of other tissues. In every individual studied the same type of phosphoglucomutase has been found in all the tissues investigated. Moreover, when small pieces of skin were taken and cells were grown in tissue culture the characteristic individual patterns were observed even after many cell generations. These findings, and the fact that repeated blood samples from the same individual always give the same results, make it clear that these different enzyme types represent individual characteristics.

The three common types of phosphoglucomutase, referred to as phenotypes PGM 1, PGM 2–1 and PGM 2, occur in England in about 58, 36 and 6 per cent respectively of the population. Extensive family studies have shown that the differences are genetically determined and indicate that a pair of allelic autosomal genes are involved. The isoenzyme components characterizing the three phenotypes, and the presumed genotypes determining the phenotypes, are as follows:

Phenotype	*Isoenzyme components*	*Genotype*
PGM 1	a c e f g	PGM^1PGM^1 (homozygous)
PGM 2	b d e f g	PGM^2PGM^2 (homozygous)
PGM 2–1	a b c d e f g	PGM^1PGM^2 (heterozygous)

This suggests that the isoenzyme components a and c determined by PGM^1 may be molecular alternatives of components b and d determined by PGM^2. Possibly these pairs of isoenzymes contain a common polypeptide chain and the difference between the two homozygous phenotypes depends on a small structural difference in this, involving perhaps the substitution of a different amino acid at a single point in the chain. If this is so, then presumably this polypeptide chain is not present in the isoenzyme components e, f and g, since they appear to be unaffected by this gene substitution, and their structures are presumably therefore determined at another locus. Support for this idea has now been obtained by the discovery of an uncommon variant involving components e, f and g, but not affecting a, b, c or d (Hopkinson and Harris, 1965). This variant was found to be inherited independently from PGM 1, 2–1 and 2, and the family study showed that it was determined at a separate and not closely linked gene locus.

Red cell acid phosphatase

The acid phosphatase present in erythrocytes differs both in its substrate specificity and in its inhibition characteristics from the acid phosphatases present in other tissues. Its precise function is not known.

Hopkinson, Spencer and Harris (1963) examined the enzyme in preparations from the erythrocytes of a series of normal people, using an electrophoretic procedure, and found that in every instance more than one isoenzyme component was present. Furthermore there were clear-cut individual differences in the number, electrophoretic mobilities and relative activities of the isoenzyme components. Five common phenotypes were identified. They are referred to as A, BA, B, CA and CB, and in England they occur respectively in about 13, 43, 36, 3 and 5 per cent of the population.

The initial family studies showed that these phenotypes are genetically determined and led to the hypothesis that three allelic genes (P^a, P^b and P^c) at an autosomal locus are involved. It was inferred that the phenotypes are determined as follows:

Phenotype	*Genotype*
	Homozygous:
A	P^aP^a
B	P^bP^b
	Heterozygous:
BA	P^aP^b
CA	P^aP^c
CB	P^bP^c

On this hypothesis it was predicted that there must be a sixth phenotype, C, corresponding to a genotype P^cP^c, and indeed a few examples of what appears to be this phenotype were subsequently found. The fact that the heterozygotes having CA and CB are relatively uncommon means that homozygotes with the phenotype C will be found rather infrequently—in about 1 in 625 of the population.

With the five common phenotypes fifteen different mating types are possible and the pattern of inheritance in most of these has now been studied (Hopkinson, Spencer and Harris, 1964; Harris, 1966). These quite extensive family data have proved to be fully consistent with the hypothesis, and the findings have been confirmed by several other groups of workers investigating different populations. There seems little doubt therefore that these acid phosphatase variations reflect a polymorphism involving at least three alleles, and a variety of studies on the properties of the isoenzymes in the different phenotypes makes it appear reasonably certain that these allelic genes determine the synthesis of structurally different forms of the enzyme.

A particularly interesting feature of this polymorphism is that the qualitative differences between the phenotypes are reflected quantitatively in differences in the levels of enzyme activity (Spencer, Hopkinson and Harris, 1964b). Levels of the total acid phosphatase activity were determined by a standard method in a series of samples from individuals of the different phenotypes. Although there was considerable variation in the activity between individuals of any one phenotype, nevertheless quite marked differences between the mean values for different phenotypes could be demonstrated. Thus type B red cells showed on

average about 50 per cent more acid phosphatase activity than type A red cells and type BA red cells were intermediate in activity, while type CB red cells showed a greater average activity than those of type CA or type B.

It is of interest that if red cell acid phosphatase activities are determined in a series of randomly selected individuals they show a continuous unimodal distribution (see figure 1), which in fact is not dissimilar in form to the distributions usually obtained when enzymes not so far known to be polymorphic

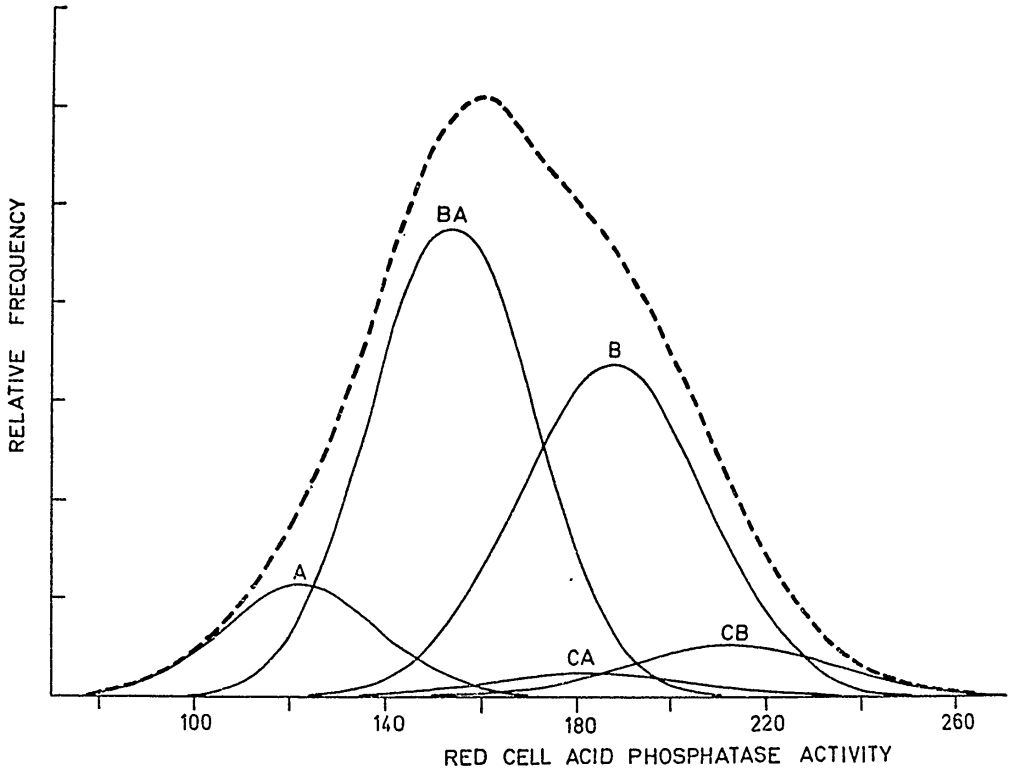

FIGURE 1

Diagram showing distribution of red cell acid phosphatase activities in the general population (broken line), and in the separate phenotypes. (From Harris, 1966.)

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are examined quantitatively in randomly selected populations. In particular the variance, when related to the mean, is of the same order of magnitude as is found with many other enzymes. In the present case, however, it is clear that the overall distribution (shown by a dotted line in the figure) represents a summation of a series of separate but overlapping distributions corresponding to each of the qualitatively different phenotypes. Furthermore in the overall distribution the genetical component of the variance can be largely, if not entirely, attributed simply to the different effects of the three allelic genes. It is not unreasonable therefore to suppose that the genetical component of the continuous variation in the levels of other enzymes may have a similar basis.

Acetyl transferase and placental alkaline phosphatase

It is clearly difficult in human beings to carry out genetical studies on tissue enzymes that do not happen to occur also in blood cells and may appear only occasionally in blood plasma. It is therefore perhaps not without significance

that two examples of polymorphism involving such relatively inaccessible enzymes have already been discovered. One of these concerns an acetyl transferase that occurs in liver, the other an alkaline phosphatase apparently peculiar to the placenta.

Significant levels of this acetyl transferase are evidently only found in about 50 per cent of individuals (Price Evans and White, 1964). In other people the level of activity is very low or even absent. These differences in enzyme activity were discovered because they result in differences in the metabolism of the drug isoniazid. These may be detected by determining levels of the drug in the plasma at an appropriate time after its administration. Family studies (Price Evans, Manley and McKusick, 1960) have shown that these metabolic differences are genetically determined and that two autosomal allelic genes with frequencies of about 0·3 and 0·7 in the general population are involved. It is apparently the less common of these genes that determines in some way the appearance of significant amounts of the acetyl transferase activity in the liver, and this is associated with fast inactivation of isoniazid.

The alkaline phosphatase that is present in relatively large amounts in the human placenta is evidently a different enzyme from the alkaline phosphatases present in such tissues as bone, intestine, kidney and liver. In terms of the electrophoretic characteristics of the enzyme (Boyer, 1961), it has been found possible to classify placentas into at least six quite distinct types (Robson and Harris, 1965). These types are referred to as S, SF, SI, F, FI and I, and in a series of placentas obtained from European women after normal pregnancies they were found to occur with frequencies of about 41, 35, 11, 7, 5 and 1 per cent respectively. On the basis of the electrophoretic characteristics of the phosphatase in the different types and of the relative frequencies of these types, a simple genetical hypothesis that could account for the variations was constructed. This suggested that three common autosomal allelic genes are concerned, types F, S and I representing the homozygous genotypes and types SF, SI and FI the heterozygous genotypes. It is of course impossible to carry out family studies of the ordinary kind in the case of a characteristic peculiar to the placenta. However, it proved possible to test the hypothesis by studying a series of pairs of placentas from dizygotic twin births, since such twins can be regarded as pairs of sibs. With six types of placentas, twenty-one different combinations may occur in twin pairs. The relative frequencies of these different combinations in a series of 380 placentas from 190 dizygotic twin pairs were found to be in close agreement with the frequencies expected on the genetical hypothesis. The results also make it clear that the differences in placental alkaline phosphatase are determined by the genotype of the foetus, not the mother. Although the biological implications of this polymorphism are still quite obscure, it seems not unlikely that it may have relevance to problems connected with maternal–foetal interrelationships.

The extent of enzyme diversity

In the investigation being carried out by the Human Biochemical Genetics Research Unit three of the ten enzymes so far studied have been found to show polymorphism. Although firm conclusions can hardly be drawn from such a small series, it seems at least possible that unless there has been an excessive degree of luck in the choice of enzymes for study, polymorphism may be a

fairly common phenomenon among the very large number of enzymes that occur in the human organism. If this is so, it implies a considerable degree of individual diversity, and some idea of how extensive this may be can be obtained by considering together the various enzymes that are now known to exhibit some degree of polymorphism in the English population. Relevant data on seven such enzymes are given in table 1. For the present purpose only those variations where two or more allelic genes have been found with frequencies greater than 0·01 have been included. In the case of one enzyme, serum cholinesterase, the variation is governed by genes at two different loci, so eight gene loci are represented in all. Of these at least six can be regarded as ' structural ' loci since the variation that results appears to involve qualitative differences. In the other two cases—serum cholinesterase E_2 and acetyl transferase—only quantitative differences in the enzyme have so far been found, but it is possible that these also reflect differences in the structure of the enzyme.

TABLE 1*

Enzyme polymorphism in the English population

Enzyme	Number of alleles with frequency greater than 0·01	Frequency of commonest phenotype	Probability of two randomly selected individuals being of the same phenotype	Reference
Red cell acid phosphatase	3	0·43	0·34	Hopkinson, Spencer and Harris (1963)
Phosphoglucomutase	2	0·58	0·47	Spencer, Hopkinson and Harris (1964a)
Placental alkaline phosphatase	3	0·41	0·31	Robson and Harris (1965)
Acetyl transferase	2	0·50	0·50	Price Evans and White (1964)
Adenylate kinase	2	0·90	0·82	Fildes and Harris (1966)
Serum cholinesterase				
Locus E_1	2	0·96	0·92	Kalow and Staron (1957).
Locus E_2	2	0·90	0·82	Harris, Hopkinson, Robson and Whittaker (1963)
6-Phosphogluconate dehydrogenase	2	0·96	0·92	Fildes and Parr (1963)
Combined		0·037	0·014	

* From Harris (1966); reproduced by courtesy of the Royal Society.

Each of these variants occurs independently of the others. Thus a fairly large number of different combinations of phenotypes may be found in the general population; indeed, the commonest of these combinations will occur in less than 4 per cent of the population and the probability that two randomly selected people would have the same combination of phenotypes is less than

1 in 70. Thus quite a high degree of individual differentiation in enzymic make-up can already be demonstrated even from this very limited series of examples, and it is of interest that most of this is not simply quantitative but is probably attributable to variation in the molecular structure of the enzymes. Since these various enzyme combinations are all to be found among individuals who can be regarded as normal and healthy, it is apparent that there must be many different versions of so-called normality. Indeed one may plausibly imagine that in the last analysis every individual may be found to have a unique enzymic constitution.

Rare variants

Besides the relatively common variants listed in table 1, a number of rather less frequent variants of some of these enzymes have also been discovered during the course of population and family studies; in each case these unusual phenotypes appear to be determined by genes in heterozygous combination with one or other of the common forms. For example several rare phosphoglucomutase phenotypes are known (Hopkinson and Harris, 1965) and a number of relatively uncommon placental alkaline phosphatase phenotypes have also been identified (Robson and Harris, 1965). Uncommon variants of serum cholinesterase (Harris and Whittaker, 1961; Liddell, Lehmann and Silk, 1962) and of 6-phosphogluconate dehydrogenase (Fildes and Parr, 1964) have also been found. Extensive surveys have been carried out on several enzymes which, at least with the methods used, do not appear to have common variants, and in a number of cases rare variants have also come to light here. For example in an electrophoretic survey of lactate dehydrogenase in more than 1000 English people two examples of a genetically determined variant form of the enzyme were found (Davidson *et al.*, 1965), and a number of other uncommon variants of lactate dehydrogenase and of several other enzymes have also been reported in various human populations (see Shaw, 1965).

Since the screening programmes required to uncover such infrequent variations are necessarily very laborious and often technically difficult, it is not surprising that as yet only a few enzymes have been looked at in this way. However, it is reasonably certain even from the data available at the moment that a large number of such rare variants must exist. The genes that determine them appear to have frequencies of between about 0·01 and 0·001 in the general population. They are in this respect similar to the genes that determine many of the classical inborn errors of metabolism, though they have been discovered in a quite different way and they are not necessarily associated with a reduction in enzyme activity.

* * *

Each of the different enzyme polymorphisms and rare variants that have been mentioned poses a whole range of intriguing problems in biochemistry, medicine and genetics. For example, we do not know what is the precise nature of the structural differences between the variant forms of an enzyme, or whether these are reflected in kinetic differences and in differences in functional activity. The discovery that even in homozygous individuals many enzymes apparently occur in multiple molecular forms is a recent development in enzymology; further investigation of these isoenzyme systems and of the variant forms may well help to elucidate the biological significance of the phenomenon.

It must also be asked whether, and to what extent, the different enzyme phenotypes result in differences in metabolism or other differences between individuals—whether, for example, individuals with different phenotypes respond differently to different environments, to different diets, to particular types of stress and so on. Moreover, do the various phenotypes involve differences in susceptibility to particular diseases, or in response to particular types of pathological processes or different drugs? Among the enzymes listed in table 1, certain relatively uncommon serum cholinesterase phenotypes do result in an excessive sensitivity to the muscle relaxant drug suxamethonium (Kalow and Staron, 1957), and the different acetyl transferase phenotypes involve differences in the metabolism of isoniazid and sulphamethazine (Price Evans and White, 1964).

We should also like to discover why the different forms of an enzyme occur with the particular frequencies that are observed, why some occur quite commonly while others are relatively rare, and why the gene frequencies (as in the case of red cell acid phosphatase and placental alkaline phosphatase, for example) may vary quite widely from one population to another. Probably they are determined by factors important in natural selection but at the moment we have scarcely any idea what these might be. It is reasonable to hope, however, that we shall identify the metabolic and functional differences that presumably result from the various enzyme differences; this knowledge may then provied us with some indication of what selective factors are important, and thsn give us greater insight into the genetical and biochemical structure of human populations.

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THE GENETICS OF SCHIZOPHRENIA

Schizophrenia is one of the most serious forms of mental illness, and is common in all countries of the world; in Europe and North America nearly one per cent of the population can expect to have a schizophrenic illness at some time in their life. Studies on the genetics of schizophrenia have a long history, but even now no universally accepted conclusions have been reached. Whereas in Britain and Europe biological theories of causation predominate, in Canada and the United States the view prevails that the major factors are psychological and have their effect during the first years of life. Some of the results of family investigations, such as those that show an above-average incidence of schizophrenia in the relatives and particularly in the parents of schizophrenics, can be interpreted in alternative ways. The geneticist is inclined to think that these findings support the view that a specific predisposition to the illness is passed on from parent to child via the genes; but the believer in psychological causation prefers the view that the predisposition is transmitted from one generation to the next through family traditions and upbringing. Much attention has been directed towards the ' schizophrenogenic ' mother, who has been thought to endanger her child through her coldness and lack of love, or her dominance and possessiveness. A large amount of work has been done along these lines. Briefly, the abnormalities of personality in the parents of schizophrenic patients have not been shown to have any specific quality. Where control studies have been done, mothers of schizophrenics have not been found to differ in any definable way from the mothers of neurotics or psychopaths. Furthermore, the upbringing of children who later became schizophrenic has not been shown to differ from that of their sibs who remained well.

There is another observation which is strongly in favour of a genetical causation, but which does not fit environmental theories. It would be expected on the environmental hypothesis that any psychological abnormality of the

mother would be much more fateful for the child than abnormality of the father. We find a high proportion of schizophrenics among both the parents and the children of schizophrenic patients, and we should naturally expect to find more schizophrenic mothers than fathers among them and more schizophrenics among the children of female than of male schizophrenic patients. When appropriate adjustments are made for ages and risks periods, neither of these expectations is borne out. Despite their greater psychological remoteness from the infant and young child, fathers are just as likely as mothers to transmit the predisposition to schizophrenia. This is just what one would expect on the genetical hypothesis. In the light of present knowledge, however, both genetical and environmental factors would seem likely to play a part in the causation.

In rare cases, a mental illness clinically indistinguishable from schizophrenia can be produced by specific environmental causes. Illnesses of this kind have been observed in patients—especially drug addicts—who have been taking amphetamine ('benzedrine') in excessive doses or over a long time (Connell, 1958). No other poison is known to produce an effect just like this. However, some patients with brain damage—for example patients who have had epilepsy for a number of years, and have suffered damage to a temporal lobe of the brain—sometimes pass for days or months, and even for years, into a mental condition so like schizophrenia that mistakes in diagnosis are sometimes made. People who have had a 'schizophrenia-like' mental illness arising from one or other of these causes have been found to have families unaffected by schizophrenia, and it would thus seem that no genetical factor has contributed to their illness (Slater, Beard and Glithero, 1963). These observations suggest that the mental symptoms of schizophrenia may depend on a breakdown in particular functional systems in the brain, most likely deep in the central parts and perhaps involving particular biochemical pathways. If a specific genetical predisposition to schizophrenia were shown to cause a similar deviation of body chemistry, this would mean that schizophrenia in which a genetical factor plays a part would have essentially the same mechanism as the relatively rare forms of the illness which are known to be environmentally caused. A great deal of the research directed towards finding biochemical differences between schizophrenics and others depends on this idea. Some of this work is very promising. Recent large-scale investigations by Bourdillon *et al.* (1965) have confirmed the repeated reports that one abnormal product of metabolism (dimethoxyphenylethylamine, seen as a pink spot after chromatography of the urine) is to be found in schizophrenics but not in other psychiatric patients. The 'pink spot' was not found by Bourdillon and his colleagues in those relatives of 'positive' schizophrenics whom they tested, and so would seem more likely to be related to the disease process than to the underlying genetical predisposition. It is noteworthy that dimethoxyphenylethylamine is related in chemical structure to mescalin, which has been used by American Indians as an intoxicant for its vivid hallucinatory effects.

Studies on twins

The biological difference between 'similar' or monozygotic (MZ) and 'dissimilar' or dizygotic (DZ) twins provides the means of making the most sensitive single test of the significance of hereditary factors. MZ twins are genetically duplicates of one another; DZ twins share about half their genetic

material in common, like ordinary brothers and sisters. Environmental factors that produce their effects regardless of family groupings are found to be associated with low degrees of similarity (concordance) between twin pairs, both DZ and MZ, with regard to the condition in question. Environmental factors which operate to different degrees in different families, and which tend to affect members of the same family about equally, go with high rates of concordance both in MZ and in DZ pairs, with little difference between the two kinds of twin. For instance, one of the best twin investigations into the causes of criminality (Kranz, 1936) showed concordance rates of respectively 66 and 54 per cent in MZ and in same-sexed DZ pairs in respect of having a police record. Where there is so little difference in concordance rates between MZ and DZ twins we are likely to attribute the characteristic in question to upbringing and family standards of behaviour. By contrast, in those conditions determined by genetical factors there are likely to be high rates of concordance within MZ pairs, and much lower concordance within DZ pairs, which may be no more alike than ordinary brothers and sisters. This is what has usually been found in the case of schizophrenia.

In a series reported by Slater (1953), working with a grant from the Council, there were 156 schizophrenic patients who were one of a twin pair; of the 41 MZ pairs 28 were concordant for schizophrenia, and of the 115 DZ pairs 13 were concordant. This is one of the few series that have been reported in full clinical detail. The pairs of MZ twins were found to resemble one another not only in the fact that a schizophrenic illness had occurred but also in features such as age at onset, type of illness at onset and clinical course. There have been a number of other studies on series of twins, including a very large one reported by Kallmann (1946) in the United States. In the cumulative reports from the literature reviewed by Essen-Möller (1963), the concordance rate for MZ pairs was 194 out of 280 (69 per cent), as against the figure of 59 out of 448 (13 per cent) for DZ pairs. While these findings suggest that it is the genetical factor that causes the specific predisposition to schizophrenia, they also suggest that whether or not a mental illness actually occurs may depend on environmental factors.

Following the publication of the complete case data in Slater's report, the American worker Rosenthal (1959, 1961, 1962) made an intensive study of all the available case reports on twins. He found that, in the MZ pairs, female twins resembled one another more closely than did male twins, and in the DZ pairs concordance was higher in the same-sexed than in the opposite-sexed pairs. Taking the pairs from Slater's study, Rosenthal found a striking difference between the concordant pairs and the discordant pairs: in the families of the latter there was only one out of 13 in which a further member had suffered from schizophrenia, while 13 out of the 22 families of the concordant twins had further cases of schizophrenia. The suggestion that Rosenthal makes is that the diagnosis of schizophrenia perhaps covers what is in reality a variety of disorders, of which some are genetically determined while others are not.

In recent years further series of schizophrenic twins have been collected in Japan, Denmark, Norway, Finland and England. The British work has been carried out by Gottesman and Shields (1966) at the Council's Psychiatric Genetics Research Unit at the Maudsley Hospital in London. They have

investigated 57 twin pairs from an uninterrupted series of hospital admissions between 1948 and 1964. Once again there is a contrast between the MZ and the DZ pairs, with 10 out of 24 of the former and 3 out of 33 of the latter proving concordant. The results confirmed another finding of Rosenthal's, namely that concordance was more probable if the schizophrenic illness was a severe one. If there are both genetical and environmental schizophrenias, one might perhaps expect the former to be more severe.

The recent Japanese and English studies have produced results corresponding with the expected pattern. The Norwegian and the Finnish data have shown much lower concordances. In Norway (Kringlen, 1966) only 14 out of 50 male MZ pairs and in Finland none of the 16 pairs were concordant. However, the Finnish investigator notes that 3 of the twins of the schizophrenics were on the borderline of psychosis, and 9 of the remainder had schizoid personalities (Tienari, 1963); the actual discrepancy between these results and those of other workers is thus less than the crude figures suggest.

Nevertheless it is an interesting fact that the Scandinavian results have shown concordances lower than those found in other countries. One possible explanation—assuming that the twins studied are not unrepresentative—would be to postulate a different pattern of interaction between genetic and environmental factors. Scandinavians may be a genetically more homogeneous people than other Europeans, and are certainly more so than Americans. This would tend to depress the apparent effect of a genetical contribution to causation. It may also be the case that the physical environment in which the people of Norway and Finland live runs more to extremes than that of more southern lands, varying as it does from the harshness of the northern countryside to the benign conditions of the south and of the cities; if so, the members of a twin pair might well be exposed to environmental conditions that differ more profoundly than would be likely in many other countries. It must also be remembered that so far only male twins in Norway and Finland have been studied, and that these tend in any case to have lower rates of concordance than females.

The results of twin studies, then, support the hypothesis of a genetical contribution of an important and specific kind to the causation of schizophrenia. The great bulk of schizophrenic illnesses would seem to depend on this genetical predisposition, although it is demonstrably lacking in the rare cases with an organic causation where identical clinical symptoms are present. The environmental factors that act as precipitating causes in the general run of cases are better established on the physical than the psychological side; it seems fairly certain that both severe head injuries and the regressive changes of old age may suffice to bring about a schizophrenic psychosis in people who have only a relatively weak genetical predisposition to the illness. There is no evidence that the genetical contribution is made through a chromosomal abnormality; and the question that awaits decision is whether the genetical factor consists in the action of one or more single genes of major effect or in the combined action of many genes of minor effect. There are arguments in favour of both possibilities.

Incidence of schizophrenia in the relatives of schizophrenics

The mode of inheritance of schizophrenia might be clarified by information on the incidence of schizophrenia in the general population and in the various

classes of relatives of schizophrenic patients. A large number of studies have been carried out, in several countries, and results are in fair agreement with one another. The probability of the occurrence of the illness in a relative of a schizophrenic depends on whether there is a blood relationship, and on how close it is. Thus the husband or wife of a patient, not related by blood but sharing some of the same environment, has only a slightly raised risk of schizophrenia—about 2 per cent as against 1 per cent in the general population. According to Kallmann, the risk for the half-brothers and half-sisters of a schizophrenic is about 7 per cent; for full brothers and sisters, for DZ twins and for children it is between 14 and 16 per cent and for MZ twins 86 per cent.

The simplest explanation of this high incidence of schizophrenic illnesses in the blood-relatives of schizophrenics would be to postulate polygenic factors; this is the hypothesis of causation by multiple genes of small effect. This is the model we use to explain quantitative variation between individuals, for instance in such characteristics as intelligence and bodily stature. However, Edwards (1960) has argued that polygenic inheritance may also be at work in conditions which are of an all-or-none kind, such as biochemical disorders like gout, and disorders of development like hare-lip. One supposes that if a deviation from the average state (biochemical, developmental etc.) of the individual goes beyond a certain margin, the capacity of the organism to adapt to it is exceeded, and some new, and possibly pathological, process goes into operation; quantitative variation in the cause produces qualitative variation in the end-result. This might well be one of the most usual modes of genetical causation in common disorders (that is, any condition affecting more than 1 in 1000 individuals). Edwards shows that the incidence of a polygenically determined condition among the first-degree relatives of an affected individual should be approximately the square root of the incidence in the general population—so that a disease occurring in say 1 in 100 of the population would affect about 1 in 10 of the first-degree relatives. As the incidence of schizophrenia in the general population is about 0·8–1·0 per cent the polygenic theory gives us an expectancy of schizophrenia in the sibs and children of schizophrenics of 9 or 10 per cent, which is not far from the observed 14 per cent.

The alternative theory of single-gene causation agrees with observation at least as well. This theory was advanced by Böök (1953) and has been further developed by Slater (1958). We suppose that the specific gene involved is an intermediate one, at neither extreme of dominance or recessivity. This means that it shows its effects in all homozygotes (double gene carriers) and in a proportion of heterozygotes (single gene carriers). If the proportion of heterozygotes showing the effects of the gene is very small, then the mode of inheritance approximates to simple recessivity; if the proportion is very high, then we have an approximation to simple dominance.

It comes as a surprise to find that, away from these extremes, the intermediate gene has effects that do not lie somewhere between dominance and recessivity. The expected proportions of affected relatives tend to be lower than those associated with complete dominance or complete recessivity. This is illustrated in figure 1, where the proportions expected with complete recessivity are shown

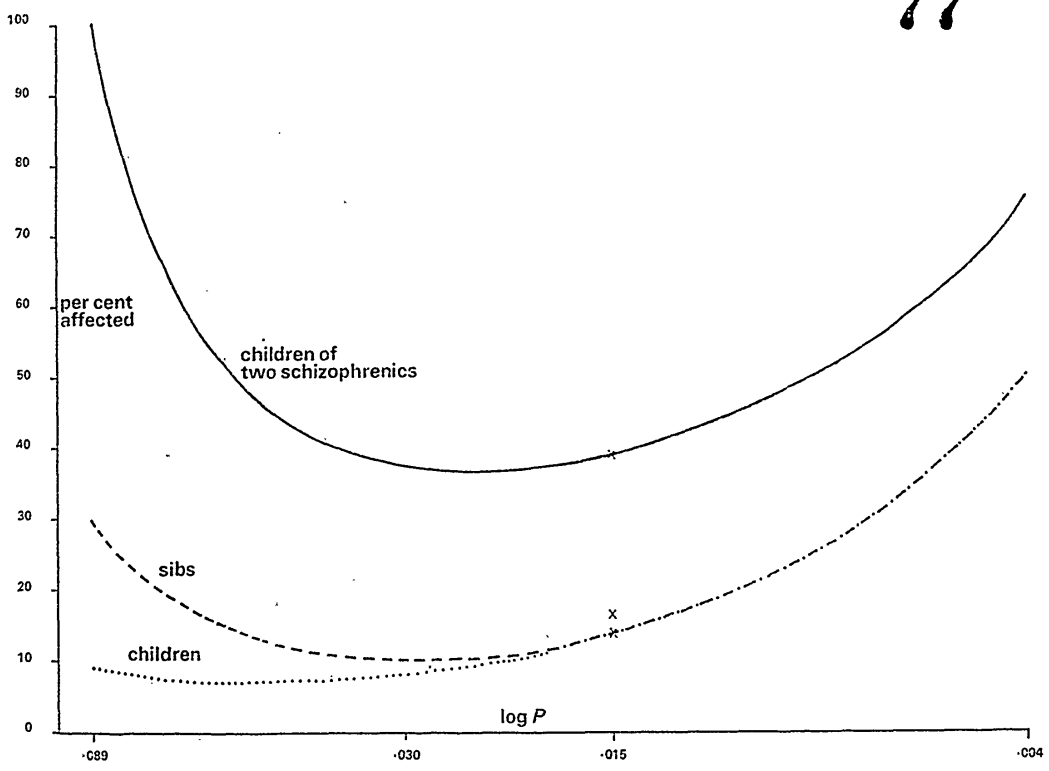

FIGURE 1

Theoretical expectancies of schizophrenia in relatives of schizophrenics for different degrees of recessivity and dominance of the gene (logarithmic scale). The three curves show the expected incidence of schizophrenia in three classes of relatives of schizophrenics, the basic assumption being that the incidence of schizophrenia in the general population is 0·8 per cent. The three crosses show the observed age-corrected incidence of schizophrenia in the children of two schizophrenic parents, in the children of a single schizophrenic parent and in the sibs of a schizophrenic. These points find their best fit with the corresponding curves where the gene frequency is 0·015 and the gene effects lie about halfway between those of complete dominance and those of complete recessivity.

on the left and those expected with complete dominance on the right. At the recessive extreme, to account for an incidence of schizophrenia of 0·8 per cent in the general population, the necessary frequency of the schizophrenic gene would be 0·089, one out of every 6 people in the population being a carrier. At the dominant extreme the gene frequency would be much lower, 0·004, one in every 125 people in the population being a carrier. A gene intermediate between dominance and recessivity would have a frequency somewhere between these values. A gene frequency of 0·015 (with approximately one in every 33 individuals a carrier) gives the values that best fit the observed incidences:

	Percentage expectancy of schizophrenia	
	Theoretical	*Observed*
Brothers and sisters of a schizophrenic	14·4	14·2*
Children of a schizophrenic	14·3	16·4*
Children of two schizophrenics	39·6	39·2†

* From Kallmann (1953)
† From Elsässer (1952)

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Genetic polymorphism

It is a somewhat striking feature of the observed incidences of schizophrenia in the relatives of schizophrenics that they come close to the theoretical minima of the curves in the figure. This coincidence suggests that the gene frequency is the result of a balance between opposed forces. These are on the one hand the natural selective processes tending to eliminate the gene, through its effect in producing schizophrenia, and on the other hand some selective advantage attaching to the gene when it does not actually cause this disastrous illness. One of the clearest examples of a gene that is kept at a high frequency in some populations, despite the lethal effects it can produce, is the gene for sickle-cell anaemia. Homozygotes, carrying two such genes, succumb to an early and usually fatal anaemia; but in heavily malarial regions heterozygotes have an advantage over persons without the gene in that they are more resistant to the malarial parasite (see article on abnormal haemoglobins on p. 37). Huxley and his colleagues (1964) have suggested that this balanced genetic polymorphism (or ' morphism ') is operating in schizophrenia.

There is much to be said for this view, but so far little solid evidence has been collected to support it. However, schizophrenia is a condition with such serious consequences to the sufferers that their fertility is reduced to 70 per cent of the average; and unless there were some advantage attaching to possession of the schizophrenic gene or genes, to compensate for this disadvantage, one would expect schizophrenia to be a rare condition. In fact the gene frequency is maintained at a high and steady level not only in America and Europe but probably nearly equally in all countries of the world. This problem has been considered by Moran (1965b). Normal genes can mutate into abnormal genes, and if the rate of elimination of the schizophrenic gene were not very high mutation might make up for the loss. Moran considers that this by itself would not be sufficient. However, a ' morphism ' giving the heterozygote not suffering from the disease some advantage over both kinds of homozygote (those with two normal and those with two Sc genes) might provide an adequate explanation. One would be most tempted to look for such an advantage in those stages of the life process in which mortality is at its heaviest—that is, before birth and in the first year of life.

A second possibility suggested by Moran (1965a) is connected with the fact that there is an association between incidence of schizophrenia and social class, the lowest social class having the highest incidence. This seems to be due to a drift downwards of those who later develop schizophrenia, since their parents are normally distributed socially. Moran points out that one way in which schizophrenia is maintained at its present frequency could be by this social drift, since higher fertility is found in the lowest social class. These and other suggestions that might be made open up new and interesting avenues of research.

* * *

There is good evidence that genetical factors contribute to the aetiology of schizophrenia; what we want to know more than anything else is what their most immediate effects are. To put the question in another way, one might ask: what are the aspects of the disorder that stand in closest relationship to the action of the genes? One would expect to find a difference at the metabolic

or physiological level between individuals highly predisposed to schizophrenia and others in whom the predisposition was slight or absent. This is the field in which research would seem to have the brightest prospects. However, so far all the biochemical differences between schizophrenics and others have been found to be associated with the illness itself, and none of them have been found to be a constant feature of the individual in both sickness and health. It is, perhaps, a commonplace to say that the greatest hope of making further progress lies in cross-disciplinary collaboration, and in applying in family studies the techniques provided by advances in other fields. One may hope, for instance, that research workers who investigate any of the wide range of problems, whether clinical, biochemical, psychological or sociological, will include among their subjects not only schizophrenics but also the sibs of schizophrenics; this would give an added dimension to their investigations.

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THE THYMUS AND IMMUNITY

For a long time there has been some uncertainty about the functions of the thymus. Some considered that it was a gland producing hormones but gave no direct proof for this belief. Others thought that it was a useless, vestigial organ. In recent years new knowledge of the physiology of the thymus has been gained, and this has brought us closer to an understanding of certain clinical and experimental states of immunological deficiency and autoimmunity and is also throwing light on mechanisms relevant to the development of cancer.

The thymus in man is an irregular bilobed organ, lying behind the upper part of the breast bone above the heart and extending for a variable short distance into the neck. It is a relatively large organ in the infant, and it reaches its maximum size at about the time of puberty (when it weighs roughly 35–40 grams), after which it regresses. In late adult life it is little more than a vestigial structure, but in the young adult it is still of considerable size. This fact is not often realized because in individuals dying of some illnesses it is very small; it is well known that stress, such as occurs in infections, causes a considerable atrophy of the thymus, and it is in this condition that the organ is generally seen at autopsy. But in healthy adults dying suddenly—in an accident, for example—it is still quite large.

The thymus forms part of the lymphoid system of the mammal. Lymphatic tissue is scattered throughout the body, mainly in the thymus, tonsils, spleen, lymph nodes, bone marrow and lining of the alimentary canal. If it could all be collected together, it would form an organ of some considerable size, roughly 1 per cent of the body's weight. It consists of a framework of specialized epithelial cells—cells with some similarities to those lining the skin and body cavities—and a mass of lymphocytes—round cells, varying in size but mostly small (diameter less than 8 microns), and possessing a large nucleus and relatively little cytoplasm. Lymphocytes are also found in lymph and blood and constitute one of the types of white cells circulating in the blood. They are manufactured in all lymphoid tissues but they are produced in far greater numbers in the thymus than in any other lymphoid tissue. This extraordinary efficiency of the thymus in producing lymphocytes is thought to be dependent on the presence of special types of cell found only in the thymus. Metcalf (1958), at the Walter and Eliza Hall Institute of Medical Research in Melbourne, has suggested that these special cells may produce some substance that stimulates lymphocytes to multiply.

The small lymphocytes

There has been some controversy about the fate of the lymphocytes produced in the thymus. Nossal (1965)—also at the Walter and Eliza Hall Institute—labelled the lymphocytes directly by injecting a radioactive substance into the thymus of the guinea pig and followed the fate of the labelled cells. Some of these were found in other lymphoid tissues after short periods of time. This, and other evidence, favours the view that the thymus may be an important source of the lymphocytes which circulate in blood and lymph and which may be distributed to other lymphoid organs. Such distribution may be particularly important in early life when lymphoid tissues other than the thymus are only poorly formed. Ford (1966) and his colleagues at the Council's

Radiobiological Research Unit have found that some cells which migrate from the thymus to the lymph nodes—and which in the thymus behave as typical thymus lymphocytes—have themselves migrated from the bone marrow.

Immune responses have for long been known to be a function of the lymphoid system. It is only recently, however, that direct, unequivocal evidence has been obtained that the small lymphocyte is an immunologically competent cell—that is, a cell that is fully qualified to initiate immune reactions when given the appropriate stimulus by ' foreign ' antigens (in other words by cells foreign to the body). These reactions include both those performed by lymphocytes, which after making contact with foreign tissue cells kill them (transplantation immune reactions), and those mediated by plasma cells that secrete circulating antibodies. In a series of very elegant experiments, Gowans and his colleagues at the Sir William Dunn School of Pathology in Oxford have clearly shown that small lymphocytes in the rat's thoracic duct (which is the main lymph vessel) are not newly formed cells but are recirculating from lymph to blood, through lymphoid tissue, out by efferent lymphatic vessels and back to the thoracic duct (Gowans and Knight, 1964). Other experiments showed that these small cells have a long life span, a finding that strongly supports the theory of recirculation. Gowans (1965) also showed that the small lymphocytes of the thoracic duct are capable of initiating transplantation immune reactions. He postulated that as the cells migrated through the lymph nodes they would make contact with macrophages (specialized cells with the function of ingesting foreign antigen) and differentiate either into antibody-producing plasma cells or into lymphocytes capable of destroying foreign tissue.

The role of the thymus

However, these immunologically competent small lymphocytes do not normally circulate through the thymus in adult life. Moreover, few, if any, of the small lymphocytes of the thymus can initiate transplantation immune reactions when stimulated by the presence of foreign tissue; indeed, the production of lymphocytes in the thymus of mice kept germ-free under sterile conditions is as active as it is in conventional animals, which are subjected to constant challenge by foreign antigens (such as those of micro-organisms). Nor does the thymus produce plasma cells in response to circulating foreign antigens, and its removal in adult life is not normally associated with any decrease in antibody response. Thus it used to be thought that the thymus did not play an important part in immunity. Experiments performed since 1961, however, have shown that in spite of this immunological inertia it has a role of fundamental importance in the development and maintenance of an adequate pool of immunologically competent cells.

Since the thymus is the major lymphoid organ and the main factory for producing lymphocytes in early life, it was suspected that thymectomy of the newborn would cause serious defects. Experiments carried out by Miller (1961, 1962a, 1962b) at the Chester Beatty Research Institute in London have shown this to be the case. Thymectomy was performed in mice of various strains soon after birth; they gained weight and developed and, for a time, no effect of the operation was apparent. Between the age of 6 weeks and 4 months, however, from 60 to 100 per cent of the mice of some strains suddenly became sick, wasted and died. One group of thymectomized mice was killed before 6 weeks of age and their lymphoid tissues and blood were examined.

It was evident that the population of small lymphocytes throughout the body was severely reduced. The capacity of the thymectomized mice for immune response was tested and found to be deficient; for instance, skin transplanted on to such mice from animals of another strain was not rejected but grew luxuriant tufts of hair and was tolerated until the animal died, and these mice had an impaired capacity to produce antibodies in response to some antigens such as those of sheep red cells. The results were confirmed by investigators in Minneapolis who had approached the same problem independently (Good *et al.*, 1962). At the National Institute for Medical Research and at the Imperial Cancer Research Fund's Laboratories at Mill Hill, it was shown that, in mice thymectomized soon after birth, capacity for synthesizing antibodies was reduced in the case of a few foreign antigens but not in the case of others (Humphrey, Parrott and East, 1963).

Removal of the thymus of the newly hatched chick impairs immune reactions to transplanted tissue but not antibody-producing capacity. On the other hand, removal of the bursa of Fabricius, a lymphoid organ of birds situated near the cloaca, prevents the development of the antibody-producing system but does not impair the capacity for transplantation immune reactions (Szenberg and Warner, 1962). The equivalent of the bursa of Fabricius in mammals has not been found, but a possible candidate is the tonsil, which bears certain resemblances—in its mode of development and its structure, for example—to the bursa of birds.

The wasting disease which occurs in some strains of mice thymectomized at birth does not develop when the animals are kept germ-free under sterile conditions (McIntire, Sell and Miller, 1964). This suggests that the disease is precipitated by environmental factors, probably infections; thymectomized mice, because of their impaired immunological reactivity, would presumably be particularly susceptible to such factors.

Studies on the mechanisms by which the thymus exerts its effects on the immune system have been performed at the Chester Beatty Research Institute. The following facts have been established experimentally.

The earlier in life thymectomy is performed, the greater are the defects in immunological reaction (Miller, 1962b). Thymectomy in the adult animal is not associated with any immediate significant immunological defects. However, when mice thymectomized in adult life are subsequently exposed to ionizing radiation, they fail to recover the capacity to mount some types of immune reaction (Miller, 1962c). Irradiated control mice, which have not been thymectomized, have impaired immune reactions for a few weeks after irradiation but soon recover and react like normal mice. These findings suggest that the thymus, even in the adult, must still continue to function whenever the immune system is damaged or destroyed and ensures its recovery. Thymectomy in adult mice is eventually followed by defects in immune capacity if a *new* foreign antigen is introduced into the animal between 6 and 9 months (but not earlier) after thymectomy. Thus throughout life the thymus evidently ensures the maintenance of an adequate pool of immunologically competent cells: only when the pool becomes depleted as a result of the finite (even though long) life span of its cells can defects in immune capacity become evident in the animal thymectomized in adult life (Miller, 1965a).

Further evidence for the hypothesis that the thymus normally builds up and maintains an adequate pool of competent cells was obtained by Miller (1964).

An injection of spleen or lymph node cells taken from adult mice of the same inbred strain corrects the immunological inadequacies of mice thymectomized at birth. The cell population in these tissues presumably contains long-lived immunologically competent cells that could function in the new host even in the absence of thymus tissue. Moreover, if a cannula is inserted into the thoracic ducts of normal mice and pure suspensions of lymphocytes recovered from the lymph are inoculated into mice thymectomized at birth, these mice immediately become capable of immunological reactions (Miller, 1965c). This provides further support for the view that one of the effects of neonatal thymectomy is a reduction in the number of small lymphocytes. In fact, when the thoracic duct of mice thymectomized at birth was cannulated, the output of small lymphocytes was found to be 0·5–1 per cent of that of normal control mice.

Implantation of thymus tissue just beneath the skin or on the kidney can also correct the immunological defects of thymectomized mice (Miller, 1961, 1962a, 1962b, 1964), only the epithelial cells of thymus tissue being essential for this correction. By employing two inbred strains, the cells of one being identifiable by the presence of a marker chromosome, it was found that the lymphoid cell population of the implant was progressively replaced by cells immigrating from the host, even if the latter had been thymectomized at birth. Furthermore, the majority of cells dividing in the lymphoid tissues were of host-type, though a few cells derived from the implanted thymus tissue were found (Miller and Osoba, 1963; Dukor *et al.*, 1965). This suggests that a thymus implant acts not only by directly providing cells to the host but also by inducing the differentiation of the host's lymphoid precursor cells into small lymphocytes with full immunological competence.

Strong evidence for this possibility has been obtained. Thymus tissue was enclosed in millipore diffusion chambers, the walls of which were impermeable to the passage of cells, and these chambers were placed in the peritoneal cavity of mice thymectomized at birth. When the mice received sheep red cells and foreign skin grafts they were capable of reacting normally to the immunological challenge (Osoba and Miller, 1963). It would thus appear that the thymus influences the development of the immune system by means of some substance it secretes into the blood (Miller, 1964), though attempts to isolate an active factor from the thymus have so far been unsuccessful. The current hypothesis (Miller, 1964, 1965b) is that the thymus ' instructs ' certain cells—presumably those stem cells of haemopoietic origin immigrating into the organ—to differentiate exclusively along lymphoid pathways, thus becoming thymus lymphocytes. By means of a substance secreted into the blood the thymus then ensures that some of the lymphocytes which migrate out of the organ and which are presumably long-lived cells become immunologically competent and thus able to respond to antigen in the manner postulated to occur by Gowans.

The thymus and immunological disease

This new work on the role of the thymus in the development of the immune system has focussed attention on human diseases in which immunological abnormalities are associated with some pathological condition of the thymus. There are clear-cut immunological deficiency syndromes in infants that can be linked to a failure of development of the thymus. For instance, when there is a complete lack of gamma globulin and an almost complete absence of

lymphocytes, as in the condition studied extensively by Hitzig and Willi (1961), there is a failure to produce antibodies and to reject foreign tissues. The thymus is often very small, weighing less than 1 gram, and it lacks small lymphocytes and may be in an abnormal position. In other disease syndromes characterized by immunological deficiencies (for example acquired hypogammaglobulinaemia) there are tumours of the thymus. The possibility of treating some thymic deficiency syndromes by grafting normal thymus tissue ought to be carefully explored. In conditions believed to be autoimmune in nature, when the body produces antibodies against its own constituents, there are often associated thymic lesions and sometimes tumours; myasthenia gravis, a chronic condition characterized by extreme weakness of the muscles, is one such disease (van der Geld and Strauss, 1966). The exact relationship between thymic dysfunction and the development of such diseases is unknown and clearly requires further study. Moreover, the recent work suggesting that the thymus exerts at least part of its effect by means of a blood-borne substance urgently calls for the extraction and purification of the biologically active thymus fraction; it may then prove possible to use this in clinical practice.

Implications for cancer research

Many tumours induced by viruses and chemical agents are now known to have their own antigenic individuality—that is, to have antigens ' foreign ' to those present in the host. It may seem paradoxical that antigenic tumour cells can multiply in an individual and not be eliminated by an immune reaction of the transplantation type against their foreign antigens. There are, however, a number of factors that facilitate the growth of antigenic tumours. The capacity to mount a transplantation type of immune reaction is less developed at birth than later, and newborn rodents are more susceptible to tumour-inducing viruses and chemicals than are older animals; thymectomy at birth renders animals more susceptible to these agents in adult life (Miller, Grant and Roe, 1963; Miller, Ting and Law, 1964; Grant and Miller, 1965; Miller 1966). Furthermore, chemical carcinogens have been shown to depress immunological reactivity. It can thus be seen that the development of some tumours will be facilitated by an inadequacy of transplantation immune reactions. Since these reactions are dependent on the thymus it can be assumed that the thymus forms part of a ' surveillance ' system, the function of which is to eliminate antigenically foreign cells before they can multiply. Correlations have been made between the increasing frequency of cancer with age, the increasing inability to react against a new antigen as the animal ages and the final regression and atrophy of the thymus in old age (see, for example, Burnet, 1965).

As antigenic differences (even though they may be slight) exist in many cases between normal and cancer cells, anything that would enable the immunological system to discriminate between cells of normal and altered antigenic constitution could be beneficial. What is required is a factor which produces ' the converse of the effect of cortisone in damping down immunological reactivity ' (Burnet, 1957). A logical place to look for such a factor is in the thymus, since it has been shown that a blood-borne substance originating in the thymus is operating during the development of the immune system. This then is a further reason for investigating the biological activity of thymus fractions.

This knowledge of the part played by the thymus in natural resistance to tumours has opened up a new chapter in cancer research. Logical development of research in this field must increase our understanding not only of the normal function of the thymus but also of the role of immune processes in resistance to chemically induced and viral cancers. It will certainly shed some light on the means by which resistance to cancer may be increased.

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A NEW THEORY OF TEMPERATURE CONTROL IN THE HYPOTHALAMUS

The brain is not a compact mass of tissue but contains a number of communicating cavities, the cerebral ventricles, which are filled with cerebrospinal fluid. To study the functions of the brain drugs can be introduced into these cavities so that they penetrate the ventricular walls and act on the nervous structures contained in them, or fluid that has been perfused through the cerebral ventricles can be tested for substances released into it from the nervous structures.

During the last twelve years, relatively simple methods have been developed for injecting drugs into the cerebral ventricles of animals (Feldberg and Sherwood, 1953; Hasselblatt and Sproull, 1961) and for perfusing the cerebral ventricles of cats (Bhattacharya and Feldberg, 1958; Carmichael, Feldberg and Fleischhauer, 1965; Feldberg and Myers, 1966). A number of modifications have made it possible to confine the perfusion of drugs to selected parts of the ventricles, and to detect in the outflowing fluid substances released into it from various specific parts of the ventricular walls. One recent outcome of these studies is a new theory of temperature control in the hypothalamus.

Some substances, when artificially administered in minute amounts, are found to have a particular effect on a part of the body in which they are normally present, though in an inactive form (that is, bound to some tissue constituent from which they have to be freed in order to become active); the problem then arises of whether the effects that follow the injection of these substances mimic a physiological function. Three substances, the monoamines noradrenaline, adrenaline and 5-hydroxytryptamine (5-HT), are naturally present in and exert an effect on the hypothalamus or, more precisely, the anterior hypothalamus, which is situated in the walls of the ventral half of the third ventricle, a cleft-like cavity in the middle of the brain near its base. In a study of the distribution of these monoamines in the brain of the dog, Vogt (1954) and Amin, Crawford and Gaddum (1954), working in the University of Edinburgh, found that noradrenaline was present in the hypothalamus in a concentration of 1 microgram per gram of fresh tissue, and that adrenaline and 5-HT were present in weaker concentrations. The physiological function that these monoamines are thought to imitate when they are administered to this part of the brain is the control of body temperature.

It has long been known that the hypothalamus influences body temperature. But what happens in this part of the brain when changes in temperature occur? Are noradrenaline, adrenaline and 5-HT released, as suggested by the effects when they are injected into the cerebral ventricles? It was known that when 5-HT was injected into the cerebral ventricles of cats it produced shivering whereas noradrenaline and adrenaline had the opposite effect and stopped shivering (Domer and Feldberg, 1960). Moreover, injections of bacterial pyrogens into the cerebral ventricles of the cat were known to produce not only fever but also vigorous shivering. Could it be that this pyrogen-induced shivering would similarly be abolished by intraventricular noradrenaline and adrenaline and, if so, would these substances affect body temperature as well—would they reduce fever and perhaps even lower normal temperature? Could it be that 5-HT is a pyrogen, causing fever as well as shivering when injected into the cerebral ventricles?

In this article some attempts to answer these questions are discussed. A great deal of the work has been carried out during the last three years by Feldberg and Myers (1963; 1964a, b; 1965a, b; 1966) at the National Institute for Medical Research. These workers observed that intraventricular injections of adrenaline in unanaesthetized cats lowered for several hours normal rectal temperature as well as temperature elevated by bacterial pyrogens. The injections also stopped the shivering that accompanied fever produced by the bacterial pyrogens. On the other hand, 5-HT injected intraventricularly caused a long-lasting rise in rectal temperature. All these effects result from the action of the monoamines on the anterior hypothalamus, for similar changes in rectal temperature occurred when these substances were introduced directly into this part of the hypothalamus by micro-infusion. Only a few micrograms were required—in fact, in one experiment only half a microgram of adrenaline produced a fall in temperature of over 0·5°C. The anterior hypothalamus occupies both walls of the third ventricle, but the micro-infusions were made unilaterally. Thus it seems that levels of 5-HT or of adrenaline or noradrenaline on only one side of the anterior hypothalamus determine the level of body temperature. Micro-infusion of these monoamines into the posterior or ventro–medial hypothalamus did not affect temperature.

The most common changes in body temperature are the rise produced by bacterial pyrogens (that is, the fever of infectious diseases) and the fall which occurs in anaesthesia. So far little is known about the action of bacterial pyrogens. It is possible that they may act by causing increased production and release of 5-HT, perhaps with inhibition of the release of adrenaline and noradrenaline. Moreover, the pyrogens may render the hypothalamus more sensitive to the action of 5-HT, and there is the further possibility that they do not act solely through the release of the monoamines, but that they themselves mimic the effect of 5-HT.

In anaesthesia the mechanism of temperature regulation ceases to function; the animal becomes poikilothermic (cold-blooded) and therefore temperature will tend to fall to the level of the environmental temperature. The fall in temperature has been shown to be due to an action of the anaesthetics on the anterior hypothalamus. Feldberg's and Myers' evidence for this was as follows: (1) In unanaesthetized cats a fall in rectal temperature was obtained when anaesthetics were injected into the cerebral ventricles in doses that were far too small to be effective when injected intravenously. (2) Perfusion of an

anaesthetic through the ventral half of the third ventricle—the walls of which contain the hypothalamic nuclei—produced a fall in temperature; this did not happen when the anaesthetic was perfused through the dorsal half of this ventricle. (3) One anaesthetic, chloralose, was shown to lower temperature when minute amounts (a few micrograms) were introduced directly into the anterior hypothalamus.

Some anaesthetics, such as pentobarbitone sodium, produce not only a fall in temperature but a fall followed by a rise accompanied by strong shivering. When successive injections of small doses of this anaesthetic were made into the cerebral ventricles of unanaesthetized cats, each injection produced a fall followed by a rise beyond the pre-injection level, so that finally fever level was reached. The onset of each rise was associated with shivering. In man anaesthesia produced by halothane is associated with shivering.

What then is the mechanism of the fall in temperature during anaesthesia? And why do some anaesthetics produce a fall followed by a rise accompaned by vigorous shivering? Does the fall result from an ' anaesthetizing ' action on the hypothalamus, rendering this structure insensitive to the action of the monoamines? This may happen when anaesthesia is very deep, but it does not explain the fall that occurs during a somewhat lighter anaesthesia because in this condition the hypothalamus still responds to the monoamines, as was shown in experiments in which adrenaline, noradrenaline or 5-HT was injected intraventricularly into cats during general anaesthesia. Adrenaline and noradrenaline postponed the return to normal temperature for many hours, whereas 5-HT had the opposite effect—in fact it not only accelerated the return to normal temperature but also raised temperature to fever level.

We have to assume therefore that the fall in temperature during anaesthesia is brought about because the anaesthetics modify the rate of release of the monoamines. One possibility would be that they increase the release of noradrenaline and adrenaline. An increased release of 5-HT may occur at the same time but, initially at least, the more pronounced effect of the noradrenaline and adrenaline would prevail and mask that of the 5-HT. The release of one monoamine may well be affected to a greater or lesser extent than that of the others by particular anaesthetics. For instance, an increased release of 5-HT during anaesthesia may be a characteristic feature of pentobarbitone sodium in cats and of halothane in man, which would account for the shivering seen after the administration of these anaesthetics in the two species. Although we cannot yet say for certain how anaesthetics modify the release of the monoamines, the new theory at least enables us to explain in physiological terms peculiar features—such as shivering—associated with certain anaesthetics.

However, is it permissible to generalize and to assume that the results obtained with cats are valid for other species, including man? This question is pertinent because Cooper, Cranston and Honour (1965), working in the Council's Body Temperature Research Unit in Oxford, found that in rabbits the monoamines, when injected into the cerebral ventricles or into the hypothalamus, produced effects opposite to those observed in cats: noradrenaline and adrenaline raised and 5-HT lowered body temperature. The hyperthermic effect of adrenaline injected into the cerebral ventricles of rabbits had already been described a few years earlier by von Euler, Linder and Myrin (1943). Although these responses are the opposite of those obtained in cats, the results show that in the rabbit too the hypothalamus is sensitive to the monoamines. Further,

the response seen in the rabbit appears to be the exception because Feldberg, Hellon and Myers (1966) found that the hypothalamus of dogs and monkeys responded to the monoamines in the same way as that of the cat. In dogs they recorded not only rectal temperature but skin temperature as well (as an index of skin vasodilatation) and showed that at least two central mechanisms were involved in the temperature-lowering effect of noradrenaline and adrenaline—a reduction of heat production by abolition of shivering and by reduction of muscle tone, and an increase of heat loss by skin vasodilatation. The first mechanism was activated by lower doses of the amines than was the second mechanism. According to Allen and Marley (1966), working at the Maudsley Hospital, London, the hypothalamus of birds appears to respond to the monoamines in the same way as that of cats, dogs and monkeys.

The occurrence of the monoamines in the hypothalamus and their effects when they are injected into this structure, though strongly suggestive, do not prove that they have a physiological role in the control of body temperature. Proof would be the demonstration that they are released in the hypothalamus and that their release affects temperature. How could this evidence be obtained?

If the amines released in the hypothalamus were to diffuse from the ventricular walls into the cerebrospinal fluid of the third ventricle, they would most likely also diffuse into fluid perfused through this ventricle. So the next step would be to perfuse the third ventricle and to test the outflowing perfusate for the monoamines. This has so far been done only for 5-HT, which can be assayed in minute amounts by measuring its effect on a preparation of the isolated strip of the rat's stomach fundus. The use of the fundus strip for assaying 5-HT was introduced by Vane (1957), working in the Department of Physiology at the Royal College of Surgeons, London. When the strip is suspended in a bath containing 5 ml of fluid, less than one nanogram (a millionth of a milligram) of 5-HT will cause it to contract.

Feldberg and Myers perfused the third ventricle of anaesthetized cats with fluid resembling cerebrospinal fluid and collected the perfusate. When they then added small amounts of the perfusate to a bath in which the fundus strip was suspended, the strip contracted. This in itself was not proof that the fluid contained 5-HT because a number of other substances would also cause the strip to contract. But when they found that a specific antagonist of 5-HT, 2-bromolysergic acid diethylamide, inhibited the contraction to the same extent as it inhibited a contraction produced by 5-HT, they could be reasonably sure that the contraction produced by the perfusate was due to the presence of 5-HT. The amounts of 5-HT assayed were small and often only just within the limits that could be detected by the assay. Thus a regular and definite correlation between temperature and the amount of 5-HT in the perfusate could not be established, although in some experiments an increase in 5-HT was noted in samples collected at a time when the low temperature produced by the anaesthesia began to rise. It became clear that without some means whereby the 5-HT in the perfusate could be increased, so that changes in 5-HT level could be readily recorded, it would not be possible to get much further.

Anticholinesterases (inhibitors which prevent the enzymatic destruction of the released acetylcholine) have been of invaluable help in the past in demonstrating the release of acetylcholine from cholinergic nerve endings and it was thought that a similar procedure might be used for 5-HT. Two possibilities

suggested themselves—the use of inhibitors of monoamine oxidase, the enzyme that destroys 5-HT, and the use of 5-hydroxytryptophan (5-HTP), the precursor of 5-HT. So far only the latter procedure has been tried (El-Hawary and Feldberg, 1966). 5-HTP was added to the fluid used for perfusing the third ventricle of anaesthetized cats. The output of 5-HT in the effluent increased between 50- and 100-fold, the cat began to shiver and its temperature rose, provided a toxic side-effect of 5-HTP (a central depressant action) could be overcome.

In the course of these experiments great individual variations were observed in the 5-HT output before the addition of 5-HTP to the perfusion fluid, and in cats with an initially high output the content of 5-HT in the effluent rose much higher during the 5-HTP perfusion than it did in those with an initially low output. These individual variations in turnover and synthesis of 5-HT could be correlated with the changes in temperature obtained when 5-HTP was given by simple intraventricular injections. In some cats the injections produced large rises in temperature with vigorous shivering, in others small rises with mild shivering. When the third ventricle was subsequently perfused under anaesthesia, those cats that had shown a large rise in temperature were found to have an initially high output of 5-HT, which reached very high levels during 5-HTP perfusion, whereas those that had shown a small rise in temperature had an initially low output, which did not reach very high levels during 5-HTP perfusion. Individual variations in turnover and synthesis of 5-HT in the hypothalamus, which explain the variations observed in the response to intraventricular 5-HTP, may also provide a plausible explanation of why some individuals develop high fever more readily than others.

Another application of the new theory of temperature regulation concerns a phenomenon that has puzzled neurosurgeons for a long time: the high fever and shivering bouts that occur in certain cases of brain injury. Feldberg and Myers tried to find out how long it would take for the 5-HT to disappear from the perfusate when perfusion of the third ventricle was continued after the cat was killed. To their surprise they found that the 5-HT activity did not disappear at once, but that on the contrary it increased, sometimes over 20-fold, in the samples collected during the first 30–60 minutes after death, and then diminished gradually. What is the significance of the post-mortem rise in 5-HT output, the ' life after death ' in the hypothalamus? On the assumption that normal temperature depends on a fine balance in the release of noradrenaline, adrenaline and 5-HT in the hypothalamus, the basic mechanism to keep up temperature would appear to be the release of 5-HT. As soon as the blood supply to this part of the brain is interrupted, 5-HT is released at an abnormally high rate. This happens after death—and if the animal were not dead its temperature would rise and it would shiver! The same may happen in cases of brain injury in which small vessels in the hypothalamus tear or contract spastically, since abnormally large amounts of 5-HT are released in the regions that no longer receive their normal blood supply, with the result that temperature rises and shivering sets in.

The fact that fever and bouts of shivering occur also in brain injuries that affect the midbrain does not render this interpretation invalid. According to recent fluorescent microscope studies by Swedish workers (Carlsson, Falck and Hillarp, 1962; Dahlström and Fuxe, 1964) the monoamines in the hypothalamus are mainly located not in the nerve cells but in the nerve endings surrounding them. The ' monoaminergic ' nerve fibres were found to originate

in more caudal structures of the brain, in particular in the midbrain. Therefore interruption of the blood supply in this part of the brain might well result in an increased release of the 5-HT from the nerve fibres that terminate in the hypothalamus.

There is still a long way to go before this new theory of temperature control in the hypothalamus is firmly established and before the conditions in which the three monoamines are released are fully elucidated. But just as, over thirty years ago, the discovery of the role of acetylcholine in the transmission of nerve impulses across cell boundaries in the peripheral nervous system changed our outlook on practically all problems of neuromuscular and ganglionic transmission, so also may knowledge of the role of the three monoamines in the hypothalamus change our approach to the problem of temperature control.

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MOTOR MECHANISMS IN THE HUMAN GASTROINTESTINAL TRACT

The development of modern physiological techniques and their application to the investigation of clinical problems has rapidly led to spectacular advances in recent years in our knowledge of normal and abnormal function in such organs as the heart, lungs and kidneys. The digestive tract is more difficult to study, partly because of its sheer length and inaccessibility and also because its cellular structure is so complex and its functions so varied. Our knowledge of its secretory, digestive and absorptive activities is much more precise than that of its motor functions, because the secretions and products of digestion can be collected and analysed, and because much of the information about digestion derived from animal experiments is directly applicable to man. The physiology of gastrointestinal muscle, on the other hand, is difficult to study even in animals and its behaviour varies from species to species and from one level of the digestive tract to another. Over the past few years, however, some remarkable advances have been made in our knowledge of the cellular physiology of intestinal muscle (see review by Burnstock, Holman and Prosser, 1963), and new methods have been developed for recording and analysing its behaviour in man. Much of the work described in this article was carried out in the Council's Gastroenterology Research Unit at the Central Middlesex Hospital, London.

A better understanding of the physiology of gastrointestinal movements is important to the clinician because these movements are involved in many of the commonest and most serious diseases affecting the swallowing, transit, digestion and absorption of food. Moreover, it is commonly assumed that a disorder of muscular function is responsible for a wide variety of syndromes that are characterized by attacks of pain in different parts of the abdomen (sometimes accompanied by vomiting or diarrhoea). Symptoms of this kind are very common and usually recurrent and intractable, though all investigations—including exploratory operations in the most severe cases—prove negative. These symptoms are usually attributed to distension or incoordination of segments of muscle, or to abnormal contractions somewhere along the bowel, possibly induced reflexly in response, for example, to the ingestion of food. All this was little more than surmise until recently, when more refined methods for the clinical investigation of such disorders were developed. The application of these new methods has not only improved diagnostic accuracy and provided a guide to treatment but has also increased our understanding of normal physiology.

Layers of smooth muscle line the whole of the digestive tract with the exception of the mouth and throat, where the muscles are skeletal in type. The muscles of the mouth and throat, like those of the limbs, contract and relax quickly and only in response to impulses from the central nervous system, whereas most smooth muscle is spontaneously active and may contract slowly and rhythmically, even after all its nervous connections have been severed. Two different tracts of apparently similar smooth muscle may show opposite responses to stimulation, so that identical nervous impulses may cause a contraction in one and a relaxation in the other. This unpredictable behaviour of smooth muscle is one of the fundamental problems of physiology, but the application of modern electrophysiological techniques at the cellular level has already shed enough light on the problem to remove any justification for invoking a biological ' Uncertainty Principle ' to explain it. Briefly, it has been shown that the electrical potential of the membrane of a smooth muscle cell is continually fluctuating and that this electrical instability is related to the membrane's high permeability to sodium and other ions that move across it, the energy required for the process being supplied by metabolic reactions within the cell. The response of the cell to stimulation probably depends on the state of its membrane potential at the time—that is, whether it is polarized or depolarized.

The electrophysiological state and therefore the response of smooth muscle to stimulation vary so much from species to species that advances in the clinical field must depend on a study of the behaviour of smooth muscle in man himself. One approach to this problem has been made possible by the development of a technique for recording the contractions of strips of human muscle taken from tissue removed during operations and kept alive in the laboratory. The responses of the strips of muscle, both to direct stimulation with drugs, hormones and electrical impulses and to indirect stimulation through the nerve cells and plexuses enmeshed between the layers of muscle, can be studied, and in this way it is possible to analyse the nature of the defective mechanism in some neuromuscular disorders, including those affecting the gastrointestinal tract.

All attempts to devise direct methods for recording the activity of intestinal muscle *in situ* in a living individual, whether by mechanical methods or by electrical techniques analogous to electrocardiography, have proved unsuccessful. There are, however, two valuable indirect methods—cineradiography and techniques for the accurate measurement of pressure within the channel of the intestine (either by means of fine polyethylene tubes or by using radiotelemetering capsules). Cineradiography became practicable with the development of image intensifiers, which enable the radiation hazard to be reduced to an acceptable level. This technique solved the problem of analysing rapid movements because the cinefilm can be projected at any speed and studied at leisure.

X-rays, however, reveal no more than the shape and movement of barium in the gastrointestinal tract. If at the same time pressure within the channel is recorded, the muscular forces that move and mould the barium can be studied and assessed, particularly in those areas where the bore of the channel is narrow or relatively constant, as for example in the oesophagus and sphincters. Measurements of pressure in the stomach and intestine are more difficult to interpret,

because the bore of the channel and resistance to the flow of the contents are continually changing. However, the development of the transistorized pressure-sensitive radiotelemetering capsule (popularly known as the radio-pill because it can be so easily swallowed) was a major advance. It provides a freely mobile observation platform within the intestine and transmits data, not only about the changing pressures but also about its own movements, from all parts of the digestive tract, most of which was previously inaccessible except by methods involving the swallowing of tubes—an uncomfortable and often distressing procedure (Connell *et al.*, 1963). By recording data simultaneously from different levels in the digestive tract it is possible to study the reflexes and other mechanisms that control and coordinate its motor functions in health and disease.

The sphincter mechanisms and disorders of swallowing

These new methods have proved much more successful for analysing the rapid sequence of neuromuscular events involved in the act of swallowing than for clarifying the often sluggish but subtle movements of the stomach and intestines (Edwards and Rowlands, 1960). After the food or fluid has been swallowed, it passes through the pharynx and down the oesophagus into the stomach. Pressure measurements show that the oesophagus is closed at both ends by the contraction of the sphincter muscles, which relax reflexly during swallowing, and contract again immediately after the bolus of food has passed through (Code, Creamer and Schlegel, 1958; Atkinson *et al.*, 1957a). Since the pharynx is a common channel for breathing and swallowing, the air-passages to the nose and lungs have to be blocked momentarily during swallowing by contraction of the palatal and laryngeal muscles. Meanwhile the constrictor muscles of the pharynx contract to drive the food through the upper oesophageal sphincter, which relaxes before the food enters the pharynx. Then the sphincter closes and the food passes rapidly down the oesophagus, followed by a wave of contraction, and enters the stomach through the lower oesophageal sphincter, which relaxes reflexly as soon as the food enters the pharynx. Then this sphincter closes and the wave of oesophageal contraction passes through it.

Difficulty in swallowing may arise if this sequence of neuromuscular events is disturbed, at any point between the mouth and the stomach, by any one of a wide variety of diseases of nerve and muscle. The skeletal muscles of the mouth, palate or pharynx may be paralysed by diseases which affect their nerve supply. For example, in those cases of diphtheria in which the nervous system is affected food may regurgitate through the back of the nose because the palatal muscles are paralysed, and in poliomyelitis food may accumulate in the pharynx because the pharyngeal muscles are too weak to propel it through the upper sphincter. The oesophagus and its lower sphincter, being composed of smooth muscle, are rarely affected by diseases of the central nervous system but they are frequently affected by diseases of muscle. For example, in patients suffering from systemic sclerosis, a condition in which there is widespread degeneration of muscles throughout the body, the muscle of the oesophagus is often affected and may be too weak to contract when the patient swallows. This in itself, however, does not cause difficulty in swallowing because the muscle of the lower sphincter is also affected by the disease and the food passes through it by the force of gravity. The observation that the oesophagus fails

to contract when a patient swallows can, however, provide an important clue to the diagnosis of systemic sclerosis and related diseases, which are difficult to diagnose, especially in their early stages.

In achalasia of the cardia, the commonest and most serious neuromuscular disorder of swallowing, the lower sphincter fails to open and the coordinated oesophageal wave of contraction is replaced by irregular contractions occurring intermittently here and there. Strips of muscle taken from the body of the oesophagus of patients with this disorder respond normally when the muscle fibres are stimulated directly, but they do not respond at all to indirect stimulation through the nerve cells and plexuses between the layers of muscle. Examination with the microscope shows the muscle cells to be normal but the nerve cells degenerated and sparse. It is these nerve cells that control and coordinate the muscular movements to produce the wave of contraction that progresses down the oesophagus. Strips of sphincter muscle also fail to respond to indirect stimulation, though this normally produces a prompt relaxation (Adams *et al.*, 1961). The only drug which can be used clinically for relaxing the sphincter is octyl nitrite, which acts directly on the muscle cells; unfortunately it is not possible to give adequate doses for effective treatment because this drug acts on smooth muscle throughout the body, producing unpleasant and dangerous side-effects (Edwards, 1964). For the same reason it is not possible to treat the disease by the administration of the chemical transmitter substances that are normally released as a result of nervous impulses. In the past, both medical and surgical treatment of this condition was largely based on the assumption that the sphincter muscle was in spasm, but pressure measurements show that this is not the case and that the only difference from the normal is that the pressure in the sphincter fails to fall during swallowing. The only effective treatment available at present for this very serious disease is to cut the sphincter muscle.

Another type of neuromuscular disorder, oesophageal spasm, is characterized by the sudden onset of an intense, sustained muscular contraction that is localized to one part of the oesophagus and blocks the channel. This usually happens during a meal, causing a severe attack of pain associated with retching and vomiting. The cause is unknown but the symptoms may be triggered off in some patients by regurgitation of acid from the stomach into the oesophagus.

The oesophagus passes out of the chest through a slit in the diaphragm to join the stomach in the abdomen a few centimetres below the diaphragm. The physiology of the oesophago–gastric junction is enigmatic and controversial and the very existence of a sphincter at this point was denied until quite recently because, unlike the other sphincters of the digestive tract, it is not recognizable anatomically as a thickened ring of muscle. It is now generally accepted, however, that the smooth-muscle coats of the last four centimetres or so of the oesophagus are normally contracted so that they perform the physiological functions of a sphincter, relaxing only during the act of swallowing to allow food to pass into the stomach. The question that remains is whether the sphincter plays an important part in the mechanisms that prevent reflux from the stomach, where the pressure is positive and may rise as high as 100 centimetres of water, into the oesophagus, where the pressure is subatmospheric. When this anti-reflux mechanism breaks down, as it frequently does, the acid and pepsin secretions of the stomach can flow backwards into the oesophagus,

where they cause inflammation, heartburn and regurgitation of acid into the mouth, and sometimes obstructive stricture with severe pain and vomiting. Medical treatment is ineffective in severe cases and the results of surgery are often disappointing. Several different operations have been tried but it will not be possible to plan a definitive surgical procedure to cure the disorder until the mechanisms that prevent reflux have been identified and understood. Many contradictory theories have been advanced to explain the anti-reflux mechanism, mostly based on observations made on animals, on anaesthetized patients at operation, or on the cadaver. A new theory based on pressure measurements and cineradiography seems to fit the clinical facts rather better.

The primary mechanism for the prevention of reflux seems to depend on the fact that the oesophagus normally joins the stomach below the diaphragm, so that the terminal inch or so is subjected to the positive pressure within the abdominal cavity. The walls of the oesophagus are held close together as it passes through the slit in the diaphragm, and the positive intra-abdominal pressure forces them more firmly together. The higher the pressure rises in the abdominal cavity (during lifting or coughing, for example) the more tightly will it keep the channel of the abdominal oesophagus closed (Creamer, Harrison and Pierce, 1959; Edwards, 1961). The oesophageal sphincter alone cannot be the principal barrier against reflux because it normally relaxes with every swallow and it can be destroyed surgically (in the treatment of achalasia, for example) without any evidence of reflux. This theory appears to be confirmed by observations on those patients who suffer most severely from reflux, namely those with hiatus hernia (Atkinson *et al.*, 1957b). In this condition a portion of the stomach herniates through the slit in the diaphragm into the chest, so that the oesophagus joins the stomach in the chest, where the pressure is negative. When this happens the sphincter is the only possible barrier against reflux of acid and pepsin secretions from the herniated portion of the stomach into the oesophagus. If there is free communication across the diaphragm between the main part of the stomach and the herniated portion, the sphincter is not strong enough to prevent reflux, and the patient suffers from intractable and incapacitating reflux oesophagitis. In many patients, however, the channel between the stomach and the hernia is narrow, and only opens during certain postural movements, such as turning or twisting the trunk, which alter the shape and size of the slit in the diaphragm. In these circumstances the sphincter may be strong enough to withstand the pressure in the hernia, which is much lower than is that of the main part of the stomach, and the symptoms of oesophagitis are likely to be mild and intermittent (Edwards, Phillips and Rowlands, 1964).

If this new theory is correct, the normal anti-reflux mechanism can be breached only if the pressure within the stomach rises higher than the pressure in the abdominal cavity surrounding the abdominal oesophagus, or if the walls of the oesophagus are pulled apart as they pass through the slit in the diaphragm. These are probably the mechanisms involved in belching and vomiting respectively. In the majority of patients who complain of belching, however, the air that they swallow never passes through the sphincter into the stomach but simply moves in and out of the oesophagus.

Measurements of pressure in the rectum and anal canal indicate that anal continence may depend on a similar mechanism. The anal sphincter alone is not strong enough to resist the sudden increases in abdominal pressure that take place during coughing and lifting, but the anal canal passes through

a slit in the muscular floor of the pelvis just as the oesophagus passes through the diaphragm, and a similar mechanism may operate in both cases (Phillips and Edwards, 1965). The pyloric sphincter, however, which is at the narrow exit from the stomach into the duodenum, does not function in the same way as do the oesophageal and anal sphincters: it is not a barrier that opens reflexly to allow gastric contents to pass through. It seems rather to act as a filter because of its narrow bore, and as part of a pumping machine to promote gastric emptying and prevent reflux from the duodenum into the stomach (Rowlands, 1963).

Normal and abnormal intestinal movements

Only a slight change of pressure seems to be necessary to empty the stomach and facilitate the flow of its contents through the intestines. Paradoxically, most of the muscular contractions have the effect of delaying rather than propelling the intestinal contents, thus ensuring sufficient time for the digestion and absorption of food. By recording pressures from the right and left side of the colon simultaneously it has been shown that the pattern and frequency of the pressure waves is quite different on the two sides, even at points only a few centimetres apart (Connell, 1959). Evidently these dissociated, segmenting contractions delay the transit of food residues through the colon so as to allow time for absorption of water and salts, and this explains the somewhat surprising fact that colonic contractions are diminished in patients suffering from diarrhoea (Connell, 1962). It seems likely that these contractions also control the rate at at which the faeces pass on to the sensitive areas of the rectum, since there is no demonstrable sphincter mechanism at the junction of colon and rectum.

These observations have shed some light on the mechanism of one of the commonest and most puzzling of abdominal disorders, the so-called 'irritable colon syndrome'. This is characterized by recurrent attacks of pain, often associated with some disturbance of bowel habit, for which no cause can be found by routine investigations or at operation. The colonic contractions are diminished in those patients whose main symptom is diarrhoea, whereas in those who suffer from severe attacks of pain and constipation muscular contractions are exaggerated, especially in response to meals and to drugs that stimulate smooth muscle (Chaudhary and Truelove, 1961). In some patients (who develop their symptoms during meals) exceptionally high pressures are recorded in the colon after eating (Connell, Jones and Rowlands, 1965). Presumably the intense muscular contractions cause transient functional obstructions of the bowel and the formation of pockets of gas, resulting in distension and pain.

There is increasing evidence that another common disease of the colon, diverticulosis, is associated with exceptionally high colonic pressures (Arfwidsson *et al.*, 1964; Painter and Truelove, 1964). In this disease, diverticula or pockets in the mucous membrane lining the colon are extruded between the muscle layers; on X-ray films they have the appearance of berries or grapes. Infection, abscess formation, perforation and bleeding are common complications. It is not yet known whether the very high colonic pressures recently observed in patients suffering from this disease are causally related to it, although this theory was advanced at least half a century ago. There is, however, some evidence that high pressures are already present in the prediverticular stage of the disease.

To what extent the reflexes and other mechanisms for controlling and co-ordinating the motor functions of the tract depend on local intestinal factors and to what extent on the extrinsic nerves is far from clear (Rowlands, 1965). Both the sympathetic and the parasympathetic nerves connecting the bowel to the central nervous system are often cut in the surgical treatment of various diseases without any obvious effect on the motor functions of the small intestine or colon. On the other hand, in patients in whom the lower part of the spinal cord is completely destroyed pressure waves in the colon are exaggerated and irregular (Connell, Frankel and Guttmann, 1963). The extrinsic nerves probably exercise a subtle modulating effect and they may well be the pathways for psychogenic influence on the intestinal movements. Morever the muscle of the digestive tract is affected by a wide variety of hormones and other chemical substances present in the blood and tissues, and it seems likely that some of these may also be concerned in the mechanisms that control and co-ordinate the intestinal movements. One such substance that has been intensively studied over the past few years is serotonin, which is present in most of the body tissues, the largest amounts being found in the digestive tract. It has recently been shown that serotonin, both *in vivo* and *in vitro*, stimulates the small intestine and the anal sphincter to contract, but it inhibits contractions of the colon and has a variable effect on the stomach (Fishlock, Parks and Dewell, 1965; Misiewicz and Waller, 1966). Its physiological role, if any, is still unknown, but it is secreted in large quantities by carcinoid tumours and is almost certainly the cause of the intractable diarrhoea that is one of the most serious symptoms of the carcinoid syndrome. It is therefore of considerable interest that in patients suffering from this disease the muscular contractions of the small intestine are grossly exaggerated compared with those in normal people, whereas the contractions of the colon are greatly diminished.

Although these new methods have only recently been applied to the investigation of clinical problems, they have already clarified our views about some of the motor mechanisms of the digestive tract. Further progress, however, depends on the continuing development of more refined and more direct methods for recording and analysing the muscular activity of the gut and for relating it to the processes of digestion, absorption and transit of food in the stomach and intestines. Because the physiology of intestinal muscle is so much affected by the psyche, ideally the patient should not be aware that he is being studied at all. Ingenious new methods to replace the use of swallowed tubes are continually being developed, involving radiotelemetering devices, radio-isotopes, ultrasonic techniques and so on, and these promise to be of great value.

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THE PROBLEM OF DECOMPRESSION SICKNESS IN DIVING AND CIVIL ENGINEERING

Man has long explored below the ocean's surface and to do so he must somehow adapt himself to the great pressure to which he becomes exposed. At a depth of no more than 33 ft of water, the absolute pressure is already 30 lb per sq in—twice that of his normal environment. To counteract the effects of such pressure, he can do one of two things: the first is to construct a rigid suit, which isolates him physically from the pressure. If the suit is to have sufficient strength, however, it becomes very heavy and unwieldy and in addition, because of the enormously increased frictional forces in the joints of the suit, movement becomes severely limited. The second approach, on which

almost all modern developments are based, is to allow the diver's body to be exposed to the surrounding water pressure, and to supply air at this pressure for him to breathe; he can then move freely and use all his normal manual skills.

The acceptance, physiologically, of an increased pressure brings in its turn three main hazards. Oxygen, which the diver must have, is poisonous at high pressures, producing as its most dramatic effect frank convulsions and loss of consciousness. This means that the partial pressure of oxygen respired must be kept suitably low, by diluting the air breathed with some inert gas. No gas, however, is totally inert; even the least chemically reactive, such as nitrogen and argon, when given at sufficiently high pressure prove to be narcotic, probably because they dissolve in the fatty elements of the brain. Helium, however, is not narcotic at pressures required for the depths that can be reached at present, so that divers can be protected from oxygen poisoning without incurring the risk of narcosis if they use helium and oxygen mixtures. Now the third problem arises: the inert gases breathed (whether nitrogen in air or helium in some artificial mixture) dissolve in the blood and tissues of the body according to Henry's Law, in proportion to their partial pressure. When a diver who has been breathing gases at high pressure is ' decompressed ', by returning to the surface, his body fluids are supersaturated with gas, and just as when the stopper is removed from a bottle of carbonated drink, bubbles tend to form. In animal experiments and in post-mortem examinations of humans such bubbles have been observed in the arteries, veins and heart, the brain and spinal cord, fatty tissue and other parts of the body. To these bubbles are attributed the various symptoms: pain in or near a joint (' bends '), itching of the skin (' sandhog itch '), pulmonary disturbances (' the chokes '), and a variety of neurological lesions. These effects occur, of course, only when the pressure is reduced; they constitute the condition called ' decompression sickness ' and can be relieved by recompression. From what has been said, it is clear that a risk of decompression sickness attends all exposures to high pressure.

The Medical Research Council supports research in this field in two main ways: through the Underwater Physiology Subcommittee of the Royal Naval Personnel Research Committee, a joint committee of the Royal Navy and the Council; and through the Decompression Sickness Panel, which is primarily concerned with work in compressed air in civil engineering. Most of the practical work described in this article was carried out under the auspices of one or other of these committees. Since diving on the one hand and industrial work in compressed air on the other present different aspects of the problem, advances in knowledge in these fields will be discussed separately.

Decompression sickness in diving practice

If decompression sickness is to be avoided, we must either know or make reasonable assumption about two things: first, the rate at which the body takes up gas when pressure is raised and loses it when pressure is lowered (processes usually called ' saturation ' and ' desaturation '), and second, the amount of supersaturation that can take place during decompression before the normally smooth elimination of excess gas (by diffusion into the air that is exhaled) is disturbed by the formation of bubbles in the body. The first successful approach to this problem was by Haldane over fifty years ago. He seized on the fact that it is almost always possible for a diver to surface from a depth

of 33 ft, or a little more, without symptoms of decompression sickness; the reduction of pressure involved—from 2 atmospheres to 1 atmosphere, or in other words a reduction to a half—thus appeared to be safe. Haldane argued that the volume of gas released from the body tissues would (by Boyle's law) always be constant provided that the proportional reduction in pressure was constant, so that a drop in pressure from 4 to 2 or from 6 to 3 atmospheres would be as safe as a drop from 2 to 1. Haldane also concluded, for various reasons, that the rate of saturation and desaturation would follow an exponential time-course, and that this rate would vary widely in different body tissues, but that in no tissue would the process take longer than about 5 hours. He was thus able to construct ' decompression tables ', which laid down the rates at which pressure should gradually be reduced to normal after exposure to any given higher pressure. These tables ensured that the pressure of the gas in any of the tissues of the body was never more than twice the pressure of the atmosphere in the decompression chamber at any time during the decompression process. (This rule was slightly relaxed, however, in the later stages of decompression.) The decompression procedure consisted of two stages: a primary reduction to half the initial absolute pressure, followed by a second stage in which pressure was gradually reduced to normal over a period that varied with the extent to which the body had become saturated.

Haldane's tables proved very effective for a time and were internationally used both for naval divers and for tunnel and caisson workers. However, when diving to greater depths and for longer periods was attempted, deficiencies appeared; the tables were found to be unnecessarily cautious for the shallower depths and shorter exposures, but not safe enough for greater depths and longer exposures. As a result, a variety of arbitrary adjustments were made, both by Haldane himself and by others, but the rationality of the method was reduced. Recently, Hempleman, of the Royal Naval Physiological Laboratory, suggested a completely new approach (Hempleman, 1952; Rashbass, 1954); this was based on the fact that the uptake of gas was limited, not as Haldane postulated, by the rate at which it was carried by the blood to the various organs, but by the rate at which the gas could diffuse from the capillaries into the surrounding tissues. Tables constructed on this basis were much simpler to devise, and proved to be superior to Haldane's for shorter exposures. However they were again not completely satisfactory, and arbitrary adjustments were required as deeper and longer dives were attempted (Crocker and Hempleman, 1957).

At this point an experimental reassessment of the underlying theory by Hempleman (1957, 1960, 1961) brought to light certain important facts. Hitherto, theoretical considerations had implied that if the pressure was rapidly lowered after any given exposure, the risk of decompression sickness depended only on the degree of saturation at the time of the rapid decompression and on the ratio by which the pressure fell. In principle, therefore, the risk of a given decompression should be the same for the same conditions of saturation, regardless of how those conditions were arrived at. Hempleman tested these ideas by devising compound dives in which after a period at a suitable pressure there was a further exposure to a higher or lower pressure, followed by a rapid decompression. The risk attached to a particular degree of saturation could then be assessed, according to how far, in the final rapid decompression, the pressure could safely be lowered. The experiments showed that a given saturation carried a greater risk if it had been preceded by a fall of pressure than if it

had been preceded by a rise; in other words, saturation and desaturation, so far as risk of decompression sickness was concerned, were not the symmetrical processes, analogous to the uptake and elimination of anaesthetics, that they had been believed to be. Second, it was shown that the risk incurred as a result of a given proportionate fall in pressure is much increased if it is followed by subsequent falls in pressure. These results can be accounted for by a tentative theory that on decompression so-called ' silent ' bubbles may be formed which do not produce symptoms, but which can interfere with the elimination of gas, and can expand so as to cause symptoms if there is a further reduction of pressure.

A word must be said about the method used in investigations of this sort. Decompression sickness in a form at all comparable to that in man can be induced in only one experimental animal, the goat, and for this reason a good deal of experimental work and testing of possible procedures are done with these animals. The susceptibility of the goat is not identical with that of man, however, and sooner or later human trials are necessary. Great credit is due to the courage and skill of the naval teams who have conducted these trials. Recently a group of naval divers in this country demonstrated how a dive to a depth of 600 ft could be made safely for a useful working period. Though there have been more spectacular dives, in which individuals have for a brief period been to greater depths, this achievement is an outstanding one, unexcelled elsewhere.

Compressed air workers and bone necrosis

In civil engineering, the medical problem is rather different. The pressures are relatively low—sufficient to keep water out of a tunnel working or caisson—and are usually no higher than 50 lb per sq in gauge (i.e. 50 lb per sq in above atmospheric pressure); but in place of a limited amount of diving, often for quite short periods, by few highly trained and disciplined naval personnel, during a single tunnel contract shifts of up to 8 hours a day are worked by a population of several score, made up to a considerable extent of unskilled labourers who travel round the country for work at different sites. Because the pressures are not very high, and work is in free air, many of the diver's problems are avoided; and indeed until recently compressed air work has not seemed to present many problems, provided that recommended procedures were followed. In 1954, however, Paton and Walder, reporting on a study of decompression sickness during the construction of a tunnel, noted some unsatisfactory features. First, although the type of decompression sickness known as ' bends ' occurred (on the average) after less than two per cent of all compressions, nevertheless virtually all shift workers suffered from it at some time before their work in compressed air ceased, simply because their exposures were so numerous. It is true that ' bends ' seem to be painful rather than dangerous, and an incidence of under two per cent has long been accepted as satisfactory. But if some longer-lasting harm were found to be associated with it, the fact that so large a number of workers eventually suffer would be disquieting. Further, the method of treating bends was unsatisfactory. The procedure is to recompress the worker until the pain disappears or leaves at most some residual soreness, and then to decompress him in such a way that pain does not recur. This has proved very difficult, and multiple therapeutic recompressions were, and still are, a very common feature of medical

care. Finally, it was noted that cases of decompression sickness came in waves, almost epidemic in character. This proved to be associated, not with any environmental factor, such as deterioration of working conditions, but with the introduction of new recruits to the labour force. Men were found to 'acclimatize' to work in compressed air, so that the chance of suffering an attack of bends after a standard shift and standard decompression fell from around 10–15 per cent on the first day to 1–2 per cent after ten days. The acclimatization was lost over a similar period of absence from work under pressure. These observations greatly assisted both the interpretation of data obtained during a particular contract and the comparison of the results from different contracts. But they also raised a question: should the decompression schedules be framed for the new recruit, and therefore waste the time of the acclimatized, or should they be suited to the acclimatized at the expense of the new recruit? And if, as is clearly desirable, it were decided to frame them to give protection to the recruit, how could one find an industrial undertaking where the necessary practical trial could be carried out—an undertaking with a continuing entry of new recruits as well as suitable environmental conditions?

Doubts about the full effectiveness of existing decompression procedures were greatly strengthened by later discoveries. First was the observation that severe cases of decompression sickness could be associated with pathological changes in the lungs (Campbell Golding *et al.*, 1960). In two instances, an air cyst was found in the lungs, the expansion of air within which during decompression could be supposed to discharge air bubbles into the circulation. This suggested the possibility that, more generally, decompression sickness might be due in part at least to the production of bubbles by the expansion of air trapped in the lung beyond regions of bronchial or bronchiolar occlusion; such a situation could readily occur with quite minor bronchial abnormalities. A search for signs of pulmonary abnormality in men susceptible to decompression sickness has not been fruitful, and cases resembling the two mentioned prove so far to be uncommon. Provisionally, then, the results suggest that any man with abnormalities of the lung should be excluded from work in compressed air; but they do not support a more general theory that decompression sickness is to any great extent due to bubbles produced by the expansion of air trapped in the lungs.

Second, and more important, was the question of bone damage. It had long been known that among the sequelae of decompression was arthritis of the hip or shoulder; but its incidence was quite unknown, it was not very widely recognized as being associated with decompression, and it could reasonably be questioned whether the described cases were *certainly* due to decompression sickness. Accordingly, during the construction of a later tunnel, the Decompression Sickness Panel made a deliberate radiographic search, to discover the incidence of such damage. This brought to light a considerable number of cases of early bone lesions (Campbell Golding *et al.*, 1960); and a subsequent more extensive survey on another contract indicated that, as judged by radiology, nearly 20 per cent of all shift workers develop a bone lesion of some sort, and that in 5 per cent it is so placed, near an articular surface, that arthritic changes are likely (McCallum and Walder, 1966).

From what is already known, some picture of the process can be built up. When the lesion is fully developed in a shoulder or hip, radiology shows a wedge-shaped area of articular surface and underlying bone delimited by an

area of increased calcification; associated with this is a degree of disorganization of the articular surface. There are good reasons for believing that these signs represent, not the primary lesion, but the result of repair processes, and that the original lesion may have been much more widespread. The first radiological changes may not be detectable until months after the last exposure to pressure; and since symptoms of arthritis will only develop if and when the articular surfaces come to be involved, clinical recognition may be slower still.

This discovery poses a very difficult problem in preventive medicine. Decompression procedures have hitherto been formulated so as to protect the diver or worker from acute forms of decompression sickness. Now some way must be found of formulating safe procedures to prevent these chronic effects even though it will be necessary to wait for months or years before the results of their use can be assessed. Nor do we have much guidance in the preliminary stages of this task. It is true that bone lesions are most common in men exposed frequently and to the higher pressures; but they have also occurred in men who have experienced single or very few exposures at quite low pressures, and in men with no history of acute decompression sickness of the ordinary kind. There is no firm evidence of how the regions of bone concerned take up gas, precisely how the lesions are produced, what degree of supersaturation is safe, or the full natural history of the lesion.

To deal with the situation three things are being done. First, wherever possible radiographic surveillance of the working force is undertaken. Second, to establish a continuing follow-up a Central Decompression Sickness Registry has been set up at the Department of Industrial Health, 10 Claremont Place, Newcastle upon Tyne. Detailed records were kept of all the exposures to pressure and attacks of bends for the whole working force during the study by Paton and Walder, and much additional information has been obtained subsequently. It is hoped that as complete a record as possible of the working experience of all compressed air workers may be obtained, which will be correlated by computer with the accumulating radiographic data. Third, the first steps have been taken in an attempt to draw upon a pool of wider experience, through international cooperation. An International Working Party was organized recently, at which it became clear that similar problems and difficulties were being met elsewhere. In certain countries, decompression procedures are employed differing from those used in Britain; and if data could be obtained from countries using such different procedures, it would offer some hope of shortening the search for an adequate decompression procedure.

It seems clear, however, that completely satisfactory regimes of decompression and of therapeutic recompression will not be evolved unless carefully controlled practical trials of different regimes can be carried out over a long period in an industrial setting. The difficulties are obvious, but the encouraging degree of collaboration with contractors and engineers now achieved gives hope that successful arrangements will be made.

The future

In spite of the outstanding problems, there is good reason to believe that the advances of recent years have conjointly opened the way to a much wider exploration of the biological effects of high pressures. It is true that the fundamental physico-chemical events which initiate decompression sickness, despite

much past and current work, still elude us. But as sometimes happens in medicine, prevention is in advance of fundamental theory. From studies on divers, a rational foundation for the design of decompression schedules is emerging; from work on the larger populations of civil engineering workers, the means by which we can learn how to control bone necrosis are becoming clear. The time is rapidly approaching when there will be no bar, in principle, to a full exploitation of such benefits as can be developed from the use of high pressures in medicine, and more generally of the scientific and economic rewards of underwater exploration.

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* Obtainable from the Ministry of Defence.

RESEARCH SUPPORTED BY THE MEDICAL RESEARCH COUNCIL

The following section of the report takes the form of a handbook providing information about the activities of Council establishments—the National Institute for Medical Research and the Council's research units—and of members of their external scientific staff. In each case the summaries of research are preceded by lists of staff employed by the Council and of others who have worked in association with the establishment in question. In addition to members of the Council's scientific staff, these lists include, under the heading 'Other senior staff', the names of those working in the following categories: Senior Technical Officers; Technical Officers; Chief Technicians II; Technical Research Assistants (Higher); Senior Executive Officers and Higher Executive Officers (including library staff of equivalent grades).

After the lists of the Council's own establishments and external staff information is given, in summary form, about other projects supported by the Council under various schemes of grants and training awards—namely, institutions assisted by block grants, research groups, short-term research grants, fellowships and scholarships.

National Institute for Medical Research

Mill Hill, London N.W.7

(Mill Hill 3666)

The National Institute for Medical Research, the largest of its kind in the Commonwealth, is the Council's principal research establishment. It was originally set up at their Hampstead Laboratories (formerly the Mount Vernon Hospital) in 1920, but in 1950 most of the Institute's Divisions moved to a new building at Mill Hill. Three Divisions (as indicated below) are, however, still housed in the building at Hampstead.

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

Director

Sir Peter Medawar, CBE, D SC, FRS

Deputy Director

J. H. Humphrey, MD, FRS

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Scientific staff

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P. A. Bell, BA*
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R. K. Callow, D PHIL, FRS (*until Feb. 1966*)
J. R. Chapman, D PHIL
Mrs J. Gigg, PH D
R. H. Gigg, PH D
E. A. Johnson, D PHIL
P. E. Linnett, B SC
C. D. Warren, PH D

Other senior staff

W. A. L. Marshment
N. Schunmann
E. V. Wright

BIOPHYSICS

Scientific staff

A. S. McFarlane, MB, B SC (*Head of Division*)
P. A. Charlwood, PH D
T. Freeman, BM, MC PATH
A. H. Gordon, PH D
S. B. Henriques, DR MED (*until June 1965*)
G. S. Hodgson, DR MED (*until Oct. 1965*)
R. C. Holloway, M SC
E. L. Regoeczi, DR MED
R. C. Valentine, PH D
N. G. Wrigley, BA

Other senior staff

G. Dickinson
L. N. Louis
C. D. Sutton
M. R. Young, FRPS, FRMS

Attached workers

P. Jacques, DR MED (*University of Louvain; British Council Bursar*)
Miss L. Mutschler, PH D (*US Public Health Service Postdoctoral Fellow*)

BIOCHEMISTRY

Scientific staff

T. S. Work, D SC (*Head of Division*)
H. R. V. Arnstein, D SC (*until Oct. 1965*)
I. B. R. Bowman, PH D (*until Dec. 1965*)
M. Cannon, PH D
N. R. Cohen, B SC
R. A. Cox, PH D
C. P. Fawcett, PH D
N. M. Green, PH D
S. Jacobs, PH D, FRIC†
C. G. Knight, M SC
E. M. Martin, PH D
M. D. Melamed, M SC
Miss A. Minter, B SC (*until Dec. 1965*)
D. Peel, D PHIL
Mrs R. V. Pitt-Rivers, PH D, FRS
J. R. Tata, D-ÈS-SC
C. C. Widnell, PH D‡
A. R. Williamson, PH D

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* Transferred to the staff of the Dunn Nutritional Laboratory in April 1966.
†On leave of absence at the University of Ibadan.
‡ On leave of absence at Argonne Cancer Research Hospital, Chicago.

Other senior staff

A. D. Brownstone
J. L. Coote
A. W. Hemmings
E. J. Toms

Attached workers

Z. Awdeh, MS (*American University of Beirut*)
J. J. Betheil, PH D (*Albert Einstein College of Medicine, New York*)
Miss S. A. Bonanou, B SC
P. D. Cooper, PH D (*National University of Australia, Canberra*)
H. Edelhoch, PH D (*US National Institutes of Health*)
C. A. Gonzalez, MD (*University of Venezuela*)
Mrs H. G. Gould, PH D (*US Public Health Service Postdoctoral Fellow*)
D. Haldar, D PHIL (*Indian Institute for Biochemistry and Experimental Medicine, Calcutta; 1851 Scholar*)
T. H. Hamilton, PH D (*University of Texas; Guggenheim Fellow*)
L. Konieczny, DR MED (*Ministry of Health, Poland*)
T. de Leo, PH D (*University of Naples; NATO Fellow*)
R. J. Naftalin, MB, M SC (*MRC Junior Research Fellow*)
H. L. Schwartz, PH D (*Downstate Medical Center, State University of New York; US Public Health Service Fellow*)

EXPERIMENTAL BIOLOGY

Scientific staff

N. A. Mitchison, D PHIL (*Head of Division*)
D. R. Bainbridge, MB (*until Sept. 1965*)
R. H. R. Bomford, PH D
L. Brent, PH D (*until Apr. 1965*)
D. W. Dresser, PH D
J. Farrant, PH D
G. Gowland, PH D (*until July 1965*)
M. Ruszkiewicz, PH D *
Miss A. U. Smith, MB, D SC
Mrs A. Taylor, PH D (*honorarium; part-time*)
R. B. Taylor, PH D, B VET SC

Other senior staff

F. H. Crisp, AIST

Attached workers

P. J. Chesterman, MB, FRCS (*St. Mary's Hospital, London*)
C. J. Inchley, B SC (*University of Edinburgh*)
Miss S. V. Jooste, B SC (*Atomic Energy Board, Pretoria*)
M. Laurence, MB, FRCS (*St. Mary's Hospital, London*)
R. H. Levey, MD (*Harvard Medical School*)
S. Utsumi, MD, PH D (*University of Pennsylvania; Wellcome Trust Research Fellow*)
H. H. Wortis, MD (*Stanford Medical Center, Palo Alto; US Public Health Service Research Fellow*)

PHYSIOLOGY AND PHARMACOLOGY

Scientific staff

Professor W. S. Feldberg, CBE, MD, FRS (*Head of Division*)
G. W. Bisset, MD, D PHIL
Miss B. J. Clark, MB
R. F. Hellon, D PHIL
O. F. Hutter, PH D
D. H. Sproull, MD, B SC
Mrs A. E Warner, PH D

Other senior staff

A. Spratt
J. P. B. Stean

Attached workers

M. B. El-Hawary, MD (*University of Cairo; Riker Fellow*)
Professor K. J. M. Fleischhauer, MD (*University of Hamburg; Wellcome Trust grant-holder*)
Mrs J. Haldar, M SC (*Indian Institute for Biochemistry and Experimental Medicine, Calcutta; Wellcome Trust grant-holder*)
G. H. Hall, PH C (*Tobacco Research Council*)
M. C. Harris, DIP TECH (*MRC Scholar*)
V. J. Lotti, PH D (*Center for Health Sciences, Los Angeles; US Public Health Service Research Fellow*)
W. C. de Mello, MD (*Institute of Biophysics, Rio de Janeiro; Rockefeller Fellow*)
R. D. Myers, PH D (*US Office of Naval Research contract-holder*)
E. Reit, DR VET MED (*US Public Health Service Special Fellow*)
M. Rocha e Silva, DR MED (*University of São Paulo; British Council Scholar*)
J. Stekar, DR MED (*Pathophysiological Institute, Ljubljana; British Council Scholar*)

* On leave of absence at the Jackson Laboratory, Bar Harbour, Maine.

HUMAN PHYSIOLOGY

NIMR (Hampstead Laboratories), Holly Hill, London N.W.3

Scientific staff

O. G. Edholm, MB, B SC (*Head of Division*)
R. H. Fox, MB
R. Goldsmith, MB
I. F. G. Hampton, B SC
T. J. Hunt, D PHIL
H. E. Lewis, MB, B SC
Miss M. C. C. Lobban, PH D, MRCVS
L. G. C. E. Pugh, BM
Miss B. E. Tredre, PH D

Other senior staff

E. A. Crowley, B SC
J. W. Jack, BEM
G. R. Plimsaul
C. R. Underwood, FRMS
E. J. Ward

Attached workers

Col. J. Adam, MB, B SC (*RAMC*)
Mrs P. Bradbury (*MRC external staff*)
J. Brotherhood, MB (*British Antarctic Survey*)
Miss M. A. Chambers, B SC (*MRC grant-holder*)
R. W. M. Corner, MB (*British Antarctic Survey*)
E. R. Hillier, MB (*British Antarctic Survey*)
M. Rice, MB (*British Antarctic Survey*)

BIOMEDICAL ENGINEERING

NIMR (Hampstead Laboratories), Holly Hill, London N.W.3

Scientific staff

H. S. Wolff, B SC (*Head of Division*)
A. G. A. Pickford, GRAD IERE
A. J. Solman, B SC

Other senior staff

J. A. Baker
K. Callan

Attached workers

A.S. Velate, B SC (*MRC grant-holder*)
C. Weller, GRIEE (*Institute of Psychiatry, London*)

VIROLOGY AND BACTERIOLOGY

Scientific staff

H. G. Pereira, DR MED (*Head of Division*)
A. C. Allison, BM, D PHIL
J. P. T. Boorman, BA (*until Jan. 1966*)
P. Draper, D PHIL
Miss F. C. Fildes, B SC
Miss E. W. Garbutt, M SC (*until Apr. 1965*)
P. M. D'Arcy Hart, CBE, MD, FRCP (*part-time; until June 1965*)
J. M. H. Pearson, BM, MRCP *
Mrs A. Porebska, DR MED
J. S. Porterfield, MD
R. J. W. Rees, MB, B SC, FC PATH
W. C. Russell, PH D
M. F. R. Waters, MB, MRCP

Other senior staff

D. Busby, AIST
C. V. Gibbs
V. G. Law

Attached workers

L. Berman, MD (*US Public Health Service Fellow*)
P. M. D'Arcy Hart, CBE, MD, FRCP (*MRC grant-holder*)
L. Kjellen, MD (*Mälmo Allmanna Sjukhus*)
L.-G. Lundin, FIL LIC (*University of Uppsala*)
L. Mallucci, MD (*Italian National Research Council grant-holder*)
A. R. Salim, DKSM, DIP BACT (*University of Khartoum*)
Mrs T. Steimatsky, PH D (*Ministry of Health Virus Laboratory, Tel-Aviv; Action for the Crippled Child grant-holder*)

LABORATORY OF CYTOPATHOLOGY

Scientific staff

Miss J. S. F. Niven, MD, FC PATH (*Head of Laboratory*)
J. A. Armstrong, MB, M SC

Other senior staff

F. J. Higginson

* On secondment for work in Malaysia.

LABORATORY FOR RESEARCH ON INTERFERON

Scientific staff

A. Isaacs, MD, FRS (*Head of Laboratory*)
J. A. Sonnabend, MB, MRCPE

Attached workers

F. Himmelweit, MD, PH D, FRCPE
E. Mecs, PH D (*Institute of Microbiology, Szeged, Hungary; Wellcome Trust Research Fellow*)
Z. Rotem, PH D (*Israeli Embassy, London*)
J. G Tilles, MD (*Boston City Hospital; US Public Health Service Special Fellow*)

MICROBIOLOGY

Scientific staff

M. R. Pollock, MB, FRS (*Head of Division until Apr. 1965*)
H. J. Rogers, PH D (*Head of Division from May 1965*)
J. F. Collins, D PHIL (*until Aug. 1965*)
K. G. H. Dyke, PH D
A. J. Garrett, PH D*
R. Holliday, PH D
R. C. Hughes, PH D
J. Mandelstam, PH D
B. T. Pickering, PH D (*until June 1965*)
D. A. Reaveley, PH D
M. H. Richmond, PH D (*until July 1965*)
W. M. Waites, PH D
S. C. Warren, D PHIL
N. S. Willetts, BA (*until Aug. 1965*)

Other senior staff

Miss J. M. Fleming, (*until May 1965*)
I. G. Mathison

Attached workers

M. Fodor, DR MED (*Medical University of Debrecen, Hungary; WHO Fellow*)
H. Gest, PH D (*University of Washington, St. Louis; National Science Foundation Senior Postdoctoral Fellow*)

IMMUNOLOGY

Scientific staff

J. H. Humphrey, MD, FRS (*Head of Division*)
Miss B. A. Askonas, PH D
Miss B. M. Balfour, BA, MRCS
D. C. Dumonde, MB (*until Jan. 1966*)

Other senior staff

Mrs R. M. De Rossi

Attached workers

A. C. Aisenberg, MD (*Massachusetts General Hospital; Guggenheim Fellow*)
Mrs B. Argyris, PH D (*University of Syracuse; US Public Health Service Research Fellow*)
Miss I. Auzins, PH D (*University of Adelaide; Commonwealth and Industrial Research Organization Student*)
M. Frank, MD (*US Public Health Service grant-holder*)
C. A. Janeway, BA (*Harvard Medical School*)
H. Jaquet, MD (*Swiss Academy of Medical Sciences grant-holder*)

PARASITOLOGY

Scientific staff

F. Hawking, DM, FRCP, DTM (*Head of Division*)
I. N. Brown, B SC
K. N. Brown, PH D
Miss H. G. P. Dixon, M SC
A. T. Fuller, PH D
C. D. Ginger, PH D †
D. J. Hockley, B SC
Mrs V. E. Jones, PH D
S. R. Smithers, PH D
P. I. Trigg, PH D
D. C. Warhurst, PH D
J. Williamson, PH D
R. J. M. Wilson, PH D ‡

Other senior staff

M. J. Worms, B SC

Attached workers

Miss B. M. Ogilvie, PH D (*Wellcome Trust Fellow*)
R. J. Terry, PH D (*SE Essex Technical College*)

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* On leave of absence at Tufts University School of Medicine, Boston.
† On leave of absence at University of Massachusetts.
‡ On leave of absence at Harvard University.

BIOLOGICAL STANDARDS

Scientific staff

D. R. Bangham, MB (*Head of Division*)
S. G. Anderson, MD, D SC
Miss J. M. Bond, PH D
P. J. Campbell, PH D
Miss P. M. Cotes, MB, PH D
V. Houba, DR MED (*until Mar. 1966*)
Mrs M. Kogut, PH D
Miss N. M. I. Kovacic, DR MED, DR SCI, PH D
J. W. Lightbown, M SC, DIP BACT
Miss M. V. Mussett, B SC
J. A. Parsons, BM
M. P. Stack-Dunne, PH D
P. L. Walton, PH D
Miss P. M. Woodward, B SC

Other senior staff

K. R. Hobbs
P. H. Isaacson
J. Prasad, B SC
L. Ward, AIST

Attached worker

R. J. Summers, B PHARM (*MRC Scholar*)

IMMUNOLOGICAL PRODUCTS CONTROL

NIMR (Hampstead Laboratories), Holly Hill, London N.W.3

Scientific staff

F. T. Perkins, PH D (*Head of Division*)
L. R. Boulger, MB
L. D. Brookes, BM
Miss M. Clarke, MB, DCH
E. G. Hartley, MRCVS
L. F. Hewitt, D SC
Mrs M. C. Holness, B SC
J. P. Jacobs, MA
D. I. Magrath, PH D
T. W. Osborn, MB
Miss G. R. Paton, B SC
G. Sander, DR MED
F. W. Sheffield, MB
Miss M. A. Westwood, PH D
Miss R. A. Yetts, B SC

Other senior staff

H. Ward, AIST

Attached workers

E. Ferreira, MD (*Government of Portugal grant-holder*)
J. R. Thayer, B SC (*National Biological Standards Laboratory, Parkville, Victoria; WHO Fellow*)

ENGINEERING

Scientific staff

W. C. Lister, B SC, MIEE, F INST P (*Head of Division*)
J. Edwards, M SC
B. C. Elford, B SC
N. L. Gregory, M SC
W. J. Perkins, MIEE, MIERE
F. G. Tattam, ME
B. M. Wright, MB

Other senior staff

R. B. Bower, AIST
C. F. Doré, AIST
B. J. Hammond, AMIEE, AMIERE
J. E. Lewin, AMIERE
E. A. Piper
L. L. Woodget, AIST

ANIMAL DIVISION

Scientific staff

A. W. Gledhill, SC D, MRCVS (*Head of Division*)

Other senior staff

D. J. Short, MBE, FIAT

Attached worker

D. L. J. Bilbey, MB, PH D (*King's College, London*)

LABORATORY OF HUMAN BIOMECHANICS

NIMR (Hampstead Laboratories), Holly Hill, London N.W.3

Scientific staff

R. J. Whitney, PH D (*Head of Laboratory*) D. W. Grieve, PH D

Other senior staff

Mrs R. J. Gear

UNATTACHED MEMBER OF INSTITUTE

D. G. Smyth, PH D

COMMON COLD RESEARCH UNIT

Harvard Hospital, Salisbury
(Salisbury 22485)

Scientific staff

D. A. J. Tyrrell, MD, FRCP (*Head of Division*)
Sir Christopher Andrewes, MD, FRCP, FRS (*Consultant Adviser*)
Mrs J. E. Acornley, B SC
F. E. Buckland, DM (*died May 1965*)
M. L. Bynoe, MB, DTM & H, D OBST RCOG
P. J. Chapple, PH D
N. J. Dimmock, PH D
Miss J. M. Liptrot, B SC
D. Taylor-Robinson, MD
Miss G. H. Walker, MB (*until Feb. 1966*)

Attached workers

M. Albanese, DR MED (*University of Palermo*)
Miss M. Dimic, MD (*Institute of Hygiene, Belgrade; WHO Fellow*)

WORKS AND MAINTENANCE

J. Cree (*Building Superintendent*)
J. C. Tyler (*Maintenance Engineer; NIMR Hampstead Laboratories*)

LIBRARY

L. T. Morton, FLA (*Librarian*)
Mrs R. E. Arnstein, BA, ALA
R. J. Moore, ALA

ADMINISTRATIVE STAFF

L. J. Hale (*Personnel Officer*)
Mrs M. E. A. Lang (*Administration; NIMR Hampstead Laboratories*)
J. H. Platts (*Finance Officer*)
Miss P. M. Towend (*Director's Secretary*)

The work of the Institute is generally designed to cover as wide a field as possible in basic non-clinical medical research, and is 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 the mechanisms of protein synthesis, the actions of viruses on cells, and the nature and control of the immunological response, 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 investigations on the growth of leprosy organisms, the storage of tissues, the action of pharmacological agents infused into the cavity of the brain, and many others besides.

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*) Mechanism of haemoglobin synthesis by reticulocyte ribosomes.
   (*b*) Protein synthesis by isolated mitochondria.
   (*c*) Control mechanisms in protein biosynthesis.
   (*d*) Mechanism of synthesis of immunoglobin.
   (*e*) Enzyme synthesis in synchronized yeast cells.
2. Protein structure:
   (*a*) Interaction between avidin and small molecules.
   (*b*) Chemical modification of biologically active peptides.
   (*c*) Specific chemical methods for rupture of peptide chains.
   (*d*) Quantitative amino acid analysis of proteins.
   (*e*) Structural studies on thyroglobulin.
3. Nucleic acids:
   (*a*) Purification of messenger RNA.
   (*b*) Fractionation of polynucleotides on acrylamide gel.
   (*c*) Secondary structure of ribosomal RNA.
   (*d*) Nucleotide sequence studies on ribosomal RNA.
4. Hormones:
   (*a*) Effect of various hormones on nucleic acid turnover.
   (*b*) Enzyme changes during amphibian metamorphosis.
   (*c*) Purification of neurohormones from the median eminence of the hypothalamus.
5. Virus replication:
   (*a*) Synthesis of EMC-virus RNA in cell-free systems.
   (*b*) Synthesis of EMC-virus proteins in cell-free systems.
6. Subcellular organelles:
   (*a*) Effect of thyroxine on mitochondria.
   (*b*) Specific active sites for attachment of RNA to ribosomes.
   (*c*) Preparation of mammalian cell walls.

BIOPHYSICS

1. Physical characterization of proteins:
   (*a*) Electron microscope studies of protein molecules.
   (*b*) Ultracentrifugal analysis of commercial human immunoglobin for standardization purposes.
   (*c*) Chemical and physico-chemical characteristics of human and rat transferrins.
2. Metabolism of plasma proteins:
   (*a*) Site of catabolism of plasma proteins.
   (*b*) Role of liver subcellular particles in catabolism of plasma proteins.
   (*c*) Effect of shock on synthesis of glycoproteins by the perfused liver.
   (*d*) Distribution of extravascular plasma proteins in the mouse.
   (*e*) Metabolic aspects of defibrination syndrome due to snake venom.
   (*f*) Clinical studies of haptoglobin metabolism.
3. Electron microscope studies of bacteria and viruses.
4. Investigation of aberrations in the interference optical system of the ultracentrifuge.
5. Acrylamide gel electrophoresis as a preparative technique.
6. Quantitative immunoelectrophoresis of pathological sera.

1. Filariasis:
   (*a*) Periodicity of microfilariae and its relation to the circadian rhythms of the host.
   (*b*) Control of human filariasis by drugs.
   (*c*) Filariasis in British wild birds and African mongooses.
   (*d*) Immunological reactions to filarial infections.
   (*e*) Fine structure of microfilariae and of adult worms.
2. Malaria:
   (*a*) Experimental immunology.
   (*b*) Development and nature of drug resistance to chloroquine.
   (*c*) Attempts to cultivate endoerythrocytic forms of *Plasmodium*.
   (*d*) Synchronization of the endoerythrocytic cycle.
3. Schistosomiasis and other helminthic infections:
   (*a*) Mechanism of acquired resistance to *Schistosoma* and *Nippostrongylus*.
   (*b*) The role of reaginic-like antibodies in infections with *Schistosoma* and *Nippostrongylus*.
   (*c*) Identification and fractionation of allergens in *Schistosoma* and *Nippostrongylus*.
   (*d*) Factors responsible for the stimulation of acquired resistance to *Schistosoma* in monkeys.
   (*e*) Study of the host–parasite relationship of *Schistosoma* in the albino rat.
   (*f*) Characterization of polysaccharide antigen in eggs and cercariae of *Schistosoma*.
4. Trypanosomiasis:
   (*a*) Immunology of pathogenic trypanosomes.
   (*b*) Effects of trypanocidal drugs on the metabolism and fine structure of trypanosomes.
   (*c*) Platelets as contaminants in metabolic studies on trypanosomes.
   (*d*) Constitution and metabolism of lipids of *Trypanosoma rhodesiense*.
   (*e*) Cordycepin (3-deoxyadenosine) as a new trypanocidal agent.

ORGANIC CHEMISTRY

1. Biosynthesis of thiamine.
2. Chemistry of the micrococcin antibiotics.
3. Chemistry of thiazoles and thiazolines.
4. Improvements in chromatographic techniques.
5. Physico-chemical studies on salts of amidines with carboxylic acids.
6. Haemoglobin:
   (*a*) Quantitative characterization of haemoglobin variants in selected clinical material.
   (*b*) Chemical and physical studies of haemoglobins.
   (*c*) Study of genetically determined unstable haemoglobin variants.
   (*d*) Formation and properties of sulphaemoglobin.
   (*e*) Non-haemoglobin proteins in red cells.
7. Preparation, purification and quantitative spectroscopic characterization of model compounds and proteins.
8. Spectroscopic study of structural perturbations of proteins and related compounds.
9. Antihistaminic compounds in plant tissues.
10. Metabolism of vitamin D.
11. Chemical releasers and pheromones of Apidae.
12. Synthesis of plasmalogens.
13. Synthesis of derivatives of muramic acid.
14. Syntheses of sphingolipids.
15. Gas chromatographic analysis of aromatic chlorination products.
16. Chemical structure of the cell wall of *Bacillus subtilis*.

GENERAL MICROBIOLOGY AND ANTIBIOTICS

1. Bacterial surface structures:
   (*a*) Control of the biosynthesis of cell surface components.
   (*b*) Structure of the cell walls of *Bacillus licheniformis*, *Clostridium welchii* and *Mycobacteria*.
   (*c*) Relationship of cell wall and membrane formation to cell division and growth.
2. Control of metabolism:
   (*a*) Biochemistry of spore formation in *Bacillus subtilis*.
   (*b*) Mechanism of enzyme repression in *Escherichia coli*.
3. Microbial genetics:
   (*a*) Mechanism of recombination in *Ustilago*.
   (*b*) Radiation-sensitive mutants in *Ustilago*.
   (*c*) Cytoplasmic inheritance and ageing in fungi.

4. Leprosy and mycobacteria:
   (*a*) Attempts to cultivate *Myco. lepraemurium* in cell free medium.
   (*b*) Studies on *M. lepraemurium* and *leprae* in cell cultures.
   (*c*) Studies on human leprosy in experimental animals.
   (*d*) Isolation of mycobacteria from skin ulcers.
5. Attempts to produce sarcoidosis in animals.
6. Antibiotics:
   (*a*) Isolation and investigation of antibiotics from soil bacteria.
   (*b*) Mode of action of streptomycin.
   (*c*) Mode of action of penicillins and other antibiotics interfering with biosynthesis of cell walls.
   (*d*) Evolution of resistance to new antibiotics.

VIRUS RESEARCH

1. Adenoviruses:
   (*a*) Structure and antigenic composition of adenoviruses.
   (*b*) Carcinogenic action of adenovirus serotypes of human and animal origins.
2. Immune reactions in virus-induced tumours.
3. Arboviruses:
   (*a*) Growth in mammalian and mosquito cells *in vitro*.
   (*b*) Characterization of sandfly fever virus.
   (*c*) Transmission of arboviruses in Britain.
4. Common cold:
   (*a*) Mechanisms of transmission of the viruses of common colds.
   (*b*) Propagation of viruses in organ cultures of respiratory epithelium.
   (*c*) Characterization of some ' new ' respiratory viruses.
   (*d*) Mechanism of the inactivation of picornaviruses.
   (*e*) Antigenic studies of rhinoviruses as part of a WHO-sponsored collaboration.
   (*f*) Testing of rhinovirus vaccines in human volunteers.
   (*g*) Studies of substances that inhibit the multiplication of rhinoviruses.
   (*h*) Role of rhinoviruses and other viruses in severe infections of the lower respiratory tract.
   (*i*) Search for new *in vitro* methods of detecting viruses.
   (*j*) Testing of some allegedly non-specific methods of preventing colds.
5. Interferon:
   (*a*) Production and mode of action of interferon.
   (*b*) Effect of interferon on metabolism of uninfected cells.
   (*c*) Relationship between interferon and viral interference.
   (*d*) A naturally occurring blocker of interferon production.
   (*e*) Carcinogens and interferon production.
6. Murine viruses:
   (*a*) Growth of hepatitis virus in tissue culture.
   (*b*) Pathogenesis of leukaemias.
   (*c*) Epidemiology of ectromelia.
   (*d*) Development of mice infected *in utero* with lymphocytic choriomeningitis virus.
7. Mycoplasmas:
   (*a*) Rapid and simple methods of identifying mycoplasmas.
   (*b*) Biophysical characteristics of mycoplasmas.
   (*c*) Relationship of mycoplasmas to non-specific urethritis, chronic bronchitis and rheumatoid arthritis.
8. Viruses in *Paramecium*.
9. Studies on vaccinia–*B. subtilis* transfection.
10. Effects of penicillin and metabolic inhibitors on ultrastructure of the lymphogranuloma venereum agent.
11. Electron microscope studies of virus-infected cells.
12. Assessment of neurovirulence of poliovirus and its correlation with *in vitro* marker tests.
13. World Health Organization reference laboratory investigations with influenza and other respiratory viruses and arboviruses.

IMMUNOLOGY

1. Mechanism of cell damage by complement.
2. Fate of radioactively labelled antigens and haptens in relation to antibody production and induction of tolerance.
3. Mechanisms of tolerance in humoral immunity and delayed-type hypersensitivity.

4. Immunological response systems:
   (*a*) Identification of single cells producing antibody.
   (*b*) Functions of the thymus.
   (*c*) Life span of immunologically competent cells.
   (*d*) Specific reactions of macrophages in delayed-type hypersensitivity.
   (*e*) Subcellular mechanisms of antibody synthesis.
5. Cellular receptors for antigen.
6. Population dynamics of antibody-forming cells.
7. Tissue transplantation:
   (*a*) Normal lymphocyte transfer reaction and its histological analysis.
   (*b*) Analysis of the action of anti-thymocytic antisera.
   (*c*) Homograft reactions *in vitro*.
8. Antibody production by cells in diffusion chambers.
9. Investigation of immunization schedules in infants.
10. Development of immunity in foetal Rhesus monkeys.

BIOLOGY, CYTOLOGY AND PATHOLOGY

1. Freezing and storage of tissue:
   (*a*) Pharmacology of protective agents; uptake of non-electrolytes by smooth muscle.
   (*b*) Orthotopic grafting of hyaline cartilage; mechanism of liquid transport through cartilage.
   (*c*) Development of cryogenic equipment.
   (*d*) Ultrastructure of smooth muscle exposed to low temperatures.
2. Transplacental transfer in Rhesus monkey.
3. Physiology of erythropoietin secretion.
4. Isolation and pharmacological study of insect toxins.
5. Lysosomes:
   (*a*) Activation of lysosomal enzymes in virus-infected cells.
   (*b*) Concentration of carcinogenic and fluorescent drugs in lysosomes.
6. Electron donation and acceptance by molecules of biological importance.
7. Relationship of glucose-6-phosphate deficiency to cataract.
8. Cytology of pituitary gland of the Patas monkey.
9. Karyology of human diploid cell strains.
10. Euchrysine in fluorescence microscopy.

PHYSIOLOGY AND PHARMACOLOGY

1. Neural control of the release of vasopressin and oxytocin.
2. Inhibition of oxytocin by its analogues.
3. Role of amines in the hypothalamic control of body temperature.
4. Drugs acting from the cerebral ventricles and subarachnoid space.
5. Release of acetylcholine and monoamines from the brain.
6. Regions of the brain stem involved in the defence reaction.
7. Effects of polypeptides on the suprarenal medulla and sympathetic ganglia.
8. Histamine uptake and formation by animal tissue.
9. Effects of pH on electrical and mechanical properties of heart and skeletal muscle.

HUMAN PHYSIOLOGY AND BIOMECHANICS

1. Thermoregulation in man:
   (*a*) Physiological responses in controlled hyperthermia.
   (*b*) Stress in relation to hyperthermia.
2. Environmental studies in Antarctica.
3. Diurnal rhythms:
   (*a*) In psychosis and neurosis.
   (*b*) In blind subjects.
   (*c*) Cold diuresis.

4. Peripheral circulation in man:
   (*a*) In skin grafts.
   (*b*) Effects of temperature.
5. Effects of exercise: measurement of cardiac output and oxygen consumption.
6. Biomechanics of standing and sitting postures.
7. Analysis of complex movements of work and athletics (simultaneous use of force analysis platform, cinephotography and electromyography).
8. Biomechanics of human locomotion during infancy and adolescence, and comparison with adult locomotion.
9. Effects of prolonged inactivity and sitting on muscular function.

BIOLOGICAL STANDARDS AND CONTROL OF IMMUNOLOGICAL PRODUCTS

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 40 international and 20 British national or research standards or reference preparations.
   (*b*) Standardization of penicillin PAM preparations on behalf of WHO anti-yaws campaign.
4. Relative assessment of different penicillins and penicillin preparations on the basis of *in vitro* and *in vivo* experiments.
5. Methods of assay of streptokinase, urokinase and other activators of the fibrinolytic system.
6. Method of assay and characterization of heparins of various origins.
7. Methods of assay and characterization of pituitary hormones.
8. Control testing:
   (*a*) Inactivated poliomyelitis vaccine, oral poliomyelitis vaccines, inactivated measles vaccine, live attenuated measles vaccines, influenza vaccines and smallpox vaccine.
   (*b*) Diphtheria, tetanus, pertussis and BCG vaccines.
   (*c*) Development of new methods for control of rubella vaccine.
9. Clinical trials of efficacy of measles vaccines.
10. Methods of assay of combined vaccines.
11. Investigations of toxicity of pertussis vaccines.
12. Assessment of neurovirulence of poliomyelitis virus and its correlation with *in vitro* marker tests.
13. Tissue culture:
   (*a*) Provision of national tissue culture service.
   (*b*) Investigation of human diploid cell cultures for preparation of virus vaccines.
   (*c*) Karyology of human diploid cell strains.

BIOLOGICAL ENGINEERING AND INSTRUMENTATION

1. Use of analogue computer for the synthesis of mathematical models in biology, particularly in biochemistry and microbiology.
2. Use of TV scanning system for data processing of visual signals.
3. Physical methods of chemical analysis using gas chromatography, electron capture and mass spectrometry.
4. Factors governing breath/blood alcohol ratio and associated measuring techniques.
5. Development of particle separation methods.
6. Design and construction of special equipment, including cryogenic equipment, urine flow recording, cell counting, drop counting, servo controlled animal fluid balance, electronic microbalance, single and multichannel peristaltic pumps, apparatus for cartilage grafting and slow injection devices.
7. Development of fully automatic patient monitoring system.
8. Radio aids for survival at sea.
9. Development of methods for long-term implantation of ' radio pills '.
10. Design of implantable EEG radio transmitter for small animals.
11. Development of very small recording instruments to measure simple environmental and physiological variables on ordinary members of the population.
12. Fast access literature retrieval system (' FAIR ').
13. Apparatus for the measurement of metabolism during rest and sleep.
14. Equipment for the recording of behaviour and physiological parameters in the newborn.

Research Units

One of the chief means adopted by the Council for the long-term support of research has been the creation of research units in which they employ their own staff. The principle determining the establishment of units is that scientists of proven ability should be given the opportunity of leading a team working, within fairly wide terms of reference, in a particular field. Such units may be set up to further research into new subjects not yet appropriate for inclusion in the university framework, or to develop subjects which require support on a scale beyond the resources of a university or hospital or which have been hitherto neglected.

The majority of the Council's units are situated within or in close proximity to a university or hospital, but they are normally independent of the host institution both in function and in administration.

DEPARTMENT OF CLINICAL RESEARCH

University College Hospital Medical School, University Street, London W.C.1
(Euston 5861)

Director

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

Scientific staff

C. F. Barnaby, M SC, PH D
E. R. Beck, MB, B SC, MRCP
C. J. Edmonds, MD, B SC, MRCP
D. A. W. Edwards, MA, MD, MRCP †
B. M. Jasani, M SC
Miss J. C. Marriott, B SC
E. N. Rowlands, MD, B SC, FRCP †
C. T. Stockel, B SC
B. D. Thompson, B SC, PH D

Other senior staff

A. G. Cronquist, FBHI, DIP STA

Attached workers

R. J. Orton, B SC, GRAD INST P (*Apsley Grammar School, Hertford*)
Mrs H. Triantaphyllidis, DR MED (*Faculté de Médecine, Paris; until Nov. 1965*)

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*) Behaviour of normal and overactive glands, and of the metabolites discharged from them.
   (*b*) Nature of metabolites formed during ablation of normal thyroids in man and animals and during treatment of overactive glands with radioactive iodine.
2. Thyroid cancer:
   (*a*) Evaluation of the radioiodine treatment of thyroid cancer, criteria of suitability for any given case, 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 and overactive glands.

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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; Dr Edwards is also a part-time member of this Unit (p. 102).

(*d*) Relationship between tumour histology, metabolite formation and radioiodine turnover.
(*e*) Investigation of large-area solid or liquid scintillation counters, particularly for measurements of whole-body radioactivity in man and animals.
(*f*) Development of techniques for measurement of low-level radioactive sources, using solid or liquid scintillation counters for tracer studies.
(*g*) Computation of the distribution of radioactive sources within the human body corresponding to observed distributions of counting rates at the body surface.

3. Gastroenterology:
   (*a*) Achalasia, diffuse spasm and the hypertensive cardiac sphincter: manometric and cineradiographic studies.
   (*b*) Applied pharmacology of the oesophagus: manometric and cineradiographic studies.
   (*c*) Mechanisms concerned in (i) gastro-oesophageal reflux, aerophagy and vomiting; (ii) the production of oesophageal stricture; and (iii) the causation of symptoms of dysphagia from various causes and of the hiatus hernia syndrome.
   (*d*) Measurement of gastrointestinal pH and mucosal potential *in situ*.
   (*e*) Mechanisms of anal continence, defaecation and colon transport.
   (*f*) Clinical and radiological studies on the effects of treatment of hiatus hernia and achalasia.
4. Electrolyte distribution: passage of labelled sodium, potassium and other materials across the intestinal wall; electrical potentials across the wall and their variation with luminal electrolyte concentrations.
5. Inhibition of antidiuretic hormone production by alcohol ingestion.

GASTROENTEROLOGY RESEARCH UNIT

Central Middlesex Hospital, Park Royal, London N.W.10
(Elgar 5733)

Director

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

Scientific staff

H. B. Cook, MB, MRACP
D. A. W. Edwards, MD, MRCP*
D. J. Holdstock, MB, M SC, MRCP
T. D. Kellock, MD, MRCP (*honorary*)
J. E. Lennard-Jones, MD, MRCP (*part-time*)
J. J. Misiewicz, MB, B SC
Mrs M. Shiner, MRCS, DCH (*part-time*)
T. Smith, M SC
Miss S. L. Waller, MB, B SC
H. S. Wiggins, PH D

Attached workers

M. Eisner, MD (*University of Basle*)
E. A. Napier, PH D (*University of Michigan*)
T. C. Northfield, MB, MRCP (*Central Middlesex Hospital*)
J. D. Townsend, MD (*Permanente Medical Group, Walnut Creek, California*)

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

Summary of research

1. Pathogenesis and treatment of achalasia and oesophageal spasm.
2. Mechanisms of gastro-oesophageal reflux, aerophagy, flatulence and vomiting.
3. Gastric motility in anorexia nervosa.
4. Pressure-movement relationships in stomach and intestine.
5. *In vitro* responses of gastrointestinal smooth muscle removed at operation.
6. Effect of serotonin on human gastrointestinal smooth muscle *in vivo* and *in vitro*.
7. Effect of stress on gastric and colonic motility.
8. Mechanisms of colonic symptoms; comparison of motility of proximal and distal colon in health and disease.

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*Dr Rowlands and Dr Edwards work also in the Department of Clinical Research, University College Hospital Medical School, London (p. 101).

9. Measurement of transit rate in the gastrointestinal tract in health and disease.
10. Biochemical studies of the intraluminal phase of fat absorption and electron microscopy studies of the intracellular phase.
11. Correlation of mucosal changes in jejunal biopsies with clinical findings.
12. Origin of faecal fat in normal subjects.
13. Assessment of Lundh's pancreatic function test.
14. Investigation of intestinal bacterial flora.
15. Effect of carbenoxolone on gastric secretion.
16. Effect of anti-secretory drugs in the Zollinger–Ellison syndrome.
17. Effect of gastric freezing in the dog.
18. Therapeutic trials of oestriol and carbenoxolone and of high protein and high carbohydrate diets in the treatment of duodenal ulcer.
19. Assessment of therapy in Crohn's disease.
20. Therapeutic trials in ulcerative colitis.
21. Assessment of adrenal function during steroid therapy in ulcerative colitis.
22. Assessment of tests of vitamin B_{12} absorption.
23. Development of tubeless devices for measuring pressure and pH, for detecting the site of bleeding in gastrointestinal haemorrhage and for obtaining samples of intestinal contents.
24. Construction of a shielded whole-body counter for clinical studies and assessment of radiation to various organs.

DEPARTMENT OF EXPERIMENTAL MEDICINE

Tennis Court Road, Cambridge
and
Shaftesbury Road, Cambridge

(Cambridge 52252)

Director

Professor R. A. McCance, CBE, MD, D SC, FRCP, FRCOG, FRS*

Assistant Director

Miss E. M. Widdowson, D SC

Scientific staff

J. W. T. Dickerson, PH D (*until Oct. 1965*)
G. C. Kennedy, MB, PH D
L. Lawn, MD (*honorarium*)
M. J. Purves, MD, MRCP, PH D
D. A. T. Southgate, PH D
Miss M. W. Stanier, D PHIL (*until Sept. 1965*)
A. E. Thorn, MB, D OBST RCOG

Other senior staff

R. A. Spires, MIST

Attached workers

Miss H. M. Bruce, B SC (*MRC grant-holder*)
A. R. Hamad El Neil, MB, PH D (*University of Khartoum*)
D. Lister, PH D (*University of Cambridge; ARC scientific staff*)
K. J. McCracken, B SC, B AGRIC (*MRC Scholar*)
R. N. Misra, MD (*University of Lucknow; Colombo Plan Fellow*)
Miss A. W. Mitchell, M SC (*University of Birmingham*)
Miss C. W. Rintoul, MB, MRCP (*MRC Junior Research Fellow*)
Professor J. R. Robinson, MD, PH D (*University of Otago, New Zealand*)
Mrs M. Robinson, PH D (*University of Otago, New Zealand*)
Miss L. Thomas, M SC (*University of Edinburgh; Joseph Rank Ltd Student*)
J. M. Walshe, MB, SC D, FRCP (*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 dietary deficiency and disease. The work includes studies of normal infants and adults, of patients and of animals.

* Professor McCance is also Honorary Director of the Infantile Malnutrition Research Unit in Uganda (p. 151).

Summary of research

1. Effect of development, deficiencies of calories and protein, and rehabilitation from these deficiencies, on the composition of the tissues and cells of the body in human beings, pigs, poultry and rats.
2. Metabolism of the protein-and-calorie-deficient animal.
3. Food, growth and homoeostasis in the neonatal period.
4. Development of respiratory control in the foetus and newborn infant.
5. Fat and mineral metabolism in the newborn infant.
6. Development and use of an artificial placenta.
7. Hypothalamic regulation of water and energy expenditure, with special reference to hormone production and the blood supply to the kidneys.
8. Copper metabolism in man.
9. Pathogenesis and treatment of Wilson's disease.
10. Treatment of Paget's disease with fluorides.
11. Lead poisoning in small battery factories.

RHEUMATISM RESEARCH UNIT

Canadian Red Cross Memorial Hospital, Taplow, Maidenhead (Burnham 543)

Honorary Director

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

Scientific staff

Miss B. M. Ansell, MB, MRCP (*part-time*)
Mrs P. C. Brown, MD
R. Consden, PH D, FRIC
A. M. Denman, MB, MRCP
L. E. Glynn, MD, FRCP
E. J. Holborow, MD
A. Howard, B SC
G. Loewi, DM
Miss J. M. Phillips, PH D (*until June 1965*)
J. E. Scott, D SC
D. P. Page Thomas, MB
T. L. Vischer, DR MED
D. J. Ward, MB, MRCP (*until July 1965*)

Other senior staff

G. D. Johnson, FIMLT

Attached workers

R. D. Barnes, MD (*Guy's Hospital Endowments Fund Fellow*)
E. H. Beutner, PH D (*State University of New York; National Institute of Dental Research Fellow*)
W. V. Epstein, MD (*University of California; US Public Health Service grant-holder*)
M. Espiritu, MD (*University of St. Thomas, Philippines; Colombo Plan Fellow*)
H. J. Kaufmann, MD (*Ciba Ltd, Basle*)
D. H. Kearns (*US Public Health Service grant-holder*)
J. A. Kirrane, MB (*Beit Fellow*)
R. M. Kivel, MD (*Stanford University; National Institute of Arthritis and Metabolic Diseases Fellow*)
O. A. Räsänen, MD (*University of Oulu, Finland; Council of Europe Fellow*)
W. J. Reynolds, MD, FRCP CAN (*Canadian Arthritis and Rheumatism Society Fellow*)
E. L. Rhodes, MB (*King's College Hospital*)
S. D. Roberts, MD (*Arthritis and Rheumatism Council grant-holder*)
Mrs A. Sukonthamarn, MD (*University of Chulalenghorn, Ceylon; Colombo Plan Fellow*)
Mrs M. Tuffrey, B SC (*Hospital for Sick Children, Great Ormond Street*)

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

Summary of research

1. Changes in connective tissue with age and disease.
2. Use of immunofluorescent methods:
   (*a*) to detect autoantibodies in human and animal sera;
   (*b*) to study the distribution in the tissues of native and foreign antigens and of antibody;
   (*c*) to study immune responses at a cellular level.

3. Experimental study of autoantibodies and autoimmune disease.
4. Nature of immune responses to polysaccharide-containing antigens.
5. Family study of rheumatic fever, systemic lupus erythematosus and Still's disease, with reference to genetic constitution.
6. Long-term surveys of the course of rheumatic fever and rheumatoid arthritis in children.
7. Effects of prophylaxis in the prevention of rheumatic fever recurrences.
8. Controlled therapeutic trials in various connective tissue diseases.

CLINICAL ENDOCRINOLOGY RESEARCH UNIT

2 Forrest Road, Edinburgh 1
(Caledonian 3186)

Director
John A. Loraine, MB, D SC, FRCPE

Scientific staff

W. P. Barnard, B SC
E. T. Bell, PH D
Miss H. E. C. Cargill-Thompson, PH D (*until Nov. 1965*)
G. P. Crean, MB, PH D, MRCPE
Mrs M. M. Evans, B SC
R. A. Harkness, MB, PH D, MRCPE
Mrs J. K. Higgs, PH D (*until Aug. 1965*)
W. M. Hunter, PH D
W. J. Irvine, MB, B SC, MRCPE
K. E. Kirkham, PH D
Mrs M. Krishnamurti, MB (*until Dec. 1965*)
Miss M. W. Marshall, B SC
E. Menini, PH D
Mrs P. A. Sadler, M SC
Miss J. M. Sowerby, M SC
Miss R. M. Standeven, M SC
Miss P. M. Wilson, B SC

Other senior staff

H. A. F. Blair, AIST
D. W. Davidson
D. N. Love
Miss M. A. Mackay, FATA, AIST

Attached workers

P. M. Adhikary, M SC (*Department of Medicinal Plants, Katmandu, Nepal; British Council Scholar*)
L. Faro, DR MED (*St. Maria Hospital, Lisbon*)
P. C. Ganguli, MB, MRCPE (*MRC grant-holder*)
A. A. Gunn, MB, FRCSE (*Bangour General Hospital, Edinburgh*)
F. Halter, MD (*University of Berne; British Council Scholar*)
A. L. Herbst, MD (*Harvard University*)
D. Hogg, MB, FRACS (*University of Edinburgh*)
A. A. A. Ismail, B PHARM (*University of Cairo*)
K. Mašek, MD (*Postgraduate Institute of Medicine, Prague; WHO Scholar*)
A. Papanicolaou, DR MED (*Evangelismos Hospital, Athens*)
S. Sulimovici, M SC (*Tel-Hashomer Government Hospital, Tel-Aviv*)
Galina Truevtseva, CAND MED SCI (*Research Institute of Obstetrics and Gynaecology, Moscow; WHO Fellow*)
Pachara Visutakul, MB, PH D (*Colombo Plan Fellow*)

The main research interests of this Unit are: firstly, the development of assay methods for the quantitative determination of hormones and their metabolites in human body fluids; secondly, the application of such methods to a variety of clinical problems; thirdly, investigations designed to obtain information on the mechanism of action of hormones; and, finally, studies relating clinical and experimental endocrinology to other medical specialties, with particular reference to gastroenterology and autoimmunity.

Summary of research

1. Induction of ovulation in immature rats by administration of gonadotrophic hormones.
2. Interrelationships between thyroid function and the response to gonadotrophic stimulation in immature rodents.
3. Development of radioimmunological assay methods for luteinizing hormone and human chorionic gonadotrophin.
4. Effect of various compounds on pituitary gonadotrophic function in normal and pathological conditions.

5. Assay of follicle-stimulating hormone, luteinizing hormone and urinary steroids in patients receiving treatment with oral progestational agents and with clomiphene (MRL–41), in an attempt to elucidate the site and mode of action of these compounds (with Dr E. Mears, London; Dr M. C. N. Jackson, Exeter; Dr D. Charles, University of Pittsburgh, USA; Dr G. L. Foss, Bristol Royal Hospital, and Dr W. I. Morse, University of Dalhousie, Canada).

6. Establishment of a radioimmunological assay method for insulin.

7. Measurement of plasma growth hormone and insulin levels after glucose administration in normal adults, normal children and diabetics (with Dr J. A. Strong, Western General Hospital, Edinburgh; Mr W. M. Rigal, University of Edinburgh, and Dr L. J. P. Duncan, Royal Infirmary, Edinburgh).

8. Diagnostic value of serial estimations of plasma growth hormone in acromegaly and dwarfism (with Drs J. A. Strong and J. McClelland, Western General Hospital, Edinburgh, and Dr J. W. Farquhar, Royal Hospital for Sick Children, Edinburgh).

9. Development of a radioimmunological assay method for thyroid-stimulating hormone (TSH).

10. Biological nature of the long-acting thyroid stimulator and its separation from TSH in body fluids.

11. Serum TSH levels, in children and adolescents, in thyroid endocrinopathies and after hypophysectomy and yttrium implantation (with Dr J. W. Farquhar and Dr L. J. P. Duncan).

12. Chemical methods for the hydrolysis of steroid conjugates.

13. Assay methods for oestrogens, progesterone and its metabolites, pregnanetriol and corticosterone, with special reference to the development of techniques for the systematic analysis of steroids.

14. Development of a new assay method for the estimation of urinary testosterone and the application of the procedure to studies in normal men, normally menstruating women, patients with hirsutism and subjects with an abnormal sex chromosome constitution.

15. Endocrinology of puberty and of the menopause.

16. Endocrinology of anorexia nervosa and of dermatological conditions, with special reference to acne vulgaris (with Dr G. F. M. Russell, the Maudsley Hospital, London, and with the Department of Dermatology, Royal Infirmary, Edinburgh).

17. Hormonal interrelationships in abnormal gynaecological conditions, especially anovulatory cycles and the Stein–Leventhal syndrome, and in rhesus-immunized pregnancy (with Dr D. V. I. Fairweather and Dr D. G. Millar, Royal Victoria Infirmary, Newcastle upon Tyne).

18. Effect of age and parity on hormone excretion in normal pregnancy (with Dr D. V. I. Fairweather).

19. Experimental and clinical gastroenterology:
    (*a*) Development of a radioimmunological assay method for gastrin.
    (*b*) Factors regulating the growth of gastric mucosa, with special reference to the influence of the endocrine system, nutrition and experimental procedures, such as duodenal obstruction and vagotomy.
    (*c*) Gastric secretion in rats with chronic fistulae.
    (*d*) Hormone excretion patterns in patients with gastrointestinal diseases, especially those cases complicated by malnutrition.

20. Assessment of current methods of radioiodine therapy for thyrotoxicosis.

21. Studies in autoimmunity:
    (*a*) Establishment of a radioimmunological assay method for vitamin B_{12}
    (*b*) Function of the reticuloendothelial system in autoimmune *NZB* mice.
    (*c*) Changes in the thymus in patients with evidence of autoimmunity (with Dr M. D. Sumerling and Mr J. R. Cameron, Royal Infirmary, Edinburgh).
    (*d*) Clinical significance of thyroid antibodies in the diagnosis and management of thyroid diseases (with Dr J. N. Harcourt-Webster, University of Edinburgh).
    (*e*) Autoimmunity in relation to atrophic gastritis in man, with special reference to Addisonian pernicious anaemia.

ATHEROMA RESEARCH UNIT 125

Western Infirmary, Glasgow W.1

(Western 8822)

Acting Honorary Director

Professor Sir Edward Wayne, MD, PH D, FRCP, FRCPG

Scientific staff

T. B. Begg, MB, MRCP, MRCPG
C. J. W. Brooks, PH D, (*part-time*)
T. Fyfe, MB
W. A. Harland, MB, PH D, MC PATH, FRCPC
J. W. Kerr, MB, MRCP, MRCPG (*until Feb 1966*)
W. D. Mitchell, AH-WC (EDIN)
Miss L. E. Murchison, MB
R. Pirrie, MB, MRCPE (*part-time*)
G. Steel, B SC

Other senior staff

V. M. Wells, AIST (*until June 1965*)

This Unit is engaged in clinical and laboratory investigation of ischaemic heart disease and other occlusive vascular disorders. Particular attention is being given to some aspects of lipid metabolism and to the mechanisms of thrombosis.

Summary of research

1. Biochemical analysis of tissue lipids, with special reference to:
   (*a*) blood platelets;
   (*b*) minor steroids and hydrocarbons in atheroma;
   (*c*) adipose tissue;
   (*d*) serum-free fatty acids.
2. Effect of environmental factors, e.g. temperature and smoking habits, on lipid metabolism.
3. Dietary and other environmental factors affecting platelet aggregation and the viscosity of the blood.
4. Electrophoretic mobility of erythrocytes in occlusive vascular disease.
5. Patterns of faecal bile acid and neutral steroid excretion in health and disease.
6. Gastrointestinal lipolytic activity in ischaemic heart disease.
7. Morphological studies of atheroma.
8. Effects of lowering plasma cholesterol and other lipids on the incidence of ischaemic heart disease.
9. Histamine metabolites in the urine and metabolism of ^{14}C-histamine in allergic asthma.

CARDIOVASCULAR RESEARCH UNIT*

Postgraduate Medical School of London

Ducane Road, London W.12

(Shepherds Bush 2030)

Director

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

Scientific staff

D. H. Bergel, MB, PH D
I. Gabe, MD, MRCP
Miss D. N. Reid, PH D
M. Thomas, MB, MRCP

Attached workers

P. Avasthey, MD (*Nuffield Fellow*)
S. J. Fillmore, MD (*US National Institutes of Health Fellow*)
G. Makin, FRCS (*Postgraduate Medical School of London; Surgical Research Fellow*)
H. Miller, MD (*US National Institutes of Health Fellow*)
C. J. Mills, B SC (*Royal Society Paul Instrument Fund Research Fellow*)
A. Mourdjinis, MD (*University of Athens Fellow*)
F. Nager, MD (*University of Zurich Medical School*)
B. L. Pentecost, MB, MRCP (*Postgraduate Medical School of London*)
M. Pertle, MD (*Wellcome Research Fellow*)
D. Pomerantz, MD (*Canadian Heart Foundation Research Fellow*)
J. A. Reid, MD (*US National Institutes of Health Fellow*)
C. Valori, MD (*British Council Fellow*)
L. Zatz, MD (*US National Institutes of Health Fellow*)

* The former Cardiovascular Research Group became a research unit on 1 February 1966.

The Unit is concerned with the study of the circulation in health and disease, with special emphasis on coronary heart disease. The research programme includes the development of new methods designed to improve the early diagnosis of heart disease and the investigation of both coronary and hypertensive heart disease. These investigations are augmented by basic laboratory studies, including research into the biophysics of circulation.

Summary of research

1. Studies in association with the intensive care unit for coronary thrombosis.
2. Direct measurement 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. Study of the circulation by indicator substances including radioisotopes:
   (*a*) Measurement of cardiac output and coronary artery flow.
   (*b*) Measurement of local venous flow and its application to the study of renal and arterial disease.

BODY TEMPERATURE RESEARCH UNIT

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

Honorary Director

Professor Sir George Pickering, MD, FRCP, FRS

Assistant Director

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

Scientific staff

R. H. Johnson, MB, D PHIL

W. R. Keatinge, MB, PH D

Attached workers

P. A. Murphy, MB, B SC, MRCP

B. J. Prout, MB, PH D, MRCP (*Radcliffe Infirmary Oxford*)

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

Summary of research

1. Action of endogenous pyrogens within the hypothalamus.
2. Mode of action of antipyretics.
3. Reaction between bacterial pyrogens and leucocytes.
4. Location and mode of response of central temperature receptors.
5. Nerve pathways involved in reflex and centrally induced vasodilatation.
6. Mechanism of action of arterial smooth muscle.
7. Studies of patients with abnormalities of temperature regulation.

REPRODUCTION AND GROWTH RESEARCH UNIT

Princess Mary Maternity Hospital, Newcastle upon Tyne 2 (Newcastle 814352)

Director

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

Honorary Consultant in Obstetrics

Professor J. K. Russell, MD, FRCOG

Scientific staff

W. Z. Billewicz, M SC — F. E. Hytten, MD, PH D

Other senior staff

G. A. Cheyne, FIMLT — Miss R. M. Holliday, AIS

The Unit was formed in October 1965 from a section of the former Obstetric Medicine Research Unit, Aberdeen. Much of the work is undertaken in collaboration with the Departments of Obstetrics and Gynaecology and of Child Health, University of Newcastle upon Tyne.

Summary of research*

1. Growth and health of young children in a rural African village (with the Council's laboratories in the Gambia).
2. Changes in body composition during pregnancy and the puerperium.
3. Measurement of total body fat with ^{85}Kr.
4. Anaemia and oedema in pregnancy.
5. Obstetrical implications of maternal height and weight and of gain in body weight during pregnancy.
6. Carbohydrate metabolism in pregnancy, with special reference to ' pre-diabetes '.

DENTAL RESEARCH UNIT

Dental School, Lower Maudlin Street, Bristol 1
(Bristol 20473)

Honorary Director

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

Scientific staff

R. J. Andlaw, M SC, LDSRCS (*until May 1965*)
G. H. Dibdin, M SC
N. W. Johnson, MD SC, FDSRCS
D. F. G. Poole, PH D
L. M. Silverstone, B CH D, LDS, LDSRCS
M. V. Stack, PH D
J. E. Tyler, ARIC

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 occurring in these properties as caries develops.

Summary of research

HISTOLOGICAL STUDIES

1. Development and structure of ' normal ' enamel and the significance of structural features in the initiation and spread of enamel caries.
2. Fine structure of enamel, including the arrangement and packing of the crystalline elements, as shown by polarized-light and electron microscopy and by X-ray diffraction.

CHEMICAL STUDIES

1. Characterization of enamel proteins by pyrolysis and gas chromatography.
2. Analysis of amino acids and hexoses by gas chromatography of volatile derivatives.
3. Production of caries-like lesions of enamel by acidified gels; comparison of simulated and natural caries with respect to the successive stages of breakdown.
4. Pattern of dissolution of enamel crystallites treated with various acids and chelating agents as seen with the electron microscope.

PHYSICAL STUDIES

Porosity of enamel and dentine as shown by sorption techniques.

* The work described here was previously undertaken as part of the programme of the Obstetric Medicine Research Unit, which was disbanded in September 1965 on the retirement of the Honorary Director, Professor Sir Dugald Baird.

TUBERCULOSIS AND CHEST DISEASES RESEARCH UNIT

Lynton House, 7–12 Tavistock Square, London W.C.1
(Euston 7862)

Director

Wallace Fox, MD, FRCP (*from June 1965*)*
P. M. D'Arcy Hart, CBE, MD, FRCP (*until June 1965*)

Scientific staff

Miss J. F. Heffernan, MB, DPH
D. M. Macfadyen, MRCP, MB†
A. B. Miller, MB, MRCP
Miss Christine Miller (Mrs Manning), BM (*part-time*)
D. N. Mitchell, MD
D. K. Robinson, MB, DCH
Miss R. Tall, B SC

Tuberculosis is still a very serious problem in many developing countries and by no means a negligible one in Britain. Statistically controlled clinical trials of the value of different chemotherapeutic agents and methods have been undertaken by the Unit in Britain and overseas (notably in India and also in East Africa, where the Council have scientific responsibility for the trials), and associated problems (e.g. drug resistance) have been studied, the work being increasingly orientated to the community rather than the individual. Studies of various methods of treatment of tuberculosis of the spine have been initiated through the Orthopaedic Subcommittee of the Council's Committee for Research on Tuberculosis in the Tropics. The national trial of the value of measures of specific immunization in tuberculosis continues. The investigations of the Unit have been extended to include the study of certain methods of treatment of thoracic carcinoma and the aetiology of sarcoidosis. The Unit cooperates actively with the Council's Statistical Research Unit and the Unit for Research on Drug Sensitivity in Tuberculosis.

Summary of research

1. Chemotherapy of tuberculosis:
   (*a*) Chemotherapy of pulmonary tuberculosis with pneumoconiosis (with the Miners' Chest Diseases Treatment Centre, South Wales).
   (*b*) Chemotherapy of tuberculosis in East Africa:
      (i) the use of combinations of thiacetazone with isoniazid;
      (ii) the use of these two drugs intensified by adding streptomycin initially;
      (iii) the value of two levels of intensity of home-visiting in out-patient supervision;
      (iv) comparison of out-patient treatment and in-patient followed by out-patient treatment;
      (v) a comparison of four regimens of pyrazinamide and streptomycin for the treatment of cases that have failed to respond to other treatment;
      (vi) ethionamide dosage schedules.
   (*c*) The incidence of side-effects from the combination of thiacetazone with isoniazid in various racial communities.
   (*d*) Treatment of pulmonary tuberculosis in South India (with the World Health Organization, the Indian Council of Medical Research and the Madras State Government, at the Tuberculosis Chemotherapy Centre, Madras), in particular:
      (i) effectiveness and practicability of several regimens of supervised intermittent chemotherapy;
      (ii) the use of thiacetazone with isoniazid;
      (iii) metabolism of several antituberculous drugs.
   (*e*) The use of thiacetazone with streptomycin in comparison with that of thiacetazone with isoniazid in Rhodesia.
   (*f*) Studies of thiacetazone plus isoniazid in Hong Kong.
2. Prevalence of drug resistance in tuberculosis:
   (*a*) Primary resistance in Britain (for comparison with the 1955–56 MRC survey).
   (*b*) Resistance in newly diagnosed cases in East Africa.

* Dr Fox, already a member of the staff of the Unit, succeeded Dr D'Arcy Hart as Director on the latter's retirement in June 1965.
† Working in Nairobi.

3. Radiographic sampling survey of severity of disease in newly diagnosed cases in Kenya, and a one-year evaluation of the results of chemotherapy as currently applied in the routine service in the area.
4. Protection afforded by BCG and vole bacillus vaccines in adolescence and early adult life in Britain.
5. Comparisons of treatment of certain types of carcinoma of the bronchus:
   (*a*) by surgery or by radiotherapy;
   (*b*) by two cytotoxic agents.
6. Aetiology and prevalence of sarcoidosis in young adults; mechanism of the Kveim test; standardization of Kveim test material.
7. Methodology of controlled clinical trials.

UNIT FOR RESEARCH ON DRUG SENSITIVITY IN TUBERCULOSIS

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

(Shepherds Bush 2030)

Honorary Director

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

Scientific staff

Mrs A. Csillag-Szekeley, D PHIL
Miss J. M. Dickinson, LRCPI & SI
G. A. Ellard, PH D
M. J. Lefford, MB*

Other senior staff

J. K. Clancey†
E. A. Edwards†

Attached workers

P. Cavanagh, MB, BAO (DUBLIN) (*University of Khartoum; MRC grant-holder*)

The Unit studies the bacteriological aspects of mycobacterial infections in man. Particular attention is given to bacteriological methods in the chemotherapy and epidemiology of tuberculosis and to the classification of mycobacteria. The Unit works in close association with the Council's Tuberculosis and Chest Diseases Research Unit and Statistical Research Unit.

Summary of research

1. Provision of centralized bacteriological services for:
   (*a*) National survey of the prevalence of drug resistance in tubercle bacilli from newly diagnosed patients with pulmonary tuberculosis.
   (*b*) Study of chemotherapy with thiacetazone-containing combinations in Hong Kong.
2. Survey of virulence in the guinea pig, thiacetazone sensitivity and susceptibility to hydrogen peroxide of tubercle bacilli from various countries (with the World Health Organization).
3. *In vitro* and animal experiments on intermittent chemotherapy in tuberculosis.
4. Comparison of several sensitivity test methods.
5. Classification and life cycle of mycobacteria.

UNIT FOR RESEARCH ON THE EXPERIMENTAL PATHOLOGY OF THE SKIN

The Medical School, The University, Birmingham 15

(Selly Oak 2103)

Director

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

Scientific staff

M. Baxter, M SC
A. O. T. Charles, PH D
A. E. Fairburn, MD, MRCP (*honorary*)
Professor P. G. H. Gell, MB (*honorary*)
K. R. Haye, MB
Mrs E. A. Hell, D PHIL
G. I. Horsfield, MB
R. F. Oliver, PH D
B. C. Tate, MBE, MD, FRCP (*honorary*)
Mrs S. Tittensor, PH D
M. D. Trotter, PH D
H. J. Yardley, PH D

* On leave of absence from December 1965 at Trudeau Laboratory, Saranac Lake, USA.

† Working on the East African Tuberculosis Chemotherapy Trial (Mr Clancey in Uganda and Mr Edwards in Kenya).

Other senior staff

J. R. Cooper, FIMLT

Attached workers

J. F. Kennedy, B SC (*MRC Scholar*)
Miss D. M. Rimmer, B SC (*MRC Scholar*)
R. Summerly, MB, MRCP (*MRC Clinical Research Fellow*)

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 metabolic processes *in vitro* and upon a study of allergy.

Summary of research

1. Metabolic pathways in skin (studied by various methods, including the use of radioactive isotopes), particularly the fatty acid and cholesterol metabolism of skin.
2. Effects of hormonal, chemical and physical agents on the metabolism and cytology of skin *in vitro*.
3. Effects of hormones and vitamin A on the synthesis of mucopolysaccharides of the dermis and epidermis.
4. 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.
5. 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.
6. 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.
7. Role of the basophil and mast cell in allergic and other tissue reactions.
8. Mechanism of keratin digestion by dermatophytic fungi.
9. Factors initiating regeneration of epithelium after skin injury; comparison of epidermal cell replacement in normal and psoriatic skin.
10. Trace metals and enzymes in the sera of patients with skin disease.
11. Investigation of materials suspected of causing industrial skin disease.

MINERAL METABOLISM RESEARCH UNIT

The General Infirmary, Great George Street, Leeds 1
(Leeds 32799)

Director

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

Assistant Director

A. Hodgkinson, PH D, FRIC

Scientific staff

J. Fitzpatrick, B SC
D. J. Lea, PH D
C. Oxby, PH D
M. Peacock, MB
W. G. Robertson, B SC
Miss M. M. Young, MB

Other senior staff

C. F. Knowles, FIMLT
P. M. Zarembski, M SC, FIMLT

Attached worker

G. Schwarz, MD (*University of Heidelberg*)

The Unit is concerned with the study of nephrolithiasis, metabolic bone disease with particular reference to osteoporosis, and the behaviour of bone-seeking isotopes.

Summary of research

1. Nephrolithiasis:
   (*a*) Ionic products of calcium phosphate and calcium oxalate in urine of normal subjects and patients with renal calculus.
   (*b*) Epidemiology of renal lithiasis.
   (*c*) Assay of parathyroid hormone and diagnosis of primary hyperparathyroidism.
   (*d*) Aetiology of idiopathic hypercalciuria.
   (*e*) Medical treatment of renal calculi based on *in vitro* studies of stone solubility.
2. Metabolic bone disease:
   (*a*) Quantitative X-ray studies, including spinal densitometry.
   (*b*) Bone in tissue culture.
   (*c*) Calcium absorption and requirement in osteoporosis.
   (*d*) Ageing in bone.
3. Bone-seeking isotopes:
   (*a*) Measurement of bone turnover.
   (*b*) Calcium absorption and transport.
   (*c*) Factors governing absorption and retention of strontium.

DEMYELINATING DISEASES RESEARCH UNIT

13 Framlington Place, Newcastle upon Tyne 2
(Newcastle 25131)

Honorary Director
E. J. Field, MD, MS, PH D, MRCP

Honorary Clinical Adviser
Professor Henry Miller, MD, FRCP, DPM

Scientific staff
E. A. Caspary, M SC
C. S. Raine, B SC
P. A. H. Millac, MB, MRCP

Other senior staff
D. Hughes, B SC
Miss G. Joyce, AIMLT

The Unit is concerned with the clinical and experimental investigation of aetiological factors in multiple sclerosis, with particular reference to the relationship between experimental allergic encephalomyelitis, multiple sclerosis and post-exanthematous encephalitis. The biology of glial cells is an important subject of study.

Summary of research

1. Electron microscope study of:
   (*a*) Experimental allergic encephalomyelitis.
   (*b*) Material from cases of multiple sclerosis (as available).
   (*c*) *In vitro* myelination.
2. Role of circulating and cell-bound antibodies in the causation of experimental demyelination *in vitro*.
3. Platelet agglutination studies in multiple sclerosis, with particular reference to agglutination resulting from antigen–antibody interactions.
4. Pathogenicity for animals (especially sheep, goats and mice) of material from cases of multiple sclerosis.
5. Antibodies in multiple sclerosis and other nervous diseases.

EXPERIMENTAL HAEMATOLOGY RESEARCH UNIT

Wright-Fleming Institute of Microbiology, St. Mary's Hospital Medical School, London W.2
(Paddington 1662)

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

Scientific staff

M. C. Adinolfi, MD (*until Oct. 1965*)
S. Ardeman, BM (*honorary*)
P. Barkhan, MD, PH D, MC PATH (*honorary; until July 1965*)
I. Chanarin, MD, B SC, DCP, MC PATH (*honorary*)
Miss J. Economidou, MD
N. C. Hughes Jones, DM, PH D
Miss A. McLean, PH D
Miss M. J. Polley, PH D*

Attached worker
F. S. Morrison, MD (*US Navy*)

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

Summary of research

1. Comparison of kinetics of γM and γG anti-A.
2. Methods of determining concentration and binding constant of Rh antibodies.
3. Characteristics of antibody produced by single cells.
4. Incidence and characteristics of γA blood group antibodies.
5. Blood group and bacterial antibodies in colostrum.
6. Relation between amount of antibody on red cells and rate of clearance from the circulation.
7. Estimation of amount of antibody on red cells in haemolytic disease of the newborn.
8. Comparison of ^{51}Cr and DF ^{32}P as red cell labels.
9. Physiology and pathology of intrinsic factor secretion; influence of steroids.
10. Folic acid metabolism in megaloblastic anaemia.
11. Significance of intrinsic factor antibodies in control patients without pernicious anaemia.
12. Viability of red cells from whole blood frozen in liquid nitrogen.

BLOOD GROUP RESEARCH UNIT

Lister Institute of Preventive Medicine, Chelsea Bridge Road, London S.W.1
(Sloane 4042)

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

Scientific staff

Miss E. J. Gavin, B SC
Miss J. E. Noades, B SC
Miss R. A. Sanger, PH D
Miss P. A. Tippett, PH D

The Unit is searching for unrecognized blood group antigens and studying the inheritance of those already known. Information about the antigens is being applied to the cartography of the human chromosomes and to the investigation of chromosomal abnormalities. The antigens are also involved in problems of haemolytic disease of the newborn and adverse reaction to transfusion. All the investigations listed below except the first have been carried out in collaboration with numerous colleagues in this country and abroad.

* On leave of absence, working in the Division of Experimental Pathology, Scripps Clinic and Research Foundation, La Jolla, California.

Summary of research

1. The X-linked blood group system Xg.
2. Use of Xg in the investigation of abnormalities of form or of number of the sex chromosomes.
3. Use of Xg in the mapping of genes on the X chromosome.
4. Xg in anthropoid apes.
5. Blood groups and abnormalities of the autosomes.
6. Blood groups and problems of twinning, chimerism, mosaicism and dispermy.
7. Identification of an antigen, Do^a, which defines a new blood group system.
8. Rh system: the ' D-like ' antigen LW; the presence of anti-D in D-positive people.
9. P system: the antigens P^k and ' Luke '.
10. Examination of sera suspected of containing new blood group antibodies.

BLOOD GROUP REFERENCE LABORATORY

(Administered by the Council for the Ministry of Health)

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

(Sloane 2152)

Director

K. L. G. Goldsmith, MB, PH D, FC PATH (*from Sept. 1965*)*
A. E. Mourant, DM, D PHIL, FRCP, FC PATH, FRS (*until Sept. 1965*)

Scientific staff

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

The Laboratory is responsible for large-scale processing of blood grouping serum of human origin and for issuing it to the National Blood Transfusion Service, the Armed Forces, and hospitals in the United Kingdom and overseas, and for the production of animal sera both for routine issue and for experimental purposes. Technical and clinical advice and instruction are given to visiting workers, both individually and by means of organized courses, and general assistance over a wide field is given to a large number of laboratories, transfusion centres and research institutes. The Laboratory is continuing to carry out comparative trials of new techniques, to develop lines of research arising from cases of clinical and scientific interest referred for investigation, and to cooperate with scientific and clinical colleagues in the study of immunological problems arising from transplant surgery.

Summary of activities

1. Large-scale production and issue of blood-grouping sera of both human and animal origin, including work on the preparation of International Standards.
2. Experimental production of blood grouping sera in animals.
3. Experimental production, preparation and standardization of anti-human-globulin sera of various specificities (with the Council's Blood Transfusion Committee).
4. The provision of reference facilities, including full red cell grouping of laboratory and hospital staffs for use as control panels, and the investigation of human and animal sera submitted by laboratories for checking prior to their use as grouping sera.
5. ABO and Rh grouping of all recruits to the London Red Cross Blood Transfusion Service.
6. Full red cell grouping of donors for the National Panel of Blood Donors, maintenance of Panel records, and periodic issue of revised Panel lists.

*Dr Goldsmith succeeded Dr Mourant as director of the Laboratory in September 1965 when the latter transferred to the Council's external scientific staff for work at the serological population genetics laboratory at St. Bartholomew's Hospital, London.

7. Investigation of cases referred to the Laboratory for clinical or scientific reasons, including the determination of red cell and serum groups and the specificity of red cell, leucocyte and platelet antibodies.
8. Follow-up research, including family studies, arising from cases referred, and the investigation of ' new ' blood group antigens and antibodies.
9. Development of immunological methods for selecting donors and recipients of organ and tissue grafts, and of reliable *in vivo* and *in vitro* compatibility tests, examination of pre- and post-graft sera, and follow-up of patients.
10. Investigation of red cell antigens in blood stored in liquid nitrogen.
11. Plant haemagglutinins.
12. Possible associations between blood groups and disease (in collaboration with clinicians).

BLOOD COAGULATION RESEARCH UNIT

Churchill Hospital, Headington, Oxford
(Oxford 64841)

Director

Professor R. G. Macfarlane, CBE, MD, FRCP, FRS (*part-time*)

Scientific staff

Mrs E. Bidwell, PH D, FRIC
Miss R. Biggs, PH D, MD
S. Goldenberg, MB (*part-time; until Dec. 1965*)
Miss A. E. Vartan, MB (*part-time*)

Other senior staff

K. W. E. Denson, FIMLT
G. W. R. Dike

Attached workers

R. B. Davis, MD (*University of Minnesota*)
R. Failace, MD (*University of Rio Grande do Sul, Brazil; British Council Bursar*)
C. Hougie, MD (*University of Washington; Established Investigator of the American Heart Association*)
F. Jobin, MD (*Canadian Rhodes Scholar*)
J. M. Matthews, MB (*MRC Clinical Research Fellow*)
Miss L. Nahas, MD (*Instituto Butantan, São Paulo*)
Mrs R. Sen, MB (*British Council Bursar*)
T. S. Song, MD (*National Medical Center, Seoul; British Council Bursar*)

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, diagnosis and treatment of cases of abnormal bleeding due to deficiency of clotting factors or to 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 of 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. 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 Dr J. E. French and Dr A. G. Sanders, the Sir William Dunn School of Pathology, Oxford).
7. Standardization of methods and reagents used for the routine assay of clotting factors (with the International Committee for Haemostasis and Thrombosis and Dr Jean Grant, Oxford Regional Blood Transfusion Service).

8. Blood level of clotting factors and their natural inhibitors in the normal population in cases of thrombosis.
9. The organization of a Haemophilia Centre and plasma fractionation plant in Oxford (with Dr Jean Grant).

ABNORMAL HAEMOGLOBIN RESEARCH UNIT

University Department of Biochemistry,
Tennis Court Road, Cambridge
(Cambridge 63240)

Honorary Director
H. Lehmann, MD, SC D, FRCP, FRIC, FC PATH

Scientific staff
D. Beale, B SC
Miss D. A. Davies, PH D

Other senior staff
D. Irvine

Attached workers
R. W. Carrell, MB, B SC (*New Zealand Government and Wellcome Trust research grant-holder*)
W. A. Isaacs, BM, MA (*World Health Organization Trainee, Regional Office, Brazzaville*)
Fl/Lt A. Marengo Rowe, MB (*Royal Air Force, Halton*)
Barbara Wyslouch, MD (*British Council Visitorship grant-holder*)

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

Summary of research

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

CELLULAR IMMUNOLOGY RESEARCH UNIT

Sir William Dunn School of Pathology, University of Oxford
(Oxford 57321)

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

Attached workers
J. C. Howard, BA (*MRC Scholar*)
P. J. McCullagh, MB (*Rhodes Scholar*)

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

Summary of research

1. Macrophage–lymphocyte interactions in antibody formation.
2. Activities of small lymphocytes from immunized and tolerant animals.
3. Cellular basis of immunological memory.

CLINICAL PULMONARY PHYSIOLOGY RESEARCH UNIT

King's College Hospital Medical School, Denmark Hill, London S.E.5
(Brixton 6222)

Director
P. Hugh-Jones, MD, MA, FRCP (*part-time*)

Scientific staff
E. N. O'Brien, MB, MRACP (*part-time*)
N. B. Pride, MB, MRCP

Attached workers
M. J. Grayson, MD, MRCP (*King's College Hospital; until Oct. 1965*)
A. R. Tanser, MB, MRCP (*King's College Hospital*)
J. Jordanoglou, MD (*Evangelismos Hospital, Athens*)
T. K. Wheeler, MB (*King's College Hospital*)
P. Meisner, MB (*Asthma Research Council Scholar*)

The Unit is studying the effects of disease in the human lung using, among other methods, new techniques that show the distribution of air and blood to each of the different pulmonary lobes. These methods can be used to assess the indications for medical or surgical treatment and their results.

Summary of research

1. Regional distribution of gas and blood in normal lungs and the changes caused by disease:
   (*a*) Topographical distribution, studied by the use of radioactive gases, without intubation of patients (with the Cyclotron Unit and the Postgraduate Medical School of London).
   (*b*) Distribution in individual lobes and segments, studied with a mass spectrometer sampling system and flow-meter during routine diagnostic bronchoscopy.
2. General and regional lung function in chronically breathless patients at rest and during exercise as a basis for definition of different clinical conditions; indications for surgery when localized emphysema is found.
3. Functional abnormality in the lungs of patients with different clinical types of asthma; the changes which occur during status asthmaticus and its treatment by different methods.

VISION RESEARCH UNIT

Institute of Ophthalmology, Judd Street, London W.C.1
(Euston 9621)

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

Scientific staff
C. D. B. Bridges, PH D
J. D. Moreland, PH D
J. N. Lythgoe, PH D
Mrs P. H. Silver, PH D

The Unit is concerned with the pigmentary, photochemical and physiological 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. 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 distribution of visual pigments and to correlate the findings with taxonomy and environmental demands; (*b*) to elucidate the structures and chemical reactions of the visual pigments, and (*c*) to measure and interpret visual characteristics.

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 by means of skin diving techniques to obtain fishes from known depths in the seas).
2. Effects of changing environment, e.g. influence of day length, light intensity and quality and water salinity on visual pigments in migratory and non-migratory fishes.
3. Visual pigments in rod and cone preparations.
4. Measurement of visual sensitivities with automatic apparatus.
5. Measurement of lens and corneal pigmentation.
6. Purkinje's blue arcs.
7. Relationship between the fine structure of photoreceptor outer segments and photochemical data.
8. Effect of drugs on colour vision in humans.
9. Human peripheral colour vision.

TRACHOMA RESEARCH UNIT

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

Medical Research Council Laboratories,
Fajara, Bathurst, Gambia

Honorary Director
Professor L. H. Collier, MD

Scientific staff

W. A. Blyth, PH D
Miss D. M. Graham, M SC (*until Oct. 1965*)
Mrs E. F. Hart, B SC (*until Apr. 1965*)
P. Reeve, PH D
Miss A. E. Smith, B SC
J. Sowa, M SC (*Gambia*)
Mrs S. C. I. Sowa, MB, DO (*Gambia*)
Mrs J. Taverne, PH D (*part-time*)

At the Lister Institute trachoma and related microorganisms are studied, with particular attention to their pathogenicity for cell cultures, chick embryos and animals, including primates; their serological reactions; and their immunogenicity, with special reference to the production of a trachoma vaccine.

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 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,
London W.C.2
(Holborn 3474)

Honorary Director
Professor Arnold Sorsby, CBE, MD, FRCS

Scientific staff
J. P. Newhouse, B SC (*until June 1965*)
H. W. Reading, PH D

Attached workers
G. R. Fraser, MB, PH D (*Godfrey Robinson Unit, Royal College of Surgeons; until Nov. 1965*)
A. I. Friedmann, MB, FRCS (*Godfrey Robinson Unit, Royal College of Surgeons*)
G. A. Leary, FSMC (*Royal Eye Hospital, London*)

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

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, protein structure and vitamin A.
3. Clinical studies:
   (*a*) Classification of the causes of blindness found in schools for the blind.
   (*b*) Isolation of new genetic entities.
4. Refraction of the eye:
   (*a*) Components of ocular refraction in man, and their genetic behaviour in human families.
   (*b*) Changes of the components of refraction during growth.

OTOLOGICAL RESEARCH UNIT

National Hospital for Nervous Diseases,
Queen Square, London W.C.1
(Terminus 3611)

Honorary Director†
Sir Terence Cawthorne, FRCS

Director (until July 1965)
C. S. Hallpike, CBE, MB, FRCP, FRCS, FRS

Scientific staff
S. K. Bosher, FRCS (*until Nov. 1965*)
J. D. Hood, D SC, F INST P
Miss M. R. Dix, MD, FRCS

Other senior staff
E. Trinder, AMIEE

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. The Unit was disbanded in June 1966 on the retirement of Professor Sorsby.

† Since the retirement of Dr Hallpike in July 1965 Sir Terence Cawthorne has been acting as Honorary Director pending further consideration of the future of the Unit.

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
(Brixton 4744)

Director
T. S. Littler, PH D, F INST P (*until December 1965*)

Honorary Clinical Director
Sir Terence Cawthorne, FRCS

Attached worker
Surg. Cdr. R. R. A. Coles, MB, DLO, RN

This Unit, which has been investigating medical and physical aspects of deafness, was disbanded in December 1965 on the retirement of Dr Littler from the Council's service. The Unit collaborated with the Post Office Research Station and the Ministry of Health in research on the development of hearing aid and audiometry equipment, and was associated with the Ear, Nose and Throat Department of King's College Hospital in clinical investigations. The cost of the Unit's work was met mainly from Alexander Pigott Wernher Memorial Trust funds but the audiometric surveys—which are continuing—have been financed by the Ministry of Pensions and National Insurance.

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 (with the Greater London Council).
4. Speech audiometry in children and adults.
5. Continuous recording threshold audiometry.
6. Audiometric surveys in industrial situations and hearing-conservation programmes (with the National Physical Laboratory).

RADIOBIOLOGICAL RESEARCH UNIT

Harwell, Nr. Didcot, Berkshire
(Rowstock 393)

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

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

DIRECTOR'S GROUP

Scientific staff

M. J. Ashwood-Smith, PH D
D. W. H. Barnes, BM, FC PATH
H. S. Micklem, D PHIL
D. G. Papworth, B SC
L. A. Stocken, D PHIL, FRIC (*honorarium*)

Other senior staff

E. J. Lucas, MBE (*until Apr. 1965*)

BIOCHEMISTRY

Scientific staff

J. St. L. Philpot, MA, B SC (*Head of group*)
J. H. Barnes, M SC, ARIC
G. W. Bazill, B SC
A. J. P. Phillips, B SC

Other senior staff

J. V. Horgan
D. A. Stock

BIOPHYSICS

Scientific staff

G. J. Neary, SC D (*Head of group*)
A. L. Batchelor, PH D
B. A. Bridges, PH D
D. R. Cowdrey, PH D (*until Feb. 1966*)
R. J. Munson, PH D
R. J. Preston, BA
D. M. Robinson, PH D
J. R. K. Savage, PH D

Other senior staff

D. A. Bance
M. J. Corp, MSR
P. Gray
D. G. Martin
W. S. G. Weal
C. F. Wright, FIST

CYTOGENETICS

Scientific staff

C. E. Ford, D SC, FRS (*Head of group*)
Mrs C. M. Clarke, PH D (*part-time*)
E. P. Evans, PH D
D. A. Ogden, B SC

Other senior staff

G. Breckon

GENETICS

Scientific staff

Miss M. F. Lyon, PH D (*Head of group*)
Miss M. J. Lamb, PH D
T. W. McSheehy, B SC
T. Morris, B SC
Miss R. J. S. Phillips, B SC
C. E. Purdom, PH D
A. G. Searle, D SC

CELL BIOLOGY

Scientific staff

H. J. Evans, PH D (*until Jan. 1966*)
D. Scott, B SC

EXPERIMENTAL PATHOLOGY

Scientific staff

R. H. Mole, BM, FRCP, MC PATH (*Head of group*)
G. T. Bungay, MB
P. W. Edmondson, MRCS, FC PATH
E. V. Hulse, MD, MC PATH

PHYSIOLOGY

Scientific staff

O. A. Trowell, MD, FRSE (*Head of group*)
R. O. Jones, B SC
D. R. Lucas, MD, FC PATH

Other senior staff

W. R. Lush

Scientific staff

G. E. Harrison, D SC, F INST P (*Head of group*)
T. E. F. Carr, B SC
D. R. Cowdrey, PH D
Mrs A. Harrison, PHARM CHEM
E. R. Humphreys, PH D
B. J. Parsons, PH D (*until Sept. 1965*)
G. Patrick, BA

Other senior staff

R. O. R. Brooks
K. B. Edwards, B SC (*until June 1965*)
K. C. Gould
G. R. Howells (*until Aug. 1965*)
K. J. Kapota (*until Sept. 1965*)

ADMINISTRATIVE STAFF

F. D. Bushell (*Administrator*)
L. C. G. Manwaring, FLA (*Librarian*)

ATTACHED WORKERS

H. M. J. Bazin, DR VET LIC SCI (*Institut du Radium, France; Euratom Bursar*)
Captain J. F. P. Clemenger, B VET MED, MRCVS, RAVC (*Ministry of Defence*)
J. A. M. Heddle, PH D (*Oak Ridge National Laboratory, USA; James Picker Foundation Fellow*)
Mrs J. E. Heddle, MA (*Oak Ridge National Laboratory, USA*)
Captain A. W. Horne, B V SC, MRCVS, RAVC (*Ministry of Defence; until Dec. 1965*)
A. Y. Leonard, PH D (*Centre d'Étude de l'Énergie Nucléaire, Belgium*)
D. Oldroyd, B SC (*University of Southampton*)
V. S. Šljivić, MD (*Institute of Nuclear Sciences, Yugoslavia; International Atomic Energy Agency Fellow*)
R. L. Tapp, PH D (*University of Cambridge*)

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. Dosimetry for exposure of large and small animals to fast neutrons or γ-rays.
2. Relation of ^{24}Na activity in plasma to fast neutron dose in goats.
3. Development of heavy-ice target for use in accelerator for production of fast protons.
4. Measurement of energy spectra of heavy particles and of soft X-rays.
5. Development of a rapid continuous-flow electrophoretic separator for purifying enzymes etc.

CHEMICAL STUDIES

1. Examination of serum proteins in radiation chimeras.
2. Analysis of alginic acid by column chromotography for the guluronic and mannuronic constituents.
3. DNA replication: attempts to replicate biologically active DNA *in vitro*, and related enzymatic studies.
4. Antiradiation drugs: enzymatic indicators of radiation damage for use in screening protective substances and for other purposes.

PHYSIOLOGICAL STUDIES

1. Radiation chimeras:
   (*a*) Lymphoid aplasia and secondary disease.
   (*b*) Role of the thymus in lymphopoiesis.
   (*c*) Serial passage of bone marrow.
2. Gastric function after, and conditioning by, whole-body or localized irradiation.
3. Sensitivity of acute and delayed responses to irradiation in relation to age, including comparisons between different kinds of penetrating radiation.
4. Quantitative aspects of recovery from whole-body irradiation and its cellular basis.
5. Quantitative comparisons of lethal and other effects of fast-neutron radiation and γ-radiation, especially in large animals.
6. Modification of delayed effects of whole-body irradiation by cell grafting.
7. Pathological mechanisms underlying the deleterious action of selected mutants in the mouse.

8. Plasma levels, excretion and body retention of ^{47}Ca, ^{85}Sr, ^{133}Ba and ^{223}Ra after intravenous injections in a healthy man.
9. Application of neutron activation analysis to the study of diurnal variations in the concentrations of strontium and barium in human plasma.
10. Effect of dietary supplements of sodium and calcium alginates on the uptake of radioactive strontium in rats.
11. Toxicological assay in rats of sodium alginate used as a dietary supplement.
12. Transport of barium and radium across segments of rat intestine.
13. Effect of dietary additives of sodium, potassium, magnesium, calcium or phosphorus on the blood levels and turnover of alkalis and alkaline earths in the rat (with Dr K. Kostial, Institute of Medical Research, Zagreb).
14. Transmissability of scrapie in irradiated lambs treated with haematopoietic inocula (with the Nuffield Institute for Medical Research, Oxford).

FUNDAMENTAL STUDIES

1. Induction of chromosome aberrations by radiation:
   (*a*) Development of a general theory of the relative biological effectiveness of different qualities of radiation, checked by experiments with protons and α-particles of various energies and soft X-rays.
   (*b*) Numbers and distribution of intranuclear sites for chromosome exchange in *Tradescantia*, and their relation to radiosensitivity in respect of the production of aberrations.
   (*c*) Dose fractionation and recovery phenomena.
2. Cell-killing by radiation:
   (*a*) Influence of trypsinization on radiosensitivity of mammalian cells in culture.
   (*b*) Influence of linear energy transfer (LET) and particle track length on radiosensitivity.
   (*c*) Effect of storage of cells at liquid nitrogen temperature on various physiological parameters, with special reference to radiosensitivity.
   (*d*) Pollen germination as a measure of cell survival after irradiation by hard X-rays or by fission neutrons.
3. Mutagenic and lethal action of radiations on bacteria:
   (*a*) Experiments bearing on the site of lethal damage in *Escherichia coli* B/r growing in minimal medium.
   (*b*) Mutagenesis induced by ultraviolet light and ionizing radiations and the influence of the host cell reactivation (excision repair) enzyme system.
   (*c*) The LET dependence of mutagenic and lethal efficiencies of ionizing radiations in various auxotrophic strains of *Escherichia coli*.
   (*d*) Synergism between the mutagenic action of ultraviolet light and ionizing radiations.
4. Mechanisms of damage in microorganisms by ultraviolet radiation at sub-zero temperatures.
5. Influence of oxygen in radiation-induced dominant lethals in mouse spermatozoa.
6. Cell population studies using chromosome markers in the mouse.
7. Cytogenetics of neoplasia in experimental animals.
8. Cytogenetics of chromosome rearrangement in the mouse.
9. Dose fractionating experiments on human peripheral blood leucocytes *in vitro* and on *Drosophila*, to study the mechanism of induction of chromosome aberrations and mutation by X-rays.
10. Dose response determinations for chromosome aberrations induced by X-rays and ultraviolet light in cultured human leucocytes.
11. Preliminary determinations of the relative biological effectiveness of γ-rays and fast neutrons in producing chromosome aberrations in cultures of human leucocytes.
12. Actions of radiomimetic compounds and base analogues in inducing chromosome damage in human leucocytes.
13. DNA and RNA synthesis in mammalian sex chromosomes.
14. The combined effect of X-rays and radiomimetic chemicals in inducing chromosome aberrations at different phases of the mitotic cycle.
15. Use of radioactive nucleosides to study the structure and replication of chromosomes in normal and X-irradiated cells.
16. Dose response studies on the action of alkylating agents on chromosomes (with workers at the Chester Beatty Research Institute, London).
17. The relation between cell survival and chromosome aberration yield in plant cell systems exposed to X-rays and fission neutrons.
18. Survival of Chinese hamster cells cultured *in vitro*, after X-irradiation given at different times during development.

19. Identification of four different patterns of damage in lymphocytes exposed to various noxious agents.
20. Occurrence in organ cultures of salivary gland of early and reversible vacuolation of the acinar cells.
21. Correlation of histological, ultrastructural and metabolic changes in X-irradiated organ cultures (retina, lymph nodes, liver).
22. Factors affecting the radiosensitivity of visual cells in organ cultures of retina.
23. Prevention by soya bean trypsin inhibitor of rapid autolysis in organ cultures of rat pancreas.
24. Induction of growth in certain epithelia, in some organs but not in others, by a ' factor ' prepared from submandibular glands of male mice.

GENETICS

1. Effects of radiation dose, intensity and quality of induction of mutations in immature germ cells of *Drosophila melanogaster.*
2. Genetic effect of ^{14}C in *Drosophila melanogaster.*
3. Radiation and ageing in *Drosophila.*
4. Mutagenic effects of radiation in fish.
5. Induction of genic and chromosomal mutations in mice by chronic γ-irradiation, acute X-irradiation and neutrons; the effect of dose fractionation.
6. Gene action in the mammalian X chromosome.
7. Genetics and development of a number of mouse mutants.
8. Chromosomal abnormalities in the mouse.
9. Investigation of the possible mutagenic effects of oral contraceptives in the mouse.

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

1. Effects of irradiation on thiol content of nuclei (rat thymus).
2. Analysis of thiol-containing compounds in thymic nuclei, especially histones.
3. Repression of DNA-dependent RNA synthesis by histones after oxidation, alkylation and irradiation.

EXPERIMENTAL RADIOPATHOLOGY RESEARCH UNIT

Hammersmith Hospital, Ducane Road, London W.12
(Shepherds Bush 4594)

Director

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

Scientific staff

P. E. Bryant, B SC
W. A. Cramp, PH D
Miss B. M. Cullen, B SC
B. Dixon, B SC
N. T. S. Evans, PH D
Mrs S. Hornsey, B SC
M. Key, PH D
R. J. Littleton, B SC
N. J. McNally, B SC
J. L. Moore, B SC
J. A. Simmons, PH D (*until Dec. 1965*)
R. H. Thomlinson, MB
D. K. Watkins, PH D

Other senior staff

D. Dowson
Miss B. Hodgkins

Attached workers

D. P. S. Chan, MB (*Institute of Radiology, Hong Kong*)
G. Harris, MRCP (*Hammersmith Hospital*)
A. I. Hashmi, M SC (*Pakistan Atomic Energy Commission, Karachi*)
U. K. Misera, PH D (*University of Delhi*)
N. Watanabe, MD (*University of Tokyo*)

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. Electron-spin resonance signals from amino acids exposed to radiations of different qualities.
2. Action of radiation on bacteriophages:
   (*a*) Investigation of host cell reactivation, using free phage and phage–host complexes.
   (*b*) Comparative radiosensitivities, in presence and absence of oxygen, of dry phage and of phage DNA after injection into host bacteria.
3. Attempts to determine the nature of the agent for scrapie by means of radiobiological investigations (with Dr D. Haig, ARC Institute for Research on Animal Diseases).
4. Oxygen enhancement ratio for the effect of radiation on DNA synthesis in mammalian cells.
5. Oxygen enhancement ratios for inhibition of β-D-galactosidase induction by radiations of various LET (linear energy transfer) values.
6. Chemical protection and sensitization:
   (*a*) Chemical protection against ultraviolet light and against ionizing radiations of various LET values.
   (*b*) Effects of copper and copper compounds on bacteria and higher cells irradiated in anoxic conditions; mechanism of cell killing by cuprous ions.
7. Effects of dose fractionation on various systems:
   (*a*) Small intestine of mouse, irradiated in aerobic and anoxic conditions.
   (*b*) Mammalian cells *in vitro*, in aerobic and anoxic conditions.
   (*c*) Solid tumours in rats.
8. Effect of oxygen on radiosensitivity of *Chlamydomonas* at various values of LET.
9. Studies with mammalian cells *in vitro*:
   (*a*) Comparative radiosensitivities of normal and transformed hamster fibroblasts.
   (*b*) Differences in radiobiological response arising from variations in methods of growth before irradiation.
   (*c*) Cultivation of cell lines derived from solid tumours in rats.
10. Measurement of oxygen tension on surface of human tissues: variations with changes in respired gas.
11. Effects of radiation on growing cartilage in the tails of young rats and the dependence of these effects on oxygen at various concentrations.
12. Changes in growth rate of irradiated solid tumours, and their relationship to vascular damage; the effect of a first dose of radiation on the proportion of anoxic cells present at the time of subsequent irradiation.
13. Mechanism of stimulation of rabbit spleen cells by exposure to antigen, and of the transfer of the stimulus between cells; quantitative study of numbers of antibody-secreting cells in spleen by the Jerne plaque technique.

CLINICAL EFFECTS OF RADIATION RESEARCH UNIT

Western General Hospital, Crewe Road, Edinburgh 4

(Dean 1361)

Director

W. M. Court Brown, OBE, MB, B SC, FRCPE, FFR

Honorary Consultant Physician

J. A. Strong, MBE, MB, FRCPE, FRCP

Scientific staff

Miss K. E. Buckton, B SC
Miss E. Day, BA
T. R. Elsdale, PH D
M. J. W. Faed, PH D
D. G. Harnden, PH D
Miss J. Hilditch, B SC
Mrs A. L. Hutchison, MB, DCH (*part-time*)
Miss P. A. Jacobs, D SC
Mrs C. F. von Kuenssberg, MB (*part-time*; *until Jan. 1966*)
A. O. Langlands, MB, B SC, FFR
Miss M. E. McIlree, B SC
W. H. Price, MB, B SC, MRCPE
D. Rutovitz, PH D
P. G. Smith, DIP TECH
Miss I. M. Tough, B SC
E. R. D. Williamson, MB
D. E. Young, PH D

Other senior staff

A. S. J. Farrow, B SC
A. Ross, FIMLT
B. Stein, BA

The work of the Unit is particularly concerned with the delayed effects of radiation exposure in man, with all branches of human cytogenetics and with the application of experimental virological techniques to the study of human tumours.

Summary of research

1. The effects of *in vivo* radiation exposure (acute irradiation and chronic exposure) in man in producing chromosome damage (with the United Kingdom Atomic Energy Authority).
2. Chromosome changes and ageing.
3. Chromosome polymorphism in man.
4. Study of human meiotic chromosomes.
5. Studies of families with marker chromosomes for purposes of genetic linkage (with the Human Biochemical Genetics Research Unit and Statistical Research Unit).
6. Frequency of subjects with abnormal sex chromosome complements in various population sub-groups, with particular reference to abnormalities involving the Y chromosome and their possible effect on sex differentiation and behaviour.
7. Benzene exposure and the production of chromosome abnormalities (with HM Factory Inspectorate).
8. Cytogenetic structure of leukaemias.
9. The application of experimental virological techniques to the study of leukaemias and related neoplasms.
10. Organization of a registry of abnormal karyotypes.
11. Epidemiological studies on groups of therapeutically irradiated human subjects (with the Statistical Research Unit).
12. Automation of counting and analysis of human chromosomes.

BONE-SEEKING ISOTOPES RESEARCH UNIT

The Churchill Hospital, Headington, Oxford
(Oxford 64841)

Honorary Director
Dame Janet Vaughan, DBE, DM, FRCP

Scientific staff

A. T. Andrews, BA
Miss P. J. Bingham, BA
Mrs B. I. Bleaney, B SC (*part-time*)
G. M. Herring, D PHIL
S. G. Kshirsagar, PH D (*until April 1965*)
Mrs E. Lloyd, D PHIL*
D. Oldroyd, B SC
Mrs M. E. Owen, D PHIL
Mrs M. C. Williamson, B SC (*part-time*)

Other senior staff

Miss I. Brazell
Miss F. Schofield

Attached worker
Professor M. R. Shetlar (*University of Oklahoma*)

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, in addition to problems of dosimetry in relation to carcinogenesis.

* On leave of absence from April to December 1965 at Argonne National Laboratory, Illinois.

Summary of research

1. A quantitative study of the synthesis of nucleic acids, and protein and carbohydrate components by the cells of the osteogenic connective tissue, using labelled precursors and autoradiographic techniques, with particular reference to the effects of various metabolic inhibitors and hormones on the metabolism of these cells.
2. Physical characteristics, metal-binding properties and carbohydrate composition of a sialoprotein, a chondroitin sulphate and three other mucoprotein fractions isolated from bovine bone and of acellular teleost bone (Dr A. R. Peacocke and Mr P. Williams, Biochemistry Department, Radcliffe Infirmary, are collaborating in some of these studies).
3. Histochemical and histological character of the surfaces on which plutonium and americium are concentrated.
4. Dosimetry of plutonium on bone surfaces and in the bone marrow.
5. Distribution of radium and calculation of radiation dose in trabecular bone of human patients with radium poisoning in whom cortical bone has already been studied.
6. Occurrence of carcinomas of the ear in rabbits given ^{90}Sr by injection.

ENVIRONMENTAL RADIATION RESEARCH UNIT

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

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

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

Scientific staff

L. Burkinshaw, PH D
L. D. Davis, MA
D. Gvozdanovic, GRAD IN SCI
Mrs S. Gvozdanovic, GRAD IN SCI
M. S. Huq, PH D (*until Oct. 1965*)
C. B. Woodcock, B SC
G. D. Zanelli, B SC

Other senior staff

D. B. Appleby
B. Oldroyd

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. Measurement of γ-radioactivity in soil and biological specimens.
7. Measurement of α- and 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 pathogenesis of autoimmune diseases, with particular reference to the effect of radiation on ageing processes.
11. Measurement of cosmic-ray neutron dose.
12. Measurement of radiation dose to marrow in trabecular bone by means of thermoluminescent dosimetry.

RADIOLOGICAL PROTECTION SERVICE 147

(Jointly with the Ministry of Health)

Clifton Avenue, Belmont, Sutton, Surrey

(Meville 5441)

Director

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

Deputy Director

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

Scientific staff

W. F. Bland, B SC, A INST P
Miss J. E. Challiss, B SC
B. L. Davies, B SC, A INST P
M. J. Duggan, B SC
A. A. Edwards, B SC
P. L. Entwistle, B SC
P. C. Escott, B SC
B. E. Godfrey, M SC, A INST P
S. G. Goss, B SC
E. I. Hamilton, D PHIL
G. Hems, PH D
Mrs G. D. Parry Howells, PH D
B. E. Jones, B SC, F INST P
T. O. Marshall, B SC
Miss M. J. Minski, B SC
D. L. Newman, B SC
M. C. O'Riordan, B SC
M. A. Shaw, B SC
Miss R. M. Standeven, M SC *(until Oct. 1965)*
G. R. Stevenson, PH D *(until March 1966)*
J. Vennart, B SC, F INST P

Other senior staff

T. V. Bird
L. J. F. Brotherton
P. N. Casbolt
J. J. Cleary
J. W. Davies, DIP TECH *(until Nov. 1965)*
E. Greenslade
A. E. Greinig, GRAD BRIT IRE
R. T. Hankins
C. L. Harvey
P. B. Roberts, AIST
S. C. Stephenson, B SC

BIRMINGHAM REGIONAL CENTRE

Queen Elizabeth Hospital, Edgbaston, Birmingham 15

(Selly Oak 1213)

Honorary Director

R. F. Farr, MA, F INST P

Scientific staff

R. Gelder, B SC
Miss D. E. Gillion, B SC
D. L. O. Humphreys, M SC

Other senior staff

R. C. Hampton

LEEDS REGIONAL CENTRE

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(Leeds 32799)

Honorary Director

F. W. Spiers, CBE, D SC

Scientific staff

T. Ashton, B SC, A INST P
A. P. Hudson, B SC

MANCHESTER REGIONAL CENTRE

Christie Hospital and Holt Radium Institute, Withington, Manchester 20

(Didsbury 8123)

Honorary Director

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

Scientific staff

M. J. MacHugh, M SC

Other senior staff

D. N. Craven (*until Aug. 1965*) G. C. Roberts

SCOTTISH CENTRE

(*Jointly with Scottish Home and Health Department*)

31 Sherbrooke Avenue, Glasgow S.1

(Ibrox 0508)

Honorary Director

J. M. A. Lenihan, M SC, PH D, AMIEE, F INST P

Scientific staff

B. H. Crichton, B SC D. A. Simpson, B SC (*until Aug. 1965*)

N. T. Harrison, B SC, A INST P

Other senior staff

A. Gall G. C. Jardine

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

RADIATION MONITORING AND ADVISORY SERVICES

1. Operation of a personnel radiation monitoring service employing punched 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 in new uses of radioactive isotopes.
4. Calibration of radiation monitoring instruments.
5. Leakage testing of sealed radioactive sources.
6. 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.
7. Miscellaneous measurements of environmental radioactivity, e.g. continuous measurement of the local γ-radiation due to fallout and measurement of the natural radioactivity of some drinking waters.
8. Tests of the effectiveness of protective materials.

1. Improvement of the accuracy of techniques for measuring external radiation received by workers:
   (*a*) Improvement of methods of film dosimetry.
   (*b*) Improvement of track plate methods for neutron dosimetry.
   (*c*) Development of equipment for measuring low-energy X-rays.
   (*d*) Studies on the use of lithium fluoride for personnel dosimetry.
2. Automation in film densitometry and dose evaluation.
3. 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.
4. Measurement of radium body burdens of persons formerly engaged in the luminizing industry (with Dr J. T. Boyd, Statistical Research Unit).
5. Relationship between radium in the bodies of workers and in the working environment of radium luminizing departments.
6. Relationship in humans between radium in the body and radon in breath.
7. Radon concentration in coal mines.
8. Size distribution of radon decay products.
9. Investigation of current practice in the use of tritium luminous compound and of mechanisms whereby tritium can enter the bodies of workers.
10. ^{40}K in humans and its relationship to obesity and pregnancy (with Dr G. R. Wadsworth, Queen Elizabeth College, London).
11. Fallout ^{137}Cs in members of the population.
12. Variations in local background γ-radiation due to nuclear weapon tests.
13. Stable isotope concentrations in organs of the body studied by neutron activation and other methods.
14. Variation of organ weights with age.
15. Distribution in different organs and retention in the body of organic compounds tagged with ^{14}C and ^{3}H, including observations on humans and on experimental animals.
16. Manufacture and use of solid-state devices for the absolute calibration of very low levels of radioactive materials and for α-ray spectrometry.
17. Electronic equipment for radiation measurements, particularly utilizing transistors.
18. Theoretical and practical studies on the scattering of X- and γ-radiation from surfaces and volumes; design of maze entrances; investigation of airshine.
19. Protective properties of various materials (e.g. water, concrete, paraffin wax) against fast neutrons.
20. Investigation on the performance of available neutron site-monitoring equipment and the development of new designs, with emphasis on improved portability and sensitivity.

CYCLOTRON UNIT

Hammersmith Hospital, Ducane Road, London W.12
(Shepherds Bush 4594)

Director

D. D. Vonberg, B SC

Scientific staff

D. K. Bewley, PH D
G. Burton, B SC
J. C. Clark, B SC
S. B. Field, PH D
Professor J. F. Fowler, PH D, F INST P (*honorarium*)
A. W. G. Goolden, MB, DMRT (*honorary*)
T. Jones, M SC
Miss P. M. Kibby, BA
Miss C. M. E. Matthews, PH D
R. L. Morgan, MB, B SC, DMRT, FFR (*part-time*)
C. J. Parnell, B SC
R. J. Post, AMIEE
T. E. Saxton, B SC
J. Sharp, B SC
D. J. Silvester, PH D
P. C. R. Turner, M SC

Other senior staff

L. C. Baker, FIST
P. C. Buckingham
M. B. Coyne
K. Finding, AMI MECH E
G. F. S. Harding
D. M. Leslie, B SC

This 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.

Summary of research

1. Clinical use of cyclotron-produced radioactive isotopes:
   (*a*) ^{15}O, ^{11}C and ^{13}N in pulmonary and circulatory studies (with the Postgraduate Medical School of London).
   (*b*) ^{18}F in dental studies (isotope material supplied to the London Hospital Medical College).
   (*c*) ^{52}Fe in studies of iron metabolism after treatment with ^{32}P (isotope material supplied to the Royal Marsden Hospital and Radiotherapy Department, Hammersmith Hospital).
   (*d*) ^{11}CO for measurement of blood volume (with Departments of Obstetrics and Medical Physics).
   (*e*) ^{129}Cs for scanning of myocardial infarcts (with Department of Medical Physics).
2. Investigations associated with the use of cyclotron-produced isotopes:
   (*a*) Development of a positron camera for *in vivo* isotope distribution studies.
   (*b*) Concentration of niobium isotopes in rat tumours.
   (*c*) Control of ventilation using $^{11}CO_2$ and analogue computer (with the Postgraduate Medical School of London).
   (*d*) Use of ^{129}Cs to study blood flow in heart muscle (with the Postgraduate Medical School of London).
   (*e*) Comparison of radioactive substances used in brain scanning.
   (*f*) Study of collimators used for scanning.
3. Investigations associated with the production of radioisotopes by the cyclotron:
   (*a*) Development of new methods of preparation of isotopes in high specific activity.
   (*b*) Preparation of labelled compounds with high specific activity.
   (*c*) Absolute standardization of cyclotron-produced isotopes.
   (*d*) Radioactivation analysis with the cyclotron.
   (*e*) Radiochemical investigations associated with the heavy-ion beam project.
4. Radiobiological studies using radiations of specified linear energy transfer:
   (*a*) Variation of relative biological efficiency, and effectiveness of chemical protectors, with linear energy transfer of radiation, with dose and with concentration of oxygen, on the basis of survival of human kidney cells, bacteria and plant cells exposed to X-rays, to α-particles, and to deuterons of various energies (with Dr G. W. Barendsen of the Radiological Institute, Rijswijk, Netherlands, and members of the Experimental Radiopathology Research Unit).
   (*b*) Variations in the production of free radicals in alanine with linear energy transfer of radiation, using the electron spin resonance technique (with the Experimental Radiopathology Research Unit).
5. Development of fast-neutron dosimetry and facilities for radiotherapy with fast neutrons.
6. Radiobiological experiments with fast neutrons to determine:
   (*a*) Comparative effect of fast neutrons and 8-MeV X-rays with various fractionation schemes, using the skin of pigs and mice.
   (*b*) Comparative effectiveness of fast neutrons and 250-KV X-rays in the treatment of transplanted tumours in rats, using single and fractionated exposures.
   (*c*) Relative biological efficiency of the fast-neutron beam for various biological systems (with the Experimental Radiopathology Research Unit, the Churchill Hospital, Oxford, and St. Mary's Hospital, London).
7. Engineering studies:
   (*a*) Conditions in the cyclotron for accelerating ions of heavy nuclei, such as nitrogen and ^{3}He, to high energies by methods compatible with normal functioning of the machine.
   (*b*) Focussing conditions in Van de Graaff accelerating tubes and design of a new tube for use in the machine when it is recommissioned.
   (*c*) The use of ion pumps and cryosorption pumps in a hydrocarbon-free pumping system for the Van de Graaff machine.
8. Use of 8-MeV X-ray and electron beams for radiobiological studies, particularly in relation to dose-rate effects and protection by anoxia (with the Experimental Radiopathology Research Unit and Dr E. A. Wright of St. Mary's Hospital, London).

CLINICAL GENETICS RESEARCH UNIT

Institute of Child Health,
30 Guilford Street, London W.C.1
(Chancery 9789)

Director
C. O. Carter, DM, FRCP

Scientific staff
Miss I. H. M. Blyth, MB, D OBST RCOG
Miss M. I. Dunsdon, PH D
R. M. C. Huntley, BA, B ED
D. J. Mantle, MRCS
Mrs J. Slack, BM, DCH
J. Wilson, MB, PH D, MRCP

Attached worker
N. C. Nevin, B SC, MD, B CH, BAO (*MRC Clinical Research Fellow*)

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. A genetics counselling clinic is held weekly at The Hospital for Sick Children.

Summary of research

1. Common congenital abnormalities: pyloric stenosis, spina bifida cystica, congenital heart disease, inguinal hernia, harelip and cleft palate, congenital dislocation of the hip, Hirschsprung's disease, Down's syndrome and polycystic kidneys.
2. Studies on coronary artery disease, including estimations of serum lipoprotein lipase and sugar tolerance in families.
3. Genetics and biochemistry of Leber's optic atrophy and other neurological diseases.
4. Genetics of cystic fibrosis of the pancreas and the survival rate of patients.
5. Genetics of childhood muscular dystrophies.
6. Quantitative human variation: physical and mental measurements on a series of twins and their relatives to obtain estimates of degrees of resemblance.

POPULATION GENETICS RESEARCH UNIT

Old Road, Headington, Oxford
(Oxford 62834)

Director
A. C. Stevenson, MD, B SC, DPH, FRCP

Scientific staff
A. Barr, PH D (*part-time*)
D. J. Bartlett, MB, PH D
M. Bobrow, MB, B SC
Miss B. C. C. Davison, MB, DPH, DRCOG
H. A. Johnston, MB, DPH (*until Sept. 1965*)
C. B. Kerr, MB (*until Dec. 1965*)
W. G. Pearce, MD, FRCS, FRCSE (*part-time*)
P. L. Pearson, B SC
D. F. B. Roberts, D PHIL (*until Oct. 1965*)
I. B. Shine, MB (*until Dec. 1965*)

Other senior staff
Mrs J. Bedford, B SC
G. Clarke, AIMLT

Visiting worker
M. A. Abul-Enein, MB, DGO (*University of Alexandria; WHO Fellow*)

The Unit is concerned primarily with work designed to illuminate the genetic structure of human populations by means of the pattern of distribution of traits of medical importance. The cytological laboratory is concerned with the relationship of chromosomal aberrations to developmental anomalies, abortions and infertility. Four advice and referral clinics are held monthly in the hospitals of the Oxford Regional Hospital Board.

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 the population of an island.
6. Cytology of chorion and hydatidiform mole.
7. Association of consanguinity with certain congenital malformations and disorders of pregnancy.
8. Contribution of sex-linked mutations to the incidence of atresia ani and to hydrocephalus.

MUTAGENESIS RESEARCH UNIT

Institute of Animal Genetics, West Mains Road, Edinburgh 9
(Newington 1011)

Honorary Director
Miss C. Auerbach, D SC, FRS

Scientific staff

B. M. Cattanach, PH D
C. H. Clarke, PH D
J. Corran, MA
I. C. Felkner, PH D
Mrs M. E. Griffiths, B SC
B. J. Kilbey, PH D*
B. M. Slizynski, DR PHIL

Attached workers

M. J. Allison, B SC (*MRC Scholar*)
N. Anwar, M SC (*British Council Fellow*)
N. J. Brink, PH D (*University of Tasmania; University of Edinburgh Junior Fellow*)
V. L. Chopra, B SC (*Indian Agricultural Research Institute, New Delhi; Commonwealth Scholarship Commission scholar*)
Miss S. K. Quah, B SC (*Ministry of Education, Singapore; Commonwealth Scholarship Commission scholar*)
W. Ratnayake, B SC (*University of Ceylon; Commonwealth Scholarship Commission scholar*)

The Unit is engaged in an analysis of the process of mutation, with particular emphasis on the events leading from the primary lesion in DNA to the emergence of the mutant cell.

Summary of research

1. Bacteria:
   (*a*) The lethal and mutagenic action of irradiated medium.
   (*b*) Attempts to study mutagen specificity by means of transforming principle.
   (*c*) Influence of caffeine on ultraviolet-induced killing and reverse mutation in hcr+ and hcr− strains of *Escherichia coli* B/r.
   (*d*) Analysis of mutagen specificity in three diauxotrophic strains of *Escherichia coli* B/r.
2. *Neurospora:*
   (*a*) Analysis of mutagen specificity for reverse mutations to prototrophy.
   (*b*) Analysis of the delayed action of chemical mutagens, using the recessive lethal technique.
   (*c*) Production and analysis of resistance mutations to acriflavine.
3. *Schizosaccharomyces pombe:*
   (*a*) Production and study of replicating instabilities by radiation and chemical mutagens.
   (*b*) Study of a system showing a high degree of mutagen specificity.
4. *Drosophila:*
   (*a*) Analysis of the delayed action of chemical mutagens.
   (*b*) Analysis of delayed chromosome breakage produced by triethylenemelamine.
   (*c*) Action of chemically treated medium on mutation and recombination.

* On leave of absence in the United States.

5. The mouse—genetical studies:
   (*a*) Analysis of the mechanism of non-disjunction in translocation stocks.
   (*b*) A search for inactivation centres in the X chromosome.
6. The mouse—cytological studies:
   (*a*) Sex chromosome and nucleolus in spermatocytes with the ' flecked ' translocation.
   (*b*) Analysis of the ' flecked ' translocation in the pachytene oocyte.
   (*c*) Opportunities for repair of premutational damage during spermatogenesis.
   (*d*) Relation between the morphology of the oocyte and its sensitivity to radiation.

PSYCHIATRIC GENETICS RESEARCH UNIT

Institute of Psychiatry, Maudsley Hospital, Denmark Hill, London S.E.5
(Rodney 9600 or 8585)

Director
E. T. O. Slater, CBE, MD, FRCP, DPM (*part-time*)

Assistant Director
Mrs V. A. Cowie, MD, DPM (*part-time*)

Scientific staff
Mrs J. G. Carr, BA (*part-time; until Nov. 1965*) J. S. Price, BM, DPM
J. Kahn, PH D

Other senior staff
Miss V. G. Seal

Attached workers
L. L. Heston, MD (*University of Oregon Medical School; US National Institutes of Health Special Fellow*)
J. Shields, BA (*Institute of Psychiatry*)
M.-T. Tsuang, MD (*National Taiwan University Hospital, Formosa; Sino-British Trust Fellow*)

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—because appropriate material is available, for instance, or because methodological advances have made the problems amenable to solution. Examples of such problems are the investigation of genetic–environmental interactions in a large collection of twins whose records are are available at the Institute of Psychiatry, and the multidimensional study of mongolism in a population sample by means of special cytogenetical techniques now available.

Summary of research

1. A multidimensional study of mongolism in a population-based sample, with chromosomal, dermatoglyphic, familial, psychological and general clinical investigations, including a special longitudinal study of neurological development beginning in the neonatal period.
2. Hormonal factors in mothers of mongols (with Dr A. J. Coppen, St Ebba's Hospital, Epsom, and Dr Margaret Stern, Chelsea Hospital for Women).
3. Chromosome studies of cases of psychiatric interest referred by hospitals.
4. Aetiological factors and later effects in female delinquency: a study of delinquent girls admitted to a classifying school, with a 5-year follow-up.
5. Birth order and maternal age in psychiatric patients.
6. Follow-up study of monozygotic and same-sexed dizygotic twin pairs of which one member has been under treatment at the Maudsley Hospital for neurosis, personality disorder or schizophrenia since 1948.
7. Investigation of pairs of sibs both treated in hospital for mental illness.

8. Study of children of schizophrenic mothers reared in a foster-home.
9. Clinical, biochemical and psychometric investigation of sibs of patients with schizophrenia and affective psychosis.
10. Serum proteins in Huntington's chorea (with Dr D. Gammack, Department of Biochemistry, Institute of Psychiatry).

EXPERIMENTAL GENETICS RESEARCH UNIT

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

(Euston 7050)

Honorary Director

Professor H. Grüneberg, MD, D SC, FRS

Scientific staff

M. S. Deol, PH D*
Mrs H. M. Murphy, PH D
Mrs L. E. Riles, MA (*until Dec. 1965*)
Miss G. M. Truslove, PH D

Attached workers

S. L. Beck, PH D (*University of Michigan*)
D. R. Johnson, B SC (*MRC Scholar*)
Miss H. Randelia, M SC (*Indian Cancer Research Centre, Bombay*)

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 and their genetic background, and a study of the pathology and development of these conditions. The genetic background in the absence of major pathological entities is also studied both in inbred laboratory strains and in wild populations.

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: their development, with special reference to anomalies of the central nervous system.
5. Cerebral degeneration in the mouse.
6. Genes affecting embryonic haemopoiesis.
7. A search for differences in proteins and smaller molecules associated with genes ascertained through their morphological effects.
8. A search for effects in adult life of genes ascertained through their effects in early development.
9. A search for genetic effects of radiation in areas with high background radiation (Kerala, South India).
10. Genes and genotypes affecting the dentition of the mouse.
11. Tests of the ' single active X chromosome ' hypothesis in the mouse.
12. Embryology of inherited syndactylism in cattle.

CELL GENETICS RESEARCH UNIT

Department of Genetics, University of Glasgow, Glasgow W.2

(Western 8855)

Honorary Director

Professor G. Pontecorvo, PH D, FRSE, FRS

Scientific staff

D. Bell, PH D
Mrs J. C. M. Macnab, B SC

* On leave of absence for one year from October 1965 for work at Jackson Laboratory, Bar Harbor, Maine, USA.

This Unit is concerned with genetic analysis at the cellular level in human and other tissue.

Summary of research

1. Induction of whole chromosomal segregations in cultured human cells.
2. A search for conditions determining the division in culture of human peripheral blood lymphocytes.

MICROBIAL SYSTEMATICS RESEARCH UNIT

The University, University Road, Leicester

(Leicester 50000)

Director

P. H. A. Sneath, MD, DIP BACT

Scientific staff

Mrs D. Wood, PH D, DIP BACT

This Unit is engaged in research on the classification of microorganisms, with special reference to numerical taxonomy and computer methods. The application of these methods to other fields of medical and biological science is also being explored.

Summary of research

1. Systematics of pseudomonads and related bacteria.
2. Influence of environment on the classification of bacteria.
3. New statistical methods in taxonomy.
4. Systematic study of primary structure of proteins.
5. Development of computer programs for systematics.
6. Systematics of coryneform bacteria.
7. Relationship between pasteurellas and enterobacteria.

MICROBIAL GENETICS RESEARCH UNIT

Hammersmith Hospital, Ducane Road, London W.12

(Shepherds Bush 4594)

Director

W. Hayes, MB, D SC, DPH, FRCPI, FRS

Scientific staff

J. M. Boyle, M SC (*until Nov. 1965*)
P. M. A. Broda, PH D (*until Sept. 1965*)
R. C. Clowes, PH D (*until Sept. 1965*)
G. M. Crowley, PH D
W. D. Donachie, PH D
K. W. Fisher, PH D
S. W. Glover, PH D
J. D. Gross, PH D
J. G. Scaife, PH D*
K. A. Stacey, PH D (*until Sept. 1965*)
N. D. Symonds, PH D (*until Sept. 1965*)

Attached workers

J. Aronovitch, PH D (*Hebrew University Medical School, Jerusalem; British Council Fellow*)
S. Cooper, PH D (*US National Science Foundation Fellow*)
J. M. Erskine, B SC (*New Zealand Dairy Research Fellow*)
Z. Evenchik, PH D (*Israel Institute for Biological Research; Rothschild Foundation Fellow*)
Mrs T. Gottfried, B SC (*University of Pennsylvania; US Public Health Service Fellow*)
D. Karamata, B SC (*University of Geneva*)
G. Kerszman, PH D (*University of Lodz; British Council Fellow*)
Miss A. M. Macfarren, B SC (*MRC Scholar*)
Miss M. Masters, PH D (*US National Institutes of Health Fellow*)
N. Mendelson, PH D (*US National Science Foundation Fellow*)
Mrs E. Meynell, MB (*MRC grant-holder*)
L. Pearce, PH D (*University of Otago; New Zealand Dairy Research Fellow*)
K. E. Sanderson, PH D (*Wellcome Trust Fellow*)
A. Siccardi (*University of Pavia*)

* On leave of absence for one year from September 1965 to work at Harvard Medical School.

Microorganisms in recent years have proved to be uniquely adapted to highly refined analyses of genetic structure, organization and function. The Unit is undertaking detailed study of the fine structure of genes and chromosomes in microorganisms and the mechanisms of their replication and transfer to other cells (i.e. sexuality). Research is concerned primarily with the genetics of bacteria and their viruses, which are relevant to such problems as 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. Investigation of non-recombining mutant strains of bacteria and bacteriophages.

HUMAN BIOCHEMICAL GENETICS RESEARCH UNIT

Galton Laboratory, University College London, Gower Street, W.C.1

(Euston 7050)

Honorary Director

Professor H. Harris, MD, FRS

Scientific staff

T. E. Cleghorn, MD (*honorary*)
R. A. Fildes, PH D (*until Dec. 1965*)
Miss A. M. Glen-Bott, MB (*until Aug. 1965*)
D. A. Hopkinson, MB
W. H. P. Lewis, B SC
Miss J. E. Luffman, B SC
Mrs P. M. H. Mazumdar, MB (*until June 1965*)
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. Human enzyme polymorphisms and variants: their genetical and biochemical basis and clinical significance, with particular reference to serum cholinesterase, red cell acid phosphatase, phosphoglucomutase, placental alkaline phosphatase, adenylate kinase and aminopeptidases.
2. Electrophoretic studies on inherited variants of serum proteins.
3. Quantitative and qualitative studies on serum alkaline phosphatase in relation to the ABO blood groups and the secretor status and to gastrointestinal function (with the Statistical Research Unit).
4. Biochemical markers in twin studies: a survey of multiple births in Birmingham (with Dr J. H. Edwards, Department of Social Medicine, University of Birmingham) and in Oxford (with Dr G. Corney, Radcliffe Infirmary).
5. Linkage studies (with the Clinical Effects of Radiation Research Unit and the Blood Group Research Unit).

BIOPHYSICS RESEARCH UNIT 157

Department of Biophysics, University of London, King's College,
26–29 Drury Lane, London W.C.2
(Temple Bar 8851)

Director
Professor Sir John Randall, D SC, FRS (*part-time*)

Deputy Director
Professor M. H. F. Wilkins, CBE, PH D, FRS

Honorary Biological Adviser
Professor Dame Honor B. Fell, DBE, D SC, FRS

Scientific staff

J. B. Alexander, B SC
S. Arnott, PH D
Miss A. I. Bailey, PH D
Mrs A. V. W. Brown, PH D (*part-time*)
G. L. Brown, PH D
Miss N. Brown, B SC
H. G. Davies, PH D
G. F. Elliott, PH D
Miss E. J. Hanson, PH D
Mrs S. Lee, PH D
J. Lowy, PH D
D. W. McMullen, B SC (*until July 1965*)
B. M. Millman, PH D
S. R. Pelc, D PHIL
E. G. Richards, PH D
M. Spencer, PH D
J. R. Warr, PH D (*until Sept. 1965*)
M. R. Watson, M SC
Miss M. G. E. Welton, B SC

Other senior staff

J. M. Hopkins
Miss R. D. Hynes
R. L. Jones, AIST
Z. Kosinski, M SC
H. R. Munden, FIST

Attached workers

J. Anker, M SC (*University of Geneva and Department of Radiobiology, Mol-Donk, Belgium*)
J. N. Champness, B SC (*MRC Scholar*)
Chang Yu-shang (*Institute of Biochemistry, Shanghai*)
Miss Chou Yung-chin (*Peking Agricultural University*)
D. A. Cowburn, B SC (*MRC Scholar*)
S. D. Dover, BA (*MRC Scholar*)
C. J. Garrett, B SC (*University of York*)
J. Gillis, PH D (*University of Louvain*)
R. G. Gosling, PH D (*University of the West Indies*)
P. M. D. Hardwicke, B SC (*MRC Scholar*)
U. Loening, PH D (*University of Edinburgh*)
Miss S. Lowey, PH D (*Children's Cancer Research Foundation, Boston; American Heart Association Investigator*)
P. McPhie, B SC (*MRC Scholar*)
N. Marsden, PH D (*University of Uppsala*)
Miss V. Mautner, B SC (*MRC Scholar*)
F. Mavrommatis, PH D (*University of Gottingen*)
J. Palau, PH D (*University of Madrid; British Council and Rockefeller Foundation grant-holder*)
J. F. Pardon, B SC (*MRC Scholar*)
W. J. Pigram, B SC (*MRC Scholar*)
I. N. Rabinowitz, PH D (*Damon Runyan Foundation for Cancer Research grant-holder*)
R. A. Rifkind, PH D (*Columbia University; Guggenheim Foundation grant-holder*)
Miss E. M. Rome, B SC (*MRC Scholar*)
J. H. Venable, PH D (*Yale University; National Science Foundation grant-holder*)
P. J. Vibert, B SC (*MRC Scholar*)
Miss F. I. Yen Mu, PH D (*Lima, Peru*)
M. Zade, PH D (*University of Uppsala*)

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. Primary and secondary structure of RNA; role of RNA in protein synthesis.
2. X-ray investigation of the structures of RNA, DNA and nucleoprotein.
3. Contraction in muscle and bacterial flagella studied by electron microscopy and X-ray diffraction; associated biochemical studies on structural 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

(Cambridge 48011)

*Chairman of Governing Board**

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

Deputy Chairman

J. C. Kendrew, CBE, SC D, FRS

Honorary Adviser

Sir Lawrence Bragg, OBE, MC, FRS

STRUCTURAL STUDIES

Scientific staff

J. C. Kendrew, CBE, SC D, FRS (*Head of Division*)
U. W. Arndt, PH D
D. M. Blow, PH D
W. Bolton, PH D
W. Brown, PH D (*until Nov. 1965*)
Miss J. M. Cox, BA
R. Diamond, PH D
J. T. Finch, PH D
Miss L. C. G. Goaman, PH D
T. H. Gossling, MA
K. C. Holmes, PH D
H. E. Huxley, MBE, SC D, FRS
Mrs P. L. King, BA
A. Klug, PH D
R. Leberman, PH D
J. F. C. Mallett, BA
B. W. Matthews, PH D
A. Miller, PH D
H. C. Watson, PH D
R. J. Watts-Tobin, PH D

Attached workers

L. J. Banaszak, PH D (*University of Indiana; US Public Health Service Fellow*)
J. Berger, MD (*US National Institutes of Health Fellow*)
P. A. Bretscher, BA (*MRC Scholar*)
Y.-S. Chang, PH D (*Institute of Biochemistry, Shanghai*
R. A. Crowther, BA (*MRC Scholar*)
D. J. De Rosier, PH D (*University of Chicago; US Air Force Office for Scientific Research Fellow*)
J. Greer, AB (*Princeton University; Fulbright Scholar*)
S. C. Harrison, AB (*Harvard University; Henry Fellow*)
J. C. Haselgrove, B SC (*MRC Scholar*)
A. D. Kaiser, PH D (*Stanford University, California; US National Science Foundation Fellow*)
J. V. Kilmartin, BA (*MRC Scholar*)
R. Kretsinger, PH D (*Massachusetts Institute of Technology; Helen Hay Whitney Foundation Fellow*)
J. B. Leigh, BA (*MRC Scholar*)
M. Lubin, MD (*Harvard University; Guggenheim Foundation Fellow and US National Institutes of Health grant-holder*)
F. S. Mathews, PH D (*Massachusetts Institute of Technology; US National Institutes of Health Fellow*)
J. K. Moffat, B SC (*Nuffield Foundation Biological Sciences Bursar*)
C. L. Nobbs, PH D (*University of Auckland, New Zealand; Shell Scholar and Royal Society Stothert Research Fellow*)
M. K. Reedy, MD (*University of Washington, Seattle; US Public Health Service Fellow*)
B. P. Schoenborn, PH D (*University of California*)
P. B. Sigler, PH D (*US National Institutes of Health; Helen Hay Whitney Foundation Fellow*)
L. E. Webb, PH D (*University of Chicago; US National Science Foundation Fellow*)

MOLECULAR GENETICS

Scientific staff

F. H. C. Crick, PH D, FRS } (*Joint Heads*
S. Brenner, MB, D PHIL, FRS } *of Division*)
Mrs M. L. Barnett, B SC
M. S. Bretscher, PH D
B. F. C. Clark, PH D
B. K. Davis, PH D
R. E. Monro, PH D
A. S. Sarabhai, PH D
J. D. Smith, PH D
A. O. W. Stretton, PH D

* The Heads of Divisions and Dr Huxley are the members of the governing board of the Laboratory.

Attached workers

J. N. Abelson, PH D (*Johns Hopkins University, Baltimore, Maryland; US National Institutes of Health Fellow*)
J. S. Anderson, PH D (*University of Wisconsin; US Public Health Service Fellow*)
J. W. Drake, PH D (*University of Illinois, Urbana; Guggenheim Foundation Fellow*)
D. P. Fan, PH D (*Massachusetts Institute of Technology; US National Science Foundation (NATO) Fellow*)
R. P. Freedman, BA (*MRC Scholar and Fellow of King's College, Cambridge*)
H. M. Goodman, PH D (*Massachusetts Institute of Technology; Helen Hay Whitney Foundation Fellow*)
S. Kaplan, PH D (*University of California; US National Institutes of Health Fellow*)
G. S. Martin, BA (*MRC Scholar*)
J. R. Menninger, PH D (*Harvard University; Helen Hay Whitney Foundation Fellow*)
R. H. Rownd, PH D (*Harvard University; US National Institutes of Health Fellow*)
F. W. Stahl, PH D (*University of Oregon*)
G. P. Tocchini-Valentini, DOTT (*International Laboratory of Genetics and Biophysics, Naples*)
A. A. Travers, BA (*MRC Scholar*)

PROTEIN AND NUCLEIC ACID CHEMISTRY

Scientific staff

F. Sanger, CBE, PH D, FRS (*Head of Division*)
R. P. Ambler, PH D (*until Sept. 1965*)
J. B. Clegg, PH D
J. I. Harris, PH D
B. S. Hartley, PH D
J. Hindley, PH D (*until Mar. 1966*)
Miss D. A. Kauffman, BA (*until Sept. 1965*)
K. Marcker, DR PHIL
C. Milstein, PH D
K. Murray, PH D
R. E. Offord, BA
L. F. Smith, PH D (*until Oct. 1965*)
A. G. Weeds, BA
J. Williams, MB, B SC (*until Sept. 1965*)

Attached workers

W. S. Allison, PH D (*Brandeis University, Waltham, Mass.; US National Institutes of Health Fellow*)
G. G. Brownlee, BA (*MRC Scholar*)
P. J. G. Butler, BA (*MRC Scholar*)
B. E. Davidson, B SC (*University of Melbourne; Commonwealth Scientific and Industrial Research Organization Overseas Scholar*)
P. Fellner, BA (*MRC Scholar*)
B. Foltmann, PH D (*University of Copenhagen; Carlsberg Foundation grant-holder and Danish State Fellow*)
R. Heinrikson, PH D (*Rockefeller University, New York; US National Science Foundation (NATO) Fellow*)
G. M. T. Jones, BA (*MRC Scholar*)
K. Marcker, PH D (*Royal Dental College, Copenhagen; Carlsberg–Wellcome Trust Fellow*)
D. Marinkovic, DIP CHEM (*Institute of Nuclear Science, Belgrade*)
H. Noller, PH D (*University of Oregon; US Public Health Service Fellow*)
R. E. Offord, BA (*MRC Scholar*)
J. R. L. Pink, BA (*MRC Scholar*)
D. M. Shotton, BA (*MRC Scholar*)
J. Tang, PH D (*Oklahoma Medical Research Foundation; Guggenheim Foundation Fellow*)

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 and nucleic acid 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. Determination of protein structure by X-ray methods:
   (*a*) Haemoglobin: extension of three-dimensional study of horse methaemoglobin to a resolution of 3 Å; studies of deoxy and other derivatives, with a view to gaining a better understanding of oxygenation and the Bohr effect; formation of complexes with xenon.
   (*b*) Myoglobin: refinement of the structure at a resolution of 1·4 Å and assignment of atomic coordinates; studies of deoxy- and oxy-myoglobins and of the mode of attachment of other ligands besides oxygen, including metal ions and xenon.
   (*c*) Chymotrypsin: three-dimensional structure at a resolution of 2 Å.
   (*d*) Glyceraldehyde phosphate dehydrogenase: relation between subunits; low resolution study.

2. Determination of virus structure by X-ray diffraction, electron microscopy and chemical analysis, with particular reference to tobacco mosaic, turnip yellow, turnip crinkle, human wart and tomato bushy stunt viruses.
3. Studies of muscle and muscle proteins by X-rays and electron microscopy to establish the structure and mechanisms of contraction.
4. Theoretical work in protein crystallography; development of methods for finding the symmetry of protein molecules in crystals and for the determination of phases; development of methods for refining partly determined structures of very complex molecules.
5. Developments in techniques and instrumentation:
   (*a*) Computer-controlled methods for automatic recording of intensities of X-ray reflections.
   (*b*) New methods for detecting X-ray reflections.
   (*c*) Use of computer-controlled oscilloscope display for the preparation of Fourier maps, for manipulating representations of molecular structures, for the densitometry of X-ray photographs and for other related purposes.
   (*d*) Use of new types of high-power X-ray tubes and focussing cameras.
   (*e*) Use of optical transforms for examining electron microscope images.

MOLECULAR GENETICS

1. Mutants, especially of the acridine type, of the r_{II} locus of the bacteriophage T4.
2. Characterization of the triplets for chain termination as UAG (*amber*) and UAA (*ochre*).
3. Characterization of the amino acids inserted by the three *amber* suppressors su^{+}_{I}, su^{+}_{II} and su^{+}_{III} as serine, glutamine and tyrosine respectively.
4. Genetic mapping of *amber* and *ochre* suppressors.
5. Polar effects of *amber* and *ochre* mutants.
6. The mechanism of suppression, studied in the cell-free system.
7. Studies on polypeptide chain initiation: the role of *N*-formyl-methionyl transfer RNA.
8. Fractionation of transfer RNA.
9. The mechanism of protein synthesis: the role of guanosine triphosphate and the action of puromycin.
10. Regulatory mechanisms in T4 growth.
11. Integration and growth of temperate bacteriophages.

PROTEIN AND NUCLEIC ACID CHEMISTRY

1. Structure and activity of glyceraldehyde 3-phosphate dehydrogenase from muscle and yeast.
2. Structure and activity of yeast alcohol dehydrogenase.
3. Amino acid sequence homologies in pancreatic proteolytic enzymes.
4. Development of ' diagonal ' techniques for the study of sequences around specific amino acid residues in proteins.
5. Purification of methionine-activating enzymes.
6. Amino acid sequence around all the cysteine residues in myosin.
7. Amino acid sequence of cytochrome *c* from *Pseudomonas* and of penicillinase.
8. Variation of the amino acid sequence around the disulphide bridges of type K Bence-Jones proteins and its significance in the structure and synthesis of antibodies.
9. Amino acid sequence of an immunoglobulin λ chain.
10. Structure of the protein and nucleic acid components of tobacco rattle virus.
11. Further development of fractionation procedures for digests of RNA and DNA and their application.
12. Nucleotide sequence of 5*S* ribosomal RNA.
13. Purification of phenylalanyl and methionyl transfer RNAs and studies on their composition and nucleotide sequences.
14. Significance of formyl-methionine transfer RNA and its role in chain initiation of protein synthesis.

CELL METABOLISM RESEARCH UNIT

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

Honorary Director
Professor Sir Hans Krebs, MD, D SC, FRCP, FRS

Scientific staff

K. Burton, PH D
Miss P. Lund, B SC
Miss M. R. Lunt, D PHIL (*until Oct. 1965*)
E. A. Newsholme, PH D
D. S. Robinson, PH D
Mrs J. M. Uo, DR SCI
D. H. Williamson, B SC

Other senior staff

L. V. Eggleston, B SC
R. Hems

Attached workers

Miss M. W. Bates, SC D (*University of Pittsburg*)
Mrs K. N. Bojanowska, PH D (*University of Warsaw; Polish Ministry of Health Scholar*)
J. Borensztajn, MD (*University of Brazil; Ministry of Overseas Development Student*)
Mrs H. Cole, BA (*MRC Scholar*)
J. A. Cole, BA (*MRC Scholar*)
C. J. Fielding, PH D (*University College London; Guinness Research Fellow, New College, Oxford*)
W. Gevers, BA, MB (*Cape Town; Sir Robert Kotze Scholar*)
Miss D. Keane, B SC (*University College, Dublin*)
N. J. Kuhn, BA (*MRC Scholar*)
F. Kunz DR MED (*University of Innsbruck; until Dec. 1965*)
L. H. Opie, MB, D PHIL (*University of Cape Town; Wellcome Trust Fellow*)
M. Pring, D PHIL (*Junior Research Fellow, Balliol College, Oxford*)
Miss L. Raijman, MD, B SC (*University of Cordoba; until Nov. 1965*)
Miss J. Robinson, BA (*MRC Scholar*)
F. S. Rolleston, BA (*Wellcome Trust Scholar*)
B. D. Ross, MB, B SC (*University of London; MRC Junior Research Fellow*)
Mrs C. Start, BA (*MRC Scholar*)
V. I. Tanyashin (*University of Kazan, USSR; British Council Scholar*)
A. H. Underwood, BA (*Wellcome Trust Scholar*)
J. C. Wallace, PH D (*Monash University, Victoria; 1851 Scholar*)
Mrs P. G. Wallace, PH D (*Monash University, Victoria; 1851 Scholar*)
M. J. Weidemann, PH D (*University of Melbourne; Commonwealth Scientific and Industrial Research Organization Overseas Studentship*)
M. Wilson, PH D (*University of the West Indies; Wellcome Research Travelling Fellowship*)

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

1. Rate-controlling factors in respiration and glycolysis.
2. Gluconeogenesis.
3. Metabolism of ketone bodies.
4. Regulation of blood triglyceride level and glycerol metabolism.
5. Factors affecting clearing factor lipase formation in adipose tissue.
6. Biochemistry of bacteriophages.
7. Primary and secondary structure of nucleic acids.
8. Development of techniques:
   (*a*) Degradation methods for determining the structure of DNA.
   (*b*) Ancillary equipment of gas–liquid chromatography.
   (*c*) Fractionation of subcellular particles in non-aqueous systems.
   (*d*) Radiochemical assays for enzymes and metabolic intermediates.
   (*e*) Perfusion of isolated liver and kidney.

BRAIN METABOLISM RESEARCH UNIT

Department of Pharmacology, University Medical School,
Teviot Place, Edinburgh 8
(Newington 1011)

Honorary Director
Professor W. L. M. Perry, OBE, MD, DSC, MRCPE

Scientific staff

H. M. Adam, MB (*honorary*)
G. W. Ashcroft, MB, DORCOG, DPM, MRCPE
T. B. B. Crawford, PH D (*honorary*)
D. Eccleston, MB, DPM
F. Knight, MB, DA
I. Laszlo, GRAD IN MED, PH D
Miss E. J. McDougall, MB, DPM (*honorary*)
A. T. B. Moir, MB, B SC
Miss E. E. Robertson, MB, FRCPE, DPM (*honorary*)
Miss C. M. Yates, M SC

Attached workers

Y. Abou, MB (*University of Baghdad*)
A. J. Cooper, MB, DPM (*University of Edinburgh*)
H. Guldberg, MB, B SC (*University of Edinburgh*)

The work of the Unit is concerned with the metabolism of amino acids and other substances in the brain and tissue fluids of animals and in the tissue fluids of normal and psychotic humans, and with the action of psychotropic drugs on the metabolism. The clinical studies are carried out in the Unit's ward at the Royal Edinburgh Hospital and also in cooperation with the Neurological Department, Western General Hospital, and the Neurological Unit, Northern General Hospital. The approach to clinical problems is based on principles defined in the animal studies.

Summary of research

ANIMAL STUDIES

1. Development of techniques for the study of cerebral metabolism in the intact animal:
   (*a*) Examination of concentrations of cerebral metabolites in cerebrospinal fluid.
   (*b*) Cerebral ventricular perfusion.
2. Properties of blood–brain barrier:
   (*a*) Transport of amino acids into brain and cerebrospinal fluid.
   (*b*) Removal of acid metabolites from brain and cerebrospinal fluid.
3. Analytical procedures for measurement of precursors, active substances and degradation products in the metabolic pathways of indolalkylamine, catecholamine, histamine and substance P.
4. Effects of psychotropic drugs on the metabolic pathways described above and in particular on interactions between the pathways.
5. Examination of differences in amine metabolism between specific areas of the brain.
6. Correlation of biochemical changes in amine metabolism with histochemical changes as demonstrated by fluorescence microscopy.

CLINICAL STUDIES

1. Blood and urine—estimation of amino acid precursors, amines and metabolites:
   (*a*) In normal controls.
   (*b*) In patients with psychotic illnesses.
   (*c*) Changes induced by psychotropic drugs.
2. Cerebrospinal fluid:
   (*a*) Techniques for the estimation of amino acid precursors, amines and acid metabolites in cerebrospinal fluid.
   (*b*) Factors controlling cerebrospinal fluid levels of acid metabolites, e.g. site of cerebrospinal fluid sampling (lumbar, cisternal, ventricular).
   (*c*) Changes in amine metabolism as reflected in cerebrospinal fluid levels of metabolites (i) in pathological states, e.g. depression, Parkinsonism; (ii) induced by psychotropic drugs.
3. Brain tissue: investigation of the possibility of measuring levels of amines and their metabolites in small biopsy samples, e.g. from the basal ganglion in Parkinsonism.

METABOLIC REACTIONS RESEARCH UNIT

Biochemistry Department, Imperial College, London S.W.7
(Kensington 5111)

Honorary Director
Professor E. B. Chain, D PHIL, FRS

Scientific staff

D. M. Blond, D PHIL
Mrs R. Catanzaro-Quintiliani, DR MED
C. Chlouverakis, DR MED
K. R. L. Mansford, M SC
S. P. R. Rose, PH D
A. Wiseman, PH D (*until Oct. 1965*)

Other senior staff

A. E. Lowe
G. Moffat

Attached worker
H. F. Bradford, PH D (*MRC Junior Research Fellow*)

The research programme of this Unit is concerned with the study of the mode of action of hormones, in particular insulin, and certain aspects of brain metabolism.

Summary of research

1. Mode of action of insulin:
   (*a*) The fate of ^{14}C-glucosamine and other slowly metabolized hexoses under the influence of insulin in different insulin-sensitive tissues; identification of the phosphorylated intermediates that accumulate.
   (*b*) The fate of ^{14}C-glucosamine in the liver of normal rats and of rats rendered insulin-deficient by treatment with insulin antiserum.
   (*c*) The metabolic pattern of ^{14}C substrates in the perfused heart in the presence and absence of insulin.
   (*d*) The metabolic pattern of ^{14}C substrates in isolated tissues of reptiles and amphibia in the presence and absence of insulin.
   (*e*) Studies on adipose tissue in the rat: mode of action of insulin as regards its effect on various lipases; metabolic patterns of this tissue during starvation and diabetes.
2. The action of various nucleotides on the pattern of glucose metabolism in different tissues.
3. Brain metabolism:
   (*a*) Comparative study of metabolic patterns of glucose, fructose, galactose, maltose and glucosamine in rat brain cortex.
   (*b*) Specific role of hexoses in amino acid transport.
   (*c*) Preparation of neuronal and glial enriched fractions from brain cortex and their biochemical and physiological characterization.
   (*d*) Measurement of electrical potentials in isolated neurones.
   (*e*) Building of computer models of metabolic pathways in brain slices.
4. Instrumentation: adaptation of bidimensional radiochromatogram scanner for direct quantitative evaluation of radioactive spots by computer; computer evaluation of data from separation of intermediates by column chromatography.

EXPERIMENTAL VIRUS RESEARCH UNIT

Institute of Virology, Church Street, Glasgow W.1
(Western 8855)

Honorary Director
Professor M. G. P. Stoker, MD, FRSE

Staff

R. Bürk, PH D
L. V. Crawford, PH D
F. G. Wingfield Digby, PH D (*died Mar. 1966*)
E. A. C. Follett, PH D
G. Le Bouvier, MD
I. A. Macpherson, PH D
C. H. O'Neill, PH D
J. D. Pitts, PH D
Miss S. E. Reed, MB (*part-time*)
H. Subak-Sharpe, PH D
M. A. Thomas, MD (*honorarium; until Aug. 1965*)
H. V. Thorne, PH D

Other senior staff

W. House, FIMLT

Visiting and attached workers

K. B. Fraser, MD, FRSE (*University of Glasgow*)
Miss M. Gharpure, MB, PH D (*University of Glasgow; Indian Government Polio Research Unit*)
P. Gill, PH D (*McGill University; Medical Research Council of Canada Fellow*)
P. Gomatos, MD (*US Public Health Services Fellow*)
I. P. Gormley, B SC (*University of Glasgow; MRC Scholar*
Mrs L. Holroyd, B SC (*University of Glasgow*)
O. Jarrett, BVMS (*University of Glasgow; Horse Race Betting Levy Board Scholar*)
Miss S. Milliken, B SC (*University of Glasgow*)
Miss S. Reed, MB (*University of London*)
Miss W. Shepherd, B SC (*University of Glasgow; MRC Scholar*)
Miss M. E. Smart, B SC (*University of Glasgow; MRC Scholar*)
P. Urbano, MD (*University of Florence; Italian Research Council Fellow*)
D. Warden B SC (*University of Glasgow; British Empire Cancer Campaign grant-holder*)
J. M. Whalley, B SC (*University of Glasgow; British Empire Cancer Campaign grant-holder*)
J. Závada, PH D (*University of Bratislava; International Atomic Energy Agency Fellow*)

The Unit carries out research on virus structure and function, with particular reference to hereditary changes in animal cells induced by tumour viruses.

Summary of research

1. Mechanism of neoplastic transformation by polyoma, papilloma and SV40 viruses studied in cell culture.
2. Characteristics of the DNA and protein components of polyoma and papilloma group viruses.
3. Reversion in cells transformed by Rous sarcoma virus.
4. Characterics of cells of tumours induced by viruses compared with those of normal and of spontaneously appearing neoplastic cells.
5. Genetically stable biochemical variants of a stable diploid cell line.
6. Identification of RNAs and proteins specified by the herpes virus genome.
7. Analysis of virus–virus and virus–host relationships using the nearest-neighbour nucleotide patterns in the DNA.

VIRUS RESEARCH UNIT

Medical Research Council Laboratories, Woodmansterne Road,
Carshalton, Surrey
(Melville 4461)

Director

F. Kingsley Sanders, D PHIL

Scientific staff

A. T. H. Burness, PH D
P. Faulkner, PH D (*until Aug. 1965*)
M. L. Fenwick, PH D (*until Aug. 1965*)
S. M. McGee-Russell, D PHIL
A. D. Vizoso, PH D

Other senior staff

F. W. Clothier, AIST

Attached workers

F. Galibert, CNRS (*Hôpital St. Louis, Paris; Council of Europe grant-holder*)
G. Gosztonyi, MD (*University of Pecs, Hungary; Wellcome Trust Research Fellow*)

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 started simultaneously in a large number of cells, and (*b*) cells at different stages of infection can subsequently be investigated by chemical, morphological and virological methods, are being used to investigate the process involved both in virus synthesis and in the accompanying cellular alterations.

1. Intracellular events during the growth of several variants of a cell-destroying virus in mouse ascites tumour cells.
   (*a*) Significance of differences in the biochemical and biophysical make-up of virus particles in relation to differences in their interaction with susceptible cells.
   (*b*) The relation between the mode of assembly of virus particles and their cytopathic effect.
2. Development of new cell–virus systems for the study of cellular events during the growth of viruses of varying sizes and pathogenicity containing different sorts of nucleic acid.
3. Cell strains adapted to growth in agar suspensions as tools in virological research.
4. Characterization of a new virus recently isolated from wild grey squirrels, which causes morphological transformation of mammalian cells in tissue culture.
5. Electron microscope investigations of the mode of interaction of viruses attacking the central nervous system with their host cells.

HUMAN NUTRITION RESEARCH UNIT

Nutrition Building, National Institute for Medical Research,
Mill Hill, London N.W.7
(Mill Hill 3378)

Director

Professor B. S. Platt, CMG, MB, PH D

Scientific staff

Miss I. M. Barrett, B SC
Mrs B. A. Christie, M SC
B. H. Doell, M SC
C. R. C. Heard, D PHIL
D. J. Naismith, PH D
P. R. Payne, B SC
M. R. Turner, M SC

Other senior staff

Mrs S. N. Payne
Miss H. G. Sheppard
R. J. C. Stewart
P. Ward

Attached workers

Miss Y. Chou, B SC (*Singapore; Commonwealth Scholar*)
H. R. Gayed, MB (*UAR Military Forces; UAR Government grant-holder*)
P. V. J. Hegarty, M SC (*Evans Medical Ltd research student*)
M. A. Hossain, MB (*University of Dacca; Commonwealth Scholar*)
Miss N. M. Ibrahim, B SC (*Iraq*)
E. O. Idusogie, B SC (*Nigerian Government grant-holder*)
Mrs S. H. Khatun, M SC (*University of Dacca*)
B. Laksesvela, PH D (*Norwegian Government grant-holder*)
Mrs A. K. Lebshtein, MB (*University of Assiut, Egypt*)
Miss K. K. Narula, MB (*University of Delhi; Commonwealth Scholar*)
Mrs S. S. Nasser, MB (*University of Cairo; WHO Fellow*)
M. Soyuer, MD (*University of Ankara; WHO Fellow*)

At the London School of Hygiene and Tropical Medicine

W. R. Aykroyd, CBE, MD, SC D
Miss M. E. Cameron, B H SC, DIP DIET (NZ)
G. R. Wadsworth, MD
} *Department of Human Nutrition*

T. P. Eddy, CBE, MRCS, DPH
Miss A. Nicholson, B SC
P. L. Pellett, PH D, ARIC
Miss M. S. Prosper, DIP DOM SC
Miss E. F. Wheeler, B SC, DIP DIET (LOND)
} *Nuffield Provincial Hospitals Trust grant-holders*

Mrs J. Doughty, B SC
D. C. Morley, MD, DPH
Miss J. A. S. Ritchie, M SC
} *UNICEF grant-holders*

The main study of the Unit has been the malnutrition of people in Commonwealth territories and other tropical and subtropical 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–calorie deficiency. 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.

Summary of research

1. The various forms and manifestations of malnutrition, especially the effects in man and animals of low-protein, high-carbohydrate diets:
   (*a*) Interrelationships of dietary and endocrine factors.
   (*b*) Effects on the foetus and infant, on the reproductive system, 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

The University, Milton Road, Cambridge
(Cambridge 55444)

Director
E. H. Kodicek, MD, PH D

Scientific staff
M. J. Barnes, PH D
D. E. M. Lawson, PH D
C. I. Levene, MD, MC PATH
J. B. Mason, BA
I. M. Sharman, PH D, FRIC

Other senior staff
D. R. Ashby
B. J. Constable
P. W. Wilson

Attached workers
Miss E. M. Cruickshank, PH D (*MRC grant-holder*)
D. R. Fraser, B V SC (*University of Sydney*)
T. K. Murray, PH D (*Food and Drug Directorate, Department of National Health and Welfare, Ottawa*)
D. Tillotson, BA (*MRC Scholar*)

The Unit is engaged in research on vitamins and other nutrients, including the elucidation of the biochemical and physiological processes underlying their mode of 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; effect on collagen and elastin synthesis; carbohydrate and amino acid composition of granulation tissue.
2. Niacytin (the bound nicotinic acid in cereals): elucidation of chemical structure and biochemical pathways.
3. Vitamin A: mode of action, particularly at subcellular levels; effects of deficiency; blood levels in human subjects; significance for farm animals.
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 animal tissues and subcellular fractions; metabolism of tritiated and ^{14}C-labelled vitamin D_2 and vitamin D_3 in rats and tissues cultivated *in vitro*; effect of vitamin D and parathyroid on absorption of ^{45}Ca; comparison of the effect of dihydrotachysterol and vitamin D_3 on healing of rickets in rats; mechanisms affecting calcium homeostasis; effect of vitamin D on viruses; estimation of vitamin D in natural products by gas–liquid chromatography; identification of metabolites of vitamin D.
6. Biosynthesis of bacterial lipids: investigations on isoprenoid compounds, phospholipids, fatty acids.
7. Nutritional requirements of fibroblasts in tissue culture.
8. Experimental calcium deficiency: influence on bone structure in the rat; balance between iron, calcium and copper; mineral deficiencies induced by meat diets.

MEDICAL RESEARCH COUNCIL LABORATORIES, GAMBIA

Fajara, Nr. Bathurst, Gambia, West Africa

Director

I. A. McGregor, OBE, MRCP, DTM & H

Scientific staff

D. S. Harling, MD, MRCP, DTM & H
G. H. Harverson, MB
D. P. M. Howells, MB, MRCP
Miss E. Topley, MD
Miss G. H. Walker, MB (*until May 1965*)
Mrs M. E. Wilson, MB, DTM & H

Other senior staff

A. W. M. Cooke (*Administrative Officer*)

Attached workers

J. Hamburger, M SC (*Hebrew University, Jerusalem; US Army grant-holder*)
Professor Avivah Zuckerman, PH D (*Hebrew University, Jerusalem; US Army grant-holder*)

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. Epidemiology of malaria, with special reference to the acquisition of immunity.
2. Measurement of communal malarial immunity by fluorescent and haemagglutination techniques.
3. Antigenic composition of Gambian plasmodia, especially *Plasmodium falciparum*.
4. Serological changes in Gambians caused by malarial infection.
5. Placental infection in malaria.
6. Field assessment of repository antimalarial drugs.
7. Macroglobulin (IgM) levels in a rural population, with special reference to trypanosomiasis (with Dr R. Masseyeff, University of Dakar, and Dr P. Mattern, Pasteur Institute, Dakar).
8. Levels of the various immunoglobulins in the sera of rural Africans (with Dr D. S. Rowe, University of Birmingham).
9. Fluorescent immunology in the epidemiological study of virus infection prevalent in Gambia (with Dr R. G. Sommerville, Belvidere Hospital, Glasgow).

10. Pattern of illness in Gambian children and adults.
11. Factors responsible for high rates of mortality in Gambian children (with the Reproduction and Growth Research Unit).
12. Pattern of growth of Gambian children (with the Reproduction and Growth Research Unit).
13. Effect of socio-economic influences on growth and mortality of Gambian children (with the Medical Sociology Research Unit).
14. Incidence and aetiology of anaemia in rural African populations.
15. Contribution of hookworm infection to the development of prevalent anaemia of the iron deficiency type.
16. Incidence, aetiology and importance of seasonal oedematous states in Gambian adults.
17. Incidence and aetiology of cardiac disease in Gambians.

See p. 180 for an account of work undertaken at the MRC Laboratories in the Gambia by Dr M. E. C. Giglioli, a former member of the staff of the Laboratories and until November 1965 a member of the External Scientific Staff at the London School of Hygiene and Tropical Medicine.

TROPICAL METABOLISM RESEARCH UNIT

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

Director
Professor J. C. Waterlow, MD, MRCP

Assistant Director
J. S. Garrow, MD, PH D, MRCPE (*until Sept. 1965*)

Scientific staff

G. A. O. Alleyne, MB, MRCP
Miss A. Ashworth, PH D
H. V. Chan, MB (*until Sept. 1965*)
K. Fletcher, PH D (*until Sept. 1965*)
D. Halliday, B SC
W. P. T. James, B SC, MB, MRCP
D. I. M. Picou, MB, PH D
Miss J. M. L. Stephen, PH D

Attached workers

A. M. Hay, B SC (*University of London; Wellcome Trust grant-holder*)
B. Lewis, MD, PH D, MRCP (*University College of Rhodesia; Wellcome Trust grant-holder*)

The Unit is concerned mainly with the clinical and biochemical effects of malnutrition in infants and young children, and particularly with the study of protein metabolism and body composition. The Unit collaborates with WHO, with members of the staff of the Department of Medicine of the UWI and with the Government of Jamaica in the study of practical nutritional problems.

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 and the whole body counter.
3. Renal and cardiac function and electrolyte disturbances.
4. Protein turnover, studied with ^{35}S- and ^{15}N-labelled amino acids and with ^{131}I-labelled proteins.
5. Mechanism of fatty infiltration of the liver.
6. Protein requirements of infants.
7. Activity of tissue enzymes in malnutrition.

STUDIES ON ADULTS

Calorie cost of work in relation to food intake.

EXPERIMENTAL WORK

1. Fatty acid synthesis by liver tissue *in vitro*.
2. Adaptive changes in protein turnover in the rat caused by low protein intakes.

INFANTILE MALNUTRITION RESEARCH UNIT

Mulago Hospital, Kampala, Uganda

Honorary Director

Professor R. A. McCance, CBE, MD, D SC, FRCP, FRCOG, FRS*

Officer in Charge

R. G. Whitehead, PH D

Scientific staff

D. R. Hadden, MD
P. S. E. G. Harland, MB (*until Nov. 1965*)
Mrs R. H. Harland, MB (*until Nov. 1965*)
Miss I. H. E. Rutishauser, B SC (NUT)
B. A. Wharton, MB, MRCP, DCH

Other senior staff

G. R. Howells

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. Biochemical abnormalities that may be due to malnutrition.
2. Assessment of marginal malnutrition.
3. Utilization of locally produced foods for the prevention and treatment of nutritional disease.
4. Long-term effects of malnutrition.

SOCIAL PSYCHIATRY RESEARCH UNIT

Institute of Psychiatry, Maudsley Hospital, Denmark Hill, London S.E.5
(Rodney 6333)

Director

J. K. Wing, MD, PH D, DPM

Scientific staff

J. L. T. Birley, MA, BM, MRCP, DPM
G. W. Brown, PH D
J. E. Cooper, BM, MRCP, DPM (*until Jan. 1966*)†
Miss R. D. S. Lang, BA
Mrs M. H. Rayfield, BA
E. P. Razzell, B SOC SC

Attached workers

V. Lotter, BA (*Inner London Educational Authority*)
Professor D. Mechanic, PH D (*University of Madison; US National Institutes of Health Fellow*)
P. Pullen, MA (*University of Houston and Birkbeck College*)
Miss B. Stevens, BA (*Mapother Research Fellow*)
Mrs L. G. Wing, MD, DPM (*MRC External Staff*)

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 and classification of social and clinical abnormalities and to the evaluation of the effects of social methods of treatment.

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* Professor McCance is also Director of the Council's Department of Experimental Medicine (p. 103).

† Joint appointment with the Unit for the Study of Environmental Factors in Mental and Physical Illness (p. 156).

Summary of research

1. (*a*) Standardization of diagnosis and subclassification of mental illness.
   (*b*) Measurement of clinical changes in psychiatric patients.
   (*c*) Standardization of social and psychiatric history-taking.
   (*d*) Development of a questionnaire for use in screening general populations.
2. (*a*) Measurement of social functioning of members of families.
   (*b*) Measurements of impact of psychiatric illness on the family.
3. Cumulative Psychiatric Disease Register based on the population of a London Borough (supported by a grant from the Ministry of Health).
4. (*a*) Factors affecting social and clinical outcome in schizophrenic patients admitted to hospital for the first time.
   (*b*) Clinical and social handicaps of schizophrenic patients in a London Borough, and their need for services.
   (*c*) Expectation of mental illness in close relatives of schizophrenic patients.
   (*d*) Measurement of psychological abnormalities in close relatives of schizophrenic patients.
   (*e*) Fertility of women with schizophrenic and affective disorders.
5. Information needed for planning psychiatric services in a London Borough.
6. Characteristics of patients from a London Borough who are receiving psychotherapy.
7. Birth order, sibship size, parental characteristics and other features of a series of autistic children.
8. Social and psychiatric characteristics of individuals consulting their general practitioner frequently and infrequently.

UNIT FOR RESEARCH ON THE EPIDEMIOLOGY OF PSYCHIATRIC ILLNESS

Edinburgh University Department of Psychiatry,
Royal Edinburgh Hospital,
Morningside Park, Edinburgh 10
(Morningside 7489)

Honorary Director
Professor G. M. Carstairs, MD, FRCPE, DPM

Assistant Director
G. A. Foulds, PH D (*from Sept. 1965*)
W. I. N. Kessel, MD, MRCP, DPM (*until Sept. 1965*)

Scientific staff

Mrs E. L. Cay, MB, DPM
Mrs D. L. Dinwoodie, MB, D OBST RCOG (*part-time; until July 1965*)
Miss E. C. Hassall, DIP SOC SC
A. Scott Henderson, MB, MRCP, DPM
K. Hope, PH D
N. B. Kreitman, MD, DPM
W. McCulloch, M SC
P. R. Mayo, B SC, DCP (*until July 1965*)
A. Munro, MD, MB, MRCPE, DPM (*until June 1965*)
A. E. Philip, MA, DIP CLIN PSYCHOL
Miss M. E. Whiteley, MA

Attached workers
Miss U. M. Maclean, MD, DPH (*MRC Junior Research Fellow*)
Miss S. Wolff, BM, MRCP, DPM, DCH (*Mental Health Research Fund grant-holder*)

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

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. Relationship of role behaviour to neurotic illness in pregnant women.
4. Behaviour disorders in children referred for psychiatric treatment.

5. Standardization, on a mental hospital inpatient population, of Symptom–Sign Inventory, Hysteroid Obsessoid Questionnaire and Hostility Battery.
6. Changes in symptoms, attitudes and traits concomitant with clinical change in cases of depression.
7. Hostility patterns of patients in a maximum security hospital.
8. Relationship between ratio of 'psychological' to 'somatic' symptoms and modes of expression of hostility.
9. Interrelation of varied types of personality disorder.
10. Significance of secondary diagnosis in mental hospital inpatients.
11. Psychiatric disorders in adolescents.
12. Clinical and social factors in alcoholism occurring in early adult life.
13. Measures of attitudes to mental illness in specific population groups.
14. Thought disorders in the schizophrenias.

NEUROPSYCHIATRIC RESEARCH UNIT

Medical Research Council Laboratories, Woodmansterne Road, Carshalton, Surrey
(Melville 4461)

Clinical Investigation Ward, Greenbank, West Park Hospital, Epsom, Surrey
(Epsom 24771)

Director
D. Richter, PH D, MRCP

Scientific staff

R. Balazs, DR MED, DR PHIL
J. B. Brierley, MD, FC PATH
B. W. L. Brooksbank, PH D
A. W. Brown, B SC
A. J. Coppen, MD, DPM (*part-time*)
M. K. Gaitonde, PH D
Mrs B. Herzberg, MB, MRCP
Miss T. L. Julian, MBE, M SC
B. S. Meldrum, MB, PH D
Mrs M. Metcalfe, DIP PSYCOL (*part-time*)
Miss O. M. Ricard, MD, B SC
D. M. Shaw, MB, PH D, MRCP
R. Vrba, DR ING

Other senior staff
G. W. Morris

Attached workers

G. E. Gaull, MD (*Children's Hospital Medical Centre, Boston, Mass.; US National Institutes of Health Fellow*)
Y. Machiyama, MB, D MED SC (*University of Tokyo; British Council Fellow*)
R. E. Martenson, PH D (*Harvard University; US National Institutes of Health Fellow*)
J. G. Nievel, MD (*University of Budapest; Riker Fellow*)
E. H. Reynolds, MB, MRCP (*The National Hospital, London*)
A. Rizzoli, MD (*University of Padua*)

The Unit carries out basic and clinical research on the causes and treatment of mental disorders. A Clinical Investigation Ward has been set up at West Park Hospital, Epsom, for special metabolic investigations not ordinarily available in mental hospitals.

Summary of research

1. Biochemical and biophysical factors related to depressive illness and schizophrenia.
2. Biochemistry of the brain in normal subjects and in mental hospital patients.
3. Metabolic changes associated with maturation and with the functional activity of the brain.
4. Action of drugs and electrical shock treatment on the brain.
5. Anoxic damage to the brain during birth asphyxia and open-heart surgery.
6. Characteristics of evoked electrical responses in the brain.
7. Neurological sequelae of meningoencephalitis.
8. Metabolic factors related to mental subnormality and to epilepsy.

NEUROPHARMACOLOGY RESEARCH UNIT

Department of Experimental Neuropharmacology, The Medical School, Birmingham 15
(Selly Oak 1642)

Honorary Director
Professor P. B. Bradley, D SC

Scientific staff

B. J. Key, PH D (*honorary*)
A. R. King, PH D
Mrs M. Nikolova, DR MED (*until Dec. 1965*)
M. I. Phillips, B SC
M. H. T. Roberts, B SC (*until Oct. 1965*)
J. H. Wolstencroft, PH D

Attached workers

G. L. Avanzino, MD (*University of Genoa*)
S. A. Grillo, M SC (*Nigerian Government Scholar*)
F. N. Johnson, B SC (*MRC Scholar*)

The Unit is studying the actions of drugs on the central nervous system, with particular reference to the correlation between electrophysiological and behavioural effects and to interactions with sensory stimuli. 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 that 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 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
(Chichester 83288)

Director
P. Sainsbury, MD, MRCP, DPM

Scientific staff

B. M. Barraclough, MB, MRACP, DPM
W. R. Costain, MB, DPH, DPM (*until Jan. 1966*)
Miss J. C. Grad, PH D
J. B. Knowles, PH D (*until Sept. 1965*)
N. B. Kreitman, MD, DPM (*until Feb. 1966*)
J. C. Shaw, B SC

Other senior staff

J. D. Haines
Miss B. Nelson
G. C. Ongley

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

Summary of research

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.
4. Clinical characteristics of mania.

EPIDEMIOLOGY

1. Factors determining referral rates of psychiatric patients.
2. Incidence of suicide in an ' open ' hospital and in a community care service.
3. Factors affecting the incidence of suicide in the elderly on retirement.

PSYCHOSOMATIC AND NEUROPHYSIOLOGICAL STUDIES

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

EXPERIMENTAL PSYCHOLOGY

Experimenter characteristics and verbal conditioning effects.

UNIT FOR RESEARCH ON THE CHEMICAL PATHOLOGY OF MENTAL DISORDERS

Department of Physiology, The Medical School,
Birmingham 15
(Selly Oak 1301)

Hollymoor Hospital, Northfield,
Birmingham 31
(Priory 2271)

Physician-in-charge

F. A. Jenner, MB, PH D, DPM (*part-time*)

Scientific staff

A. A. Boulton, PH D
J. C. Goodwin, M SC
E. F. Legg, B SC
R. J. Pollitt, PH D
Mrs J. E. W. A. Trotter, B SC

Other senior staff

N. E. Chard, AIMLT
L. Grant, AIST MRSH

Attached workers

Miss M. E. Burns, MB, MRCPE, DTM & H (*Hollymoor Hospital*)
D. Wynne Davies, MB, MRCP (*Birmingham Regional Hospital Board*)
S. M. Hanna, MB, DM, DTCD, LMSSA (*Hollymoor Hospital*)
L. Honigsberger, MB, DPM (*Birmingham Regional Hospital Board*)
T. Nilsson, FIL LIC (*University of Lund; Wellcome Trust Fellow*)
Miss S. Slater, B SC (*Mental Health Research Fund*)

The aims of this Unit are to investigate possible biochemical, humoral and electrophysiological abnormalities in patients with mental disorders, and aspects of physiology, biochemistry and animal behaviour which may bear on these problems.

Summary of research

CLINICAL STUDIES

1. Factors producing water retention in periodic psychosis, and the relationship between these changes and changes in mental state.

2. Nitrogen and electrolyte metabolism in changing mental states and the psychological and metabolic consequences of influencing these with thyroxine and steroids.
3. Steroid and amino acid metabolism in mental illnesses.
4. Correlation of EEG changes with changes in mental state.
5. Diagnostic implications of the presence of the ' pink spot ' and dimethoxyphenylethylamine in the urine of schizophrenic patients and its relationship to drug treatment.

BIOCHEMICAL STUDIES

1. Development of apparatus for automatic scanning and digitizing of paper chromatograms.
2. Improved methods for estimating amino acids and amines.
3. Behaviour of the ' pink spot ' and dimethoxyphenylethylamine in various electrophoretic and chromatographic systems.
4. Attempts to simplify methods of estimating individual steroids clinically.

ANIMAL STUDIES

1. Methods for the bioassay of antidiuretic substances.
2. Development of cages and recording apparatus for timing and collecting specimens in combined studies of rhythms in rat behaviour and metabolism.

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

London School of Economics, Houghton Street, Aldwych, London W.C.2
(Holborn 7686)

Director
J. W. B. Douglas, BM, B SC

Scientific staff
J. E. Cooper, BM, MRCP, DPM (*part-time*)*
Miss M. L. Gilchrist, OBE, MD, DPH (*part-time*)
Mrs A. LeVay Lawson, PH D
Miss J. M. Ross, B SC
R. K. Turner, BA

Attached workers
Mrs M. C. Ferreira, BA (*Catholic University of São Paulo, Brazil*)
Miss P. S. Green, B SC (ECON) (*Science Research Council grant-holder*)
Miss K. Kelly, AB (*University of California*)
D. M. Nelson, MA (*Science Research Council grant-holder*)
B. Pless, MD (*University of Western Ontario*)
Mrs M. Scotford-Morton, BA (*London School of Economics*)

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

Summary of research

1. National Survey of Health and Development—a longitudinal study of 5000 children born in March 1946. The following studies are now in progress:
   (*a*) Environmental factors in secondary education (with Rothamsted Experimental Station).
   (*b*) Delinquency and maladjustment (supported by grant from the Home Office).
   (*c*) 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. Development of observational techniques for assessing the social development of children.
5. Vocational training and technical education (supported by grant from the Science Research Council).

* Joint appointment with the Social Psychiatry Research Unit (p. 151).

NEUROENDOCRINOLOGY RESEARCH UNIT

University Department of Human Anatomy, South Parks Road, Oxford
(Oxford 58686)

Honorary Director
Professor G. W. Harris, CBE, DM, SC D, FRS

Scientific staff

J. Chamberlain, PH D
H. M. Charlton, D PHIL
D. Exley, D PHIL
D. J. El Kabir, MB
Miss M. Reed, PH D
A. W. Rogers, MB, PH D

Attached workers

K. Brown-Grant, MD (*Royal Society Locke Research Fellow*)
A. W. Burrows, BA (*MRC Scholar*)
G. Fink, MB (*Monash University, Victoria; Nuffield Dominions Demonstrator*)
B. F. Good, PH D (*University of Adelaide; Fellow of the National Health and Medical Research Council of Australia*)
J. A. Grayburn, BA (*MRC Scholar*)
Miss M. Lindburgh, PH D (*Stanford University*)
R. D. Nadler, PH D (*University of California*)
D. F. Salaman, BA (*MRC Scholar*)
W. N. Adams Smith, MB, MA (*New Zealand; Beit Memorial Research Fellow*)

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. Study of cyclic endocrine activity in normal males and females.
3. Chemical mediators by which the hypothalamus regulates the activities of the anterior pituitary gland.
4. Mode of action of the progestational compounds (including contraceptive steroids) on metabolism and on ovarian function.
5. Mechanism of ovulation at the ovarian level.
6. Estimation of thyrotrophic hormone in blood in man and in the experimental animal.
7. The properties of the long-acting thyroid stimulator.
8. Thyroid–ovarian interrelationships.
9. Neuroendocrine factors in induced ovulation in the immature rat.
10. Endocrine activity in psychiatric patients during different phases of mental illness.
11. Studies on steroid hormones:
    (*a*) Development of methods for the estimation of steroid hormones in body fluids.
    (*b*) Gas chromatographic analysis of steroids derived from biological material.
12. The possible role of the pineal gland and its hormone melatonin on pituitary–gonadal interrelationships including histological and electron microscope studies of the pineal gland in different vertebrates.
13. Techniques of autoradiography, with particular reference to absolute measurements of radioactivity in sources of microscopical dimensions.

APPLIED PSYCHOLOGY RESEARCH UNIT

15 Chaucer Road, Cambridge
(Cambridge 55294)

Director
D. E. Broadbent, SC D

Assistant Directors

R. Conrad, PH D
E. C. Poulton, MB

(93778) F4

Scientific staff

Mrs P. M. E. Altham, BA
A. D. Baddeley, PH D
M. J. F. Blake, B SC (*until Oct. 1965*)
I. D. Brown, B SC
A. Carpenter, MB
W. P. Colquhoun, PH D
D. W. J. Corcoran, PH D
H. C. A. Dale, PH D
P. R. Freeman, MA (*until Sept. 1965*)
M. Hammerton, PH D
J. D. Ingleby, BA
J. Morton, PH D
P. M. A. Rabbitt, PH D
L. H. Shaffer, PH D (*until Sept. 1965*)
R.T. Wilkinson, PH D
Miss M. M. Woodhead

Other senior staff

A. Davidson
Mrs M. H. P. Gregory, MB

Attached workers

Miss N. S. Anderson, PH D (*University of Maryland; National Science Foundation Fellow*)
M. Brandon, BA (*Science Research Council/ NATO grant-holder*)
G. R. J. Hockey, B SC (*MRC Scholar*)
T. B. Roby, PH D (*Tufts University, Massachusetts*)
Professor R. O. Rouse, PH D (*Williams College, Massachusetts*)

The purpose of the Unit is to observe and measure human behaviour with the aim of establishing the general principles governing 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*) Effect of context on sensory judgments.
   (*d*) Factors affecting the intelligibility of speech.
2. Thinking:
   (*a*) Information theory.
   (*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*) Teaching of skills.
   (*c*) Factors affecting verbal learning.
6. Personality:
   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

14 Welbeck Street, London W.1
(Welbeck 1144)

Honorary Director
C. B. Frisby, PH D *(from Oct. 1965)*
Professor G. C. Drew, MA *(until Oct. 1965)*

Honorary Deputy Director
J. W. Whitfield, MA *(until Nov. 1965)*

Scientific staff

L. J. Buck, B SC
Mrs G. C. de la Mare, MA *(part-time)*
Mrs N. Harris, B SC
Miss H. A. Long, B SC
Miss D. Monnington, B SC
R. Sergean, MA
J. Walker, PH D
Mrs A. Zajaczkowska, PH D *(until Oct. 1965)*

The aim of the Unit is to obtain better knowledge of the relation between conditions of employment, including methods of work, and the satisfaction and effectiveness of people in all kinds and levels of occupation.

Summary of research

1. Investigation of industrial motivation and behaviour, with particular emphasis on field studies of individual and social factors affecting behaviour:
   (*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 errors of performance and accidents:
   (*a*) Individual differences.
   (*b*) Retrospective and prospective identification of causative factors by the study of data on both accidents and normal performance.
   (*c*) Relation between accidents and the sensory information available, with particular reference 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.
4. Analysis of skills.
5. Perception studies: geometry of visual space.

UNIT FOR THE EXPERIMENTAL INVESTIGATION OF BEHAVIOUR

Department of Psychology, University College London, Gower Street, W.C.1
(Euston 7050)

Honorary Director
Professor G. C. Drew, MA

Assistant Director
I. S. Russell, PH D*

Scientific staff

Mrs C. M. Coulouris, B SC *(part-time; until Aug. 1965)*
N. Mrosovsky, PH D†
H. Plotkin, B SC
G. A. Tolliver, MA

* On leave of absence at Indiana University Medical Center from October to December 1965
† On leave of absence at the University of Pennsylvania until February 1966.

Attached workers

D. Kleinman, B SC (*Science Research Council Student*)
R. T. Rentoul, BA (*MRC Scholar*)
D. A. Oakley, B SC (*Science Research Council Student*)

The Unit is undertaking experimental studies of the neurological correlates of behaviour in animals. These studies are concerned with analysing mechanisms of learning, conditioning and motivation.

Summary of research

1. Use of stimulation, ablation and stereotactic lesions in the cerebral cortex, limbic system and hypothalamus 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

(Royal 5351)

Honorary Director

Professor L. S. Hearnshaw, MA

Honorary Medical Adviser

Professor A. B. Semple, CBE, VRD, MD, DPH, QHP

Honorary Scientific Advisers

D. B. Bromley, PH D
M. G. Davies, PH D

Scientific staff

Mrs S. M. Chown, PH D (*honorarium*)
R. C. Cooper, PH D
F. I. M. Craik, PH D (*until Sept. 1965*)
Mrs A. D. M. Davies, PH D
Mrs G. R. Hearnshaw, PH D (*part-time*)
G. H. Jamieson, M ED
Mrs A. C. Owens, MBE, PH D (*part-time*)
R. L. Payne, BA (*until Sept. 1965*)
G. S. Tune, PH D

Other senior staff

A. Hackwood

Attached worker

H. H. Whincup, MB (*British Railways Area Medical Officer*)

The Unit is studying psychological changes that accompany ageing, with particular reference to changes considered likely to be of occupational importance. Both laboratory and field investigations are carried out.

Summary of research

1. Vigilance behaviour and temporal expectancy, with special reference to ageing.
2. Adult learning and the problems of retraining and rehabilitation of older persons.

MEDICAL SOCIOLOGY RESEARCH UNIT*

Foresterhill, Aberdeen
(Aberdeen 23423)

Honorary Director
Professor Raymond Illsley, PH D

Scientific staff

W. R. Bytheway, B SC
G. Horobin, B SC (ECON)
D. J. Oldman, MA

Other senior staff

Miss J. Aitken-Swan, AIMSW, AHA
Miss E. B. D. Thompson, PH D, AIMSW

Attached workers

Professor E. Milner, PH D (*Brooklyn College, New York*)
P. Nylander, MB, MRCP, MRCOG (*University of Ibadan*)
Professor W. R. Rosengren, PH D (*Western Reserve University, Ohio; Fulbright Scholar*)

The Unit collaborates with the University Departments of Midwifery, Child Health and Sociology in Aberdeen in studying the effect of social factors on reproduction and child development. Within this broad field the Unit's work is primarily focussed on four problems: (*a*) the social origin of complications of pregnancy and abortions and perinatal death; (*b*) the effect on children's physical and mental development of pregnancy complications and of their condition at birth; (*c*) the identification and diagnosis of handicap in children; (*d*) the sociological study of the family, community and other social factors influencing the course of pregnancy and the development of children.

Summary of research

1. Social and obstetric factors in the history of physically and mentally handicapped children.
2. Social antecedents and development consequences of low birth weight.
3. Pregnancy complications and their sequelae.
4. Social and educational influences on intellectual development in children.
5. Transmission of cultural values.
6. Social influences on health and mortality of children in an African village (with the Medical Research Council Laboratories in the Gambia).
7. Social factors in the aetiology of cervical cancer.

SOCIAL MEDICINE RESEARCH UNIT

The London Hospital Research Laboratories, Ashfield Street,
London E.1
(Stepney Green 5257)

Director
Professor J. N. Morris, D SC, FRCP, DPH

Assistant Director
J. A. Heady, PH D

Scientific staff

M. R. Alderson, MD, DCH, DPH
J. S. A. Ashley, MB
Mrs M. D. Crawford, MD (*part-time*)
M. J. Gardner, B SC, DIP MATH STAT
J. A. H. Lee, MD, B SC, DPH
T. W. Meade, BM, MRCP
D. C. Pattison, MB, D OBST RCPG, DPH
C. M. Phillipson, MA (*until Jan. 1966*)
M. J. Power, DIP SS
Miss E. Shoenberg, MA, MRCS, DPM (*part-time*)
Mrs M. S. Smith, MB (*part-time*)
S. Yasin, MA

* This Unit was set up in October 1965 to continue and expand the sociological part of the programme of the Obstetric Medicine Research Unit, which was disbanded on the retirement of the Honorary Director, Professor Sir Dugald Baird.

Other senior staff

Miss A. Howlett, SRN

Miss J. W. Marr, SRD

Attached workers

T. H. D. Arie, BM, DPM (*London Hospital Medical College*)

M. L. Bierenbaum, MD, FACP (*New Jersey, USA; Milbank Memorial Fund Fellow*)

C. J. Burns-Cox, MB, MRCP (*Central Middlesex Hospital*)

J. Cassel, MB, MPH (*University of North Carolina*)

Miss P. M. Fulton, MB, MRCPE, DPH (*Central Middlesex Hospital*)

G. J. L. Hall, MB (*West Middlesex Hospital*)

Miss P. Olgun, DIP MATH (*School of Public Health, Ankara; WHO Fellow*)

Miss P. Weiskopf, B SC (*The Hebrew University, Jerusalem*)

The Unit investigates the influence of social factors upon health and sickness, and the relationship of social to other factors. Studies are made of populations and their environments, and individuals are studied in relation to these.

Summary of research

CARDIOVASCULAR STUDIES

1. Ischaemic heart disease in relation to nature of work and to other factors, including physique and obesity, diet, blood pressure, blood lipids and family history.
2. Factors affecting obesity, blood pressure and blood lipids in men.
3. Prognosis of ischaemic heart disease in relation to diet (therapeutic trial with several hospitals).
4. Relationship of cardiovascular disease to the hardness of the water and other local factors in British towns.
5. Trial of reduction of blood lipid levels in healthy men (with Department of Cardiology, University of Edinburgh).
6. Epidemiology of ruptured cerebral aneurysm and subarachnoid haemorrhage (with St. George's Hospital, London).

SOCIAL STUDIES

1. Patterns of leisure in middle-aged men.
2. Juvenile delinquency in East London.

CURRENT TRENDS IN MORBIDITY AND MORTALITY

1. Incidence of ischaemic heart disease and peptic ulcer in physicians and others.
2. ' Sickness-absence ' and disability rates.
3. Mortality and major morbidity in young people.
4. Death rates in British towns in relation to social features.

THE WORKING OF HEALTH SERVICES

1. Background of patients with hyperplasia of prostate admitted to several hospitals in the North-East Metropolitan Region, their condition on admission, the care received, and postoperative morbidity and mortality.
2. Prescribing in general practice and its relationship to other aspects of the National Health Service (with the Department of Pharmacology, London Hospital Medical College).

MISCELLANEOUS STUDIES

1. Morbidity and mortality in leukaemia and other malignant disease in relation to season of year.
2. Community picture of Addison's disease.
3. Methods:
   (*a*) Assessment of individual physical activity apart from work.
   (*b*) Short-cut methods for assessment of individual diets.
   (*c*) Development of food tables for diet surveys.

PSYCHOLINGUISTICS RESEARCH UNIT*

Institute of Experimental Psychology, 1 South Parks Road, Oxford
(Oxford 57651)

Honorary Director
Professor R. C. Oldfield, MA

Scientific staff

J. H. Clark, MA, MB, DPM
M. B. Clowes, PH D (*until Dec. 1965*)
Mrs G. M. Geffen, BA
D. Gerver, BA
J. C. Marshall, BA
Mrs A. M. Treisman, D PHIL
Mrs M. Williams, D PHIL (*part-time; until Dec. 1965*)
A. Wingfield, MA

Other senior staff
Mrs J. W. Clarke

Attached workers

P. Twitchell Smith, BA (*MRC Scholar*)
M. Treisman, MB, D PHIL (*University of Oxford*)

The aim of the Unit is the investigation of psychophysiological processes underlying language and other forms of communication in both normal and pathological conditions.

Summary of research

1. Mechanisms of selective attention and message segregation.
2. Statistical features of speech and language:
   (*a*) Properties of stochastically generated samples.
   (*b*) Changes in statistical features of speech in the presence of noise.
   (*c*) Statistical aspects of dysphasic speech.
3. Psychological processes connected with grammatical, syntactical and semantic aspects of normal and disordered speech.
4. Object-naming processes in normal and brain-injured individuals.
5. Factors affecting control of amount, speed, loudness and articulation of speech.
6. Visual perception of characters and reading:
   (*a*) Computer simulation of perceptual processes.
   (*b*) Automatic character recognition and picture discrimination.
   (*c*) Communication between man and computer.
   (*d*) Grammatical aspects of dyslexia.
7. Development of language in the infant.
8. Linguistic routines in hypnotic induction.

STATISTICAL RESEARCH UNIT

University College Hospital Medical School,
115 Gower Street, London W.C.1
(Euston 7651)

Director
W. R. S. Doll, OBE, MD, D SC, FRCP, FRS

Scientific staff

J. T. Boyd, MB, DPH
Mrs P. A. Gregory, MRCS
I. D. Hill, B SC
M. J. S. Langman, MD, MRCP
M. C. Pike, PH D
Miss N. J. Seyd, B SC
I. Sutherland, D PHIL

* In October 1966 the Unit will be transferred to the University of Edinburgh and its title changed to Speech and Communication Research Unit. Professor Oldfield will then become full-time Director of the Unit.

Attached workers

A. Nagy, MD (*Institute of Oncology, Budapest; WHO Fellow*)

N. G. Usunov, MD (*Oncological Scientific Institute, Sofia; WHO Fellow*)

R. Saracci, MD (*University of Pisa; Euratom Commission award-holder*)

The Unit is concerned with the development and application of statistical methods in medicine and in the associated sciences, including research into the epidemiology and aetiology of disease, the promotion and analysis of vital statistics, the design and analysis of therapeutic trials of new drugs and other agents, the design and analysis of field trials of prophylactic agents and the application of mathematical-statistical techniques to the solution of laboratory and epidemiological problems. The investigations listed in the summary of research include not only the individual researches of members of the Unit's staff but also the main items of collaborative work undertaken 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. Epidemiological features of mortality from leukaemia and from cancer of bone, stomach, large bowel and cervix uteri.
3. Intestinal phosphatase in gastric cancer and pernicious anaemia.
4. Incidence of cancer in tropical countries.
5. Comparisons between human and experimental data on carcinogenesis.
6. Epidemiological data in relation to cancer mechanisms.
7. Long-term effects of therapeutic irradiation.
8. Effects of small amounts of absorbed radium.
9. Effects of smoking on mortality.
10. Aetiology of chronic bronchitis.
11. Mortality of gasworkers.
12. Sugar consumption and myocardial infarction.
13. Blood group substances and their secretion in gastro-duodenal diseases.
14. Perinatal mortality in high-risk obstetric groups.
15. Cyanide metabolism in subacute combined degeneration of the spinal cord.
16. World-wide survey of measles.

THERAPEUTIC AND PROPHYLACTIC TRIALS

1. BCG and vole bacillus vaccine in the prevention of tuberculosis in adolescents.
2. Drugs in respiratory tuberculosis in the United Kingdom and abroad.
3. BCG vaccine in the prevention of leprosy.
4. Treatment of leprosy.
5. Treatment of leukaemia.
6. Radiotherapy under high-pressure oxygen.
7. Treatment of gastric and duodenal ulcer.
8. Vaccines for the prevention of trachoma.
9. Manipulation for acute back pain.
10. Hormones for osteoporosis.
11. Treatment of hypertension.
12. Treatment of renal infections.
13. Treatment of tetanus.

MATHEMATICAL STATISTICS AND COMPUTER SCIENCE

1. Fitting mathematical models to observations on cancer incidence.
2. Application of bioassay techniques to radiobiology.
3. Computer-aided diagnosis of hypercalcaemia.
4. Computer program for describing mathematical functions in terms of polynomials.

1. Use of enzyme tests in screening for pre-invasive carcinoma of the cervix uteri.
2. Carcinogenicity of mineral oils.
3. Reactions to Kveim antigen in healthy subjects.
4. Natural history of clinical tuberculosis in adolescents.
5. Screening for phenylketonuria.
6. Prognostic value of clinical features in infantile malnutrition.
7. Genetic linkage of serological and red cell traits and their association with marker chromosomes.

INDUSTRIAL INJURIES AND BURNS RESEARCH UNIT

Birmingham Accident Hospital, Bath Row, Birmingham 15
(Midland 7041)

Director
J. P. Bull, MD, MRCP

Scientific staff

G. A. J. Ayliffe, MD, FC PATH
Miss S. Baar, FRIC
Mrs G. M. Buck, B SC
Mrs S. A. Carney, PH D (*part-time*)
J. W. L. Davies, PH D
Miss S. P. Farrow, B SC
D. MacG. Jackson, MD, FRCS (*part-time*)
R. J. Jones, PH D
J. C. Lawrence, PH D
E. J. L. Lowbury, DM, FC PATH
Miss F. A. Pettit, B SC
C. R. Ricketts, D SC

Other senior staff

M. Hall, AIMLT
H. A. Lilly, FIMLT

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. Special studies of hospital infection (12—19 below) are made at the Hospital Infection Research Laboratory, Summerfield Hospital, Birmingham.

Summary of research

1. Types, causes and prevention of common injuries; special study of burns caused by clothes catching fire and of burns involving bones and joints.
2. Laboratory studies and clinical trials of colloid replacement fluids, including various dextran and plasma protein solutions.
3. Role of oral and intravenous saline solution in the treatment of burns; sodium requirements and half-life of ^{22}Na in patients with burns.
4. Plasma protein changes and fibrinolysis in burns; metabolism of labelled fibrinogen in burns and other injuries.
5. 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.
6. Skin metabolism in relation to healing of wounds and grafts:
   (*a*) Effects of thermal damage on collagen formation.
   (*b*) Collagen formation in ' transparent ' skin of rheumatoid patients (with Drs K. Walton and B. McConkey, University of Birmingham).
   (*c*) Effects of laser light and radar microwaves on the biochemistry of the skin.
7. 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 burns.
8. Experimental infection of burns in mice; assessment of antisera and antibiotics in preventing deaths from infection.
9. Development of methods for identification of bacterial flora in wounds.
10. 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.

11. Controlled trials of local chemotherapy and chemoprophylaxis for burns and open wounds; tests of silver nitrate solution for local therapy and of its fate in the body.
12. Incidence of infection in hospitals and the association of infection rate with environmental factors; development of methods of study.
13. Alternative methods of air conditioning and of ultraviolet ' screens ' to prevent infection of patients in isolation rooms by the bacterial flora of the hospital.
14. Survival of pathogens outside the body.
15. Comparative trials of alternative methods for floor cleaning and disinfection; study on role of floor bacteria in the transfer of infection.
16. Epidemiology of infection in neurosurgery and eye surgery.
17. Ecology of antibiotic-resistant staphylococci in hospital; the possible role of transduction in the emergence of resistant strains.
18. Ecology of *Pseudomonas aeruginosa*, investigated with the aid of phage typing (with the Central Public Health Laboratory, Colindale).
19. Nasal carriage of *Staph. aureus*; investigation of alternatives to neomycin for removal of *Staph. aureus* from the nose; study on the mechanisms that determine ability to carry or resist colonization by *Staph. aureus*.

TOXICOLOGY RESEARCH UNIT

Medical Research Council Laboratories, Woodmansterne Road, Carshalton, Surrey

(Melville 4461)

Director

J. M. Barnes, CBE, MB

Scientific staff

W. N. Aldridge, PH D
W. H. Butler, MB
Miss V. M. Craddock, PH D
Miss J. E. Cremer, PH D
F. De Matteis, PH D, LAUREA MED CHIR
Miss P. M. Fullerton DM, MRCP (*part-time*)
D. F. Heath, D PHIL
M. K. Johnson, PH D, ARCS, ARIC
R. A. Little, B SC
A. E. M. McLean, BM, PH D
P. N. Magee, MB, MC PATH
L. Magos, DR MED
A. R. Mattocks, PH D, ARIC
Miss M. J. Ord, PH D*
V. H. Parker, B SC
M. S. Rose, B SC
Miss R. Schoental, D SC
H. B. Stoner, MD, B SC
P. F. Swann, M SC
C. J. Threlfall, B SC
S. Villa-Trevino, DR MED, PH D

Other senior staff

R. C. Emery
A. R. Henderson
J. A. E. Jarvis
Mrs J. I. Jenkins, B SC
C. R. Kennedy, AIMLT
B. W. Street, AIMLT
K. D. Wilford

Attached workers

M. E. Fowler, BS, DVM (*University of California; US National Institutes of Health Fellow*)
D. D. Leaver, BV SC, M SC (*University of Melbourne*)
Miss E. Reiner, PH D (*Institute of Medical Research, Zagreb; WHO Fellow*)
A. A. Seawright, PH D, BV SC, MRCVS (*University of Queensland*)
R. C. Shank, PH D (*Massachusetts Institute of Technology; US National Institutes of Health Fellow*)
H. P. Witschi, MD (*Institute of Forensic Medicine, Berne*)

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.

* Working in the University of Southampton.

1. Chemical, biochemical and physical properties of substances that uncouple oxidative phosphorylation.
2. Biochemical properties of trialkyltin and lead compounds, including studies of the distribution and binding to biological material using triethyltin (^{113}Sn).
3. Influence of organotin and organolead compounds on the oxidation of glucose and pyruvate by slices of rat brain, liver and kidney and rat brain *in vivo*.
4. Influence of triethyltin on the incorporation of ^{32}P into phospholipids of rat brain.
5. Inhibition of esterases by carbamates and the process of spontaneous reactivation of carbamylated and phosphorylated esterases.
6. Chronic neurotoxic effects of organophosphorus compounds and the sensitivity of the esterases of the central nervous system of the fowl to these compounds.
7. Electrophysiological and histological studies of peripheral neuropathies produced by lead and acrylamide and by local pressure.
8. The inhibition of enzymes by beryllium and the mechanism of liver necrosis produced by beryllium salts.
9. Effect of diet and DDT on liver injury produced by poisons.
10. Effect of griseofulvin and some of its analogues on cholesterol and porphyrin metabolism in the liver.
11. Glutathione and *S*-alkyl transferase and the reaction of methyl iodide with glutathione.
12. Alkylation of glutathione *in vivo* after giving chloroethanol.
13. Toxicity of pyrrolizidine alkaloids from *Amsinkia intermedia* and other plants toxic to livestock.
14. Toxicity of chemical modifications of pyrrolizidine alkaloids.
15. Development of a sensitive colorimetric method for the detection and estimation of hepatotoxic pyrrolizidine alkaloids.
16. Studies of certain Ethiopian and Rhodesian plants for hepatotoxicity.
17. Pathology of acute and chronic tissue injury and carcinogenesis induced by dialkylnitrosamines and nitrosamides.
18. Chronic toxicity and possible carcinogenicity of dimethylsulphate.
19. Alkylation of cellular components by nitroso compounds and alkylating agents; investigation of other possible intracellular reactions of nitrosamines.
20. Quantitative determination of degree of alkylation *in vivo* of nucleic acids of different organs by nitroso compounds and other alkylating agents, including dimethylsulphate, methyl methane sulphonate and methyl iodide.
21. Excretion of alkylated purines in the urine of animals treated with nitrosamines and other hepatotoxins and carcinogens.
22. Mechanism of action of cycasin (methylazoxymethanol glucoside), a naturally occurring hepatotoxin resembling dimethylnitrosamine.
23. Comparison of inhibition of hepatic protein synthesis by dialkylnitrosamines, cycasin and aflatoxin, using known inhibitors including ethionine, actinomycin D and puromycin.
24. Mechanism of liver injury by hydrazine.
25. Interaction of *N*-alkyl-*N*-nitrosourethanes and *N*-alkyl-*N*-nitroso-*N*-nitroguanidine (potent carcinogens) with thiol and other cell constituents *in vitro*.
26. Fate of ^{14}C-methyl from *N*-methyl-*N*-nitrosourethane and *N*-methylurethane *in vivo*.
27. Mechanism of toxic injury to renal tubules by dichlorovinylcysteine.
28. Effect of metabolic inhibitors on mercury uptake and liberation by the kidney.
29. Quantitative studies on $Hg \rightarrow {}^{203}Hg$ exchange reaction and its application to the determination of atmospheric and urinary Hg.
30. Quantitative studies on the reactions of glycolysis, gluconeogenesis and the tricarboxylic acid cycle *in vivo* after physical injury (using tourniquet shock as the standard physical injury).
31. Theoretical treatment of linked pathways for carbohydrate metabolism *in vivo*.
32. Fat metabolism after physical injury.
33. Changes in the adenine nucleotides and the RNA and DNA fractions of the liver after physical injury.
34. Influence of cold-acclimation and environmental changes on the effects of physical injury.
35. Effect of catecholamines and adrenergic blockade drugs on the temperature changes after physical injury.
36. Sites of metabolic heat production in the rat.

37. Radiotelemetry observations on the body temperature of patients with multiple injuries (at Luton and Dunstable Hospital and St. Peter's Hospital, Chertsey).
38. Role of bacterial products from gut flora in the response to physical injury.
39. Pathogenic effects of *Clostridium welchii* (with Dr J. J. Bullen, Rowett Research Institute).

ENVIRONMENTAL PHYSIOLOGY RESEARCH UNIT

London School of Hygiene and Tropical Medicine,
Keppel Street, London W.C.1
(Museum 6084)

Director
Professor J. S. Weiner, PH D, MRCS

Scientific staff

C. R. Bell, BA
K. J. Collins, D PHIL
G. W. Crockford, B SC
C. T. M. Davies, B SC
J. D. Few, M SC
K. G. Foster, B SC
Miss J. L. Hubbard, B SC
Mrs A. N. Watts, B SC

The investigations of the Unit are concerned with anatomical, physiological and ergonomic problems arising in the working environment.

Summary of research

1. Limits of tolerance for work at high temperatures and humidity, with reference to different patterns of work and posture, and in relation to age and physique.
2. Physiology of muscular work, including athletic performance.
3. Survey of fitness as measured by work capacity in various groups, e.g. schoolchildren, industrial workers, sportsmen.
4. Relationship of raised body temperature to performance in high-temperature environmental conditions.
5. Intense radiant heat in relation to the development of protective clothing.
6. Biochemistry and histochemistry of sweat gland activity in man and animals.
7. Growth and heat tolerance of animals at high temperatures, with particular reference to genetic factors.
8. Role of endocrine glands in heat adaptation.
9. Fluid and electrolyte balance during heat exposure in man.
10. Neurological basis of temperature regulation.

PNEUMOCONIOSIS RESEARCH UNIT

Llandough Hospital, Penarth, Glamorgan
(Penarth 58761)

Director
J. C. Gilson, OBE, MB, FRCP

Scientific staff

D. P. G. Bolton, BM (*part-time; until June 1965*)
B. W. B. Chan, MB, MRCP
W. G. Clarke, MSR
Miss H. A. C. Cockburn, MB
G. W. Cook, MA (*until Sept. 1965*)
J. E. Cotes, BM, MRCP
G. Lakshmipathi, MD (*until July 1965*)
Mrs M. McDermott, B SC
C. B. McKerrow, MD, MRCP
T. G. Morris, PH D
P. D. Oldham, MA
N. Pearl, MD (*until July 1965*)
R. R. Peset, DR MED
C. E. Rossiter, MA
G. O. Thomas, MB (*part-time*)
V. Timbrell, PH D
J. C. Wagner, MD

Other senior staff

N. E. Bevan, B SC
Miss M. M. Collins
G. F. Cory (*Administrative Officer*)
F. Meade
J. A. Reynolds, AMIRE
R. E. Silverton, FIMLT
J. W. Skidmore

Attached workers

G. Ostiguy, MD (*McLaughlin Foundation Fellowship*)
Bengt-Eric Skoogh, BM (*Renstromska Hospital, Gothenburg, Sweden*)

The Unit is investigating alterations in the structure and function of the lungs resulting from exposure to specific industrial dusts and general air pollution. The studies concerned with asbestos are carried out in collaboration with several university departments, technical colleges and local and other authorities and include international comparative studies.

Summary of research

EPIDEMIOLOGY

1. Prospective survey of byssinosis in the cotton industry.
2. Prevalence of chronic respiratory disease in women (with Lower Swansea Valley Project).
3. Surveys of beryllium and foundry workers and coal- and ex-coal-workers.
4. Relation between the type of asbestos dust exposure and lung function and lung and other tumours.

CARDIOPULMONARY FUNCTION

1. Theoretical basis and practical applications of measurements of the gas transfer factor (diffusing capacity) of the lung.
2. Development of methods of measuring lung compliance in large groups of subjects.
3. Normal values of lung functions and the effect on these of seasonal and other factors.

CLINICAL AND EXPERIMENTAL PATHOLOGY

1. Immunology of complicated pneumoconiosis of coal-workers and its relation to rheumatoid arthritis (with Dr J. N. McCormick).
2. Standardization of the morphological assessment of chronic non-specific lung disease.
3. Relation between content and composition of the dust in the lungs and lung pathology and X-ray appearances.
4. Quantitative studies of the deposition and retention of fibrous and other dusts in animals.
5. Carcinogenic action of dusts administered by intrapleural injection and inhalation in animals.

PHYSICS AND CHEMISTRY

1. Inhalability of fibrous dusts and the relation of falling speed of respirable particles to shape, size and other factors.
2. Development of dust sampling instruments giving direct measurements of respirable mass and number of particles.
3. Development of physical gas analysers for oxygen, carbon monoxide and other gases.
4. Use of gas chromatography in studies of respiratory function.

RADIOLOGY

Classification of radiographs of workers who have been exposed to asbestos.

TREATMENT

Theory of clinical trials and its application to chemotherapy in early chronic bronchitis, complicated pneumoconiosis of coal-workers with and without tuberculosis, and other diseases.

EPIDEMIOLOGICAL RESEARCH UNIT (SOUTH WALES)

4 Richmond Road, Cardiff
(Cardiff 20376)

Honorary Director
Professor A. L. Cochrane, MBE, FRCP, DPH

Honorary Assistant Director
W. E. Miall, MD*

Scientific staff

H. Campbell, MB, FSS (*part-time*)
P. C. Elwood, MD, DPH
P. A. Graham, FRCS (*honorarium*)
F. C. Hollows, MB, FRCS, DO (*until June 1965*)
T. Khosla, M SC (*part-time*)
Miss J. B. Landsman, MB, MRCP
R. McGuinness, MB (*until Mar. 1966*)
J. W. Palmer, BA, DPSA (*until Sept. 1965*)
W. E. Waters, MB, BS, DIH

Other senior staff
G. F. Cory (*part-time*)†

The Unit is developing epidemiological techniques for the study of the prevalence, attack rates and progression rates of common diseases with the ultimate objective of obtaining clues to aetiology and prevention. 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 coal-workers' pneumoconiosis, in particular the more serious form, progressive massive fibrosis.
2. Social factors associated with juvenile delinquency in the Rhondda.
3. Controlled trials of the reformative effects of punishments in schools.
4. (*a*) Studies of the epidemiology and prevention of iron deficiency in the community (with the Medical Unit and Department of Pathology of the Welsh National School of Medicine and Cardiff City Public Health Department).
   (*b*) Studies of the symptomatology of iron deficiency (with the Social Psychiatry Research Unit).
5. Factors influencing the prevalence and incidence of glaucoma in communities.
6. Factors influencing the prevalence of lens opacities.
7. Development of techniques for keeping a census up to date in a local authority area.
8. Sampling techniques for drawing a random sample of the population for a national survey of anaemia.
9. Epidemiology of dental disorders (with Professor J. Miller, Department of Dentistry, Welsh National School of Medicine).
10. Epidemiology of carcinoma of the cervix in Cardiff (part of a large collaborative study).

EPIDEMIOLOGICAL RESEARCH UNIT (JAMAICA)

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

Director
W. E. Miall, MD‡

Scientific staff

M. T. Ashcroft, DM, DPH, DTM & H
M. Clarke, MB (*from Jan. 1966*)§
H. G. Lovell, BA
H. I. McKenzie, B SC (*until Feb. 1966*)
P. Nash, MB (*until Dec. 1965*)§
K. A. Smith, MB, MPH§
K. L. Standard, MD, MPH (*honorary; part-time*)

* Also Director of the Epidemiological Research Unit (Jamaica) (See below).
† Based at the Pneumoconiosis Research Unit, Llandough Hospital (p. 168).
‡ Also Honorary Assistant Director of the Epidemiological Research Unit (South Wales).
§ Seconded from the Ministry of Health, Jamaica.

Other senior staff
R. Grant (*part-time*)

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

Summary of research

CARDIOVASCULAR RESEARCH

1. Longitudinal study of the influence of environmental and genetic factors on arterial pressure, and of the relationship between arterial pressure levels and prognosis in Jamaica and South Wales.
2. Role of bacteriuria in the aetiology of hypertension in Jamaica and South Wales (with Dr E. H. Kass, Harvard Medical School, and Dr K. L. Stuart, University of the West Indies).
3. Clinical, electrocardiographic and radiological studies of heart disease in middle-aged Jamaican adults in rural and urban populations.
4. Radiological comparisons of the size of heart and aorta in random samples of Jamaican and Welsh agricultural adult populations.
5. Anaemia in urban and rural populations in Jamaica (with Dr P. Milner, University of the West Indies).

STUDIES ON CHILD DEVELOPMENT AND MORTALITY

1. Factors influencing child development in a rural population in Jamaica (studies designed to be parallel to investigations carried out at the Medical Research Council Laboratories in the Gambia and the Reproduction and Growth Research Unit, Newcastle upon Tyne).
2. Measurement of heights and weights of schoolchildren in rural and urban areas of Jamaica; establishment of standards for international and secular comparisons.
3. Investigations of socio-economic factors contributing to high risk of mortality in children aged from 6 months to 3 years (with Jamaican Ministry of Health and the Tropical Metabolism Research Unit).
4. Electrocardiographic and radiological studies of previously malnourished infants, to determine the possible role of malnutrition in the aetiology of cardiomyopathies (with the Tropical Metabolism Research Unit).

DEVELOPMENT OF HEALTH SERVICES IN THE CARIBBEAN

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
(Clerkenwell 1537)

Director
P. J. Lawther, MB, FRCP

Scientific staff

B. T. Commins, PH D, FRIC
J. McK. Ellison, PH D
T. Nash, MA, ARIC
R. E. Waller, B SC

Other senior staff

B. J. Biles
A. G. F. Brooks

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. Analytical techniques in determination of pollutants in the extreme dilutions occurring in urban atmospheres.
3. Possible adsorption of sulphur dioxide on particles and its oxidation to sulphuric acid.
4. Determination of carcinogenic substances in town air and in industrial atmospheres.
5. Health hazards of emissions from motor vehicles, with special attention to polycyclic hydrocarbons and carbon monoxide.
6. Effects of pollutants on pulmonary function.
7. Variations in mortality, in the demands for hospital admission and in the clinical condition of patients with chronic bronchitis and emphysema in relation to daily changes in weather and air pollution.
8. Analysis of data on lung cancer mortality in relation to urban factors.
9. Daily variations in the respiratory function of normal subjects.
10. Respiratory function in patients with occupational disease of the lungs.
11. Chemical constitution of irritant and toxic chemicals, including carcinogens, and their mode of action.
12. Optical methods of assessing particulate pollution and of identifying pollutants.
13. Theoretical study of the lung as a pneumatic system.
14. Chemical and physical properties of various forms of asbestos in relation to their carcinogenicity.

CARCINOGENIC SUBSTANCES RESEARCH UNIT

Washington Singer Laboratories, The University, Exeter
(Exeter 75817)

Honorary Director
Sir James Cook, D SC, FRIC, FRS

Scientific staff

J. M. Barker, PH D
W. Carruthers, PH D
I. D. Entwistle, B SC
H. N. M. Stewart, AH-WC, ARIC

The Unit is investigating the chemistry of tobacco and 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. The chemical constituents of tobacco leaf are also being examined, and 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 and their relation to components of tobacco leaf.
3. Investigation of constituents of 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. Analysis of mixtures of polycyclic aromatic hydrocarbons by gas-liquid chromatography.

LABORATORY ANIMALS CENTRE

Medical Research Council Laboratories, Woodmansterne Road,
Carshalton, Surrey
(Melville 4461)

Director

J. Bleby, B VET MED, MRCVS

Scientific staff

Miss A. M. Brown, PH D
Miss M. Dinsley, PH D
D. T. M. Forrest, BVMS
Mrs T. M. Fox, B PHARM
Professor R. Hare, MD (*honorarium*)

Other senior staff

J. L. Izard
G. Porter, M INST BIOL

Attached workers

M. A. Chaudary, B SC (*Department of Animal Husbandry, Pakistan; UFAW grant-holder*)
A. Farooqi, B SC (*West Pakistan Veterinary Research Institute; UFAW grant-holder*)
V. M. Jhala, B V SC (*Government of India; UFAW grant-holder*)
V. Monaco (*Comitato Nazionale per L'Energia Nucleare, Italy; ICLA Scholar*)
A. Retnasabapathy, M V SC, DIP BACT (*University of Malaya*)
K. Suzuki, MD (*University of Tokyo; ICLA Scholar*)

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 newsletters, catalogues, films and other material for distribution to other laboratories, and administers an accreditation scheme for commercial breeders; (2) to maintain, under controlled (pathogen-free) conditions, primary-type colonies of special strains for issue as breeding nuclei (these at present include fifteen inbred and two non-inbred strains of mice, one inbred and one non-inbred strain of rats, one non-inbred strain of guinea pigs and one non-inbred strain of rabbits in addition to many other species and strains of animals maintained under conventional conditions); (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 genetic specification and to certain standards of health and nutrition, including the development of specified pathogen-free (SPF) colonies.
2. Control of health in large laboratory populations of high density, especially in conditions of rigorous isolation.
3. Formulation, compounding and assessment of diets for laboratory animals, and methods of sterilizing the food.
4. Assessment of differences in response to various stimuli between different strains of mice (mostly inbred), and analysis by electrophoresis of serum samples from inbred mice, in order to compare the content of haptoglobulins, ceruloplasmin and lipoproteins.
5. Assessment of the effects of selection for various aspects of fertility during the formation of inbred mouse strains from the random-bred strain *CFW*.
6. Observations on the effects of housing SPF rats under conventional conditions and the effects of environment on reproduction in mice.
7. Compilation of a bibliography on the effects of genetics and environment on the responses of animals to drugs (financed by WHO).

External Scientific Staff

The Council appoint to their staff a small number of individual research workers, who are based for the most part in university departments.

Birmingham

GENERAL HOSPITAL

Department of Surgery

J. A. WILLIAMS, CH M, FRCS (*part-time*)

The effects of different gastric operations on the structure and function of the remaining gastric mucosa:

1. Histological structure and gastric secretory capacity before and after total vagotomy and pyloroplasty; measurement of the output of acid, pepsin and intrinsic factor.
2. Structure and function of gastric mucosa ten years or more after partial gastrectomy for duodenal ulcer.
3. Detailed metabolic and functional studies on postgastrectomy patients with the bile vomiting syndrome who have been submitted to a conversion gastrectomy.
4. Investigation of post gastrectomy deficiency states resulting from atrophy of gastric mucosa, with particular reference to the effects of treatment with iron and vitamin B_{12}.

UNIVERSITY

Chemistry Department

R. G. H. B. BODDY, PH D

Development of microchemical methods for the analysis of dusts causing pneumoconiosis.

Experimental Pathology Department

P. WOLF, MD

1. Immunological assay of human AHF and plasminogen (with Dr K. W. Walton, University of Birmingham).
2. Immunochemistry of human platelets.
3. Relationship of the platelet phospholipid in blood to thrombosis.

Experimental Pathology Department and Queen Elizabeth Hospital

J. D. BLAINEY, MD, FRCP (*part-time*)

1. Long-term study of the natural history of glomerulonephritis, the nephrotic syndrome and pyelonephritis by biopsy and biochemical techniques.
2. Metabolic studies in acutely and chronically administered haemodialysis.
3. Development of improved dialysing and proportionating systems in acutely and chronically administered dialysis.
4. Studies of protein of low molecular weight in the urine in disease.

Cambridge

STRANGEWAYS RESEARCH LABORATORY*

Miss J. M. ALLEN, B SC

Phagocytosis and intracellular digestion of particles and bacteria by mammalian macrophages in culture, and the effect of drugs on these processes.

Miss M. CAFFREY, M SC

1. Uptake of cobalt by rat tissues.
2. Nature and synthesis of protein in normal muscle and metal-induced myosarcomas.

* The Strangeways Research Laboratory receives a block grant from the Council and further information about its work is given on pp. 193–195. Many of the investigations listed above were made in collaboration with other staff at the Laboratory.

G. D. CLARKE, PH D

1. Factors influencing survival and growth rate of normal fibroblasts in culture at low and very high cell densities.
2. Action of aflatoxin on cells in culture (with Dr J. M. Barnes, Toxicology Research Unit).
3. Cultivation of liver parenchymal cells for infection with malaria.

G. M. W. COOK, PH D

1. Morphogenic processes in connective and skeletal tissue: biosynthesis of carbohydrate polypeptide polymers.
2. Nature of the surfaces in connective and skeletal tissue cells as indicated by electrophoretic and biochemical properties.

J. T. DINGLE, PH D (see also under Dr J. A. Lucy)

Mrs S. ADAMS, B SC (*until Dec. 1965*)

Mrs E. D. NYBERG, B SC

1. Effects of antisera on embryonic bone and cartilage in culture (with Dame Honor Fell and with Dr R. R. A. Coombs of the Department of Pathology, University of Cambridge).
2. Effects of oxygen on limb bone rudiments in culture.
3. Effects of sucrose on skeletal tissue in culture (with Dame Honor Fell).
4. Effects of sucrose on fibroblasts in clone culture.
5. Effect of hormones on the lysosomal acid phosphatase activity of the rat prostate glands in culture.
6. Lysosomal activity of sheep corpus luteum (with Miss M. Hay, Dr L. Rowson and Dr T. Moor, ARC Unit of Reproductive Physiology, Cambridge).
7. Lysosomal activity of spermatozoa (with Dr M. Dott, ARC Unit of Reproductive Physiology, Cambridge).
8. Effect of carcinogenic hydrocarbons on rat adrenal lysosomes (with Dr A. C. Allison, National Institute for Medical Research).
9. Electrophoretic properties of lysosomes (with Dr J. A. Lucy).

J. W. DODSON, PH D (*until Oct. 1965*)

Morphogenic interactions of dermis and epidermis.

Miss S. FITTON JACKSON, PH D

1. Morphogenic processes in connective and skeletal tissue: stages in formation of collagen and protein polysaccharides.
2. Factors concerned in regulating synthetic balance in skeletal tissue in culture: selective depletion of chondroitin sulphate.
3. Interactions between intercellular macromolecules and surfaces of skeletal and connective tissue cells.

J. A. LUCY, PH D

1. Reactive forms of vitamin A (with Dr J. T. Dingle).
2. Chemical properties of retinol in an aqueous environment.
3. Oxidation of colloidal retinol in an aqueous dispersion.

D. A. T. NEW, PH D

1. Nutrition and respiration of rat embryos *in vitro*.
2. Methods for growing rabbit embryos *in vitro*.

D. S. O'DELL, PH D

1. Morphogenic processes in connective and skeletal tissue: preparation and characterization of antibodies to various subunits of collagen.
2. Factors concerned in regulating synthetic balance in skeletal tissue in culture: selective depletion of collagen.
3. Modes of collagen breakdown *in vitro* and in multiple myeloma.

M. WEBB, D SC

1. Magnesium in bacterial physiology: (*a*) utilization; (*b*) differential effects of deficiency on polysome structure and protein synthesis in Gram-positive and Gram-negative bacteria.
2. Heavy-metal uptake by bacteria, mammalian cells and isolated mitochondria.
3. Metal carcinogenesis: (*a*) intracellular distribution of cadmium, cobalt and nickel in primary tumours induced by these metals; (*b*) structure and function of nucleic acids of normal muscle and of metal-induced rhabdomyosarcomas.
4. Zinc-rich component(s) of rat dorsolateral prostate.

Department of Biochemistry: Sub-department of Chemical Microbiology

R. DAVIES, PH D

1. Stimulation of enzyme formation in yeasts by cyclic dipeptides of arginine and proline.
2. Action of sulphydryl compounds on yeast cell-wall structures.
3. Synthesis of cyclic dipeptides.

B. A. NEWTON, PH D

1. Protein and nucleic acid metabolism in trypanosomid flagellates.
2. Mode of action of trypanocidal drugs and mechanisms of drug resistance.
3. Attempts to establish *in vitro* conditions for the growth of pathogenic trypanosomes.

Chemical Laboratory

Mrs O. KENNARD, MA, F INST P

1. Analysis of the structure of cyclohexylammonium phosphoenol pyruvate, geranyl phosphate and 2,4-dinitrophenyl phosphate as part of an X-ray investigation of the high energy phosphate bond.
2. Structure of natural products of biological interest: monobromoneotigogenin, dibromoneotigogenin, tomatidine hydrobromide, 2α-bromoarborinone, acetylcholine-selenoiodide (with the Chemical Crystallography Laboratory, University of Oxford), aspidospermidine, vallesachotamine, eunicellin, repanduline; commissioning and testing of an automatic diffractometer and a system of computer programs in connection with these investigations.
3. Computer analysis and refinement of published structures, to study laws governing molecular associations (with Professor J. D. Bernal, Birkbeck College, London).

Molteno Institute

Mrs E. W. SMART, PH D (*part-time*)

1. Axenic cultivation of *Entamoeba invadens.*
2. Cytochemistry of oocysts from normal and drug-resistant strains of *Plasmodium gallinaceum.*

Psychological Laboratory

W. E. HICK, MD

1. Study of skill, with special reference to control and supervision of machines (including vehicles, aircraft etc.) 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 in 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

1. Development of psychological tests: Self-judging Vocabulary, Shapes Analysis, Word-in-Context and two versions of a high-grade intelligence test.
2. Brook Reaction: a test to assess interests and personal adjustment.
3. Use of these tests in experimental inquiries into such problems as student selection and specialization.

Miss M. A. VINCE, BA

S. H. SALTER, BA (*honorarium*)

Mrs A. J. WATSON (*part-time; until May 1965*)

Communication between embryos and the synchronization of hatching in quail:

1. Signals produced by embryos that can accelerate or retard their siblings' time of hatching.
2. Developmental stages associated with these signals and the mechanism of synchronization.
3. Possible effects of pre-hatching stimulation on later behaviour.

School of Agriculture

Miss R. DEANESLY, D SC (*with grant for assistance*)

Reproductive physiology of the female:

1. Corpus luteum reactions to agents and experimental techniques affecting pituitary and uterus in the guinea pig.
2. Synchronization of oestrus in the guinea pig.

Federal Cameroon Republic

KUMBA

Helminthiasis Research Unit

B. O. L. DUKE, OBE, MD, DTM & H

1. Trials of drugs for treatment and prophylaxis of onchocerciasis.
2. Experimental infections with *Onchocerca volvulus* in chimpanzees.
3. *Onchocerca–Simulium* complexes in different bioclimatic and geographical zones.
4. Bionomics and control of *Simulium damnosum.*

Cirencester

EPIDEMIOLOGICAL RESEARCH UNIT

R. E. HOPE-SIMPSON, OBE, MRCS (*part-time*)

1. Elucidation of the peculiar natural history and symptomatology of the individual viruses causing the common respiratory infections, using a general practice as an unselected population.
2. Participation in a long-term cooperative study of the significance of convulsive disorders in persons under 20 years.
3. Herpes zoster as an example of a latent infection.

East Grinstead

MCINDOE MEMORIAL RESEARCH UNIT*

D. A. L. DAVIES, D SC
Miss B. J. ALKINS (*technical staff*)
A. J. MANSTONE (*technical staff*)

1. Chemical nature of mouse and human transplantation isoantigens.
2. Purification of mouse leukaemic cell-specific antigens.
3. Antigenic completeness of the thymus.

A. R. SANDERSON, PH D

1. Serological techniques for the detection and assay of human transplantation antigens.
2. Purification of a factor involved in clotting of chick plasma and implicated in terminal graft-versus-host disease.

Edinburgh

ROYAL INFIRMARY

Surgical Neurology Department

J. P. LAIDLAW, MB, MRCPE (*part-time*)

Development and application of methods of analysing the background rhythmic activity of the human EEG.

WESTERN GENERAL HOSPITAL

Gastro-Intestinal Unit and Department of Medicine

W. SIRCUS, MD, PH D, FRCP (*part-time*)

1. Studies in diseases characterized by malabsorption.
2. Detailed studies in cases of Zollinger–Ellison syndrome.
3. Controlled trials of therapeutic agents for the management of aphthous ulceration.

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* This Unit receives a block grant from the Council: see p. 196.

Elstree

LISTER INSTITUTE OF PREVENTIVE MEDICINE

Mrs J. M. DOLBY, PH D (*until Oct. 1965*)

Immunological and pharmacological properties of purified *Bordetella pertussis* antigens.

Miss M. E. MACKAY, PH D

1. Proteolytic enzyme in human plasma.
2. Pharmacologically active substances in human plasma fractions.

London

BRITISH MUSEUM (NATURAL HISTORY)

D. J. LEWIS, SC D

1. Phlebotomine sand-flies of West Pakistan.
2. Variation of *Simulium damnosum* in relation to transmission of *Onchocerca volvulus*.

CENTRAL PUBLIC HEALTH LABORATORY, COLINDALE

Cross-Infection Reference Laboratory

O. M. LIDWELL, D PHIL

D. KINGSTON, MA

1. Cross-infection in hospitals: the part played by airborne transmission of microorganisms, especially *Staphylococcus aureus*, and the effects of ward and hospital design on this.
2. Attempts to recover respiratory syncytial virus from the surroundings (including the air) of infants suffering from acute bronchiolitis.
3. Comfort conditions in operating theatres (with Professor R. E. O. Williams of St. Mary's Hospital Medical School; see grant no. 571, p. 242).

COMPUTER SERVICES CENTRE

M. J. R. HEALY, BA

Miss J. TROOP, BA

A. V. SWAN, B SC

1. Statistical problems arising from the records of the Hypogammaglobulinaemia Working Party.
2. Statistical extreme-value problems arising from tumour detection by radioisotopes.
3. Quality control of biochemical laboratory readings.

GUY'S HOSPITAL MEDICAL SCHOOL

Anatomy Department

W. A. GAUNT, PH D

1. Quantitative analyses of the growth of teeth and jaws.
2. The dental follicle.
3. Innervation and vascularity of teeth and associated tissues.

Chemical Pathology Department

B. MCARDLE, MD, FRCP, DCH (*with grant for assistance*)

Miss H. PELS, AIST (*technical staff*)

1. The levels in various neuromuscular disorders of total and individual phosphatides, total plasmalogens, RNA and DNA and certain glycolytic enzymes of muscle.
2. Biochemical changes in myopathy induced by plasmocid in rats.

Department of Medicine, Radioisotopes Laboratory

N. VEALL, B SC, F INST P

J. D. PEARSON, B SC

M. D. O'BRIEN, MB

J. R. GREEN (*technical staff*)

1. Cerebral blood flow and other circulation studies using ^{133}Xe.
2. Use of ^{47}Ca for clinical metabolic studies.
3. General clinical applications of radioactive tracers.

INSTITUTE OF CANCER RESEARCH*

Chester Beatty Research Institute

E. J. DELORME, MD, FRCS(C)

1. Specific anti-tumour effect of immune lymphoid cells and the capacity of isolated immune RNA to bring about this effect through a transfer mechanism.

INSTITUTE OF NEUROLOGY

J. A. V. BATES, MB, MRCP (*part-time*)

H. W. L. KOK, MB (*part-time*)

N. DE M. RUDOLF, BM (*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. Surgical relief of epilepsy.

A. M. HALLIDAY, MB, B SC

J. R. PITMAN (*technical staff*)

1. Factors affecting the form of cortical evoked responses in healthy subjects.
2. Changes in cerebral evoked potentials produced by various lesions of the nervous system.
3. Clinical trial of the therapeutic effect of unilateral electroconvulsive therapy in depression and a comparison of its effect on memory with that of conventional bilateral ECT.

P. W. NATHAN, MD, FRCP

1. Studies on tracts of the spinal cord in relation to anterolateral cordotomy, rhizotomy and other pain-relieving procedures.
2. Studies on spasticity, with particular reference to its treatment by rhizotomies with phenol solutions and by drugs given intravenously.

Miss M. C. SMITH, MD, B SC, MRCP, FC PATH (*part-time*)

1. Correlation between post-mortem findings and the clinical effects of stereotactic operations.
2. Functional anatomy of the human central nervous syste.., studied by investigations of neurological conditions.

INSTITUTE OF ORTHOPAEDICS, STANMORE

Clinical Research Wing

A. MCPHERSON, MB, MRCP

L. JUHÁSZ, PH D (*until May 1965*)

V. SKORPIL, DR MED

1. Viscerosomatic reflexes.
2. Haemodynamics of bone.
3. Changes in myoglobin content after nerve cross-union.

Sir Henry Dale Laboratory

J. A. WILKINSON, M CH, FRCS (*part-time*)

1. Genetic factor in the aetiology of congenital dislocation of the hip: family studies.
2. Epiphysial bone growth: effects of experimental shortening and lengthening of the intervening diaphysis.
3. Neonatal surveys for orthopaedic congenital anomalies.

INSTITUTE OF PSYCHIATRY

Mrs L. G. WING, MD, DPM

The Camberwell Register: compilation of a cumulative Psychiatric Disease Register to provide epidemiological information and a sampling frame for intensive studies of specific problems.

N. O'CONNOR, PH D†

P. E. BRYANT, PH D†

Mrs B. M. HERMELIN, PH D†

1. Learning and behaviour problems of psychotic children.

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* The Institute of Cancer Research receives a block grant from the Council: see p. 187.

† Members of staff of the Social Psychiatry Research Unit until September 1965.

2. Transfer and discrimination in the severely subnormal.
3. Specific linguistic disabilities in psychotic children.

Neurosurgery Department

L. SYMON, MB, FRCS (*part-time*)

1. Cerebrovascular resistance in the pial circulation of primates.
2. Experimental production and study of arterial spasm in the cerebral circulation.
3. Local flow and pressure patterns in arterial collateral fields of the brain.

LISTER INSTITUTE OF PREVENTIVE MEDICINE

Department of Experimental Pathology

J. NEWSOME, MD, DTM & H

1. Mechanism of phagocytosis.
2. Methodology of opsonic and avidity indices.

LONDON HOSPITAL

Medical Unit

F. B. BYROM, MD, FRCP

Production, mechanism and effect of experimental hypertension.

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE

C. N. DAVIES, D SC, F INST P

1. Nucleation of homogeneous aerosols.
2. Human inhalation of aerosol.
3. Deposition mechanisms of aerosol in turbulent flow.

M. E. C. GIGLIOLI, PH D (*until Nov. 1965*)*

1. Studies on *Anopheles gambiae melas*, with particular reference to breeding and age composition.
2. The mangrove swamps of Keneba, lower Gambia river basin:
   (*a*) The climate and the physical composition of the soils (with Mr I. Thornton, Gambia Department of Agriculture).
   (*b*) pH changes in air-drying swamp soils (with Mr I. Thornton).
   (*c*) Seasonal variations in the chloride and water content of swamp soils, with observations on the daily levels and the salinity of free soil water during the dry season (with Mr D. King).
3. A simple recording wind gauge:
   (*a*) Mechanism and method of recording.
   (*b*) Interpretation of the recorded wind trace.

POSTGRADUATE MEDICAL SCHOOL OF LONDON

Cyclotron Building (*Medical Research Council*)

N. B. MYANT, DM, B SC, MRCP

Miss V. J. ILIFFE, B SC

K. A. MITROPOULOS, GRAD IN CHEM

C. MOUTAFIS, MD

1. Regulation of the metabolism of fatty acids and cholesterol, using cell-free mammalian preparations.
2. Disorders of lipid metabolism in humans.
3. Influence of the thyroid on the metabolism of brain phospholipids.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

Pharmacology Department

Mrs H. M. PAYLING WRIGHT, PH D, LMSSA

1. Histology and reactions of small blood vessels.
2. Effect of splenectomy, with and without anaemia, on platelet behaviour.
3. Platelet behaviour in multiple sclerosis and certain other clinical conditions.
4. Effect of experimental microplatelet emboli on brain tissue.

* This work was conducted at the MRC Laboratories in the Gambia (p. 149) but written up at the London School of Hygiene.

Physiology Department

N. AMBACHE, MA, MRCS

Mrs J. M. C. WHITING, B SC

Miss M. J. WOOD, B SC

1. Investigation of physiological role and characterization of irin-like unsaturated hydroxy-acids, including prostaglandins, found in extracts and perfusates of parts of the brain, eyes and other tissues (with development of sensitive techniques); possible species differences in the various hydroxy-acids and in the response of effectors to them.
2. Neurotoxic effects of purified fractions of tetanus toxin and of types A and D botulinum toxins.
3. Atropine-resistant nerve effects in atropinesterase-free rabbits and in other species.

ROYAL FREE HOSPITAL AND INSTITUTE OF NEUROLOGY

A. ELITHORN, MD, MRCP, DPM (*part-time; with grants for assistance*)

T. J. BARNETT, BA

D. JONES, PH D*

Miss P. PICKBOURNE, B SC

Miss J. D. SMITH, BA

1. Relationship between perceptual capacity and intellectual capacity.
2. Relationship between anxiety and depression.
3. Computer simulation of human problem solving.

THE ROYAL INSTITUTION

Davy Faraday Research Laboratory†

D. W. GREEN, PH D

1. X-ray crystallography determination of the structure of β-lactoglobulin.
2. Studies of reversible conformation changes in proteins in solution (with Dr R. Aschaffenburg, National Institute for Research in Dairying, Shinfield, Reading).

A. C. T. NORTH, PH D, A INST P

1. Investigation of the structure of lysozyme and other proteins by X-ray diffraction.
2. Explanation of enzymic activity in terms of chain conformation.
3. Development of computational methods for the determination of protein structures.

D. C. PHILLIPS, PH D, F INST P

1. Investigation of the structure and enzymic properties of lysozyme by X-ray diffraction.
2. Development of theoretical and experimental methods of X-ray analysis for the determination of protein structures.
3. Theoretical and computational study of the folding of protein molecules.

ST. BARTHOLOMEW'S HOSPITAL

Serological Population Genetics Laboratory

Serological Section

A. E. MOURANT, DM, D PHIL, FRCP, FC PATH, FRS

Miss B. G. GLASGOW, B SC

Miss M. J. GOODWIN, B SC

Full determination of the erythrocyte groups, haemoglobins, and a large range of genetically determined plasma protein groups, in blood samples collected on a population basis, especially by expeditions sponsored by the International Biological Programme.

Statistical Section (*St. Paul's Churchyard*)

Miss S. HEATH, B SC

Mrs A. C. KOPEC, D-ES-SC

1. Collection, tabulation and statistical treatment of all available data, published and unpublished, showing the incidence of genetically determined serological and biochemical characters in human populations.

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* On leave of absence for one year at the State University of Iowa.

† The Laboratory receives a block grant from the Council: see p. 195 for further details of its research projects.

2. Operation as the world information centre for such data.
3. Survey of the distribution of the ABO and Rh blood groups in the population of the United Kingdom.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL

Department of Medicine

A. ANTONIS, PH D, MC PATH, FRIC

1. Metabolic studies on the dietary control of serum lipoprotein concentration and composition.
2. Effect of different carbohydrates and catecholamines on ketosis.
3. Epidemiological studies:
   (*a*) Bus conductors and drivers and their siblings (with the Social Medicine Research Unit).
   (*b*) Rayon workers exposed to carbon disulphide and hydrogen sulphide (with the Social Medicine Research Unit and the Department of Remedial Health, London School of Hygiene and Tropical Medicine).

ST. MARY'S HOSPITAL

Department of Chemical Pathology

J. S. GARROW, MD, PH D, MRCPE*

1. Influence of nutritional factors on protein metabolism in man.
2. Effect of protein depletion on electrolyte metabolism.

THE TAVISTOCK INSTITUTE OF HUMAN RELATIONS

E. J. M. BOWLBY, MD, FRCP (*part-time*)

Short-term effects of the temporary loss of a mother-figure.

R. D. SHEPHERD, B SC†

Cognitive interference and interpersonal experience: experimental studies of the susceptibility to disorganization of some basic cognitive skills.

UNIVERSITY COLLEGE

Physiology Department

H. DAVSON, D SC (*with grant for assistance*)
C. PURVIS (*technical staff*)

1. Exchange of material between blood, cerebrospinal fluid and brain and cord.
2. The extracellular space of brain.

Psychology Department

Mrs S. JONES, PH D†

1. Effect of linguistic variables in instructions.
2. Comprehension of complex rules expressed in visual and verbal forms.

P. C. WASON, PH D†

1. The interaction between thinking and perception.
2. Effect of word order in the interpretation of formally ambiguous sentences.
3. Development of algorithmic procedures for understanding and learning complex rules.

Mrs A. ZAJACZKOWSKA, PH D†

1. Effects of muscle afferents on visual perception of distance.
2. Effects of visual estimates of distances on the mechanics of movements.
3. Some numerical links between visual and kinaesthetic space.

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* Formerly Assistant Director of the Tropical Metabolism Research Unit (p. 150).
† Members of the staff of the Industrial Psychology Research Unit until October 1965.

WEST HENDON HOSPITAL

Centre for Muscle Substitutes

A. B. KINNIER WILSON, MB, MRCP, DPM

A. H. BOTTOMLEY, MB

R. P. J. G. MCWILLIAM, MA

S. R. MONTGOMERY, MA, SC D (*part-time*)*

R. E. REILLY, M SC

P. J. STYLES, ASSOC IEE

Advanced motor and control system for artificial limbs and splints:

1. Ranges of arm positions and their simplification.
2. Characteristics of normal movement in relation to its mechanical substitution.
3. Functional analysis of disability of upper limbs in relation to design of prostheses and splints and their attachments.
4. Methods of acquisition and use of noise-free myoelectric and other proportional signals for control and coordination of movement of prostheses.

Malaysia

SUNGEI BULOH SETTLEMENT

Research Unit

J. H. S. PETTIT, MD, MRCP

J. M. H. PEARSON, BM, MRCP†

1. Controlled clinical trials in leprosy, with particular reference to the effects of low dosage of diaminodiphenyl sulphone on the morphological index.
2. Studies on B.663 (a rimino-phenazine derivative):
   (*a*) Effect on cases of sulphone-resistant leprosy.
   (*b*) Use in the management of erythema nodosum leprosum.
   (*c*) Use in the treatment of infection with *Mycobacterium ulcerans*.
3. Tuberculin and lepromin sensitivity in leprosy patients and contacts.
4. Epidemiology of leprosy in an isolated Chinese community.

Manchester

PATERSON LABORATORIES, CHRISTIE HOSPITAL AND HOLT RADIUM INSTITUTE‡

Experimental Chemotherapy Department

H. JACKSON, MB, D SC

1. Effects of sulphonic esters and related compounds on mammalian spermatogenesis and fertility; structure–activity relationship.
2. Embryopathic effects mediated by direct action on the developing foetus and possibly via the paternal germ cell.
3. Possible correlation between antispermatogenic effects, mutagenicity and antitumour activity.

UNIVERSITY

Turner Dental School

A. S. HALLSWORTH, PH D (*until Oct. 1965*)

1. Aspects of the molecular biology of collagen relating to dental research.
2. Specific problems associated with the calcification of bone, dentine and enamel.
3. Nature and distribution of fluoride in dental plaque.

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* On secondment from the Department of Mechanical Engineering, University College, London

† Seconded from the Virology and Bacteriology Division of the National Institute for Medical Research (see p. 92).

‡ The Paterson Laboratories, Christie Hospital and Holt Radium Institute, receive a block grant from the Council (see p. 192).

Nottingham

UNIVERSITY

Psychology Department

J. A. LEONARD, PH D

1. Mobility of blind people:
   (*a*) Field observations, on familiar and on new routes.
   (*b*) Role of visual cues in static and mobile balancing.
   (*c*) Relationship between intensity of stimulation of artificial or natural signals and walking speeds.
2. Development of keyboard skills:
   (*a*) Role of vision in acquiring skill at a simple keyboard task.
   (*b*) Utilization of sequential redundancy as a function of the typing progress.

Oxford

THE CHURCHILL HOSPITAL

Central Workshop

F. D. STOTT, D PHIL

Miss A. D. M. GLASS, BA (*technical staff*)

1. Pulmonary systemic blood flow and pressure measurements in man (with Dr G. de J. Lee, Radcliffe Infirmary).
2. Long-term continuous recording of blood pressure in ambulant patients (with the Department of the Regius Professor of Medicine).
3. Assistance to Professor R. G. Macfarlane (Blood Coagulation Research Unit) in the study of thrombus formation.

Department of the Regius Professor of Medicine

L. I. WOOLFE, PH D (*with grant for assistance*)

B. L. GOODWIN, D PHIL

Miss N. G. KENNAWAY, B SC

1. Biochemical genetics, diagnosis and treatment of phenylketonuria; metabolism of phenylalanine, tyrosine and tryptophan; population screening for inborn errors of metabolism.
2. Renal tubular reabsorption of amino acids and sugars.
3. Chemistry of glycolipids etc. in inborn errors of metabolism.
4. Urinary metabolites of imipramine.

Sir William Dunn School of Pathology

J. C. F. POOLE, DM

1. Electron microscope studies of natural and artificial thrombi.
2. Phagocytosis of platelets.
3. Cellular mechanisms in experimental atherosclerosis.

A. M. WOODIN, PH D

Miss A. A. WIENEKE, DRS

1. Interaction of leucocidin with lipids.
2. Properties of leucocyte cell membranes.
3. Sulphydryl reagents in protein secretion and granule movement.

Penarth, Glamorgan

LLANDOUGH HOSPITAL

Department of Psychological Medicine, Welsh National School of Medicine

J. G. INGHAM, PH D*

M. M. WOOD, B SC*

1. Comparative studies of the distribution of psychiatric disorders in a mining area and an agricultural area.
2. Development of scales for the assessment of subjective symptoms.
3. Investigation of individual differences in the parameters of stimulus detection.
4. Application of statistical detection theory to the detection of physiological changes.

* Members of staff of Social Psychiatry Research Unit until November 1965.

Reading

UNIVERSITY

Department of Zoology

A. D. BERRIE, PH D

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 Tanzania.

Sheffield

NETHER EDGE HOSPITAL

Rheumatism Research Unit

H. F. WEST, MD, FRCP, DTM (*with grant for assistance*)

1. Metabolism of cortisol and its analogues and the disposition of these hormones and their metabolites in the body fluids of patients and controls.
2. Therapeutic studies for rheumatoid arthritis.

Republic of South Africa

DURBAN, NATAL

Institute for Parasitology, Durban, and Zoology Department, British Museum (Natural History), London

D. S. BROWN, PH D

1. Taxonomy of the intermediate snail hosts (genera *Bulinus* and *Biomphalaria*) of *Schistosoma* in Africa.
2. Distribution of freshwater snails in South Africa and Ethiopia (field work at Haile Selassie University College, Addis Ababa).

St. Lucia

CASTRIES

Research and Control Department

P. JORDAN, MD, DTM & H

Epidemiology of *Schistosoma mansoni* infection prior to application of control methods.

Tanzania

TANGA

WHO/MRC Tanzania Bilharziasis Chemotherapy Centre

A. DAVIS, MB, MRCPE, DTM & H

1. Methodology of clinical trials in bilharziasis.
2. Field and laboratory studies of a new oral schistosomicide in *Schistosoma haematobium* infections.

Trinidad

UNIVERSITY OF THE WEST INDIES

Trinidad Regional Virus Laboratory

D. C. J. BASSETT, MB, DIP BACT

Streptococcal diseases in connection with epidemic acute glomerulonephritis.

Uganda

MAKERERE UNIVERSITY COLLEGE MEDICAL SCHOOL, KAMPALA

Department of Surgery

D. P. BURKITT, MD, FRCSE*

1. Chemotherapy of African lymphoma (Burkitt tumour).
2. Geographical distribution of selected cancers throughout East Africa and some of the neighbouring territories on an interterritorial basis.

Wickford, Essex

RUNWELL HOSPITAL

J. DAWSON, MB, M SC (*until Nov. 1965*)

1. Influence of alterations in electrolyte and water metabolism on the electroencephalogram in patients with affective disorders and periodic psychoses.
2. Effect of vasopressin and psychotropic drugs on the electrolyte and water metabolism of brain slices.
3. Effect of urinary extracts on the distribution of water, sodium and potassium in brain slices.

* Now at 164 Tottenham Court Road, London W.1.

Institutions Assisted by Block Grants

The Council are also able to assist the progress of research through their scheme of block grants. These grants are used to support, in whole or in part, the research activities of a number of autonomous institutions. In addition, individual members of the Council's staff are working in most of these institutions; further details will be found under the appropriate entry in the section 'External Scientific Staff' (p. 174).

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, FRIC, F INST P

Secretary
N. P. Hadow, OBE, MA

The Institute was recognized in 1927 as a school of the University of London; since 1951 it has had similar status as an Institute of the British Postgraduate Medical Federation. The work of the Institute is centred in the Chester Beatty Research Institute and in the research activities of the Departments of Physics, Biophysics, Radiotherapy and Clinical Research, which are joint departments of the Institute of Cancer Research and of the Royal Marsden Hospital. Since 1951 the Council has made an annual block grant to the Institute; substantial support is also received from the British Empire Cancer Campaign for Research. Detailed accounts of the Institute's scientific work are available in the Annual Reports of the British Empire Cancer Campaign, and only a brief survey will be given here.

CHESTER BEATTY RESEARCH INSTITUTE

Director
Professor Sir Alexander Haddow, MD, D SC, FRS

For many years this Institute has studied the mechanisms of carcinogenesis and its programme of research is still concentrated upon the solution of the problems of the causation, development, prevention and treatment of cancer; new approaches and techniques are being used wherever possible. During the past year there has been a shift of emphasis leading to increased concentration upon the biological approach to the problem and the development of work in the fields of molecular biology and immunology. New techniques have allowed problems of tumour invasiveness and cell redifferentiation to be studied more effectively. In particular, study of the role of the thymus gland in immunology and leukaemogenesis has increased understanding of cell surfaces, cell movement and invasion, and may lead to further consideration of tumour antigens. The techniques of cell biology, electron microscopy and tissue and organ culture are particularly valuable in this work.

Special attention is also being paid to the effects of radiation in bacterial and mammalian cells and to the development of drug resistance. One of the

most interesting aspects of research into the effects of radiation is the study of repair in cells exposed to X-rays. At the moment bacteria, such as *Micrococcus radiodurans*, are being used for this work but it is hoped that in due course studies will be carried out in mammals.

In cytology and cytogenetics progress has been made by means of quantitative studies, particularly of mutagenesis induced by various means in *Drosophila*.

Recent investigations have included work on the structure and function of enzymes and other proteins, with particular reference to histones, xanthine oxidase, and asparaginase. Work in the field of experimental chemotherapy has included further investigation of alkylating agents, among them derivatives that might be useful for the treatment of head and neck tumours. New types of compounds are constantly being sought and, among the antimetabolites, some intermediate compounds have shown potential antiviral effects. It is hoped that synthesis of such compounds will lead to the discovery of a more detailed knowledge of their mechanism of action. From these varied approaches a glimpse is now being obtained for the first time of the way in which carcinogenic transformation may be effected by the action of chemical carcinogens or the nucleic acids of the oncogenic viruses on the nucleic acids governing cellular heredity.

PHYSICS DEPARTMENT

Professor J. W. Boag, D SC, F INST P

The clinical work of the Physics Department is concerned with the measurement of radioactive isotopes used in the diagnosis and therapy of malignant disease and with the measurement of the high-energy radiation beams used in radiotherapy. In the Low Background Laboratories at Sutton accurate measurements of total body activity and of isotope distribution in the body can be made down to much lower levels than hitherto. This more accurate measurement of whole-body radioactivity should render unnecessary the collection and measurement of excreta in patients who have received large doses of radioisotopes.

The X-ray spectrum of the 6-MeV linear accelerator has been determined by scintillation spectrometry and the factors that influence spectral shape have been investigated. The use of modern photocopying techniques to extract isodensity lines from exposed films has made photographic film dosimetry much more convenient. The development of an electronic analogue computer for the immediate calculation and display of isodose distribution charts has made further progress.

In the department's work on environmental radiation, special attention has been focussed on the isotope polonium-210. The levels of polonium-210 in human tissues from different population groups have been studied in relation to dietary and smoking habits. The polonium-210 content of cigarette tobacco from different regions has been measured and reports that there are individual variations in the deposition of polonium-210 in the bronchial epithelium of cigarette smokers have been studied. The apparent affinity of polonium-210 for certain specific proteins is under investigation. The radiation dose to the

population from fast neutrons and heavy charged particles arising from cosmic radiation has been measured more accurately and is found to be much lower than had been reported.

Research on the basic physical properties, biological effects and possible clinical applications of ultrasound has continued and is being developed further. Some work has been done on the degradation of DNA, and studies are in progress on the effect of ultrasound on the permeability of tissues to drugs and metabolites with a view to developing clinical applications of this technique.

A new research project on the initial chemical effects of ionizing radiation has been begun. This will employ the techniques of pulse radiolysis and flash photolysis to study the transient chemical species formed in irradiated liquids and their reactivities with biological molecules.

The Instrument Group has designed and constructed special apparatus for both clinical and experimental work. Patient monitoring equipment for the reverse barrier nursing wards, apparatus for perfusing excised tumours, a clinical isotope scanner and an ultrasonic scanner have been completed during the year.

BIOPHYSICS DEPARTMENT

Professor L. F. Lamerton, D SC, F INST P

The major preoccupation of the Department is the study of cell proliferation in normal and malignant tissues in order to achieve a better understanding of factors responsible for the maintenance and breakdown of tissue homeostasis, and to obtain information that will provide guidance in the choice of radiotherapeutic and chemotherapeutic procedures.

Studies are continuing on the effects of partial resection, continuous irradiation, and lactation on the cell proliferation pattern in the small intestine of the rat. The response of the bone marrow to continuous irradiation is being investigated, with particular reference to the changes seen in the recognizable precursors of the red cell and the effects on those cells which carry repopulating ability. The migration of ' repopulating ' cells from the shielded limbs of irradiated mice has also been studied. The effect on the red cell system of substantial bleeding and of the induction of anaemia by phenylhydrazine is also being examined.

Cell proliferation in specimens of human tumours has been studied by labelling with tritiated thymidine, with particular reference to investigations of tumour growth.

Various techniques are being used to study the cell proliferation in transplanted rat tumours and to compare fast and slowly growing tumours. Studies on cell proliferation and the effect of continuous irradiation are also being carried out on mouse lymphoma cells in culture.

Biochemical studies of the regenerative process have been made on the kidney during the compensatory growth that follows unilateral nephrectomy, and also after the administration of folic acid. The programme of work on the possible reutilization of isologous DNA by lymphoma cells *in vitro* has been continued.

Another aspect of the Department's work is the study of the metabolism of the actinide elements and trace metals. Work on the carcinogenic action of plutonium and americium has continued and chemical studies on trace elements in human subjects, particularly in cases of primary biliary cirrhosis, have been carried out.

RADIOTHERAPY DEPARTMENT

Director
Professor D. W. Smithers, MD, FRCP, FRCS, FFR

Clinical studies of tumours have continued throughout the period under review, with special emphasis on a survey of over 6000 patients with carcinoma of the bronchus. A study has also been made of patients with carcinoma of the breast in the early stages who have been treated by local removal of the mass and by irradiation. Work has continued on tumours of the eye and orbit, the larynx and pharynx, the kidney, bladder, prostate and testicle. A new caesium-137 dispenser, which is a combined mobile store and handling device for radioactive material, has been designed and built. Investigations of the potentialities of fast neutrons in radiotherapy have continued, in collaboration with the Medical Research Council's Cyclotron Unit and the Radiotherapy Department of the Hammersmith Hospital.

Tumour growth and tumour spread have been studied, both to test the general theory on the growth of neoplasms and as a guide in treatment. Most measurements have so far been made on radiographs of metastatic lesions in lungs, on lymph nodes containing radio-opaque material, and by direct methods on some accessible tumours. External radioisotope scanning techniques have been used to detect tumours in the brain, liver and skeleton, and to assess the response to treatment.

Investigations are being carried out in an attempt to shed light on the mechanism underlying radioresistance, which stands in the way of further progress in radiotherapy. Comparative studies on radiosensitivities *in vivo* and *in vitro* have been carried out using transplantable rat fibrosarcoma and have included investigations into the effects of hyperbaric oxygen and of dose fractionation. The influence of the stromal environment, and particularly of connective tissue, on cell sensitivity has been examined by studying the effects of irradiation and of the administration of thyroid hormones on collagen synthesis. The effects of radiation on nerve function have been studied in view of the possible implication of nerves in regeneration. Hyperbaric oxygen has been used in a trial, conducted in collaboration with other centres, under the guidance of the Medical Research Council Steering Committee on the Evaluation of Different Forms of Cancer Therapy, in randomly selected patients with advanced carcinoma of the cervix and with anaplastic carcinoma of the bronchus.

Another important aspect of the work of this department is the investigation of some of the immunological, haematological and neurological side-effects of tumours of the thymus and lymphoid system. A panel has been established, in collaboration with several other hospitals, to review cases of thymic tumours. A technique has been investigated for detecting the presence of factors in pathological sera which, when injected into lethally irradiated mice, reduce

the ability of the bone marrow cells to recover erythropoietic function. Evidence of the existence of such factors has been found in two patients with thymic tumours. The radiosensitivities, rates of production and rates of migration through the blood stream of lymphoid cells responsible for the graft-versus-host reaction have been studied in rats by means of the technique of extracorporeal irradiation of the blood. This is a preliminary step towards the introduction of this technique as a method of treating certain types of human leukaemia.

CLINICAL RESEARCH DEPARTMENT

Director

P. E. Thompson Hancock, MB, FRCP

The clinical research programme is divided into two main sections: (1) investigation into patients' defence mechanisms, their environmental background and the characteristics of their tumours; and (2) studies of new methods of treatment. In all these projects clinical research is closely integrated with the fundamental research at the Institute.

The investigatory work is mostly incorporated in a project known as the 'Characterization of Human Cancer', in which a series of investigations is carried out by small teams. There is a collection, registration and distribution service which supplies specimens for all purposes. Studies are carried out on tumour cell culture (including the inhibitory effect of a range of drugs), the relationship of enzymes and coenzymes, respiratory behaviour, trace metal content, karyotypes, immunological response, level of thiols and disulphides, and tissue and tumour storage. The environmental pathology of the patients from whom the tumours were removed is also investigated.

Special groups of patients are kept under observation, including (1) those known to have been exposed to a carcinogen, e.g. rubber and cable workers, (2) women who, at routine cervical smear screening, have shown some abnormal enzyme content (with or without cytological changes) and (3) gas and tar workers.

Normal women and women with breast tumours and cysts are being studied to see if thermographic scanning of the breasts yields useful information.

Clinical trials of systemic chemotherapy continue to be carried out, with particular reference to the use of Melphalan in myelomatosis, merophan in alimentary and pulmonary carcinoma and chlorambucil or mannitol Myleran in ovarian carcinoma. The response to hormone therapy of patients with inoperable carcinoma of the kidney is being studied. During the year a sterile ward has been brought into operation to provide facilities for the treatment of patients with greatly reduced immune response and marrow depletion. The treatment of skin tumours with local applications of cytotoxic drugs continues.

Regional chemotherapy by arterial infusion also continues and efforts are being made to improve the delivery of a drug to the site of the tumour and to make it effective in that region only. Two experimental systems are used, one employing an isolated human tumour with an extracorporeal circulation, the other using a transplanted tumour in the rat.

ROYAL BEATSON MEMORIAL HOSPITAL
132–138 Hill Street, Glasgow C.3

CANCER RESEARCH DEPARTMENT

Director
P. R. Peacock, MB, FRCPG, FC PATH

The Cancer Research Department of the Royal Beatson Memorial Hospital has received a block grant from the Council since 1957. It also receives financial support from the British Empire Cancer Campaign for Research. The ordinary maintenance costs of the Department are met by the Western Regional Hospital Board.

The work of the Department includes studies on problems with a clinical bearing as well as investigations of the mechanism of carcinogenesis and aetiological studies.

Recent investigations into the effects of the administration of isoniazid in two strains of mice, one in which the incidence of spontaneously occurring pulmonary adenoma (PA) is high and one in which it is low, have shown that isoniazid causes earlier and higher incidence of PA than would normally be expected in both strains; but the results are more striking in the strain in which the incidence of spontaneous PA is low. Histological studies show that alveolar hyperplasia (AH) occurs at the same anatomical sites as PA, though it occurs earlier. Both lesions are frequently present together and can be distinguished by the presence of normally distributed elastic tissue in AH and its deficiency or absence in PA. The anatomical site, subpleural or perivascular, of AH and PA is thought to be of aetiological importance and related to airborne or blood-borne carcinogens respectively. Wistar rats, given similar doses of izoniazid, proved much less susceptible to the induction of AH and PA than either strain of mice; desert rats and hamsters showed no adverse response to the drug.

Asbestos-induced tumours in the respiratory tract of domestic fowls are histologically unlike mesothelioma or carcinoma associated with asbestosis in man. They resemble malignant lymphoma or reticulosarcoma and are invasive and transplantable but not transmissible by cell-free extracts.

The molecular biology of cell growth and differentiation is being studied by a combination of techniques of biochemistry, tissue culture, optics and electron microscopy.

CHRISTIE HOSPITAL AND HOLT RADIUM INSTITUTE
Withington, Manchester 20

PATERSON LABORATORIES

Director
L. G. Lajtha, MD, D PHIL

During the past twelve months 32 research scientists and a supporting staff of 70 have been working in the Laboratories. Administrative services are provided by the South Manchester Hospital Management Committee and the Laboratories are under the immediate control of the Cancer Research Executive Advisory Committee.

The research interest of the Laboratories is strongly slanted towards radiotherapy and is based on two main principles. The first is that progress in the understanding of malignant disease and, eventually, its rational treatment must depend on the furtherance of chemical and biological knowledge of fundamental cellular processes and the effects of radiation on them. To this end the radiation chemistry group has vigorously pursued the study of the immediate effects of radiation on chemical systems of biological interest. The cytogenetic group has analysed the chromosome duplication pattern and behaviour of various mammalian cells, including human cells originating from malignant and other pathological tissue, and genetic studies on the effects of radiation have been continued in mice and *Drosophila*. Studies on cell killing by radiation have been carried out on dormant and dry cells as well as on mammalian tissues *in vivo*. In addition, the effects of low-dose-rate radiation on the survival of human cells in tissue culture have been vigorously investigated, and related to chromosome damage and the growth rate of cell colonies. The regulation and control of growing and steady-state cell populations has been investigated in a variety of experimental systems, ranging from monolayer cultures to bone-marrow stem cells *in vivo*. The complexity of these cell population kinetic studies necessitates the use of computers. All the biological systems except those used for radiation studies are also employed in the study of a variety of alkylating agents. These compounds have considerable tissue specificity and some appear to have useful antitumour effect in some forms of malignancy.

The second approach rests on the belief that immediate advances in the techniques of radiotherapy are most likely to come about through close contact between research workers and medical men, and through a deliberate effort by the former to solve problems that arise in the experience of the latter. A device for the extracorporeal irradiation of the circulating blood of leukaemic patients has now been tested and has been applied to some suitable cases. Study of the response of monkeys to whole-body irradiation has given much information relevant to the care and management of patients who have been exposed to radiation or tumour chemotherapy and of the victims of radiation accidents. The problem confronting the radiotherapist in his attempt to achieve the maximum effect on the tumour while sparing adjacent normal tissue underlie much of the effort that has been made to measure the sensitivity of tissues to radiation and to study oxygen supply and other factors controlling this sensitivity.

STRANGEWAYS RESEARCH LABORATORY

Wort's Causeway, Cambridge

Director

Professor Dame Honor Fell, DBE, D SC, LL D, FRS (*Research Professor of the Royal Society*)

Deputy Director

A. Glucksmann, MD (*Senior Gibb Fellow, British Empire Cancer Campaign for Research*)

The Laboratory is an independent institution devoted to the study of cell biology. The property is vested in a Board of Trustees, and the management in a Board of five Governors, two of whom are nominated by the Medical Research Council. Usually between 30 and 35 graduate scientists, including guest workers, are accommodated.

During the year much attention has been paid to various aspects of skeletal physiology and pathology. Cultures of differentiated skeletal tissue have been extensively used for this work because cultures have the special advantage that both the tissue and its humoral environment are available for biochemical examination. For a detailed study of the synthetic activities of cartilage cells under different experimental conditions, a method (based on work carried out in the Experimental Biology Division of the National Institute for Medical Research) has been developed whereby mass cultures of chondrocytes differentiating in a chemically defined medium can be obtained from the cartilage of pigs. The factors concerned in maintaining the normal synthetic equilibrium between the various components of the skeletal matrix are being investigated by growing the embryonic limb-bones of the chick in medium to which hyaluronidase or collagenase has been added; such treatment, which selectively and continuously depletes one component of the matrix, changes the balance of the cell's synthetic activities during both treatment and subsequent regeneration.

The direct action on cartilage and bone of other experimental agents has been examined in chemically defined media. It has been found that ascorbic acid prevents excessive hydration of cartilage matrix, promotes ossification and maintains a normal ratio of hydroxyproline to hexosamine; the simultaneous addition of hydrocortisone raises the content of hydroxyproline-containing material above normal by reducing the amount released by the explants into the medium. The breakdown of extracellular material has been induced by complement-sufficient antiserum (a reversible effect) and also by means of hyperoxia; both the antiserum and the oxygen much increase the synthesis and release of lysosomal acid protease. The breakdown can be inhibited by either hydrocortisone or an inhibitor of the protease.

Surprisingly little is known about the properties and normal functions of the lysosomal enzymes; the major acid protease is therefore being purified and its characteristics examined. The physiological role of lysosomal enzymes has been investigated in several other biological systems. In the sheep lysosomal activity of the corpus luteum is greatly enhanced during its regression; in rats deficient in vitamin E the kidney lysosomes become very unstable, an effect that is aggravated by diets rich in highly unsaturated fatty acids. Lysosomal activity is known to be closely linked to endocytosis. This relationship is being studied in cells and tissues exposed to sucrose, which not only stimulates endocytosis but is found greatly to increase the synthesis and secretion of lysosomal enzymes; it is also being examined in macrophages during the ingestion of living bacteria.

Further work has been done on the membrane systems of the cell. Biochemical studies indicate that the agranular endoplasmic reticulum actively participates in the synthesis of glycoproteins. The immuno-chemical and physico-chemical properties of the plasma membrane are being investigated in cells of different types and in different physiological states.

Studies on the biological action and biochemical properties of retinol and retinoic acid have been continued, and the inhibitory effect of these agents on keratinization has been investigated. The uptake of radioactive vitamin A in the rat prostate gland in organ culture has been observed by autoradiography, and the chemical properties of retinol in an aqueous environment have been examined.

Developmental studies include experiments on the nutritional requirements of whole rat embyros in culture, and combined autoradiographic and histological analyses of the hair cycle in mice and of the cell growth cycle of the developing rat retina.

The biological importance of heavy metals, both in normal cell physiology and in carcinogenesis, has been investigated further. It has been found that nickel, cadmium and cobalt are incorporated into the nuclear material of sarcomas induced by these metals.

The action of carcinogens has been studied both in organ culture and *in vivo;* for example, human foetal lung grown in the presence of a highly purified fraction of hydrocarbons isolated from a condensate of cigarette smoke showed increased mitosis, hyperplasia and some squamous metaplasia of the bronchial epithelium. The effects of hormones on the ovary, prostate and epithelial component of the thymus have been investigated in organ culture; in a long series of experiments on rats, chemical carcinogenesis was found to be profoundly influenced by hormonal status. Another aspect of cancer research concerned the differences between malignant and non-malignant cell lines in culture in their response to various physical and nutritional factors.

In further experiments on mouse leukaemia, a new pteridine has been tested which cured a proportion of the mice treated; when subsequently reinoculated with leukaemic cells, these animals failed to develop the disease. More data have been obtained on the cellular mechanism through which testosterone stimulates the bone marrow in children suffering from aplastic anaemia.

Radiological work has included studies on intracellular dosimetry and on the relationship between varying degrees of chromosomal damage inflicted on individual cells with a microbeam and the cell's reproductive integrity. Long-term clinico-pathological research on the effects of radiotherapy on human carcinoma of the cervix has been continued, and recent results suggest that tumour type has a greater influence on survival rate than variation in the radiation dose received in treatment.

THE ROYAL INSTITUTION OF GREAT BRITAIN

21 Albemarle Street, London W.1

DAVY FARADAY RESEARCH LABORATORY

Director
Sir Lawrence Bragg, OBE, FRS

Assistant Director
Professor Ronald King, PH D

Since 1960, the Council have supported, by a means of a block grant, research into the structures of protein molecules at the Davy Faraday Research Laboratory. The Laboratory was set up in 1896 under an endowment by Dr Ludwig Mond ' to promote by original research the development and extension of chemical and physical science ' and is administered in trust by the Managers of the Royal Institution. It is financed partly by income derived from the original endowment and by donations from industrial organizations. For the last ten years the study of proteins has been a major part of the research and this has drawn substantial support from the United States National

Institutes of Health in addition to the Council's grant. Three members of the Council's external staff (see p.181) have been attached to the laboratory and have played a major part in leading the research, and there has always been close collaboration with the Council's Laboratory of Molecular Biology.

The primary aim of the research programme is the determination of the detailed atomic arrangements in protein molecules and the study of these arrangements in relation to biological function. The structures are being studied by X-ray diffraction methods and a significant contribution from the Laboratory has been the development of new apparatus and techniques, including automatic diffractometers, which have enabled such studies to be carried out more expeditiously.

Work is currently proceeding on the structure of lysozyme, lactoglobulin, rennin and seal myoglobin, and preliminary studies are being made of a number of other proteins. The study of lysozyme has been particularly fruitful, leading to a very clear image of the structure at a resolution of 2 Å, in which the amino acid arrangement can be closely correlated with chemical data on the sequence. It has also been possible to locate the position of attachment of certain inhibitor molecules to the lysozyme molecule and further study should throw light on the mechanism of the action of lysozyme on bacterial cell walls.

McINDOE MEMORIAL RESEARCH UNIT

Blond Laboratories, Queen Victoria Hospital, East Grinstead, Sussex

Director

Morten Simonsen, MD (*Honorary Professor, Royal College of Surgeons*)

The Unit, which is administered by the East Grinstead Research Trust, receives financial support from several sources, including the Leverhulme Trust as well as the Council. Its work, which is centred on the study of the biological problems of tissue transplantation, is chiefly concerned with two major aspects of this subject. First, the differences between strong and weak histocompatibility antigens are being studied by means of chemical and immuno-genetic investigations. Second, an important part of the work of the Unit is the study of the behaviour of grafted immunologically competent cells in chick embryos and mice. Particular attention is being paid to the study of the dynamics of cell populations during the course of graft-versus-host reactions. In addition, the Unit is investigating a syndrome of haemorrhagic diathesis in chick embryos produced by injection of normal allantoic fluids and inhibited by a normal serum factor.

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.

University of Birmingham

RESEARCH GROUP IN BASIC IMMUNOLOGY

Department of Experimental Pathology, The Medical School,
Birmingham 15
(Selly Oak 1301)

Director
Professor P. G. H. Gell, MB

The Group aims to investigate, on a long-term basis, the molecular and cytological genetics of antigen recognition and antibody formation. The study is continuing of the chemistry and inheritance of allotypes (genetically labelled γ-globulins) in rabbits, together with the relationship of this system to antibody production. This will be used as a model system to elucidate the biochemistry of γ-globulin and of antibody production in the cell.

Summary of research

1. Immunochemical study of allotypic determinants in rabbits.
2. Effects of antigen on normal and sensitized cells; biochemistry of the process of recognition of foreignness.
3. Immunological significance of lymphocyte blast transformation.
4. Phylogeny of immunological functions.

RESEARCH GROUP ON MECHANISMS OF MICROBIAL PATHOGENICITY

Department of Microbiology, The University,
Birmingham 15
(Selly Oak 1301)

Director
Professor H. Smith, D SC

The Group is investigating the chemical basis of mechanisms of microbial pathogenicity, with special reference to infections which show an apparent localization of growth in particular tissues. In addition, organisms isolated from infected animals will be examined for virulence attributes which hitherto may have gone unrecognized.

Summary of research

1. Nutritional basis of growth of *Vibrio fetus* in bovine foetal tissue.
2. Factors influencing the localization of trachoma in conjunctival tissue of primates.

VIRUS RESEARCH GROUP

Department of Virology and Bacteriology, The Medical School, Birmingham 15

(Selly Oak 1301)

Director

Professor N. P. L. Wildy, MB, FRSE

The Group is investigating the multiplication of animal viruses, with particular reference to the early phases of infection.

Summary of research

1. Isolation and characterization of the new enzymes and other proteins formed during virus growth.
2. Structure and assembly of herpes virus particles.

University of Bristol

RESEARCH GROUP ON NEUROSECRETION

Department of Pharmacology, The Medical School, Bristol 8

(Bristol 24161)

Director

Professor H. Heller, MD, PH D, MRCP

The Group aims to investigate neurosecretion in all its aspects by using morphological, biochemical and pharmacological approaches. Current investigations are chiefly concerned with the evolution of neurosecretory systems and their products.

Summary of research

1. Electron microscopy of neurosecretory neurones: changes in response to experimental stimuli.
2. Ultrastructural study of the neurosecretory systems of Annelids.
3. The occurrence of acetylcholine in the hypothalamo-neurohypophysial system in a variety of mammalian species; its possible significance in hormone release.
4. Chromatographic and pharmacological investigation of the active principles in the neurohypophysis of elasmobranchs.
5. Chemistry of neurohypophysial hormones of reptiles and elasmobranchs.
6. Chemical structure of the protein carrier of neurohypophysial hormones.

University of London

RESEARCH GROUP ON CONTROL OF PROTEIN BIOSYNTHESIS IN ANIMAL CELLS

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

(Temple Bar 5454)

Director

Professor H. R. V. Arnstein, D SC

The long-term aim of the Group is to investigate the biochemical mechanisms controlling the synthesis of specific proteins, particularly during cell differentiation and development.

Summary of research

1. Control of chain initiation in haemoglobin biosynthesis.
2. Isolation and fractionation of haemoglobin messenger RNA (with Dr R. A. Cox, National Institute for Medical Research).
3. Effect of homologous and heterologous messenger RNA on cell-free protein biosynthesis.
4. Structure and function of ribosomal RNA.

RESEARCH GROUP ON THE BIOLOGY OF AGEING

Department of Zoology, University College London, W.C.1
(Euston 7050)

Director
A. Comfort, MB, D SC

The Group is concerned with the documentation and study of ageing processes at all levels, in man and animals and in cells and tissues. A library and information service on ageing is maintained.

Summary of research

1. Animal statistics:
   (*a*) Ageing patterns in captive fish populations.
   (*b*) Analysis of mammalian age records.
2. Ageing processes and causes of death in cells fixed in the postmitotic phase:
   (*a*) Nature and histology of the senile changes in striped muscle.
   (*b*) Survival of *Drosophila* imagos and the temperature coefficient of imaginal longevity.
   (*c*) Protein turnover and marker incorporation in *Drosophila* imago protein.
   (*d*) Longevity and histochemical studies in nematodes.
3. Descriptive pathology of age processes in *Lebistes* spp.(with Dr A. Woodhead and Mrs S. Ellett, Ministry of Agriculture, Fisheries and Food Fisheries Laboratory, Lowestoft).
4. Irradiation studies in *Drosophila* (with Dr M. J. Lamb, Radiobiological Research Unit).

CEREBRAL FUNCTIONS RESEARCH GROUP

Department of Anatomy, University College London, Gower Street, W.C.1
(Euston 7050)

Director
J. de C. Downer, PH D

The basic aim of the Group is the investigation of brain mechanisms involved in sensorimotor integration, learning and memory, and the role of the limbic system in experimentally induced psychopathological states.

Summary of research

1. Role of brain commissures in mediating non-visual crossed tactile placing reactions.
2. Prism-induced errors in visuomotor guidance in the normal and ' split-brain ' monkey.
3. Exploration of the neocortex to localize the area subserving temperature sensibility.
4. Transfer of monocularly learned visual discrimination habits in monkeys following midsagittal division of the optic chiasma and following unilateral resection of the visual association areas and the inferior temporal neocortex.
5. Quantitative biochemical changes in the level of DNA, RNA and in DPNH-diaphorase activity of the lateral geniculate nucleus following unilateral suppression of the optic nerve.
6. The effect of bilateral removal of the amygdaloid nucleus on the transfer of visual learning.
7. Differences in memory functions (recognition and recall) following extensive extirpation of the hippocampal complex.

RESEARCH GROUP IN HAEMOLYTIC ANAEMIA

Department of Haematology, University College Hospital Medical School, Gower Street, London W.C.1

(Euston 5861)

Director

Professor T. A. J. Prankerd, MD, FRCP

The aims of the Group are to study the causation of haemolytic anaemias at the biochemical, cellular and clinical levels.

Summary of research

1. Haemoglobin synthesis in normal and thalassaemic red cell precursors.
2. Determination of the molecular abnormality in various abnormal haemoglobins.
3. Dissociation of haemoglobin.
4. Transport of iron to the foetus and into body stores.
5. Methods of detecting organ pooling of red cells in man and the relevance of pooling to red cell survival and dilution anaemia.
6. Metabolic changes in human red cells during *in vitro* incubation and in haemolytic anaemias.

RESEARCH GROUP ON RENAL INFECTION

Department of Medicine, Charing Cross Hospital Medical School, Fulham Hospital, London W.6

(Riverside 9161)

Director

Professor Hugh E. de Wardener, MBE, MD, FRCP

The Group is studying the incidence, aetiology, diagnosis and treatment of renal infection.

Summary of research

1. Prevention of pyelonephritis of pregnancy; incidence of prematurity and foetal abnormality in bacilluria of pregnancy.
2. Controlled trial of long- and short-term administration of antibiotics in acute and chronic pyelonephritis.
3. Value of cineradiology in diagnosing chronic pyelonephritis.
4. Intrarenal localization of isotopically labelled antibiotics in isolated perfused kidney.
5. The urinary protein pattern in renal disease.
6. Long-term follow-up of patients who have had bacilluria of pregnancy.

RESEARCH GROUP ON RESPIRATION AND ENERGY METABOLISM IN THE NEWBORN

Department of Physiology, The London Hospital Medical College, Turner Street, London E.1

(Bishopsgate 5454)

Director

Professor K. W. Cross, MB, D SC, FRCP

The Group is engaged in studies on the oxygen consumption, ventilation and lung mechanics of the newborn in relation to age, environmental temperature and oxygen pressure. The subjects of the study are normal and sick newborn infants as well as laboratory animals.

Summary of research

1. Minimal oxygen consumption of the normal full-term infant and the premature infant at birth, and the change of the oxygen consumption with age.
2. Thermogenic response of the normal full-term infant and the premature infant to an environment below the critical temperature.
3. Metabolic potential of babies who have suffered cold injury.
4. Studies on thermoregulation in babies with congenital defects of heat control.
5. Oxygen consumption related to environmental temperature in babies of diabetic mothers and babies with the respiratory distress syndrome, anencephaly or other abnormality.
6. Ventilatory response to varying environmental temperatures when the environment of the face is different from that of the body.
7. Lung mechanics in normal babies and in babies who have suffered respiratory distress.
8. The treatment of asphyxia neonatorum, in the baby and in the experimental animal.

RESEARCH GROUP ON GLYCOGEN METABOLISM

Royal Free Hospital School of Medicine,
8 Hunter Street, London W.C.1
(Terminus 5385)

Director
Professor W. J. Whelan, D SC, FRIC

The Group is studying all pathways of glycogen metabolism lying between glucose, its derivatives and the polymer. Special emphasis is placed on hydrolytic pathways of degradation since these are now recognized to be of major importance. The Group is also acquiring expertise in the examination and typing of glycogen-storage diseases, congenital disorders of metabolism that lead to malfunctioning in the muscles, liver, heart, blood cells and other organs of glycogen storage.

Summary of research

1. Characterization of glycogen in erythrocytes and leucocytes and new methods for its determination.
2. Glycogen-hydrolysing enzymes of skeletal muscle and liver; their purification and characterization, with special reference to the hydrolysis of the branch linkages of glycogen.
3. Synthesis of specific substrates for the glycogen-debranching enzymes, suitable for enzyme assay in tissue biopsies.
4. Enzymic synthesis of the branch linkages of glycogen.
5. Reactivity of glycogen towards enzymes as a function of molecular weight and molecular surface area.
6. Correlation of glycogen-metabolizing enzymes of animals with those of the glycogen-storing plant sweet corn (*Zea mays*).

RESEARCH GROUP IN ENZYMOLOGY

Department of Chemical Pathology, St. Mary's Hospital Medical School,
London W.2
(Ambassador 1280)

Director
Professor A. Neuberger, CBE, MD, PH D, FRCP, FC PATH, FRS

The work of the Group is concerned mainly with the control mechanisms involved in the adaptation of photosynthetic bacteria to anaerobic metabolism in the light and aerobic metabolism in the dark. The work is also concerned with the characterization of various enzymes involved in the biosynthesis of haems and chlorophylls and of lipids and proteins in these organisms.

Summary of research

1. Involvement of lipids or lipoproteins in the chelation of iron with porphyrins to give haem and in the formation of the magnesium–protoporphyrin complex.
2. Changes in particulate protein and in phospholipid that take place when photosynthetic bacteria adapt to anaerobic conditions.
3. Resemblance between the enzymatic composition of chromatophores and the cytoplasmic membrane fraction.

RESEARCH GROUP IN IMMUNOCHEMISTRY

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

(Paddington 1664)

Director

Professor R. R. Porter, PH D, FRS

The Group is investigating the chemical structure of immunoglobulin and its relation to antibody specificity. It is also studying the basis of the antigenic specificity of myoglobin.

Summary of research

1. Amino acid sequence of the heavy chain of pathological human IgG.
2. *N*- and *C*-terminal of the Fd-fragment of normal rabbit IgG.
3. Structure of peptides from myoglobin which retain the capacity to combine with rabbit antimyoglobin.

CLINICAL RESPIRATORY PHYSIOLOGY RESEARCH GROUP

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

(Shepherds Bush 2030)

Director

J. B. West, MD, PH D

This Group is studying the physiological mechanisms controlling the distribution of blood flow and ventilation in the lung. Studies are made of the normal lung and of patients with lung and heart disease.

Summary of research

1. Site of vascular resistance in the lung.
2. Effect of lung volume history on the distribution of blood flow.
3. Distribution of ventilation in isolated lung.
4. Effect of pulsatility of pulmonary arterial pressure on the distribution of pulmonary blood flow.
5. Topographical differences in lung morphology.
6. Diffusion rates of gases in lung airways.

RESEARCH GROUP ON HAEMOLYTIC MECHANISMS

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

(Shepherds Bush 2030)

Director

Professor J. V. Dacie, MD, FRCP, FC PATH

The Group is studying the mechanism of haemolysis in various types of haemolytic anaemia. The complex interrelationship between coagulation *in vivo* and haemolysis is also being examined.

Summary of research

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1. The mechanism of haemolysis after the administration of coagulants to laboratory animals.
2. A clinical study of patients presenting with the haemolytic–uraemic syndrome, with particular reference to the value of heparin in treatment.
3. Haemolytic anaemia developing in patients taking the anti-hypertension drug α-methyl dopa; the pathogenesis of the apparent autoimmunization.

RESEARCH GROUP FOR THE STUDY OF MEGALOBLASTIC ANAEMIAS*

Postgraduate Medical School of London,
Ducane Road, London W.12
(Shepherds Bush 2030)

Director
Professor D. L. Mollin, MB, B SC, MRCP, MC PATH

The Group is concerned with the study of the pathogenesis of megaloblastic anaemia and with the metabolism of vitamin B_{12}, folic acid and pyridoxine. It acts as the reference centre for studies on vitamin B_{12} and folic acid for the WHO Research Project on Nutritional Anaemias and is responsible for the coordination of the Wellcome Research Study on Tropical Nutritional Anaemia. The Group also carries out B_{12}, folic acid and iron assays for the MRC Laboratories in the Gambia.

Summary of research

1. Determination of the severity and cause of the widespread folate deficiency revealed by new methods of studying folic acid metabolism.
2. Interrelationship of the function of vitamin B_{12} and folic acid.
3. Definition and classification of the group of conditions referred to as the sideroblastic anaemias.
4. Experimental production of sideroblastic anaemia in animals.
5. Development of biochemical and microbiological methods for investigating pyridoxine metabolism in man.

RESEARCH GROUP IN IMMUNOLOGY

Institute of Child Health, The Hospital for Sick Children,
Great Ormond Street, London W.C.1
(Holborn 9200)

Director
J. F. Soothill, MB, MRCP

The main aim of the Group is the study of immunopathological disease in childhood, especially the antibody deficiency syndrome and glomerulonephritis.

Summary of research

1. Collection of quantitative data on immunoglobulin levels and on antibody and cellular immune responses to antigens of various physical forms in healthy children at different ages.
2. Abnormalities of immune mechanisms (specific and nonspecific) in congenital rubella (with the Department of Virology).
3. Characterization of functionally defective immunoglobulins in the antibody deficiency syndrome.
4. Detailed characterization of patients with steroid-resistant nephrotic syndrome; comparative study of immunosuppressive agents (with the Department of Paediatric Medicine).

*Dr Mollin has recently been appointed Professor of Haematology at St. Bartholomew's Hospital Medical College and the Group will be moving to St. Bartholomew's later this year.

RESEARCH GROUP ON THE IMMUNOLOGICAL ASPECTS OF DERMATOLOGY

Institute of Dermatology, St. John's Hospital for Diseases of the Skin, Homerton Grove, London E.9

(Amherst 7061)

Director

J. L. Turk, MD, MC PATH

The Group is investigating the mechanism of contact sensitivity and delayed hypersensitivity in the guinea pig. The work is particularly concerned with certain large pyroninophilic cells present in greatest concentration four days after primary contact with a sensitizing agent, one day before the animal begins to manifest sensitivity. The Group is also instituting research on the development and application of immunological methods and techniques for the investigation of skin diseases.

Summary of research

1. Chemical characterization of proteins and peptides produced by large pyroninophilic cells, using the techniques of immunofluorescence, incorporation of ^{14}C-labelled amino acids, autoradio-immunoelectrophoresis and ion-exchange chromatography.
2. Cytochemistry of cells during the development of contact sensitivity.
3. Investigation of the chemical contact sensitizing agent involved in the 'Dogger Bank Itch'.
4. Investigation of the possible immunological basis of certain skin diseases (with the clinical staff of St. John's Hospital).

CLINICAL IMMUNOLOGY RESEARCH GROUP

Institute of Diseases of the Chest, Brompton Hospital, London S.W.3

(Flaxman 3707)

Director

J. Pepys, MB, MRCP

The Group is investigating the immunological responses in man to the common pathogenic and non-pathogenic fungi, to organic vegetable dusts, dusts of animal origin, and to mycobacteria, and the relationship of the immunological findings to clinical manifestations in pulmonary disorders. Controlled studies in the management of allergic disorders are being conducted.

Summary of research

1. (*a*) Separation and identification of antigens and allergens from *Aspergillus fumigatus* and their investigation in patients suffering from broncho-pulmonary aspergillosis.
   (*b*) Incidence of *A. fumigatus* infection in patients with open-healed cavities in treated pulmonary tuberculosis (with the British Tuberculosis Association).
2. (*a*) Nature and development in mouldy hay and other vegetable matter of antigens responsible for farmer's lung, and their testing in affected subjects; antigenic composition of vegetable matter produced under laboratory conditions (with Dr P. H. Gregory, Rothamsted Experimental Station).
   (*b*) Epidemiological and immunological aspects of farmer's lung.
   (*c*) Epidemiological and immunological aspects of fog fever in cattle (with the Veterinary Clinical Observation Unit).
   (*d*) Antigenicity of mesophilic and thermophilic actinomycetes in man and animals.
3. (*a*) Nature of antigens in bird excreta responsible for bird breeder's (fancier's) lung; investigations of the clinical and other features of this disease and of other examples of farmer's lung type of disease.
   (*b*) Nature and development in various vegetable and other organic dusts of antigens relevant to immunological responses in exposed subjects: correlation of results with clinical findings.
   (*c*) Antigenic relationships between vegetable dusts and other mycological flora.

4. Immunological responses in man to the antigens of *Mycobacterium tuberculosis* and the 'atypical' mycobacteria.
5. Analysis of clinical features and immunological mechanisms in 'extrinsic' and 'intrinsic' asthma.
6. Controlled studies of the role of allergy to house dust in asthma and the effects of specific hyposensitization (with the British Tuberculosis Association).

RESEARCH GROUP IN APPLIED NEUROBIOLOGY

Institute of Neurology, Queen Square, London W.C.1
(Terminus 3611)

Director
J. B. Cavanagh, MD, MRCP

The general aim of this Group is to study the relationships of the supporting and neuroglial cells in the peripheral and central nervous system to nerve cells and axons.

Summary of research

1. Fine structure of the Ranvier's nodes.
2. Fine structure of the muscle spindle.
3. Protein synthesis of Schwann cells.
4. Action of diphtheria toxin on Schwann cells.
5. Metabolic lesion in organophosphorus and other experimental neuropathies.
6. Quantitative cell relationships around a brain wound.

OCULOGENITAL VIRUS RESEARCH GROUP

Virus Research Laboratory, Department of Clinical Ophthalmology, Institute of Ophthalmology, Judd Street, London W.C.1
(Euston 9621)

Director
Professor Barrie R. Jones, B SC, MB, FRCS

The Group is interested in certain aspects of the biology of TRIC agent, a member of the psittacosis–lymphogranuloma–trachoma (PLT) group of agents, and in disease caused by this agent. It is particularly concerned with TRIC agent infection of the eye in adults and the newborn, and with associated disease of the genital tract; patients with nonspecific urethritis or with Reiter's disease and the sexual contacts of these patients are being investigated. The relationship between TRIC agent and the agent causing lymphogranuloma venereum is being studied. Attempts are being made to evaluate the importance of mycoplasmas and trichomonads in ocular and genital infection. Clinical, virological, immunological and epidemiological methods are employed in this work.

Summary of research

1. Clinical, cytological and microbiological studies to detect TRIC agent, mycoplasmas, trichomonads and other infective agents in:
   (*a*) the eye and genital tract in cases of trachoma and inclusion conjunctivitis, in both adults and the newborn;
   (*b*) the urethra in cases of nonspecific urethritis, the urethra, eye and joints in cases of Reiter's disease;
   (*c*) the genital tract of the sexual contacts of patients with trachoma, inclusion conjunctivitis, nonspecific urethritis and Reiter's disease.

(Dr D. Taylor-Robinson, Common Cold Research Unit, Salisbury, and Professor C. F. Barwell and Dr A. E. Wilkinson, The London Hospital, are collaborating in these studies.)

2. Comparison of established cytological methods, fluorescent-antibody methods and virus isolation methods in the diagnosis of TRIC agent infections.
3. Immunofluorescent methods in the estimation of local and general immunological response in patients with TRIC agent infection.
4. Electron microscope studies of TRIC agent with respect to antigenic structure.
5. Production of hypersensitivity to TRIC agent and related microorganisms in experimental animals; its role in the formation of pannus in trachoma.
6. Determination of the range of animal hosts and of the pathogenicity of TRIC agent and clarification of the relationship between it and other members of the PLT group.
7. Epidemiology of TRIC agent infections, with special reference to their sexual transmission in the United Kingdom.

RESEARCH GROUP IN MEDICAL DEMOGRAPHY

Department of Medical Statistics and Epidemiology,
London School of Hygiene and Tropical Medicine,
Keppel Street and Gower Street, London W.C.1
(Museum 3041; Langham 7621)

Director
W. Brass, MA

Medical demography is concerned both with the effects of changes in population size and structure on disease (particularly in terms of vital statistics and morbidity) and with the influence of medical developments on population characteristics. The main sources of material for investigation are population censuses, vital registration and special surveys. The Group has been established to carry out theoretical and applied research on the interrelations of population distribution and disease incidence, the uses of demographic techniques in the study of medical problems and the development of methods for improving the reliability of vital and health statistics and for deriving significant measures from them.

Summary of research

1. Techniques for the projection of time series of fertility and mortality rates as an aid to forecasting.
2. Comparison of mathematical models of the age incidence of mortality with observations and uses of the models for forecasting and for adjusting unreliable data.
3. Birth spacing and infant mortality rates.
4. Loss and replacement in the medical practitioner population of Great Britain.
5. Trends of mortality in Europe classified according to cause of death.

RESEARCH GROUP ON THROMBOSIS

Department of Pharmacology, Royal College of Surgeons of England,
Lincoln's Inn Fields, London W.C.2
(Holborn 3474)

Director
Professor G. V. R. Born, MB, D PHIL

The Group is concerned with research into chemical substances which promote or prevent the adhesion and aggregation of platelets in the blood and which affect the formation of thrombi.

Summary of research

1. Mechanisms that cause blood platelets to adhere to vascular endothelium and to each other to form aggregates *in vivo* and *in vitro*.
2. Experimental production of thrombosis in animals and its inhibition by chemical substances.
3. Influence of chemical substances on thrombogenesis in man.
4. Biochemical mechanism controlling the concentrations of circulating platelets in animals and in man.
5. Effects on the microcirculation of drugs and other active substances applied by iontophoresis.

University of Newcastle upon Tyne

RESEARCH GROUP ON THE RELATION OF FUNCTIONAL TO ORGANIC PSYCHIATRIC ILLNESS

Department of Psychological Medicine, 11 Framlington Place, Newcastle upon Tyne 2

(Newcastle 25136)

Director

Professor M. Roth, MD, FRCP, DPM

The Group is specially concerned with investigations 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 in order 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 and (*c*) anxiety neurosis; computer analysis of a large number of items to assess the relative discriminating value of a wide range of physical and psychiatric features.
2. Neuropathology of functional and organic mental disorders in old age.
3. Relationship between clinical and psychometric scores of dementia and quantitative assessment of cerebral degenerative change in old people at necropsy.
4. The contributions of genetic, organic and environmental factors to the aetiology of schizophrenia, studied by:
   (*a*) systematic psychiatric and medical evaluation of a consecutive sample of schizophrenic patients;
   (*b*) psychometric and EEG investigations;
   (*c*) a comprehensive family survey in which genetic and environmental factors, together with current personality features, are assessed in first-degree relatives.
5. Computer analysis of psychiatric and social observations in patients suffering from anxiety, phobic and depressive states.
6. Biochemical and physiological changes associated with affective disorders.

University of Oxford

RESEARCH GROUP ON ADRENERGIC MECHANISMS

University Laboratory of Physiology, Oxford

(Oxford 57451)

Director

Professor Sir Lindor Brown, CBE, MB, M SC, FRCP, FRS

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 noradrenaline by the isolated perfused spleen.
2. Factors controlling storage and synthesis of transmitter.

University of Sheffield

RESEARCH GROUP ON BIOCHEMISTRY AND PHYSIOLOGY OF INTRACELLULAR ORGANELLES

University Department of Biochemistry, Sheffield 10

(Sheffield 78555)

Director
Professor W. Bartley, PH D

The Group is studying the metabolic implications of the segregation of biochemical reactions within organized subcellular structures.

Summary of research

1. Measurement of turnover rates of mitochondrial constituents, particularly protein fractions and phospholipids.
2. Role of the essential fatty acids (EFA): studies on the effect of EFA deficiency in rats on liver mitochondria and intestinal function coupled with electron microscope studies of the ultrastructure of deficient tissues.
3. Development of a ferritin-labelled antibody technique for specific staining of preparations for electron microscopy.
4. Structure of ferritin.
5. Immunochemical studies on the morphogenesis of yeast mitochondria.
6. Immunochemical localization of enzymes in plant tissues.
7. Enzyme changes in the tissues of rats deficient in EFA.
8. Enzyme and structural changes produced in yeast in response to changed growth conditions.

RESEARCH GROUP ON INTESTINAL ABSORPTION

University Department of Physiology,
Western Bank, Sheffield 10

(Sheffield 78555)

Director
Professor D. H. Smyth, MD

The Group is concerned with a study of absorption from the intestine by *in vivo* and *in vitro* methods. One of the main objects is to attempt to locate in the epithelial cells the processes related to transfer. Most of the work so far has been done with the rat, but it is now proposed to extend these studies to other species, with particular emphasis on young animals at different stages of development.

Summary of research

1. Transfer of amino acids and peptides.
2. Transfer of hexoses.
3. Transfer of sodium and fluid.
4. Transfer of volatile fatty acids and their glycerides.
5. Electrical changes in the epithelial cell in relation to transfer.
6. The sources of energy for transfer processes and the competition between different systems for this energy.

University of Southampton 227

RESEARCH GROUP IN TISSUE TRANSPLANTATION IMMUNOLOGY
University Department of Zoology, Southampton
(Southampton 56331)

Director
Professor L. Brent, PH D

The Group is studying the immunological basis of tissue graft rejection, with emphasis on the cellular antibodies thought to play a dominant role in the mechanism of rejection.

Summary of research

1. Cellular antibodies in graft rejection and delayed hypersensitivity.
2. Investigation of the normal lymphocyte transfer reaction using isotopically labelled cells.
3. Specificity and nature of antilymphocyte antibody.

University of Sussex

RESEARCH GROUP FOR GENETIC AND BIOCHEMICAL STUDIES ON BACTERIA AND BACTERIAL VIRUSES
School of Biological Sciences, University of Sussex, Falmer, Brighton
(Brighton 66755)

Director
Professor N. Symonds, PH D

The Group is engaged in a number of studies that centre on the metabolism of DNA in bacteria and especially on those aspects that involve repair and recombination.

Summary of research

1. Mechanism of host-controlled modification in *Escherichia coli.*
2. Behaviour of bacterial and bacteriophage mutants unable to complete successfully the process of genetic recombination.
3. Thymine metabolism in *E. coli* and the physico-chemical basis of death following deprivation of thymine.

University College of South Wales and Monmouthshire

RESEARCH GROUP ON THE BIOCHEMISTRY OF CONNECTIVE AND LUNG TISSUES
Department of Biochemistry, University College of South Wales and Monmouthshire, St. Andrew's Place, Cardiff
(Cardiff 24892)

Director
Professor K. S. Dodgson, D SC

The Group is engaged on fundamental biochemical studies on the connective tissues and on the response of lung tissue to the stimulus of mineral particles.

Summary of research

1. Molecular status of heparin in relation to the fine structure of mast granules from loose connective tissue and serous fluid.
2. Metabolism of heparin.

3. Metabolic routes involved in the disposal of connective tissue aminopolysaccharides in mammals.
4. Enzymes as analytical tools in studies on connective tissue constituents.
5. Purification and properties of hyaluronidases and chondroitinases.
6. Biochemical changes induced in mammalian lung in response to coal and silica dusts.
7. Ultracentrifuge examination of sera from patients exhibiting Caplan's syndrome.
8. Effects of ionizing radiations on compounds related to aminopolysaccharides.

RESEARCH GROUP ON THE STRUCTURE AND FUNCTIONS OF MICROORGANISMS

Microbiology Department, University College of South Wales and Monmouthshire, Cathays Park, Cardiff

(Cardiff 23590)

Director
Professor D. E. Hughes, PH D, F INST BIOL

The Group is investigating the relationship between structure and function in bacteria, algae and protozoa. Particular attention is paid to enzyme systems bound in membraneous structures such as mitochondria and to the effect of physical methods of isolation, including ultrasonics.

Summary of research

1. Relationship between a soluble cytochrome *c* and hydrogenase.
2. Control of coenzyme levels in bacteria.
3. Mitochondria of colourless algae.
4. Amino acid and fatty acid metabolism in algae and fungi.
5. Biological effects of mechanically and sonically generated liquid shear gradients.

University of Edinburgh

RESEARCH GROUP ON BACTERIAL ENZYME VARIATION

University Department of Molecular Biology, West Mains Road, Edinburgh 9

(Newington 1011)

Director
Professor M. R. Pollock, MB, FRS

The general aims of the Group are to study the molecular basis for the genetic and environmental control of the biosynthesis and function of bacterial enzymes.

Summary of research

1. Transformation of penicillinase and other markers in *Bacillus licheniformis*.
2. Specific control of penicillinase biosynthesis in *Staphylococcus aureus*.
3. Compatibility relationships amongst plasmids controlling penicillinase synthesis in *Staphylococcus aureus*.
4. Properties of altered penicillinase proteins formed by penicillinase-loss mutants of *Bacillus licheniformis*.

EPIGENETICS RESEARCH GROUP

Institute of Animal Genetics, West Mains Road,
Edinburgh 9
(Newington 1011)

Director
Professor C. H. Waddington, CBE, SC D, FRS

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 microscope 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 and experimental study on certain enzyme systems in *Neurospora*.
5. Synthesis of ribosomal RNA in normal and anucleolar embryos of *Xenopus* and determination of the number of DNA cistrons coding for ribosomal RNA.
6. Sedimentation constants of the RNAs synthesized in different tissues at various stages of early embryonic development in newt and chick embryos.
7. Effects of inhibitors of DNA or RNA synthesis on the development of competence, on the evocation reaction and on short-term differentiation in newt embryos.
8. Statistical mechanics of systems involving feed-back and biological rhythms.

RESEARCH GROUP FOR THE STUDY OF GENETIC PROBLEMS IN ORTHOPAEDIC DISEASES

University Department of Orthopaedic Surgery, 12 George Square,
Edinburgh 8
(Newington 1011)

Director
Professor J. I. P. James, MS, FRCS

The work of this Group is concerned with genetic and other factors in the causation of developmental abnormalities of the locomotor system in man, and with the role of inheritance in orthopaedic disease.

Summary of research

1. Genetics of congenital dislocation of the hip and of congenital and idiopathic scoliosis.
2. Abnormalities of the skeleton associated with chromosome anomalies (with the Clinical Effects of Radiation Research Unit and with Mr J. Chalmers, Department of Orthopaedic Surgery, University of Edinburgh).

RESEARCH GROUP ON THE EXPERIMENTAL AND CLINICAL PROBLEMS OF TRANSPLANTATION

University Department of Surgical Science, Edinburgh 8
(Newington 5272)

Director
Professor M. F. A. Woodruff, MD, D SC, MS, FRCS

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. Immunosuppressive properties of heterospecific antilymphocytic serum.
2. Specific immunological tolerance of homotransplants.
3. The role of enhancing antibody in (*a*) prolonged survival of homotransplants; (*b*) the escape of tumours from immunological control and their resistance to immunotherapeutic procedures.
4. Autoimmune haemolytic anaemia in mice.
5. Evidence for the transformation of lymphocytes into macrophage during graft-versus-host reaction and after stimulation of the reticuloendothelial system with *Corynebacterium parvum*.
6. Induction of antibody formation *in vitro* by adding RNA fractions prepared from spleens and Kupffer cells of mice injected with T4 bacteriophage to lymphocytes.
7. Reticuloendothelial function during BCG-modified graft-versus-host reaction and the neonatal-thymectomy syndrome.
8. Experimental immunotherapy of cancer, with special reference to the use of sensitized immunologically competent cells.
9. Clinical study of renal isografts and homografts, including the development of techniques for the prolonged maintenance of a sterile environment.

RESEARCH GROUP ON THE ORGANIZATION OF CENTRAL MECHANISMS SUBSERVING VISION

Department of Physiology, University Medical School,
Teviot Place, Edinburgh 8
(Newington 1011)

Director
Professor D. Whitteridge, DM, FRCP, FRS

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 of visual patterns.

Summary of research

1. Normal pattern and regeneration of optic nerves in the goldfish.
2. Sensitivity to movement in the superior colliculus.
3. Relations between Visual I, II and III.
4. Callosal connections in the visual cortex.

University of Glasgow

RESEARCH GROUP IN ADRENAL AND ENDOCRINE PATHOLOGY

University Department of Pathology, Royal Infirmary, Glasgow C.4
(Bell 3535)

Director
Professor T. Symington, MD, B SC, FRIC, FRCPG, FC PATH, FRSE

The general aim of the Group is the relation of the structure of the adrenal gland to its function under normal and pathological conditions.

Summary of research

1. Investigation of vascular anatomy, physiology and pathology of adrenal glands, particularly of muscular veins.
2. *In vitro* studies on adrenal gland:
   (*a*) Androgen formation, particularly C-7-oxygenated steroids.
   (*b*) Intermediates in aldosterone biosynthesis in Conn's syndrome adenomas.
   (*c*) Steroid synthesis in the presence of ACTH and actinomycin D.

3. Preparation of ACTH with high specific activity, for autoradiographic and electron microscope investigation of the site of ACTH action in the adrenal.
4. Electron microscope investigation of the structure of adrenal mitochondria in normal and pathological conditions.
5. (*a*) Plasma binding of adrenal steroids.
   (*b*) Mechanism of potentiation by corticosteroids of catecholamine action on vascular smooth muscle.

University of Strathclyde

BIOMECHANICS RESEARCH GROUP

Bio-engineering Unit, Department of Mechanical Engineering,
University of Strathclyde, Glasgow C.1
(Bell 4400)

Director
Professor R. M. Kenedi, PH D, ARCST, AMI MECH E, AFR AE S, FRSE

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.

Summary of research

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.
   (*d*) Histological studies of stressed skin (with Dr J. E. Craik and Dr I. R. R. McNeil, Victoria Infirmary, Glasgow).
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 the movement of the rib cage.
   (*c*) Development of techniques for the transplantation of the articular cartilage of the hip joint.

Research Work Aided by Grants

The Council have always attached much importance to their scheme of grants. These are awarded, normally for a three-year period, to research workers who are not members of their own staff for particular research projects carried out at universities and other centres. Such grants may be for the personal remuneration of individual workers, for the provision of scientific and technical assistance, or for special research expenses. The cost of grants is mostly met from the Council's grant-in-aid, and special reference is made where this is not the case. Grants are also given in a limited number of cases to universities for the purchase of costly equipment ('Special Departmental Apparatus') which will advance the work of one or more departments. These grants are specifically indicated in the following list, which includes grants awarded up to the end of 1965. Information about the number of grants awarded by the Council and the acceptance rate of applications will be found on p. 18.

Aberdeen

ROWETT RESEARCH INSTITUTE

Enzymology Department

Dr G. A. LEVVY—glycosidases, with particular reference to the structure of glycoproteins. (1)

TEACHING HOSPITALS

Dr W. N. ROLLASON—use of nitrous oxide-oxygen mixtures for the relief of postoperative pain. (2)

UNIVERSITY

Biological Chemistry Department

Dr D. C. BURKE—production of interferon. (3

Dr J. W. PORTEOUS—biochemical and electron microscope investigations on intestinal epithelium. (4)

Dr J. L. SIMKIN—role of the microsome material in protein biosynthesis in mammalian cells. (5)

Chemical Pathology Department

Professor S. C. FRAZER and Mr W. MICHIE—thyroidectomy and parathyroid function (also at Aberdeen Royal Infirmary and the Rowett Research Institute). (6)

Mr N. G. C. HENDRY—relationship of glycosidases to abnormalities of connective tissue (also at Aberdeen Royal Infirmary). (7)

Child Health Department

Professor R. G. MITCHELL—respiratory distress syndrome of newborn infants (also at Aberdeen Maternity Hospital). (8)

Materia Medica and Therapeutics Department

Dr P. S. BROWN—study of anterior pituitary function by the assay of gonadotrophin. (9)

Dr J. CROOKS—thyroid function and iodine metabolism in normal and abnormal pregnancy. (10)

Dr J. M. STOWERS—metabolic defects in diabetes mellitus, with particular reference to fat metabolism. (11)

Medical Physics Department

Professor J. R. MALLARD—development of improved quantitative scanning techniques for radioisotope localization. (12)

Mental Health Department

Professor W. M. MILLAR—(1) relationship between the mental health services and psychiatric morbidity in the North-East of Scotland; (2) computer assistance and programming for psychiatric research. (13)

Natural History Department

Dr D. M. GUTHRIE—physiology of regenerating nerve fibres in insects. (14)

Obstetrics and Gynaecology Department

Professor Sir Dugald BAIRD—(1) social factors in the aetiology of carcinoma of the cervix uteri; (2) assay of oestriol and pregnanediol in urine. (15)

Dr A. I. KLOPPER—functions of steroid hormones in pregnancy. (16)

Dr A. C. TURNBULL—uterine activity, with special reference to prolonged pregnancy and labour. (17)

Physiology Department

Dr C. V. GREENWAY—cardiac output, regional blood flow and oxygen uptake in haemorrhagic shock. (18)

Professor J. L. MALCOLM—the sera of schizophrenic patients, with particular reference to their effects on the cerebral cortex in animals. (19)

Surgery Department

Mr N. A. MATHESON—intravascular red cell aggregation. (20)

Professor G. SMITH—hyperbaric oxygenation for the treatment of barbiturate coma, coronary artery occlusion and left ventricular failure and in tissue culture. (21)

Alverstoke

ROYAL NAVAL MEDICAL SCHOOL

Professor W. L. M. PERRY—the causation and treatment of motion sickness. (22)

Ascot

IMPERIAL COLLEGE FIELD STATION

Zoology and Applied Entomology Department

Dr Elizabeth U. CANNING—mode of sexual differentiation in *Coccidia.* (23)

Aylesbury

ST. JOHN'S HOSPITAL

Dr J. L. CRAMMER and Dr D. C. WATT—relation of the metabolism of imipramine to clinical response. (24)

STOKE MANDEVILLE HOSPITAL

National Spinal Injuries Centre

Sir Ludwig GUTTMANN—effects of disease and injury to the spinal cord. (25)

Oxford Regional Rheumatic Diseases Research Centre

Dr A. G. S. HILL—connective tissue disorders. (26)

Babraham

AGRICULTURAL RESEARCH COUNCIL INSTITUTE OF ANIMAL PHYSIOLOGY

Dr Ruth DEANESLY—reproductive physiology of the guinea pig. (27)

Dr R. A. MILLAR—(*a*) acid-base changes and baroreceptor and sympathetic activity during general anaesthesia; (*b*) respiratory and metabolic changes during prolonged neurosurgical operations (also at Addenbrooke's Hospital, Cambridge). (28)

Barton-on-Humber

PUBLIC HEALTH DEPARTMENT

Dr J. S. ROBERTSON—toxoplasmosis as a cause of stillbirth, infant deaths and morbidity in children. (29)

Bath

ROYAL NATIONAL HOSPITAL

Dr G. D. KERSLEY and Dr J. A. COSH—neuropathy and myopathy in connective tissue diseases. (30)

Beckenham

BETHLEM ROYAL HOSPITAL

Dr W. LINFORD REES—psychological relationships in depressive illness. (31)

Belfast

ROYAL MATERNITY HOSPITAL

Professor J. H. M. PINKERTON—survey of pregnant women likely to be pre-diabetic (also at the Jubilee Maternity Hospital and the Metabolic Unit, Royal Victoria Hospital). (32)

ROYAL VICTORIA HOSPITAL

Professor J. W. DUNDEE—survey of side-effects and efficacy of standard and new analgesic drugs (also at Musgrave Park Hospital). (33)

Metabolism and Neurology Departments

Dr L. J. HURWITZ and Dr D. A. D. MONTGOMERY—electromyographic study of certain neuromuscular complications of diabetes. (34)

THE QUEEN'S UNIVERSITY

Botany Department

Dr D. PARK and Dr P. M. ROBINSON—effects of ageing on fungal cultures. (35)

Child Health Department

Professor I. J. CARRÉ and Dr D. W. NEILL—inborn errors of metabolism in handicapped children. (36)

Dental Department

Mr C. P. ADAMS—dental growth and development in children (also at the Royal Victoria Hospital). (37)

Department of Medicine

Professor G. M. BULL—tactile influences directing the movement of schistosomes. (38)

Dr Mary G. MCGEOWN—assay of parathyroid hormones in man. (39)

Psychology Department

Dr R. G. A. STRETCH—effects of stress in pregnant rats on the behaviour of the offspring. (40)

Surgery Department

Dr A. M. CONNELL—mechanism of the gastrocolic feeding responses. (41)

Student Expedition

Mr R. MCCLELLAND—adaptation to voluntary dehydration during the Expedition to Goulimini, South Morocco, 1965 (from private funds at the Council's disposal). (42)

Birmingham

BIRMINGHAM AND MIDLAND EYE HOSPITAL

Mr S. J. CREWS—vitreous body of the eye. (43)

BIRMINGHAM AND MIDLAND HOSPITAL FOR WOMEN

Clinical Endocrinology Department

Dr A. C. CROOKE—(1) action of certain oral contraceptives; (2) gynaecological endocrinology. (44)

COLLEGE OF ADVANCED TECHNOLOGY

Biological Science Department

Professor A. J. MATTY—(1) role of thyroid and pituitary hormones in the tissue metabolism of lower vertebrates; (2) effect of hormones on the permeability and transport activity of isolated membranes. (45)

THE GENERAL HOSPITAL

Nutritional and Gastrointestinal Unit

Dr W. T. COOKE—(1) jejunal biopsies; (2) investigation of the pH changes in the duodenum and jejunum of man in normal and pathological states. (46)

Surgery Department

Professor A. L. D'ABREU—pathogenesis and natural history of liver disease complicating ulcerative colitis and Crohn's disease. (47)

THE MIDLAND CENTRE FOR NEUROSURGERY AND NEUROLOGY

Dr M. V. SALMON—morphological and cytochemical changes in the central nervous system. (48)

QUEEN ELIZABETH HOSPITAL

Clinical Biochemistry Department

The late Professor J. R. SQUIRE—evaluation of the potential use of data processing systems at the Council's projected Clinical Research Centre. (49)

Department of Medicine

Dr S. C. MELNICK—aetiology of farmer's lung. (50)

Neurosurgery Department

Professor E. B. C. HUGHES—production of focal lesions in the central nervous system. (51)

Mr R. M. BADDELEY—gastric acid secretion in experimental liver disease and after portacaval shunts. (52)

Wellcome Surgical Research Laboratories

Mr D. B. CLARKE—a method of preserving viability of the isolated lung prior to transplantation. (53)

UNIVERSITY

Anatomy Department

Professor Sir Solly ZUCKERMAN—(1) response of foetal tissues to X-irradiation; (2) gametogenesis; (3*a*) anatomical variations associated with differences in posture and locomotion; (3*b*) dimensions and growth of the craniomandibular apparatus; (4) the structure and function of the hypothalamo-hypophysial tract in the ferret; (5) role of the motoneurone in the determination of functional properties of skeletal muscle. (54)

Biochemistry Department

Dr H. G. KLEMPERER—enzymes concerned in RNA synthesis and their relationship to protein synthesis. (55)

Professor S. V. PERRY—(1) biological activity and subunit structure of myosin; (2) enzymatic adaption to contractile activity in skeletal muscle. (56)

Dr D. G. WALKER—development and control of enzyme systems within the developing mammalian foetus and newborn animal. (57)

Chemistry Department

Dr S. A. BARKER—carbohydrate moieties of γ-globulins (also in the Experimental Pathology Department). (58)

Dr A. S. JONES—relationship between chemical structure and biological function of nucleic acids. (59)

Professor M. STACEY—preparation of a range of fluorocarbon compounds for test as anaesthetic agents. (60)

Institute of Child Health

Professor D. V. HUBBLE—(1) growth hormone assays and the observation of the biochemical effects of administration of growth hormone in the differential diagnosis of short stature in children; (2) Turner's syndrome in children. (61)

Dental Pathology Department

Professor E. A. MARSLAND—chemical and histological investigation of enamel formation, with particular reference to maturation. (62)

Experimental Neuropharmacology Department

Dr G. B. ANSELL—relative importance of different pathways of phospholipid synthesis in the various anatomical areas of the brain. (63)

Experimental Pathology Department

The late Professor J. R. SQUIRE—hypogammaglobulinaemia. (64)

Dr J. HARDWICKE—physical and biological properties of antigen-antibody complexes. (65)

Dr P. W. DYKES—(1) use of isotopically labelled substances in clinical research problems, studied by means of the whole-body counter; (2) metabolism of the elements selenium, magnesium, manganese, copper, zinc and cobalt, using radioactive isotopes and the whole-body counter. (66)

Dr K. W. WALTON—reaction of rheumatoid factor with isolated polypeptide chains of γG-globulin. (67)

Medical Biochemistry and Pharmacology Department

Professor A. C. FRAZER—(1) problems of fat absorption and other metabolic studies; (2) folic acid metabolism. (68)

Dr R. R. A. DILS—development of gas-liquid radiochromatography for lipid analysis. (69)

Dr J. N. HAWTHORNE—inositol phospholipids and cation transport in nervous tissue. (70)

Dr G. H. A. HÜBSCHER—(1) carbohydrate metabolism and the electron transfer system in the mucosal cell of the small intestine; (2) lipid metabolism in the mucosa of the small intestine. (71)

Dr W. F. R. POVER—basic physical problems associated with the whole-body radiation counter, and the development of relevant data processing techniques. (72)

Department of Medicine

Professor W. M. ARNOTT—(*a*) metabolic effects of exercise; (*b*) human plasma lipids. (73)

Dr J. M. BISHOP—chronic bronchitis and emphysema. (74)

Dr C. W. CRANE—protein metabolism in patients suffering from malnutrition. (75)

Neurocommunications Research Unit

Dr I. C. WHITFIELD—neural mechanisms of hearing. (76)

Pathology Department

Dr D. B. BREWER and Dr D. A. HEATH—pathology of emphysema and its relation to disturbances of respiratory function and pulmonary haemodynamics. (77)

Dr D. L. WOODHOUSE—biological testing of mineral oil fractions (on behalf of the Committee on the Carcinogenic Action of Mineral Oils). (78)

Physics Department

Dr J. H. FREMLIN—(1*a*) structure of mature enamel; (1*b*) fluoride content of the dental plaque; (2) charged particle activation analysis of the hard tissues. (79)

Physiological Chemistry Department

Dr Sybil P. JAMES—formation of mercapturic acids. (80)

Dr C. E. ROWE—lipid metabolism in brain tissue. (81)

Physiology Department

Dr F. A. JENNER—diuresis and antidiuresis in periodic psychotics. (82)

Dr Bertha SINGER—regulation of aldosterone secretion in normal and pathological conditions. (83)

Social Medicine Department

Professor T. MCKEOWN—effect of prenatal factors on postnatal development. (84)

Bradford

INSTITUTE OF TECHNOLOGY

Biological Sciences Department

Mr T. CROSS—taxonomy of actinomycetes. (85)

Chemical Technology Department

Dr G. SHAW—nucleic acid synthesis. (86)

Pharmacy Department

Dr J. M. FOY—factors affecting water transport in the gastrointestinal tract. (87)

Dr G. D. H. LEACH—location, distribution and release of sympathomimetic amines. (88)

Braintree

BLACK NOTLEY HOSPITAL

Mr M. C. WILKINSON—skeletal tuberculosis and rheumatoid arthritis. (89)

Brighton

ROYAL SUSSEX COUNTY HOSPITAL

Biochemistry Department

Dr C. RILEY—sterol ester metabolism in relation to the adrenal gland. (90)

UNIVERSITY OF SUSSEX

Biological Sciences Department

Professor J. MAYNARD SMITH—protein synthesis and ageing in *Drosophila.* (91)

Bristol

COLLEGE OF SCIENCE AND TECHNOLOGY

Pharmacy School

Dr M. R. W. BROWN—effect of Tween 80 on the resistance of *Pseudomonas aeruginosa* to chemical inactivation. (92)

GENERAL HOSPITAL

Pathology Laboratory

Miss M. P. ENGLISH—laboratory study of otomycosis and its causal fungi. (93)

ROYAL HOSPITAL

Medical Physics and Radiodiagnosis Department

Mr H. F. FREUNDLICH and Mr M. A. BULLEN—use of ultrasonics in medical diagnosis (also at Department of Medicine, Bristol Royal Infirmary). (94)

Radiotherapy Department

Dr R. C. TUDWAY—malignant tumour activity assessed by radiophosphorus uptake. (95)

ROYAL HOSPITAL FOR SICK CHILDREN

Dr D. BURMAN—iron deficiency anaemia in infancy. (96)

ROYAL INFIRMARY

Dr R. P. WARIN—chronic urticaria. (97)

Radiodiagnosis Department

Dr J. H. MIDDLEMISS—mechanical effectiveness of coughing in patients with chronic non-specific lung disease. (98)

Surgery Department

Mr J. H. PEACOCK—the role of the catecholamines in the maintenance and production of portal hypertension. (99)

Dr M. O. SYMES—treatment of malignant neoplasms by immunologically competent cells and cytotoxic drugs. (100)

SOUTHMEAD HOSPITAL

Professorial Department of Obstetrics and Gynaecology

Dr P. M. DUNN—foetal adaptation at birth. (101)

Pathology Department

Dr J. B. HOLTON—dietary treatment, inheritance and pathogenesis of histidinaemia. (102)

UNIVERSITY

Bacteriology Department

Professor K. E. COOPER—(1) electrophoresis of colicines; (2) antibiotic action in relation to age of cells. (103)

Dr Anna J. MAYR-HARTING—colicin receptors of the bacterial cell. (104)

Dr D. B. PEACOCK—respiratory syncytial virus. (105)

Biochemistry Department

Professor P. J. RANDLE—(1) control and interaction of glucose and glyceride metabolism in mammalian tissues; (2) studies on chondromucoprotein complex; (3) biochemical reactions controlling insulin release. (106)

Dr J. B. CHAPPELL—mechanism of transport of ions and metabolites across the mitochondrial membrane. (107)

Department of Medicine

Dr J. R. CLAMP—isolation and investigation of amyloid. (108)

Dr P. B. GARLAND—coenzyme-A-linked reactions in mitochondria. (109)

Dr A. E. READ—neuropsychiatric complication in patients with liver disease. (110)

Dr D. J. WARD—rheumatic diseases. (111)

Organic Chemistry Department

Dr L. HOUGH—(1) biosynthesis of antibiotic amino sugars; (2) carbohydrate prosthetic group of immunoglobulins. (112)

Physiology Department

Dr J. M. N. BOSS—maturation of the nephron in mammals during the sucking period. (113)

Dr C. P. HALLET—extraction and animal assay of gastrin. (114)

Dr P. F. MILLINGTON—effects of hormones on the development of phosphatase activity in the small intestine. (115)

Dr T. D. WILLIAMS—(1) nerve inputs to the globus pallidus and neighbouring structures of the basal ganglia; (2) the role of the sensory nervous system in the physiology of the caudate nucleus; (3) connections between the thalamus and the caudate nucleus, and the part they play in the rhythmic response of the caudate nucleus to sensory stimuli. (116)

Psychology Department

Dr J. H. CROOK—(1) factors affecting avoidance behaviour and fear responses in monkeys; (2) field and laboratory study of the behaviour of the Sykes monkey. (117)

Zoology Department

Dr H. E. HINTON—biology and physiology of the Simuliidae. (118)

Dr A. F. W. HUGHES—(1) neuroembryological studies on *Xenopus laevis*; (2) ontogeny of cutaneous innervation in anuran amphibians. (119)

Cambridge

ADDENBROOKE'S HOSPITAL

Investigative Medicine Department

Professor I. H. MILLS—effect of human pituitary fractions on adrenal steroid synthesis. (120)

John Bonnet Laboratories

Dr H. LEHMANN—biochemistry of skin disease. (121)

Radiotherapeutics Department

Professor J. S. MITCHELL—(1) physicochemical studies, including the effects of ionizing radiation on deoxyribonucleoprotein; (2) biochemical studies on Synkavit and menadione. (122)

DUNN NUTRITIONAL LABORATORY

Dr Ethel M. CRUIKSHANK—metabolism of ^{14}C-labelled vitamin D_2. (123)

THE MATERNITY HOSPITAL

Dr Janet BOTTOMLEY and Dr D. GAIRDNER—the use of amnioscopy and analysis of blood from foetuses. (124)

STRANGEWAYS RESEARCH LABORATORY

Dr E. M. BRIEGER—host-parasite relationship in leprosy (also at the National Institute for Medical Research). (125)

Dr T. MOORE—mode of action of vitamins A and E. (126)

UNIVERSITY

Anatomy School

Dr C. C. D. SHUTE and Dr P. R. LEWIS—histochemical investigation of the central nervous system after lesions involving fibre tracts in the rat. (127)

Dr P. A. G. MONRO—microcirculation in man and animals. (128)

Sir William Dunn School of Biochemistry

Dr E. J. BUTLER—biochemistry of manganese. (129)

Dr T. M. CHALMERS—characterization of urinary fat-metabolism substance. (130)

Dr H. B. F. DIXON—chemistry of corticotrophin and the melanophore-stimulating hormone. (131)

Dr Anne STOCKELL HARTREE—purification of hormones from human pituitary glands. (132)

Dr A. KORNER—(1) hormone control of protein biosynthesis; (2) mechanism of protein biosynthesis in mammalian tissue. (133)

Dr Alison A. NEWTON—(1) biochemistry of animal viruses; (2) deoxynucleotide synthesis in normal and virus-infected cells. (134)

Dr P. K. TUBBS—study at the enzyme level of the inhibition of fatty acid biosynthesis by fatty acids. (135)

Professor F. G. YOUNG—hormone control of the activity of the pancreatic islets. (136)

Botany Department

Dr H. L. K. WHITEHOUSE—genetic investigations of recombination in *Neurospora crassa*. (137)

Colloid Science Department

Dr D. A. HAYDON—cell membrane structure and behaviour. (138)

Education Department

Professor O. L. ZANGWILL—laterality in relation to backwardness in reading. (139)

Department of Experimental Medicine

Miss H. M. BRUCE—reproductive physiology and behaviour. (140)

Genetics Department

Professor J. M. THODAY—genetic variation and endocrine function. (141)

Investigative Medicine Department

Professor I. H. MILLS—mechanism controlling the excretion of sodium by the kidney (also at Addenbrooke's Hospital). (142)

Department of Medicine

Dr D. M. T. GAIRDNER—respiratory failure in the newborn (also at Cambridge Maternity Hospital). (143)

Dr J. L. GEDYE—fundamental psychological problems relating to the development of automated guidance systems for use in the industrial rehabilitation of patients with brain damage. (144)

Professor J. S. MITCHELL—techniques of short-term culture of haemic cells and the use of cytochemical and autoradiographic methods in the analysis of cell behaviour in normal and in certain pathological states. (145)

Metallurgy Department

Dr T. P. HOAR—corrosion, passivity and protection of implant alloys. (146)

Molteno Institute

Dr Ann BISHOP—biology of protozoa, with special reference to drug resistance. (147)

Dr H. W. LASER—(*a*) immediate biochemical changes occurring during application of ionizing irradiation; (*b*) resistance to radiation. (148)

Pathology Department

Dr R. D. BARRY—nucleic acids produced in cells infected with influenza viruses. (149)

Dr R. R. A. COOMBS—chemical coupling of red cell antibodies with protein allergens. (150)

Dr R. M. FRY—preservation of living cells by freezing and drying and the effect of intracellular and extracellular additives on survival. (151)

Pharmacology Department

Professor A. S. V. BURGEN—(1) microelectrode study of chromaffin cells; (2*a*) sympathetic nerve terminals; (2*b*) uptake and release of catecholamines. (152)

Dr J. F. MITCHELL—release of transmitter substances from central synapses. (153)

Physiological Laboratory

Dr G. S. BRINDLEY—the functions of the cerebellum. (154)

Professor A. L. HODGKIN—(1) giant nerve fibres in the squid (also at the Plymouth Laboratory of the Marine Biological Association); (2) mechanism of the sodium pump and related projects (from private funds at the Council's disposal). (155)

Professor A. S. PARKES—preimplantation development in mammals. (156)

Dr E. N. WILLMER—ionic movements in the amoeba *Naegleria gruberi* in relation to cell form and differentiation. (157)

Psychological Laboratory

Mr R. L. GREGORY—distance perception and its limitation by ' neural noise '. (158)

Mr G. C. GRINDLEY—role of attention in visual perception. (159)

Mr A. W. STILL—factors controlling complex learning in the rat. (160)

Mr A. J. WATSON—studies in exploratory behaviour in animals. (161)

Dr L. WEISKRANTZ—(1) cerebral mechanisms of memory in the monkey; (2) cerebral mechanisms in visual discrimination and memory. (162)

Radiotherapeutics Department

Professor J. S. MITCHELL—(1) clinical and laboratory studies, using the linear accelerator, on the therapeutic applications of 15-MeV X-rays (from special funds at the Council's disposal); (2) 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; (3) measurement of total body radioactivity in health and disease. (163)

Mrs I. SIMON-REUSS—the effects of ionizing radiations and chemical agents on malignant cells. (164)

Zoology Department (Animal Behaviour Laboratory)

Professor R. A. HINDE—mother-infant interaction in rhesus monkeys. (165)

Student Expedition

Mr D. G. THOMAS—the role of the baboon in the transmission of bilharzia: Cambridge Mwanza Expedition, 1965 (from private funds at the Council's disposal). (166)

Cardiff

ROYAL INFIRMARY

Medical Unit

Dr R. HARVARD DAVIS—calcium urinary excretion in a general practice population (also at Dr Harvard Davis's surgery and other centres). (167)

Surgical Unit

Mr R. SHIELDS—bidirectional transport of water, sodium and potassium across the intestinal mucosa. (168)

VELINDRE HOSPITAL

South Wales Radiotherapy Centre

Dr P. B. KUNKLER—(1) randomized controlled trial of radiotherapy under high-tension oxygen; (2) clinical trial of endolymphatic therapy in malignant melanoma. (169)

UNIVERSITY COLLEGE OF SOUTH WALES AND MONMOUTHSHIRE

Anatomy Department

Professor J. D. LEVER—catecholamines in adrenergic neurones. (170)

Biochemistry Department

Professor K. S. DODGSON—biochemical studies at cellular and subcellular levels (from special funds for the purchase of costly apparatus). (171)

Professor K. S. DODGSON and Dr A. G. LLOYD—bacterial degradation of algal hetero-polysaccharides and their monomers. (172)

Psychology Department

Dr J. O. ROBINSON—personality characteristics and symptoms in individuals with high blood pressure who consult general medical practitioners. (173)

WELSH COLLEGE OF ADVANCED TECHNOLOGY

Chemistry and Biology Department

Dr R. E. HUGHES—passage of ascorbic acid across biological membranes. (174)

Welsh School of Pharmacy

Mr K. S. JAMES—comparative study of the lower testosterone esters. (175)

WELSH NATIONAL SCHOOL OF MEDICINE

Anaesthetics Department

Professor W. W. MUSHIN—uptake and distribution of inhaled anaesthetic agents (also at the Royal Infirmary, Cardiff). (176)

Social and Occupational Medicine Department

Professor C. R. LOWE—breast cancer and lactation. (177)

Surgery Department

Professor A. P. M. FORREST—gastric hypothermia in man and experimental animals. (178)

Dr A. J. U. ANDERSON and Mr R. G. HARVEY—medical and physical anthropological studies on the Commonwealth Islands Expedition. (179)

Dartford

BEXLEY HOSPITAL

Dr D. BANNISTER—conceptual relationships in schizophrenic patients. (180)

JOYCE GREEN HOSPITAL

Dr H. CLOSE—incidence of triple-X females in the general population. (181)

Douglas, Isle of Man

NOBLE'S ISLE OF MAN HOSPITAL

Professor T. FERGUSON—hospital-treated sickness in the Isle of Man (also at other hospitals on the island). (182)

Dumfries

CRICHTON ROYAL HOSPITAL

Dr W. MCADAM—alcoholism in relation to conditioning and conditioned aversion therapy. (183)

Dundee

QUEENS COLLEGE, UNIVERSITY OF ST. ANDREWS

Anatomy Department

Professor R. E. COUPLAND—organ culture using high pressures of oxygen. (184)

Biochemistry Department

Dr G. J. DUTTON—mechanism and significance of extrahepatic glucuronide synthesis. (185)

Dr D. A. STANSFIELD—mode of action of gonadotrophins on the corpus luteum and the function of ascorbic acid in the corpus luteum. (186)

Dr J. TIBBS—biochemical changes responsible for and accompanying motility in micro-organisms. (187)

Dr G. C. BARR—the primary effects of mutagens in the causation of errors of replication during DNA and RNA biosynthesis *in vitro*. (188)

Chemistry Department

Dr R. FOSTER—charge transfer in drug action. (189

Child Health Department

Professor J. L. HENDERSON—adrenal function in newborn infants and children. (190)

Gynaecology and Midwifery Department

Professor J. WALKER—steroid studies in pregnancy. (191)

Pharmacology and Therapeutics Department

Professor R. B. HUNTER—adrenal inhibitors. (192)

Dr P. B. MARSHALL—relationship of histidine decarboxylase to other amino acid decarboxylases. (193)

Dr D. M. SHEPHERD—hepatocarcinogenesis with diethylnitrosamine. (194)

Dr I. H. STEVENSON—penicillin binding in *Staphylococcus aureus*. (195)

Psychiatry Department

Professor I. R. C. BATCHELOR—impared selective attention and short-term memory in schizophrenia and organic cerebral disease. (196)

Dr A. MCGHIE—clinical and experimental study of disturbances of attention and perception in schizophrenia. (197)

ROYAL INFIRMARY

University Department of Pathology

Professor H. G. MORGAN—formation of calcium oxalate renal calculi in man. (198)

Durham

UNIVERSITY

Psychology Department

Mr I. P. HOWARD—cyclofusion and stereoscopic vision. (199)

Zoology Department

Professor D. BARKER—innervation of skeletal muscle. (200)

Edinburgh

CITY HOSPITAL

University Department of Respiratory Diseases and Tuberculosis

Professor J. W. CROFTON—physiology of the bronchus. (201)

Medical Research Council Clinical Endocrinology Research Unit

Dr W. I. CARD—immunological method for the assay of gastrin in tissues and body fluids. (202)

MOREDUN INSTITUTE

Professor A. St.G. HUGGETT—location of fructose in the sheep foetus. (203)

NORTHERN GENERAL HOSPITAL

Rheumatic Diseases Unit

Dr J. J. R. DUTHIE—pathogenesis of rheumatoid arthritis. (204)

ROYAL EDINBURGH HOSPITAL

Psychological Medicine Department

Dr J. I. EVANS—sleep and allied spontaneous and induced alterations of consciousness. (205)

ROYAL INFIRMARY

Clinical Chemistry Department

Professor L. G. WHITBY—enzymology, with particular reference to the development of diagnostically useful procedures. (206)

Dr D. W. MOSS—comparison of alkaline phosphatase from different animal tissues. (207)

University Department of Medical Physics

Dr J. R. GREENING—dosimetry of low-voltage X-rays. (208)

Dr J. R. GREENING and Dr P. TOTHILL—application of a multichannel analyser to clinical research (from special funds for the purchase of costly apparatus). (209)

Dr P. TOTHILL—liquid scintillation counter applied to the use of radioisotopes in clinical research (from special funds for the purchase of costly apparatus). (210)

Department of Medicine

Professor K. W. DONALD—blood gas tensions in respiratory insufficiency, and the use of oxygen as treatment. (211)

Dr A. DOIG—unilateral renal disease. (212)

Dr A. R. LIND—cardiovascular responses to muscular exercise. (213)

University Department of Therapeutics

Professor R. H. GIRDWOOD—bile salt metabolism. (214)

Dr I. W. DELAMORE—effect of iron deficiency on gastric function. (215)

UNIVERSITY

Anatomy Department

Dr A. PETERS—architecture of the cerebral cortex as shown by the electron microscope. (216)

Institute of Animal Genetics

Professor G. H. BEALE—genetic and biochemical studies of the antigens of *Paramoecium*. (217)

Dr J. O. BISHOP—gene-controlled specificity of protein synthesis. (218)

Bacteriology Department

Professor R. CRUICKSHANK—(*a*) possible role of mycoplasma in human infection; (*b*) antibiotic levels in respiratory infection. (219)

Dr D. M. WEIR—immunoglobulins of high molecular weight. (220)

Dr J. F. WILKINSON—continuous culture of bacteria. (221)

Biochemistry Department

Professor R. B. FISHER—role of thyroglobulin in thyroid hormone biosynthesis. (222)

Dr P. C. JOCELYN—inhibitory effect of vitamin B_{12} on the oxidation of glutathione in human erythrocytes and the role of serum copper on this oxidation. (223)

Dr J. H. OTTAWAY—(1) control of metabolism in muscle; (2) kinetics of biological systems in intermediary metabolism. (224)

Dr G. S. BOYD—bile acid production *in vitro*. (225)

Chemistry Department

Dr D. J. MANNERS—structure and metabolism of glycogen, with special reference to glycogen storage diseases. (226)

Child Life and Health Department

Dr T. T. S. INGRAM—retarded speech development in children. (227)

Dr J. W. FARQUHAR—screening methods for phenylketonuria (on behalf of the Council's Working Party on Phenylketonuria). (228)

Clinical Chemistry Department

Dr F. L. MITCHELL—metabolism of C_{19} and C_{21} steroids in the foetus and newborn infant. (229)

Clinical Surgery Department

Professor Sir John BRUCE—clinical and laboratory studies of gastric function under various conditions. (230)

Medical Physics Department

Dr J. R. GREENING—chemiluminescence. (231)

Orthopaedic Surgery Department

Professor J. I. P. JAMES—changes in the nature, structure and activity of bone and cartilage cells with age. (232)

Pharmacology Department

Dr B. L. GINSBORG—effects on synaptic transmission of the various ganglion-blocking agents. (233)

Phonetics Department

Professor D. ABERCROMBIE—speech of Tristan da Cunha islanders. (234)

Physiology Department

Dr G. H. HAGGIS—high-resolution electron microscope study of proteins and lipoproteins. (235)

Psychiatry Department (Neuropharmacology Laboratory)

Dr D. W. STRAUGHAN—(1) psychomimetic drugs and their congeners in the brain; (2) chemical transmission in the limbic system. (236)

Psychological Medicine Department

Dr J. R. SMYTHIES—cerebral amines and major psychoses. (237)

Surgical Science Department

Professor M. F. A. WOODRUFF—immunological aspects of cancer. (238)

Dr D. MICHIE—(1) quantitative study of problem-solving behaviour; (2) biomedical computing on an ' open-shop ' basis. (239)

The Ashworth Laboratory of Zoology

Professor M. M. SWANN—effects of ultraviolet radiations and radiophosphorus on the cell cycle. (240)

Mrs K. M. G. ADAM—DNA-mediated transformation of free-living amoebae. (241)

Dr P. A. G. WILSON—economy of free-living stages of parasites. (242)

WESTERN GENERAL HOSPITAL

Dr Joyce BAIRD—clinical and laboratory study of the relationship between growth hormone and diabetes mellitus. (243)

Bacteriology Department

Professor J. W. McLEOD—(*a*) thermostable toxin in staphylococcal infection; (*b*) control of infection of the urinary tract. (244)

Clinical Surgery Department

Professor Sir John BRUCE—telemetering of biological information in medical and surgical research. (245)

Gastro-Intestinal Unit

Dr W. I. CARD—action of gastrin on human gastric secretion. (246)

Pathology Department

Dr N. MACLEAN—chromosome anomalies in normal and mentally retarded subjects. (247)

Elstree

LISTER INSTITUTE OF PREVENTIVE MEDICINE

Mr A. F. B. STANDFAST—identification of the two immunizing antigens of *Bordetella pertussis.* (248)

Mrs J. M. DOLBY—studies on immunity in *Bordetella pertussis.* (249)

Epsom

Dr E. J. C. KENDALL—acute respiratory infections occurring in a general practice population. (250)

Exeter

UNIVERSITY

Physics Department

Mr K. P. S. CALDWELL and Dr F. C. FLACK—control of rectal and urinary incontinence. (251)

Postgraduate Medical Institute

Dr D. MATTINGLY—free 11-hydroxycorticoids in human plasma and urine. (252)

Psychology Department

Dr R. LYNN—autonomic reactivity, orientation reactions and speed of habituation in children aged 0–15 years. (253)

Fajara, The Gambia

MEDICAL RESEARCH COUNCIL LABORATORIES

Mrs M. E. WILSON—the incidence of malaria. (254)

Glasgow

ROYAL HOSPITAL FOR SICK CHILDREN

Child Health Department

Professor J. H. HUTCHISON and Dr J. M. A. LENIHAN—strontium content of human tissue. (255)

ROYAL INFIRMARY

Biochemistry Department

Sir David CUTHBERTSON—metabolic response to physical injury, with particular reference to the effects of diet and temperature and to injuries induced by various types of radiation. (256)

Department of Medicine

Professor A. S. DOUGLAS—(1) thrombolytic therapy and fibrinolytic states; (2*a*) MRC trial of anticoagulant therapy in acute myocardial infarction; (2*b*) fibrinolysis. (257)

Department of Steroid Biochemistry

Dr J. K. GRANT—secretion and metabolism of testosterone in normal and virilized subjects. (258)

Surgery Department

Professor W. A. MACKEY—(1) physiology of cerebral blood in relation to metabolism; (2) cerebral blood flow. (259)

Mr J. M. ANDERSON—homograft rejection. (260)

UNIVERSITY

Anatomy Department

Dr A. H. BAILLIE—3β-hydroxysteroid dehydrogenase activity. (261)

Bacteriology Department

Professor R. G. WHITE—influence of mycobacterial peptidoglycolipids on the biosynthesis of antibody in the guinea pig. (262)

Dr D. A. R. SIMMONS—immunochemistry of lipopolysaccharides from *Shigella flexneri.* (263)

Biochemistry Department

Professor H. N. MUNRO—protein metabolism of cestode tapeworms. (264)

Dr W. H. HOLMS—adaptive enzyme synthesis in staphylococci. (265)

Wellcome Laboratory for Experimental Parasitology

Dr C. A. HOPKINS—electron microscope study of structure of tapeworm cuticle. (266)

Genetics Department

Dr J. H. RENWICK—the sequence of gene loci in man. (267)

Dr M. A. FERGUSON-SMITH—possible factors leading to chromosomal non-disjunction in man. (268)

Pathology Department

Professor T. SYMINGTON—densitometric and electron microscope study of tissue cultures of the adrenal. (269)

Institute of Physiology

Dr I. A. BOYD—(*a*) muscle spindle as a transducer; (*b*) release of acetylcholine in skeletal muscle (also at the Boyd Medical Research Institute). (270)

Dr J. V. G. A. DURNIN—investigation of the diets of pre-school children in the Glasgow area. (271)

Dr J. S. GILLESPIE—(1) possible reincorporation of adrenergic transmitter into postganglionic nerve endings; (2) storage and release of catecholamines in adrenergic nerves. (272)

Dr B. R. MACKENNA—storage and release of noradrenaline in the subcellular fractions of the cat spleen. (273)

Zoology Department

Mr S. A. BARNETT—(1) physiology of social stress in wild rats; (2) effects of breeding mice in a cold environment. (274)

UNIVERSITY OF STRATHCLYDE

Applied Microbiology and Biology Department

Dr J. A. BLAIN—oxidizability of unsaturated plasma lipids. (275)

Dr G. J. O'NEILL—isolation of blood group antigens from human erythrocyte membranes. (276)

Pharmacy Department

Dr Mary DAWSON—antibacterial substances of animal origin. (277)

Dr N. G. WATON—histamine formation in mammals. (278)

WESTERN INFIRMARY

University Department of Medicine

Dr A. GOLDBERG—(*a*) measurement of the haem enzymes of human marrow erythropoietic cells in various blood diseases; (*b*) studies on iron absorption. (279)

University Department of Orthopaedic Surgery

Professor Roland BARNES—prospective survey of intracapsular fractures of the neck of the femur. (280)

Surgery Department

Professor A. W. KAY—hyperbaric oxygenation. (281)

VETERINARY HOSPITAL

Wellcome Laboratory

Professor W. A. MACKEY—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. (282)

VICTORIA INFIRMARY

Pathology Department

Dr J. E. CRAIK—microarchitecture of skin and its behaviour under stress. (283)

Hull

UNIVERSITY

Biochemistry Department

Dr G. W. CROSBIE—glycine and glyoxylate metabolism in microorganisms. (284)

Professor E. A. DAWES—(1) diauxic growth effect in *Pseudomonas aeruginosa*; (2) role of poly-β-hydroxybutyrate in the genus *Azotobacter*, with reference to endogenous metabolism and survival. (285)

Chemistry Department

Dr G. W. GRAY—studies on the sensitivity of gram-negative bacteria to ethylenediaminetetra-acetic acid. (286)

Ibadan, Western Nigeria

UNIVERSITY COLLEGE

Chemical Pathology Department

Dr J. C. EDOZIEN—biochemical studies in kwashiorkor. (287)

Physiology Department

Professor J. GRAYSON—the use of internal calorimetry in the determination of blood flow in solid organs. (288)

Kampala, Uganda

MAKERERE UNIVERSITY COLLEGE

Pharmacology Department

Mr J. A. LOCK—isolation, characterization and pharmacology of materials from *Bersama abyssinica* var. *paullinoides*. (289)

Physiology Department

Dr P. G. WRIGHT—peripheral circulation in the monkey. (290)

Dr R. E. THIES—post-tetanic potentiation at motor nerve terminals. (291)

Keele

UNIVERSITY

Communication Department

Professor D. M. MACKAY—electrophysiological steady-state responses to periodic stimuli. (292)

Kingston, Jamaica

UNIVERSITY OF THE WEST INDIES

Biochemistry Department

Professor C. von HOLT—degradation of leucine in protein-deficient rats. (293)

Morbid Anatomy Department

Dr J. A. HAYES—relationship of emphysema to pulmonary vasculature and pulmonary heart disease in Jamaica. (294)

Kumi, Uganda

KUMI LEPROSY CENTRE

Dr J. A. KINNEAR BROWN—trial of BCG in leprosy. (295)

THE GENERAL INFIRMARY

Electromyography Department

Dr D. TAVERNER—electrophysiological study of the peripheral neuromuscular system in patients with renal failure. (296)

University Department of Medical Physics

Dr J. B. DAWSON—development of spectrochemical techniques for the study of mineral metabolism. (297)

Department of Medicine

Dr George A. ROSE—metabolic bone diseases. (298)

Dr M. S. LOSOWSKY—(1) lipid metabolism in acute renal failure; (2) assay of plasma fibrin stabilizing factor activity in patients with congenital and acquired deficiencies. (299)

Renal Research Unit

Dr F. M. PARSONS—(1) investigation to compare and contrast the effect of natural protein feeding with that of a mixture of essential amino acids; (2) renal transplantation using kidneys from cadavers (also in the University Chemical Pathology Department). (300)

Urology Department

Mr M. FOX—some basic immunological and cellular problems of homotransplantation. (301)

UNIVERSITY

Anaesthetics Department

Professor J. F. NUNN—arterial and tissue hypoxia during anaesthesia and surgery. (302)

Anatomy Department

Dr Julia M. FOURMAN—water conservation by the kidney. (303)

Bacteriology Department

Dr J. G. SHOESMITH—effects of heat and irradiation on tetanus spores. (304)

Biochemistry Department

Professor S. DAGLEY—effect of antibiotics on bacterial cell constituents. (305)

Dr F. W. CHATTAWAY—(1) mode of inhibition of growth of fungi by certain steroids; (2) factors affecting growth and morphology of pathogenic fungi. (306)

Chemical Pathology Department

Professor P. FOURMAN—(1) osteomalacia after gastrectomy; (2) metabolism *in vitro* of bone from cases of osteomalacia. (307)

Professor G. H. LATHE—mechanisms of bile secretion. (308)

Dr S. R. STITCH—(1) biosynthesis of oestrogen by the ovary after sterilization with X-irradiation; (2) investigation of ovarian and extra-ovarian oestrogens; (3) mechanism and locus of action of gonadotrophic hormones in the control of steroid biosynthesis by the ovary. (309)

Dr C. TOOTHILL—haem synthetase in normal subjects and patients with familial hypochromic microcytic anaemia. (310)

School of Dentistry (Oral Biology Unit)

Professor S. M. WEIDMANN—(1) the mechanism of calcification; (2) biological activity of enamel and bone. (311)

Experimental Pathology and Cancer Research Department

Professor H. N. GREEN—biological testing of mineral oil fractions (on behalf of the Committee on the Carcinogenic Action of Mineral Oils). (312)

Proctor Department of Food and Leather Science

Dr H. E. NURSTEN—interaction between elastin and simple acid dyestuffs. (313)

Medical Physics Department

Mr G. W. REED—quantitative histology of cortical bone. (314)

Pathology Department

Professor C. E. LUMSDEN—immunological studies in experimental allergic encephalitis and in human disseminated sclerosis. (315)

Dr C. G. WOODS—microscopical study of iliac crest biopsies from patients with intestinal malabsorption. (316)

Pharmacology Department

Dr D. MACKAY—kinetics and mode of action of neuromuscular-blocking drugs. (317)

Physiology Department

Professor A. HEMINGWAY and Dr R. J. LINDEN—basic physiology of cardiovascular system. (318)

Dr W. J. O'CONNOR—water and sodium balance in dogs. (319)

Dr C. KIDD—central connections of cardiovascular afferent fibres. (320)

Surgery Department

Mr C. G. CLARK—absorption from intestine after procedures that alter gastric secretion. (321)

Zoology Department

Professor J. M. DODD—(*a*) comparative studies on goitrogenesis; (*b*) bioassay of thyroid-stimulating hormone and thyroid hormones in microamounts of body fluids and pituitary fractions. (322)

Leicester

UNIVERSITY

Chemistry Department

Dr B. CAPON—intramolecular catalysis in glycoside hydrolysis. (323)

Engineering Department

Dr J. M. NIGHTINGALE—automatic upper-arm prosthesis. (324)

Leigh (Lancashire)

LEIGH INFIRMARY

Dr M. C. STONE—very low density lipoprotein levels and their relation to sex, age and body weight in a randomly selected group of 1000 subjects. (325)

Lincoln

ST. GEORGE'S HOSPITAL

Biochemical Laboratory

Dr L. NAFTALIN—changes in aminoaciduria after therapeutic irradiation. (326)

Liverpool

ROYAL INFIRMARY

Dermatology Department

Dr C. F. H. VICKERS—epidermal reservoir phenomenon. (327)

SEFTON GENERAL HOSPITAL

Surgery Department

Mr J. G. GOW—effect of gastric hypothermia on acute haematemesis. (328)

UNIVERSITY

Building Science Department (Acoustics Research Unit)

Dr M. E. BRYAN—(1) middle ear reflex; (2*a*) evaluation of the Bekesy audiometer for the diagnosis of hearing disorders; (2*b*) variation in the threshold of hearing in normal subjects. (329)

Computer Laboratory

Professor A. YOUNG—computer studies of extraction processes in the liver. (330)

Dental Science Department

Professor R. L. HARTLES—experimental dental caries in the rat. (331)

Materia Medica, Pharmacy, Pharmacology and General Therapeutics Department

Professor A. WILSON—(1) metabolism and excretion of neostigmine; (2) ultramicrobiochemical methods for observing the effects of drugs in histologically distinct structures of voluntary muscle. (332)

Obstetrics and Gynaecology Department

Professor T. N. A. JEFFCOATE—(1) 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; (2) aetiology of defective folate metabolism in pregnancy. (333)

Organic Chemistry Department

Dr R. A. W. JOHNSTONE—composition of cigarette smoke. (334)

Physiology Department

Dr G. L. KIDD—electrophysiological study of the intrafusal fibres of the mammalian muscle spindle. (335)

School of Tropical Medicine

Professor B. G. MAEGRAITH—(1) electron microscopy of liver lesions in experimental malaria; (2) effect of malarial and other protozoal infections on the enzymes of tissue and mitochondria. (336)

Professor W. E. KERSHAW—effect of particulate insecticide on the fauna, including *Simulium*, in streams and rivers. (337)

Veterinary Anatomy Department

Professor A. S. KING—senile changes in the vertebral column and associated variations of vascularity of the vertebral column in the rat. (338)

WALTON HOSPITAL

Laryngology Department

Mr A. TUMARKIN—speech transmission systems. (339)

London

ATKINSON MORLEY'S HOSPITAL

Research Laboratories

Dr Helen M. B. BUCKELL—metabolic studies in neurosurgical patients. (340)

BATTERSEA COLLEGE OF TECHNOLOGY

Biochemistry Unit

Dr E. REID—control of nucleic acid metabolism in normal and cancerous liver. (341)

Metallurgy and Materials Technology Department

Professor L. W. DERRY—corrosion of surgical implants. (342)

BEDFORD COLLEGE

Chemistry Department

Dr Margaret E. FARAGO—metal ions and transamination reactions. (343)

Physiology and Biochemistry Department

Mr G. H. WRIGHT—water and electrolyte transport across foetal gastric mucosa. (344)

Professor W. F. WIDDAS—the facilitated transfer of glucose and related sugars. (345)

Dr J. R. LAGNADO—amine oxidases in developing brain tissue. (346)

Psychology Department

Dr Monica LAWLOR—activity patterns in the golden hamster. (347)

BOROUGH POLYTECHNIC

Food Science and Technology Department

Dr D. B. SMITH—methods of folic acid assay in foods. (348)

BRITISH MUSEUM

Physical Anthropology Department

Mr D. R. BROTHWELL—reassessment of certain continuous and discontinuous variations of a polygenic nature in man. (349)

CENTRAL MIDDLESEX HOSPITAL

Cardio-Thoracic Department

Dr K. P. BALL—clinical trial of diet in coronary thrombosis (with Professor J. N. Morris). (350)

Dr K. P. BALL and Dr H. JOULES—management of respiratory failure in chest and other diseases (also at the Pulmonary Physiology Unit, Hammersmith Hospital). (351)

Dr K. P. BALL and Dr M. W. MCNICOL—haemodynamic and respiratory changes in acute myocardial infarction. (352)

Gastroenterology Department

Dr F. AVERY JONES—(1) peptic ulceration; (2*a*) genetic studies in ulcerative proctocolitis and Crohn's disease; (2*b*) maintenance treatment of patients with proctocolitis after successful treatment of an acute attack. (353)

CHARING CROSS HOSPITAL MEDICAL SCHOOL

Anatomy Department

Dr T. W. GLENISTER—biology of implanting mammalian blastocysts (also at the Electron Microscope Unit, West London Hospital). (354)

Bacteriology Department

Dr H. I. WINNER—pathogenic mechanisms of yeast-like fungi with particular reference to the genus *Candida*. (355)

Chemical Pathology Department

Dr J. SPENCER-PEET—relationship between deficiency of glycogen synthetase and the occurrence of hypoglycaemia in man. (356)

Department of Medicine

Dr K. D. BAGSHAWE—trophoblastic tumours. (357)

Professor H. E. DE WARDENER—presence of synalbumin antagonism in the relatives of diabetics and others. (358)

Dr Doreen M. NUTBOURNE—control of the renal excretion of sodium and water by hormones other than aldosterone and vasopressin. (359)

Obstetrics and Gynaecology Department

Professor N. F. MORRIS—human placental metabolism in normal and abnormal pregnancies. (360)

Pharmacology Department

Professor J. B. E. BAKER—myocardial needs in relation to coronary flow. (361)

CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY

Biophysics Department

Dr D. ROSEN—electrical properties of phospholipids and proteins in model systems. (362)

Chemistry Department

Dr D. F. EVERED—amino acid uptake in various animal tissues. (363)

School of Pharmacy

Dr N. D. HARRIS—further development of a temperature gradient incubator. (364)

Physiology and Pharmacology Department

Dr D. T. PLUMMER—enzymes present in serum and urine. (365)

GUY'S HOSPITAL

Anaesthetics Department

Dr J. M. HALL—development of non-explosive anaesthetic agents (in collaboration with Dr T. H. S. Burns, St. Thomas's Hospital). (366)

Handicapped Children's Centre, Newcomen House

Dr Mary D. H. SHERIDAN—developmental tests for infants and young children, with special reference to visual and language disorders. (367)

GUY'S HOSPITAL MEDICAL SCHOOL

Anatomy Department

Dr M. BROOKES—vascularization of bone. (368)

Professor R. WARWICK and Professor C. B. ALLSOPP—biological effects of ultrasonic vibrations (also in the Physics Department). (369)

Bacteriology Department

Professor R. H. GORRILL—experimental bacillary pyelonephritis. (370)

Professor R. KNOX—work on steam pressure sterilizers (on behalf of the Council's Working Party on Steam Pressure Sterilizers). (371)

Biochemistry and Chemistry Department

Dr A. N. DAVISON—lipid and protein metabolism in disseminated sclerosis. (372)

Dr D. B. GOWER—biosynthesis of androst-16-en-3α-ol and other 3-hydroxy-Δ-16 steroids. (373)

Chemical Pathology Department

Professor R. H. S. THOMPSON—(1) action of lysolecithin and phospholipase A on the nervous system; (2) certain biochemical disturbances in neurological disorders. (374)

Professor S. COHEN, Professor P. C. C. GARNHAM and Dr J. D. FULTON—isolation of protective malarial antigens (also at the London School of Hygiene and Tropical Medicine). (375)

Professor S. COHEN—mechanism of malarial immunity in Gambian adults. (376)

Dr B. MCARDLE—human and experimental (plasmocid) myopathy. (377)

Experimental Medicine Department

Dr R. T. GRANT—blood circulation in skeletal muscle. (378)

Department of Medicine

Professor W. J. H. BUTTERFIELD—metabolism of isolated mammalian islets of Langerhans. (379)

Dr M. E. ABRAMS—biochemical studies of the surface-active lipoprotein isolated from mammalian lung. (380)

Paediatric Research Unit

Professor P. E. POLANI and Dr J. A. FRASER ROBERTS—autosomal anomalies and some hereditary defects in a population sample. (381)

Pathology Department

Dr J. N. BLAU—(*a*) blood-thymus barrier to radioactive-labelled proteins, vital dyes and antigens; (*b*) relationship of lymphocytes and germinal centres. (382)

Pharmacology Department

Dr J. A. NISSIM—(1) pharmacological inhibition and stimulation of intestinal absorption; (2) mechanism of intestinal absorption. (383)

Professor J. M. ROBSON—(1) analgesic properties of anaesthetic agents; (2) effect of drugs on pregnancy; (3) *in vivo* and *in vitro* action of drugs and immune mechanisms on the multiplication of *Mycobacterium leprae*. (384)

Physiology Department

Dr J. N. CROSSLEY—dietary carbohydrate absorption and its influence on lipid metabolism. (385)

Surgery Department

Professor H. J. B. ATKINS—bladder motility. (386)

HOSPITAL FOR TROPICAL DISEASES

Dr D. S. RIDLEY—histology of leprosy. (387)

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

Chemistry Department

Dr Margaret GOODGAME—complexes of substituted benzimidazoles with metal ions. (388)

Dr J. WALKLEY—diffusion in the mechanism of inert gas anaesthesia. (389)

Physics Department

Dr W. T. WELFORD—Mach effects on microscopical vision. (390)

INSTITUTE OF BASIC MEDICAL SCIENCES,
ROYAL COLLEGE OF SURGEONS OF ENGLAND

Anaesthetics Department

Professor J. P. PAYNE—circulatory, respiratory and metabolic responses to high concentrations of carbon dioxide during anaesthesia. (391)

Biochemistry Department

Professor C. LONG—(1) brain lipids; (2) structure of the erythrocyte membrane; (3) pathogenesis of hereditary retinal dystrophy in the experimental rat. (392)

Pathology Department

Professor G. J. CUNNINGHAM—cytochemical studies on early cell damage, particularly in the liver. (393)

Dr A. J. M. REESE and Dr M. S. ISRAEL—role of the thymus in the development of immune response. (394)

Pharmacology Department

Dr J. R. VANE—pharmacology of renin, angiotensin, catecholamines and gastrin. (395)

Professor G. V. R. BORN—physicochemical factors involved in the action of glycosides on ion transport. (396)

INSTITUTE OF CANCER RESEARCH

Chester Beatty Research Institute

Dr P. ALEXANDER—(1) susceptibility of cells to ionizing radiations (also at the Botany Department, Imperial College of Science and Technology); (2) effect of immunological procedures on radiosensitivity of tumours. (397)

Dr R. C. BRAY—(1) isolation of milk xanthine oxidase in a state suitable for physical studies; (2) mechanism of action of xanthine oxidase studied by electron spin resonance (also at the Inorganic Chemistry Department, Imperial College of Science and Technology). (398)

Professor J. A. V. BUTLER—multiplication of bacteriophage ϕX174. (399)

Dr R. A. M. CASE—cohort studies of mortality from various diseases in the British Isles. (400)

Dr K. S. KIRBY—(1) methods of separating DNA and RNA from the same tissue; (2) isolation and fractionation of DNA and RNA from *B. subtilis* and *E. coli*; (3) studies of nucleic acids in normal and tumour tissue; (4) DNA and messenger RNA and protein biosynthesis. (401)

Professor P. C. KOLLER—(1) role of chromosomes in carcinogenesis; (2) influence of environmental factors on karyotype stability. (402)

Dr F. J. C. ROE—carcinogenicity of combinations of cigarette smoke condensate and air pollutants and related problems, including the effects of thymectomy. (403)

Dr R. C. BRAY and Dr D. M. P. PHILLIPS—studies on proteins labelled with ^{14}C-iodoacetamide and ^{14}C-iodoacetic acid. (404)

Dr E. O. FIELD—effects of ionizing radiation on nervous function. (405)

Dr D. M. P. PHILLIPS—amino acid sequences in histone fractions from calf thymus and other tissues. (406)

Professor D. W. SMITHERS—radiosensitivity and radioresistance in human tumours. (407)

Dr A. R. CRATHORN—processes associated with DNA synthesis in synchronously dividing mammalian cells. (408)

INSTITUTE OF CHILD HEALTH AND HOSPITAL FOR SICK CHILDREN

Dr O. H. WOLFF—disturbances of lipid metabolism in childhood. (409)

Chemical Pathology Department

Dr Barbara E. CLAYTON and Professor J. M. TANNER—growth hormone in children. (410)

Dr Barbara E. CLAYTON—insulin levels in blood in relation to (*a*) mental retardation, and (*b*) problems of growth. (411)

EEG and Clinical Neurophysiology Department

Dr G. PAMPIGLIONE—electroencephalograms of children before and after measles. (412)

Growth and Development Department

Professor J. M. TANNER—(1) development of adrenal function in children; (2) growth and development of children (Harpenden Growth Survey). (413)

Haematology Department

Dr R. M. HARDISTY—(1) blood coagulation; (2) acute leukaemia in children; (3) preparation and clinical use of human antihaemophilic globulin concentrates. (414)

Dr A. E. CLAIREAUX—chromosomal abnormalities in leukaemias and other neoplastic diseases of childhood. (415)

Microbiology Department

Dr J. A. DUDGEON—congenital abnormalities, with particular reference to the effects of rubella in pregnancy. (416)

Neonatal Department

Professor J. P. M. TIZARD—metabolism of brown adipose tissue in newborn animals. (417)

INSTITUTE OF DENTAL SURGERY

Mr A. S. T. FRANKS—temporomandibular joint studies. (418)

Biochemistry Department

Dr W. G. ARMSTRONG—components of sound and carious human dentine. (419)

INSTITUTE OF DERMATOLOGY

Professor C. D. CALNAN—effect of antimalarial and other substances and of ultraviolet light on the porphyrin metabolism of humans and animals. (420)

Dr I. A. MAGNUS—(1) photosensitivity of skin; (2) phosphate esters in psoriatic skin; (3) identification of DNP haptene-protein complexes in skin; (4) ultraviolet radiation and the ageing of skin. (421)

Dr Elizabeth A. RYAN—degenerative changes in human skin. (422)

Dr G. C. WELLS—mitotic indices in human skin. (423)

INSTITUTE OF DISEASES OF THE CHEST

Dr Lynne M. REID—(1) certain aspects of mucus secretion in the bronchial tree; (2) intracellular changes associated with mucus secretion; (3) production and control of mucus secretion in the normal and diseased human bronchus (from special funds for the purchase of costly apparatus). (424)

Dr Margaret E. H. TURNER-WARWICK—immunological aspects of (*a*) interstitial pulmonary fibrosis and (*b*) intrinsic and extrinsic asthma. (425)

INSTITUTE OF EDUCATION

Mr B. M. FOSS—effect of signal strength on time taken to detect and localize auditory stimuli. (426)

Professor J. TIZARD—cytogenetical and psychiatric aspects of mongolism in Surrey. (427)

INSTITUTE OF LARYNGOLOGY AND OTOLOGY

Dr R. HINCHCLIFFE—(*a*) clinical investigation of vertigo; (*b*) bioelectric potentials in the cochlea of the cat. (428)

Professor D. F. N. HARRISON—normal and malignant larynges studied by serial section. (429)

INSTITUTE OF NEUROLOGY AND NATIONAL HOSPITAL FOR NERVOUS DISEASES

Dr L. J. HERBERG—neurological basis of motivation. (430)

Dr E. H. REYNOLDS—electrolyte distribution in epilepsy (also at the MRC Neuropsychiatric Research Unit and at West Park Hospital, Epsom). (431)

Dr P. C. BARRINGTON—application of numerical taxonomy to clinical neurology. (432)

Applied Electrophysiology Department

Dr W. A. COBB—cerebral electrical activity which precedes spontaneous and voluntary movements and certain discharges in the EEG. (433)

Chemical Pathology Department

Professor J. N. CUMINGS—study of post-mortem material in chronic neurological disease. (434)

Dr G. CURZON—(1) aromatic amine metabolism in the brain; (2) biochemical studies on caeruloplasmin. (435)

Clinical Neurology Department

Professor R. W. GILLIATT—(1) motor unit innervation ratios in forelimb muscles in primates; (2) toxic neuropathy in the baboon. (436)

Dr T. A. SEARS—nervous mechanism of respiration. (437)

Electron Microscope Laboratory

Dr P. K. THOMAS—electron microscope study of experimental allergic neuritis. (438)

Neuropathology Department

Dr T. G. SCOTT—microanatomical localization in cerebellar cortex. (439)

Neurosurgical Unit

Mr V. LOGUE—(1) analysis of disorders of motor skill in patients with cerebral lesions; (2) mental function and the human optic thalamus (also at the Middlesex Hospital). (440)

Pathological Department

Professor W. H. MCMENEMEY—(1) presenile dementias; (2) comparison between the protein fractions of the cerebrospinal fluid and those in the blood. (441)

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY AND QUEEN CHARLOTTE'S MATERNITY HOSPITAL

Professor J. C. MCCLURE BROWNE—oxytocic lipids in human amniotic fluid. (442)

Professor S. G. CLAYTON and Dr I. F. SOMMERVILLE—human ovarian function in dysfunctional uterine haemorrhage. (443)

Dr Rosalinde HURLEY—(1) 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; (2) pathogenicity of commensal species of the genus *Candida* and the mechanisms of their sensitivity to nystatin and other polyene antibiotics. (444)

Mr W. G. MACGREGOR—measurement of peripheral blood flows in normal pregnancy and the puerperium. (445)

Dr M. SANDLER—investigation of 5-hydroxyindole metabolism in laboratory animals. (446)

Mr H. G. DIXON—morphology of the placental bed and placenta in normal and abnormal pregnancy. (447)

INSTITUTE OF OPHTHALMOLOGY

Dr G. B. ARDEN—analysis of retinal activity. (448)

Professor N. ASHTON—hypertensive retinopathy. (449)

Sir Stewart DUKE-ELDER—investigation of the potentialities of lasers in ophthalmology. (450)

Mr J. S. CONWAY—cryogenic surgery of the ciliary body, to determine the effect of cold applied to the ciliary body on the intra-ocular pressure. (451)

Dr R. A. WEALE—ageing of the crystalline lens. (452)

INSTITUTE OF ORTHOPAEDICS

Dr C. H. LACK—(1) ' thrombolysometers ' in the diagnosis and treatment of thrombosis; (2) staphylococcal toxins, with particular reference to their effect on lysosomes. (453)

Dr J. T. SCALES—' levitation ' in the treatment of large-area burns. (454)

Professor Sir Herbert SEDDON—evaluation of treatment of osteogenic sarcoma of the femur and tibia (on behalf of the Council's Working Party on Bone Sarcoma). (455)

INSTITUTE OF PSYCHIATRY

Biochemistry Department

Dr D. B. GAMMACK—chemical investigation of cerebral constituents. (456)

Professor H. MCILWAIN—chemical contributions to electrical studies of the mammalian brain. (457)

Dr R. W. RODNIGHT—phosphopeptides from membrane proteins. (458)

Experimental Neurology Department

ablations of tae brain on complex behaviour in the monkey. (459)

cerebral cortex associated with epileptogenic lesions; (2) effect of epileptogenic lesions and

ProfessorG. D. DAWSON—(1) alterations of functional and anatomical organization in the

Dr G. ETTLINGER—effects of damage to the cerebral cortex on the ability to make sensory discrimination. (460)

Neuroendocrinology Department

Professor J. T. EAYRS—cerebral mechanisms involved in assembling information from sensory channels. (461)

Neuropathology Department

Dr L. W. DUCHEN—cellular proliferation in the neurohypophysis. (462)

Dr Sabina J. STRICH—congenital malformation of the nervous system. (463)

Physiology Department

Dr H. J. CAMPBELL—determination of the extrahypothalamic regions of the central nervous system involved in anterior pituitary responses to emotional stress. (464)

Psychiatry Department

Professor Sir Aubrey LEWIS—comparative trial of conditioning treatment of neuroses. (465)

Dr R. P. MICHAEL—(1) action of hormones on the activity of the brain; (2) investigation of the mechanisms underlying the expression of sexual behaviour in the female primate; (3) microtelemetry in experimental studies of sexual behaviour and the action of hormones. (466)

Dr E. MARLEY—central effects of sympathomimetic and allied amines, with particular regard to temperature regulation. (467)

Dr M. L. RUTTER—child development. (468)

Psychology Department

Professor H. J. EYSENCK—(1) structure of mental ability; (2) conditioning and personality. (469)

Dr G. W. GRANGER—effect of alcohol on human visual thresholds. (470)

Dr P. SLATER—(1) standardization and revalidation of the Sutton Booklet and the Selective Vocabulary Test; (2) development of a service for analysing repertory grids by computer. (471)

INSTITUTE OF UROLOGY

Mr J. D. FERGUSSON—possible relationship between 'endemic', or primary, bladder stones and malnutrition. (472)

Dr George A. ROSE—parathyroid hormone in urine. (473)

KING'S COLLEGE

Anatomy Department

Dr R. M. H. MCMINN—functional cytology of intestinal absorption and malabsorption. (474)

Biochemistry Department

Dr A. DARBRE and Dr K. H. F. BLAU—amino acid sequence studies of peptides and proteins (from special funds for the purchase of costly apparatus). (475)

KING'S COLLEGE HOSPITAL MEDICAL SCHOOL

Chemical Pathology Department

Professor C. H. GRAY—(1) metabolism of cortisol; (2) metabolism of steroids in disease; (3) biochemical abnormality in acute intermittent porphyria; (4) enzymatic degradation of haem proteins to bile pigments. (476)

Haematology Department

Professor W. M. DAVIDSON—nuclear sex and human chromosomal abnormalities and their relation to various developmental abnormalities. (477)

Medical Physics Department

Dr S. B. OSBORN and Professor J. F. FOWLER—radiation dose to bone from ^{22}Na. (478)

Medical Unit

Professor J. ANDERSON—sodium transport. (479)

Department of Medicine

Dr K. W. TAYLOR—insulin synthesis and secretion in normal and diabetic human serum (also in the Diabetic Unit). (480)

Professor J. ANDERSON and Dr S. B. OSBORN—development of techniques for neutron activation analysis in man *in vivo* (also in the Department of Medical Physics). (481)

Obstetrics and Gynaecology Department

Dr P. F. DIXON—protein binding of steroids in plasma. (482)

Pathology Department

Dr Una M. KROLL—aetiology and recurrence rate of cervical erosion and its relationship to carcinoma. (483)

Surgical Unit

Professor J. G. MURRAY—stomach emptying after pyloroplasty. (484)

LEWISHAM GENERAL HOSPITAL

Dr J. S. STAFFURTH—plasma volume and total body-water in various conditions. (485)

LISTER INSTITUTE OF PREVENTIVE MEDICINE

Dr J. M. CREETH—(1) physico-chemical studies of blood group substances and their derivatives; (2) characterization of protein by the ultracentrifugal steady-state method. (486)

Professor W. T. J. MORGAN—chemical basis of blood group specificity in man. (487)

Dr G. M. GRAY—structural analysis of glycolipids and lipoproteins. (488)

Dr Winifred M. WATKINS—(1) enzymic decomposition of blood group specific substances; (2) biosynthesis of blood group specific glycoproteins and red cell antigens. (489)

Dr W. E. PARRISH—allergic reactions in bacterial infection. (490)

LONDON HOSPITAL

Dr D. G. PENINGTON—(1) methods for preparation of erythropoietin and studies of the factors governing its secretion in animals and in man; (2) aetiology of idiopathic thrombocytopenic purpura. (491)

Physiology Department

Mr A. G. PARKS—*in vitro* study of the physiology and pharmacology of human intestinal muscle (also at the Research Department, St. Mark's Hospital). (492)

LONDON HOSPITAL MEDICAL COLLEGE

Bacteriology Department

Professor C. F. BARWELL—(1) antigenic differences between various strains of trachoma virus; (2) cytophilic antibody and the fate of intracellular organisms. (493)

Dr C. S. CUMMINS—cell wall polysaccharide antigens in gram-positive bacteria. (494)

Dr G. L. ASHERSON—(1) cytotoxic action of immune cells *in vitro*; (2) mechanism of immune deviation and the passive transfer of delayed hypersensitivity. (495)

Dental Anatomy Department

Mr R. W. FEARNHEAD—X-ray probe microanalysis of tooth enamel. (496)

Dental Pathology Department

Professor A. E. W. MILES—pigmented enamel of various vertebrates. (497)

Dental School

Professor G. L. SLACK—(1) bacteriology of dental disease; (2) metabolism of oral filamentous organisms. (498)

Forensic Medicine Department

Dr Barbara E. DODD—detection of blood group substances in stains from body fluids and other body products. (499)

Bernhard Baron Institute of Pathology

Dr D. O. HOURIHANE—asbestosis and mesotheliomas of the pleura and peritoneum. (500)

Pharmacology Department

Professor M. WEATHERALL—effectiveness of various therapeutic procedures. (501)

Physiology Department

Dr R. L. SPEIRS—relation between the chemical composition of teeth and resistance to caries. (502)

Bacteriology and Immunology Department

Dr I. G. MURRAY—mycetoma. (503

Department of Clinical Tropical Medicine

Professor A. W. WOODRUFF—toxocariasis in man. (504)

Entomology Department

Dr M. G. R. VARMA—culture of tissues from arthropods and cold-blooded vertebrates for infection with arboviruses. (505)

Medical Statistics and Epidemiology Department

Professor P. ARMITAGE—statistical analysis of the results of clinical trials with γ-globulin conducted by the Council's Working Party on Hypogammaglobulinaemia. (506)

Dr Geoffrey A. ROSE—the use of steroids in the nephrotic syndrome in adults. (507

Mycological Reference Laboratory

Dr I. G. MURRAY—serology in the classification of fungi and in the diagnosis of mycoses. (508)

Occupational Health and Applied Physiology Department

Professor R. S. F. SCHILLING—(1) prospective clinical, physiological and environmental survey of cotton-mill workers for the study of byssinosis; (2*a*) mortality of cohorts of workers at Cape Asbestos Factory, Barking; (2*b*) asbestos exposure in patients diagnosed as suffering from mesothelioma. (509)

Dr M. L. THOMSON—(1) human lung function in the home and in industry; (2) prospective study of asbestosis (also at Cape Asbestos Factory, Barking); (3) measurement of mucociliary efficiency in the normal and diseased lung (also at the Institute of Nuclear Medicine, Middlesex Hospital Medical School). (510)

Parasitology Department

Dr J. D. FULTON—(*a*) development of new tests for antibodies to *Toxoplasma*; (*b*) preparation of vaccine for malaria. (511)

Dr W. E. ORMEROD—protein metabolism of the malarial parasite. (512)

Ross Institute of Tropical Hygiene

Professor G. MACDONALD—genetics of anopheline mosquitoes. (513)

Virology Department

Professor F. FULTON—(*a*) immune adherence to tissue culture; (*b*) transmission of arboviruses by arthropods. (514)

MIDDLESEX HOSPITAL MEDICAL SCHOOL

Anatomy Department

Dr J. G. BEARN—(*a*) foetal endocrinology; (*b*) biological activity of DNA. (515)

Courtauld Institute of Biochemistry

Dr Patricia MCLEAN—carbohydrate metabolism in the mammary glands. (516)

Dr I. M. ROITT—(1*a*) hypersensitivity in human autoimmune disease; (1*b*) investigation of the autoimmune nature of thyrotoxicoses; (2) connective tissue diseases. (517)

Dr A. E. KELLIE—plasma levels of progestational steroids. (518)

Dr P. N. CAMPBELL—correlation between morphological structure and protein synthesizing activity in rat liver. (519)

Dr K. J. ZILKHA—fatty acid metabolism in multiple sclerosis. (520)

Department of Biology as Applied to Medicine

Dr F. S. BILLETT—effect of nucleic acid antimetabolites on the early development of avian embryos. (521)

Dr N. E. GILLIES—restoration of bacterial cells exposed to ionizing or ultraviolet radiation. (522)

Mr R. F. WITHERS—action of lactones and related compounds on human chromosomes. (523)

Institute of Clinical Research

Dr F. R. BETTLEY—(1) transepidermal water loss; (2) action of soap and detergents on keratin. (524)

Mr N. THOMPSON—survival and reinnervation of free autogenous transplants of skeletal muscles in dogs. (525)

Dr J. D. N. NABARRO—(*a*) idiopathic hirsutism; (*b*) the adrenocortical and metabolic response to acute medical stress. (526)

Ear, Nose and Throat Department

Mr W. S. LUND—motor nerve supply of the larynx and the mechanism and treatment of vocal cord paralysis. (527)

Institute of Nuclear Medicine

Dr J. L. H. O'RIORDAN—immunoassay of glucagon. (528)

Dr W. S. REITH—iodotyrosines and thyroid hormones in various states of thyroid function. (529)

Ferens Institute of Otology

Dr C. S. HALLPIKE—(*a*) histological studies of temporal bone; (*b*) biology of the inner ear fluids. (530)

Pharmacology Department

Professor C. A. KEELE—(1) identification of an intracellular substance which causes the sensation of pain; (2) studies on bradykinin and related peptides. (531)

Academic Department of Psychiatry

Dr J. M. HINTON and Dr V. MEYER—clinical tests of the sensorium in psychiatric patients (from private funds at the Council's disposal). (532)

Dr V. MEYER—control of stammering. (533)

Psychological Medicine Department

Mr S. H. COATES—analysis of results of the Middlesex Hospital Medical School High Altitude Physiological Expedition, 1960. (534)

MOUNT VERNON HOSPITAL

Mr I. F. K. MUIR—blood flow of pedicle and flap grafts used in plastic and reconstructive surgery. (535)

NATIONAL INSTITUTE FOR MEDICAL RESEARCH

Human Physiology Division

Dr S. BLACK—mechanisms involved in the inhibition, by direct suggestion under hypnosis, of allergic skin reactions. (536)

Miss Margaret A. CHAMBERS—dietary survey of Tristan da Cunha islanders. (537)

Physiology and Pharmacology Division

Professor W. FELDBERG—physiology and pharmacology of the brain, with particular reference to temperature regulation and convulsive activity. (538)

Virology and Bacteriology Division

Dr P. M. D'ARCY HART—(*a*) mechanism of the antituberculous effect of macrocyclon; (*b*) growth of leprosy bacilli in cell-free media. (539)

NATIONAL PHYSICAL LABORATORY

Dr I. P. PRIBAN—control of breathing, using control systems theory and an analogue computer. (540)

NEW END HOSPITAL

Dr E. S. SHALOM—iodine constituents in the blood and urine. (541)

NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD

Mr M. WARD—survey of a high altitude population during an expedition to Bhutan, in connection with the International Biological Programme. (542)

NUFFIELD INSTITUTE OF COMPARATIVE MEDICINE

Dr P. A. J. BALL—immunity to *Necator americanus*. (543)

Dr L. G. GOODWIN—immunofluorescent techniques in the study of malaria and helminth infections of man and animals. (544)

Pathology Department

Dr S. B. ROSALKI—composition and function of lactate dehydrogenase isoenzymes in normal and diseased muscle. (545)

POSTGRADUATE MEDICAL SCHOOL OF LONDON AND HAMMERSMITH HOSPITAL

Anaesthesia Department

Dr M. K. SYKES—effect of applied pressure waveforms on differences in alveolar-arterial gas pressure and pulmonary blood flow during mechanical ventilation in the dog. (546)

Professor J. G. ROBSON—effect of anaesthetic drugs on the central nervous system. (547)

Bacteriology Department

Dr Naomi DATTA—(1) transmissible drug resistance among Enterobacteriaceae; (2) antibacterial chemotherapy (grant previously held by the late Professor Mary Barber). (548)

Chemical Pathology Department

Dr K. FOTHERBY—metabolism of ovulation-suppressing agents. (549)

Dr I. MACINTYRE—(1) experimental magnesium deficiency in the rat; (2) isolation, structure and physiological effects of calcitonin. (550)

Professor I. D. P. WOOTTON and Dr J. R. HOBBS—protein studies during MRC therapeutic trial in myelomatosis. (551)

Professor J. F. FOWLER and Dr I. MACINTYRE—magnesium absorption from the gut (also in the Medical Physics Department). (552)

Medical Physics Department

Professor J. F. FOWLER—(1) effect of fractionated irradiation of normal tissue and tumours in animals; (2) thermoluminescent dosimetry; (3) improved radioisotope localization techniques for clinical diagnosis and for studies of turnover *in vivo*. (553)

Department of Medicine

Dr C. C. BOOTH—compensatory mechanisms in the small intestine. (554)

Dr E. J. M. CAMPBELL—(1) particle deposition in the lungs; (2) development of a method for the measurement of mixed venous carbon dioxide tension during exercise; (3) proprioceptive mechanisms in the control of breathing and in the sensation of dyspnoea. (555)

Dr C. L. COPE—aldosterone metabolism in human disease. (556)

Dr C. M. FLETCHER—preclinical stages of chronic bronchitis. (557)

Professor T. RUSSELL FRASER—(1) clinical trials of human growth hormone (on behalf of the Council's Clinical Endocrinology Committee); (2) assay of growth hormone in serum; (3) nature of serum 'atypical' insulin-like activity; (4) radioimmunoassay of protein hormone and a study of electrolyte kinetics in endocrine and metabolic disorders. (558)

Professor Sir John MCMICHAEL—relationship of gout to hypertension. (559)

Dr O. M. WRONG—(1) action of aldosterone on the electrolyte composition of human cells grown in tissue culture; (2) determination of the organic content of faeces. (560)

Dr C. T. DOLLERY—studies in retinopathy (grant previously held by Professor Sir John McMichael). (561)

Microbial Genetics Research Unit

Dr Elinor W. MEYNELL—participation in the Unit's programme, with particular reference to work on resistance-transfer factors. (562)

Morbid Anatomy Department

Dr B. E. HEARD—obliteration of small bronchi and non-respiratory bronchioles. (563)

Pathology Department

Dr H. K. WEINBREN—regeneration of the liver after resection, and related work. (564)

Dr A. G. E. PEARSE—elucidation of the sites of the effect and the mechanism of the activity of calcitonin and localization of its source. (565)

Radiotherapy Department

Professor J. F. FOWLER and Dr R. MORRISON—a technique for *in vivo* studies of hormone dependence of tumour growth. (566)

Dr R. MORRISON—(1) analysis of the results of treatment of malignant disease by Council's 8-MeV linear accelerator; (2) treatment of carcinoma of the bladder by supervoltage radiotherapy and hyperbaric oxygen. (567)

Surgery Department

Mr H. DAINTREE JOHNSON—mechanisms of gastric emptying, with special reference to the effects of surgery. (568)

Mr M. A. E. KULATILAKE—isolated kidney perfusion with whole blood. (569)

PUBLIC HEALTH LABORATORY SERVICE

PUBLIC HEALTH LABORATORY SERVICE BOARD—coordinated studies of the pattern of infection in acute respiratory virus infections. (570)

Cross-Infection Reference Laboratory

Professor R. E. O. WILLIAMS and Dr O. M. LIDWELL—comfort conditions in operating theatres. (571)

Epidemiological Research Laboratory

Dr T. M. POLLOCK—γ-globulin in the prevention of congenital defects. (572)

QUEEN ELIZABETH COLLEGE

Chemistry Department

Dr A. M. JAMES—(1) ionizable surface groups and their relationship to known antigens in staphylococci; (2) lipid material in the cell walls of various strains of streptococci (also at the Central Public Health Laboratory, Colindale). (573)

Nutrition Department

Professor J. YUDKIN—(1) dietary composition and the efficiency of food utilization; (2) dietary and blood chemistry of subjects with non-traumatic arterial disease; (3) protein–calorie interrelationships; (4) sugar intake and arterial disease. (574)

Physiology Department

Dr B. C. WHALER—ionic movements at the nerve endings of normal and botulinum-poisoned nerve-muscle preparations. (575)

QUEEN ELIZABETH HOSPITAL FOR CHILDREN, HACKNEY

Dr Patricia E. MORTIMER—family study of coeliac disease (also at the Hammersmith Hospital). (576)

QUEEN MARY COLLEGE

Chemistry Department

Dr E. W. RANDALL—hydrogen bonding, structure and tautomerism in molecules of biological importance. (577)

ROYAL DENTAL HOSPITAL

School of Dental Surgery

Dr W. G. ARMSTRONG—nature of the modifications to the dentine matrix caused by dental caries. (578)

ROYAL EYE HOSPITAL

Professor A. SORSBY—variations in the components of refraction during growth. (579)

ROYAL FREE HOSPITAL

Chemical Pathology Department

Professor D. N. BARON—(1) computer studies on the correlation between signs and symptoms and laboratory findings in liver disease (also at the University of London Institute of Computer Science); (2) purification, properties and distribution of isoenzymes of NADP-specific isocitrate dehydrogenase. (580)

Dermatology Department

Dr I. SARKANY—organ culture of human skin, with particular reference to drug-induced stimulation of peripheral lymphocytes *in vitro*. (581)

Ophthalmology and Diabetes Departments

Mr H. E. HOBBS—effects of retinal photocoagulation in halting the progress of diabetic retinopathy. (582)

Anatomy Department

Dr P. R. DAVIS—effects of material-handling methods on respiratory and trunk mechanics. (583)

Biochemistry and Chemistry Department

Dr H. BAUM—biochemistry of induced thermogenesis in the neonate. (584)

Haematology Department

Dr Katharine M. DORMANDY—investigation into the problems of children with coagulation disorders. (585)

Medical Physics Department

Dr N. F. KEMBER—(1) effects of radiation on the cellular complement of rat bone; (2) effects of radiation on cartilage cells in organ and tissue culture. (586)

Professor H. A. B. SIMONS—possible protective action against ionizing radiations of a series of compounds incorporating the thioureido and guanidino structures. (587)

Department of Medicine

Dr Barbara H. BILLING—bile pigment metabolism in jaundice. (588)

Dr A. M. DAWSON—the effect of bile salts on the esterification of fatty acids by the small gut mucosa. (589)

Professor Sheila SHERLOCK—drug metabolism in liver disease. (590)

Dr Ten FEIZI—cold agglutinins caused by *Mycoplasma pneumoniae* infection. (591)

Dr E. SAMOLS—interrelationships between hormones and metabolites in health and disease. (592)

Morbid Anatomy Department

Dr G. B. D. SCOTT—(1) thrombotic sequelae of the generalized Schwartzman reaction; (2) *in vivo* studies of coagulation and thrombosis. (593)

Pharmacology Department

Dr J. R. HODGES—mechanisms controlling adrenocorticotrophic activity. (594)

Professor Eleanor J. ZAIMIS—(1) mode of action of reserpine; (2) drug-induced myocardial abnormalities. (595)

Physiology Department

Dr J. C. G. COLERIDGE—reflexogenic receptors in the pulmonary circulation. (596)

Professor C. B. B. DOWNMAN—(1) supraspinal control of visceral activity; (2) transplantation of canine pulmonary tissue (also at the Buckston-Browne Farm of the Royal College of Surgeons of England); (3) supraspinal control of sympathetic outflows. (597)

Dr R. E. MOORE—(1) control of heat production in the newborn; (2) discriminative capacity of the infant rat in response to a change in environmental temperature. (598)

ROYAL HOLLOWAY COLLEGE

Zoology Department

Dr G. I. TWIGG—*Leptospira* in rodent populations. (599)

Dr J. C. BROWN—central nervous control of salivation. (600)

ROYAL MARSDEN HOSPITAL

Clinical Pathology Department

Dr H. E. M. KAY—collection and preservation of foetal tissues. (601)

Clinical Research Department

Dr C. B. CAMERON—role of 6-phosphogluconate dehydrogenase and related enzymes in the development of neoplasia, with special reference to the early diagnosis of uterine cancer. (602)

ROYAL VETERINARY COLLEGE

Student Expedition

Mr M. T. SHEPPARD—collection of specimens during the College's East African Expedition, 1965 (from private funds at the Council's disposal). (603)

Dr J. FRY—outcome of acute otitis media n children (also at Dr Fry's general practice at Beckenham, Kent). (604)

ST. BARTHOLOMEW'S HOSPITAL MEDICAL COLLEGE

Bacteriology Department

Dr R. B. HEATH—serological studies of respiratory virus infection (from special funds for the purchase of costly apparatus). (605)

Biochemistry and Chemistry Department

Professor E. M. CROOK—(1) imidazole-sulphydryl hydrogen bonding and the active sites of enzymes; (2) isolation and study of the active principles of *Clibadium sylvestre* and *Cissampelos ovalifolia.* (606)

Dr G. E. FRANCIS—chemistry of natural products of British Guiana of medicinal importance. (607)

Pathology Department

Professor W. G. SPECTOR—(1) mechanics of increased capillary permeability; (2*a*) lymphoid cell factors as mediators of local hypersensitivity reactions; (2*b*) origin and fate of mononuclear cells in inflammatory exudates. (608)

Pharmacology Department

Professor J. P. QUILLIAM—(1) relation of electron-microscopic structure of ganglion cells to pharmacological action; (2) isolation and study of the active principles of *Clibadium sylvestre* and *Cissampelos ovalifolia.* (609)

Physics Department

Professor J. ROTBLAT—age factor in radiation sensitivity of mammals. (610)

Physiology Department

Professor M. DE BURGH DALY—mechanisms underlying the control of the circulation by chemoreceptors. (611)

Dr B. N. DAVIES—synthesis and release of noradrenaline at postganglionic nerve endings. (612)

Dr E. W. HORTON—metabolism and physiological significance of the prostaglandins. (613)

Zoology and Comparative Anatomy Department

Professor D. LACY—mammalian spermatogenesis. (614)

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL

Bacteriology Department

Dr H. P. LAMBERT—Eaton agent in chronic respiratory disease. (615)

Dr L. O. BUTLER—studies on DNA. (616)

Chemical Pathology Department

Professor N. H. MARTIN—nature of the interaction of metals with proteins, with special reference to the naturally occurring metalloproteins. (617)

Haematology Department

Dr J. L. STAFFORD—comparative study of blood coagulation and fibrinolysis in West African and English males (in association with the University of Ibadan). (618)

Department of Medicine

Professor A. C. DORNHORST—clinical trial of diet in coronary thrombosis (with Professor J. N. Morris). (619)

Psychiatry Department

Mr H. GWYNNE JONES—visual perceptual functioning in patients with localized cerebral lesions. (620)

Professor D. CURRAN—(*a*) psychological effects of localized brain lesion; (*b*) effects of stress on performance; (*c*) aspects of ' behaviour therapy '. (621)

Surgical Unit

Professor B. N. BROOKE—steroid therapy in ulcerative colitis. (622)

ST. LUKE'S HOSPITAL, MUSWELL HILL

Professor Sir Denis HILL—orienting reaction. (623)

ST. MARK'S HOSPITAL

Dr B. C. MORSON—(*a*) pathogenesis of inflammatory diseases of the large intestine; (*b*) mechanism of venous embolism in cancer of the large intestine; (*c*) histopathology of anal cancer. (624)

Dr A. C. YOUNG—angiography of the colon in neoplasm, diverticular disease and ulcerative colitis. (625)

Mr A. G. PARKS—*in vitro* study of human alimentary smooth muscle. (626)

ST. MARY'S HOSPITAL

Mr M. TAYLOR—repair and grafting of the tympanic membrane. (627)

Paediatric Unit

Dr J. A. AMBROSE—nature of distress reactions in infancy (also at Medical Research Council Laboratories, Hampstead). (628)

ST. MARY'S HOSPITAL MEDICAL SCHOOL

Anatomy Department

Dr A. d'A. BELLAIRS—wound healing and regeneration in reptile embryos. (629)

Dr A. S. BREATHNACH—electron microscopy of human skin. (630)

Bacteriology Department

Professor R. E. O. WILLIAMS—(1) classification of non-haemolytic streptococci; (2) chemical investigation of staphylococci and their extracellular products during the early stages of subcutaneous injection. (631)

Professor R. E. O. WILLIAMS and Dr Margot SHINER—intestinal bacterial flora in healthy humans. (632)

Dr R. R. DAVIES—promotion of fungal infection by antibiotic and other drug treatment. (633)

Dr G. W. CSONKA—aetiology of non-gonococcal genital infections (also at Central Middlesex Hospital and Twyford Virus Laboratory). (634)

Biology Department

Dr Marjorie ALLANSON—cytological and histochemical study of the mammalian adeno-hypophysis. (635)

Chemical Pathology Department

Dr H. D. BARNES—porphyrin metabolism. (636)

Immunology Department

Dr S. COHEN—association of the A and B chains of human γ-globulin. (637)

Professor R. R. PORTER—chemical structure of γ-globulin. (638)

Medical Unit

Professor W. S. PEART—(1) definition of the role of the renal enzyme renin in the control of aldosterone secretion, electrolyte balance by the kidney and renal hypertension; (2) physiological and pathological role of the renin-angiotensin system; (3) mode of action and enzyme specificity of renin and its localization in the kidney. (639)

Obstetrics and Gynaecology Department

Professor I. MACGILLIVRAY—electrolyte studies in pregnant women. (640)

Dr D. B. PAINTIN—electrolyte studies in pregnant women. (641)

Pathology Department

Dr K. A. PORTER—immunological study of X-irradiated animals with marrow transplants (also in Bacteriology Department). (642)

Pharmacology Department

Dr P. A. NASMYTH—relationship of adenosine 3′,5′-phosphate to the activity of sympathomimetic amines. (643)

Physics Department

Dr S. ROWLANDS—flow of red cell suspensions through artificial capillary beds. (644)

Physiology Department

Dr R. CREESE—(1) sodium exchange in isolated muscle; (2) labelled depolarized drugs in striated muscle. (645)

Dr Pamela HOLTON—(1) chemical transmitters at nerve endings; (2) secretion, vascular resistance and oxygen consumption in the stomach of the anaesthetized dog. (646)

Professor A. D. M. GREENFIELD—effects of acute and chronic changes in the viscosity of blood on the reactivity of blood vessels responsible for peripheral resistance. (647)

Surgical Unit

Mr J. R. KENYON—deep hypothermia with exsanguination and total circulatory arrest, and its application to human patients for certain surgical procedures. (648)

Professor W. T. IRVINE—homograft response and tumour immunity. (649)

ST. THOMAS'S HOSPITAL

Anaesthetics Department

Dr T. H. S. BURNS—development of non-explosive anaesthetic agents (in collaboration with Dr J. M. Hall, Guy's Hospital). (650)

Dr H. C. CHURCHILL-DAVIDSON—neuromuscular transmission in man. (651)

Radiography Department

Dr G. WIERNIK—effect of ionizing radiation in tissues. (652)

ST. THOMAS'S HOSPITAL MEDICAL SCHOOL

Anatomy Department

Professor D. V. DAVIES—physical properties of synovial fluid. (653)

Chemical Pathology Department

Professor F. T. G. PRUNTY—steroid metabolism. (654)

Gynaecology Department

Dr Maureen YOUNG—(1) placental transfer of amino acids; (2) regional blood flow changes during a reduction in systemic pulse pressure and during asphyxia in young animals. (655)

Medical Microbiology Department

Professor A. P. WATERSON—(1) viral structure and multiplication, using electron microscopy; (2) diagnosis and nature of rubella. (656)

Department of Medicine

Dr S. J. G. SEMPLE—chemical control of ventilation in man and the respiratory and cardiovascular effects of tracheostomy and artificial ventilation. (657)

Pathology Department

Professor R. C. CURRAN—mucopolysaccharides in (*a*) atherosclerosis and (*b*) fibrous repair. (658)

Professor R. C. CURRAN and Dr A. J. HALE—development of a scanning X-ray microanalyser for quantitative cytochemistry. (659)

Physiology Department

Professor H. BARCROFT—effect of altitude on cardiac and pulmonary physiology. (660)

Dr M. T. JONES—regulation of pituitary adrenocorticotrophic activity. (661)

Dr F. J. IMMS—catecholamine production and excretion, and interrelationships between the autonomic nervous system, the adrenal medulla and the adrenal cortex. (662)

Surgery Department

Professor J. B. KINMONTH—(*a*) endolymphatic therapy of transplantable tumours; (*b*) lymphangiography. (663)

SCHOOL OF PHARMACY

Dr W. C. BOWMAN—mechanism of action of adrenaline on muscle. (664)

Professor G. A. H. BUTTLE—effect of pregnancy and of steroid hormones in inhibiting the growth of certain tumours. (665)

Dr G. B. WEST—uptake, storage and release of labelled histidine and histamine by tissues of different species. (666)

Anatomy and Embryology Departments

Professor J. Z. YOUNG—(1) synaptic structure in the autonomic nervous system; (2) fine structure of the nervous system. (667)

Anthropology Department

Professor N. A. BARNICOT—(1) the human karyotype in various populations; (2) genetical variation in natural populations of the baboon in Uganda; (3) chemical composition of some primate haemoglobins. (668)

Biochemistry Department

Professor E. H. F. BALDWIN—structural and enzymatic studies on myosin. (669)

Mrs F. H. CLARKE—(1) structure and mode of synthesis of cell walls of *Pseudomonas* spp; (2) studies on amidase production by mutant strains of *Pseudomonas aeruginosa.* (670)

Dr S. P. DATTA—kinetic and calorimetric study of the reaction catalysed by the enzyme isocitrate lyase. (671)

Dr A. L. GREENBAUM—(1) control of metabolism by the pyridine nucleotides; (2) a computer program for studies on carbohydrate and fat metabolism. (672)

Dr L. Margaret KERLEY—amino acid metabolism in the perfused rat liver. (673)

Dr K. L. MANCHESTER—hormones and protein synthesis in muscle. (674)

Dr A. P. MATHIAS—(1) isolation of the messenger RNA responsible for the synthesis of amidohydrolase in *Pseudomonas aeruginosa*; (2) isolation and characterization of messenger RNA from avian reticulocytes. (675)

Dr D. B. RODYN—protein synthesis in mitochondria. (676)

Dr B. R. RABIN—the mechanism of action of glutamic dehydrogenase. (677)

Biophysics Department

Dr P. FATT—(1) mechanism of visual excitation; (2) photoconductive charges in rod outer segments. (678)

Botany and Chemistry Departments

Dr D. WILKIE and Dr D. V. BANTHORPE—genetics and chemistry of actidione action in yeast. (679)

Professor D. LEWIS—characterization of mitochondrial DNA and its role in the morphogenesis of the mitochondrion of *Saccharomyces cervisiae.* (680)

Chemistry Department

Dr C. A. VERNON—(1) enzymic transamination; (2) structure and biological activity of the wasp venom kinins. (681)

Dr A. WASSERMANN—molecular size and shape of muscle proteins in dilute solution. (682)

Crystallography Department

Professor Dame Kathleen LONSDALE—X-ray studies of endemic bladder stones. (683)

The Galton Laboratory

Professor C. A. B. SMITH—statistical study of factors associated with spontaneous abortion. (684)

Pharmacology Department

Professor H. O. SCHILD and Dr C. A. VERNON—identification of urogastrone. (685)

Professor H. O. SCHILD—(1) histidine decarboxylase in sensitized lymph node cells; (2) the action of psychotropic drugs. (686)

Physiology Department

Dr H. DAVSON—mechanism of formation and drainage of the cerebrospinal fluid. (687)

Professor J. A. B. GRAY—transmission of information about external stimuli in primary and second-order receptor neurones. (688)

Dr O. C. J. LIPPOLD—(1) long-term effects of polarizing currents on the rat cerebral cortex; (2) the mechanism by which polarizing currents produce long-lasting changes in the spontaneous firing of cortical cells. (689)

Mr J. E. PASCOE—(1) central control of muscle spindles; (2) relative importance of activation of α and γ motor neurones in muscle reflexes; (3) discharge pattern of semitendinosus fusimotor neurones in the rabbit and the effect of spinal transection and stimulation and of drugs; (4) histological identification of α and γ motor neurones. (690)

Dr M. SCHACHTER—possible physiological significance of kinins and of the enzymes which release them. (691)

Dr D. R. WILKIE—muscle physiology (also at the Plymouth Laboratory of the Marine Biological Association). (692)

Dr Barbara BANKS and Dr J. DIAMOND—isolation and characterization of γ-amino butyric transaminase. (693)

Dr L. H. SMAJE—the role of kinins in the regulation of blood flow. (694)

Dr R. D. HARKNESS—nature of mechanical linkages in connective tissue frameworks. (695)

Psychology Department

Miss G. H. KEIR—psychological study of the children of school age in the Tristan da Cunha settlement. (696)

Mr J. W. WHITFIELD—affective disorders in schizophrenia (grant previously held by Dr A. A. Robin at Runwell Hospital, Wickford). (697)

Student Health Service

Dr C. J. LUCAS—prevalence of mental ill-health in a population of university students. (698)

UNIVERSITY COLLEGE HOSPITAL

Clinical Pathology Department

Dr F. V. FLYNN—proteinuria accompanying generalized renal tubular malfunction. (699)

Obstetrics Department

Dr Mavis GUNTHER—development of immune responses to cows' milk in infants during the first weeks of life. (700)

Respiratory Function Laboratory

Dr P. J. D. HEAF—(*a*) effects of respiratory stimulants on ventilation; (*b*) cinebronchography; (*c*) circulatory failure in cases of intermittent positive pressure ventilation. (701)

UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL

Bacteriology Department

Dr J. P. STEVENSON—virus morphology and cell-virus interaction. (702)

Chemical Pathology Department

Dr H. HEATH—metabolism of the retina and other ocular tissues in alloxan-produced diabetes. (703)

Dr T. F. SLATER—energy mechanisms in biliary secretion. (704)

Dr K. R. REES—protein synthesis and liver injury. (705)

Dermatology Department

Dr R. I. C. SPEARMAN—epidermal growth and keratinization. (706)

Medical Unit

Professor C. E. DENT—(1) osteoporosis in young people; (2) uses of a computer in the diagnosis of disorders of calcium metabolism. (707)

Dr D. C. CUSWORTH—metabolic disorders in man, particularly those involving amino acids. (708)

Dr C. J. DICKINSON—(*a*) renal pulse pressure in relation to the rate of urine excretion; (*b*) cerebral vascular resistance in the control of blood pressure. (709)

Mr R. G. WESTALL—inherited diseases which exhibit disorders of amino acid metabolism. (710)

Obstetric Unit

Professor W. C. W. NIXON—aetiology and diagnosis of carcinoma of the cervix. (711)

Dr C. N. SMYTH—relation of posture to the duration, discomfort and forces of labour in human subjects. (712)

Paediatrics Department

Dr L. B. STRANG—pathogenesis of hyaline membrane disease. (713)

UNIVERSITY OF LONDON INSTITUTE OF COMPUTER SCIENCE

Professor R. A. BUCKINGHAM and Dr A. ELITHORN—factors which determine failures in problem solving by human subjects. (714)

Zoology Department

Dr J. A. RIEGEL—functional mechanism of the cray-fish antennal gland. (715)

WEST MIDDLESEX HOSPITAL

Dr P. M. MCALLEN—clinical trial of diet in coronary thrombosis (with Professor J. N. Morris). (716)

WESTMINSTER HOSPITAL

Mr P. D. TREVOR-ROPER—long-term preservation of human cornea. (717)

Dr J. H. WILKINSON—specificity of serum enzyme tests. (718)

Dr V. J. REDDING—(*a*) myocardial blood flow; (*b*) effects of drugs of potential value in coronary disease. (719)

WESTMINSTER MEDICAL SCHOOL

Chemical Pathology Department

Professor N. F. MACLAGAN—(1) origin and absorption of blood phospholipids; (2) familial hypercholesterolaemic xanthomatosis. (720)

Surgery Department

Mr A. G. HORSBURGH—transference of mucosa in the gastrointestinal tract, with reference to the treatment of ulcerative colitis. (721)

Surgical Unit

Dr A. D. M. SMITH—cyanide metabolism in man. (722)

WHITTINGTON HOSPITAL

Dr A. M. JOEKES—abnormalities of renal function in man (also at St. Philip's Hospital). (723)

Paediatric Department

Dr S. YUDKIN—serum proteins in children. (724)

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Lady M. MELLANBY—the structure of teeth. (725)

Dr A. RYLE—neuroticism and family relationships of 14-year-old children. (726)

Manchester

COLLEGE OF SCIENCE AND TECHNOLOGY

Biochemistry Department

Dr S. SHALL—synthesis of heavy atom derivatives of bovine pancreatic ribonuclease. (727)

Chemical Engineering, Fuel Technology and Metallurgy Department

Professor T. K. Ross—isolation of aromatic hydrocarbons from petroleum (grant formerly held by Professor F. Morton). (728)

Electrical Engineering Department

Dr J. B. KNOWLES—microminiaturized biological amplifiers (729)

ROYAL INFIRMARY

Dr K. G. WORMSLEY—gastric and duodenal function in health and in peptic ulceration. (730)

Clinical Haematology Department

Dr M. C. G. ISRAELS—(*a*) folic acid metabolism; (*b*) metabolism in renal disease; (*c*) vitamin D metabolism (from special funds for the purchase of costly apparatus). (731)

Department of Medicine

Dr Pamela E. AYLETT—(*a*) gastric physiology and peptic ulcer; (*b*) serotonin and histamine in ulcerative colitis. (732)

Neurosurgery Department

Mr R. TYM—growth-rate kinetic studies, and studies of radiation sensitivity in human and experimental malignant cerebral tumours. (733)

University Department of Surgery

Mr D. Ll. GRIFFITHS—tuberculosis of the spine in the tropics. (734)

UNIVERSITY

Bacteriology Department

Dr G. TAYLOR—byssinosis antigen research. (735)

Chemistry Department

Dr G. R. BARKER—RNA and tumour growth. (736)

Dr F. R. JEVONS—(1) mode of action of enzymes acting on the carbohydrate moieties of mucoproteins; (2) naturally occurring glycopeptides. (737)

Dr W. D. STEIN—(1) isolation of the glucose transport system from the membrane of the human red blood cell; (2) direct visual localization of a transport system in the membrane of the human red blood cell. (738)

Dr C. H. WYNN—specificity of the collagenolytic activity of rat liver lysosomes. (739)

Pathology Department

Dr A. H. GOWENLOCK—determination of vitamin D in serum. (740)

Pharmacology Department

Professor H. SCHNIEDEN—urinary dopamine in patients with tremor. (741)

Preventive Dentistry Department

Professor J. L. HARDWICK—fluoride content of the dental plaque. (742)

Social and Preventive Medicine Department

Dr Zena A. STEIN—(*a*) mental illness in Salford, with analyses by electronic computer; (*b*) school health studies in Leigh (also at the Computing Laboratory and the Salford City Mental Health Department). (743)

Dr M. W. SUSSER—programming medical and survey data for analysis by the Atlas computer. (744)

Menston, Ilkley

HIGH ROYDS HOSPITAL

Dr R. P. HULLIN and Dr R. MCDONALD—changes in body water and electrolytes in manic-depressive psychosis and depressive illness. (745)

Mickley-on-Tyne

Professor G. R. CLEMO—chemical constituents of cigarette smoke. (746)

Newcastle upon Tyne

ROYAL VICTORIA INFIRMARY

University Department of Child Health

Professor S. D. W. COURT—viruses in chronic respiratory disease in children and in cross-infection in children's wards. (747)

Clinical Biochemistry Department

Professor A. L. LATNER—studies of isoenzymes by starch gel electrophoresis. (748)

Dermatology Department

Professor S. SHUSTER—(1) effect of various diseases on skin connective tissues; (2) internal manifestations of cutaneous disease. (749)

Midwifery and Gynaecology Department

Dr D. V. I. FAIRWEATHER—effect of age and parity on the urinary excretion of sex hormones in normal pregnancy. (750)

University Department of Psychological Medicine

Professor M. ROTH—psychometric assessment of cerebral damage. (751)

Anatomy Department

Professor R. J. SCOTHORNE—correlated studies of structure and function in the developing parathyroid and salt glands. (752)

Biochemistry Department

Dr A. H. EMSLIE-SMITH—strain recognition of coliform bacilli in recurrent urinary tract infection. (753)

Chemistry Department

Professor J. WEISS—(1) mechanism of the chemical action of ionizing radiations on nucleic acids, nucleoproteins and related compounds; (2) radiation-induced structural changes in nucleic acids. (754)

Dr G. SCHOLES—pulse radiolysis of aqueous solutions of nucleoproteins, nucleic acid and related substances. (755)

Sutherland Dental School

Professor C. H. TONGE—histological studies of the developing tooth and its supporting structures, including the examination of the teeth and jaws in undernourished pigs. (756)

Professor G. N. JENKINS—the proteins and mucopolysaccharides of the dental plaque. (757)

Nuffield Department of Industrial Health

Mr D. N. WALDER—decompression sickness (on behalf of the Council's Decompression Sickness Panel). (758)

Pharmacology Department

Professor J. W. THOMPSON—(*a*) enzymic and subcellular aspects of adrenergic transmission; (*b*) drug metabolism. (759)

Physiology Department

Professor A. A. HARPER—hormonal and nervous effects on gastric and pancreatic secretion. (760)

Dr B. SCHOFIELD—intramural nerve plexuses in the control of gastric secretion. (761)

Dr H. S. A. SHERRATT—(*a*) hypoglycaemic compounds; (*b*) energy metabolism of the pancreas. (762)

Dr W. TAYLOR—*in vitro* and *in vivo* metabolism of progesterone. (763)

Dr H. J. LAKE—hormones of the gastrointestinal tract. (764)

Dr A. J. MCCOMAS—neuronal control of cells in the dorsal column nuclei. (765)

Psychology Department

Dr K. GIBBINS—effect of temporal variations of stimuli on visual threshold phenomena. (766)

Surgery Department

Mr D. N. WALDER—(1) decompression sickness in Tyne Tunnel workers; (2) bone necrosis in compressed air workers: radiographic surveys (on behalf of the Council's Decompression Sickness Panel). (767)

Northampton

PUBLIC HEALTH LABORATORY

Dr L. HOYLE—(1) physical and chemical structure of the influenza virus; (2) chemical reactions of myxovirus proteins. (768)

Nottingham

MAPPERLEY HOSPITAL

Dr D. MACMILLAN—subsequent history of schizophrenic patients admitted in 1956 to the Mapperley, Netherne and Severalls Hospitals. (769)

UNIVERSITY

Pharmacology Laboratories

Dr J. CROSSLAND—nature and behaviour of chemical transmitter substances in the central nervous system. (770)

Pharmacy Department

Dr W. C. EVANS—formation of the ditigloyl esters of tropine in the roots of various species of *Datura*. (771)

Psychology Department

Professor C. I. HOWARTH—(1) temporal characteristics of the visual system; (2*a*) mobility of blind people; (2*b*) development of keyboard skills. (772)

Zoology Department

Dr Rosalind S. M. KENT—reticulo-endothelial system of vertebrates. (773)

Oswestry

THE ROBERT JONES AND AGNES HUNT ORTHOPAEDIC HOSPITAL

Mr N. W. NISBET—experimental problems of transplantation. (774)

Oxford

CHURCHILL HOSPITAL

Neurology Department

Dr C. W. M. WHITTY—referred pain. (775)

Dr E. W. POOLE—time relationship between EEG phenomena, internal bodily events and external stimuli. (776)

Radiotherapy Department

Dr F. ELLIS—modification of radiation effects by physical and pharmacological means. (777)

RADCLIFFE INFIRMARY

Accident Service

Mr J. C. SCOTT—reactions of the blood to injury. (778)

Nuffield Department of Clinical Biochemistry

Dr M. P. ESNOUF—interactions of the plasma proteins concerned in blood coagulation. (779)

Dr A. R. PEACOCKE—(1) complexes of non-basic proteins and histones with DNA; (2) effects of ionizing radiations and other mutagenic agents on the structure of soluble nucleoprotein. (780)

Nuffield Department of Clinical Medicine

Dr E. D. ACHESON—multiple sclerosis in immigrants. (781)

Dr Sheila T. E. CALLENDER—(1) family study of pernicious anaemia and ' latent ' pernicious anaemia; (2) importance of iron deficiency, autoimmunity and other factors in the Plummer-Vinson syndrome (grant previously held by Professor L. J. Witts). (782)

Dr S. C. TRUELOVE—aetiology of ulcerative colitis, with special reference to immunological aspects. (783)

Dr S. C. TRUELOVE and Dr G. M. ARDRAN—human colonic motility in health and disease. (784)

Department of the Regius Professor of Medicine

Professor Sir George PICKERING—(1) clinical aspects of genetically determined errors of amino acid metabolism; (2) arterial pressure regulation during sleep. (785)

Neurology Department

Dr W. RITCHIE RUSSELL—war wounds of the brain. (786)

Dr J. M. K. SPALDING—autonomic function in normal and diseased man. (787)

Pathology Department

Dr M. S. DUNHILL—quantitation in morbid anatomy. (788)

Nuffield Department of Surgery

Mr A. J. GUNNING—(1) the use of homologous aortic valve transplants in the surgical treatment of aortic incompetence; (2*a*) long-term fate of transplanted heterologous heart valves; (2*b*) an immunological study of these valves. (789)

Mr J. S. S. STEWART—frozen blood. (790)

Anatomy Department

Dr T. P. S. POWELL—cerebral connections of certain sensory systems. (791)

Biochemistry Department

Dr K. DALZIEL—enzyme kinetics. (792)

Dr C. A. PASTERNAK—control of sulphur and amino sugar metabolism in the mast-cell tumour P815. (793)

Dr L. A. STOCKEN—(1) biochemical effects of ionizing radiation on mammalian systems; (2) X-irradiation of thiol groups in thymus nuclei (from special funds for the purchase of costly apparatus). (794)

Dr M. A. FOSTER—cellular functions of vitamin B_{12} and folic acid in microorganisms. (795)

Chemical Crystallography Laboratory

Professor Dorothy C. HODGKIN—detailed structure determination of vitamin B_{12}. (796)

Dyson Perrins Laboratory

Dr G. LOWE—(1) studies related to the antibiotic cephalosporin C; (2) structure and mechanism of action of the proteolytic enzyme papain. (797)

Institute of Experimental Psychology

Dr E. R. F. W. CROSSMAN—analysis of human motor control mechanisms. (798)

Dr M. TREISMAN—investigation of the hierarchical mechanisms in auditory and visual perception. (799)

Dr D. M. VOWLES—role of the forebrain structures in learning and motivation in the pigeon. (800)

Professor R. C. OLDFIELD—effect of reproductive hormones on the behavioural responses to stress in the rat. (801)

Dr M. KINSBOURNE—short- and long-term memory processes and their impairment in organic cerebral disease. (802)

Dr N. J. MACKINTOSH—animal discrimination learning. (803)

Human Anatomy Department

Dr S. BRADBURY—localization of mucopolysaccharides by electron histochemistry. (804)

Dr D. A. T. DICK—ion fluxes in single cells. (805)

Dr A. G. M. WEDDELL—structural changes in skin and sensory nerve trunks associated with leprosy and psoriasis. (806)

Professor G. W. HARRIS—electron microscopy studies of histopathological changes in skin and nerves (from special funds for the purchase of costly apparatus). (807)

Dr K. BROWN-GRANT—experimental analysis of the thyroid-ovary interrelationship. (808)

Dr G. A. HARRISON—population genetics and the growth and development of children in selected rural areas around Oxford. (809)

Inorganic Chemistry Department

Dr R. J. P. WILLIAMS—metalloprotein complexes, especially in relation to enzymes. (810)

Dr L. M. VENANZI—metal-containing histochemical stains. (811)

Department of Regius Professor of Medicine

Professor Sir George PICKERING—arterial occlusion. (812)

Nuffield Laboratory of Ophthalmology

Dr S. G. WALEY—(*a*) proteins of the lens; (*b*) structure and function of related glycolytic enzymes. (813)

Mrs Antoinette PIRIE—metabolism of the lens in relation to cataract formation. (814)

Sir William Dunn School of Pathology

Dr E. P. ABRAHAM—(1) isolation, structure and mode of action of a peptide-like substance produced by *B. subtilis*; (2) biosynthesis, structure and function of some microbial products. (815)

Dr A. G. SANDERS—behaviour of platelets and other cells in living vessels. (816)

Dr W. E. VAN HEYNINGEN—isolation of a toxin of *Clostridium septicum* and *C. sordellii* and determination of its mode of action. (817)

Dr M. L. FENWICK—RNA synthesis in normal and virus-infected cells. (818)

Pharmacology Department

Dr H. BLASCHKO—biochemical pharmacology of catecholamines and of neurophysin. (819)

Dr Edith BÜLBRING—physiology and pharmacology of smooth muscle. (820)

Professor W. D. M. PATON—(1) drug receptors and uptake of drugs by tissues; (2) studies on the renin-angiotensin system. (821)

Physical Chemical Laboratory

Dr A. C. R. DEAN—variations in enzyme activity during the growth cycle and during the continuous culture of *Aerobacter aerogenes*. (822)

Physiology Laboratory

Lord FLOREY—investigation of the structure of blood vessels, with particular reference to the endothelium. (823)

Professor Sir George PICKERING and Professor Sir Lindor BROWN—cardiovascular afferent fibres in animals and in man (also at the Radcliffe Infirmary). (824)

Professor Sir Lindor BROWN—electron-microscope studies of the fine structure of blood vessels and nerve cells (from special funds for the purchase of costly apparatus). (825)

Mr B. H. COLMAN—temporal bone microtomy, studied by means of animal experimentation and by investigations of human otopathology. (826)

Dr G. GORDON—functional organization of somatosensory nuclei in the mammalian nervous system and their control by the higher parts of the brain. (827)

Social Medicine Department

Dr Alice STEWART—(1) survey of leukaemia in adults and children; (2) malignant diseases in childhood; (3) Oxford Cancer Surveys (children and adults). (828)

Nuffield Department of Surgery

Professor P. R. ALLISON—venous thrombosis and the natural history of pulmonary emboli. (829)

Zoology Department

Dr J. B. GURDON—changes in the function of living cell nuclei on exposure to different cytoplasmic environments. (830)

Professor J. W. S. PRINGLE—physiology of mouse trophoblast and the effect of extra-uterine pregnancy on the oestrus cycle. (831)

Peaslake

Dr G. I. WATSON—infectious diseases in a rural community. (832)

Portsmouth

PORTSMOUTH AND ISLE OF WIGHT AREA PATHOLOGICAL SERVICE

Dr J. R. O'BRIEN—platelet stickiness. (833)

Reading

UNIVERSITY

Dr J. D. CUMMING—relationship between the secretory activity of the stomach and gastric blood flow. (834)

Physics Department

Professor R. W. DITCHBURN—eye movements in relation to visual perception. (835)

Redcar

Dr G. K. H. HODGKIN—(1) records of age, diagnosis and morbidity in a general practice; (2) ulcer dyspepsia and its relation to peptic ulcer. (836)

St. Andrews

UNIVERSITY

The Gatty Marine Laboratory

Dr G. A. HORRIDGE—(1) activation of contraction of striated muscle; (2) electrophysiological experiments on memory as a factor in movement perception in the crab. (837)

Natural History Department

Dr G. A. T. TARGETT—serology and protective immunology in experimental animals infected with or immunized against malaria. (838)

Physiology and Biochemistry Department

Dr G. R. TRISTRAM—structure and selective degradation of collagen and the analysis of leaf protein. (839)

Sheffield

THE JESSOP HOSPITAL FOR WOMEN

Endocrine Investigation Centre

Dr G. W. PENNINGTON—source of polar steroids and their excretion in biological fluids, including changes in excretion in both normal and pathological pregnancy. (840)

University Department of Obstetrics and Gynaecology

Professor C. SCOTT RUSSELL—computer analysis of obstetric and paediatric data. (841)

NETHER EDGE HOSPITAL

Dr H. F. WEST—excretion of corticosteroid hormones in urine and saliva. (842)

ROYAL HOSPITAL

University Department of Medicine

Dr J. R. COX—control of aldosterone secretion. (843)

Professor C. H. STUART-HARRIS—relationship between blood gas tensions and the pulmonary blood pressure. (844)

Dr Margaret M. PLATTS—water and electrolyte shifts during recovery from uraemia in man. (845)

THE ROYAL INFIRMARY

Therapeutics Department

Professor G. M. WILSON—effects of drugs on tissue transport mechanisms and subcellular localization of drug action. (846)

Surgery Department

Professor H. L. DUTHIE—effect of vagotomy on the digestion and absorption of fat. (847)

UNIVERSITY

Biochemistry Department

Mrs P. M. HARRISON—structure and function of ferritin. (848)

Dr M. A. G. KAYE—the biochemical lesion in phenylketonuria. (849)

Professor J. R. QUAYLE—mammalian glyoxylate metabolism. (850)

Genetics Department

Dr B. BURNET—physiological genetics of melanotic tumours in *Drosophila melanogaster*. (851)

Professor J. A. ROPER—polytene chromosomes of *Zaprionus*. (852)

Human Biology and Anatomy Department

Professor R. BARER—(1) development and application of histochemical methods in electron microscope studies; (2) development of electromagnetic flowmeters. (853)

Dr P. F. HARRIS—isolation and study of cell fractions from bone marrow after irradiation. (854)

Dr E. J. CLEGG—effects of exposure to lowered atmospheric pressures on the reproductive system of laboratory animals. (855)

Microbiology Department

Dr B. A. FRY—structure and morphogenesis of the temperate bacteriophage λ. (856)

Pharmacology and Therapeutics Department

Dr D. S. MUNRO—nature and significance of the long-acting stimulator of hyperthyroidism. (857)

Physiology Department

Dr V. R. PICKLES—(*a*) endometrial prostaglandins in simian and human reproduction; (*b*) the mechanism of action of intrauterine contraceptive devices. (858)

Professor D. H. SMYTH—(1) intestinal absorption; (2) functional topography of the intestinal epithelial cell. (859)

Psychology Department

Dr N. P. MORAY—mechanisms of learning and inheritance of behaviour. (860)

Surgery Department

Professor H. L. DUTHIE—gastric hypothermia. (861)

WHITELEY WOOD CLINIC

Mr P. R. F. CLARKE and Dr I. PILOWSKY—hypochondriasis and the effect of emotional 'meaning' on recall and the processing of information. (862)

Shenley

HARPERBURY HOSPITAL

Professor L. S. PENROSE—genetic aspects of mental subnormality. (863)

Dr J. M. BERG—genetic aspects of mental deficiency. (864)

Smethwick

SMETHWICK HOSPITAL

Midland Centre for Neurosurgery

Dr A. L. WOOLF—innervation and metabolism of muscle. (865)

Southampton

GENERAL HOSPITAL

Dr R. S. WILLIAMS—iron absorption in cirrhosis and haemochromatosis. (866)

UNIVERSITY

Physiology and Biochemistry Department

Dr M. AKHTAR—(*a*) synthesis of 19-tritiated steroids; (*b*) synthesis of tritiated vitamin D_3 and mechanism of the conversion of previtamin D_3 into vitamin D_3. (867)

Zoology Department

Professor L. BRENT—electrical and chemical properties of the heart muscle of *Anodonta* and their significance in muscle function. (868)

Stock (Essex)

ANIMAL HEALTH TRUST FARM LIVESTOCK RESEARCH CENTRE

Dr L. F. TAFFS—fluorescent antibody staining in the serodiagnosis and immunology of helminth parasites in man and animals. (869)

Stoke-on-Trent

CITY GENERAL HOSPITAL

Respiratory Physiology Department

Dr M. C. S. KENNEDY—natural history of the asthma-bronchitis-emphysema syndrome. (870)

Sunderland

TECHNICAL COLLEGE

School of Pharmacy

Dr E. G. BEVERIDGE—stability of pharmaceutical preservatives to microbial attack. (871)

Dr W. G. SMITH—effects of anaphylaxis on the subcellular components of lung tissue and their modification by anaphylactic agents. (872)

Wickford

RUNWELL HOSPITAL

Neuropathological Laboratory

Dr J. A. N. CORSELLIS—(*a*) neuropathological, clinical and EEG findings in epilepsy; (*b*) relation of vascular disease, cerebral degeneration and mental disorder in old age. (873)

Wigan

ROYAL ALBERT EDWARD INFIRMARY

Pathological Department

Dr J. SCHRAGER—carbohydrate and amino acid components of the gastric mucopolysaccharides. (874)

Wye (Kent)

WYE COLLEGE

Biological Sciences Department

Mr C. A. FINN—artificial decidual cell reaction in the uterus of the mouse. (875)

York

YORK GROUP OF HOSPITALS

Dr C. N. PULVERTAFT—gastro-duodenal ulceration. (876)

Fellowships and Scholarships

Various forms of assistance are provided by the Medical Research Council for suitably qualified medical, dental and scientific graduates who wish to prepare themselves for careers in research. These awards are ordinarily restricted to British subjects resident in the United Kingdom. Details of the awards made for the academic year 1964–65 were given in the Report for 1963–65.

MEDICAL RESEARCH COUNCIL TRAVELLING FELLOWSHIPS

These fellowships are intended for medical or scientific graduates of registrar or lecturer status, resident in the United Kingdom, who have undertaken some training in research in clinical medicine, surgery or some other branch of medical science and who are likely to profit by a period of work at a recognized centre abroad before taking up appointments in higher teaching or research in the United Kingdom.

The following appointments were made by the Council for the academic year 1965–66:

Dr D. T. BAIRD (*Simpson Memorial Maternity Pavilion, Edinburgh*): basic methods useful in the investigation of reproductive physiology—at the Worcester Foundation for Experimental Biology, Shrewsbury, Mass. (under Dr G. Pincus).

Dr M. HARTOG (*Hammersmith Hospital, London*): development of an immunological technique involving the culture of lymphocytes—at the San Francisco Medical Center, University of California (under Professor P. H. Forsham).

Dr D. R. LONDON (*Department of Chemical Pathology, St. Thomas's Hospital, London*): transport and metabolism of amino acids in various endocrine disorders—at the National Institute of Arthritis and Metabolic Diseases, US National Institutes of Health, Bethesda (under Dr S. Segal).

Dr W. I. MCDONALD (*National Hospital, London*): experimental demyelination and other pathological states and their effects on normal nervous function—at the Department of Neurology, Harvard University Medical School, Boston, Mass. (under Professor D. Denny-Brown).

Dr N. MROSOVSKY (*MRC Unit for the Experimental Investigation of Behaviour, University College London*): an investigation of the apparent similarity between obese rats with ventromedial lesions and naturally obese hibernators—at the Department of Psychology, University of Pennsylvania, Philadelphia (under Professor P. Teitelbaum).

SIR HENRY WELLCOME TRAVELLING FELLOWSHIPS IN MEDICINE

These fellowships, which have been made available through the generosity of the Wellcome Trustees, are of similar standing to the Medical Research Council Travelling Fellowships. They are open to medical and scientific graduates with research experience in any field of medical science, although—in accordance with the wishes of the Trustees—the subjects of physiology, biochemistry, pharmacology and tropical medicine are given preference.

The following appointments were made by the Council for the academic year 1965–66:

Dr L. J. BEILIN (*Department of Medicine, King's College Hospital Medical School, London*): interrelationships between the effects of adrenal and pituitary hormones on ion transport and carbohydrate metabolism—at the Endocrine Unit, University of Southern California, Los Angeles (under Professor D. Nelson).

Dr I. D. COOKE (*Department of Obstetrics and Gynaecology, University of Aberdeen*): foetal metabolism of oestrogens—at the Karolinska Sjukhuset, Stockholm (under Professor E. Diczfalusy).

Dr R. N. HERRINGTON (*Department of Psychological Medicine, University of Glasgow*): interrelations of physiological and psychological processes—at the Brain Research Laboratories, Department of Psychiatry, New York Medical College (under Dr E. Roy John).

Dr J. G. WALKER (*Medical Unit, Royal Free Hospital, London*): immunology and immunological techniques and their application to gastroenterological problems—at the Belle Vue Hospital, New York (under Professor L. Thomas).

LILLY FOREIGN EDUCATIONAL FELLOWSHIP

After nomination by the Council the following appointment was made by Eli Lilly and Company, Indianapolis, USA, to a Lilly Foreign Educational Fellowship for the academic year 1965–66:

Dr T. K. C. KING (*Department of Social and Occupational Medicine, Welsh National School of Medicine, Cardiff*): alteration of pulmonary mechanics in disease—at the Cardiopulmonary Laboratory, Belle Vue Hospital, New York (under Dr W. A. Briscoe).

UNITED STATES PUBLIC HEALTH SERVICE FELLOWSHIPS

In 1958 the National Institutes of Health of the United States Public Health Service inaugurated a programme of research fellowships for European scientists and invited the Council to nominate candidates from the United Kingdom. The fellowships are open to medical or scientific graduates, and preference is given to candidates who have obtained a doctoral degree in one of the medical sciences and have shown outstanding research ability. After nomination by the Council, the following candidates were elected by the United States Public Health Service to fellowships for 1965–66:

Dr J. H. DAGG (*Department of Medicine, University of Glasgow*): studies of iron metabolism—at the University of Washington, Seattle (under Professor C. A. Finch).

Dr A. J. GARRETT (*National Institute for Medical Research, London*): investigation into the possibility of an integrated synthesis of mucopeptide and teichoic acid *in vitro* and into the effects of antibiotics on their synthesis—at the Tufts University School of Medicine, Boston, Mass. (under Dr J. T. Park).

Dr G. J. R. MCHARDY (*Department of Medicine, Postgraduate Medical School, London*): pressure–flow relationships in the airways and the blood vessels of the lung—at the Johns Hopkins University, Baltimore (under Dr R. L. Riley).

Dr D. MACKAY (*Department of Pharmacology, University of Leeds*): microelectrode techniques and experiments on the effects of drugs on the neuromuscular junction—at the Department of Pharmacology, University of California, Los Angeles (under Professor D. B. Taylor).

Dr D. L. MILLER (*Public Health Laboratory Service, Colindale, London*): epidemiological research methods at present in use in the United States, particularly as applied to studies of whole communities—at the Department of Epidemiology, School of Hygiene and Public Health, Johns Hopkins University, Baltimore (under Professor P. E. Sartwell).

ALEXANDER PIGOTT WERNHER MEMORIAL TRUST FELLOWSHIPS IN OPHTHALMOLOGY AND OTOLOGY

These awards are provided from a special fund placed at the disposal of the Council by the trustees of the late Lady Ludlow under the terms of a bequest

in memory of her son, to be used ' towards the prevention and cure of blindness and deafness in the United Kingdom and the British Empire, and, in particular, research in connection therewith by financing medical men and students within the Empire to study methods and practices in all countries of the world '. Reference is made elsewhere (pp. 120–1) 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 1965–66:

Mr A. L. CROMBIE (*Department of Ophthalmology, Royal Infirmary, Edinburgh*): the sympathetic control of intraocular dynamics—at the Wilmer Ophthalmological Institute, Johns Hopkins University School of Medicine, Baltimore (under Dr M. E. Langham).

Mr D. G. DAVIES (*Royal National Throat, Nose and Ear Hospital, London*): functional manifestation of strial atrophy in the guinea pig—at the Harvard Medical School and the Massachusetts Eye and Ear Infirmary, Boston, Mass. (under Professor H. F. Schuknecht).

DOROTHY TEMPLE CROSS RESEARCH FELLOWSHIPS

These fellowships, provided from an endowment by the late Mrs Odo Cross, are awarded to suitably qualified British graduates who are devoting themselves to the advancement by teaching or research of the curative or preventive treatment of tuberculosis in any of its forms, or to increasing knowledge of other diseases of the lung.

No award was made by the Council for the academic year 1965–66.

KATHLEEN SCHLESINGER RESEARCH FELLOWSHIP

This fellowship has been provided from an endowment made by the late Mr and Mrs Eugen M. Schlesinger, in memory of their daughter, for research in the field of neuropathology. On the advice of the Fellowship Advisory Committee, preference has been given in recent years to candidates who propose to investigate mechanisms underlying degenerative processes affecting the brain. The fellowship has been held since January 1964 by Dr Clara Margoles at the National Hospital for Nervous Diseases, Maida Vale, London. The endowment has now expired (see p. 19).

MAPOTHER BEQUEST RESEARCH FELLOWSHIP

This fellowship is provided from a benefaction by the late Dr and Mrs Edward Mapother for research in psychiatry. It has been held since February 1963 by Miss Barbara C. Stevens at the Institute of Psychiatry, Maudsley Hospital, London.

NATHAN TRUST 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. Mr D. R. Sweetnam (Middlesex Hospital) was awarded this fellowship in 1960 for a study to be carried out under the auspices of the Bone Sarcoma Working Party of the Council's Committee on Evaluation of Different Methods of Cancer Therapy.

CLINICAL RESEARCH FELLOWSHIPS

These fellowships, which are normally tenable for up to three years, are offered to suitably qualified medical graduates who wish to prepare for careers in clinical research. It is intended that each fellow appointed should have the opportunity, as part of his training, of studying methods of research in the basic subjects most relevant to his particular clinical interest, his training preferably being given in departments other than his own.

The following appointments were made for the academic year 1965–66:

Dr D. BARNETT (*Department of Medicine, University of Leeds*): Department of Medicine Postgraduate Medical School, London (under the direction of Professor T. R. Russell Fraser).

Dr T. CHARD (*Department of Gynaecology, St. Thomas's Hospital Medical School, London*): Department of Immunology, Guy's Hospital Medical School, London (Dr R. Batchelor).

Dr P. B. C. FENWICK (*Academic Department of Psychiatry, Middlesex Hospital Medical School, London*): Academic Unit of Psychiatry, National Hospital, London (Dr W. A. Cobb).

Dr E. HOUSLEY (*Department of Medicine, Queen Elizabeth Hospital, Birmingham*): Department of Medicine, University of Birmingham (Professor W. Melville Arnott).

Dr J. HOUSLEY (*Queen Elizabeth Hospital, Birmingham*): Department of Experimental Pathology, University of Birmingham (Professor P. G. H. Gell).

Dr N. C. NEVIN (*Department of Medicine, Queen's University, Belfast*): MRC Clinical Genetics Research Unit, Institute of Child Health, London (Dr C. O. Carter).

Dr D. K. PETERS (*Department of Medicine, Cardiff Royal Infirmary*): Department of Experimental Pathology, University of Birmingham (Professor J. R. Squire).

JUNIOR RESEARCH FELLOWSHIPS

These fellowships, which are normally tenable for up to three years, 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 1965–66:

Dr N. B. BENNETT: Department of Medicine, University of Aberdeen (under the direction of Professor H. W. Fullerton).

Dr H. F. BRADFORD: Department of Biochemistry, Imperial College of Science and Technology, London (Professor E. B. Chain).

Dr J. A. EDWARDSON: Department of Neuroendocrinology, Institute of Psychiatry, London (Professor J. T. Eayrs).

Dr N. D. C. FINLAYSON: Department of Therapeutics, University of Edinburgh (Professor R. H. Girdwood).

Dr A. T. FLORENCE: Department of Pharmacy, University of Strathclyde (Dr P. H. Elworthy).

Dr C. S. HENNEY: Department of Experimental Pathology, University of Birmingham (Dr D. R. Stanworth).

Dr M. J. LARGEN: Department of Zoology, Queen Mary College, London (Professor G. E. Newell).

Dr G. A. LEWIS: Department of Anthropology, London School of Economics and Political Science (Professor R. W. Firth).

Dr C. E. R. MADDOX: Department of Molecular Science, University of Warwick (Professor V. M. Clark).

Dr R. J. NAFTALIN: Division of Biochemistry, National Institute for Medical Research, London (Dr T. S. Work).

Dr R. M. PIGACHE: MRC Cerebral Functions Research Group, University College London (Dr J. de C. Downer).

Dr J. T. RICK: Department of Physiology and Biochemistry, University of Southampton (Dr J. Kerkut).

Dr M. R. SALAMAN: Department of Biochemistry, University College London (Dr K. L. Manchester).

Dr A. B. SHAW: Department of Medicine, University of Manchester (Professor D. A. K. Black).

Dr S. Smith: Department of Medical Biochemistry and Pharmacology, University of Birmingham (Dr D. Dils).

Mr D. J. WIGGLESWORTH: Royal Dental Hospital, London (Professor R. B. Lucas) and Strangeways Research Laboratory, Cambridge (Professor Dame Honor Fell).

Dr A. D. WRIGHT: Department of Clinical Endocrinology, Postgraduate Medical School, London (Professor T. Russell Fraser).

FRENCH EXCHANGE SCHOLARSHIPS IN MEDICAL SCIENCE

These awards are made in collaboration with the Centre National de la Recherche Scientifique and allow for the annual exchange of two workers from each country for a full academic year.

The following scholar was nominated by the Council for an award to be held in France during the academic year 1965–66:

Miss T. KATKOV (*Department of Biochemistry, University College London*): Laboratoire des Isotopes, Hospital Necker, Paris (under Dr Etling).

The award made for the academic year 1964–65 to Dr L. Dalgarno (National Institute for Medical Research, London) for work at the Institut de Biologie Physico-Chimique, Paris, under Dr François Gros, has been extended until June 1966.

No French scholars were nominated by the CNRS for awards to be held in Great Britain during the academic year 1965–66.

ANGLO-FRENCH CLINICAL RESEARCH SCHOLARSHIPS

The first awards were made to a new class of scholarships, introduced under an agreement between the French Institut National d'Hygiène (which is responsible for clinical research in France) and the Council. Four scholarships are available annually to enable two British and two French workers to undertake clinical research in France and Great Britain respectively.

The following scholars were nominated by the Institut National de la Santé et de la Recherche Médicale for awards to be held in Great Britain during the academic year 1965–66:

Dr S. P. COUDERT (*Collège de France, Paris*): Department of Clinical Studies, School of Veterinary Medicine, Cambridge (under Dr R. V. Short).

Dr F. L. TURPIN (*Hôpital Saint-Louis, Paris*): Department of Haematology, Postgraduate Medical School, London (under Professor J. V. Dacie).

The following scholars were nominated by the Council for awards to be held in France during the academic year 1965–66:

Mr A. R. H. BLISS (*Royal Sussex County Hospital, Brighton*): Raymond Poincaré Hospital, Garches, Seine-et-Oise (under Professor R. Judet).

Dr M. J. PECKHAM (*Department of Radiotherapy, University College Hospital, London*): Institut Gustav Roussy, Villejuif, Seine (under Professor M. Tubiana).

SCHOLARSHIPS FOR TRAINING IN RESEARCH METHODS AWARDS FOR FURTHER EDUCATION IN THE MEDICAL SCIENCES AWARDS TO MEDICAL AND DENTAL STUDENTS FOR INTERCALATED COURSES IN A BIOLOGICAL SCIENCE

Scholarships are awarded to recent medical, dental or scientific graduates of special promise who wish to be trained in research techniques in order to pursue a career in medical research.

Awards for Further Education in the Medical Sciences are made to enable graduates with a medical or dental qualification or a first degree in science to receive approved postgraduate instruction—as distinct from training in research methods—in a subject ancillary to their main research interest in the field of the biological or medical sciences.

One hundred and eighty two new Scholarships and Awards for Further Education were made for the academic year 1965–66 and the total number of awards held during this academic year was 410. The numbers of awards according to subject were:

Subjects studied	*No. of awards*
Biochemistry	118
Physiology	64
Psychology	40
Pharmacology	31
Biophysics	23
Microbiology	20
Genetics	19
Zoology	14
Chemistry	13
Radiation	12
Anatomy	11
Immunology	11
Pathology	7
Biology	5
Dental science	4
Social and environmental health	4
Tropical medicine	4
Virology	3
Endocrinology	2
Cancer	1
Nutrition	1
Psychiatry	1
Unclassified	2

Scholarships and awards for further training were held at the following centres:

Aberdeen University	11
Aberystwyth: University College of Wales	1
Belfast: Queen's University	1
Birmingham University	21
Bristol University	6
Cambridge: University	50
MRC Laboratory of Molecular Biology	11
Strangeways Research Laboratory	1
Cardiff: University College of South Wales and Monmouthshire	14
Dublin: Trinity College	2
Edinburgh University	19
Glasgow: University	14
University of Strathclyde	2
Hull University	7
Leeds University	6
Leicester University	6
Liverpool University	12
London: University	
Bedford College	3
Birkbeck College	1
Imperial College of Science and Technology	1
King's College	11
London School of Economics and Political Science	2
Queen Elizabeth College	2
Queen Mary College	1
Royal Holloway College	1
School of Pharmacy	5
University College	39
Guy's Hospital Medical School	2
London Hospital Medical College	2
Middlesex Hospital Medical School	1
Royal Free Hospital School of Medicine	1
St. Bartholomew's Hospital Medical College	1
St. Mary's Hospital Medical School	1
St. Thomas's Hospital Medical School	4
British Postgraduate Medical Federation	
Institute of Cancer Research	5
Institute of Psychiatry	11
London School of Hygiene and Tropical Medicine	4
Chelsea College of Science and Technology	8
Sir John Cass College	2
MRC Microbial Genetics Research Unit	1
National Institute for Medical Research	2
Royal College of Surgeons	1
Loughborough College of Technology	1
Manchester University	11

Newcastle upon Tyne University	7
Nottingham University	7
Oxford University	67
Reading University	1
St. Andrews University	1
Sheffield University	9
Southampton University	8
Sussex University	1
Swansea: University College	1

Awards to Medical and Dental Students for Intercalated Courses in a Biological Science are made to enable selected undergraduates who have completed their second MB or BDS examinations to extend their studies by intercalating a course in a biological science leading to a first degree. One hundred and one awards were made for the academic year 1965–66.

MRC Headquarters Office and other Council establishments

HEADQUARTERS OFFICE
20 Park Crescent, London W.1
(Museum 5422)

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Private secretary: Miss Valerie Potts, MA

SECOND SECRETARY
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B. S. Lush, MD, FRCP

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PRINCIPAL SENIOR MEDICAL OFFICER
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SENIOR MEDICAL OFFICER
M. P. W. Godfrey, MB, MRCP

MEDICAL OFFICERS
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Katherine Lévy, MB
Sheila Howarth, MB

Divisional assistant: Miss Margaret Grieve, MA

MEDICAL DIVISION B

Radiobiology; industrial medicine; toxicology; nutrition; infectious diseases; immunology and microbiology; molecular biology and biophysics; experimental genetics; services research; non-clinical subjects; Biological Research Board and Tropical Medicine Research Board business; training awards

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R. C. Norton, MA, MB, D OBST RCOG

Other senior staff
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L. D. Hamlyn, OBE

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E. M. B. Clements, MB
P. J. Chapman, MB
Elizabeth Neale, BM, MRCP

Divisional assistant
Miss Stephanie Jones, MA

ADMINISTRATIVE DIVISION

HEAD OF DIVISION
J. G. Duncan, MA, LL B

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ADMINISTRATIVE OFFICER
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CHIEF EXECUTIVE OFFICER
D. F. Green

Other senior staff
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C. R. Russell
Miss Patricia Cross
P. G. Daly
H. A. Garling
H. D. Harwood, BA

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ADMINISTRATIVE OFFICER
F. Rushton

Junior Administrative Officer
J. E. A. Hay, MA
Other senior staff
M. A. F. Barren
D. G. Metcalfe

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ADMINISTRATIVE OFFICER
J. C. R. Hudson, MA

Grants and training awards
D. B. H. Clark
Miss Elizabeth Mackenzie, MA
A. E. White
Supplies
J. A. Brown

Finance

ADMINISTRATIVE OFFICER
R. F. Smart

CHIEF EXECUTIVE OFFICER
J. M. Jeffs, AACCA
(*Accountant*)

Accounts
P. J. L. Farrow, AAIA
Miss Edna Pickavance
Miss Marjorie Biedermann

GENERAL DEPARTMENT

Council business; constitutional matters; parliamentary liaison; library and information retrieval; publications; press and general information

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Joan Faulkner, MB, DPH

ADMINISTRATIVE OFFICER
D. J. Cawthron, MA

Publications
Miss Daphne Gloag, MA
Library
Mrs Norma Morris, MA
Parliamentary liaison
B. M. Jones, BA
Information
Mrs Anne Sanderson

* * * *

CONSULTANT ADVISERS
Sir Charles Harington, KBE, SC D, FRS
Sir Robert Platt, Bart, MD, M SC, FRCP

SPECIAL DUTIES
Sir Landsborough Thomson, CB, OBE, DSC

CLINICAL RESEARCH CENTRE

Planning and Administrative Offices
164 Tottenham Court Road, London W.1
(Euston 5381)

Director-designate
Professor G. M. Bull, MD, FRCP

Deputy Director-designate
W. R. S. Doll, OBE, MD, DSC, FRCP, FRS

Senior staff
D. Cox, ACIS
Mrs L. E. Hill, MD, MRCP, DCH
Miss M. Harvey, BA, BLS (*Library*)

A short account of the Clinical Research Centre project has been included in the Council's main Report (p. 1). An appreciation of the late Professor J. R. Squire, the first Director-designate of the Centre, will be found on p. 28.

MEDICAL RESEARCH COUNCIL LABORATORIES, CARSHALTON

Woodmansterne Road, Carshalton, Surrey
(Melville 4461)

Administrative Officer
A. M. Gerrard, OBE, MA

Senior staff
W. E. Barker (*Chief Engineer*) T. Battersby, FIMLT

The Laboratories house the Toxicology Research Unit (p. 166). the Neuropsychiatric Research Unit (p. 153), the Virus Research Unit (p. 146) and the Laboratory Animals Centre (p. 173), and provide administrative and other services for these establishments.

COMPUTER SERVICES CENTRE

172–3 Tottenham Court Road, London W.1
(Euston 0201)

Head of Centre
B. K. Kelly, MA

Scientific staff
Miss C. M. Devine, B SC
D. A. Franklin, M SC

Other senior staff
Miss M. J. H. Arnott, B SC
T. J. Scott
Miss A. C. Bramley, B SC

The Centre provides assistance to research units and external staff in the application of computers to their research problems by carrying out programming, arranging for data preparation and running calculations on the computer. It has access to the London University Atlas Computer.

A program library is also being set up, which will aim to keep copies of all programs likely to be of use to Council workers.

STEROID REFERENCE COLLECTION

Chemistry Department, Westfield College,
Hampstead, London N.W.3
(Hampstead 7601)

Honorary Curator
Professor W. Klyne, D SC

Honorary Deputy Curator
D. N. Kirk, PH D

The Collection was set up in 1954 and now includes over 400 compounds. It provides reference samples of steroids for use as standards in chromatography, spectroscopy and so on, particularly for work related to the metabolism of steroid hormones.

The work of the Collection is carried out with the aid of a long-term grant from the Council, supplemented by assistance from the US National Institutes of Health.

CENTRAL STORE, COLINDALE

Colindale Avenue, Colindale, London N.W.9
(Colindale 0071)

Head of Store
A. Waltho

Senior staff
J. Rickards

The Central Store, which was set up in 1950, provides supplies of materials and equipment for the Council's research establishments in this country and overseas. It provides, on a repayment basis, a similar service for the Public Health Laboratory Service and the Agricultural Research Council.

ADVISORY COMMITTEES OF THE COUNCIL

At date of report

The Medical Research Council have for long greatly depended upon a series of advisory committees and working parties for assistance in the promotion of research on special subjects within the broad field of medical science and in dealing with other questions calling for expert knowledge. Of these bodies, some are standing committees keeping a particular field of research under review and giving advice from time to time; others are temporary committees concerned with particular investigations; others again are committees appointed jointly by the Council and other organizations to consider questions of common interest. All members serve in an honorary capacity. Membership of the Council's principal committees and working parties is as follows:

Non-explosive Anaesthetic Agents

Professor W. D. M. Paton, DM, FRS (*Chairman*)
J. M. Barnes, CBE, MB
T. H. S. Burns, BM, FFARCS
H. G. Epstein, PH D, FFARCS
Professor W. W. Mushin, MB, FFARCS
Professor G. S. W. Organe, MD, DA, FFARCS
Professor J. M. Robson, MD, D SC, FRS
Professor M. Stacey, CBE, D SC, FRS
Professor G. Stead, D SC
J. D. Robertson, MD, FRCPE (*Secretary*)

Nitrous Oxide/Oxygen Analgesia in Midwifery

Professor Sir Dugald Baird, MD, D SC, FRCOG, DPH (*Chairman*)
Josephine Barnes, MD, MRCP, FRCS, FRCOG
Professor J. C. McClure Browne, MB, FRCSE, FRCOG
P. V. Cole, MB, FFA, FCS
W. R. S. Doll, OBE, MD, D SC, FRCP, FRS
A. G. Doughty, MB, FFARCS
H. G. Epstein, PH D, FFARCS
I. D. Hill, B SC
Professor W. W. Mushin, MB, FFARCS
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D. Thomson, CB, MD, DPH
Professor J. P. W. Tizard, BM, FRCP, DCH
M. E. Tunstall, FFARCS, DA, DOBST RCOG
W. N. Rollason, MB, FFARCS (*Secretary*)

Subcommittee:
Specifications of apparatus

Hazards to Man of Nuclear and Allied Radiations

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Secretariat

Scientific staff	*Headquarters staff*
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Endolymphatic Therapy in Malignant Melanoma

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Epidemiology
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Anaemia
Anti-depressant Drugs in General Practice

Occupational Health

J. C. Gilson, OBE, MB, FRCP (*Chairman*)
Professor W. M. Arnott, TD, MD, FRCP, FC PATH
J. M. Barnes, CBE, MB
J. P. Bull, MD, MRCP
T. A. Lloyd Davies, MD (*Assessor: Ministry of Labour*)
W. R. S. Doll, OBE, MD, D SC, FRCP, FRS

D. E. Hickish, PH D, AMIEE
Professor C. R. Lowe, MD, PH D, DPH
A. E. Martin, MD, DPH (*Assessor: Ministry of Health*)
L. G. Norman, CBE, MD, B SC, FRCP, DPH
I. M. Richardson, MD, PH D, FRCPE, DPH
J. M. Rogan, MD, FRCPE, DPH
Professor R. S. F. Schilling, MD, FRCP, DPH, DIH
Professor T. S. Scott, MD, MRCP
W. H. Walton, B SC, F INST P
J. Watkins-Pitchford, MD, DPH, DIH (*Assessor: Ministry of Pensions and National Insurance*)
Professor J. S. Weiner, PH D, MRCS
P. J. Chapman, MB (*Secretary*)

Panels:
Measurement and Composition of Dust
Biological Activity of Dust
Decompression Sickness

Hyperbaric Oxygen Therapy

Professor Hedley J. B. Atkins, DM, M CH, FRCS (*Chairman*)
Professor W. Melville Arnott, TD, MD, FRCP, FC PATH
Catherine N. Dennis, MB, FRCS, DPH (*Observer: Ministry of Health*)
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Professor D. V. Hubble, CBE, MD, FRCP
Professor A. W. Kay, MD, FRCS
Professor W. D. M. Paton, DM, FRS
Professor G. Smith, MBE, MD, CH M, FRCSG, FACS
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Research on the Toxicity Testing of Drugs

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Professor G. A. H. Buttle, OBE, MRCS
Sir James Cook, D SC, FRIC, FRS
Professor Dame Honor B. Fell, DBE, D SC, FRS
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R. Goulding, MD
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Professor M. L. Rosenheim, CBE, MD, PRCP
Professor A. Wilson, MD, PH D, FRCPG
T. S. Work, D SC
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Professor Sir Robert Bradlaw, CBE, DDS, FRCS, FDSRCS
Professor A. I. Darling, DD SC, MRCS, FDSRCS, FC PATH
Professor A. D. Hitchin, DD SC, FDSRCSE
Rear Admiral W. Holgate, CBE, LDSRCS
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Professor R. Knox, MD, FRCP
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E. C. Cornford, BA, FRAES
Professor G. C. Drew, MA
Lt.-Gen. Sir Robert Drew, KCB, CBE, QHP, MB, FRCP
O. G. Edholm, MB, B SC
Lt.-Gen. Sir Charles H. P. Harington, KCB, CBE, DSO, MC
E. R. R. Holmberg, PH D
Lt.-Gen. Sir Charles Jones, KCB, CBE, MC
Professor P. L. Krohn, BM, FRS
Maj.-Gen. D. B. Lang, CB, DSO, MC
Professor M. L. Rosenheim, CBE, MD, FRCP
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Professor K. W. Donald, DSC, MD, D SC, FRCP
Professor G. C. Drew, MA
O. G. Edholm, MB, B SC
Surgeon Captain F. P. Ellis, OBE, MD, FRCP, RN
Surgeon Captain J. Glass, OBE, LRCP, DPH, RN
Professor R. A. McCance, CBE, MD, PH D, FRCP, FRCOG, FRS
Surgeon Captain S. Miles, MD, M SC, DTM & H, RN
A. W. Ross, OBE, MA, AMIEE
Surgeon Vice-Admiral Sir Derek D. Steele-Perkins, KCB, KCVO, QHS, FRCS, FRACS, DLO
Captain A. G. Watson, RN
N. A. B. Wilson, OBE, PH D
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Professor A. L. Cochrane, MBE, MB, FRCP, DPH
Professor Desmond Curran, CBE, MB, FRCP, DPM
Professor Sir Austin Bradford Hill, CBE, D SC, FRS
Professor Sir Denis Hill, MB, FRCP, DPM
Professor Sir Aubrey Lewis, MD, FRCP
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J. A. Fraser Roberts, CBE, MD, D SC, FRCP, FRS
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Professor Sir Edward Wayne, MD, PH D, FRCP, FRCPG
Professor O. L. Zangwill, MA
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Clinical Trials (Drugs in Psychiatry)
Psychopathic Personality
National Statistics of Mental Disorder

Epidemiology of Mental Disorders

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Eileen M. Brooke, M SC
Professor G. M. Carstairs, MB, FRCPE, DPM
Professor A. L. Cochrane, MBE, MB, FRCP, DPH
Professor D. V. Glass, PH D
E. L. M. Millar, MD, M SC, DPH

Professor W. M. Millar, MD, FRCPE
Professor J. N. Morris, D SC, FRCP, DPH
Professor Sir George Pickering, MD, FRCP, FRS
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Subcommittee:
Causes of Crime

The Human Factor in Railway Accidents

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J. Howlett, PH D, AMIEE
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H. Yellowlees, BM
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Joint Services Personnel Research

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J. P. Bull, MD, MRCP
Air Marshal Sir Harold Whittingham, KCB, KBE, MB, FRCP, FRCSE
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The Monitoring of Radioactivity from Fallout

(*Jointly with the Agricultural Research Council*)

J. F. Loutit, CBE, DM, FRCP, FRS (*Chairman*)
W. Anderson, PH D
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Elizabeth Neale, BM, MRCP } (*Joint Secretaries*)
F. J. S. Culley, LLB, B SC }

Panel:
Radiobiological Research

UK National Committee of the British Commonwealth Collections of Micro-organisms

(*Jointly with the Science Research Council and the Agricultural Research Council*)

S. T. Cowan, MD, DIP BACT (*Chairman*)
A. H. Cook, D SC, FRS
W. A. Cuthbert, M SC
J. J. Elphick, B SC
R. E. Glover, CBE, D SC, FRCVS
D. Rudd Jones, PH D
R. A. Lelliott, BA
J. G. Savory, B SC
J. M. Shewan, PH D, FRIC
S. P. Lapage, MB, DIP BACT (*Secretary*)

Lighting and Vision

(*Jointly with the Advisory Committee on Building Research of the Ministry of Technology*)

W. J. Wellwood Ferguson, MB, MI MIN E, FIES (*Chairman*)
B. H. Crawford, D SC
M. Drury, MI MECH E, AMIHVE (*Observer: Ministry of Health*)
Professor W. F. Floyd, PH D, F INST P, AMIEE
Professor R. G. Hopkinson, PH D, MIEE, FIES
J. S. McCulloch, MIEE, FIES, M CONS E
D. L. Medd, OBE, DIP ARCH, ARIBA
Professor R. C. Oldfield, MA
D. J. Petty, MBE, MA, DIP ARCH, ARIBA
R. A. Weale, D SC
A. T. Welford, SC D
Wing Commander T. C. Whiteside, MBE, MB, PH D
J. B. Collins, B SC, AMIEE, FIES } (*Joint Secretaries*)
E. M. B. Clements, MB }

Joint Medical Research Council/Atomic Energy Authority Co-ordinating Committee for Radiobiological Research

Professor Sir Brian Windeyer, MB, FRCP, FRCS, DMRE, FFR (*Chairman*)
Sir Charles Harington, KBE, SC D, FRS
J. F. Loutit, CBE, DM, FRCP, FRS
A. S. McLean, MB, DIH
Professor W. V. Mayneord, CBE, D SC, F INST P, FRS
Professor J. S. Mitchell, CBE, MD, PH D, FRCP, DMR, FFR, FRS
E. E. Pochin, CBE, MD, FRCP
Professor M. M. Swann, PH D, FRS
F. A. Vick, D SC
R. C. Norton, MB, D OBST RCOG (*Acting Secretary*)

APPENDICES

Accounts of receipts and payments

RECURRENT

1964–65 £	*Receipts*	£	£
32 455	Balance 1 April 1965		27 912
8 151 000	Parliamentary grant-in-aid		9 637 536
	Contributions from Government Departments		
(428 563)	Ministry of Health	479 876	
(102 779)	Ministry of Overseas Development	113 445	
(68 840)	Ministry of Defence	68 000	
(26 731)	Others	34 991	
626 913			696 312
	Contributions from public bodies		
(43 675)	Regional Health Boards	41 284	
(991)	National Coal Board	626	
(7 271)	Others	15 647	
51 937			57 557
	Special grants		
(40 242)	World Health Organization	48 781	
(35 827)	Others	21 417	
76 069			70 198
4 542	Contributions from bequests, donations etc.		5 330
104 302	Miscellaneous receipts		112 227
£9 047 218			£10 607 072

NON-RECURRENT

1964–65 £	*Receipts*	£
—	Balance 1 April 1965	2 588
602 000	Parliamentary grant-in-aid	450 000
7 905	Repayments for new buildings from Ministry of Health	16 419
2 554	Other receipts	410
£612 459		£469 417

for the year ended 31 March 1966

EXPENSES ACCOUNT

1964–65 £	Payments	£	£
	Administration		
(329 165)	Salaries and wages	380 886	
(142 585)	Other expenses	136 353	
471 750			517 239
	Central expenses		
(38 989)	Pensions, honoraria etc...	47 260	
(72 560)	Other expenses	71 246	
111 549			118 506
	National Institute for Medical Research		
(913 092)	Salaries and wages	976 770	
(330 918)	Other expenses	337 478	
1 244 010			1 314 248
	Research units and external scientific staff		
(3 306 277)	Salaries and wages	3 676 841	
(1 442 624)	Other expenses	1 715 537	
4 748 901			5 392 378
6 576 210	Total direct expenditure		7 342 371
1 517 096	Short-term research grants and training awards	2 113 523	
254 982	Grants to universities for research groups	407 245	
671 018	Special grants to institutions	680 905	
—	International subscription	53 536	
			3 255 209
9 019 306	Total expenditure		10 597 580
27 912	Balance 31 March 1966		9 492
£9 047 218			£10 607 072

EXPENSES ACCOUNT

1964–65 £	Payments	£
43	Balance 1 April 1965	—
460 121	New buildings	373 227
149 707	Grants to university departments for special apparatus	86 842
2 588	Balance 31 March 1966	9 348
£612 459		£469 417

APPENDIX II

During the year covered in this report the Council received valuable support from other bodies as summarized below:

SUBVENTIONS FROM GOVERNMENT DEPARTMENTS

Source		*Purpose*
Ministry of Health, Scottish Home and Health Department, and Welsh Board of Health	£499 549	Division of Immunological Products Control (National Institute for Medical Research) for control testing of therapeutic substances; Blood Group Reference Laboratory; Blood Products Laboratory; part of the cost of the Radiological Protection Service; special surveys
Ministry of Overseas Development	£113 445	Subvention towards the cost of: MRC Laboratories, Gambia; Tropical Metabolism Research Unit, Jamaica; Trachoma Research Unit, London and the Gambia; Epidemiological Research Unit, Jamaica; Abnormal Haemoglobin Research Unit; other research in tropical medicine
Ministry of Defence	£68 000	Investigations proposed by Council's Royal Naval Personnel Research Committee and Army Personnel Research Committee
Ministry of Pensions and National Insurance	£10 214	Audiometric surveys in industrial environments
Ministry of Labour	£1 471	Survey of health problems in the foundry industry
Post Office	£975	Study of code design and the design of keyboards
Department of Education and Science	£2 658	Study of educational retardation in children

GRANTS FROM OTHER BODIES

World Health Organization	£48 781	International Laboratory for Biological Standards; World Influenza Centre; International Blood Group Reference Laboratory; International Reference Centre for Respiratory Virus Diseases; International Reference Centre for Abnormal Haemoglobins; trial of chemotherapeutic agents against tuberculosis (India); contributions for special investigations at several Council establishments
Alexander Piggott Wernher Mermorial Trust	£20 000	Fellowship awards and research on blindness and deafness
Wellcome Trust	£15 000	Fellowship awards
Association for the Aid of Crippled Children	£3 992	Study of child growth and development in Jamaica
Rockefeller Foundation, New York	£2 489	Research in X-ray crystallography of proteins
Government of Uganda	£2 250	Infantile Malnutrition Research Unit, Uganda
East African Tuberculosis Investigation Centre	£6 338	East African tuberculosis chemotherapy trial
International Atomic Energy Agency	£1 746	Research into the measurement of total body potassium in malnourished Jamaican infants by whole-body counting of natural potassium
Agricultural Research Council	£1 374	Investigation into the inhibition of queen rearing in honey bees, in collaboration with Rothamsted Experimental Station

Source		*Purpose*
National Coal Board	£626	Pneumoconiosis chemotherapy trial
British Iron and Steel Research Association	£639	Study of limit of working capacity in steelworkers
United States Public Health Service	£439	Steroid Reference Collection
World Council of Churches	£712	Infantile Malnutrition Research Unit, Uganda
Nathan Trust	£500	Fellowship award

INDEXES

Subject Index

(including establishments and committees)

The italic numbers in brackets give references to individual grant-holders.

Personal Names Index

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