COMMITTEE OF PRIVY COUNCIL
FOR MEDICAL RESEARCH

REPORT OF THE MEDICAL RESEARCH COUNCIL FOR THE YEAR 1958–1959

Presented to Parliament by the Minister for Science
by Command of Her Majesty
June, 1960

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COMMITTEE OF PRIVY COUNCIL FOR MEDICAL RESEARCH

(Ex Officiis)

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The Secretary of State for Commonwealth Relations
The Secretary of State for the Colonies
The Secretary of State for Scotland
The Minister of Health
The Minister of Labour
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At Date of Report

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REPORT OF THE

COMMITTEE OF PRIVY COUNCIL FOR MEDICAL RESEARCH

FOR THE YEAR 1958–1959

TO THE QUEEN'S MOST EXCELLENT MAJESTY

May it please Your Majesty,

We, the Lords of the Committee for Medical Research of Your Majesty's Privy Council, humbly submit to Your Majesty a report of our proceedings during the year from 1st October, 1958, to 30th September, 1959.

1. During the financial year 1959–60 Parliament provided for the expenditure of the Medical Research Council a grant-in-aid of £3,471,020 on the ordinary account and £91,200 on the non-recurrent account for special apparatus and buildings.

2. The estimates of the Medical Research Council for the financial year 1959–60 were met by our provisional allocation of funds under the following heads:

For administration, including expenses of the Council and of the administrative offices and staff;

For the expenses of the National Institute for Medical Research, the Research Units and other establishments maintained by the Council; and for the salaries of members of the Council's scientific staff, working therein or independently elsewhere;

For special grants to institutions for research work, including the Institute of Cancer Research: Royal Cancer Hospital, London; the Royal Beatson Memorial Hospital, Glasgow; the Christie Hospital and Holt Radium Institute, Manchester; and the Strangeways Research Laboratory, Cambridge.

For temporary research grants to workers in universities, hospitals and other centres; and for training awards.

For non-recurrent expenditure on buildings.

3. By two Orders we appointed new members of the Medical Research Council (after the required consultation with the Medical Research Council and with the President of the Royal Society in the case of members appointed in respect of their scientific qualifications) as follows:

By an Order of 6th July, 1959, Sir Hugh Linstead, O.B.E., LL.D., F.P.S., M.P., in the vacancy caused by the death of Richard Fort, M.P.

By an Order of 4th September, 1959, Alan Lloyd Hodgkin, M.A., F.R.S. (Royal Society Research Professor in the University of Cambridge), and Robert Milnes Walker, M.S., F.R.C.S. (Professor of Surgery in the University of Bristol), in place of Robert Campbell Garry, M.B., D.Sc., F.R.F.P.S.G. (Regius Professor of Physiology in the University of Glasgow), and Herbert John Seddon, C.M.G., D.M., F.R.C.S. (Director of Studies, Institute of Orthopaedics, University of London, and Clinical Director, Royal National Orthopaedic Hospital, London), retiring in accordance with the provisions of the Charter.

4. We have received from the Medical Research Council a report, which is submitted herewith, upon the progress of their work during the year ended 30th September, 1959. This is the forty-fifth annual report upon the research work falling now to the duty of the Medical Research Council and formerly to their predecessors, the Medical Research Committee. This report illustrates once again the expanding nature of the Council's activities. In this regard the statements on certain major aspects of the Council's policy are of especial interest.

5. The Medical Research Council, in consultation with the Clinical Research Board, have completed a detailed review of their existing arrangements for the support of clinical research. They have come to the conclusion that, in addition to their existing arrangements, provision of a different kind is required to meet, to the full, foreseeable developments of medical knowledge in this field. The Council have accordingly agreed, with the approval of H.M. Treasury, to set up a Clinical Research Centre comprising a comprehensive concentration of relevant clinical and paraclinical disciplines. This Centre will not be a special hospital for research purposes but will form part of an existing hospital dealing with current medical problems.

6. Research in tropical medicine has always been of concern to the Medical Research Council both as a subject in its own right and as a complement to their investigations in temperate climates. Since the last war they have co-operated closely with the Colonial Office and, with the advice of the Colonial Medical Research Committee, appointed jointly by the Council and the Secretary of State for the Colonies, many developments have occurred in this field. In recent years new requirements have emerged, partly as a result of a change of scientific emphasis in tropical medicine and partly from the political developments which have been taking place in the status of overseas territories. These changes have made it necessary to consider the whole question of the organisation of tropical medicine research. It has accordingly been agreed that the Medical Research Council, through the Tropical Medicine Research Board which they will set up, should take over all responsibility for promoting and co-ordinating research in this field. These arrangements will, it is hoped, provide a suitable structure for medical research overseas.

7. During the year covered by their Report the Medical Research Council reviewed their arrangements for the support of research in psychiatry with a view to ensuring that no opportunity to stimulate profitable lines of research was overlooked and that full advantage was being taken of the increasing interest in this subject now evident. Within the past five years the Council's programme in this field has expanded considerably with the setting-up of particular Research Units. They have now decided to establish two further Units concerned respectively with epidemiology and genetics as applied to

psychiatric problems and, further, to set up two Committees on clinical psychiatry and on the epidemiology of mental disorders to advise them on specific aspects of this field. The Council believe that the next few years will see considerable developments in psychiatric research.

8. As a means of giving longer-term support than is possible under their scheme of temporary research grants, the Medical Research Council have inaugurated a new scheme to promote, in University departments, suitable research projects which it appears in the national interest desirable to accelerate. This new scheme of ' Research Groups ' will primarily be used to develop work which is in direct line with the main interests of the particular department, rather than work on new lines which will continue to be supported under the Council's existing scheme of Research Units.

9. Since 1939, the Medical Research Council have been responsible for administering, on behalf of the Ministry of Health, the Public Health Laboratory Service. Since the Service has been well established for a number of years, the Council have for some time felt that separate and more permanent arrangements for its administration were necessary and, in agreement with the Ministry of Health, a new Public Health Laboratory Service Board is being established under the Public Health Laboratory Service Bill, 1960.

10. Close touch has been maintained with the Ministry of Health and the Department of Health for Scotland, and other departments having problems calling for new research work or for expert advice, and with the Department of Scientific and Industrial Research and the Agricultural Research Council, acting under their respective Committees of Privy Council, on items of common interest. Co-operation with the Colonial Office has continued in the field of tropical medicine; and scientific liaison with Commonwealth countries, the United States of America and other countries overseas, and with the World Health Organization of the United Nations, has been actively fostered.

11. On the 30th October, 1959, Your Majesty was pleased to appoint a Minister for Science and to direct by Order in Council that the Minister for Science should succeed the Lord President of the Council as the Chairman of the Committee for Medical Research of Your Majesty's Privy Council.

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

HAILSHAM

Minister for Science.

HAROLD HIMSWORTH

Secretary to the Committee of
Privy Council for Medical Research.

14th June, 1960.

REPORT OF THE MEDICAL RESEARCH COUNCIL FOR THE YEAR 1958–1959

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

May it please Your Lordships,

The Medical Research Council beg leave to submit the following Report upon their proceedings during the period from 1st October, 1958, to 30th September, 1959.

Introduction

FORM OF THE REPORT

The form of this Report largely follows the pattern used in recent years although one or two minor changes have been introduced. The account of the work done under the Council's auspices is given, as in previous years, only in summary form. The fullest account of the researches promoted by them is contained in the numerous scientific publications of the individual workers; references to these are included in the Report.

SIR GEOFFREY JEFFERSON

In October, 1953, Sir Geoffrey Jefferson was appointed Chairman of the newly founded Clinical Research Board. He retired at the end of December, 1959, being succeeded by Professor E. J. Wayne.

From Sir Geoffrey's previous service with them, the Council were confident that no better choice of Chairman could be made in inaugurating this new venture. To an exceptional degree his knowledge, wisdom, foresight and wit fitted him for this task and, under his guidance, the new Board has been securely launched. During his tenure of office the Council's expenditure on clinical research has more than doubled; the number of clinical research units has increased from 24 to 42; the arrangements agreed with the Health Departments in respect of research within the National Health Service have been carried through; and a thorough review of the provision for clinical research, giving rise to far-reaching new recommendations, has been carried out.

At their meeting in December, 1959, the Council unanimously recorded their high appreciation of Sir Geoffrey's conduct of the duties involved and their gratitude for the invaluable help he had given in steering the Clinical Research Board through its formative phase and putting it on a firmly established basis, thereby making an important contribution to the development of clinical research under the Council's auspices.

Developments of Scientific Policy

From time to time the Council's Reports have contained accounts of some particular trends or aspects of their scientific policy. On this occasion some account is given below of their proposals in three major fields: clinical research, tropical medicine research and mental health research. Two shorter accounts follow on other developments that have occurred.

CLINICAL RESEARCH: A NEW DEVELOPMENT

In the Council's Report for 1955–56 an account was given of the arrangements which had been made for the further encouragement and promotion of both centrally and locally organized clinical research in relation to the National Health Service. The Council, in consultation with the Clinical Research Board, have now completed an exhaustive review of their existing arrangements for the support of clinical research at the national level, and have come to the conclusion that further provision of a different kind will be needed to meet foreseeable developments of medical knowledge in this field.

The Council finance clinical research in three main ways—by employing their own research staff, by awarding grants for research projects to workers not in their service, and by providing fellowships and scholarships for training in research. The overall cost of these activities in the field of clinical and paraclinical research has risen steadily from about £682,000 a year in 1953–54 to over £1,500,000 in the financial year 1959–60. Over the same period of six years since the appointment of the Clinical Research Board, the number of Units in the clinical and paraclinical field has increased from 24 to 42.

The Council are of the opinion that the present research grant and training schemes are well adapted to the needs of the situation and can readily be expanded according to requirements. But as instruments of research policy within the Council's control these schemes have only a limited value, in that their main use is to assist individual projects initiated by others, either directly by grants or indirectly through training awards. It follows, therefore, that for the purpose of promoting lines of investigation and meeting needs which they themselves identify the Council must rely primarily upon the staff they employ in their own Research Units, and at the National Institute for Medical Research.

In general the Council's Research Units are placed, as a matter of deliberate policy, in university departments, medical schools or hospitals, so as to provide the opportunity for collaborative work with departments having cognate or contiguous interests and also to guard against intellectual isolation. The Council are satisfied that this policy has, in general, justified itself and that the unit system, which has made an important contribution to the development of medical research in this country, must continue to constitute an essential feature of any future arrangements for the support of clinical research. The Council are, however, also convinced that by itself the unit system is insufficiently flexible and adaptable to meet the foreseeable requirements of a changing situation. In particular, the very fact that Council Units are housed in or alongside university or hospital departments has made it increasingly difficult, and indeed impracticable, to consider bringing together several Units in one place for a concerted attack on a major problem, or to develop particular Units to the

size that seemed desirable. This is inevitable because the available accommodation and general facilities at any one centre are seldom sufficient for the needs both of the host department and of more than one guest Unit. Yet there are already large areas of research in which progress depends on co-ordinated collaboration of a kind which can only be achieved by a suitable concentration of contiguous disciplines in one building.

In the preclinical field the Council have in the National Institute for Medical Research at Mill Hill a centre in which multi-disciplinary planned work of the intensity and scope that is now not only possible but necessary can be undertaken. This, together with their individual Research Units in the preclinical field, gives adequate overall provision for this particular group of research subjects. In the clinical field, however, there is no comparable centre, and the Council are wholly dependent on a series of separate and relatively small Research Units distributed throughout the country. The Council are thus restricted in their ability to promote the type of planned collaborative work that is coming increasingly to be required, or to regroup existing disciplines in new ways. Moreover, the present trend of development in medical research is towards the rapid integration of preclinical and clinical knowledge; and, since the National Institute has no clinical department, the Council are handicapped in promoting such integration.

With these considerations in mind, the Council, in consultation with the Clinical Research Board, have reached the conclusion that a centre should be set up, which would comprise an adequate and appropriately comprehensive concentration of relevant clinical and paraclinical disciplines. It would be incorporated within a general hospital which was providing, and would continue to provide, a full range of services to the community. The Council have from the outset been wholly opposed to any suggestion that a special hospital for research purposes should be built. In their view, such a concept would be inappropriate in this country; further, it would seem desirable that such a research centre should form an integral part of a hospital dealing with current medical problems and thus keep in touch with trends and changing disease patterns in day-to-day medical practice.

The Council are fully conscious of the fact that the siting, organization, structure and staffing of such a centre will present most formidable problems, and that it will be a long-term and costly development. After a full consideration of the present situation and of the trends of development that are emerging they are, however, firmly of the opinion that, if arrangements in this country are to be adequate to meet the needs of the future it is necessary not only to continue the development of existing means of promoting medical research but also to create additional and different facilities of the kind that would be provided by the new type of research centre they have proposed.

MEDICAL RESEARCH FOR THE TROPICS

To a country such as ours with extensive overseas interests, the problems of tropical medicine have long been of direct and practical importance. But it is perhaps of even more importance for medical research that all experience shows that medical knowledge is indivisible, and that, at any time, research anywhere may uncover information which, often quite unexpectedly, is of decisive importance elsewhere. The spread of epidemics, the contrasting incidences of

disease in temperate and tropical countries, the effects of race and environment upon the expression of diseases common to all countries, the opportunities for complementary research provided by locally occurring conditions, are all instances of opportunities to advance medical knowledge which not merely increase the range of individual illnesses which we can effectively control, but insensibly influence our whole orientation and thinking on illness in general. It was not, therefore, surprising that, when the Medical Research Council came to be founded, no artificial limitations, such as those of geography or climate, were put to their operations, or that the Committee of Privy Council to which they were made responsible contains those Ministers who have charge of Overseas Departments.

Up to the end of the Second World War, the operations of the Council in the tropical field were limited. This was largely due to the well-developed role of the Indian sub-continent in this field. There, the huge population and the epidemics of disease had early compelled attention, and in response there had arisen a fine medical service, universities, and research institutes upon which all could call. In 1947, India became independent. Some years earlier, however, provision was made in the first, and later in all subsequent Colonial Development and Welfare Acts, to develop research in the Colonies proper; and in 1945 the Colonial Medical Research Committee was created to advise the Secretary of State for the Colonies and the Medical Research Council on the promotion of this development.

When this Committee began its work, only two universities existed in the Colonies—those of Singapore and Hong Kong—and these had not yet recovered from the effects of the Second World War. In tropical Africa and in the Caribbean there were no centres of higher medical education, although in Uganda and in Nigeria institutions existed which gave a limited licence to practise. In several of the Colonies there were medical research institutes; but in general these were so burdened with routine that their staff could devote little time to investigation. Even had these resources been entirely available for medical research, the vast distances and the small numbers of personnel would have made them insufficient. Within ten years, however, the picture was changed substantially.

The first step was to recruit research workers and to set up bases. An Overseas Research Service was created under the Secretary of State for the Colonies. Bases were built at strategic points, and the Rockefeller Foundation, with characteristic understanding and generosity, transferred their Institutes at Lagos and Entebbe. In this period, universities began to develop, and soon full medical schools, of which any country might be proud, came into existence at the University Colleges in Uganda, Nigeria, and the West Indies. Parallel with these changes, the increasing interest in the basic medical problems related to the tropics developed in the universities and research institutes of the United Kingdom.

But, despite these encouraging developments, it was early evident that no single territory contained, or in the foreseeable future was likely to contain, sufficient resources for medical research to deal with more than a fraction of its problems and opportunities, and, further, that the division of effort between them was such as to render those resources that were available less effective than they might have been. It was therefore suggested that neighbouring

territories might combine their efforts. In this way there came into being a West African Council for Medical Research, covering Nigeria, the Gold Coast (as it then was), Sierra Leone, and the Gambia; an East African Council covering Kenya, Uganda, Tanganyika, and Zanzibar; and a Standing Advisory Committee for Medical Research in the British Caribbean. Each of these organizations contained two members from the United Kingdom, nominated by the Secretary of State for the Colonies, and was thus related to the Colonial Medical Research Committee. As a consequence of these developments the role of the latter Committee began to alter. It became less concerned with individual schemes of research overseas, and more concerned with co-ordinating policy (including the integration of home-based and overseas research programmes), initiating the opening up of promising new fields, and acting as a consulting organization and clearing-house of knowledge. In discharge of these functions an important factor was its promotion of visits to tropical territories by relevant experts and by visitors to undertake research of some duration.

By the end of their first ten years of work, therefore, the Colonial Medical Research Committee could justifiably feel that they had made a beginning in solving the problem. But by this time two new factors were entering on the scene. The first was scientific, the second political.

When the Colonial Medical Research Committee began their work, their thinking was dominated by the problems of tropical Africa. There, large populations were exposed over wide territories to the killing epidemic and endemic diseases traditionally associated with the tropics; and in Africa resources were most limited. It was inevitable, and proper, that the Committee should seek, at the earliest opportunity, to adapt to these problems the very substantial knowledge already available and to press forward all relevant research. Their primary preoccupation was, therefore, with such conditions as malaria, viral infections, helminthic diseases, and malnutrition. This chapter is, even now, only just opened; but it has been opened to the extent that one can have confidence that sooner or later it will be completed. But, with the beginnings of an establishment of control, other conditions are demanding and receiving attention. Particularly is this so of the diseases, such as tuberculosis, which are being favoured by the adoption of urbanization and other western social structures, and which, in a tropical environment, may pose new and unsuspected problems. It is evident, therefore, that in Africa we are entering on a new phase in which increasing attention will be required by conditions with which, perhaps in other variants, we have long been acquainted in this country. Some idea of what the balance of research interest in tropical Africa might become may be provided by the present position in the Caribbean. There, save perhaps in some of the mainland territories, ' bush medicine ' has been largely pushed back so that practice in general is primarily concerned with variants of conditions well known to us in this country, but which, being variants, provide most stimulating opportunities.

It is evident that the developing change in emphasis will require a reconstruction of the present Colonial Medical Research Committee. This, however, might have been delayed, were it not for coincidental administrative and political developments.

During the last few years, the Malayan territories and Ghana have become independent and self-governing. This year, similar developments will occur

in Nigeria. In the foreseeable future, the status of more territories will alter similarly. The change from Colonial to independent status necessitates that the territory passes from under the aegis of the Colonial Office and that it is, in future, related, like any other independent territory within the Commonwealth, to the Commonwealth Relations Office. Contingent on such change, the territory ceases to be eligible for aid from Colonial Development and Welfare funds (including the research allocation of these funds); and expatriate research workers who remain within its borders cease to be members of H.M. Overseas Civil Service and become employees of the new government, though provision is usually made for them to continue to be eligible for transfer to other territories with the agreement of the employing government. If the newly-independent territory is able to do so, it may find from its own resources the research funds required to replace those hitherto supplied from Colonial Development and Welfare funds. But, even so, there is an understandable reluctance among potential recruits to medical research in the tropics to commit themselves to a career where the future is uncertain or short-term, and a consequent danger arises of losing those now in posts overseas whose experience renders them invaluable.

Last year the Overseas Research Council was set up by H.M. Government and one of its primary tasks is to advise on the general policy to be pursued in regard to this problem. In regard to the particular problem of medical research in tropical countries the Medical Research Council were asked to propose a suitable scheme. This has now been officially accepted, and the Overseas Research Council have concurred with this scheme.

It has been agreed that the Medical Research Council should take overall responsibility for promoting and co-ordinating medical research for the tropics in so far as this directly or indirectly concerns this country. To this end they will set up, on the analogy of the Clinical Research Board, a Tropical Medicine Research Board to advise

(*a*) the Secretary of State for the Colonies through the Medical Research Council on all medical research in or for the Colonies financed from Colonial Development and Welfare funds;

(*b*) the Medical Research Council on all medical research in or for the independent Commonwealth financed from the United Kingdom Exchequer; and

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

It is intended that the Tropical Medicine Research Board will take over the work of the existing Colonial Medical Research Committee, including the promotion of visits abroad by experts and by home research workers who have a problem that could be developed with benefit overseas.

In regard to those investigators whose interests are primarily directed to medical problems as they occur in tropical countries and whose ' centre of gravity ' will tend to be overseas, provision needs to be made for three broad types of worker.

First are those senior men, now in key posts overseas, with years of valuable experience behind them. Given the necessary security and a relation to a home-based organization that can not only offer them a career when their posting

overseas would normally expire, but ensure that, if not at one place then at another, suitable opportunities are found for them to follow their work, it is believed that many such men might prefer to continue in the work that has been their lifelong interest. The Council believe that it is possible to make such arrangements which would suit not only the individual, but the territory or overseas organization with which he is working.

The second type of senior man is a specialised expert whose skill may be deployed in different places at different times. It is proposed that such workers be recruited to a home-based cadre to work abroad as need and opportunity offers.

The third type is the assistant. Many young research workers are interested in the medical problems of the tropics. They hesitate to take posts overseas, however, either because they consider such a career uncertain or because they are doubtful whether their interest in tropical problems is sufficiently strong. It is proposed that the Council should give such men, in the first instance, appointments to their staff for five years, the first three of which will, in any case, be spent abroad. If work in the tropics appeals to the man, and he makes a success of it, then at the end of three years he could be given a longer appointment overseas. It is from such men that it is hoped to recruit the key personnel and directors of the future who elect for a lifetime's career in the tropical field. If, on the other hand, the man finds that he has no liking for work in the tropics, he will spend the remainder of his first appointment in a home department allied to his interests.

The exact source, or sources, of finance in any particular case may be a complex matter; but it will be one for the Council to arrange with the various bodies concerned.

It is hoped that by the arrangements outlined above it may be possible to produce a career-structure which will command the confidence of medical research workers. The opportunities for advancing medical knowledge in the tropics are vast. This is so not only in relation to those diseases that are traditionally associated with the tropics, but also in regard to diseases which, although commonplace in this country, occur in different circumstances, or with variations, overseas. In many branches of medical research, the experience and opportunities available in the tropics are such as could not fail to enrich and deepen knowledge, both general and individual.

RESEARCH IN PSYCHIATRY

In January, 1959, the Council began a full review of their arrangements for the support of research in psychiatry with the aim of seeing whether these could be improved and extended. They were aware of the very great problems in urgent need of research in this field. Although the immense burden which mental illness imposes on the community is not reflected in mortality statistics, nearly half the hospital beds in the country are in mental hospitals or in institutions for the mentally sub-normal, and a substantial proportion of general practice is concerned with the care of patients with minor forms of psychiatric disability which cause much distress and economic loss. The Council were therefore anxious to make sure that they were not overlooking any opportunity to stimulate profitable lines of research, and that they were taking full advantage of

the new ideas and the increasing interest in the subject now becoming evident amongst medical scientists.

In the past, research in psychiatry has tended to lag behind research in other medical subjects and has not perhaps participated to the full in the great advances in knowledge, both of aetiology and of treatment, that have recently taken place in many other branches of medicine. Part of the reason for this less rapid progress may have been the tardy and incomplete recognition of the importance of psychiatry as an academic subject, and the relatively neglected place it has traditionally occupied in the medical curriculum. Although there has been an improvement in this respect in recent years, it is still probably true that the problems presented by mental illness, and the intellectual stimulus which they might provide for the young research worker, remain largely unknown to the majority of those passing through the medical schools. It is therefore not surprising that there has hitherto been a shortage of potential research workers in this field, and that this has shown itself in the difficulty experienced by the Council in promoting psychiatric research on a sufficient scale through any of the means at their disposal. Thus there have been relatively few applications in the psychiatric field for the Council's training awards, or for support for research projects among more senior clinical workers anxious to engage in psychiatric research; and workers in the basic sciences, upon which progress in this as in other clinical subjects now largely depends, have with few exceptions preferred to devote their energies to problems in other fields.

The improvement that is now taking place in these and other respects still falls short of what is required. Nevertheless the Council have found it possible in the past five years to make a considerable expansion in their programme; their expenditure in this field has been trebled and they now have a number of units devoted entirely to work on different aspects of psychiatry. In addition to their Social Psychiatry Research Unit, which was set up in 1948, at the Maudsley Hospital, the Council were already supporting, before undertaking their present review, a Neuropsychiatric Research Unit, now at the Council's Laboratories at Carshalton, a Clinical Psychiatry Research Unit at Graylingwell Hospital, Chichester, and a Neuropharmacology Research Unit in the Department of Experimental Psychiatry in the University of Birmingham.

As an outcome of their review the Council decided that work in epidemiology and genetics as applied to psychiatric problems was likely to be particularly fruitful at the present time, and they have accordingly established two new Research Units—one on psychiatric genetics at the Maudsley Hospital, and one on the epidemiology of mental disorders at University College Hospital, London. The Council also decided that in order to provide themselves with continuing advice on the needs and opportunities for promoting research they should set up two committees—one on Clinical Psychiatry under the chairmanship of Sir George Pickering and one on the Epidemiology of Mental Disorders under Sir Aubrey Lewis.

The Council have every hope that during the next few years some further expansion of research in psychiatry will be possible. They feel, however, that their present arrangements offer good career prospects for men and women interested in many of the varied aspects of psychiatric research. They also hope that the far-reaching changes introduced by the Mental Health Act, 1959, will provide a liberal and stimulating environment for research, and will attract a

rather larger share of young scientists and doctors into what is admittedly a difficult but nonetheless a socially important and potentially rewarding field of medicine.

RESEARCH GROUPS

At the present time the Council support research by employing their own staff or by giving temporary research grants to members of the staff of other institutions. The Council's staff are in general grouped in teams known as 'Research Units' or at the National Institute for Medical Research. Temporary research grants are given to allow workers in universities and hospitals to initiate new work and development on the understanding that if such work becomes established as a continuing activity of their department it will be taken over and financed from the departmental budget.

For some time, however, the Council have felt that there are circumstances in which, although there is not a case for creating a special Research Unit manned by members of their own staff, there is a good case for giving longer-term support than is possible under their scheme of temporary short-term research grants. They have accordingly inaugurated a scheme to promote, on a longer-term basis, suitable research projects outside their own Units or institutes, the development of which it is in the general interest to accelerate. Projects supported under this scheme will be known as Research Groups. These will differ from Research Units in that the work proposed will be in direct line with the purpose for which the Univerity or other centre created the particular department, rather than an entirely new and unforeseen development of knowledge or a highly specialised activity such as would need to be supported by a specially created research unit.

The initial period of support for such Research Groups will be related to the current or next University Grants Committee quinquennium. Possible further extension of Council support is envisaged, but this form of assistance would remain on the understanding that work assisted in this way would in due course be taken over by the University should the latter decide that it ought to be continued.

PUBLIC HEALTH LABORATORY SERVICE

On the outbreak of war in 1939 the Council became responsible for administering what was then called the Emergency Public Health Laboratory Service, which they had previously planned and organized at the request of H.M. Government. The original object of the Service was to augment the existing public health resources of England and Wales (analogous arrangements being made for Scotland in consultation with the Council) in combating outbreaks of infectious disease such as might arise from enemy action or from abnormal conditions in time of war.

Experience during the war years showed that the facilities which the Service provided could be of great value in the interests of public health quite apart from any special demands of the kind which had been envisaged; and when in 1945 the Government decided to retain the Service on a permanent footing the Council, at the invitation of the Ministry of Health, agreed to continue their administration of it for five years. In this matter, accordingly, the Council

acted as agents of the Ministry, the latter being also the channel through which funds for the purpose were provided. Statutory authority was given by Section 17 of the National Health Service Act, 1946, which empowered the Minister of Health to provide ' a bacteriological service ' for the control of the spread of infectious diseases.

Later the Council agreed to an extension of the period of their responsibility, on the understanding that they were free to delegate all detailed responsibility to a Public Health Laboratory Service Board appointed by them for the purpose; this body included representatives of the Ministry of Health and was under the chairmanship of Sir Landsborough Thomson of the Council's headquarters staff. In addition to the Director, Dr. G. S. Wilson, two senior members of the Service attended meetings of the Board as assessors.

In recent years, however, the Council have felt that, as the Service was now well established, separate and more durable arrangements for its administration had become desirable. In agreement with the Ministry of Health, therefore, provisions which the Council regard as entirely satisfactory have been embodied in the Public Health Laboratory Service Bill, 1960.

The purpose of the Bill is to establish and incorporate a new Public Health Laboratory Service Board as a statutory body capable of acting in its own right as agent of the Ministry. The Bill likewise transfers the staff of the Service from the employment of the Council to that of the Board; and transferred property from the Council to the Ministry.

Under the Bill, the members of the Board would be appointed by the Minister of Health, including two who must be appointed after consultation with the Council. The latter are happy that, while relieved of direct responsibility, they will still be associated with a Service which they have fostered for more than twenty years; and one which, although primarily performing a routine function, has always been active in research work of relevant nature. The Council particularly welcome the assurances given in Parliament that this last mentioned feature of the Service will be maintained.

In playing their part in these new arrangements, the Council have been anxious to preserve the greatest possible continuity in the administration of the Service—and not least in personal relations between headquarters and laboratory staffs. To this end Mr. D. V. T. Fairrie, a member of the Council's headquarters staff for many years, and latterly as Principal Administrative Officer, has been placed on permanent secondment so that he may take up the whole-time post of Secretary of the new Public Health Laboratory Service Board; some more junior members of the Council's headquarters staff have been similarly seconded.

The present Report includes the usual account of the work of the Service under the old arrangements, which obtained throughout the period under review.

Administration

ORGANIZATION

HEADQUARTERS STAFF

At date of Report

38, Old Queen Street, Westminster, London, S.W.1

SECRETARY
Sir Harold Himsworth, K.C.B., M.D., F.R.C.P., F.R.S.

DEPUTY CHIEF MEDICAL OFFICER
R. H. L. Cohen, M.A., M.R.C.S.

PRINCIPAL MEDICAL OFFICER
F. J. C. Herrald, M.B., F.R.C.P.E.

SENIOR MEDICAL OFFICERS
B. S. Lush, M.D., M.R.C.P.
Joan Faulkner, M.B., D.P.H. (*Information*)
R. C. Norton, M.A., M.B., D.Obst.R.C.O.G.

MEDICAL OFFICERS
E. M. B. Clements, M.B.
Margaret Gorrill, B.A., M.B.
P. J. Chapman, M.B.
H. W. Bunjé, M.D., M.R.C.P.
M. P. W. Godfrey, M.B., M.R.C.P.

PUBLICATIONS OFFICER
H. Stanley Banks, M.A., M.D., F.R.C.P., D.P.H. (*part-time*)

PRINCIPAL ADMINISTRATIVE OFFICER
J. G. Duncan, M.A., LL.B.

ASSISTANT SECRETARY
J. D. Whittaker, M.B.E.

ADMINISTRATIVE OFFICERS
D. J. Cawthron, M.A.
J. C. R. Hudson, M.A.
R. F. Smart

CHIEF EXECUTIVE OFFICERS
J. M. Jeffs, A.A.C.C.A. (*Accountant*)
F. Rushton (*Personnel*)
A. E. Turner

SENIOR EXECUTIVE OFFICER
M. A. F. Barren (*Supplies*)

SPECIAL DUTIES
Sir Landsborough Thomson, C.B., O.B.E., D.Sc. (*part-time*)
F. E. E. Smith, M.B.E.

VISIT BY THE LORD PRESIDENT

On the 14th January, 1959, Lord Hailsham, as Lord President of the Council, visited the Cell Metabolism Research Unit and the Bone-Seeking Isotopes Research Unit at Oxford.

RESEARCH ESTABLISHMENTS

The following new establishments were formally set up during the year: the Blood Coagulation Research Unit under the part-time direction of Dr. R. G. Macfarlane, at the Churchill Hospital, Oxford (p. 111); the Bone-seeking Isotopes Research Unit, under the honorary direction of Dame Janet Vaughan, also at the Churchill Hospital, Oxford (p. 122); the Mutagenesis Research Unit, under the honorary direction of Dr. Charlotte Auerbach, in the Institute of Animal Genetics, Edinburgh University (p. 125-6); the Experimental Virus Research Unit, under the honorary direction of Professor M. G. P. Stoker, in the Department of Virology, University of Glasgow (p. 132); and the Environmental Radiation Research Unit, under the honorary direction of Professor F. W. Spiers, in the Department of Medical Physics, University of Leeds (p. 123). Council also agreed during the course of the year to put arrangements in hand for the establishment of a Psychiatric Genetics Research Unit, under the direction of Dr. E. T. O. Slater, at the Institute of Psychiatry, Maudsley Hospital

and of a unit concerned with the epidemiology of mental disorders under the direction of Dr. G. M. Carstairs at University College Hospital, London.

Under arrangements agreed with the Ministry of Health and the Hospital authorities concerned, and with the advice of the Clinical Research Board, the Council formally took over financial responsibility for the research being undertaken at the Royal National Hospital for Rheumatic Diseases, Bath, and accordingly set up the Rheumatism Research Unit there, under the direction of an honorary committee (p. 102). Similarly, the Neuropharmacology Research Unit, under the honorary direction of Dr. P. B. Bradley, in the Department of Experimental Psychiatry, Birmingham University was also formally established (p. 139).

Shortly after the period covered by the Report, Council agreed that the epidemiological side of the Pneumoconiosis Research Unit at Llandough Hospital, Penarth, should be created a separate Unit under the honorary direction of Dr. A. L. Cochrane whose appointment to the David Davies Chair of Tuberculosis at the Welsh National School of Medicine had been announced just previously.

Two establishments were disbanded at the end of the year under review; the Environmental Hygiene Research Unit at the London School of Hygiene and Tropical Medicine, following the retirement of the Director, Dr. T. Bedford; and the Group for Research in Occupational Optics at the Institute of Ophthalmology, on the retirement of Mr. H. C. Weston. Arrangements were also made to disband, at the end of the calendar year 1959, the Group for Epidemiological Research on Respiratory Diseases (Air Pollution) at Sheffield, although the collection of data concerning pollution in Sheffield is being continued under the aegis of the Air Pollution Research Unit at St. Bartholomew's Hospital, London.

The Virus Research Unit transferred from the London School of Hygiene and Tropical Medicine to the Council's Laboratories at Carshalton. Council also approved arrangements for the transfer, at a later date, of the Neuropsychiatric Research Unit from the Whitchurch Hospital, Cardiff, to their Carshalton Laboratories.

On his appointment to the Chair of Psychology at University College London, Professor G. C. Drew was appointed Honorary Director of the Industrial Psychology Research Unit and of the Unit for Experimental Investigation of Behaviour, in succession to Professor Roger Russell. Dr. Alastair Heron, formerly Deputy Director of the Unit for Research on Occupational Aspects of Ageing, was appointed Director and Professor L. S. Hearnshaw, hitherto Honorary Director, became Honorary Scientific Adviser. At the same time Professor A. B. Semple accepted appointment as Honorary Medical Adviser to the Unit.

At the end of the year, the Council's establishments consisted of the National Institute for Medical Research, the Medical Research Council Laboratories, Gambia, and 71 Research Units (in some cases described by titles other than 'Unit'). Staff continued to be attached individually, as members of the Council's External Staff, to other institutions.

The Council continued to provide by a block-grant for a substantial part of the research activities of the Institute of Cancer Research, Royal Marsden Hospital, London. They also continued to provide block-grants to meet part of

the cost of the Research Department of the Royal Beatson Memorial Hospital, Glasgow, of the research programme of the Christie Hospital and Holt Radium Institute, Manchester, and of the Strangeways Research Laboratory, Cambridge.

OVERSEAS LIAISON

During the year, members of the Council's staff visited many countries overseas to attend international and other congresses, to give lectures, and to see and take part in research work at various centres.

A fairly large number of staff were again granted leave of absence to spend periods of up to one year in academic departments in various centres in the U.S.A.; these with others visiting the U.S.A., Canada and South America to attend congresses and other meetings generally took the opportunity to visit research centres elsewhere on the American continent.

Many staff visited research institutes and other centres in Europe for short periods to take part in collaborative work, to attend specialized symposia and to lecture. In addition, some 30 international congresses and other smaller meetings which took place in various European and Middle East countries were attended by members of staff, with financial assistance in most cases provided by Council: an especially large number attended the International Congress of Radiology in Munich.

Through the work of the Colonial Medical Research Committee, appointed jointly by the Council and the Secretary of State for the Colonies, and by close liaison with the East and West African Councils for Medical Research and the Standing Advisory Committee for Medical Research in the British Caribbean, the Council have continued their interest in many aspects of this field, both in the United Kingdom and in territories overseas. Several visits to both East and West Africa to call at research centres and to undertake field work were made under the Committee's auspices by members of the Council's staff and others closely associated with the Council's work.

During the year the Council have continued to maintain, out of their own funds, supplemented by support from Colonial Development and Welfare funds and other sources, their Laboratories in the Gambia, the Tropical Metabolism Research Unit in Jamaica and the Infantile Malnutrition Research Unit in Uganda. The Chairman of the Council visited the Gambia during the year to see work in progress at the Council's Laboratories at Fajara.

Progress has been maintained in the tuberculosis chemotherapy trials taking place in East Africa and India; in the latter country the project is being undertaken at the invitation of the Indian Government through the World Health Organization. On behalf of the Organization the Council have also continued to fulfil their responsibilities in connexion with biological standards and the epidemiology of influenza at the international centres maintained at the National Institute for Medical Research, and with blood grouping in the centre maintained in the Blood Group Reference Laboratory at the Lister Institute of Preventive Medicine. Members of staff have attended various WHO Standing Committees, Study Groups, and Conferences and several others, by special invitation, have attended meetings to advise on future research programmes to be carried out by the Organization in particular fields. The Secretary of the Council, as a member of the WHO Advisory Committee on Medical Research, attended the inaugural meeting of this Committee.

SCIENTIFIC COMMITTEES AND CONFERENCES

The Council have for long been closely concerned with personnel research in relation to the Defence Services, being advised by a number of specialist committees in this field. Among these is their Army Personnel Research Committee which has been recently reconstituted under the chairmanship of Professor J. R. Squire.

Following their review of the whole position of mental health research the Council have set up two committees in this field: on Clinical Psychiatry and on the Epidemiology of Mental Disorders, under the chairmanship of Sir George Pickering and Sir Aubrey Lewis respectively.

Other committees appointed during the course of the year have been those on Trachoma Research (replacing the former Trachoma Supervisory Committee); on Virus Diseases in the Tropics; on the Aetiology of Lung Cancer (an amalgamation, with certain changes of membership, of the two former Chemical and Biological Working Committees on the Chemistry of Tobacco Smoke in Relation to Carcinogenesis); on the Human Factor in Railway Accidents; and also a Working Party on Resistance of Gonococci to Penicillin.

The Council agreed that the following Committees which had completed their tasks should be disbanded: Analgesia in Midwifery; Research on Breathing Apparatus for Protection against Dangerous Fumes and Gases; Food Adulterants; Industrial Health Research Board (Committee of Chairmen); Resettlement of the Disabled; Whooping Cough Immunization; Leukaemia Research Working Party; Peripheral Paralysis and Bulbar Paralysis (Poliomyelitis) Working Parties; and the following Panels concerned with the relation of Cortisone and ACTH to Collagen Diseases and Hypersensitivity; Dermatology; and Haematology.

Continuing their policy of bringing together workers in a particular field to discuss their relevant interests or special problems where the need for a formal committee is not apparent, the Council arranged a Conference on Attenuated Polio Virus Vaccines and another to consider research in the field of virology. The Committee on the Human Factor in Railway Accidents referred to above was appointed following a Conference on this subject which was arranged after a request had been received from the British Transport Commission for advice on this problem. In addition to the research workers who were present, this Conference was also attended by representatives of the Commission, the Railway Inspectorate (Ministry of Transport) and the Trades Unions concerned.

PUBLICATIONS

The Council have published their Annual Report for 1957–58, and a reprint of the articles in the Annual Report (*see* p. 294); the publication of certain Special Reports was delayed owing to the printing dispute.

PUBLIC HEALTH LABORATORY SERVICE

The Public Health Laboratory at Bristol, which had for many years been maintained by the University Department of Bacteriology as an associated laboratory of the Service, was taken over as a constituent laboratory on the 1st January, 1959. Bristol was the last remaining associated laboratory to have been taken over in this way.

The new Laboratory at Preston Royal Infirmary, a joint pathological and bacteriological laboratory, was formally opened in December, 1958. Until then, the Service had no laboratory of its own in this densely populated area of Lancashire. Instead, through the co-operation of the Manchester Regional Hospital Board, arrangements were in operation for sanitary bacteriological examinations to be undertaken by conveniently situated hospital pathological laboratories. Eventual transfer of the sanitary bacteriological work from these 'recognized' laboratories to Preston was always envisaged, however, and it is hoped to complete the necessary arrangements for this as soon as possible.

The Central Tuberculosis Laboratory, which had hitherto been administered by the Welsh Regional Hospital Board, was transferred to the Service in April, 1959. It will in future act as the Tuberculosis Reference Laboratory of the Service.

The retirement through ill-health, at the end of December, 1958, of Dr. P. H. Martin and Dr. A. I. Messer is recorded with regret. Dr. Martin was Bacteriologist and Acting Director of the Institute for Medical Research, Kuala Lumpur, for some years before joining the staff of the London School of Hygiene and Tropical Medicine; at the outbreak of war in 1939 he joined the Service as Director, first of the Colchester and later of the Ipswich Laboratory. Dr. Messer had been Director of the Northumberland County Laboratory at Newburn since 1927; he joined the Service when the Laboratory was taken over in April, 1947, and was appointed Director of the Regional Laboratory at Newcastle in July, 1948.

FINANCE

EXPENDITURE OF PUBLIC FUNDS

In the financial year ended the 31st March, 1959, the total expenditure of public funds by the Council was £3,368,784 on ordinary account and £71,090 on non-recurrent account. The figures in the previous year were £3,032,889 and £35,514, respectively.

Most of this expenditure was met from the Parliamentary grant-in-aid, but this was augmented by sundry receipts (£52,990) arising from the Council's activities, and by contributions (£263,586) from Government departments and other official sources for special purposes. These included payments from the Ministry of Health for the Biological Standards Control Laboratory, for certain statistical work, for the maintenance of the Blood Group Reference Laboratory and for part of the cost of the Radiological Protection Service; from the Admiralty and from the War Office for investigations proposed by the Royal Naval Personnel Research Committee and the Army Personnel Research Committee respectively; and from Colonial Development and Welfare funds towards the cost of the Council's Laboratories in the Gambia, the Tropical Metabolism Research Unit in Jamaica, the Trachoma Research Unit, the Bilharzia Research Unit and for other researches in the field of tropical medicine. The World Health Organization provided funds for work on international biological standards and for the World Influenza Centre (both at the National Institute for Medical Research), for the International Blood Group Reference Laboratory in the Blood Group Reference Laboratory, and for work in the Infantile Malnutrition Research Unit in Uganda.

The allocation under main heads of the total expenditure of public funds on ordinary account was as follows :

	Per cent
Administration	4·0
Central Expenses	0·9
National Institute for Medical Research	18·5
Research Units and External Staff	61·5
Special Grants	7·0
Temporary Research Grants and Training Awards	8·1
	100·0

RESEARCH GRANTS

During the past five years the Council have received over 730 applications under their scheme of temporary research grants and accepted 629. The total number of current grants is 337.

BENEFACTIONS

Under the terms of their Charter, the Council are empowered to receive and administer private funds or properties entrusted to them by grant, gift or bequest, either for the general purposes of their work or for special objects within their field. Further valuable additions to the Council's resources have become available to them in this way during the year (see p. 295), and of these they wish to make grateful acknowledgement. During the year the legal formalities were almost completed in respect of the bequest by the late Lady Wadia of a sum of money to be spent on purposes of medical research ' by the Council within the University of Cambridge'. The sum involved, which is likely to be over £150,000, is designated, at Lady Wadia's request, the ' Sir Cusrow Wadia Fund'.

The income from benefactions for the financial year ended the 31st March, 1959, was £123,984. This included £35,715 as a further instalment of the grant from a group of tobacco manufacturers for research on cancer of the lung; £32,000 from the Alexander Pigott Wernher Memorial Trust; £21,350 from the Trustees of the late Lord Dulverton for research on coronary thrombosis; and £12,500 from the National Fund for Poliomyelitis and Other Crippling Diseases. Numerous smaller benefactions were received amounting to £4,868.

In addition, $28,000 was provided by the Rockefeller Foundation for travelling fellowships; nomination was made by the Council to awards of equivalent status at the invitation of the Eli Lilly Company, Indianapolis, the Lederle Laboratories Division of the American Cyanamid Company, and the United States Public Health Service.

PUBLIC HEALTH LABORATORY SERVICE

Financial provision for the Public Health Laboratory Service in England and Wales was made separately, the cost being borne on the Vote of the Ministry of Health. The expenditure in the financial year 1958–59 was £1,164,851 on ordinary account, and £36,404 on non-recurrent account.

Provision was similarly made by the Ministry of Health for the Blood Products Laboratory, another technical service administered by the Council on an agency basis through the Lister Institute of Preventive Medicine. The expenditure under this head was £47,506.

ACCOMMODATION

NEW BUILDING AND CONVERSION

For some years it has been realized that the accommodation for the Council's headquarters office was inadequate, at present five separate premises being occupied in the Westminster area. Most of the property developments in the Central London area have been considered in relation to the Council's requirements but all, with one exception, have been found unsuitable for a variety of reasons: the exception is the bombed section of Park Crescent, Regent's Park, which is being rebuilt and which may be ready for occupation within two years. The Council have negotiated with the developers for a lease of part of this building.

The Population Genetics Research Unit has occupied a new building at the Warneford Hospital, Oxford, and the Blood Coagulation Research Unit has moved to converted accommodation at the Churchill Hospital, Oxford.

In Cambridge, plans have reached an advanced stage for a new laboratory block for the Molecular Biology Research Unit, jointly with the University Department of Radiotherapeutics on a site on Hills Road where the new Addenbrooke's Hospital is to be built. The silent room being built in the grounds of the Applied Psychology Research Unit is nearing completion.

The extension to the block of laboratories at Hammersmith Hospital has now been completed; the part built by the Council accommodates the Microbial Genetics Research Unit and provides an additional animal house and laboratory accommodation for the Experimental Radiopathology Research Unit.

Extensive redevelopment of the Council's Laboratories at Carshalton are planned in order to provide laboratory accommodation for the Neuropsychiatric Research Unit, a specialized animal house for the Laboratory Animals' Centre, an enlarged canteen and, possibly at a later stage, an extension to provide enlarged Library and Meeting Room facilities.

A new animal house for the Rheumatism Research Unit at the Canadian Red Cross Memorial Hospital at Taplow has been completed. Plans are being prepared for a new animal house for the Radiobiological Research Unit at Harwell.

PUBLIC HEALTH LABORATORY SERVICE

A newly-built Laboratory at Maidstone has been occupied and the Exeter Laboratory has transferred to temporary accommodation kindly made available by the University.

A hut to be used as a Virus Laboratory is nearing completion at Southend and a new Public Health Laboratory being built at Chester is scheduled for completion by the summer of 1960. Building is expected to start shortly on a new Joint Hospital and Public Health Laboratory as part of a large hospital development scheme at Glangwili, Carmarthen, and extensions to the Laboratories at Coventry, Lincoln and Sheffield are under discussion.

PERSONNEL

OBITUARY

The Council record with deep regret the death on the 16th May, 1959, of Richard Fort, M.P. Since his appointment in January, 1955, as the member drawn from the House of Commons, Richard Fort had taken a full and valuable part in the deliberations of Council. His own scientific background fitted him admirably for this, and his informed advice has been greatly missed.

The Council also noted with regret the death of a former member of their body, Sir Robert Muir, M.D., F.R.C.P.E., F.R.C.P., F.R.F.P.S.G., F.R.S., on the 31st March, 1959, and of Major-General Sir John Taylor, C.I.E., D.S.O., M.D., I.M.S. (Retd.), on the 7th February, 1959.

Sir Robert Muir, a member of the Council from 1928 to 1932, was Professor of Pathology at Glasgow University from 1899 to 1936. He was also Pathologist to the Western Infirmary, Glasgow, where most of his own research was carried out; he made valuable pioneer contributions to immunology, haematology and research on malignancy. The author of important scientific papers and textbooks, Sir Robert was also a great teacher; he received many honours, and was elected F.R.S. in 1911 and created Knight Bachelor in 1934.

Sir John Taylor was Director of the Central Research Institute at Kasauli, in India, from 1932 until 1944. He then took up an appointment on the Council's Headquarters Staff, serving as joint secretary of the Colonial Medical Research Committee until his retirement in 1954. In this work Sir John's long experience of tropical medicine and research into tropical diseases proved extremely valuable. He was knighted in 1942.

RETIREMENTS AND RESIGNATIONS

Dr. T. Bedford (Director, Environmental Hygiene Research Unit) and Mr. H. C. Weston (Director, Group for Research in Occupational Optics), retired from the Council's staff after many years of loyal service. The Council are glad to report that both Dr. Bedford and Mr. Weston continue their association with them through the work they are undertaking in an advisory capacity.

Dr. J. L. Malcolm (National Institute for Medical Research) resigned to take up the Regius Chair of Physiology at the University of Aberdeen and among the other more senior members of the staff who left the Council's service during the year were the following: Dr. D. A. Long (National Institute for Medical Research) to take a post as Chief Medical Adviser to the Wellcome Foundation; Mr. G. R. Newbery (Radiotherapeutic Research Unit) to become Head of the Physics Section at the Radiochemical Centre, Amersham; Dr. P. Howard-Flanders (Experimental Radiopathology Research Unit) to take a post as Associate Professor at Yale University School of Medicine; Dr. T. C. Carter (Radiobiological Research Unit) and Dr. Joyce Wright (External Staff, St. Anne's Hospital, London).

Other staff who left the Council's service included the following: Dr. C. J. Shepherd (Chemical Microbiology Research Unit) on appointment to the staff of the Australian Commonwealth Scientific and Industrial Research Organization; Dr. V. M. Ingram (Molecular Biology Research Unit) to take a post in the Department of Biology at the Massachusetts Institute of Technology; Dr. C. S. Hunter (Tuberculosis Research Unit) to return to general practice; Dr. S. L.

Sherwood (National Institute for Medical Research) to take a post at the Illinois State Psychiatric Institute; Mr. D. R. Westgarth (Radiobiological Research Unit) on appointment as Head of the Division of Statistics and Operational Research at the Rubber Research Institute, Malaya; Dr. G. Holti (Unit for Research on the Experimental Pathology of the Skin) on appointment as Consultant Dermatologist to the United Newcastle-on-Tyne Hospitals and Lecturer at the University of Durham; Dr. M. E. Langham (Ophthalmological Research Unit) to take a post as Associate Professor in Experimental Ophthalmology at the Johns Hopkins Medical School, Baltimore; and Dr. J. H. Renwick (Population Genetics Research Unit) to take up a Fellowship in the Department of Genetics at the University of Glasgow.

HONOURS

Among the Birthday Honours, Her Majesty the Queen conferred a Baronetcy on Dr. Robert Platt, President of the Royal College of Physicians and a former member of Council and of the Clinical Research Board; the K.C.V.O. on Dr. Wilfrid Sheldon, a former member of the Clinical Research Board; knighthoods on Professor Aubrey Lewis, a former member of Council and of the Clinical Research Board and also Honorary Director of their Social Psychiatry Research Unit, and on Professor Dugald Baird, a former member of the Clinical Research Board and Honorary Director of the Council's Obstetric Medicine Research Unit; and the C.B.E. on Professor L. J. Witts, also a former member of Council.

The following members of the Council's staff have been honoured by Her Majesty during the year: Dr. E. E. Pochin (Director, Department of Clinical Research, University College Hospital Medical School, London) with the award of the C.B.E.; Dr. T. Bedford (Director, Environmental Hygiene Research Unit), Mr. H. C. Weston (Director, Group for Research on Occupational Optics) and Dr. I. A. McGregor (Director, M.R.C. Laboratories, Gambia) with the O.B.E. Dr. J. H. Hale, who has recently joined the staff of the Public Health Laboratory Service was also awarded the O.B.E.

Shortly after the opening of the year under review the award was announced of the Nobel Prize in Chemistry to Dr. F. Sanger, a member of the Council's External Staff working in the Department of Biochemistry at Cambridge. Dr. Sanger was honoured in this way for his work on insulin, which showed for the first time the chemical constitution of a protein. This award makes the third Nobel Prize awarded in the past seven years to members of the Council's staff.

Dr. C. S. Hallpike (Director, Otological Research Unit) was awarded the Guyor Prize by the University of Gröningen for the best work in otology for the past five years and one of the members of the staff of his Unit, Dr. J. D. Hood, received the Norman Gamble Prize from the Royal Society of Medicine for the best original work in otology for the past four years, and the Carpenter Medal from the University of London. Sir Stewart Duke-Elder (Director, Ophthalmological Research Unit) was awarded the Charles Mickle Fellowship for 1959 by the University of Toronto; Dr. L. H. Collier (Honorary Director, Trachoma Research Group) the 1959 Medaille d'Or Chibret by the League against Trachoma; Professor A. Bradford Hill (Honorary Director, Statistical Research Unit) the Galen Medal in Therapeutics for 1959 by the Worshipful Society of Apothecaries; and Dr. A. T. James (National Institute for Medical Research),

with Dr. A. J. P. Martin and Dr. R. L. M. Synge, a John Price Wetherill Medal of the Franklin Institute, Philadelphia.

The following were elected to the Fellowship of the Royal Society; Dr. Anne Bishop (Director, Chemotherapy Research Unit); Dr. F. H. C. Crick (Molecular Biology Research Unit); and Dr. M. H. F. Wilkins (Biophysics Research Unit). Two former members of the Council's staff, Dr. J. F. Tait and Dr. Sylvia Tait, and Professor F. Bergel (Institute of Cancer Research) were similarly honoured.

The Secretary of the Council, Sir Harold Himsworth, has recently been awarded the honorary degree of Doctor of Laws by the University of Wales.

STAFF NUMBERS

The number of staff employed by Council for their own purposes at the end of the period covered by the Report was 2,432. This figure was made up of 709 scientific staff (of whom 222 were medically qualified and 50 were part-time), 890 technical staff (of whom 11 were part-time), 492 administrative and clerical staff (73 part-time) and 341 maintenance staff (73 part-time). Not included in the total were 69 African staff employed full-time at the Council's establishments in Gambia (58) and Uganda (11).

The Council, as agents of the Ministry of Health in this matter, also employed 1,116 members of the Public Health Laboratory Service. This figure was made up of 153 scientific staff (of whom 126 were medically qualified and seven were part-time), 526 technical (one part-time), 183 administrative and clerical staff (13 part-time) and 254 maintenance staff (104 part-time).

ADVISERS, COMMITTEES AND ASSESSORS

The Council wish to express their gratitude to all the independent medical and other scientists—in addition to members of their own staff—who have assisted them with advice, whether individually or as members of special committees. A list of their committees is given on pp. 278–294.

The Secretaries of the Department of Scientific and Industrial Research and of the Agricultural Research Council, the Chief Medical Officers of the Ministry of Health and the Department of Health for Scotland are Assessors, *ex officiis*, to the Council. Sir Harry Melville and Sir William Slater, in this capacity, received papers on a reciprocal basis; and Sir John Charles, Sir Kenneth Cowan and Sir Geoffrey Jefferson (before his retirement from the Clinical Research Board) have attended meetings.

LIMERICK
Chairman of the Medical Research Council

HAROLD HIMSWORTH
Secretary of the Council
38, Old Queen Street,
Westminster,
London, S.W.1.

22nd April, 1960.

The subjects of the following articles have been selected for review out of the large number of research studies which the Council now supports. It is intended that every important subject coming within the Council's field should be dealt with in this way once in a few years. In order to present a reasonably balanced picture of the research on a particular subject it has frequently been necessary to refer to contributions made by workers unconnected with the Council; where workers are associated with the Council in the relevant research as members of the staff, grant-holders, or in an honorary capacity, this is indicated in the text in various ways at the first mention of their names, except where a name appears only in a reference.

OCCUPATION AND CORONARY HEART DISEASE

Perhaps the most striking feature of the vital statistics of our own and of certain other countries since the decade 1920–30 is that the fall in mortality which set in at the turn of the century has almost ceased for middle-aged males and not for middle-aged females. Thus, while the death rate of men aged 55–64 has fallen by only 10 per cent since the nineteen twenties and has remained stationary at about 22 per 1,000 since the end of the second world war, the death rate of women in middle age has undergone a steady reduction, the fall being 40 per cent since the nineteen-twenties in England and Wales. The rate for women is now about 11 per 1,000—half that in men. There are, however, a few highly developed countries, Sweden and Holland for example, where this trend is much less in evidence.

In seeking for an explanation of this check in the improvement of male mortality, there is no reason to think that men have not shared in the benefits of antibiotics and of other advances in treatment. For example, since the introduction of streptomycin, the death rate from tuberculosis among middle-aged men has fallen by more than half (Registrar General, 1958). Of possible contributory factors, the relatively higher liability of men than of women to develop coronary heart disease (and also lung cancer) in middle age, seems to be of outstanding importance, especially since there is good reason to suppose that the incidence of both these conditions has been increasing since the nineteen-twenties (Morris, 1951).

Dietary and Occupational Factors in the Causation of Coronary Heart Disease

Coronary thrombosis and coronary heart disease are characteristic of highly developed countries. From comparative studies of populations at different stages of social and economic development, suspicion has been thrown on diet as an important cause, and particularly on the animal, or 'saturated', fat content of the diet; much laboratory study is now devoted to this aspect of the problem. While these investigations are proceeding, studies of the disease in populations in Western countries have been chiefly concerned with factors other than diet, and the Council's Social Medicine Research Unit has been engaged for some years in investigations on the possible influence of occupation on the production of coronary heart disease.

Comparative Incidence in 'Light' and 'Heavy' Workers

An early result of studies on the frequency of coronary heart disease in various occupations was the observation that the conductors of London's double-decker

buses were less often affected than the drivers (Morris *et al.*, 1953). The advantage to the conductors was most marked among younger men and in respect of severe coronary disease; thus, ' sudden death ' under 50 as the first clinical manifestation of this disease was three times more common among the drivers than among the conductors. A similar situation was observed among men in Government service: executive officers, telephonists, and clerks were found to have broadly an equal incidence of coronary heart disease, which was higher than that of postmen, and the difference was greatest with the rapidly fatal type in the younger age groups. A further investigation covered men in a variety of occupations throughout the country, and showed that the coronary death rate was greatest in sedentary and ' light ' workers, and least in those engaged in heavy work; this trend was seen both among skilled workers and among unskilled.

Two later studies confirmed the suggestion that physical inactivity is important in coronary heart disease. In a national survey of post-mortem findings (Morris and Crawford, 1958) far more fibrous scars (the result of previous episodes of the disease) were reported in the heart muscles of ' light ' than of ' heavy ' workers, and this applied particularly to the most severe type of scarring and to the early middle age group. Secondly, in Birmingham (Brown *et al.*, 1957) the prevalence of the disease was studied in a large sample of men of 60–70 years of age, and here again more coronary heart disease was found in those who had been mostly engaged on physically light jobs than in those who had been on heavy work. An electrocardiographic survey in S. Wales by the Council's Pneumoconiosis Research Unit also indicated some excess of heart disease in ' light ' workers (Higgins, 1960). Surveys in several European countries have yielded the same result. Some studies in the United States have failed to confirm it, although in the most recent (Zukel *et al.*, 1959) the same contrasts were found between farmers and non-farmers as occur in this country between the physically more active and the physically less active.

Pathological Processes Leading to Coronary Thrombosis and Heart Disease

The walls of the coronary arteries are subject to a patchy fatty change, atheroma, and where this occurs a thrombus may form, narrowing or closing the channel. Any part of the heart muscle thus deprived of its normal blood supply is diseased and may die. The search for the biological mechanisms underlying the occupational differences in this form of heart disease has led to some interesting results and has raised even more interesting questions. Occlusion of the coronary arteries, whether occurring suddenly by massive thrombosis or gradually by narrowing of the blood vessels from atheroma or repeated lesser thrombosis, is most common in sedentary and ' light ' workers (Morris and Crawford, 1958); one contributory factor may be the tendency to relatively slow blood flow in the coronary vessels of these workers. In the laboratory it has been found that physical exercise both lengthens the time taken by blood to clot after withdrawal from the body (McDonald and Fullerton, 1958) and increases the rate of fibrinolysis, or the removal by enzyme action of the fibrin present in the clot. (Biggs, Macfarlane and Pilling, 1947; Greig, 1956). Accordingly, a field study was started in H.M. Dockyard, Portsmouth (O'Brien, 1960), to investigate aspects of blood clotting in men of different and contrasted occupations. Another effect of physical exercise, revealed by laboratory work in animals (Eckstein, 1957), is enlargement of the bed of small anastomosing blood vessels between

the two main coronary arteries; when this collateral blood supply is good the circulation to the heart muscle may be re-established after a coronary occlusion.

In several surveys, high blood lipids and high blood pressure have been noted before the actual appearance of coronary occlusion and heart disease. Both these precursors seem to be affected by occupation. Among samples of working busmen in this country, blood lipids have been found to be higher, age for age, in the drivers than in the conductors; and similar observations have been made in other countries. In the laboratory it has been shown that vigorous exercise lessens the rise in the level of blood lipids that takes place after heavy feeding (Mann *et al.*, 1955). In studies by the Pneumoconiosis Research Unit (Miall, 1959) and in the clinical survey of London busmen (Kagan, 1960) systolic and diastolic blood pressures were found to be higher in sedentary and ' light ' workers than in the more active groups; and in the national survey of post-mortem material, referred to above, evidence of serious hypertension was found most commonly in those who had been ' light ' workers. However, the results of some Scandinavian studies are not in agreement with this finding, and it is not yet clear whether the difference stems from unstandardized methods of examination or is of real importance.

It is evident that habitual physical activity or inactivity affects many physiological functions of the body, and the question arises whether, in the production of coronary heart disease, we are dealing with the results of increasing cardiovascular inefficiency in middle age, or with a specific factor related, for example, to the thrombosis itself. In the post-mortem survey it was found that, in general, ' light ' workers had pathological cardiac changes similar to those of men in heavy work who were 10–15 years older. It seems possible that the increase in coronary heart disease in the present century may in some measure reflect the increasingly sedentary nature of work, of transportation, and of leisure. If this is so, the use and enjoyment of leisure assumes an added importance in the preventive medicine of tomorrow.

Obesity and Body Build in Relation to Coronary Heart Disease

Another factor in the problem was first observed in the course of analysis of measurements of the uniforms distributed to London bus drivers and conductors. It was found that ' age for age ' the drivers were larger round the waist and chest than the conductors. This observation was checked by clinical examination, and by a study of skinfold measurements; obesity was found to be commoner in the sedentary workers, the drivers, than in the physically active workers, the conductors. Further enquiry showed, however, that such differences in physique were already substantial in the earliest years of employment. It seems likely that men of different body build, or somatotype, select different kinds of jobs, and having done so they spend many years in environments which may enhance their initial differences. An attempt is being made to sort out some of the constitutional and environmental factors involved in the production of such differences found in middle age, and to study the development of these differences in relation to occupation, body build, diet, and other factors. Meanwhile, the evidence suggests that the occupation as such is more important than physique in producing the differences found in the incidence of coronary heart disease.

Differences within Light Occupations

Whatever their social class, men in light occupations in general show high rates of coronary heart disease. However, considerable differences in frequency exist in different sections of this group of workers, and the question arises whether other factors than mere physical inactivity are concerned, for example, the nervous strain associated with certain light occupations. Various puzzling differences have been observed in this country, for instance: (*a*) higher incidence of coronary thrombosis in general practitioners than in other doctors, (*b*) particularly high mortality among radio and telegraph operators, and (*c*) relatively low mortality among leading Government officials, who are frequently faced with problems involving difficult decisions (Registrar General, 1958a and 1958b). It is proving very difficult to unravel the factors associated with such differences within the light occupations. Self selection and other forms of selection may be factors in the low mortality among higher public servants, who may reach such positions partly at least because of their ability to deal with difficult problems without undue nervous strain; or the relative immunity from coronary disease may indicate an effective social organization for coping with such problems. Some direct studies limited to such occupations are now being made. Blood pressure and blood lipid levels can undoubtedly be affected by emotional stimuli, and presumably by conditions producing emotional reactions and fatigue; but personality and temperament have so far proved difficult to correlate with cardiovascular function; this field of enquiry also is now being opened up (Friedman and Rosenman, 1959).

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STUDIES ON THE CHEMOTHERAPY OF TUBERCULOSIS IN EAST AFRICA AND INDIA

The Problem of Tuberculosis in the Less-Developed Countries

'With the encouraging progress made in the control of malaria, tuberculosis now is the most important specific communicable disease in the world as a whole, and its control should receive priority and emphasis both by WHO and by

governments' (World Health Organization, 1959a). This is the global picture that should be kept in view, and it should not be obscured by the remarkable progress in the conquest of tuberculosis made in Great Britain and some other countries in the past 10–15 years. The ravages of tuberculosis can be illustrated by events in India, where the number of infectious cases has been estimated variously at 2½ and 1½ millions (WHO, 1959b). Tuberculosis is a particularly damaging disease because of the chronic illness and the mortality to which it gives rise in the productive adult section of the population.

Practical considerations prevent many developing countries from adopting, for their population as a whole, schemes of chemotherapy like those which have been employed with great success in Britain, since they are lengthy, intrinsically expensive, and entail the heavy additional costs of complicated hospital and chest clinic facilities. The requirements for treatment in such countries are that it should be cheap, easy to administer, and effective when applied to patients living at home. The need is to organize mass campaigns of case finding, and to follow this with home treatment that is simple but sufficiently effective to break the chain of infection from person to person, and so lead to control and ultimate eradication of the disease. After some years' experience with isoniazid we now know that it is the most valuable antituberculosis drug that we possess, because of its high potency, its convenient (oral) form of administration, its low toxicity in the dosages commonly used, and its cheapness; no other known antituberculosis drug has all these advantages. Unfortunately, if isoniazid is given alone tubercle bacilli that are isoniazid resistant tend to appear in a considerable proportion of cases within a few months, and these drug-resistant organisms may cause relapse in patients who have begun to improve, and may also infect their contacts. However, it has recently been established that highly isoniazid-resistant strains of tubercle bacilli are relatively non-virulent in animals, and the disadvantages of isoniazid resistance may possibly be smaller than has been supposed. Nevertheless, when resistant bacilli appear in a patient difficulties arise as to further drug treatment. It has been found as a general principle that a combination of drugs usually delays or prevents the appearance of resistance to any one of them, and in this country either *p*-amino-salicylic acid (PAS) or streptomycin is usually given with isoniazid for this purpose, and also because such combinations are therapeutically effective; but many health authorities in developing areas consider the difficulties of administration of such combinations to be too great for widespread domiciliary application, and when thousands of cases are involved the high cost of these particular companion drugs to isoniazid cannot be disregarded.

During the past few years the Council's Tuberculosis and Statistical Research Units, and their Unit for Research in Drug Sensitivity in Tuberculosis, have been co-operating with national and local agencies in East Africa and India—and with WHO also in India—in an attempt to answer the following questions. How does drug treatment given to patients living at home, even under conditions of poverty and malnutrition, compare with its use in hospital? To what extent is the use of isoniazid alone disadvantageous to the patients, and are those in whom resistant organisms appear a source of infection to contacts? Can effective, cheap, easy-to-administer, and non-toxic regimens be found, in which a companion drug to isoniazid is employed other than PAS or streptomycin? How far does inadequate treatment result in an increase in the number of new cases with drug-resistant organisms, thus jeopardizing the

success of the whole scheme? What treatment can be applied to those primarily infected with drug-resistant organisms, and to those in whom such organisms have appeared during treatment? The need to obtain answers to these questions is urgent, since there is a very real risk that if effective regimens cannot be formulated, ineffective ones will be used, resistant organisms will be disseminated, and an increasing proportion of patients will accumulate for whom no effective treatment can be given. Indeed the proportion is already large enough to cause concern (Pepys *et al.*, 1960).

From these introductory considerations it is clear that mere automatic transference of knowledge such as that existing in Great Britain to the different conditions and requirements of many developing countries will only touch the fringe of the vast problem in tuberculosis with which these countries are confronted. Different approaches and even different drugs are needed and all these have to be tested. The value of controlled clinical trials, in the development of which the Council have been in the forefront (see CIOMS, 1959), has been further confirmed in these overseas investigations.

Studies in East Africa

In 1952 the Council's Tuberculosis Research Unit were asked by the Department of Medicine, Makerere College, Kampala, Uganda, to advise on how to conduct clinical studies of antituberculosis chemotherapy in East Africans. As a result, in 1953, for the first time in East Africa, a controlled comparative chemotherapeutic trial was undertaken in hospital patients, the majority of whom suffered from the acute severe and extensive disease which is characteristic in that area. The purpose was to assess precisely how African patients would respond to forms of chemotherapy already proven in Europeans. The response to treatment with isoniazid plus streptomycin and with isoniazid plus PAS under these conditions during a period of six months was found to be very satisfactory (Hutton *et al.*, 1956). The chest radiographs of the East African patients were then compared with those of a group of patients with a similar amount and kind of tuberculous disease treated with the same drugs in Britain. The two series of radiographs were read and reported on by independent assessors, unaware of the different origins of the patients. The results showed—unexpectedly at that time—that the response to adequate and properly controlled chemotherapy in East Africans could be at least as good as the response of British patients (Fox *et al.*, 1956).

After showing that carefully controlled trials were practicable in East Africa, the next step was to try to find an effective and non-toxic regimen more acceptable to the patient, easier to administer, and, if possible, less expensive than these two standard combinations, and thus more suitable for chemotherapy on a mass scale. A series of co-operative studies involving hospitals and laboratories in Kenya, Uganda and Tanganyika was therefore initiated and is still in progress. In one of these studies the effectiveness of diaminodiphenylsulphone (DDS), which is widely used in the treatment of leprosy, was compared with PAS in its power to prevent the emergence of resistance of the patient's tubercle bacilli to isoniazid. The result showed, unfortunately, that the use of DDS did not prevent this resistance from arising (East African/British MRC Sulphone Investigation, 1959).

More promising results were obtained in a similar study of thiosemicarbazone thiacetazone as a possible alternative to PAS; this group of drugs, originally

proposed in Germany for use in tuberculosis, has been discarded in most countries owing to toxicity of the dosages commonly used. Now, however, in combination with isoniazid, thiacetazone has been found in a first trial to be about equal to PAS in preventing resistance to isoniazid (East African/British MRC Thiacetazone Investigation, 1960). This finding has justified larger scale studies with the aim of establishing an optimal balance of dosage of the two drugs that will prove efficacious without undue side effects; these studies, which (with an eye to mass chemotherapy) include out-patients as well as in-patients, are now in progress. The prize is worth pursuing, since thiacetazone is easy to administer, acceptable, and cheap. It is, however, too early to be sure that this combination can reach a desirable standard of efficacy.

These investigations reflect the present difficulties in selecting a suitable companion drug for isoniazid when considering its large-scale use in countries like East Africa. In this state of affairs it is tempting to use isoniazid alone—which, as already mentioned, is potent, cheap, and simple to use—in spite of its tendency to result in drug-resistant bacilli. Recognizing this dilemma, a recent WHO Study Group (1957) recommended investigation of the ' pros ' and ' cons ' of such treatment, which is, in fact, already being used in many parts of the world. Accordingly the East Africa/MRC co-operative studies were extended to examine the results of treatment with two dose levels of isoniazid alone. It was concluded that neither dose was as effective as isoniazid plus PAS in severe extensive pulmonary tuberculosis. Combined therapy is to be preferred at present, despite the difficulties of administration of the PAS (East African/British MRC Isoniazid Investigation, 1960).

The admission of successive series of similar patients to these trials since 1953 has provided an opportunity of assessing the trend in the prevalence of drug-resistant organisms already present in patients seen for the first time. An unexpected and ominous rising tide of initial drug resistance, particularly to isoniazid, has been revealed in East Africa. While part of this phenomenon may be due to primary infections with resistant organisms, most is believed to be due to previous, undisclosed, therapy. The trend underlines the necessity of giving antituberculosis chemotherapy in adequate forms for adequate periods (Pepys *et al.*, 1960).

In the organization of the East African studies, local co-ordination is provided from Makerere College, and progress reports on the cases are sent to the Tuberculosis Research Unit in London, where they are analyzed. The reports are prepared at the Unit in co-operation with the clinicians and bacteriologists in East Africa. The Unit for Research on Drug Sensitivity co-operates with the local laboratories and acts as a reference laboratory.

Studies in India

In 1955 WHO invited the Council to send representatives to India to advise on the planning of mass campaigns of antituberculosis chemotherapy in that country. As a result, in 1956 a chemotherapy research centre, staffed by Indian and international personnel and sponsored by the Indian Council of Medical Research, the Madras Government, and by WHO and the Council, was set up in Madras under the scientific direction of the Council's Tuberculosis Research Unit in co-operation with the Statistical Research Unit and Unit for Research on Drug Sensitivity. The Centre has a fully equipped out-patient

clinic and laboratory, a large domiciliary service, a statistical department, and 100 sanatorium beds.

The first step was to conduct a comparative investigation of the results of treatment for a year with a standard combination of drugs (isoniazid plus PAS) in a group of about 100 patients living at home in poor sections of the City of Madras, and in a similar number of patients admitted to the sanatorium. There was little to choose between the progress made by these two groups; in both it was satisfactory. Surprisingly, factors generally regarded as adverse, such as poor diet, poor housing, little rest, little nursing, irregularity in medicine-taking, most of which were operative in the domiciliary group and not in the sanatorium group, were found to have little or no influence on the results obtained after one year's treatment with this powerful standard combination of drugs (Tuberculosis Chemotherapy Centre, Madras, 1959). A basis for mass domiciliary treatment of tuberculosis with modern drugs in India has thus been established, though the problem remains—as in East Africa—of finding the most practicable drug regimen and the best way to apply it; a particular difficulty is how to persuade patients treated at home to take their medicine regularly (Fox, 1958).

Another point investigated in this first study was whether the home contacts of the domiciliary patients were exposed to a greater risk of contracting the disease than those of the patients treated in the sanatorium. The first results of these observations have been published (Andrews *et al.*, 1960). They show that, in the early months after the diagnosis of the index case, there is a major risk to young contacts, both of patients treated at home and of those treated in sanatorium—but that in both groups the risk is rapidly reduced when the patient is brought under treatment. It thus appears that efficient treatment at home and isolation in a sanatorium are both capable of reducing the risk of infection of contacts, and that this risk is not unduly increased by the treatment of patients at home.

In this study the co-operation of both patients and contacts throughout the whole year exceeded most expectations; and the great majority of the patients and contacts have continued their co-operation for a second year, and even longer, thus ensuring that information will be obtained on relapses and their prevention. The domiciliary patients have continued in the second year to fare as well as the sanatorium patients, who are now also at home (Velu *et al.*, 1960).

Since the standard combination of isoniazid plus PAS used for the initial inquiry may not be suitable for mass domiciliary application, new comparative studies are being made and others planned on further groups of domiciliary patients to test variations from this standard as well as other combinations, and also to test methods involving intermittent or less frequent administration. An important study of this kind is concerned with the value of three different regimens of isoniazid alone. Moreover, the infectiousness of isoniazid-resistant organisms is being examined by a combination of bacteriological, clinical and epidemiological methods.

In addition to the main reports emerging from this Centre, a number of subsidiary investigations have been completed. A test for detecting isoniazid in urine has been developed and is now in routine use (Gangadharam *et al.*, 1958); improved methods for obtaining specimens for culture of the tubercle

bacillus for diagnostic purposes have been worked out (Andrews and Radhakrishna, 1959); the value of fluorescence microscopy in examining large numbers of specimens for tubercle bacilli has been reported (Holst *et al.*, 1959); and the virulence of many of the strains of tubercle bacilli found in the Indian patients before treatment has been shown to be lower in guinea pigs than that of comparable British strains—an observation of possibly great epidemiological importance (Mitchison *et al.*, 1960). A number of other studies are currently in progress.

The Wider Aspects of these Studies

In these commonwealth enterprises the Council have been instrumental in setting up organizations for the clinical assessment of drug regimens in tuberculosis that can stand comparison with the best in this country. There has been little or no duplication. On the contrary, the Indian and East African studies are largely complementary. It is gratifying that the Indian Government are considering the adoption of the Madras Centre as a permanent unit, so that it will not only serve the original purpose of investigating certain urgent problems and training some national staff, but will play a continuing part in the country's developing health scheme. Finally, it must be emphasized that these studies overseas are expected to assist in the control of tuberculosis here as well as in the tropics and in developing countries. For example, the comparison between home and sanatorium treatment in India has implications for domiciliary treatment in Britain; evidence on the infectivity of isoniazid-resistant strains is also likely to be relevant to Britain, where there is also a danger that such strains may build up in the population; and the demonstration of usefulness in new combinations of drugs may be of wide application, even where cost is less of an obstacle and hospital beds are readily available, by freeing other combinations for use as a reserve. Thus a valuable reciprocal relationship is established in which advances in the more favoured countries are applied elsewhere, and *vice versa.* Special relevancy to the local conditions must, however, remain uppermost in mind; and even if and when suitable regimens can be fully endorsed for mass domiciliary chemotherapy in Africa and India, 'operational' research, to define the best way of seeing that the drugs are, in fact, taken as ordered, may be needed. Fortunately WHO and the Indian Government have foreseen these needs, and methodological studies have already been initiated in the new National Tuberculosis Institute, Bangalore, and in the Madanapalle Tuberculosis Research Unit; and their work is being co-ordinated with that of the Madras Chemotherapy Centre.

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CLEAN AIR IN OPERATING THEATRES

Airborne Infection

The risk of airborne infection of wounds occurring during surgical operation has long been recognized and it was to combat this risk that Lister, about 90 years ago, introduced a carbolic acid spray over the operating table as part of his antiseptic technique. During the last 25 years interest has been revived in the question of airborne infection generally, and the consequent development of more reliable apparatus for determining the numbers of bacteria in the air, such as the Wells air centrifuge and the Bourdillon slit sampler, has made possible a more detailed examination of the risk of airborne infection in surgery. The pattern of the more recent investigations was set by the work of two members of the Council's staff, R. B. Bourdillon and L. Colebrook (1946), and by the Council's Special Report No. 262 ' Studies in Air Hygiene ' (Bourdillon *et al.*, 1948). These workers showed that the air of operating theatres could become heavily contaminated with pathogenic bacteria, either liberated from dressings, bedding, or the clothes of the occupants, or sucked into the theatre in contaminated air from other parts of the hospital, and further, that the exhaust fans commonly provided to free the theatre from steam often added to the contamination in this way. Bourdillon and Colebrook combated both these sources of contamination by supplying sufficient clean ventilating air to the theatre to remove the internally produced contamination by dilution or displacement, and to maintain a positive air pressure in the theatre which prevented the ingress of air from the rest of the hospital. Experimental confirmation of the improvement obtained by these methods in protecting patients from infection was obtained by E. J. L. Lowbury (1954), working in the Council's Industrial Injuries and Burns Research Unit at the Birmingham Accident Hospital. Of patients whose dressings were done while the ventilation plant was in use, 17 per cent acquired *Pseudomonas pyocyanea* infection and 25 per cent acquired antibiotic-resistant staphylococci, compared with 38 per cent and 41 per cent for the patients dressed while the ventilation mechanism was switched off.

Staphylococcal Infection in Operating Theatres

Research on the subject during the last few years has been principally concerned with infection by *Staphylococcus aureus*, which now appears to be the major cause of post-operative sepsis. In 1955 R. Blowers of the Middlesbrough Public Health Laboratory and his colleagues reported on a number of cases of sepsis in a thoracic surgery unit. Clinical evidence suggested that the infection occurred at the time of operation, and examination revealed a high level of

bacterial contamination of the air of the operating theatre. Alterations to the ventilating system reduced this contamination and were followed by a striking reduction in the frequency of sepsis in the unit. This reduction could not, however, be wholly attributed to a reduction in the risk of airborne infection in the theatre, since other improvements in technique were made at the same time in other parts of the hospital. A clearer indication of the importance of airborne infection was given by R. A. Shooter, working in St. Bartholomew's Hospital, London; Shooter and his colleagues (1956) observed a reduced frequency of sepsis in wounds when improvement of the theatre ventilation was the only change made.

It seems to be established that there is a real risk of airborne infection of a wound during operation and that this may sometimes be serious. Various aspects of the problem are being explored in certain of the Council's Units and by the Public Health Laboratory Service. Some of the investigations deal with methods for preventing or reducing the dissemination of the staphylococci; others are concerned with the control by ventilation of the airborne contamination of operating theatres.

Methods of Reducing the Dissemination of Air-borne Micro-organisms

Blowers (1958) has enumerated the measures which can be taken to reduce the dissemination of staphylococci and other organisms into the air of an operating theatre; these include precautionary measures relating to the clothing of the staff, the exclusion of contaminated bedding, the detection and exclusion of carriers among the staff, and the elimination of unnecessary movement within the theatre. Despite all precautions, however, an appreciable number of pathogenic organisms always find their way into the air, and under less than ideal conditions the numbers may be large. It is a function of the ventilation system to remove these micro-organisms from the theatre as rapidly as possible, and especially from the neighbourhood of the operating table, for the protection both of the patient immediately concerned and of those who follow him on to the table. Adequate ventilation is particularly important when the patient last operated on was already infected. Current studies are concerned with the best ways of utilizing the ventilating air for these purposes.

Ventilation by Positive Air Pressure

There is general agreement in principle, though the principle is not yet always applied in practice, that air from other parts of the hospital should be excluded from the operating theatre, and that, as suggested by Bourdillon and Colebrook, this is best attained by supplying to the theatre sufficient ventilating air under positive pressure to maintain an outward flow from the theatre at all times. This implies that any extraction fans installed should have an aggregate capacity considerably below that of the apparatus supplying the input air, preferably less than half of it, and that the net volume of air supplied to the theatre should be sufficient to maintain a positive pressure across all the leakage cracks around doors and hatches. In such a ventilating system the highest pressure is obtained by dispensing with all exhaust fans and even with planned exhaust outlets, and allowing the air to find its way out through natural openings. In well-built theatres, however, the exit of air by such natural means may be insufficient to maintain the desired rate of air change in the theatre. A simple solution, proposed by Blowers and Wallace (1960), is to install exhaust ports fitted with weighted flap valves in positions selected to produce the desired pattern of air flow in

the theatre suite. When the pressure in the theatre drops owing to opening of a door the flap valves close, so that the full volume of the input air becomes available for maintaining an outward flow through the door opening. Such valves also compensate to some extent for reduced air input due to blockage of air filters, and differential weighting of the valves in the various rooms of a theatre suite provides a simple method of regulating air flow between the rooms.

Methods of supplying input air. There are, in general, three ways in which air under positive pressure can be introduced into an operating theatre. (1) It may be admitted by openings, usually placed near the ceiling, in such a way as to keep the air movement in the theatre relatively low. (2) The velocity of the incoming air may be relatively high and its direction controlled, either for reasons of comfort or to prevent stagnant zones of air in the room. By directing such currents of ventilating air towards the operating area rapid air movement is produced in the centre of the room, and this prevents the persistence of any local region of contamination, especially in the space containing the theatre lamp and the ring of staff and equipment surrounding the patient. With this method, and the preceding one, the incoming clean air mixes freely with the contaminated air already in the room. (3) The ventilating air may be introduced into the top of the room so that it displaces the contaminated air by a continuous process of downward displacement, as suggested by Bourdillon and Colebrook. In order to maintain the best ' piston effect ' of the incoming air, it must be introduced at a temperature a few degrees warmer than the room temperature.

Experimental Investigations of Ventilating Systems

Removal of general contamination. The three methods of input of air described above were investigated by Blowers and Wallace, of the Public Health Laboratory Service, in a dummy operating theatre constructed near Middlesbrough. The relative efficiency of the three systems for ventilating purposes was compared in terms of the rate at which a cloud of non-pathogenic organisms was removed, after being uniformly dispersed into the air of the theatre. The technique employed was to determine: (*a*) the numbers of organisms settling on open culture plates so disposed in the theatre as to represent the patient's wound, and (*b*) the numbers of organisms present in a given volume of air in the room. It was found that the downward displacement method was much more effective than turbulent mixing in removing bacterial contamination from the air of the room as a whole.

During the course of this work, Blowers and Wallace determined some of the conditions needed to create an effective downward displacement movement of air. In a theatre of the usual size and shape at least six air inlets should be placed symmetrically in the ceiling. The air must be thrown horizontally around each of the distributors of the incoming air at these points, and the distributors carefully designed to reduce turbulence and aspiration effects. Air exhaust ports should be situated low down on each of the four walls. All the heating should be provided by the ventilation plant itself so that warm air is admitted to a slightly cooler room; background heating from radiators or sterilizing equipment reduces the displacement effect. In the dummy theatre these methods were highly effective in removing micro-organisms from the air. It now remains to be seen whether the activity that goes on when a theatre is in use seriously

interferes with such a system. During warm weather, when cold air is needed for ventilation purposes, the ' piston effect ' will be reduced and the bacteriological efficiency of the plant may fall to that obtained when the same volume of air is introduced by methods permitting some turbulent mixing. Only a few theatres have as yet been constructed with piston type displacement ventilation systems, so that their performance in practice cannot yet be accurately assessed. Surgeons and bacteriologists working in new operating theatres should be able to make useful contributions to our knowledge by recording assessments of cleanliness in terms of sepsis rates.

Removal of localized contamination. It is, however, possible that the methods of ventilation which are most efficient in clearing the organisms from a uniformly contaminated room, as tested by Blowers and Wallace, are not those most suited to dealing with contamination arising from a *localized* source. For several years O. M. Lidwell of the Air Hygiene Laboratory, Colindale, has been investigating the use of various gaseous tracer materials suitable for studying the behaviour of ventilation plants and the air currents in occupied places generally. Acetone vapour at concentrations well below the limits of detection by smell has been employed, and methods developed for continuous quantitative estimation. This is still the only convenient tracer material which can be estimated with simple, standard, chemical apparatus. Recently, however, with the use of an infra-red gas absorption meter to make a continuous record of gaseous concentrations in the air, nitrous oxide has been found to be a satisfactory tracer. With this equipment O. M. Lidwell and R. E. O. Williams of the Public Health Laboratory Service studied a number of operating theatres and measured the amount of the gaseous tracer which reached the operation site when standard amounts of the gas were liberated in various parts of the theatre to simulate bacterial contamination emanating from persons working in the theatre.

As would be expected the greater the volume of air supplied to the theatre the smaller was the amount of contamination which reached the operation site. In those theatres where the air movement was small, 20 feet per minute or less, contamination liberated close to the operating table tended to remain there at high concentration for much longer than in theatres where the air movement was more rapid. Displacement ventilation systems are of necessity systems with minimal air turbulence, and measurements made in theatres of this type also showed that when the contamination was liberated near the operating table high local concentrations tended to persist in this area. On the other hand, displacement theatres had the advantage that tracer gas liberated below table levels reached the operation site in much lower concentrations than in theatres with turbulent mixing. This advantage for the displacement system was greatly reduced when people in the theatre walked about.

If the gaseous tracer adequately predicts the behaviour of bacterial contamination, it follows that the merits of downward displacement ventilation cannot be assessed without more precise knowledge of the most dangerous sources of airborne contamination in the theatre, and, in particular, whether the organisms are dispersed from these sources at high or low levels. In any case the final assessment of a ventilating system must be based on clinical experience.

Another point of practical importance which has emerged from the studies made with gaseous and bacterial tracers is that in twin theatres which communicate through a common sterilizing room, or in other ways, without separating

doors, contamination liberated in one theatre of the pair usually finds its way freely into the other theatre even though there may be considerable exhaust ventilation from the linking room. The amount of contamination in the second theatre, as judged by the appropriate tests, is often as much as one quarter of that in the room where the contamination was generated.

Influence of Sterilizers

The fact that exhaust fans, installed in operating theatres to remove steam, may lead to dangerous suction of contaminated air into the theatre suite has already been stressed. Steam and heat are also a frequent cause of discomfort in theatres and sterilizing rooms. With the current trend towards the use of autoclaves for all sterilizing in the theatre, trouble from steam will be eliminated, but there is still a great need for care in thermal insulation of the autoclaves, which have too often been installed with large areas of exposed hot surfaces. These heated surfaces set up thermal circulations of air which effectively defeat all attempts at control of the direction of air flow in the theatre suite and greatly increase the transfer of air between the two theatres in a twin suite.

Further Investigations in Progress

The significance of particular levels of aerial bacterial contamination in an operating theatre must ultimately be assessed by their relation to the amount of wound sepsis initiated therein. This assessment involves the difficult decision as to which, if any, of the patients whose operation wounds become septic were infected by aerial transfer of microbes in the operating theatre, and which by microbes from elsewhere. Some indication of the ratio of theatre to ward infection may be obtainable from a survey of post-operative sepsis recently carried out in 21 hospitals by units of the Public Health Laboratory Service, and a more detailed assessment may be possible from joint studies by Dr. Shooter, at St. Bartholomew's Hospital, with support from the Council, and Dr. R. E. O. Williams of the Staphylococcus Reference Laboratory.

In the meantime it is not possible to lay down rigid standards for bacterial air contamination or ventilation. Bourdillon and Colebrook suggested 10 bacteria-carrying particles per cu. ft. of air as an upper limit for periods of quick operating during normal surgery; this represented a judgment based on general experience. It is now clear that levels of 1–2 particles per cu. ft. can be attained with efficient ventilating systems, and an outstanding problem is to discover whether a reduction in contamination to this or still lower levels will reduce the risk of post-operative sepsis. Any such standard must be defined in terms of measurements obtainable by simple means, such as the exposure of open culture plates and not by the use of complicated apparatus that is available only in a few laboratories. Studies of these aspects of the problem are in progress, but meanwhile the work already done offers useful guidance on the most efficient ways of arranging the ventilating system both in old and in new operating theatres.

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Population genetics is the study of the frequency and distribution of hereditary traits in populations. It includes the study of hereditary variations brought about through the agency of single genes or of multiple genes (each individually having only a small effect) and also of variations due to environmental influences.

Research on heredity in man is especially difficult because of the long interval between generations, small families, and the need to rely on observation rather than experiment. Nevertheless the human species offers some special opportunities for research in genetics, particularly the genetics of populations. Hundreds of millions of human beings are under sufficiently close medical observation to ensure that there is a good chance of unusual or genetically interesting variations being reported. Moreover, one can generally assume that choice of mate is essentially random. Again, some practical needs result incidentally in a great deal of information highly relevant to genetical research. Thus, for example, a side effect of the practice of blood transfusion is that vastly more is known about geographical variations in the frequencies of some of the human blood group genes than is known about the variation of any other genes, plant or animal.

The mathematical work of R. A. Fisher (1930), J. B. S. Haldane (1932) and L. Hogben (1946) in this country, and Sewell Wright (1931) in the United States, laid the foundation of theoretical calculations on which the science of population genetics has been built. Such genetical theory, applied to estimates of gene distributions in human populations, makes possible the indirect estimation of mutation rates, or rates of alteration in genes. Twenty-five years ago two mutation rates had already been estimated in man, and it is a striking fact that for a period of 20 years man was the only vertebrate in which a spontaneous mutation rate had been measured.

The relatively advanced state of genetical theory derived from experiments on animal and plant populations, as well as the paucity of data concerning man, have led at times to unduly bold assumptions about the relevance of experimental findings to human populations. In the latter there is a bewildering diversity of environment, of individual and population migrations, and of changes in the patterns of breeding and selection, and these variables introduce into the analysis of human populations complexities which do not arise with animal and plant populations.

Multifactorial Genetics

Before the discovery, or, more correctly, the re-discovery of Mendelian theory, statistical methods were developed by Francis Galton and Karl Pearson in this country for interpreting data on the distribution of continuously graded characters, such as stature, in human families and populations. The reconciliation of this work (related to conditions involving multiple genes) with Mendelian genetics (involving single genes) was begun by Udny Yule and others almost immediately after the re-discovery of Mendel's work, but unfortunately this became the subject of violent controversy. It was not until the publication of a classical paper (Fisher, 1918) that both sides realized the extent of their common ground. Since then a great many experimental studies have been devoted to the subject by plant and animal breeders, and workers with laboratory animal populations, and these have led to some advances in genetic theory.

It is almost axiomatic that continuously graded traits, however genetically determined, are strongly influenced by environmental factors; in man, whose

physical and social environment has changed so much in advanced countries during the last century, these factors are of major importance, and it is impossible in principle to separate the effects of nature and nurture. The best we can hope to do is to estimate the relative importance of hereditary and environmental influences on any particular character in the population under study. In man most studies on continuous variation have dealt with stature, head measurements, intelligence test scores, blood pressure levels, or dermal ridge patterns, and in all of these, except the last, environmental influences are of importance.

Genetic Effects of Radiation

Even before the second world war misgivings arose as to the possible effects on subsequent generations of an increase in exposure to ionizing radiations, since these were known to induce mutations in the germ cells of experimental animals. Three possible effects of mutation, not necessarily separable, had to be considered: (1) the production of congenital malformations, (2) interference with continuously graded characters including the higher attributes of man such as intellectual ability and emotional stability, and (3) reduction of fertility. It was soon realized that the influence of increased mutation in determining such effects would be very difficult to determine. A whole series of questions arose which could not be answered without the development of experimental methods. What is the relative effect on mutation rate, for example, of a given total dosage of radiation when received all at once, and when received in repeated fractional amounts? Are the spontaneously occurring and the induced mutations identical or different? What is the proportion of spontaneously occurring mutations determined by natural background radiation? What are the effects of the different types of radiation, and of the sex of those exposed? Even supposing that methods could be evolved for determining quantitative relations between the amount of potentially harmful radiations received by germ cells and the induction of particular forms of mutation, the difficulties of estimating the effects of such mutations on populations as well as on individuals would remain.

In 1935 J. B. S. Haldane and L. S. Penrose devised ingenious methods for the measurement of mutation rates in man. Two estimates were made almost simultaneously, one, by Haldane (1935), for haemophilia, and the other for epiioia, a syndrome in which localized abnormal tissue growth is often associated with mental deficiency (Gunther and Penrose, 1935). The estimates were necessarily based on limited data on the frequencies of these conditions in the population, but the advance was a notable one—as already mentioned, man remained for 20 years the only vertebrate in which a mutation rate had been measured. The genetical theory then current suggested that heterozygotes* in respect of any particular character or trait determined by a single gene either fail to exhibit that character or suffer some disadvantage because of this heterozygous state. As heterozygotes always greatly outnumber homozygotes, these presumptions of invariable disadvantage for the heterozygote suggested that many more individuals in a population would be affected for a given number of mutations induced by radiation than if harmful effects occurred only in homozygotes, and so led to most pessimistic views as to the probable

* Heterozygotes for a particular character are those individuals possessing different genes or alleles, one derived from each parent, at the locus on the chromosome determining that character; homozygotes possess two genes of the same kind at that locus.

genetic effects of radiation. Compensating mechanisms probably exist, however, although knowledge of them is still scanty. There is at least one definite example of heterozygote advantage in a particular environment, that of the gene associated with the sickle cell trait in an environment of hyperendemic malaria. In some malarious regions the heterozygous sickle cell trait carriers have as much as a 25 per cent greater chance of survival than those without the trait (*Med. Res. Coun.* Ann. Rep. 1955–56). There may well be other still unrecognized examples of heterozygote advantage, since these are decidedly more difficult to detect than examples of heterozygote disadvantage. More general knowledge is accumulating too of genetically balanced systems, in which the characters determined by different alleles at a particular locus have relative advantages or disadvantages, for example in the relationship between the blood groups and certain diseases such as duodenal ulcer (p. 43).

Estimates of Gene Frequencies and Spontaneous Mutation Rates based on Trait Frequency

Pioneer work in assessing the frequency of genetically-determined harmful traits in human populations was done in Denmark and Sweden. The work of T. Kemp in Copenhagen, G. Dahlberg in Uppsala and Sweden, and J. Sjogren in Sweden showed the value of establishing central bureaux of records of such traits and led to widespread postgraduate study of human genetics in Scandinavia. Penrose (1938) carried out a similar investigation in his analysis of the population of a colony of mental defectives and their relatives, and a few other studies of this kind have been made in Britain, Japan, and other countries; but the major contributions have come from J. V. Neel in the United States and A. C. Stevenson, then working in Northern Ireland, and now Director of the Council's Population Genetics Research Unit. Stevenson (1959) has published estimates of the frequencies of all harmful traits with a strong genetical component in the entire population of Northern Ireland.

Reasonably sound estimates of spontaneous mutation rates are now available for some fifteen harmful but uncommon dominant traits, for example achondroplasia, retinoblastoma, and multiple polypi in the colon, and similar estimates for sex-linked recessive mutations for at least three traits, including haemophilia and Duchenne muscular dystrophy. The frequency of recessive genes that determine harmful traits is a much more difficult study, and better estimates must await further knowledge on how to detect, with reasonable certainty, the heterozygote carriers of the recessive genes. About half of the more reliable estimates of mutation rates apply to populations in the United Kingdom. If these are biased they are likely to be too high rather than too low. There is, however, encouraging agreement between the estimates of the mutation rates at the same gene loci made by different observers. The mean appears to be of the order of 1–10 mutations per million gametes (ova or sperms). On theoretical grounds it might be expected that mutations would accumulate with repeated cell division, and thus we might anticipate a higher mutation rate in sperms than in ova. There is no positive evidence of this, but observations on paternal age give some suggestion that accumulation of mutations may occur.

Such studies on large and free human populations provide important knowledge complementary to that derived from experimental work. In the two large mouse populations in which the occurrence of spontaneous mutation has been studied, a total of only about two dozen, freshly arising, point mutations

(mutations involving a single locus) have been observed. In man, by contrast, observations have been made on much larger defined populations, and many hundreds of newly arisen mutations associated with different traits have been recorded. Further, in man it is possible to make indirect estimates of mutation rate when the frequency of a trait in a population is known; and where direct and indirect estimates have been made they have been remarkably similar.

Advances in such knowledge are likely to be hastened if clinicians fully realize the importance of recording every clinical finding which may have a genetic origin.

Congenital Malformations

There are both environmental and genetical factors concerned in the production of congenital malformations. Large scale studies of the distribution of such malformations in a population are extremely laborious. R. G. Record and T. McKeown (1949) in Birmingham studied 47,000 consecutive births which included some malformed offspring; no other comparable body of data on congenital malformations was available until Neel (1958) published his report from Japan, based on the work of the U.S. Atomic Bomb Casualty Commission.

The outstanding features of the population distribution of congenital malformations are: (1) the aggregation of *specific* abnormalities such as anencephaly in members of families, and the lesser aggregation of *related* conditions in the neural tube series such as anencephaly and Arnold-Chiari malformations; (2) the possible importance of intra-uterine environment as shown, for example, by the same malformation being found (too often to be explained by chance) in offspring of the same mother by different husbands; (3) the association of malformations with hydramnios in pregnancy, especially anencephaly and oesophageal stenosis; (4) the seasonal, geographical, and social trends shown in a few specific malformations, e.g., anencephaly, and cleft palate; (5) the apparently constant total rate of severe malformations in populations of different countries and the differing rates for individual malformations; (6) the suggestive evidence of an effect of consanguinity; (7) the relatively high frequency in twin pregnancies.

Attempts to implicate events during pregnancy have not been very successful in accounting for the grosser malformations which occur in the first six weeks of pregnancy, except for specific virus infection of the mother, the outstanding example of which is rubella.

The probability that defects will be produced in experimental animals by irradiation of the foetus or by nutritional or other damage to it is related more to the period of gestation at which the damage is brought about than to the type of agent producing the damage. The peculiar susceptibility of certain stocks suggests that in the production of congenital malformations we may be dealing in some cases with non-specific harmful influences, to which certain specific genotypes are particularly sensitive.

Consanguinity Studies

Studies on consanguineous mating are a valuable method of uncovering the numbers and effects of the recessive genes which are carried unobtrusively in populations. They provide, moreover, one of the few opportunities for comparing

genetical findings in man and in experimental animals. However, there may well be sharp differences between man and the lower animals, particularly as regards the hereditary element in abortion and stillbirth.

In most industrialized countries the incidence of cousin marriages is low, and, as the fact of consanguinity in such marriages comes to light only when children are born with congenital defects or in other special situations, it is difficult to obtain complete unselected data. In Catholic countries it has been possible to identify consanguineous marriages by consulting the records of ' dispensation ' with permission of the Church authorities; and in certain countries civil records of consanguinity are made at the time of marriage. However, the largest study of consanguinity so far reported is in the cities, including control cities, investigated by the U.S. Atomic Bomb Casualty Commission in Japan; there, after the whole population had been investigated, the cousin marriage rate was found to be high (Schull, 1958).

The findings of the report from Japan, when offspring from consanguineous and non-consanguineous marriages are compared, appear to show in the offspring of cousin marriages. (1) a hundred per cent higher death rate of children aged 1–8 years (2) an excess of approximately 50 per cent in the major congenital malformations detectable at birth, and (3) no excess of stillbirths or of abortions. This pattern of excess early mortality and of congenital malformations is quite unlike that to be expected from the operation of independent single recessive genes; rather it suggests deviations of phenotype associated with the undue number of homozygous loci which are to be expected in cousin marriages.

These findings are in fair agreement with those of Slatis (1958) in Chicago on the offspring of 106 full cousin marriages of Catholic spouses. Here again no excess of abortions or stillbirths was reported, but the evidence suggests an excess of childhood deaths. On the other hand, some French observations (Sutter and Tabah, 1952), while recording excess mortality in childhood, also suggest an excess both in intra-uterine loss and in malformation rate. With the exception of this unconfirmed French report, the available data suggest that an average of 3–7 single recessive genes, with harmful effect but not lethal *in utero*, are carried by each individual in the populations examined, and that their effect becomes especially apparent in the children of consanguineous marriages.

Association of Blood Group and other Genes with Disease

In 1930 R. A. Fisher pointed out the improbability of the various blood group genes being of equal value in natural selection, and E. B. Ford (1948), on the same basis, predicted that an association of particular blood groups with particular diseases would be found. The history of the search for such associations and an assessment of present knowledge, have been set out by J. A. Fraser Roberts (1957), who, with I. Aird and H. H. Bentall at the Postgraduate Medical School, London, first demonstrated one of these associations, that between group A and cancer of the stomach. The following further associations of genes at particular loci with disease have so far been established, mostly by two British groups of research workers, Aird, Fraser Roberts and associates in London, and C. Clarke, R. B. McConnell, P. M. Sheppard and colleagues in Liverpool: blood group O and non-secretors of ABO antigens with duodenal ulcer, and blood group A with pernicious anaemia.

It now appears also that the frequency of rheumatic fever is greater in non-secretors of ABO antigens than in the population as a whole (Glynn *et al.* 1959). Another probable association, not yet fully established, is that between blood group A and diabetes mellitus (Roberts, 1957). Still another association is that between the ability to taste low concentrations of phenylthiocarbamide (PTC taster response) and thyroid disorders (Harris and Kalmus, 1949). In this case the chemical similarity of PTC and some substances known to interfere with the proper metabolism of thyroxine is of particular interest.

It is difficult to measure the amount of selection that is actually taking place against the genes by reason of their association with these particular diseases. It is probably not very large, since the mortality rate from the diseases is falling, and since fertility would not seem likely to be much affected by them in view of their onset late in life. Definite information on the fertility of persons with these diseases would be helpful. The natural selection pressures so far demonstrated in the ABO system might be explained by selection against homozygotes for A and O, with probable relative heterozygote advantage; but the mechanism has not yet been elucidated. There are certain sharp fluctuations from district to district in ABO distributions compared with those in other blood groups (Mourant, 1954) and this suggests that strong environmental forces may be concerned in the diseases associated with the ABO blood group system.

Another important association of ABO blood groups is the influence of the parents' blood groups on the occurrence and severity of rhesus (Rh) sensitization in the offspring. Only about 1 in 20 Rh-negative women married to Rh-positive men becomes sensitized to the rhesus factor. One of the important protective mechanisms in this association is now known to be a difference in ABO blood grouping between the infant and the mother. When a mother does become sensitized to Rh, the infant responsible is almost always of a blood group compatible with hers; and the most probable reason for this is that only in such cases do the infants' red blood corpuscles survive long enough in the maternal circulation to reach the antibody mechanisms.

It seems probable that some of the stronger pressures of natural selection on ABO blood group frequencies have now been discovered, and that lesser pressures from other disease associations, which probably exist, are likely to prove difficult to estimate without very large scale investigations; but it remains possible that the main selective pressures operate through general fitness rather than through specific identifiable diseases.

Detection of Heterozygous Carriers of Recessive Traits

There are now a number of instances, for example, the sickle cell trait, where we can detect the heterozygote for a gene which, in the homozygote, determines a much more severe condition or disease. It is to be noted that such traits no longer meet the strict definition of 'recessive', since the heterozygote gives some evidence of their presence.

It is important to be able to detect such heterozygotes for the following reasons; (1) because it is then possible to test theories as to whether the heterozygote state is harmful, neutral, or even favourable; (2) so that, in certain rather uncommon circumstances, a person may know whether he is a 'carrier' of a harmful gene as, for instance, where marriages between relatives are contemplated; (3) so that segregation ratios of recessive traits may be studied, that is,

whether a smaller, equal, or greater number of the harmful as compared with the 'normal' genes from heterozygote parents are contributed to the next generation; (4) so that, in some traits with detectable biochemical signs, the metabolic processes involved may be more adequately studied and any disadvantages treated, and (5) so that direct estimations of mutation rates for recessive genes may be made by seeking homozygotes who do not have both parents heterozygous.

It will be clear that for purposes of (1), (3) and (5) it is essential, and for purposes of (2) and (4) highly desirable, that all heterozygote carriers be detected. Unfortunately except in sickle cell anaemia and thalassanaemia, the proportion of heterozygotic carriers of harmful genes that can be detected usually falls far short of a hundred per cent. In phenylketonuria, which determines severe mental deficiency, however, Hsia *et al.* (1956) were able to detect about 90 per cent of probable carriers of the gene by a phenylalanine tolerance test. Clinical detection of the heterozygote state is usually possible only in a very small proportion of carriers, though in sex-linked and in autosomal recessive ocular albinism, about 60 per cent and 40 per cent of carriers respectively can probably be detected by lacunae in the iris demonstrable by transillumination.

D. Y. Y. Hsia (1959) and H. Harris (1959) reviewed the literature on laboratory detection of heterozygotes. A heterozygote may be detected biochemically by finding an abnormal rate of turnover of a metabolite, and occasionally by finding traces of an abnormal metabolite present in greater amounts in the homozygote. However, there is usually an overlap between the normal values and those found in carriers, so that only in a relatively small proportion of cases can a carrier be detected with certainty. A third possibility has been suggested by Haldane (1955), namely, that a substance determined by the heterozygous state could be chemically different, for example in molecular weight, from that elaborated by either homozygote. The present position is that the ability to determine heterozygotes has not yet advanced sufficiently to be of much value in population genetics.

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CHROMOSOME ABNORMALITIES AND DISEASE IN MAN

Over the last 30 years suggestions have been made by scientists that some abnormal states of human development might be associated with abnormalities of the chromosomes, for example, human intersexes (Haldane, 1932) and the syndrome of testicular feminization in which testes are present in an individual of female appearance (Pettersson and Bonnier 1937). P. J. Waardenburg in 1932 expressed the view that non-disjunction of chromosomes, after the splitting during cell division, would bring about duplication or deficiency of these chromosomes in the daughter cells, and that this might explain the origin of mongolism. The suggestion that mongolism might be the result of chromosomal abnormality, either a duplication or a deficiency, was also made by R. Turpin (1937) in Paris and L. Penrose (1939) in London. The proof, however, came as the outcome of three important new developments in which the Council's staff played a significant part and which set the stage for the remarkable and rapid recent advances in the field of human cytogenetics.

Sex Chromatin in Somatic Cells

The first of these basic developments was the discovery in Canada of the presence of a chromatin body about 1μ in diameter on the nuclear membrane of the tissue cells of females; no such body was seen in males (Barr and Bertram, 1949; Moore *et al.*, 1953). This distinction between male and female nuclei (so-called 'nuclear sex') is conveniently made by examination of cells obtained by lightly scraping the inside of the cheek. It was considered for a time that the finding of sex chromatin in the cell nuclei of an individual indicated a female sex chromosome constitution (XX), and the lack of it a male sex chromosome constitution (XY). Later it was recognised that in three conditions of abnormal sex development the sex phenotype* is at variance with the presence or absence of sex chromatin, and it was suggested that these three

* The sum of the observable features in which the sexes differ, including primary morphological distinctions and secondary sex characters.

conditions might be examples of sex-reversal. The new studies on chromosomes have, however, provided the real explanation. The three conditions are: (1) sex-chromatin-positive cases of *Klinefelter's syndrome* with predominantly male phenotype; (2) sex-chromatin-negative cases of *Turner's syndrome* with predominantly female phenotype; and (3) *testicular feminization*, in which the somatic cells are sex chromatin-negative and the phenotype is predominantly female.

Human Chromosome Number

The second basic discovery came in 1956 when Tjio and Levan announced that they had found in tissue cultures established from aborted foetuses a regular chromosome number of 46. This observation was supported in the same year by C. E. Ford and J. L. Hamerton, working at the Council's Radiobiological Research Unit, Harwell, who examined the chromosomes of dividing cells in seminiferous tubules from the testis. Subsequently it was widely confirmed that the human chromosome number was 46, and not 48 as had previously been supposed.

Development of New Techniques

The third basic advance was the development of simple techniques for studying the somatic chromosomes; this advance, in which the Council's staff had a major share, constituted a real 'break-through' to further extensive knowledge, by providing methods through which any group of human beings could be readily examined for chromosomal abnormality. Ford, Jacobs and Lajtha (1958) showed how the individual chromosomes in human bone marrow cells could be clearly viewed in a microscopic preparation. The method was a direct adaptation of one originally developed for use on mice (Ford, Hamerton, Barnes and Loutit, 1956; Ford and Hamerton 1956a). The essential steps were: (1) the incubation *in vitro* of a suspension of marrow cells in the presence of colchicine; (2) the exposure of the suspension to a hypotonic solution, and (3) the squashing of the cells on a glass slide under a coverslip. Colchicine inhibits the formation of the mitotic spindle so that the chromosomes are scattered in the cytoplasm instead of being closely aggregated; exposure to a hypotonic solution causes swelling of the cells, so that the cytoplasm becomes hydrated and soft; and the aim of squashing is to flatten the cells and spread out the chromosomes into one optical plane. The great merit of this technique is that the period of incubation of the cells need not be more than six or seven hours, and, therefore, that the chromosomes examined are those of cells that actually existed in the body.

Another recent technical achievement applicable to the counting of chromosomes is that of raising tissue cultures from tiny pieces of skin (Tjio and Puck, 1958, Harnden, 1960); and the classical tissue culture methods have also been employed to obtain dividing cells for this purpose (Chu and Giles, 1959, Lejeune *et al.*, 1959, Fraccaro *et al.*, 1959, Nilsson *et al.*, 1959). The cells obtained by these two methods, however, will have undergone many divisions since removal from the body and it is always possible that one with an abnormal set of chromosomes may have arisen and been perpetuated selectively. This difficulty can be overcome by establishing duplicate cultures, preferably from specimens taken from different parts of the body. A third technique, originally developed by Osgood and Krippaehne (1955) and recently adapted by Hungerford *et al.* (1959) utilizes the leucocytes of peripheral blood; the culture period

is shorter than for solid tissues and there is the great practical advantage that samples of blood are readily obtainable.

The Normal Human Karyotype

With a few specialized exceptions, the normal human tissue cell has a chromosomal constitution, or karyotype, of 22 pairs of autosomes (in which the members of each pair are alike) and a pair of sex chromosomes. In the female the sex chromosomes are normally alike (XX), and in the male they are unlike (XY). The chromosomes each have two arms attached at a point called the centromere. As seen after treatment with colchicine the two arms are split longitudinally, and the four strands often form an irregular St. Andrew's cross with the centromere at the point of junction. The centromere occupies a position that varies from median or sub-median (metacentric chromosomes) to near extreme (acrocentric chromosomes). The individual pairs of autosomes (not all of which are yet distinguishable) are characterized by their relative length and their arm ratio, that is, the ratio of the length of the arms on each side of the centromere. Within the set of 22 pairs there is a five-fold difference in chromosome length, and a variation of arm ratio from 1 : 1 in some of the chromosomes termed metacentric to about 10 : 1 in some termed acrocentric. There are two additional important features of the normal karyotype: (1) the X and Y chromosomes differ so much both in length and in arm ratio as to be easily distinguishable, one from the other (though not from similar autosomes), and (2) two pairs of acrocentric chromosomes bear on their short arms bodies known as satellites. The 'stalks' that attach the satellites to the main body of the chromosome are believed to be associated with the formation of nucleoli (Figures 1 and 2).

In practice, when the chromosomes are counted in a series of normal human somatic cells, the great majority will show 46 chromosomes. In most of the remainder a slightly smaller number than 46 may be found; exceptionally, a cell may be recorded with more than 46 chromosomes. The proportion of cells recorded with such variant numbers varies considerably with the technical standard of the preparations. For this and other reasons it is considered that the numerical variation is at least largely due to artefact, mainly damage to the cells during preparation, although some of the variation might be real (Ford *et al.*, 1958; Ford, 1959); and further examination seems to indicate that part of this variation does indeed represent errors at division in ancestral cells (Court Brown *et al.*, 1960). According to recent observations on other mammalian cells, however, there is little variation of chromosome number in normal somatic cells, probably not more than two or three cells in 1,000 (Hungerford, 1955; Ford, Mole and Hamerton, 1958) and it is unlikely that man will be an exception to such a rule.

Deviations from the Normal Karyotype

Abnormalities of the karyotype so far recognized can be classified as follows:

1. *Number Abnormal in Respect of the Sex Chromosomes*

(a) *Chromatin-positive Klinefelter's syndrome:* the number is 47, the sex chromosome constitution XXY, the phenotype is male, but the individuals are almost certainly sterile (Jacobs and Strong, 1959; Ford *et al.*, 1959a; Harnden, 1960: see Figure 2).

(b) *Chromatin-negative Turner's syndrome:* the number is 45, the sex chromosome constitution XO, the phenotype is female with infantile sex development (Ford *et al.*, 1959b; Fraccaro *et al.*, 1959; Tjio, Puck and Robinson, 1959).

(c) '*Super-female*' (*the triple X state*): the number is 47, the sex chromosome constitution XXX, the phenotype is female, the tissue cells are chromatin-positive, some showing two sex chromatin bodies—a feature never yet seen in a normal female (Jacobs *et al.*, 1959).

2. *Modal Number Abnormal in Respect of the Autosomes*

(a) *Mongolism:* With one exception, mentioned below, all cases of mongolism so far reported have a number of 47, the extra chromosome being a small acrocentric autosome with satellite bodies, and indistinguishable from a member of one of the smallest pairs of autosomes. Mongols are therefore described as *trisomic* for this particular autosome. This discovery was made independently in Paris (Lejeune *et al.*, 1959) and in the Council's Clinical Effects of Radiation Research Unit, Edinburgh (Jacobs *et al.*, 1959a), and in a case of double chromosomal abnormality, Klinefelter mongolism, examined at the Council's Radiobiological Research Unit at Harwell and in London (Ford *et al.*, 1959a). This is perhaps the most important discovery that has so far resulted from the technique devised by Ford and his colleagues for counting the chromosomes, and it is gratifying that the Council's staff has again played an important part.

(b) A female child with multiple congenital abnormalities that died aged 4½ months was found to have 47 chromosomes and to be trisomic for a small autosome different from the one concerned in mongolism (Edwards *et al.*, 1960).

(c) A female child aged 1 year with multiple congenital abnormalities has been found to be trisomic for yet another small autosome (Patau *et al.*, 1960).

(d) One patient has been described with a number of 45. This is interpreted as being due to the translocation of a small acrocentric autosome on to one of the larger acrocentric autosomes. The condition was named 'polydyspondylism' because of the associated developmental abnormalities of the spinal column (Turpin *et al.*, 1959).

3. *Number Normal, but Phenotype and Karyotype at Variance*

(a) *Testicular feminization:* the characteristic individual is a phenotypic female with testes present instead of ovaries; the sex chromosome constitution is XY and the sex chromatin is absent from tissue cells (Jacobs *et al.*, 1959b). The condition is transmitted in a simple Mendelian manner through carrier mothers.

(b) *Pure gonadal dysgenesis:* the characteristic feature is the absence of gonads of either type. In the one case whose chromosomes have been examined the phenotype was female and the sex chromosome constitution XY (Harnden and Stewart, 1959).

(c) *True hermaphroditism:* gonadal tissues of both male and female are present, and the phenotype shows both male and female features. In two cases examined sex chromatin was present and the karyotype was indistinguishable from that of a normal female (Harnden and Armstrong, 1959; Hungerford *et al.*, 1959). The chromosome observations were made on

dividing cells in cultures established from skin and peripheral blood respectively. The possibility of a chromosomal difference between the types of gonadal tissue remains; these cases might be mosaics (Ford, 1960; and see 6 below).

4. *Number Normal but Morphology of Sex Chromosomes Abnormal*

A phenotypic female has been found with 46 chromosomes but with one X chromosome abnormal. The appearance of this chromosome suggests that a segment has been deleted from it. The presenting symptom in this patient was primary amenorrhoea, and examination of the buccal cells revealed that the cells showing the sex chromatin body were significantly fewer than in normal women; the sex chromatin body also appeared smaller than is usual (Jacobs *et al.*, 1960).

5. *Number Normal but Morphology of Autosomes Abnormal*

A mongol child has been found with 46 chromosomes, one autosome being abnormal. The morphology of the abnormal autosome suggests that it incorporates the greater part of the additional small acrocentric autosome that is characteristic of mongolism. This case is regarded as being genotypically equivalent to a 47-chromosome mongol (Polani *et al.*, 1960).

6. *Number Differs Between Distinct Cell Types: Mosaics*

Ford and his colleagues (1959a) reported a case in which two types of cells seem to be admixed in the bone marrow, and possibly in other parts of the body, the two types differing in their chromosome complement. This individual is presumed to have normal cells with sex chromosomes XX, as well as abnormal cells with sex chromosomes XXY. Ford *et al.* (1960) have also reported another type of mosaic which can be designated XO/XX, and in which chromosome counts are 45/46.

Jacobs *et al.* (1960) have reported a patient who is presumed to be a XXX/XO mosaic, the chromosome counts being 47/45.

7. *Abnormal Karyotype in Cancer*

Ford *et al.* (1958) reported a female with acute leukaemia whose chromosome number was only 44 but with a small fragment of nuclear material added in each cell. A. G. Baikie and his colleagues (1959) reported chromosome abnormalities in four out of five cases of acute leukaemia examined, but no demonstrated abnormality in five cases of chronic myeloid leukaemia and three cases of chronic lymphatic leukaemia; however, Nowell and Hungerford (1960) found a morphological abnormality of one of the small autosomes in two cases of chronic myeloid leukaemia.

Whether these abnormalities of the genetic material of the cell are directly related to the mechanisms of induction and development of cancer is by no means yet determined, but it would seem to be worth pursuing further studies on these lines.

Errors in Cell Division as a Cause of Chromosome Abnormalities

These abnormalities (with the exception of testicular feminization, pure gonadal dysgenesis, and possibly true hermaphroditism) must be caused by errors during the splitting of the chromosomes (mitosis) at cell division, or during the reduction-divisions (meiosis) that precede the formation of the sex

cells. Of such errors the most common is likely to be 'non-disjunction', whereby chromosomes, after splitting, fail to separate to opposite poles of the cell but migrate to the same pole. In meiosis such an error produces one gamete with 22, and another with 24 chromosomes instead of the normal 23 for a sperm or ovum. Non-disjunction during mitosis would result, after cell division, in daughter cells with 45 and 47 chromosomes respectively. Daughter cells with 45 chromosomes would also arise if one or both the daughter chromosomes lagged behind the others during separation, and were excluded from the daughter nuclei.

In theory a large number of abnormalities of the fertilized ovum can be produced as a result of non-disjunction occurring at the first or second reduction-division in either or both of the parents. Non-disjunction in the autosomes could result in a whole series of trisomic and monosomic conditions, involving the addition to, or loss of, any one member of the 22 pairs of autosomes. Some of these abnormalities may be incompatible with life in the embryo and so may result in abortion; others may be very rare. In other words miscarriages and stillbirths may sometimes be due to trisomy or monosomy. Moreover, some congenital abnormalities may be associated with lesser degrees of chromosome abnormality, such as loss or gain of small chromosomal segments in daughter cells (deletions and duplications).

The Frequency of Chromosomal Abnormalities in the Population

Practically all that is known on this subject relates to mongolism; on average the probability of a child being born a mongoloid imbecile is about 1·5 per 1,000 births (1 in 660). The risk, however, is closely related to maternal age—the range of probability is from about 0·6 per 1,000 for mothers aged 18–19 years to about 27·5 per 1,000 for mothers aged 45 to 49 years (Penrose, 1954). The data of Moore (1959) suggest that the probability of a new-born *male* child being sex-chromatin positive is of the order of 2·5 per 1,000 (1 in 400). If all such children are assumed to be chromatin-positive cases of Klinefelter's syndrome, it would appear that the probability of *any* child being born with this condition is about 1·25 per 1,000—a frequency about equal to that of mongols. The frequency of other chromosome abnormalities at birth can at present only be conjectured. Studies have, however, been initiated in the Council's Clinical Effects of Radiation Research Unit, Edinburgh, with the object of determining the frequency of sex chromosome abnormalities in the newborn population.

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NEW APPLICATIONS OF ELECTRON MICROSCOPY

With conventional microscopes light is used to illuminate the specimen, and the detail that can be observed in the image is limited to structures larger than about $0{\cdot}25\mu$ (one four-thousandth of a millimetre). This limit is the wave length of light, and is a permanent restriction to the resolution of such detail. Some 30 years ago research on the properties of electron beams led to the idea of a microscope in which electron beams and magnetic fields replaced visible light and glass lenses. The extremely short wave length of an electron beam suggested that an image might ultimately be obtained with such an instrument showing detail even below 1 $m\mu$ (one millionth of a millimetre) which is roughly the size of the diameter of a polypeptide chain in a protein molecule. The electron image is not itself visible but, like X-rays, electrons can excite a fluorescent screen or darken a photographic film so that the image may be viewed and recorded. Many years of work were required to develop the idea, but shortly after the outbreak of the last war commercial electron microscopes became available both in Germany and the United States, and the first useful electron micrographs of biological objects were obtained.

In the last 20 years the performance of the electron microscope as an instrument has been improved by a factor of only two or three, but the limit in the resolution of objects now reached is not far short of the size of an atom. The detail seen in practice, however, is much more seriously limited by the conditions under which the enlarged electron image is obtained. In the electron microscope the specimen under examination cannot be living material since it must be exposed to a high vacuum and intense radiation; in thickness it should not exceed 0·0001 mm., and if sufficient contrast in the picture of the object is to be obtained, its density should approach that of a metal. Advances in techniques have now overcome many of the limitations set by these requirements, but the full theoretical potentialities of the instrument have not even yet been completely exploited. In this article only a few topics selected from the wide field of modern electron microscopy can be examined, but they all illustrate ways in which the introduction of quite simple new ideas in technique can open up new vistas for research.

Ultrathin Sections of Material to be Examined

Sections of material for examination by the electron microscope must be at least 10 times thinner than anything previously achieved in section cutting for the light microscope; the difficulties of maintaining the architecture of biological material sliced so thinly were solved quite simply about 10 years ago. Small alterations were made in the design of the cutting instrument, the microtome, to meet the need for cutting small pieces of tissue set in a new hard embedding material, and a satisfactory cutting edge was found, somewhat unexpectedly, in broken pieces of ordinary plate glass. These and other developments have now reduced thin section cutting to a routine that can be practised in any laboratory, with a resulting vast increase in knowledge of the fine structure of almost every type of animal and vegetable tissue.

The Structure of Muscle

An excellent example of this type of work is the elucidation of the structure of muscle at the molecular level described in another article. A major difficulty with ultrathin sections is to obtain sufficient contrast to reveal the finest detail at the highest magnifications attainable, and some method of binding heavy material at specific points in the specimen is usually required in order to outline structure. H. E. Huxley, working at University College London, with support from the Council, introduced the use of alcoholic solutions of a tungsten compound to treat sections of muscle, an improvement in technique that has been a major contribution to the success of studies on this tissue.

Quantitative Measurements

The use of compounds of high density to increase the contrast in organic specimens for electron microscopy has been mentioned above. Quantitative measurements of the increase in contrast produced allow an estimate to be made of the uptake of such materials; this was first demonstrated on virus particles by C. E. Hall in the United States. The possibility thus arose of differentiating between various substances in a specimen by measuring the selective uptake of suitable compounds; at King's College, London, N. R. Silvester and R. E. Burge, working with ram spermatozoa, differentiated between the lipoprotein of the cell membrane and the nucleic acid of the nucleus. Developments of this method

are likely to achieve more extensive identification and estimation of the substances seen in specimens examined by the electron microscope.

The Structure of Viruses

With few exceptions viruses are of a size well below that of objects visible under a light microscope. As they do not require to be sectioned they are ideal objects for study by the electron microscope. The first pictures gave only a rough idea of their overall size and shape. In 1946 the situation was transformed by the introduction in the United States of the technique of metal shadowing of the objects examined. A very thin film of metal was evaporated from one side on to the prepared specimen, and this greatly improved contrast in the pictures obtained and revealed some details of surface structure. A limiting factor in this technique, however, was that at the highest magnifications the molecular detail in the object was obscured by the grain in the metal.

Metal shadowed electron micrographs showed the adenovirus to have a diameter of about 60 mμ, and to be nearly round in shape; later when the metal was evaporated upon the object from various directions a hint of a more angular profile was obtained. R. C. Valentine and P. K. Hopper, at the National Institute for Medical Research, treated the virus preparation chemically with a tungsten compound and this showed up the hexagonal shape of the virus (Fig. 3(1)). Later, a uranium salt was used in a similar way, and this gave a picture not only of the polygonal outline, but also of a distinctive dark region at the centre of the virus which is the site of nucleic acid (Fig. 3(2)).

In 1957, S. Brenner, working at the Council's Unit for Molecular Biology, and R. W. Horne at the Cavendish Laboratory, Cambridge, while trying similar methods with a bacteriophage virus devised one of the most spectacular techniques yet introduced into electron microscopy (Brenner and Horne, 1959). These workers prevented direct chemical combination of the tungsten salt with the virus, and instead dried the salt around the specimen, forming a dark surround which penetrated into the crevices on the virus surface. The effect was that of a photographic negative, with the virus appearing as a bright object on a dark background. When this technique was applied to the adenovirus (Horne, *et al.*, 1959), the virus surface was found to be formed of a regular array of molecules, and the six-sided profile was seen to be consistent with an icosahedral surface. [An icosahedron is a regular surface formed from 20 equal equilateral triangles]. This was one of two possible shapes already deduced from the profile, but the negative contrast picture not only proved the shape, but also showed that each triangular face had six molecules to each edge, making 252 molecules on the whole surface (Fig. 3(3)).

Brenner *et al.* (1959) used this technique to show up almost every surface feature of the highly complex structure of a bacteriophage virus; and Horne, with other virologists in Cambridge, produced striking pictures showing the surface features of many different viruses. This simple technique will evidently play an important role in the elucidation of further details of the structure of different viruses.

Counting Virus Particles

Electron microscopy has also provided the only exact method of estimating the number of virus particles in a suspension. It is often useful to relate this number to the proved infectivity of the suspension, and so to determine the mean number of virus particles necessary to initiate an infection. Results of such

counts, reported from the National Institute for Medical Research, were reviewed by A. Isaacs (1957). It was thus found that an infective dose of virus is seldom less than 10 virus particles.

Movement of Viruses

Another quantitative value measured with the help of the electron microscope is the rate at which viruses arrive at a surface such as that of a cell which they are going to infect. This depends upon Brownian movement, that is the incessant movement of small objects suspended in a fluid resulting from the violent irregular bombardment which they constantly receive from the molecules of the fluid. This phenomenon, which is very familiar to anyone who has used an ordinary light microscope, was first described in pollen grains in 1828 by the botanist, Thomas Brown. Valentine and Allison (1959) used the electron microscope at the National Institute for Medical Research to show, by direct counting, that it is Brownian movement that accounts almost entirely for the rate at which viruses finally arrive at a surface. In consequence, even if a virus is as close as 0·1 mm. to a cell surface, it may be a matter of hours before random Brownian motion carries it on to the surface to initiate the process of infection.

The Shape of Molecules

The negative contrast technique, combined with improved methods of metal shadowing, have provided new means of determining the shape of molecules. These methods will doubtless be exploited in the next few years to obtain electron micrographs of the larger molecules and to show up their biological interactions. In the United States pictures have already been obtained of the long thread-like molecule of nucleic acid, which is a vital component of all genetic material. In this country, by means of the negative contrast technique, Valentine (1959) has shown that the molecule of the enzyme catalase, which can be crystallized, has the approximate shape of a hollow cylinder. When the surface of a crystal of catalase was examined in this way the molecules were seen end-on as rings in regular array (Fig. 4). The molecules of other proteins have been shown to have spherical shapes, and not the asymmetrical shapes traditionally ascribed to them from indirect evidence. This finding has been confirmed by M. S. C. Birbeck and K. A. Stacey (1960) who have obtained some fine pictures of metal-shadowed preparations at the Chester Beatty Research Institute, London.

Such contributions of electron microscopy to research do not end with the results so far obtained. The mere fact of seeing, counting, and measuring objects such as viruses, which a few years ago could only be detected by indirect methods, is in itself a potent stimulus in many fields of research.

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THE STRUCTURE OF VIRUSES

Introduction

During the last few years significant advances have been made in our knowledge of the molecular structure of viruses of several different shapes. All viruses whose fine structure has been investigated can be described structurally as packets of protein containing nucleic acid.

A protein molecule consists of one or more polypeptide chains, each made up of a string of amino acids linked together in end-to-end chemical combination. There are 20 different amino acids, any of which may be present and may be repeated in a polypeptide chain. A nucleic acid molecule consists of four different types of sub-units called nucleotides; these are repeated over and over again in different orders to form a long thread-like molecule containing many thousands of nucleotides. The nucleotides of each molecule of nucleic acid are linked by one of two sugar groups, giving rise either to molecules of ribonucleic acid (RNA) or of deoxyribonucleic acid (DNA). Some viruses contain RNA, and some contain DNA.

Viruses, unlike other organisms, do not grow by ingestion of food material but are built up out of the amino acids, nucleotides and sugars of the parasitized cell under the direction of the nucleic acid of the infecting virus, which is either RNA or DNA. Virus growth has been studied particularly in the bacteriophage group of viruses—those that infect bacteria. Many bacteriophages are tadpole-shaped, with a head or body containing nucleic acid, and a tail. Like the plant and animal viruses they have variable effects on their host; some, the virulent bacteriophages, infect and kill their host bacterium, and others, the temperate bacteriophages, without killing their host, may establish a carrier state. In 1952, A. D. Hershey and Martha Chase in New York showed that when the bacteriophage T_2 infects its host bacterium, it attaches itself to the wall of the bacterium by means of its tail and injects its DNA into the bacterium. In 1956, A. Gierer and G. Schramm in Tübingen found that it was possible to infect plants directly with RNA alone, prepared and separated from tobacco mosaic virus. These and other experiments showed that the power of a virus to infect resides in its nucleic acid.

The DNA of a virulent bacteriophage, after entry into the host cell, takes control of the host's synthetic mechanisms and these are turned over to the manufacture of new virus DNA and protein. The new virus DNA is built up by replication of the injected DNA, and the new virus protein is built up under the direction of the injected DNA. The type of protein formed, virus or other, is believed to be determined by a genetic code represented by the order of the nucleotides in the DNA molecule, this code being the means by which the appropriate sequence of the amino acids in the new protein is brought about. In viruses containing RNA only, the RNA appears to take over the genetic functions normally carried out by DNA.

While much recent research has been focused on the chemical and genetic aspects of virus replication because of their obvious general implications, one of the great achievements in molecular biology is the elucidation of some of the general principles of virus structure; this has largely been accomplished through researches supported by the Council, and in co-operation with the Agricultural Research Council. Viruses differ widely in their morphology; some

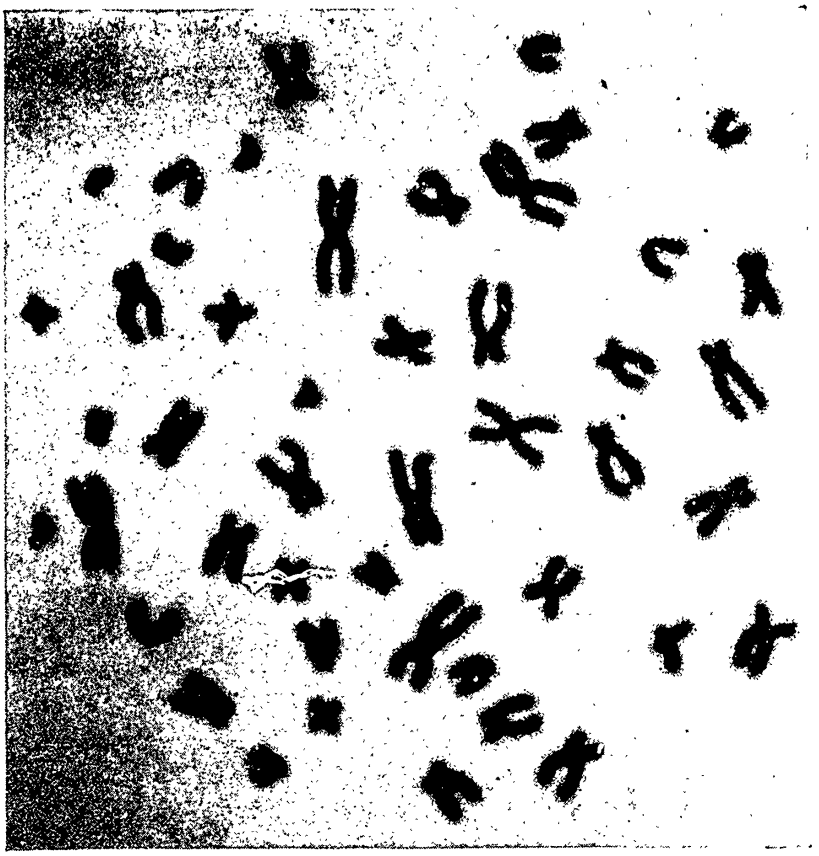

Figure 1

The 46 chromosomes in a bone marrow cell of a normal female (× 1,900).
Preparation by Dr. C. M. Clarke.

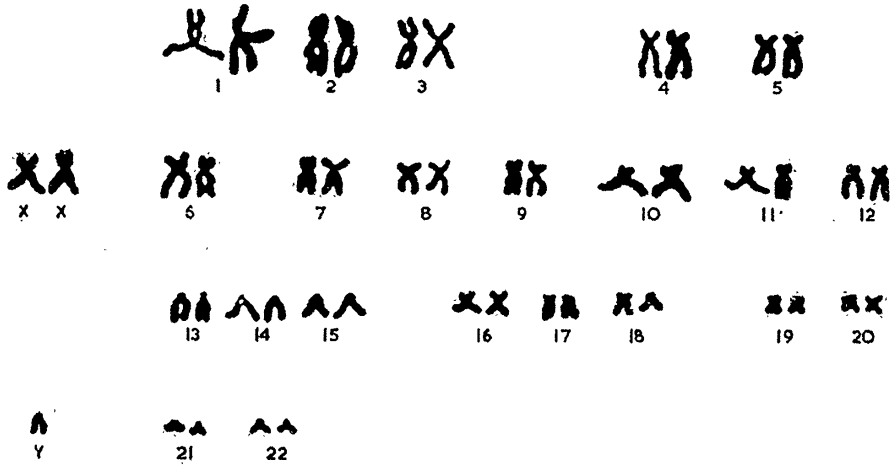

Figure 2

The 47 chromosomes of a chromatin-positive Klinefelter patient, including 2 X chromosomes and a Y chromosome. The array was prepared by cutting out the individual chromosomes from a photograph of a bone marrow cell in metaphase of mitosis (like *Figure* 1) and then re-arranging in pairs. (× 1,250.) *Standard (Denver) classification.*

(1) (2) (3)

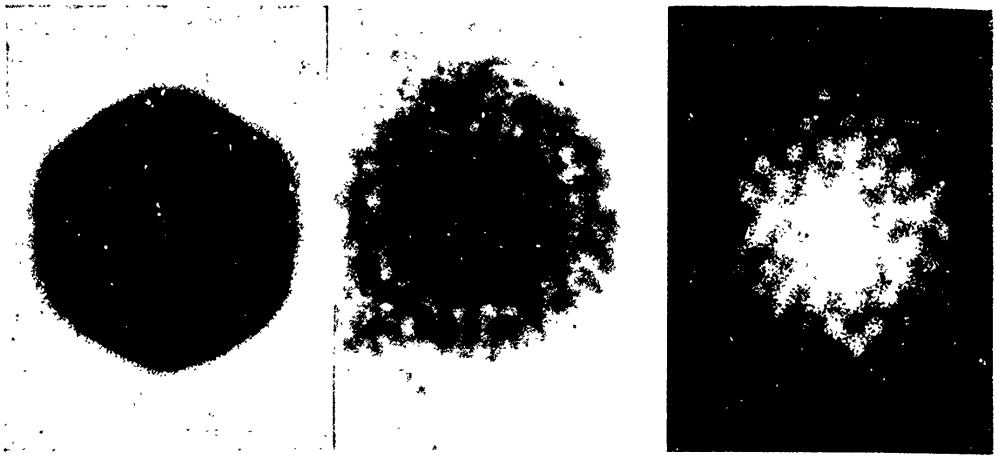

Figure 3

(1)–(3) Adenovirus (× 500,000)

(1) Phosphotungstic acid treatment showing the six-sided outline of the virus.
(2) Uranyl acetate treatment showing central body containing nucleic acid.
(3) Negative contrast technique showing surface detail. The molecules on the surface are arranged to form triangular faces.

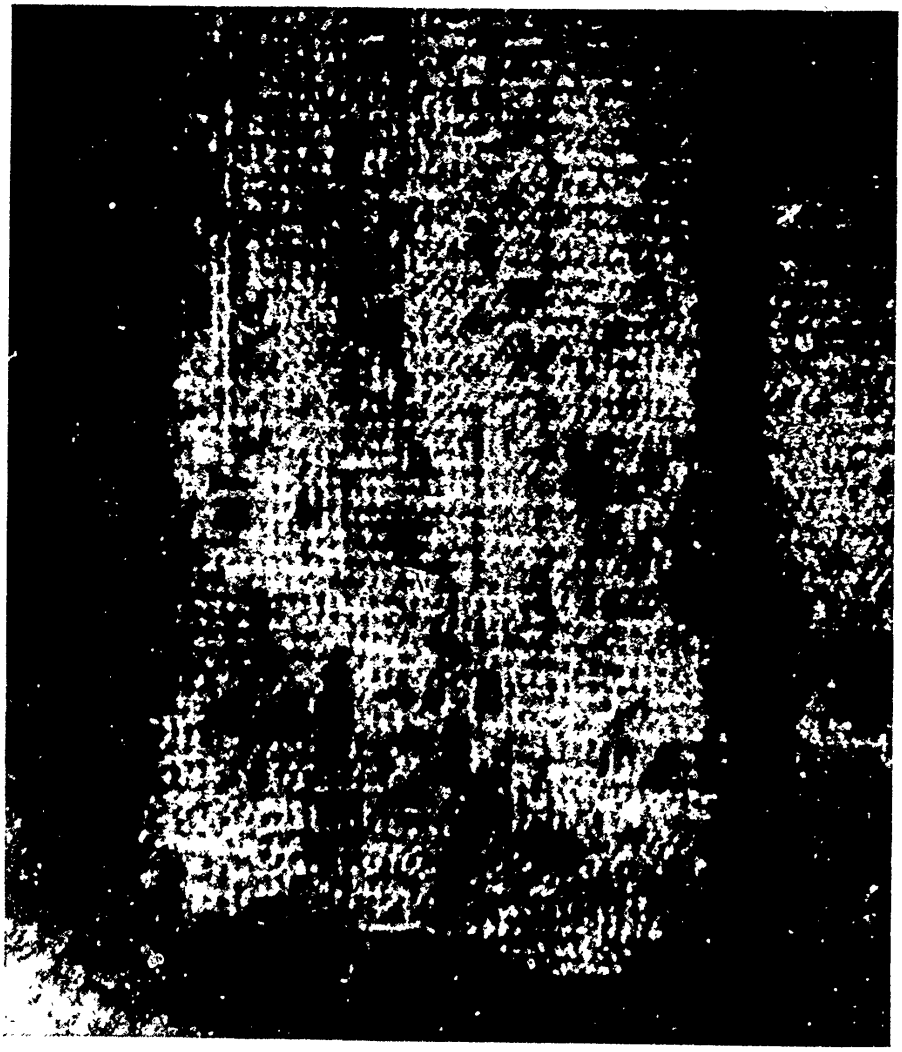

Figure 4

Surface of a small crystal of catalase showing the regular array of protein molecules; each molecule is a hollow cylinder and appears end-on as a ring. (× 300,000.)

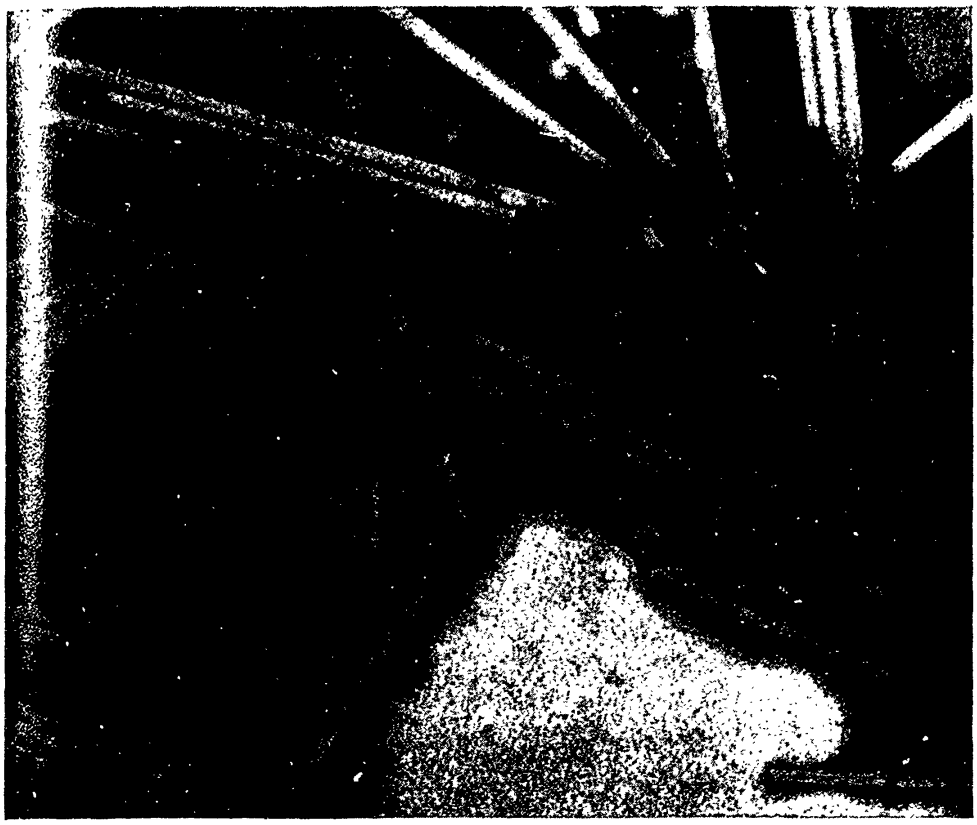

Figure 5
The rod-shaped Tobacco Mosaic Virus (TMV). (× 130,000.) Note the central hole.

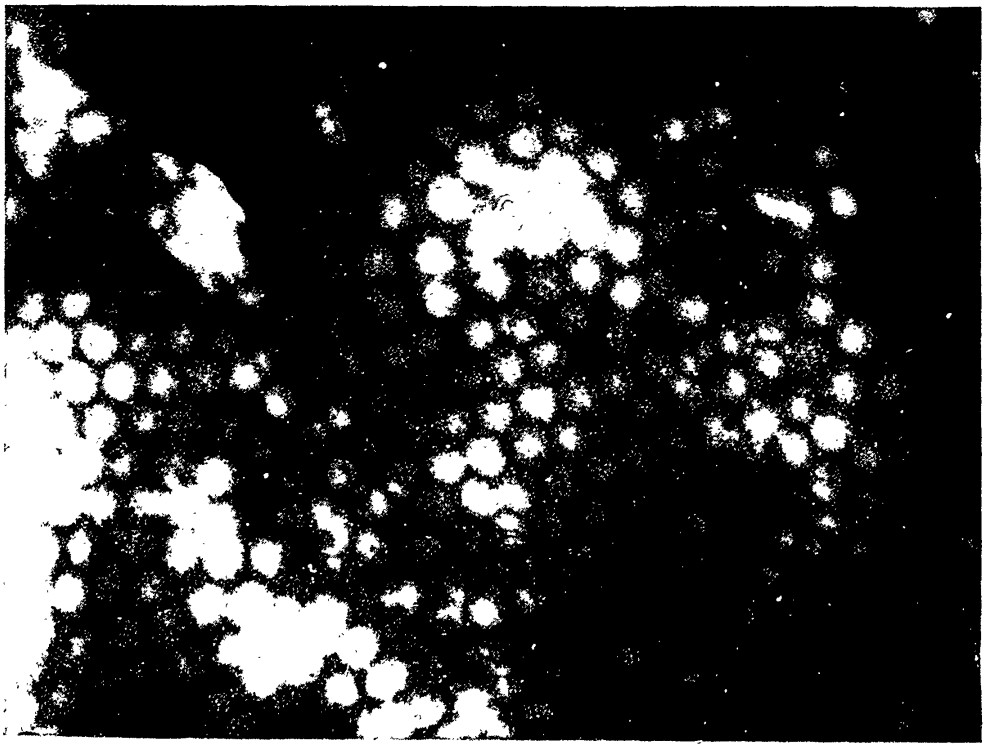

Figure 6
The spherical Turnip Yellow Mosaic Virus (TYM). (× 180,000.) Note the hexagonally packed particles.

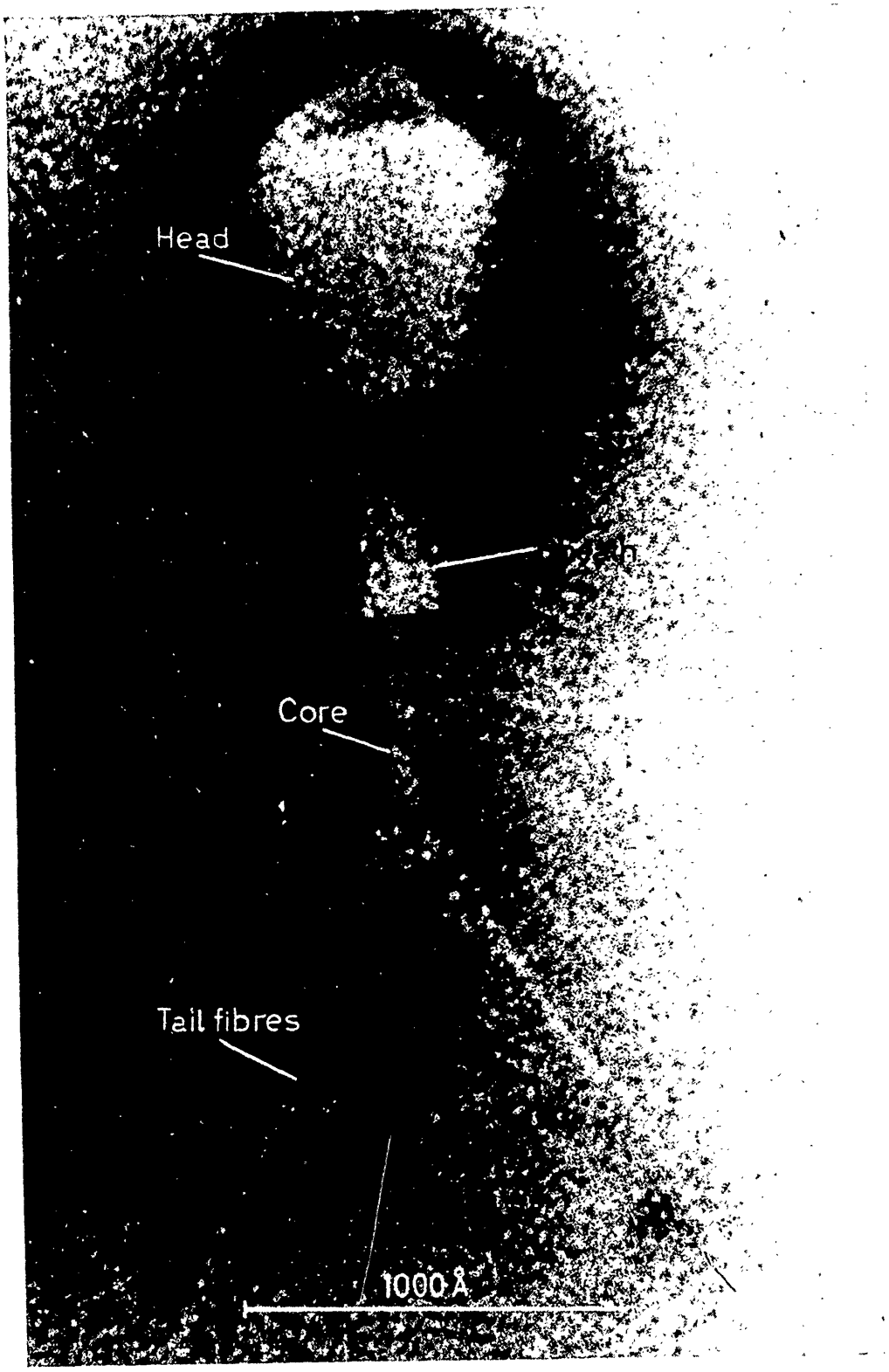

Figure 7

The tadpole shaped bacteriophage T2. (× 600,000.) The scale 1,000Å = 100 mμ. The tail has been contracted.

Figure 8

Protection of cells against the destructive action of Bunyamwera virus by interferon in a cup in the centre of the Petri dish (Technique of Porterfield, 1959).

Zone A: Zone of cells protected from destructive action of virus.
Zone B: Cells killed by virus action.
The intermediate zone contains partially protected cells.

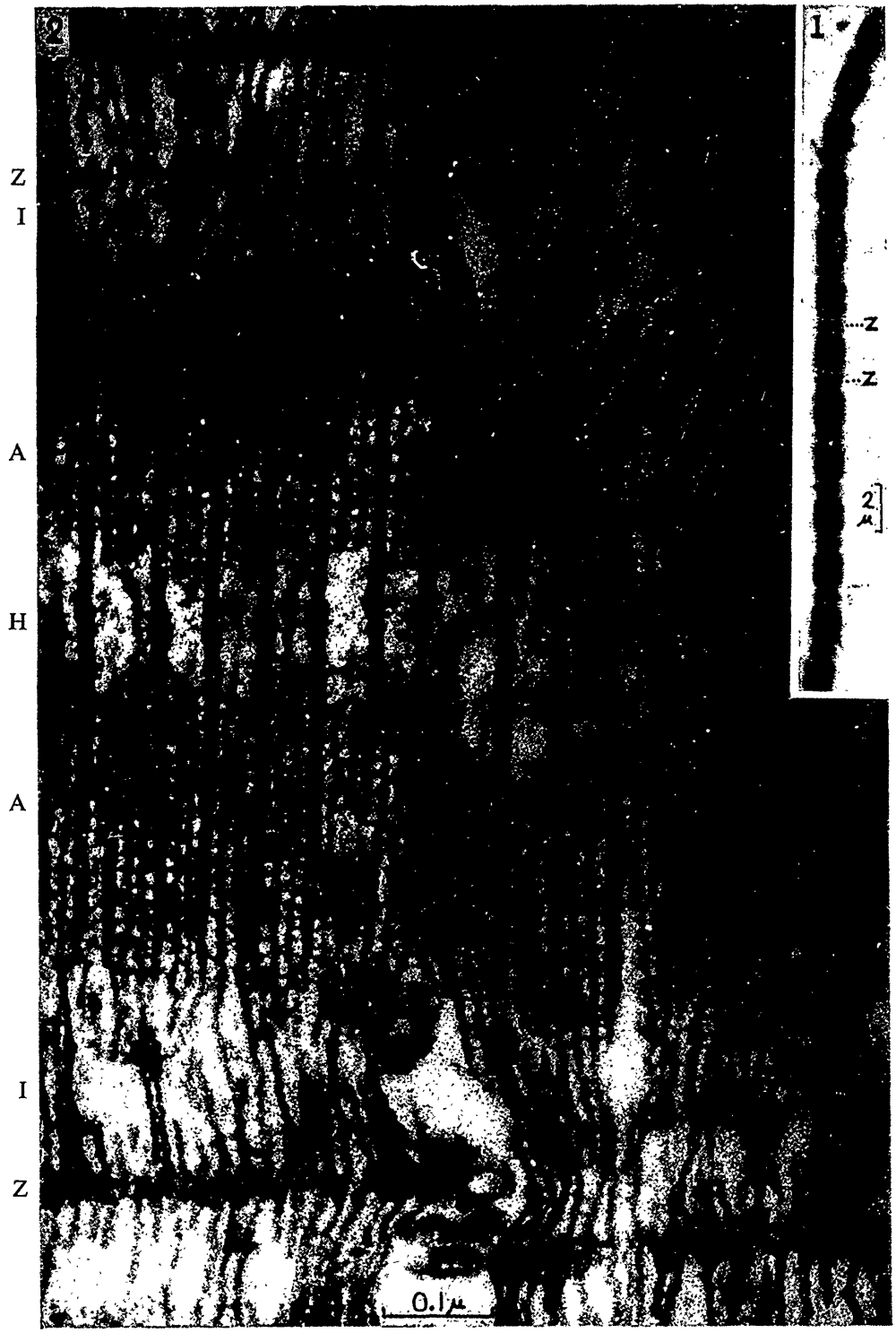

Figure 9

1. A single myofibril isolated from a cross-striated muscle and photographed in an interference microscope with about the best resolution of which the light microscope is capable. The band-pattern repeats every 2·5μ, and the detailed structure which is responsible for this pattern is shown in 2.

2. An electron micrograph of a very thin longitudinal section through two adjacent myofibrils. There are Z lines at the top and bottom of the picture, and an H zone mid-way between them. Note the thick myosin filaments (diameter about 10 mμ), confined to the A band, and the thin actin filaments (about 5 mμ), extending from the Z lines as far as the borders of the H zone where they terminate. Also note the numerous regularly-spaced transverse bridges connecting the two kinds of filaments.

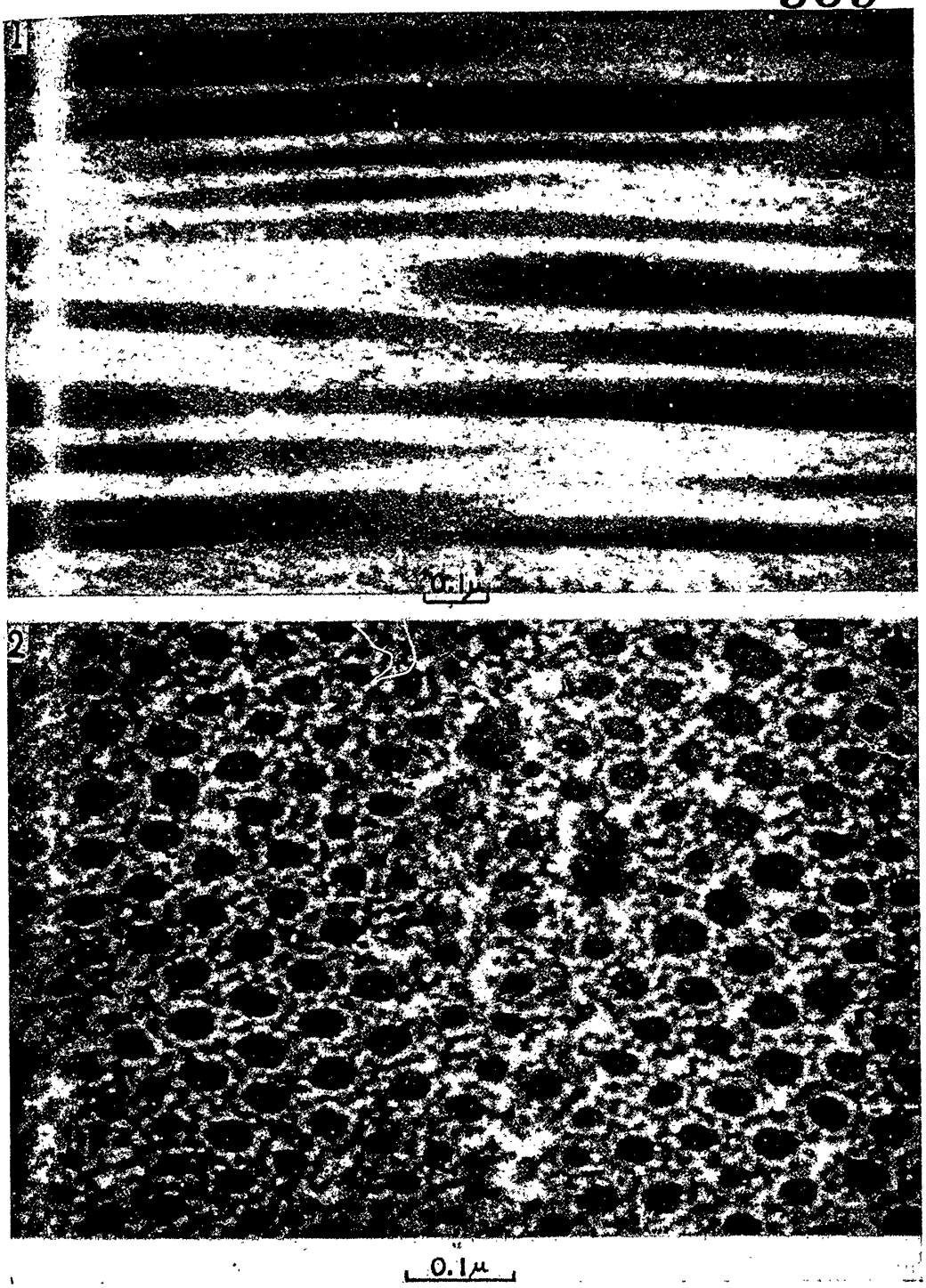

Figure 10

1. An electron micrograph of a longitudinal section through the part of a smooth muscle which is highly specialised for maintaining tension (the opaque part of the muscle which closes the shell of an oyster). The thick ' paramyosin ' filaments show a type of fine structure which is characteristic of such tonic muscles.

2. An electron micrograph of a transverse section through the other (more translucent) part of the same muscle. A large number of thin filaments (about 5 mμ in diameter) lie between the thicker filaments whose diameter ranges from 20–50 mμ. Thus, as in cross-striated muscles, there are two kinds of filaments; this, taken together with other evidence, indicates that the muscle contracts by a sliding filament mechanism.

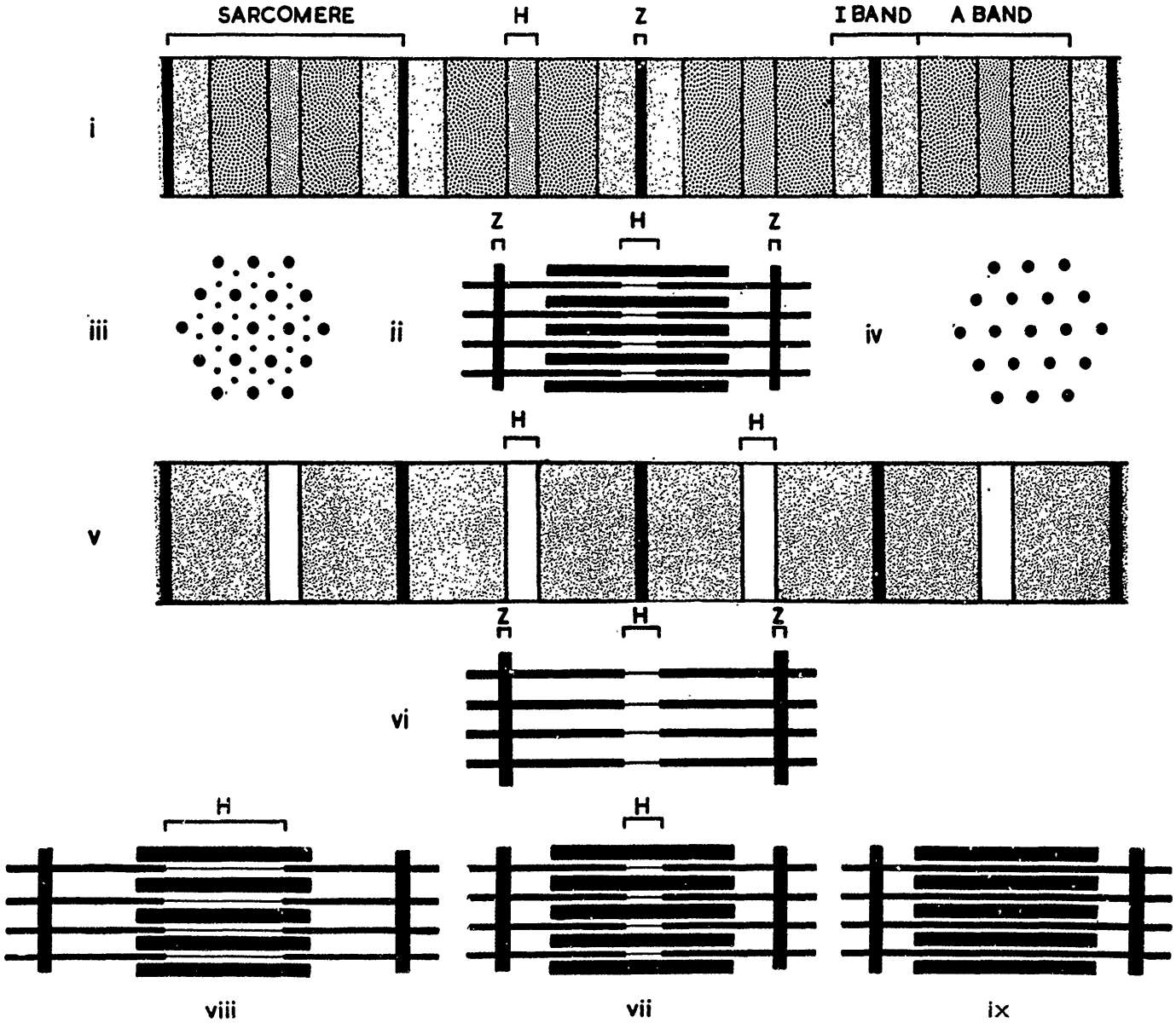

Figure 11

Figure 11

DIAGRAM OF THE CONTRACTILE ELEMENTS (MYOFIBRILS) OF A CROSS-STRIATED MUSCLE

(i) The band-pattern repeats at regular intervals along the length of the fibril. One unit in the pattern (from Z line to Z line) is called a ' sarcomere '. In a phase contrast or interference microscope the pattern appears as bands (A. I. H) of differing optical density (cf. *Figure* 9, 1) indicated here by shading.

(ii–iv) The arrangement of the actin and myosin filaments in one sarcomere is shown in these three diagrams. The thick myosin filaments extend from one end of the A band to the other (ii); it is this array of myosin filaments which is responsible for the high optical density of the A band. Two arrays of thin actin filaments extend from the Z lines as far as the borders of the H zone in the centre of the sarcomere. These arrays are exposed in the I bands. In the A band they interdigitate with the array of myosin filaments, and a cross-section through this part of the A band is shown in (iii), where one sees a double hexagonal array of filaments (the primary and secondary arrays whose existence was initially deduced from X-ray diffraction data). A cross-section through the H zone (iv) shows only the single array of thick myosin filaments.

(v and vi) After all the myosin has been extracted from the fibril, the A bands (v) and the thick filaments (vi) have disappeared. The actin filaments remain (vi), and the H zone, as seen in the light microscope (v) appears as a ' gap ' of very low optical density. Some material remains in the H zone, however, since the fibrils do not split up; this residual material is indicated diagrammatically as fine lines (ii and vi–viii).

(vii–ix) When the muscle is at the maximal length it can assume in the body, the sarcomere appears as in diagram (vii). When the muscle is stretched (viii) the arrays of actin filaments are pulled part of the way out of the A band; thus the I bands and the H zone are elongated, but the A band remains the same length. When the muscle shortens (ix) the arrays of actin filaments move inwards into the A band, and the H zone closes up while the I bands shorten, but again the A band remains unchanged.

are shaped like simple rods, some like spheres, some in geometrical configurations like an icosahedron (Figure 3), while many of the bacteriophages have a more complex 'head and tail' formation. In spite of this diversity of form there is remarkable unity in the principles underlying the structure of all viruses so far examined.

Protein Sub-units in Viruses

One of the most important of these principles is that the protein coat of the virus is not composed of a single giant protein molecule, or of many different types of protein molecule, but of small identical protein sub-units arranged in a regular manner. This general principle was deduced in the following way by F. H. C. Crick and J. D. Watson of the Council's Molecular Biology Unit at Cambridge.

The amount of genetic material required to determine the structure of a complicated organism, or complicated part of an organism, has generally been observed to be relatively large. But the amount of new genetic material introduced into a cell by an infecting virus is exceedingly small, in relation, for example, to the total genetic material of the cell. Consequently, the product which the injected genetic material determines, that is, an exact replica of the infecting virus, must be of relatively simple structure. This consideration led to the idea that the innumerable new virus particles produced in a cell must be identical, and that the protein of each of them is likely to be built up of small sub-units, either identical or of a very few different types. If, on the contrary, it were built up of a single giant protein molecule or of many different kinds of protein molecule, much more virus DNA or RNA would be required than was actually injected into the cell. It can be shown, for example, that at least three of the four available nucleotides would be required to constitute a unique code for each amino acid in a single giant protein molecule. In terms of molecular weights, this would mean that as much as 1,000 molecular weight units of single chain nucleic acid would be required for the coding of 100 molecular weight units of protein. In other words, the molecular weight of the nucleic acid in a virus particle would require to be some 10 times that of the protein coat, that is, the virus would have to contain 90 per cent nucleic acid by weight merely to specify the structure of the protein coat. But no virus is known with more than 50 per cent nucleic acid. It follows that the amino acid sequences specified by the available nucleotide sequences must be limited, and therefore used repeatedly. The most likely consequence of this limitation is that small and identical protein sub-units are used in the building of the virus particle.

Rod-shaped Viruses

The structure of the tobacco mosaic virus (TMV) is an example of one of the simpler applications of the sub-unit principle. TMV is a rod-shaped virus 300 mμ long and 15 mμ in diameter (one mμ, the millimicron=one millionth of a millimetre). Chemical studies have shown that a small protein sub-unit of molecular weight 17,000 must be part of the structure; and X-ray diffraction analysis (by J. D. Watson working for the Council in Cambridge, and the late Rosalind Franklin and her colleagues on the staff of the Agricultural Research Council) has revealed that the sub-units are arranged in the form of a screw or helix about the long axis of the particle (Figure 5). The geometry of such a helical arrangement may be envisaged by thinking of a sub-unit at a given place

in the helix and counting the number of turns made upwards until another sub-unit appears exactly above it. In tobacco mosaic virus there are three such turns; the number of sub-units encountered on the way is 49, and the pitch of the helix is 2·3 mμ. From these figures, and that for the total length of the virus, the number of protein sub-units in the virus can be calculated; this is

$$\frac{300 \times 49}{3 \times 2{\cdot}3} = 2{,}100 \text{ protein sub-units, all of them being exactly alike.}$$

Electron microscopy by H. E. Huxley of the Council's External Staff, has revealed a central hole 1·5 mμ in diameter in the structure. When the protein of the virus is separated chemically from the nucleic acid and isolated in the form of a solution of sub-units, these units reaggregate spontaneously to form rods which have the same diameter as the intact virus. X-ray diffraction analysis of these rods has shown that there is a helical groove at a radius of 4 mμ deeply embedded in the protein, in which groove the nucleic acid of the intact virus presumably lies. The length of the virus particle is related to the length of the single chain of nucleic acid which occupies this groove; the nucleic acid in this particular virus is in the form of RNA.

Small Spherical Viruses

As shown above, a rod-shaped virus has its protein sub-units arranged symmetrically in the form of a screw, that is, it has 'screw' symmetry. Can a spherical virus be constructed from identical (or similar) sub-units arranged symmetrically in a different way? This question led F. H. C. Crick and J. D. Watson (1956), at that time working together in the Council's Molecular Biology Research Unit, Cambridge, to investigate how many different kinds of regular arrangements of circles can be drawn on the surface of a sphere. They soon found that this problem had already been solved by Plato. In practical terms the only possible numbers of such circles are 12, 24 and 60, and in each case there is a different symmetry theoretically recognizable by its X-ray diffraction pattern. Crick and Watson predicted that an arrangement of 60 sub-units forming a regular polygon (a polygon in which all the faces are equivalent) was the most likely one for small spherical viruses. X-ray diffraction analysis of crystals of tomato bushy stunt virus, turnip yellow mosaic virus, and poliomyelitis virus confirmed the predicted symmetry (Figure 6). It is also likely that a small bacteriophage φX 174, has the same structure. This has not been crystallized, but electron micrographs have given indications of sub-units symmetrically arranged.

Large Icosahedral Viruses

In 1958, R. C. Williams and K. M. Smith of the Agricultural Research Council's Virus Unit described the morphology of a large insect virus which infects larvae of the species *Tipula;* the virus particles are 130 mμ in diameter and have an icosahedral shape (Figure 3). Recently the adenoviruses, of which 18 different types have been isolated from throat swabs in man, some of these being associated with upper respiratory catarrhal disease, pharyngitis and conjunctivitis, have been shown to be icosahedra; and the arrangement of the sub-units has been observed in electron micrographs, by S. Brenner and P. Wildy of the Council's staff, working with R. W. Horne and A. P. Waterson of Cambridge University. Each triangular facet has a side on which six sub-units lie, and the total number of sub-units is 252.

In the small spherical viruses described above, the surroundings of all 60 sub-units are identical. The adenovirus particles, on the other hand, are like small crystals with sharp edges and flat faces. Sub-units at the corners and edges have different surroundings from those in the middle of the faces—an arrangement which deviates from simple 60-fold symmetry. With such a design the protein shell could not possibly take up the form of an icosahedron, without some additional mechanism to determine the position of edges and corners. The most likely mechanism for this purpose is the folding of the nucleic acid chain into a polyhedral structure, upon the surface of which the sub-units of the outer shell could be packed in a regular manner.

Bacteriophage T2

Most of the known bacteriophages have a much more complicated structure than that of the animal and plant viruses. Recent studies have shown that the bacteriophage particle is built up from a number of components, each of which is of reasonably simple construction. The whole particle is tadpole-shaped. The head, which contains DNA, is a membrane in the form of a bipyramidal hexagonal prism; the cylindrical tail, which consists of an outer sheath surrounding a hollow core, is attached to the head at one end and carries a hexagonal plate at the other; from this tail plate projects six pins, to each of which a long tail is attached (Figure 7).

Chemical studies have shown that the proteins of the head, sheath and tail fibres are all different, and that the head and sheath contain protein sub-units. The head is polyhedral in shape with sharp edges and flat faces; its two ends differ in structure, one vertex being incomplete where the core is attached. It has been shown that there are about 1,000 identical protein sub-units in the virus head membrane; these could not occupy equivalent positions in the structure since some lie on faces and others on edges or corners; as in the icosahedral adenovirus, the shape is probably determined by prior folding of the DNA chain. Recent work, indeed, suggests that this is what actually happens during the synthesis of the bacteriophage in the bacterial cell.

The tail sheath is contractile, and electron micrographs suggest that its structure is helical, each sheath containing 200 protein molecules. During contraction the sheath becomes wider as well as shorter; this suggests that the helical array of sub-units becomes changed into one with fewer turns and more sub-units per turn. No details are known about the structure of the core and the hexagonal tail plate, except that the core is hollow to permit the passage of DNA during the process of its injection into a bacterial cell. The general morphology of T_2 bacteriophage had been established by research workers in the United States and elsewhere, but many of its detailed features were recognized for the first time by S. Brenner and his colleagues at the Council's Molecular Biology Unit in Cambridge.

In summary, it may be said that the general features of some of the simpler rod-shaped and spherical viruses have been determined. In both types the mode of assembly of the fully developed infective virus particle from its protein and nucleic acid components into its final geometric form can be readily understood. The shapes of these virus particles depend upon the type of symmetrical arrangement of the protein sub-units, for example, 'screw symmetry' in the rods and symmetry of a regular polygon in the spherical viruses. The structural assembly

of the icosahedral viruses and the bacteriophage head presents a more complex problem; it is not easy to see how these shapes are produced, but a probable answer is that the manner of folding of the DNA chain determines the arrangement of the protein sub-units.

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THE STRUCTURE OF MUSCLE IN RELATION TO THE MECHANISM OF CONTRACTION

During the last few years a new hypothesis about the mechanism of muscular contraction has gained wide acceptance. It arose from a fresh attack on structural problems, particularly on the long-standing question why some muscles are cross-striated.

The Double Hexagonal Array of Protein Filaments in Muscle Fibrils

Until recently it was considered that the contractile elements of muscles were constructed from the fibre-like macro-molecules of the protein actomyosin, and that contraction was brought about by a change in the manner of folding of their polypeptide chains (Astbury, 1947). Although this conclusion seemed consistent with the early results of electron microscopy obtained by examination of fragmented muscle (Hall, Jakus and Schmitt, 1946), it was difficult to explain the absence of wide-angle X-ray diffraction changes on contraction; moreover, E. Fischer (1947) had pointed out that absence of birefringence changes on stretch suggested that changes in the length of muscle took place by relative movement between large structures.

New information which suggested that some such process might be involved came in 1951 from further studies by X-ray diffraction carried out by H. E. Huxley (1951, 1952, 1953a), working in the Council's Molecular Biology Research Unit in Cambridge. Huxley obtained evidence that the fibrils of striated muscles are constructed from a *double* hexagonal array of protein filaments. Thus, if one looks down the length of a fibril, one sees a hexagonally packed 'primary' array of filaments and a 'secondary' array of other filaments lying amongst

them (Fig. 11, iii). The internal structure of the filaments repeats at regular intervals along their length, and Huxley found that the repeat-distance remains the same whatever the length of the mucle. This suggested that the filaments, and the molecules of which they are composed, do not contract when the muscle shortens. [It should be noted here that X-ray diffraction pictures give important information on sub-microscopic structure, but that, unlike electron micrographs, they can only be obtained from cells with regularly arranged components. X-ray diffraction has, however, the advantage that it can be applied to intact living tissue, for example electrically-excitable muscle, and thus provides a valuable means of checking conclusions drawn from a study of the dead material examined in an electron microscope.]

The double filament structure of a myofibril deduced from X-ray diffraction data was soon confirmed by examination of ultrathin transverse sections of striated muscle in the electron microscope (Huxley, 1953b). As a result of being able to look at different parts of the muscle fibril segment, or sarcomere (which could not be done by X-ray diffraction), Huxley discovered that the double array of filaments was present only in the mid-section of the segment, the A-band; the two end-sections of the segment, I-bands, contained only the thinner kind of filament, and these were poorly aligned; and in the centre of the A-band there was a zone (H) in which only a single array of thick filaments was present (Fig. 11, i-iv, and Fig. 9, 2).

The meaning of these results became clearer when Jean Hanson and H. E. Huxley, at that time working in the Massachusetts Institute of Technology, carried out experiments on whole isolated myofibrils under the light microscope, using a method developed by Hanson (1952) in the Council's Biophysics Research Unit. Hanson and Huxley (1953) found that the material responsible for the high optical density of the A-bands (as viewed in a phase contrast microscope—Fig. 9, 1), and for their birefringence, could be selectively extracted from the fibrils. The remainder of the fibrils (' ghosts'), when studied in the electron microscope, were found to have lost their thick filaments, except in the short H-zone in the middle of the sarcomere, but the thin filaments of the I-bands and the ' secondary ' array of thin filaments in the A-bands still remained. This result suggested that the thin filaments were continuous structures extending from the ends of each sarcomere, the Z-lines, through the I-bands and into the A-bands. Later improvements in the extracting methods (Huxley and Hanson, 1954: Hanson and Huxley, 1955), made it possible to remove the whole of the thick filaments, and it was then found that the thin filaments were discontinuous in the H-zone in the middle of the sarcomere (Fig. 11, v, vi). It became clear that the fibril could be regarded as a structure made up of two kinds of filaments, grouped into separate transverse arrays which alternate along the length of the fibril (giving the A- and I-bands) and partly overlap (as a double hexagonal array) in the A-bands. (Fig. 11, ii and Fig. 9, 2).

Constancy in Length of the Thick and Thin Protein Filaments

The functional significance of this structural plan of the myofibril of striated muscle, and further evidence for it, emerged from studies during shortening or lengthening of the sarcomere; in these the behaviour of the A- and I-bands and of the H-zones, in which the thin filaments are absent, was watched. These investigations were carried out under the light microscope, but their interpretation depended on the results of electron microscopy. A. F. Huxley and

R. Niedergerke (1954, 1958) working in the Physiological Laboratory in Cambridge, and H. E. Huxley and J. Hanson (1954) all found that as the sarcomere changed its length the A-band remained at constant length while the I-bands shortened or lengthened (Fig. 11, viii, ix); moreover Hanson and Huxley showed that the H-zone elongated when the sarcomere was stretched and disappeared altogether when it shortened (Fig. 11, viii, ix). From a study of fibrils which had been stabilized at different lengths and then treated to remove the thick filaments of the A-bands, Hanson and Huxley were able to conclude that the thin filaments as well as the thick ones remained constant in length over a wide range of muscle lengths. Indeed the changes in length of the sarcomere during shortening and lengthening affected only the length of the I-bands and the H-zone, and were produced by a *sliding filament mechanism* in which the thick and thin filaments moved relatively to one another, the arrays of thin filaments moving further in to the A-band during contraction, and being pulled out again when the relaxed muscle was re-extended (Fig. 11, vii-ix).

The sliding filament theory was propounded independently by A. F. Huxley and R. Niedergerke, and by H. E. Huxley and Jean Hanson, and both sets of authors published their results simultaneously (1954).

Electron microscopy alone could not have provided all the necessary evidence for a sliding filament mechanism, nor could light microscopy alone. With further improvements in sectioning and staining methods, H. E. Huxley (1957), now working as a member of the Council's external staff in the Department of Biophysics, University College London, obtained extremely thin longitudinal sections of sarcomeres fixed at different lengths; these showed clearly that the thin filaments had changed their positions relative to the thick filaments, and were indeed discontinuous in the middle of the sarcomere (H-zone).

Biochemical Mechanisms Associated with the Sliding Movement of the Filaments

Already in 1953 H. E. Huxley (1953b) had observed in electron micrographs that the thin and thick filaments are cross-linked by short transverse bridges where they lie in double array in the A-bands (Fig. 9, 2). These transverse bridges were later found to be projections from the thick filaments reaching out to the thin ones at regularly spaced intervals (H. E. Huxley, 1957). It was clear that such cross-links, when attached, would make the fibril inextensible, and a mechanism by which they could be attached and detached became apparent when it was discovered by Hanson and H. E. Huxley (1953, 1955) and by W. Hasselbach (1953), working in H. H. Weber's laboratory in Tübingen, that the thick filaments contained the protein myosin, and the thin filaments contained the other main muscle protein, actin.

The work of Szent-Györgyi and his colleagues in Szeged in the nineteen-forties had suggested that actin and myosin *in vitro* form a complex, actomyosin, which in solution can be dissociated into its two constituents by adenosine triphosphate (ATP), and which reforms as the ATP is dephosphorylated under the influence of an enzyme which is part of the myosin molecule. [It is very probable that the dephosphorylation of ATP supplies the energy for contraction.] Moreover, Weber and his colleagues had shown that certain preparations of muscle fibres, and also artificial threads of actomyosin, are inextensible in the absence of ATP,

but are ' plasticized ' by the addition of ATP, provided that the enzyme (ATPase) activity of myosin is suppressed. Thus Hanson and H. E. Huxley were able to suggest (1953, 1955) that cross-linkage between myosin and actin filaments in the intact muscle represents actomyosin formation, and may be controlled by ATP. Evidence that myosin is located in the thick filaments of the A-bands was obtained, simultaneously, by Hasselbach (1953), and by Hanson and H. E. Huxley (1953); all these workers found that solutions which selectively extract myosin from muscle remove the A-bands from the fibrils. Much stronger evidence was later provided when it was shown (Hanson and Huxley, 1957; Huxley and Hanson, 1957a), that the amount of myosin in the fibril, measured chemically, is equal to the amount of thick filament material in the sarcomeres, as measured by an interference microscopy method developed in the Biophysics Research Unit by H. G. Davies and M. H. F. Wilkins (Davies *et al.*, 1954).

The sliding filament *hypothesis* thus postulates that the tension produced in a muscle at the onset of activity is brought about by means of cross links formed between actin and myosin filaments, and that shortening takes place by a process (not yet understood) in which each cross-linkage site is active many times in making, breaking, re-making, and re-breaking actomyosin links as the filaments move alongside each other. That this hypothesis concerns events at a molecular level is evident from the following results: each of the transverse bridges on the myosin filaments is associated with two molecules of myosin, and for each ' step-distance ' (from one bridge to the next) of movement of an actin filament alongside a myosin filament, the amount of chemical energy used per cross-link is about the same as would become available from the dephosphorylation of a single molecule of ATP. The sliding filament hypothesis has been discussed in detail in some recent review articles (Hanson and Huxley, 1955; H. E. Huxley, 1956; A. F. Huxley, 1957; Weber, 1958; H. E. Huxley, 1960; Huxley and Hanson, 1960).

Structure of Some Smooth Muscles—a Possible Sliding Mechanism

All the work which has so far been described concerns the skeletal (cross-striated) muscles of vertebrate animals. Further studies on the flight muscles of insects (Hanson, 1956; Huxley and Hanson, 1957b) indicate that these are similar. But cross-striated muscles are highly specialized. Before we can begin to define the basic properties of contractile systems in living organisms, it is clearly necessary to study *smooth* muscles and also to try to account for some of the functional specializations of different kinds of muscle, such as the extraordinary ability of certain molluscan smooth muscles to maintain a steady high level of tension for long periods of time. The classical examples of such *tonic* muscles are the adductors of bivalve molluscs like the oyster and the mussel.

Electron microscopy has provided good evidence that these and other molluscan smooth muscles contract by a sliding filament mechanism (Hanson and Lowy, 1957, 1959, 1960 (see Fig. 10, 2)). One of the main structural differences between cross-striated muscles and these smooth muscles concerns the arrangement of the thin and thick filaments which, in the smooth muscles, are *not* segregated into separate arrays; hence there are no A- and I-bands, nor are there any Z-lines.

A number of structural features peculiar to the *tonic* muscles have been found (Hanson and Lowy, 1957, 1960). One of the most interesting concerns the thick

filaments, which are characterized by their fine structure (Fig. 10, 1). This was first described in 1945 by Hall, Jakus and Schmitt, and was one of the earliest biological applications of electron microscopy. The functional significance of this so-called ' paramyosin ' structure of the thick filaments is still a major unsolved problem, and it is one of the subjects of current investigation in the Biophysics Research Unit.

The work described by Huxley (1953b), Hanson and Huxley (1953), and Huxley and Hanson (1954) was carried out in the Massachusetts Institute of Technology.

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INTERFERON : THE PROSPECTS FOR AN ANTI-VIRAL AGENT IN MAN

In an article in the Annual Report of the Council for 1956–57, a description was given of the discovery of interferon by A. Isaacs and J. Lindenmann, working at the National Institute for Medical Research. Interferon is a substance which was first isolated from tissue cultures treated with killed influenza virus, and which has the important property of inhibiting the growth of a number of viruses *in vitro*. This discovery resulted from a laboratory investigation of the phenomenon of virus interference; hence the name ' interferon ' was given to the inhibitory substance found. It now seems that the whole process of

viral interference by killed virus can be largely accounted for by the presence of interferon; when cells are incubated with an interfering virus they produce sufficient interferon to account for their subsequent ability to resist the growth of a variety of other viruses.

Further research on the subject at the National Institute for Medical Research has advanced in two directions. First, the discovery of interferon suggested a new approach to the search for a wide-spectrum anti-viral agent, and work was set in train to determine whether the development of interferon as such an agent might prove to be a practical possibility. Secondly, the processes of virus multiplication were investigated afresh by means of the new tool provided by interferon, and this entailed comprehensive studies on its mode of action; it was hoped that this line might also lead to valuable practical results, by indicating how interferon could best be used in the control of virus infections.

Attempts to Develop an Anti-Viral Agent

Five main questions had to be answered before it could be hoped to develop interferon as an anti-viral agent in man: (1) is interferon toxic when used in doses which inhibit virus growth? (2) is it antigenic? (3) does it prevent growth of virus *in vivo* as well as *in vitro*? (4) how quickly and for how long does it act? and (5) what are the prospects for the manufacture of interferon in large amounts, and in a sufficiently concentrated and purified form for prophylaxis or therapy?

Toxicity. Whether or not interferon is toxic for man is a question that cannot yet be answered, but experiments in animals have revealed no evidence of gross toxicity. Perhaps the simplest way to demonstrate its apparent lack of toxicity is by the method devised by Porterfield (1959) for measuring the potency of interferon. This method, based on that used for measuring the potency of a bacterial antibiotic, is illustrated in Fig. 8.

A sheet of cells is placed in a Petri dish and is infected with sufficient virus to destroy all the cells. (In the example shown, an arthropod-borne (Bunyamwera) virus was used, but the same result is obtained with a variety of viruses.) The cell sheet is then covered with agar, and a small cup filled with an interferon solution is set in the centre of the agar. The interferon diffuses out of the cup through the agar to the cells in its neighbourhood. In Fig. 8 Zone A consists of healthy cells around the central cup; these are cells protected from the virus, as shown by their capacity to take up neutral red stain. Zone B at the edge of the plate consists of cells which have been killed by virus action as shown by their inability to take up the stain. Between Zone A and Zone B there is an intermediate area of partial protection. This experiment indicates that interferon, far from being toxic, does, in fact, protect cells against the toxic action of viruses.

Antigenicity. Interferon is known to be a protein, smaller than antibody globulin; if it were antigenic its usefulness would be greatly curtailed because, after it had been administered two or three times, the antibody formed in response to it might neutralize its anti-viral activity. It is encouraging, therefore, that a search for antigenicity has given wholly negative results so far.

Animal experiments. The first experiments on the protective effect of interferon in animals gave inconclusive or negative results. This was to a large extent

due to the factor of tissue specificity to which Tyrrell (1959) has drawn attention. Tyrrell found that interferon prepared in chick tissues, for example, was effective when tested *in vitro* in chick but not in calf cells, and that calf interferon was effective in calf but not in chick cells. Such specificity, however, does not appear to be absolute, although its full extent is not yet known. From the practical point of view it seems important to prepare interferon in cells of the species of animal which it is intended to protect. This approach was adopted by Isaacs and Westwood (1959a) who found that interferon prepared in cultures of rabbit kidney cells protected rabbits against skin infection by vaccinia virus, whereas interferon prepared in chick cells was only irregularly protective. For experiments in animals, therefore, and pending further knowledge of its specificity, interferon is being prepared in cells of the homologous species.

Time of action. It was first found that the optimal protective effect of interferon on cells occurred if the interferon was introduced 24 hours before the virus; with shorter intervals less protection was found. More recently Wagner (1960) has observed that significant protection of cells in tissue culture still occurs when a large dose of interferon is given one hour after the virus, although the protection is greater if the interferon is given before the virus. For use in animals and man, therefore, interferon is likely to be most effective when given early in the viral infection; perhaps it may be most effective when given in the incubation period.

The duration of action of interferon was studied by exposing cells in tissue culture to a single dose of interferon, washing the cells to remove any excess interferon and observing the duration of their resistance to infection with West Nile encephalitis virus. It was found (Isaacs and Westwood, 1959b) that the cells were resistant to infection for at least 10 days, provided they were kept in conditions under which they were unable to divide. Cell division reduces the concentration of interferon within the daughter cells, and susceptibility to virus growth returns. In most mammals cell division does not occur more often than every 24 hours, so that in theory interferon may be best administered about once a day.

Large scale production. The feasibility of preparing interferon on a large scale is still under test. Large batches of interferon have been prepared from chick tissues at the Microbiological Research Establishment, Porton, and have been found to be satisfactorily potent and stable. Considerable progress in purifying the active component has already been achieved, but further investigation is needed. For use in man it is likely that large scale cultures of human or monkey tissues will be required, and experience gained in the manufacture of poliomyelitis vaccine should be helpful in solving the problems of production.

These results were considered sufficiently encouraging to enable the Council to propose that the stage had been reached for large scale collaborative research on interferon. A method of collaboration has now been agreed between the Council, the National Research Development Corporation, and three pharmaceutical firms, with the aim of furthering research as rapidly as possible on the development of an anti-viral agent.

Mode of Action of Interferon

Early in this work it was apparent that the protective action of interferon was directed towards the infected cells, and not towards viruses outside cells, and that protection was possible against a wide range of viruses although some viruses

were more sensitive than others. At present it seems that the attack by interferon is at an early stage of virus growth, preventing the development of viral 'building blocks' as well as mature virus.

Such a fundamental point of attack suggests that interferon shifts the metabolism of the cell towards processes needed by the cell, at the expense of those needed by the invading virus. A hint of the kind of process concerned came from the observation (Isaacs, 1960) that interferon stimulates cells to increase glycolysis. Although this may be a non-specific reaction of the cell common to many stimuli it does suggest a number of interesting possibilities. Glucose is an important source of energy for the cell, and it is conceivable that stimulation of the mechanism of glycolysis during virus multiplication may interfere with the metabolic pathways needed for producing virus. Research along these lines is already giving interesting results which may lead to more efficient methods of preparing and using interferon.

Although interferon is produced rapidly by cells treated with *inactive* virus it is also produced at a late stage of infection by live virus. This applies to viruses of the influenza group and to other quite unrelated viruses. Inhibiting substances similar to interferon are produced by live vaccinia virus (Nagano and Kojima, 1958), vesicular stomatitis virus (Cooper and Bellett, 1959), and poliomyelitis virus (Ho and Enders, 1959). A uniform finding like this in a variety of viruses suggests that interferon may be produced by cells as a general response to virus infection and may be part of the natural mechanism of defence against virus infection. Recently, Henle and his colleagues (1959) showed that cells grown in tissue culture and chronically infected with virus were resistant to further virus infection as a result of the production of interferon by the culture. The development of interferon as an antiviral substance can thus be viewed as a process of exploitation of a natural cellular defence mechanism against viruses, in much the same way as the development of immunization can be viewed as stemming from the exploitation of the natural humoral defence mechanisms of the body.

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THE ARTHROPOD-BORNE VIRUSES

The arthropod-borne or 'arbor' viruses are, despite their great diversity, classified as a single group because of a characteristic common to them all—their life span includes a period of growth in an insect host. The insect, which may be a blood-sucking mosquito, tick, or sand-fly, becomes infected when it feeds upon a vertebrate host at a time when virus is present in the host's blood stream. After the virus has been taken up by the insect there is usually a latent period of 10 or 12 days, during which the virus is multiplying, before the insect

can transmit virus by feeding upon another susceptible subject. The virus appears to be harmless to the insect, which remains, however, infective for the remainder of its life. Since an infected mosquito may bite every second or third day and may live for three months or more, the potentiality for spread of these viruses is considerable. The arbor viruses are classified in a different group from that of other animal viruses which, although they may be spread by insects, do not multiply in the vector; the myxoma virus, for example, is transmitted by the bites of mosquitoes or rabbit fleas in a purely mechanical manner without any multiplication in the insect. Plant viruses, of which a number are arthropod-borne, are not considered in this review.

It is the non-arthropod cycle, which may involve man, wild and domestic animals, or birds, that makes the arbor viruses important to man. The viraemic phase in the host is usually short, lasting as a rule two to five days, and it is followed either by the development of immunity and the disappearance of virus from the blood stream, or, in certain severe infections, by the death of the host. Coincident with the viraemia the clinical symptoms of disease, if any, make their appearance; many virus attacks are symptomless. When certain tissues are affected particular disease states may arise. Thus, in yellow fever the liver is typically involved producing jaundice, although in many cases of yellow fever there is only a general reaction with fever and malaise. Certain viruses, such as Murray Valley encephalitis virus, have an affinity for nervous tissue and may produce encephalitis. Others may produce lesions in the skin, for example the rash characteristic of certain types of dengue, or a haemorrhagic disease such as has been reported from Thailand (Hammon, *et al.*, 1958). Many human infections with arthropod-borne viruses are without any characteristic symptomatology, and produce only a mild systemic illness or no overt disease at all. The diagnosis of most of these virus fevers is almost impossible without the assistance of a laboratory, and even with a first class laboratory the precise identification of a virus may be an extremely difficult and time consuming process.

World Chain of Laboratories

Scattered throughout the tropics, and in a few countries in the temperate zone, are laboratories or units in which the study of arthropod-borne virus infections is the principal interest. In Nigeria and in Uganda, laboratories were established many years ago by the Rockefeller Foundation as part of their programme of research on yellow fever. These are now known respectively as the West African Council for Medical Research Laboratories in Lagos, and as the East African High Commission Virus Research Institute in Entebbe. Whilst yellow fever studies continue in both laboratories several new viruses have been isolated, of which Chikungunya (Robinson, 1955; Ross, 1956) and Ilesha (Annual Report, 1958) are the most recent. In South Africa, a unit of the Rockefeller Foundation and the South African Institute for Medical Research have been particularly active in Tongaland, where a number of new viruses have been described (Smithburn *et al.*, 1959). In the Far East, where dengue and Japanese B encephalitis are the two most important human infections, a third potentially important reservoir of infection was uncovered in ticks (Smith, 1956). A related tick-borne virus was also isolated from human infections, some of them fatal, by workers at the Virus Research Centre operated by the Rockefeller Foundation and the Medical Research Council of India at Poona (Work, 1958). In the West Indies, the Regional Virus Laboratory established by

the Rockefeller Foundation in collaboration with the Government of Trinidad and Tobago described another new virus (Mayaro) capable of infecting man (Anderson *et al.*, 1957) and linked up an earlier strain from South America, Ilheus virus, with human infections. In the United States of America the Rockefeller Foundation Laboratories in New York have for a number of years provided a focus for research upon arthropod-borne viruses, and active groups are also present in Pittsburg, Washington, in California and a number of centres elsewhere. In Europe, tick-borne viruses of the group are under investigation in Russia, Czechoslovakia, Holland, and Scandinavia. In the British Isles, a number of different aspects of arthropod-borne virus infections are being studied at the National Institute for Medical Research, at the London School of Hygiene and Tropical Medicine, and at centres in Belfast and Glasgow.

The Council's interest in this group of viruses is both direct and indirect. Through the Colonial Medical Research Committee, which is responsible jointly to the Secretary of State for the Colonies and to the Council, and through the Council's Committee on Virus Diseases in the Tropics, research work on these viruses is directly related to that on viruses generally in the British Colonies; and indirectly the same work has an important bearing on the research in virology, supported by the Council, which is in progress in this country.

Ten years ago the isolation of a new virus in the Tropics was something of an achievement. Now it has become almost an embarrassment, and most tropical laboratories have several new or unexamined viruses stored under deep freeze conditions awaiting study. In the Annual Report for 1959 of the Rockefeller Foundation Virus Laboratories it is stated that 116 arbor viruses have been isolated, 30 in Africa, 25 in Asia, 53 in America, 15 in Europe and 1 in Australia. Many of these are common to more than one of these regions. Fortunately, in the last five years a number of advances have been made in techniques for the study of these viruses.

New Methods of Identifying the Viruses

Until recently almost all the arthropod-borne viruses were isolated by inoculation of mice, and viruses were identified by demonstrating that they could be rendered non-infective for mice after incubation with sera taken from animals which had recovered from infections with the particular virus under study. Antibodies also were demonstrated in human populations or in animals or birds by the same techniques, and these methods necessitated the use of very large numbers of mice. The demonstration that many arthropod-borne viruses could, under carefully controlled conditions, bring about the agglutination of certain avian red blood cells, and that this agglutination could be inhibited by antisera, greatly simplified laboratory procedures for their identification.

Classification of the Viruses

By this method it was shown by J. Casals and others, working at the Rockefeller Foundation Virus Laboratories in New York, that about half the known arthropod-borne viruses could be placed in one of three serological families which they designated Groups A, B and C (Casals, 1957). Five Group A viruses are known to occur on the American continent—the three equine encephalomyelitis viruses, which produce occasional disease in man, and two recently defined agents, Mayaro (Casals and Whitman, 1957) and Uruma viruses (Schmidt

et al., 1959); and at least four Group A viruses are present in Africa—Semliki Forest virus in Uganda and Nigeria, Sindbis virus in the Nile valley (Taylor *et al.*, 1955), Chikungunya virus in Tanganyika, and Middleburg virus in South Africa. Group B is a larger family of these viruses and has an even wider distribution, including as it does yellow fever virus, dengue, Japanese B encephalitis, and the Russian Spring-Summer encephalitis—louping ill group of viruses. Members of the latter group have been found in the U.S.S.R. and in other parts of Eurasia. These agents are transmitted by ticks and can cause human disease of varying clinical severity. Louping ill is the only representative of the arthropod-borne viruses known to occur naturally within the British Isles, and recent evidence from Northern Ireland suggests that it may produce a 'poliomyelitis-like' illness in addition to the influenzal or encephalitic picture previously described (Likar and Dane, 1958). Although tick transmission is probably the usual means of spread, infection may be transmitted by drinking infected goat's milk (van Tongeren, 1955; Smorodintsev, 1958). Group C viruses have so far been isolated only in South America, although antibodies to members of this group have been found in the sera of residents of West Africa.

Epidemiology

A full understanding of the epidemiology of the arthropod-borne virus infections implies a detailed knowledge not only of the manner in which human infections are acquired, but also of the way in which the virus is maintained in the different insect hosts, and of still further cycles of infection involving perhaps animals or birds. The ecological factors concerned with the spread of a mosquito-borne virus in a tropical forest are obviously very different from those which apply to the spread of a tick-borne infection in Europe, and a detailed consideration of the many and complex variables is impossible here. These factors have been suitably discussed in a recent review (Smith, 1959). Yet recent serological studies have revealed close relationships between viruses such as yellow fever and louping ill, which have utterly different ecological backgrounds. Evidence is accumulating that the existence of shared antigens and the production of group antibodies may be of considerable epidemiological importance. The greater resistance of the African to yellow fever, as compared with the unvaccinated European was in the past explained as a genetic difference; it now seems much more probable that the tolerance displayed by many Africans is the result of prior infection with one or more Group B viruses serologically related to yellow fever virus and resulting in a partial cross immunity. Such a partial protection has been demonstrated in monkeys infected with Uganda S virus (a Group B virus isolated in Uganda) and subsequently challenged with yellow fever virus (Macnamara, 1953). The close association between antibodies to yellow fever and a number of other Group B viruses has been demonstrated in Trinidad (Theiler and Casals, 1958) and in West Africa (Macnamara *et al.*, 1959). The same mechanism of serological overlapping may be used to explain the geographical zoning of infections with different arthropod-borne viruses. Thus, the absence of yellow fever from the Indian sub-continent and from the whole of the Far East in spite of the wide distribution of a suitable vector, may be explained by the presence in these areas of a widespread immunity to other Group B viruses such as dengue and Japanese B encephalitis, and perhaps in certain areas West Nile and Kyasanur Forest disease (Work, 1958). It may well be that some of the viruses isolated in the Tropics which have in the past

been regarded more as pathological curiosities than as agents of human diseases play an important part in immunizing man against the effects of more virulent infections.

Tissue Culture Techniques in Assay of Virus and Antibody

Although the existence of shared antigens may simplify the initial stage of placing an unidentified virus in the right group by its reaction in haemagglutination inhibition tests, and although field studies have shown the value of this technique in the examination of human sera (Porterfield, 1954, 1956) the presence of broad group reactions complicates the interpretation of antibody studies based upon this procedure. For a number of reasons neutralization tests are to be preferred for quantitative and other critical estimations. These may be carried out in mice, as has been standard practice for many years, but recently tissue culture techniques have been developed to a stage at which they may supplant mouse tests. When a preparation of chick embryo cells is exposed to infection with a suitable dilution of virus and subsequently overlaid with a film of agar incorporating cell nutrients, areas of cell destruction or 'plaques' develop; these may be counted to estimate the amount of virus used in the preparation (Dulbecco, 1952). A known amount of virus can thus be incubated with an antiserum and the mixture subsequently assayed by the plaque method so as to determine the strength of the particular antiserum used. (Dulbecco *et al.*, 1956; Porterfield, 1959a). An even simpler technique can be used consisting of the diffusion of antiserum from a bead placed on the surface of a layer of agar which covers chick embryo cells infected with a plaque-producing virus. If the serum under test contains antibody against the virus under study, plaque formation is prevented in an area around the bead (Porterfield, 1960; this technique adapted for interferon is illustrated in Fig. 8).

It is evident that within the last few years a much better understanding of the inter-relationship of arbor viruses in nature, and of their effect on man, has been gained by means of these newer serological and tissue culture techniques, but this can be regarded as a mere introduction to the advances that might be expected from more sustained and systematic studies in the field and laboratory.

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THE PLASMA KININS

During the last 10 years workers in several laboratories have found that, under certain conditions, potent vasodilator polypeptide substances are formed from the plasma proteins. These have been given the generic name of plasma kinin. Recent work at the Council's National Institute for Medical Research suggests that these polypeptides act as physiological mediators of vasodilatation.

Plasma kinins may be formed in the test tube by incubating plasma with proteolytic enzymes such as trypsin, kallikrein, or plasmin. Alternatively, if the proteolytic enzymes of the plasma itself are activated by contact with glass or by dilution with saline, kinin formation may take place without the addition of exogenous enzyme. The plasma kinins formed by each of these methods were originally given different names (bradykinin, kallidin, etc.), but since they are as yet indistinguishable in their biological and physico-chemical properties it is possible that they are, in fact, one and the same substance. However, this must remain uncertain until their chemical structure is known.

Pharmacological Properties

The plasma kinins were originally detected by their stimulant action on organs containing smooth muscle, such as the uterus and the intestine (Rocha e Silva, Beraldo and Rosenfeld, 1949; Frey, Kraut and Werle, 1950). In this respect they resemble acetylcholine, histamine, and 5-hydroxytryptamine, but the contraction produced by the plasma kinins is slower and is not affected by specific antagonists of these substances like atropine, mepyramine and lysergic acid diethylamide (LSD), respectively.

When injected intravenously into an animal, preparations of the plasma kinins cause a fall of blood pressure by relaxing the peripheral blood vessels. This effect is short-lived because the kinins are rapidly inactivated by an enzyme present in the blood. Kinin preparations also increase the permeability of the capillaries (Holdstock, Mathias and Schachter, 1957), thus allowing a greater proportion of the plasma constituents, especially the proteins, to pass through the capillary wall from the blood to the interstitial fluid. Moreover, the plasma kinins have a remarkable capacity for producing pain (Armstrong, Jepson, Keele and Stewart, 1957). This can be demonstrated by applying a dilute kinin solution to an area of human skin in which the nerve endings have been exposed by blistering. The amount of pain can be assessed subjectively by the subject of the experiment, who is not told which solution (active or inert) is being tested.

Under these conditions the intensity of pain experienced is found to be roughly proportional to the concentration of the kinin preparation applied.

In all these experiments crude preparations of plasma kinins were used. D. F. Elliott, E. W. Horton and G. P. Lewis (1960a, 1960b) working at the National Institute for Medical Research have recently isolated bradykinin, a plasma kinin from ox blood, and have shown that this single peptide possesses all the biological actions of the crude preparations (Elliott, Lewis and Horton, 1960). As these are the actions which characterise inflammation, it is interesting to consider the role of bradykinin as the mediator of the inflammatory response. Further work on the pure peptide at the Council's laboratories, Hampstead, has shown, that when bradykinin is injected into the brachial artery of human subjects it produces vasodilatation in the forearm and hand, and is even more active than acetylcholine or histamine (Fox, Kidd, Goldsmith and Lewis, 1960).

Physiological Role

Over a hundred years ago Claude Bernard observed that stimulation of the chorda tympani nerve results in profuse salivation and an enormous increase in vascularity of the submandibular salivary gland. After the administration of atropine, stimulation of the nerve produces no salivation, but rather surprisingly the vascular changes occur as before. S. M. Hilton and G. P. Lewis (1957), working for the Council at the National Institute for Medical Research, investigated the mechanism of this vasodilatation in the cat. They perfused the blood vessels of the salivary gland with saline and tested the perfusates for vasodilator material. It was discovered that perfusates collected during nerve stimulation contained large amounts of an enzyme which can form a plasma kinin on incubation with plasma, whereas when the nerve was not stimulated, the perfusates contained little or no enzyme. They concluded that the vasodilatation which accompanies salivation is due to the formation of a plasma kinin. These workers also showed that vasodilatation in the tongue is produced in the same way (Hilton and Lewis, 1958). R. H. Fox and S. M. Hilton working at the Council's laboratories, Hampstead, have postulated a similar mechanism for the vasodilatation in human sweat glands. In their experiments they were able to demonstrate that plasma kinin itself is present in the interstitial fluid of the forearm in increased amounts during sweat gland activity (Fox and Hilton, 1958).

Several workers have reported the presence of a vasodilator polypeptide in normal human urine. This could not be distinguished pharmacologically from three kinins prepared from plasma in different ways, and has been given the name urinary kinin (Gaddum and Horton, 1959). The output of this polypeptide in urine is continuous, and fairly constant in different people and under different conditions. It has been suggested that it may have a function in the kidney similar to that in the salivary and sweat glands, but there is no direct evidence in support of this hypothesis (Horton, 1959). The presence of a kinin in urine, however, adds further support to the belief that these substances are of physiological importance and are not merely artefacts produced in the test tube.

An interesting observation in the field of comparative physiology is that kinins, or enzymes which form them, are present in the venom of wasps and certain snakes and in the saliva of most animals so far investigated. The physiological significance of this is unknown. The presence of kinin in wasp venom undoubtedly accounts for much of the pain and swelling resulting from a wasp sting.

It has recently been shown that when bovine colostrum is incubated with calf saliva *in vitro*, a kinin is formed (Guth, 1959). This reaction almost certainly occurs during normal digestion, and it has been suggested that this kinin formation may play an important role in the newborn by increasing the permeability of the blood vessels of the gut, thus aiding the intestinal absorption of the maternal antibodies present in colostrum.

Lewis (1959) has found a plasma kinin-forming enzyme in extracts of skins. This differs from the salivary enzyme by forming kinins rather slowly. When skin is damaged, as in burns, this enzyme may be activated and bring about slow but prolonged release of kinin, thus accounting for the long lasting vascular changes in damaged skin which are not due to histamine release.

It is tempting to speculate on other vasodilator functions of the plasma kinins. They may be the vasodilator substances responsible for reactive hyperaemia and the increased blood supply to skeletal muscles during exercise, but no evidence has yet been produced to support this hypothesis. The mechanism of vasodilatation in the central nervous system is still unknown; in this connection it is interesting that a kinin has been found in human cerebrospinal fluid, during periods of increased nervous activity, and in patients with pain. The more complete determination of the functions of the plasma kinins must await the discovery of a reliable method for their estimation in body fluids. One of the main difficulties in devising such a method is the rapidity with which kinins are inactivated. This problem is being investigated at the National Institute for Medical Research.

Chemistry

Since plasma kinins can be prepared from the plasma of different species by the action of various enzymes, the existence of a considerable number of different plasma kinins is theoretically possible. It is, therefore, unlikely that full structural analysis of each of them will be achieved in the immediate future. The plasma kinins derived from one animal species by different enzymes may be a single substance, but it is probable that small structural differences will be found amongst the plasma kinins of different animal species. Such species differences in the polypeptide field, when one or more amino-acids can replace others of related structure without appreciably affecting the biological properties of a polypeptide, are of common occurrence. Ox bradykinin is the plasma kinin prepared by incubating ox plasma or plasma globulins with trypsin or the venom of the snake *Bothrops jararaca* (Rocha e Silva *et al.*, 1949); it has been studied far more intensively than the other plasma kinins. This is probably because of the greater ease with which this substance can be prepared on a large scale; even so, the preparation of sufficient pure material for chemical work remains a difficult task.

Since bradykinin is released by trypsin, it was thought that the action of the snake venom was a type of proteolytic reaction. Recent work (Hamberg and Rocha e Silva, 1957 a and b) has shown, however, that the release of bradykinin may be related to the esterase activity of the snake venom rather than to its peptidase activity. This makes it seem possible that bradykinin is not bound into the polypeptide chain of a protein precursor, thus requiring the action of a peptidase for its release, but is attached by the more labile ester bond either to the terminal, or a side-chain, carboxyl group. It is now known that bradykinin

possesses a *C*-terminal arginine residue (see below); this would be in accord with its liberation by the proteolytic action of trypsin on a protein substrate. The mechanism of bradykinin release must therefore remain an open question at present. A plasma kinin, indistinguishable pharmacologically from bradykinin, is released from partially purified plasma globulin by the enzyme plasmin, which possesses esterolytic activity and has specificity requirements similar to those of trypsin. This problem has been studied recently by Lewis (1958). Plasmin is present in blood in the form of an inactive precursor plasminogen, which can be activated *in vitro* by various means, but the mechanism of its activation *in vivo* is not fully understood. The protein precursor of bradykinin has been shown to be in fraction IV (Cohn's nomenclature) of the bovine plasma proteins (Van Arman, 1955).

The polypeptide character of bradykinin was known soon after its discovery, and various chromatographic techniques used in the peptide field have been applied in attempts to purify it (Rocha e Silva, 1955; Andrade and Rocha e Silva, 1956). Ox bradykinin, isolated in the pure state at the National Institute for Medical Research, was found to be a peptide composed of the amino acids glycine, serine, proline, phenylalanine and arginine. Now that the pure material is at hand, the elucidation of the structure and the synthesis of bradykinin should shortly follow.

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SOME FACTORS IN THE PROBLEM OF INATTENTION

Accidents arising from lack of attention are remarkably frequent. Highly skilled drivers, pilots, or factory workers, on occasion and for no apparent reason, commit errors, or fail to take some action, without being able to account for the lapse. Even when such faults do not result in immediate disaster, they

can be an important source of economic loss because they derange highly complex manufacturing and other processes, which are nowadays often controlled by single operatives. Momentary inattention by a craftsman working in traditional ways may be relatively unimportant, but if a single person is in control of forces of several hundred horse power, his inattention may have dire consequences.

The Analogy between the Nervous System and Engineering Communication Systems

In recent years attempts have been made to elucidate problems of inattention by applying to the nervous system concepts derived from communication engineering. A radio or telephone channel can transmit only a limited number of different signals at any instant, and the rate of change from one signal to another which it can support is also limited. Individual messages comprised within a given range or ' spectrum ' of messages cannot be transmitted faster than at a certain critical rate, which depends on the probability of each message being sent; this critical rate can, in fact, be expressed in terms of an exact mathematical equation. Thus the rate of transmission of messages is relatively slow if there is a large number of alternative messages, or if the probability of each being sent is equal, or if each message is independent of the one before it; the time taken in transmission does not depend on the content of the messages, provided that a satisfactory coding system is employed. The mathematical basis of this problem was studied by C. E. Shannon of the Bell telephone Laboratories (Shannon and Weaver, 1949).

On somewhat similar lines it was shown in 1952 by W. E. Hick, working as a member of the Council's Applied Psychology Research Unit, that the reaction time of trained subjects to stimuli increases proportionately to the logarithm of the number of alternative stimuli employed. Furthermore, if the subjects were allowed to speed up their reaction time at the cost of making some errors, the decrease in reaction time recorded was in accord with Shannon's mathematical formula (Hick, 1952). These findings were confirmed and extended by R. Hyman (1953) of Johns Hopkins University, and by E. R. F. W. Crossman (1953) working for the Council in Cambridge. These workers showed in different ways that the average speed of human reaction to a given signal increases as it becomes more probable that, of the possible signals, this will be the one actually given. This relationship can also be expressed mathematically by Shannon's formula. Hyman also showed that when sequences of particular signals occur with undue frequency, the average reaction time changes accordingly.

These results, however, may not apply to exceptionally familiar or simple responses, as J. A. Leonard (1959) of the Applied Psychology Research Unit, and G. H. Mowbray, and M. V. Rhoades (1959) working at Johns Hopkins University, have found. But, with this limitation, it appears that over a wide range of experiments the mathematics of well-encoded radio and telephone channels apply also to the human nervous system. This has a bearing on the problem of inattention in man. It implies that the number of different situations between which a person must be prepared to discriminate at any instant, sets an important limit to his performance. If this limit is exceeded, even a clear signal may receive no appropriate response—just as it is impossible to introduce an extra message into a fully occupied communication channel in a telephone system.

This approach to human limitations brings out an important new principle—that the performance of a task is not necessarily precluded because another task is being performed at the same time. What matters, within limits, is not the number of tasks but rather the probability that an interfering situation will occur. To test this principle experimentally, D. E. Broadbent, Director of the Applied Psychology Research Unit, asked a number of people to answer a rapid stream of questions and, at the same time, to press a key whenever a buzzer sounded. He found that they gave fewer correct answers to those questions which were synchronous with the buzzer than to the others—a result which is not surprising on any theory. But the interference produced by the buzzer was still greater if the subjects had been told that they might have to move a foot in response to a third (visual) stimulus as well. The increased interference appeared if the subjects were expecting the additional signal even though no additional signal was given. It can be concluded that as the range of alternative stimuli presented for response becomes larger, it becomes progressively more difficult for a person to deal with combined stimulus-response sequences.

Another method of testing this was adopted by P. M. Fitts and his associates at Ohio State University (Bahrick *et al.*, 1954). They trained one group of people to respond to a series of visual signals in random sequence, and another group to respond to signals repeated in a regular pattern. Then a second task was imposed on each group, to be done at the same time. After a reasonable amount of practice, this second task was carried out less efficiently when the sequence of light signals was random than when they appeared in the regular predictable pattern.

It would seem that the everyday doctrine that one cannot do two things at once needs to be qualified. The nervous system should be regarded as having a limited ' capacity ' (in the sense defined in the theory of communication); there is a limitation in the rate at which discrimination can be made between signals, although this may not hold good for situations in which there has been much practice. In the light of these findings Broadbent (1958) reviewed a number of experiments on failures of attention. Four groups of experiments, each pointing to a different factor, were distinguished.

The Distraction Factor in Inattention

In a complex task requiring response to a number of independent sources of information the more the sources the more will be the errors of omission, even when the average rate of response required remains the same. This was shown by R. Conrad (1951) of the Applied Psychology Research Unit; and N. H. Mackworth (who for some years prior to 1959 was Director of the Unit) established that the incidence of such errors could largely be predicted by considering the extent to which signals from one source were simultaneous with those from another (Mackworth and Mackworth, 1956). The frequency with which signals are likely to occur simultaneously must increase when the number of sources increases, and this explains some of the difficulties which arise when a man has to operate several machines simultaneously in industry.

In some cases the excessive stimulation of bad environmental conditions may occupy part of the available communication ' capacity ' of a worker. For example, irrelevant noise of high intensity produces occasional errors in work,

especially when the noise is one which, if it were a signal in some task, would produce a particularly efficient reaction (Broadbent, 1957, Grimaldi, 1958). Noise seems therefore to distract attention rather than to reduce efficiency generally; otherwise a particular kind of noise would be associated with poor performance, whether it was a clear signal or something to be ignored.

The Fatigue Factor in Inattention

In much of the experimental research on failures of attention a technique introduced by Mackworth in 1943 has been used. He asked the subjects to report whenever they saw a particular brief signal during a long period in which signals were only occasionally presented (Mackworth, 1950). The number of unreported signals increased very markedly after half an hour. Since the task had been designed to simulate that of a radar operator on anti-submarine work, this experimental discovery attracted immediate attention, and was confirmed by analysis of actual submarine sightings. Experimental work by Bakan (1955) and Whittenburg *et al.* (1956) showed similar rapid deterioration in performance.

While it is clear that working even for a short period can be harmful to efficiency it is not so clear whether it is fatigue that causes the reduction in capacity, or a diversion of capacity to activities other than the task in hand. Broadbent (1958), taking the latter view, argued that after an individual has been working for some time he becomes more distractable but his actual capacity is not lessened. The experimental basis for this argument is that J. Deese (1955) of Johns Hopkins University, E. Elliott (1957) for the Royal Navy, and also Broadbent (1958) found no downward trend in efficiency as work proceded on tasks in which the ill effects of momentary distraction were minimized. It is, however, still possible that prolonged work reduces communication capacity although positive evidence that this is a direct effect is lacking.

The Expectancy Factor

As has been said, when there is satisfactory coding in a communication channel transmission time is inversely related to the probability of the message being sent. While such a coding makes the best use of the available capacity, it implies some inefficiency in dealing with *unexpected* messages. Correspondingly we might expect that human beings, if they are using their capacity efficiently, will be poor at responding to unexpected signals; and this has been emphasized by Deese (1955). Deese, Jenkins of the Massachusetts Institute of Technology, and H. M. Bowen of the Applied Psychology Research Unit have all reported that when signals come more frequently in one test than they do in another, and are therefore more expected, it is more probable that any given signal will be detected. These results establish the importance of expectancy in situations demanding attention.

The Factor of Arousal

Failures of attention have so far been discussed as due either to misapplication of capacity because of 'distraction', or to disturbing side-effects of adjusting to the probability that various events will occur. They may also be due to temporary rises and falls in the capacity available.

In recent years there has been considerable interest in the role of stimulation as a means of keeping the nervous system in an efficient state. This interest derives from work by H. W. Magoun and his associates in California, the

psychological implications of which have been reviewed by R. J. Ellingson (1956) and by I. Samuels (1959). Briefly the basic concept is that stimuli not only produce specific discriminative responses in particular sensory projection areas of the cerebral cortex, but also bring about a non-specific facilitation of responses in other regions of the brain. According to this view, widespread non-specific alerting activity is effected through the reticular formation, a concentration of nerve cells at the base of the brain which has connections both with the sense organs and with the cortex; this mechanism acts in parallel with the better-known direct pathways linking the senses to the cortex. If the connecting fibres through the reticular formation are cut, a drowsy and inactive state may result, like that produced by a constant and unstimulating environment. This is illustrated by the startling experiments of D. O. Hebb and his colleagues at McGill University. Volunteers were kept under conditions which deprived them of stimulation as far as was physically possible, for example, by the use of goggles to prevent vision, and by acoustic insulation to exclude sound. Within a few days the response of these men to different stimuli and their performance of a wide variety of tasks was seriously impaired: some even seemed to suffer from hallucinations, and the experiments had to be discontinued after quite short exposures. As Hebb (1955) pointed out, the findings suggest that there is a fundamental need for general stimulation of the nervous system.

It can be inferred that exposure to unstimulating conditions, such, for example, as driving along a straight road in a modern saloon car for a long period, may bring about decreased efficiency of response to an outside signal.

Conclusion

Each of the factors discussed above has been shown, in the laboratory, to produce human errors of a type apparently similar to those which cause accidents and industrial wastage. By increasing the frequency of demands for action, or reducing the distraction factor including the noise level, these errors can in certain circumstances be made less frequent; but Mackworth (1950) adduced experimental evidence to show that such errors cannot be reduced by exhortation. Findings of this sort should influence our attitude to practical problems of inattention.

In addition, these results suggest that to some extent the nervous system acts as a whole, allocating as far as possible from a limited amount of resources those required to meet particular situations; it does not act merely as an assembly of independent stimulus-response links. Consequently the functioning of the nervous system in matters of attention seems to be more analogous to that of a single channel of limited capacity in a radio or telephone system than to the quite different kind of functioning which would be necessary if each stimulus-response connection were independent of all others.

These experiments on performance therefore contribute to our general understanding of the functioning of those mechanisms of the human nervous system which underlie behaviour.

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J. G. Graham, M.B. (*Falkland Islands Dependencies Survey*)
G. Grimby, M.D. (*Göteborg*)
I. G. F. Hampton, B.Sc. (*Falkland Islands Dependencies Survey*)
D. P. McN. Jones, M.B. (*Falkland Islands Dependencies Survey*)
R. Jonsson, Med.Lic. (*Lund*)
G. Lundin, M.D. (*Lund*)
D. J. Kidd, M.B. (*Nova Scotia*)
N. W. M. Orr, M.B. (*Falkland Islands Dependencies Survey*
H. T. Wyatt, M.B. (*Falkland Islands Dependencies Survey*)

BACTERIOLOGY AND VIRUS RESEARCH

C. H. Andrewes, M.D., F.R.C.P., F.R.S. (*Deputy Director of the Institute*)
A. C. Allison, B.M., D.Phil.
J. A. Armstrong, M.B., M.Sc.
Miss Y. M. Barr, B.A.
F. E. Buckland, D.M.
M. L. Bynoe, M.B., D.T.M. & H., D.Obst.R.C.O.G.
Miss D. M. Chaproniere, Ph.D.
Miss C. Craven, B.Sc.
Miss F. C. Fildes, B.Sc.
Miss E. W. Garbutt, B.A.
A. W. Gledhill, Sc.D., M.R.C.V.S.
P. M. d'Arcy Hart, C.B.E., M.D., F.R.C.P. (*part-time*)
Mrs. G. Hitchcock, B.A.
A. Isaacs, M.D.
Miss M. F. Jamieson, M.B., B.Sc.†
H. G. Klemperer, B.M., Ph.D.
Miss J. S. F. Niven, M.D.
Miss K. R. Parsons, B.Sc.
H. G. Pereira, Dr.Med.
J. S. Porterfield, M.D.
R. J. W. Rees, M.B., B.Sc.
D. A. J. Tyrrell, M.D., M.R.C.P.
M. F. R. Waters, M.B., M.R.C.P.‡
Miss M. A. Westwood, B.Sc.

Visiting Workers

S. M. Navashin, Cand.Med.Sci. (*Moscow*)
Miss G. Selzer, M.B. (*Cape Town*)

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* On leave of absence at the University of Illinois.
† Seconded to West African Council for Medical Research.
‡ On secondment for work in Malaya.

BACTERIAL PHYSIOLOGY

M. R. Pollock, M.B.
J. F. Collins, D.Phil.
J. Mandelstam, Ph.D.*
H. R. Perkins, Ph.D.
M. H. Richmond, Ph.D.
H. J. Rogers, Ph.D.
P. H. A. Sneath, M.D., Dip.Bact.†
D. L. Swallow, D.Phil.

Attached and Visiting Workers

R. A. Darrow, Ph.D.
J. D. Duerksen, Ph.D. (*Madison*)
Miss E. Janczura, Mgr.Chem. (*Warsaw*)
D. Kushner, Ph.D. (*Sault Ste. Marie*)

CHEMOTHERAPY

F. Hawking, D.M., M.R.C.P., D.T.M.‡
Miss L. M. Bradburn, B.Sc.
A. T. Fuller, Ph.D., F.R.I.C.
J. D. Fulton, M.B., Ph.D., D.T.M.
J. A. McFadzean, M.B.
P. J. C. Smith, Ph.D. (*until Aug., 1959*)
S. R. Smithers, Ph.D.
Miss A. E. R. Taylor, Ph.D. (*until Aug., 1959*)

Attached Worker

E. Meerovitch, Ph.D. (*Montreal*)

IMMUNOLOGY

J. H. Humphrey, M.D.
Miss B. A. Askonas, Ph.D.
Miss B. M. Balfour, B.A., M.R.C.S.
W. E. Brocklehurst, Ph.D.
C. P. Farthing, M.B.
J. L. Turk, M.D.

Attached and Visiting Workers

K. F. Austen, M.D. (*Boston, Mass.*)
S. L. Clark, M.D. (*St. Louis*)
Miss J. Rhodes, Ph.D. (*Copenhagen*)
A. B. Stavitsky, Ph.D., V.M.D. (*Cleveland, Ohio*)

BIOLOGICAL STANDARDS

D. G. Evans, D.Sc., F.R.S.
D. R. Bangham, M.B.
Miss S. Findley, B.Sc.
L. F. Hewitt, D.Sc., F.R.I.C.
Miss M. Kogut, Ph.D.
J. W. Lightbown, M.Sc., Dip.Bact.
D. A. Long, M.D. (*until March, 1959*)
Miss M. V. Mussett, B.Sc.
Miss M. Reed, B.Sc.
Mrs. J. Shewell, Ph.D. (*until Dec., 1958*)
D. E. H. Tee, M.B.

Control Laboratory:

T. S. L. Beswick, M.D., M.R.C.P.
C. R. Coid, Ph.D., M.R.C.V.S.
Miss H. Grutzner, B.Sc.
D. I. Magrath, Ph.D.
T. W. Osborn, M.B.
F. T. Perkins, Ph.D.
Miss A. Petts, B.Sc.
Mrs. K. Russell (*part-time*)
M. P. Stack-Dunne, Ph.D.
J. O'H. Tobin, B.M., Dip.Bact.
Miss R. A. Yetts, B.Sc.
Miss G. L. Williams, B.Sc.

Visiting Workers

Miss M. Cotes, M.B., Ph.D., (*London*)
G. F. Gause, Dr.Biol.Sci. (*Moscow*)
D. Ikic, M.D. (*Zagreb*)
Miss A. M. Peach, M.B. (*London*)
K. C. Sinha, R.O., V.V. (*Bareilly, India*)

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* On leave of absence at Harvard Medical School, Boston and University of Wisconsin.
† On leave of absence at Stanford University, California.
‡ On secondment for work at Central Drug Research Institute, Lucknow, India.

ENGINEERING

W. C. Lister, M.I.E.E., F.Inst.P.
A. R. Greaves (*Clerk of Works*)
W. J. Perkins, A.M.I.E.E., M.Brit.I.R.E.
S. J. Sterrett, A.M.I.Mech.E., A.M.I.Prod.E.
B. M. Wright, M.B.

LABORATORY ANIMALS DIVISION

C. R. Austin, B.V.Sc., D.Sc.
D. J. Short, M.B.E. (*Technical Superintendent*)

Dental Research

P. J. Holloway, B.D.S., L.D.S., R.C.S., Ph.D.*

Neurophysiological Research

S. L. Sherwood, L.R.C.P., L.R.C.S.E. (*part-time*) (*until Aug., 1959*)

LIBRARY

Miss J. R. Taylor, B.A.
Mrs. R. E. Arnstein, B.A.
Miss M. Harvey, B.A.

Visiting Worker

Mrs. S. Shergold (*Porton*)

Director's Administrative Staff

J. H. Platts (*Supplies Officer*)
L. J. Hale (*Personnel Officer*)

The work of the Institute is generally designed to cover as wide a field as possible in basic non-clinical medical research, and investigations undertaken there are mostly of a long-term character. In occasional instances, such as the research on the common cold, the work verges on the clinical field; and members of the scientific staff at the Institute commonly collaborate in clinical developments arising from their discoveries. Certain major themes, such as chemotherapy, especially in its biochemical and biological aspects, and virus diseases, are constantly under study; sometimes, as in the case of the Division of Human Physiology where the main task is to investigate the effects of variations in temperature on human performance, a fairly closely defined field of research may be allocated; for the rest, the direction that the work takes is largely determined by the particular interests of the senior members of the staff. This principle is at present illustrated by the preoccupation of the Division of Biochemistry with problems of biosynthesis and intermediary metabolism, by the work of the Division of Physiology and Pharmacology on the access to and action on the brain of pharmacologically active substances, and by the investigations in the Division of Experimental Biology into the survival of cells, tissues and whole animals at low temperatures, into problems of the fertilization process, and into the grafting of endocrine tissues.

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.

* On leave of absence in the Harvard School of Dental Medicine, Boston.

BIOCHEMISTRY

1. Biosynthesis:
   (1) Protein synthesis in liver cell mitochondria, with special reference to synthesis of catalase.
   (2) Effect of virus infection on RNA turnover in mouse ascites cells.
   (3) Penicillin biosynthesis; (a) evidence that cystinylvaline is a precursor; (b) isolation from *P. chrysogenum* of the aminoadipyl analogue of glutathione, and evidence for a common biosynthetic pathway for penicillin and cephalosporin N.
   (4) Role of vitamin B_{12} in biosynthesis of amino-acids in *Ochromonas malhamensis.*
   (5) Biosynthesis of phospholipids in blood; study of relative contributions of leucocytes, reticulocytes and mature red cells.
   (6) Study of the biosynthesis of thiamine in yeast.

2. Proteins and amino-acids:
   (1) Isolation of pure bradykinin and determination of its amino-acid composition.
   (2) Further studies of the synthesis of hypertensin.
   (3) Amino-acid analyses of proteins.
   (4) Further studies of the parapepsins.
   (5) Purification of spleen cathepsin D and isolation of different forms of the enzyme.
   (6) Labelling of proteins in the guanidine group of arginine as a new method for studying protein turnover.
   (7) Protein catabolism in liver and spleen.
   (8) Comparative physico-chemical study of serum albumins of different species.
   (9) Demonstration of metabolic heterogeneity of human serum albumin.
   (10) Clinical studies of plasma protein metabolism in the nephrotic syndrome and in idiopathic hypoproteinaemia.
   (11) Comparative spectrophotometric studies of haemoglobins.
   (12) Development of technique for separating haemoglobins by electrophoresis in agar gel.

3. Lipids:
   (1) Further applications of gas chromatography to analysis of long-chain fatty acids.
   (2) Analyses of fatty acid composition of human blood after prolonged exposure to cold and heavy physical work.
   (3) Studies of composition of blood lipids in atherosclerosis.
   (4) Investigation of effect of dietary fat on faecal fat in idiopathic steatorrhea; discovery of new fatty acid in human faecal fat.
   (5) Study of lipid content of influenza virus; demonstration of concentration by the virus of lipid components of the host cell.

4. Hormones:
   (1) Action of thyroid hormones on bone growth in tissue culture.
   (2) Effect of high iodide feeding on thyroid function in the rat.
   (3) Antithyroid effect of iodopyrine.
   (4) Demonstration that the thyroxine-binding protein of the blood is a complex of prealbumin with a globulin fraction.
   (5) Purification of thyroxine deiodinase and study of the properties of the enzyme.
   (6) Suppressing action of cardiac glycosides on iodide concentration by thyroid slices; role of potassium ions in this effect.
   (7) Studies of sex hormone production by the rat adrenal cortex.
   (8) Further investigations of corticotrophin with special reference to methods of assay.

ORGANIC CHEMISTRY

1. Micrococcin P; confirmation of polythiazole nature of this antibiotic; development of a new method for determining structure of substituted thiazoles.
2. Poppy alkaloids; extension of survey of poppy alkaloids in relation to epidemic glaucoma; study of fate of sanguinarine in the body and demonstration of a new type of metabolic transformation.

3. Further studies of the chemistry of the queen substance of bees.
4. Developments of the synthesis of ^{14}C-labelled vitamin D_2.
5. Synthesis of macrocyclon analogues of defined molecular size.
6. Chemical studies of an extract of oak galls showing antihistaminic activity.
7. Experiments towards the synthesis of vitamin B_{12}.
8. Further work on stereospecific synthesis of olefins.

CHEMOTHERAPY

1. Continued studies of metabolism of *Toxoplasma gondii* and *Spirochaeta recurrentis.*
2. Pathology of toxoplasma infection in the rat.
3. Attempts to transfer drug resistance in trypanosomes by means of extracts containing DNA.
4. Filariasis;
   (1) Experiments on morphology, life history and transmission of various filarial worms.
   (2) Filaricidal action of piperazine derivatives.
   (3) Role of spleen in destruction of microfilariae.
5. Fate in the body of the trypanocidal drug prothidium.
6. Immunological studies of experimental infections with trypanosomes and schistosomes.
7. Development of tissue culture method for examining action of drugs on *Theileria annulata.*
8. Study of cultivation of *Entamoeba invadens* in tissue culture.
9. Tuberculosis:
   (1) Examination of further surface-active agents in experimental tuberculosis in the mouse.
   (2) Study of chronic tuberculosis in the mouse; demonstration that bacilli are in a resting phase, and that macrocyclon is inactive in this form of infection.
   (3) Protection of *M. tuberculosis* against acid by surface-active agents.
10. Leprosy:
   (1) Further improvements in the cultivation of *M. lepraemurium* in rat fibroblasts.
   (2) Extended clinical trials of macrocyclon.
   (3) Increase of length of *M. lepraemurium* in modified bacteriological nutrient media.
   (4) Further attempts to transmit *M. leprae* to experimental animals.
   (5) Studies on the uptake of leprosy bacilli by nerves.
   (6) Electron microscopic demonstration of morphological changes in rat leprosy bacilli associated with loss of viability.

BACTERIAL PHYSIOLOGY

1. Studies of the physiological basis of the liberation of extracellular enzymes from bacteria.
2. Isolation of components of bacterial cell walls, with special reference to the use of baryta as hydrolytic agent.
3. Studies of the biosynthesis of bacterial cell wall material; demonstration of stimulating action of soluble cell components on incorporation of amino-acids into cell walls.
4. Extracellular factors influencing enzyme synthesis in *B. cereus* and *Staph. aureus;* effects of structural analogues of amino-acids.
5. Development of technique for the study of enzymic reactions in single bacterial cells.
6. Study of the soluble, non-cytochrome electron transport system of *B. subtilis,* with special reference to the action of a streptomycin antagonist.

VIRUS RESEARCH

1. Continued epidemiological studies of influenza.
2. Antigenic analysis of influenza strains.
3. Cytopathic effects of influenza virus and adenoviruses studied in tissue culture.
4. Experimental epidemiological study of Newcastle disease in chicks.
5. Factors modifying experimental virus infections, with special reference to bacterial endotoxins.
6. Studies of effect of virus infections on biochemical processes in cells.

7. Development of plaque inhibition test for virus antibodies and other anti-viral agents.
8. Determination of nucleic acid content of purified particles of different viruses; demonstration of regularities and interpretation in relation to genetic theory.
9. Rate of growth of adenoviruses in cells and correlation of stage of multiplication with development of specific antigens.
10. Study of adenovirus antigens by gel-diffusion precipitation technique.

11. Interferon:
    (1) Continued experiments on purification of interferon; demonstration that purified preparations are non-antigenic.
    (2) Demonstration that the protective effect of interferon is greater in infections of animals of the same species as that in which it was originally prepared.
    (3) Observation that interferon protects resting cells more effectively than actively dividing cells.
    (4) Study of interferon production by representative RNA– and DNA–containing viruses.
    (5) Experimental support for view that interferon protects against viral infection by deviating the cell from synthesis of virus to synthesis of interferon itself.

12. Common Cold Research Unit:
    (1) Further studies of the common cold in human volunteers.
    (2) Continued attempts to grow the common cold virus in tissue culture.
    (3) Studies of infection and antibody response in volunteers inoculated with attenuated adenovirus.
    (4) Identification of the ' U ' virus as an Echo virus.
    (5) Inoculation of volunteers with haemadsorption viruses and with Echo 20 virus.
    (6) Study of antigenic relations of influenza A viruses recovered from animals.

EXPERIMENTAL PATHOLOGY AND IMMUNOLOGY

1. Immune tolerance in rabbits; demonstration of the importance of persistence of minimal amounts of antigen.
2. Distinction between the intracellular fate of homologous and heterologous proteins.
3. Characterization of antigens by the gel diffusion technique.
4. Synthesis of γ-globulin and antibody *in vitro*, with special reference to a culture of tumour cells.
5. Localization of antigens and antibodies in the tissues of rats after injection.
6. Further studies of the heterogeneity of γ-globulins; development of fractionation techniques.
7. Continued investigation of immunochemical properties of the products of papain digestion of γ-globulin.
8. Effect of thyroid function on γ-globulin catabolism in rats and guinea-pigs.
9. Further studies of anaphylaxis, with special reference to the slow-reacting substance liberated by lung tissue during the anaphylactic reaction.
10. Further investigation of transplacental transfer of protein; transplacental movement of thyroxine and of iodide; development of technique for operations on the foetus without interruption of normal completion of pregnancy and delivery in the Rhesus monkey.
11. Study of action of bacterial toxins on tissue cultures.
12. Improvements in methods of safety and potency testing of poliomyelitis vaccines.
13. Further studies of antibody levels in persons vaccinated against poliomyelitis.
14. Tests in monkeys of factors affecting the virulence of the Brunenders strain of type 1 poliomyelitis virus.

PHYSIOLOGY AND PHARMACOLOGY

1. Study of the central tubocurarine-noradrenaline antagonism.
2. Demonstration of the passage of adrenaline from the blood stream into the ventricular-subarachnoidal space.
3. Pathways of absorption of histamine from the cerebral ventricles into the blood.
4. Experiments on the absorption of histamine and of bromophenol blue from the cerebral ventricles into the brain substances; demonstration that penetration is much greater into grey matter than into white matter.

5. Physiological studies of the antihistaminic substance extractable from oak-galls; demonstation of prolonged protection of guinea-pig against bronchospasm from a histamine aerosol.
6. Further experiments on active muscle vasodilatation produced by electrical stimulation of various areas of the brain stem; demonstration of the anatomical components of a reflex arc; relation of the observations to the defence reaction.
7. Plasma kinins:
   (1) Purification of bradykinin.
   (2) Estimation of plasma kinins in blood.
8. Experimental development in dogs of a technique for the measurement of cerebral blood flow.

HUMAN PHYSIOLOGY

1. Studies of the effect of suggestion under hypnosis on the peripheral circulation in man; conclusion that occasional positive results are probably due to emotional stimuli.
2. Quantitative measurement of acclimatization to heat in normal young men; observation that such acclimatization is lost fairly rapidly.
3. Further studies of the action of rubefacients on forearm blood flow; demonstration of the presence of cutaneous vasoconstrictor nerves in the forearm.
4. Investigation of vasodilator mechanisms in the skin of the body other than the forearm.
5. Field investigations in the Antarctic, with special reference to clothing; advisory work in connection with antarctic expeditions and further development of polar sledging rations.
6. Physiological studies of the performance of athletes.
7. Measurement of the metabolic rate during sleep.
8. Investigation of carbon monoxide content of foetal and maternal blood; demonstration that the content is higher in the foetus.
9. Studies of the effects of solar radiation on man.
10. Development of various instruments for quantitative measurements in human physiology.

EXPERIMENTAL BIOLOGY

1. Discovery that intra- and inter-strain homograft reactions and heterograft reactions in mice are diminished by induced deficiency of pyridoxine.
2. Further studies of orthotopic grafting, with special reference to ovaries.
3. Successful experiments on grafting of frozen thyroid tissue; beneficial effects of glycerol treatment before freezing.
4. Continued work on low temperature preservation of bone marrow.
5. Demonstration of power of spermatozoa to penetrate cells of the female genital tract.
6. Further studies of rat eggs by fluorescence microscopy.
7. Experiments on heterologous fertilization and hydridization in mammals.
8. Demonstration of a pregnancy block induced in recently mated female rats by placing in proximity, but not necessarily in physical contact, with strange males.
9. Study of effects of hypothermia on radiosensitivity ; demonstration in mice of protection of testis, and of spleen, by cooling to a body temperature of 0–1°C; relation of protective effect to lowered tissue oxygen tension.

BIOPHYSICS AND OPTICS

1. Ultracentrifugal and electrophoretic analysis of proteins; applications to characterization of parapepsins, spleen cathepsins and other proteins of biological interest; also to the study of the papain digestion products of γ-globulin.
2. Development of methods for showing contrast in electron microscopy; application of electron microscopy to ultra-thin histological sections.
3. Applications of spectrophotometry to problems of chemical structure.
4. X-ray crystallography of compounds of biological interest.
5. Developments in amino-acid analysis.
6. Development of radio-active counting methods.

1. Establishment of new International Standards for insulin (fourth) and streptomycin (second), and of International Reference Preparations for neomycin, novobiocin, nystatin and oleandomycin.
2. Preparatory work for International Standards of corticotrophin (third) and prolactin (second), and for International Reference Preparations of vitamin B_{12}, human menopausal gonadotrophin, penicillin PAM, amphotericin, kanamycin, leucomycin, ristocetin and vancomycin.
3. Establishment of British Standards for penicillin (third) and for poliomyelitis antisera types 1, 2 and 3.
4. Control tests on poliomyelitis vaccine and BCG vaccine.
5. Control tests on corticotrophin and insulin.
6. Advisory work for Ministry of Health (Therapeutic Substances Act) including revision of Regulations.
7. Advisory work for British Pharmacopoeia Commission, including preparation of monographs.

INSTRUMENTATION AND ENGINEERING

1. Improved diathermy equipment.
2. Development of a transistorized general purpose stimulator.
3. Blood-flow monitor.
4. Design and construction of an improved polarograph.
5. Apparatus for centrifugal paper strip chromatography.
6. Construction of phantom for radiation measurements.
7. Radioactive chromatographic scanner.
8. Development of apparatus for sustained cell culture.
9. Development of method for kinetic gas analysis.
10. Construction of many new electrical and mechanical instruments for laboratory use other than those specifically mentioned. Maintenance, servicing and modification of equipment. Constructional work to meet altered needs within the Institute.

ANIMAL DIVISION

1. Enlargement of cat colony to cover the total needs of the Institute.
2. Design and production of an improved pelleted diet for rabbits and guinea pigs.

Publications

ABRAHAMS, V. C. Venous temperature registration, and its use as an index of muscle blood flow. *J. Physiol.*, 1959, **145**, 20P.

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ARMSTRONG, J. A. and HOPPER, P. K. Fluorescence and phase-contrast microscopy of human cell cultures infected with adenovirus. *Exp. Cell Res.*, 1959, **16**, 584.

ARNSTEIN, H. R. V. Biological chemistry. 5. The biosynthesis of penicillin and some other antibiotics. *Rep. Progr. Chem.*, 1957, **54**, 339.
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Role of the rodent acrosome and perforatorium in fertilization. *ibid.*, 1958, **149**, 241.
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Presence of spermatozoa in the uterine-tube mucosa of bats. *J. Endocrin.*, 1959, **18**, viii.

AUSTIN, C. R. and LOVELOCK, J. E. Permeability of rabbit, rat and hamster egg membranes. *Exp. Cell Res.*, 1958, **15**, 260.

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Research Units

DEPARTMENT OF CLINICAL RESEARCH

UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL, LONDON, W.C.1

(1919)

*Director**

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

Staff

C. F. Barnaby, M.Sc.
Miss C. J. Cameron, M.Sc.
(*until April*, 1959)
D. A. W. Edwards, M.D., M.R.C.P.
J. Lennard-Jones, M.D., M.R.C.P.
L. G. Piaskett, B.A.
E. N. Rowlands, M.D., B.Sc., F.R.C.P.†

Attached Worker

E. S. Shalom, M.B.

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:
   (1) Study of the speed of hormonal metabolism in normal and overactive glands.
   (2) Study of the concentration of plasma iodide and organic iodine derivates in patients with abnormalities of thyroid function and with thyroid cancer; and during administration of thyroid hormone preparations.
   (3) Investigation of metabolic defects in endemic goitre.
   (4) Treatment of thyroid overactivity with radioactive iodine.
   (5) Examination of the metabolic fate of thyroxine using multiple labelling techniques.
2. Thyroid cancer:
   (1) Evaluation of the radioiodine treatment of thyroid cancer, criteria of suitability and indications for stopping treatment.
   (2) Study of body radiation received during such treatment and assessment of any consequent hazards.
   (3) Comparison of metabolites produced by cancer tissue with those from normal or overactive glands.
   (4) Study of techniques for localization of radioisotope distribution within the body.
   (5) Examination of the suitability of large plastic phosphors for determination of radioisotope distribution within the body.
3. Gastroenterology:
   (1) Manometric studies of the cardiac sphincter in achalasia.
   (2) Manometric studies on the applied pharmacology of the oesophagus in normals and in achalasia.
   (3) Comparison of open tubes and miniature balloons for studying the sphincteric mechanisms of the gut.
   (4) Study of the discriminatory value of tests of gastric secretory function in the dyspepsias.
   (5) Studies on initial rates of fat absorption in health and disease, using labelled fat.

(*Publications see p.* 154)

* Salary of post largely provided by permanent endowment from Rockefeller Foundation.
† Working also at Central Middlesex Hospital, London, N.W.10.

NEUROLOGICAL RESEARCH UNIT

NATIONAL HOSPITAL FOR NERVOUS DISEASES, QUEEN SQUARE, LONDON, W.C.1

(1933)

Director

E. A. Carmichael, C.B.E., M.B., F.R.C.P.

Staff

J. A. V. Bates, M.B.
G. D. Dawson, M.B., M.Sc.*
A. M. Halliday, M.B., B.Sc.
Miss R. Mingay, B.Sc.
P. W. Nathan, M.D., M.R.C.P.
Miss M. C. Smith, M.D., B.Sc.

Attached Worker

R. Efron, M.D. (*Harvard*)

The Unit studies the nervous system of man by observing the response of healthy persons to various applied stimuli, and the changes in function and structure resulting from disease or its treatment.

Summary of Research

1. Cerebral action potentials :
   (1) The elaboration of methods for recording cerebral action potentials.
   (2) Design and assembly of apparatus for recording direct from the cerebral cortex during surgical operations and by stereotactic methods.
   (3) Detection of focal cerebral abnormalities in epileptics.
2. Nerve and spinal cord :
   (1) Sensory and autonomic functions in inoperable cancer before and after cordotomy, and their correlation with histological changes.
   (2) Histological studies of nerve cell degeneration following posterior root section and tract degeneration following cordotomy.
   (3) Histology of lesions in the region of the basal ganglia.
3. Cerebral function:
   (1) Changes occurring following lesions surgically placed in the region of the basal ganglia and after decortication.
   (2) The underlying mechanism responsible for ' attention '.

(*Publications see p.* 154)

DEPARTMENT OF EXPERIMENTAL MEDICINE

TENNIS COURT ROAD

and

5, SHAFTESBURY ROAD, CAMBRIDGE

(1945)

Director

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

Assistant Director

Miss E. M. Widdowson, D.Sc.

Staff

Miss I. M. Barrett, B.Sc.
J. W. T. Dickerson, B.Sc.
M. Evans, M.B. (*until July*, 1959)
Mrs. L. E. Hill, M.D., M.R.C.P.
G. C. Kennedy, M.B., Ph.D.
D. A. T. Southgate, B.Sc.
Miss M. W. Stanier, D.Phil.

* Working at the Department of Physiology, University College London.

Attached Workers

P. Cannon, M.B. (*Royal Navy*)
J. Crawford, M.D. (*Assistant Professor of Pediatrics, Harvard Medical School*)
C. T. G. Flear, M.B. (*Berkeley Bye-Fellow, Gonville and Caius College*)
Mrs. E. M. Glauser, M.D. (*Kate Hurd Mead Fellow, Philadelphia*)
N. Hatemi, M.D. (*Istanbul*)
Z. Hruza (*Prague*)
W. R. Keatinge, M.B. (*Elmore Student*)
M. Kopecky (*Prague*)
J. Lát (*Prague*)
L. Lawn, M.B. (*Voluntary worker*)
Miss D. M. Nutborne, M.B. (*M.R.C. Clinical Research Fellow*)
Miss J. E. Slater, B.Sc. (*Joseph Rank Ltd., Studentship*)
J. M. Walshe, M.B., M.R.C.P.

The Department is studying certain aspects of metabolism and nutrition, and in particular the changes which take place during growth, in states of undernutrition and disease. The work includes studies of normal infants and adults, of patients and of animals. The pharmacology of chlorothiazid has recently been investigated in relation to the use of the drug in the treatment of diabetes insipidus; the effects of penicillamine on Wilson's disease are also being explored.

Summary of Research

1. Effect of development, undernutrition, and rehabilitation on the composition of the body, its tissues, and its cells in man, pigs, poultry and rats.
2. The effect of accelerated and retarded development on chemical structure and ageing.
3. The relationship between central nervous excitability and body growth.
4. Hypothalamic regulation of water and energy expenditure and hormone production.
5. Chemotherapy of diabetes insipidus.
6. Relation of overnutrition to growth and diabetes, and to renal disease.
7. Food, growth and homoeostasis in the newborn period.
8. Renal function of infants and animals before and after birth.
9. Acid-base regulation in the newborn.
10. Active ion transport in foetal membranes.
11. Electrolyte metabolism in heart failure.
12. Copper metabolism in man.
13. The control of body temperature under water and the effect of work and clothing upon it.
14. The effect of chilling on the cardiovascular system.
15. Preparation of new tables giving the composition of foods (including vitamins and amino-acids).

(*Publications see p.* 154)

RHEUMATISM RESEARCH UNIT

AREA CENTRAL LABORATORY, MANOR HOSPITAL, BATH

(1958)

Honorary Directing Committee

Professor C. Bruce Perry, M.D., F.R.C.P. (*Chairman*)

J. A. Cosh, M.D., M.R.C.P. (*Secretary*)
Professor J. E. Harris, Ph.D.
Professor H. S. Heller, M.D., Ph.D.
Professor T. F. Hewer, M.D., F.R.C.P.
L. C. Hill, M.D., F.R.C.P.
G. C. Kelly, C.B.E., M.D., B.Sc.
G. D. Kersley, M.D., F.R.C.P.
H. J. Rogers, Ph.D.

Staff

E. R. Cook, F.R.I.C.
D. P. Page Thomas, M.B.
P. J. C. Smith, Ph.D.

The Unit is studying the proliferative synovitis that occurs in rheumatoid arthritis and its relationship to an experimental synovitis produced in the rabbit.

Summary of Research

1. Comparison between carrageenin induced synovitis in the rabbit and that produced by various related polysaccharides.
2. The effect of synovial proliferation upon co-enzyme levels.
3. The variation in creatine phosphate, adenosine triphosphate and adenosine diphosphate contents of synovial tissues in relation to the proliferative process.
4. The effect and mode of action of hydrocortisone upon synovial proliferation.

RHEUMATISM RESEARCH UNIT

CANADIAN RED CROSS MEMORIAL HOSPITAL, TAPLOW, MAIDENHEAD

(1958)

Honorary Director

Professor E. G. L. Bywaters, F.R.C.P.

Staff

Miss B. M. Ansell, M.B., M.R.C.P.
Mrs. P. C. Brown, M.D.
R. Consden, Ph.D.
L. E. Glynn, M.D., B.Sc. M.R.C.P.
E. J. Holborow, M.D.
A. Howard, B.Sc.
G. Loewi, D.M.

Visiting and Attached Workers

G. L. Asherson, B.M., M.R.C.P. (*Beit Fellow*)
S. K. Banerjee, M.B., Ph.D. (*Study Leave from Indian Govt.*)
J. Baum, M.D. (*Fellow, U.S.A. National Institute of Arthritis and Metabolic Diseases*)
Mary E. Carter, M.B. (*Empire Rheumatism Council grant-holder*)
J. Colover, M.D., M.R.C.P. (*M.R.C. grant-holder*)
J. R. David, M.D. (*Fellow, U.S.A. National Institute of Arthritis and Metabolic Diseases*)
D. M. Weir, M.B. (*Empire Rheumatism Council grant-holder*)

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

Summary of Research

1. Changes in connective tissue with age and disease.
2. The use of fluorescein-labelled antibodies to localize tissue antigens and antibodies, and to study the distribution of blood group substances.
3. The experimental production of lesions by auto-immune methods.
4. The effect of sulphated polysaccharides on the processes of ossification.
5. Family study of rheumatic fever and rheumatoid arthritis, 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.

(*Publications see pp.* 155–156)

CLINICAL ENDOCRINOLOGY RESEARCH UNIT

2, FORREST ROAD, EDINBURGH, 1.

(1946)

Honorary Directing Committee

G. F. Marrian, D.Sc., F.R.S. (*Chairman*)

Professor J. Bruce, C.B.E., M.B., F.R.C.S.E.
Professor Sir Derrick Dunlop, M.D., F.R.C.P.
Professor R. J. Kellar, M.B.E., M.B., F.R.C.S.E., F.R.C.P.E., F.R.C.O.G.
Professor W. L. M. Perry, O.B.E., M.D.

Secretary to the Committee
J. A. Strong, M.B.E., M.B., F.R.C.P.E.

Assistant Directors
J. A. Loraine, M.B., D.Sc., M.R.C.P.E.
J. B. Brown, Ph.D.

Staff
Miss J. R. Brown, B.Sc.
K. Fotherby, Ph.D.
J. A. Hodgson, B.Sc.
K. C. Hooper, Ph.D.
Miss E. J. Roy, B.Sc.

Attached Workers
M. Apostolakis, M.D. (*Athens*)
Miss H. E. C. Cargill Thompson, B.Sc. (*Melville Trust*)
A. Harkness, M.B., M.R.C.P.E. (*Edinburgh University*)
Joyce D. Baird, M.B.

The Unit continues to be concerned with the development of methods of assay for hormones in biological fluids. These and other established methods are being applied to the study of a variety of clinical problems.

Summary of Research

1. Examination of methods for the assay of pituitary gonadotrophins, growth hormone and thyrotrophin in biological fluids.
2. Isolation from human placentae of enzymes destroying oxytocin and vasopressin.
3. Assay of plasma insulin-like activity.
4. Biological activity of newly discovered oestrogens.
5. Development of methods for the assay of oestrogens in blood and urine.
6. Development of methods for the assay of adrenocortical steroids in blood and urine.
7. Application of methods for the estimation of hormones and their metabolites to problems in obstetrics, gynaecology, internal medicine, cancer and psychiatry.
8. Metabolism of radio-active steroid hormones in man.
9. Effect of endocrine glands and steroids on activity and behaviour.

(*Publications see pp.* 156–157)

CHEMICAL PATHOLOGY OF STEROIDS RESEARCH UNIT

THE JESSOP HOSPITAL FOR WOMEN, SHEFFIELD, 3

(1958)

Director
J. K. Norymberski, Dr.-Ing.

Staff
Mrs. J. M. McKenna, Ph.D.
Miss R. K. Thow, B.Sc. (*until Aug.*, 1959)

The Unit is concerned with problems arising from the metabolic transformations of steroids in health and disease. Emphasis is placed on (a) analytical methods for the detection and measurement of steroids in biological material, (b) preparation of steroids of physiological interest, and (c) isolation of steroids from biological material.

Summary of Research

1. Isolation of steroid sulphates from human urine.
2. Group determination of corticosteroids.
3. Characterization of compounds from the zona glomerulosa of ox adrenal gland. (In collaboration with the Middlesex Hospital Medical School).
4. Partial reduction of steroid hormones and related substances.

CLINICAL CHEMOTHERAPEUTIC RESEARCH UNIT

WESTERN INFIRMARY, GLASGOW, W.1

(1946)

Director

J. Reid, M.D., M.R.C.P.

Assistant Director

D. H. Sproull, M.B., B.Sc. (*until Jan., 1960*)

Staff

W. D. Alexander, M.B. (*until Dec.*, 1958)
Miss M. M. Andrews, Ph.D.
C. J. W. Brooks, Ph.D.
C. M. Grant, M.B.
T. D. Lightbody, M.B.
J. F. Morman, B.Sc.
M. V. Park, B.Sc.
Mrs. W. L. Stafford, Ph.D.

Emphasis is being placed on clinical research, and the scope of the work of the Unit has widened to include current clinical problems in diabetes mellitus, and the introduction of effective new oral compounds for treatment. Work on rheumatic fever and on the chemical and biological control of metabolism and water distribution continues.

Summary of Research

1. Comparison of the action of antirheumatic drugs.
2. Studies with oral antidiabetic substances, including screening tests for new compounds and comparisons with existing ones.
3. Investigation of the metabolic effects of antirheumatic, antidiabetic and other drugs.
4. Exploration of the relation between physico-chemical properties and biological and clinical effects.

(*Publications see p.* 157)

BODY TEMPERATURE RESEARCH UNIT

DEPARTMENT OF THE REGIUS PROFESSOR OF MEDICINE, RADCLIFFE INFIRMARY, OXFORD

(1954)

Honorary Director

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

Staff

K. E. Cooper, M.B., M.Sc.
J. H. Fessler, D.Phil.
R. F. Mottram, M.B., Ph.D.

Attached Workers

Professor Ellen Brown, M.D. (*San Francisco*)
W. I. Cranston, M.D., M.R.C.P. (*at the Radcliffe Infirmary*)

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

Summary of Research

1. Mechanism of fever caused by pyrogens.
2. The chemistry of endogenous pyrogen.
3. The site of deep temperature receptors and the central pathways for reflex vasodilatation.
4. Effects of prolonged hypothermia in man.

(*Publications see p.* 157)

OBSTETRIC MEDICINE RESEARCH UNIT

UNIVERSITY OF ABERDEEN MEDICAL SCHOOL, FORESTERHILL, ABERDEEN

(1955)

Honorary Director

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

Honorary Deputy Director

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

Staff

Miss E. M. Adams, M.B.
D. H. Allcorn, Ph.D.
W. Z. Billewicz, M.Sc. (Econ.)
Mrs. A. M. Finlayson, B.A. (*part-time*)
F. E. Hytten, M.B., Ph.D.
R. Illsley, Ph.D.
A. I. I. Klopper, M.B., Ph.D., M.R.C.O.G.
Miss A. R. Taggart, B.Sc.
Miss E. D. B. Thompson, B.A. (Econ.)

Attached Worker

P. O. Paaby, M.D. (*Copenhagen*) (*WHO Fellow*)

The Unit is studying the clinical and social phenomena of maternity and family life (a) by epidemiological methods, based on the clinical and demographic records of a defined population, (2) by intensive clinical, sociological and medical surveys of samples drawn from this population, and (3) by clinical and laboratory investigation of individual patients or small groups of patients.

Summary of Research

1. Epidemiological studies:
   (1) Routine co-ordination and analysis of local maternity records.
   (2) Trends in perinatal mortality, and factors which may influence such trends.
   (3) Epidemiology of clinical abnormalities in maternity.
   (4) Social factors influencing the health, physique and ' reproductive efficiency ' of women.
2. Field investigations:
   (1) Family life and health during the first five years of marriage resulting in the birth of children.
   (2) ' Social mobility ' within family groups.
   (3) Social study of an occupational group with poor reproductive health.
   (4) Social, familial and obstetric background of handicapped children.
3. Clinical and laboratory studies:
   (1) Yield and composition of breast milk.
   (2) Control of weight gain during pregnancy in relation to pre-eclampsia.
   (3) Blood pressure levels in pregnancy, with special reference to pre-eclampsia.
   (4) Changes in body composition during normal and abnormal pregnancy.
   (5) Endocrine factors in normal and abnormal pregnancy and in various gynaecological abnormalities.

(*Publications see pp.* 157–158)

TUBERCULOSIS RESEARCH UNIT

MEDICAL RESEARCH COUNCIL LABORATORIES, HOLLY HILL, HAMPSTEAD, LONDON, N.W.3

(1948)

Director

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

Staff

H. W. Bunjé, M.D., M.R.C.P.*
W. Fox, M.D., M.R.C.P.†
C. S. Hunter, M.B. (*until March*, 1959)
Christine L. Miller, B.M. (*part-time*)
D. N. Mitchell, M.B. (*part-time*)
J. Pepys, M.B., M.R.C.P. (*part-time*)
T. M. Pollock, M.B.

* Transferred to headquarters staff, Mar., 1960.

† Seconded to the World Health Organization.

The Unit continues to study tuberculosis as it affects the community rather than the individual. Statistically controlled clinical trials of the value of different chemotherapeutic agents have been undertaken in Britain and overseas, and associated problems studied. The national trial of the value of measures of specific immunization in tuberculosis continues, a second report being in the press. The Director also works part-time in the National Institute for Medical Research on laboratory problems of tuberculosis and leprosy. The Unit co-operates actively with the Council's Statistical Research Unit and the Unit for Research on Drug Sensitivity in Tuberculosis.

Summary of Research

1. Chemotherapy in tuberculosis :
   (1) Trial of long-term chemotherapy (without surgery) in the control of chronic cavitated infective pulmonary tuberculosis.
   (2) Five-year follow-up studies of patients in the earlier M.R.C. chemotherapy trials.
   (3) Trials of new methods of chemotherapy in tuberculosis in East Africa.
   (4) Participation with the World Health Organization and the Indian Council for Medical Research in the Tuberculosis Chemotherapy Research Project, Madras, India.
2. Clinical trial of tuberculosis (BCG and vole bacillus) vaccines.
3. Survey of the present prevalence of tuberculin sensitivity in adolescents.
4. Investigation of the specificity of the tuberculin reaction.

(*Publications see p.* 158)

UNIT FOR RESEARCH ON DRUG SENSITIVITY IN TUBERCULOSIS

POSTGRADUATE MEDICAL SCHOOL OF LONDON, DUCANE ROAD, LONDON, W.12

(1954)

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

Staff

Anna Csillag-Szekely, Ph.D.
J.B. Selkon, M.B., D.C.P.*
J. G. Wallace, M.B., D.C.P. (*part-time*) (*until Nov.*, 1958)

The Unit has continued to provide a centralized bacteriological service for co-operative clinical trials of the chemotherapy of tuberculosis in Britain and E. Africa. The association between loss of virulence of tubercle bacilli in animals and its effect on human disease has been studied on strains of isoniazid-sensitive and resistant tubercle bacilli from patients in Indian and East African clinical trials. Work has continued on the mechanisms underlying chemotherapeutic action, particularly on methods determining the metabolic state of tubercle bacilli *in vivo*. Systematic studies on the classification of mycobacteria have been started.

Summary of Research

1. Chemotherapy of tuberculosis:
   (1) Centralized sensitivity tests for a trial of chemotherapy in chronic pulmonary tuberculosis in Great Britain.
   (2) Centralized sensitivity tests for clinical trials of isoniazid alone or in association with a sulphone derivative, or a thiosemicarbazone in East Africa.
   (3) The comparative sensitivity to *p*-aminosalicylic acid of British and Indian strains of tubercle bacilli.
   (4) Studies on the metabolic state of tubercle bacilli *in vivo*.
2. The relationship between the animal virulence of Indian or East African tubercle bacilli and human disease.
3. Classification of mycobacteria.

(*Publications see p.* 158)

* Seconded to the World Health Organization.

UNIT FOR RESEARCH ON THE EXPERIMENTAL PATHOLOGY OF THE SKIN

THE MEDICAL SCHOOL, UNIVERSITY OF BIRMINGHAM

(1952)

Honorary Director
Professor J. R. Squire, M.D., F.R.C.P.

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

Staff

J. Cohen, Ph.D.
Professor P. G. H. Gell, M.B. (*honorary*)
G. Holti, M.D.
B. C. Tate, M.D., F.R.C.P. (*honorary*)
M. D. Trotter, Ph.D.
S. R. Wood, M.B., M.R.C.P. (*part-time*)

The aim of the Unit is to achieve a better understanding of the underlying nature of the various types of skin disease. The scope of its activity includes research on the behaviour and metabolism of skin *in vitro*, the investigation of disease processes associated with skin infections, and clinical and laboratory studies of the reaction of normal and abnormal skin.

Summary of Research

1. Effects of hormonal, chemical and physical agents on the metabolism of skin *in vitro*.
2. The cytology of normal and abnormal skin in tissue culture, including the behaviour of pigmented and non-pigmented dendritic cells.
3. The relationship of the whisker base and dermal papilla to whisker growth in rats, using transplantation techniques.
4. The allergenic polysaccharides of the dermatophytic fungi.
5. The role of intestinal infestation with *Candida albicans* in relation to chronic urticaria and irritable colon.
6. The assessment of desensitization in the treatment of allergic conditions.
7. Skin blood flow in the eczema reaction.
8. Investigation of materials suspected of causing industrial skin diseases.

(*Publications see p.* 159)

METABOLIC DISTURBANCES IN SURGERY RESEARCH UNIT

DEPARTMENT OF UROLOGY, THE GENERAL INFIRMARY, LEEDS, 1

(1957)

Honorary Director
Professor L. N. Pyrah, Ch.M., M.Sc., F.R.C.S.

Assistant Director
F. M. Parsons, M.B., B.Sc.

Staff

F. W. Heaton, Ph.D.
A. Hodgkinson, Ph.D.
Miss M. J. Holdsworth, B.Sc.
M. J. Purton, M.Sc.

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

Summary of Research

1. Renal failure and the artificial kidney :
   (1) Evaluation of haemodialysis.
   (2) Clearance values obtained by dialysis.
   (3) The causes of uraemic symptoms.
2. Renal lithiasis :
   (1) The urinary excretion of calcium, inorganic phosphate, oxalic acid and citric acid in cases of calcium-containing renal calculi.
   (2) The nature of the defect in idiopathic hypercalciuria.
   (3) Crystallography of renal calculi and the relationship between stone structure and hypercalciuria.
   (4) Chemical changes in experimental nephrocalcinosis.
   (5) Mechanism of the action of parathormone.
3. Magnesium metabolism:
   (1) Methods of estimation of magnesium in biological fluids.
   (2) Magnesium balance studies.

(*Publications see p.* 159)

BLOOD TRANSFUSION RESEARCH UNIT*

POSTGRADUATE MEDICAL SCHOOL OF LONDON, DUCANE ROAD, LONDON, W.12

(1946)

Director

P. L. Mollison, M.D., F.R.C.P.

Staff

N. C. Hughes Jones, B.M., Ph.D.
G. C. Jenkins, M.B.
Miss. M. J. Polley, B.Sc.
Miss M. A. Robinson, B.Sc. (*until Jan.*, 1959)

The Unit's object is to improve the practice of blood transfusion by investigating its effects in man, and to use transfusion as a method of research, particularly in the study of haemolytic syndromes.

Summary of Research

1. Relation between characteristics of blood group antibodies *in vitro* and their effects *in vivo.*
2. Detection of human blood group antibodies by tests for complement-binding.
3. Sites of red cell destruction in man and in various animals.
4. Immuno-electrophoretic study of proteins taking part in the antiglobulin reaction.
5. Further studies on the preservation of red cells.
6. Development of a red cell washing machine (in collaboration with the National Institute for Medical Research and the Experimental Radiopathology Research Unit).

(*Publications see p.* 159)

BLOOD GROUP RESEARCH UNIT

LISTER INSTITUTE, CHELSEA BRIDGE ROAD, LONDON, S.W.1

(1946)

Director

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

Staff

Miss F. J. Hamper, B.Sc.
Miss J. E. Noades, B.Sc.
Miss R. A. Sanger, Ph.D.
Miss P. A. Tippett, B.Sc.

Visiting Worker

J. K. Moor-Jankowski, M.D. (U.S.A.)

* Shortly transferring to St. Mary's Hospital, Paddington, W.2, as the Experimental Haematology Research Unit.

The Unit is occupied in the search for unrecognized blood group antigens, and in the genetical analysis of those which are already known. These antigens are of importance in the study of human genetics and may be the cause of haemolytic disease of the newborn and of transfusion reactions.

Summary of Research

1. Investigation of a second family having the antigen P^k (with Dr. E. A. Kortekangas, Turku).
2. Identification of a new phenotype, Jk(a-b-), in the Kidd system (with Dr. F. J. Pinkerton, Honolulu).
3. Study of the antigens and antibodies of the I system (with Dr. W. J. Jenkins, London, Dr. A. Cahan, New York and others).
4. Recognition that red cells can acquire a B-like antigen *in vivo*. The acquisition is associated with old age or disease, or both (with Dr. C. Cameron, Dundee, Dr. I. Dunsford, Sheffield and others).
5. Study of some complexities of Rh antigens and antibodies (with Dr. F. H. Allen, Boston, Dr. A. Cahan and Dr. R. E. Rosenfield, New York and Dr. I. Dunsford, Sheffield).
6. Contributions to the establishment of the antigens called Wr^a and Vel as heralds of new systems rather than rare members of known systems.
7. Examination of sera suspected of containing new blood group antibodies (sent mostly from the United States).
8. Collaboration in twin investigations (with Professor I. Aird, Mr. J. Shields, Dr. E. Slater Professor A. Sorsby, London, and with the Council's Rheumatism Research Unit, Taplow).
9. Collaboration with Dr. P. E. Polani, London, in a study of Klinefelter's and Turner's syndromes and with Dr. P. Leyburn, Newcastle-upon-Tyne, in a study of muscular dystrophy.

(*Publications see pp.* 159–160)

BLOOD GROUP REFERENCE LABORATORY

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

LISTER INSTITUTE, CHELSEA BRIDGE ROAD, LONDON, S.W.1

Director

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

Staff

Miss C. M. Giles, B.Sc.
Miss E. W. Ikin, B.Sc.
Miss D. M. Parkin, M.R.C.S.

The main function of the Laboratory is to issue blood grouping sera for use by the National Blood Transfusion Service, by hospitals in the United Kingdom and by various laboratories overseas, and to give advice on clinical cases and technical problems referred to it by other laboratories. Special attention is given to problems encountered by laboratories which are just beginning to enter the field of blood transfusion, particularly those which have to contend with difficulties arising from local conditions; thus the actual form taken by such assistance varies widely from laboratory to laboratory. New methods of testing are tried in comparison with established techniques, with a view to their possible introduction into routine practice, with or without modification. Lines of research arising from individual cases received by the Laboratory or from questions raised by other laboratories are followed up and investigated.

Summary of Activities

1. Continued provision of blood grouping sera of both human and animal origin for the National Blood Transfusion Service, the Armed Forces and Colonies, and for other users in the United Kingdom and overseas.
2. Investigation of clinical problems referred by other laboratories.
3. Research into matters of interest arising from these cases.
4. Full blood grouping of Staff Panels from other laboratories, for use as controls.
5. Full grouping of donors for the National Panel of Donors maintained for use in transfusion cases requiring blood of rare types.
6. Rh Genotyping of all recruits to the London Red Cross Blood Transfusion Service.
7. Checking the specificity of antisera submitted by other laboratories for confirmation before they put them into use as routine grouping sera.
8. Testing of specimens received in connexion with anthropological surveys.
9. Research into new and unusual blood groups.
10. Investigation of sera from patients with rheumatoid arthritis and other rheumatic diseases for agglutinating factors inhibited by γ-globulin.
11. Full blood grouping of foetuses in relation to marrow replacement.
12. Investigation of the potentialities of the enzyme ficin in blood grouping.
13. Continued service as the World Health Organization International Blood Group Reference Laboratory.

(*Publications see p.* 160)

BLOOD COAGULATION RESEARCH UNIT

CHURCHILL HOSPITAL, OXFORD

(1959)

Director

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

Staff

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

Visiting Worker

Dr. C. R. Rizza (M.R.C. *Clinical Research Fellow*)

The Unit is studying deviations from the normal blood coagulation mechanism which may lead to excessive haemorrhage or thrombosis. The main objective is to improve the treatment of patients whose blood coagulation is abnormal.

Summary of Research

1. Investigation and diagnosis of cases of abnormal bleeding due to deficiency of clotting factors or the presence of anticoagulants, and study of their aetiology including congenital factors.
2. The production and assay of concentrated antihaemophilic globulin, and its application in the treatment of haemophilia.
3. Attempts to reduce or remove the antigenic properties of antihaemophilic globulin derived from animal blood.
4. In collaboration with the Oxford Regional Blood Transfusion Service the preparation from human blood of concentrated material for the treatment of Christmas disease and von Willebrand's disease.
5. Collaboration with Dr. G. Born and Mr. P. Esnouf of the Nuffield Institute for Medical Research, Oxford, in studies on the participation of lipoids in blood clotting.
6. Studies of the structure of thrombi as they occur *in vivo* and the factors which favour or oppose their formation.

(*Publications see p.* 160)

OPHTHALMOLOGICAL RESEARCH UNIT

INSTITUTE OF OPHTHALMOLOGY, JUDD STREET, LONDON, W.C.1

(1948)

Director

Sir Stewart Duke-Elder, G.C.V.O., M.D., D.Sc., F.R.C.S., F.A.C.S., F.R.S. (*part-time*)

Staff

N. Ambache, M.A., M.R.C.S.**
G. B. Arden, M.B., Ph.D.
D. F. Cole, Ph.D.
Mrs. D. Froomberg, Ph.D.*
J. Gloster, M.D.*
M. E. Langham, Ph.D.
D. M. Maurice, Ph.D., A.Inst.P.
Mrs. M. L. Reynolds, B.Sc.*
Miss K. Tansley, D.Sc.†
C. B. Taylor, Ph.D.*

Attached Workers

D. Ainslie, M.D., F.R.C.S.
W. E. S. Bain, M.B., F.R.C.S.‡
J. G. Dobbie, M.D. (*Chicago*)
J. H. Dobree, M.S., F.R.C.S.§
D. P. Greaves, M.B., F.R.C.S.‡
A. C. Higgitt, M.B., F.R.C.S.§
F. A. Hosni, M.B., D.S., F.R.C.S.
G. M. Krolman, B.Sc., M.D. (*Manitoba*)§
A. G. Leigh, M.D., F.R.C.S.
R. B. Niven, B.M., M.R.C.P.‡
E. S. Perkins, M.B., Ph.D., F.R.C.S.
J. Primrose, M.B., F.R.C.S.§
C. G. Tulloh, M.B., F.R.C.S.§

VISUAL RESEARCH DIVISION

Staff

H. J. A. Dartnall, Ph.D., F.R.I.C.: *Head of Division.*

C. D. B. Bridges, Ph.D.
Miss P. A. Strange, Ph.D.
R. A. Weale, D.Sc.

Attached Workers

F. W. Munz, Ph.D. (*Los Angeles*)
F. S. Said, M.Sc. (*Egypt*)

The general aims of the Unit are three-fold. In the first place, investigations are being carried out on the problems peculiar to the physiology of the eye, particularly the control of the intraocular circulation, the causes of variations in the intraocular pressure, and the metabolism of the non-vascular tissues, that is, of the cornea, lens and vitreous. These investigations are being correlated with pathological studies in the Institute of Ophthalmology and Moorfields Eye Hospital with the particular aim of elucidating the aetiology of glaucoma, uveitis and cataract, the development of corneal opacities, and the action of antibiotics on the eye.

In the second place a considerable programme is developing on the neurophysiology of the eye and the associated parts of the central nervous system. This includes the control of the intraocular pressure from the hypothalamus, the afferent and efferent paths from this region of the eye, as well as investigations into the electrophysiology of the visual pathways.

The Visual Research Division is engaged on physiological studies, with particular reference to the visual pigments and their role in the visual process. Cognate problems are also being investigated such as the pre-retinal absorption of light, and subjective measurement of visual sensitivity.

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* Salaries financed from Alexander Pigott Wernher Memorial Trust funds.
† On leave of absence at National Institutes of Health, Bethesda, Md.
‡ Wernher Research Fellow.
§ Moorfields Research Fellow.
** Now a member of the Council's External Scientific Staff working at the Royal College of Surgeons of England.

Summary of Research

1. Intra-ocular pressure ; its measurement, nervous control and pathology.
2. Pharmacology of the autonomic nervous supply to the eye.
3. Circulation of the aqueous humour.
4. The blood-aqueous barrier.
5. Metabolism of the cornea, lens and vitreous.
6. Histopathology of the retina.
7. The central nervous mechanism controlling the vegetative functions of the eye, and the electrophysiology of the visual pathways.

VISUAL RESEARCH DIVISION

1. Measurements of the relative photo-sensitivities of various visual pigments.
2. Investigation of the occurrence and distribution of visual pigments in vertebrates, particularly in river and marine fish.
3. Study of visual pigments in suspensions of retinal end-organs.
4. Study of photoproducts of visual pigments at very low temperatures.
5. Studies on the effect of light and dark environments on the visual pigments of fresh-water fish.
6. Investigation of visual pigments in human and living animals by reflection from the fundus.
7. Absorption of light by the lens of living human subjects.

Publications see pp. 160–161)

TRACHOMA RESEARCH UNIT

LISTER INSTITUTE OF PREVENTIVE MEDICINE, LONDON, S.W.1 AND MEDICAL RESEARCH COUNCIL LABORATORIES, GAMBIA

(1956)

Honorary Director

L. H. Collier, M.D.

Staff

W. A. Blyth, Ph.D. (*working in the Gambia*)
Mrs. M. Coggrave, B.A. (*working in the Gambia*)
Miss E. F. Fraser, B.Sc.
A. Frohlich, B.Sc.
Miss D. M. Graham, M.Sc.
P. Reeve, B.Sc.
J. Sowa, B.A. (*working in the Gambia*)
Mrs. S. C. I. Sowa, M.B., D.O. (*working in the Gambia*)

Attached Worker

Mrs. J. Stocker, B.Sc. (*until July*, 1959)

The aetiological role of viruses isolated by chick embryo inoculation from trachoma patients in the Gambia has been confirmed by a second experimental infection of a human volunteer.

At the Lister Institute the serological reactions of trachoma viruses are being investigated, and a study of the host-parasite relationship has been started; one strain of virus is being adapted to grow in a variety of cell cultures in which it induces easily recognizable lesions.

In the Gambia, a preliminary survey of a village community has been completed, in which clinical, virological and bacteriological investigations were

made on the eyes of 400 people. With the aid of improved techniques virus was isolated from a high proportion of patients with active trachoma. These observations are being extended; in view of the possibility that more than one agent may cause the trachoma syndrome, patients in whom repeated chick embryo inoculations have failed to detect virus will be re-examined by other methods.

In collaboration with the Institute of Ophthalmology, viruses closely resembling trachoma were isolated from several babies with neonatal inclusion blennorrhoea, and from the uterus of the mother of such an infant. The last mentioned virus induced severe inclusion conjunctivitis in baboons, providing strong evidence of its aetiological relationship to this disease, and to the associate infections of the genital tract.

Summary of Research

1. Virology of trachoma and inclusion conjunctivitis:
   (1) Mode of growth in chick embryos and cell culture.
   (2) Antigenicity, with special reference to possible vaccine production.
   (3) Relations to each other, and to other members of the psittacosis-lymphogranuloma group.
   (4) Skin reactions to intracutaneous injections of killed virus.
   (5) Experimental infections in man and animals.
   (6) Methods of purification.
   (7) Methods of preservation.
2. Field studies of trachoma:
   (1) Epidemiology.
   (2) Virology.
   (3) Influence of associated bacterial infections.

(*Publications see p.* 161)

GROUP FOR RESEARCH IN OCCUPATIONAL OPTICS*

INSTITUTE OF OPHTHALMOLOGY, JUDD STREET, LONDON, W.C.1

(1949)

Director

H. C. Weston, F.I.E.S.

The work of the Group has been concerned with visual aspects of occupational tasks and environments, with reference to health, comfort and working efficiency.

Summary of Research

1. *Ad hoc* field investigations into visual problems arising in different places of employment.
2. Effect of illumination level on the relation between accuracy and speed of visual performance.
3. Methods, criteria and data for formulating standards of working illumination.

(*Publications see p.* 161)

* This Group was disbanded on Mr. Weston's retirement in September, 1959.

WERHNER RESEARCH UNIT ON OPHTHALMOLOGICAL GENETICS

ROYAL COLLEGE OF SURGEONS OF ENGLAND,
LINCOLN'S INN FIELDS, W.C.2
(1954)

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

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

Attached Worker
M. Sheridan, F.S.M.C. (*Royal Eye Hospital*)

The Unit is studying the genetic aspects of ophthalmology, particular attention being paid to retinal dystrophy and the components of ocular refraction. It is financed from Alexander Pigott Wernher Memorial Trust Funds.

Summary of Research

1. Inherited retinal dystrophy: inbred strains of mice and rats are being used in explorations into the nature of retinal dystrophy. Special attention is being paid to enzyme systems.
2. Induced retinal degeneration: administration of various enzyme inhibitors and other agents to the intact animal in attempts to produce retinal degeneration.
3. Other studies:
   (1) The genetics and clinical course of various hereditary affections of the eye in man and animals.
   (2) The components of ocular refraction in man during growth, and their genetic behaviour in the rabbit and man.

(*Publications see p.* 162)

OTOLOGICAL RESEARCH UNIT

NATIONAL HOSPITAL FOR NERVOUS DISEASES,
QUEEN SQUARE, LONDON, W.C.1
(1944)

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

Staff
J. T. Y. Chou, D.Phil.
L. Citron, M.B., F.R.C.S. (*part-time*)*
M. R. Dix, M.D., F.R.C.S.
J. D. Hood, D.Sc., A.Inst.P.

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, 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.

* Salary provided from Alexander Pigott Wernher Memorial Trust funds.

Summary of Research

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

(*Publications see p.* 162)

WERNHER RESEARCH UNIT ON DEAFNESS

KING'S COLLEGE HOSPITAL MEDICAL SCHOOL,
DENMARK HILL, LONDON, S.E.5
(1949)

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

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

Staff
R. Hinchcliffe, M.D., B.Sc.
J. J. Knight, B.Sc., A.Inst.P.

Attached Worker
Surg. Lieut. R. R. A. Coles, M.B., D.L.O., R.N.

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

Summary of Research

1. Testing of hearing by bone conduction as a diagnostic procedure and the standardization of bone conduction audiometry.
2. Improvement in hearing aid equipment.
3. Auditory masking effect of noise and its application to clinical tests of hearing for speech and pure tones.
4. Continuous recording threshold audiometry.
5. Application of pulse signal technique in audiometry and hearing aid research.
6. The function of the round and oval windows in the mechanism of hearing.
7. Incidence and causes of deafness.
8. Speech audiometry in children and adults.
9. Audiometric surveys in industrial situations.
10. Development of technique for stapes mobilization and assessment of results.

(*Publications see p.* 162)

RADIOBIOLOGICAL RESEARCH UNIT

MEDICAL RESEARCH COUNCIL, HARWELL, DIDCOT, BERKS.

(1947)

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

Deputy Director
R. H. Mole, B.M., M.R.C.P.

Staff

S. Abrahams, B.A.
D. W. H. Barnes, B.M.
A. L. Batchelor, Ph.D.
Mrs. F. M. Bishop, B.Sc.
R. S. Bruce, D.Phil.
T. E. F. Carr, B.Sc.
T. C. Carter, O.B.E., D.Sc. (*until Sept.*, 1959)
Mrs. C. M. Clarke, Ph.D.
Miss M. T. Davison, B.Sc.
T. R. Elsdale, Ph.D.
H. J. Evans, Ph.D.
C. E. Ford, Ph.D.
J. Godfrey, Ph.D.
Miss S. M. Gray, B.Sc. (*until April*, 1959)
D. G. Harnden, Ph.D.
Mrs. A. Harrison, Ph.C.
G. E. Harrison, D.Sc., F.Inst.P.
D. B. Hope, D.Phil. (*until March*, 1959)
E. V. Hulse, M.D.
H. G. Jones, Ph.D. (*attached to Agricultural Research Council, Compton*)
Miss H. J. Jones, B.Sc. (*until June*, 1959)
K. W. Jones, B.Sc.
D. R. Lucas, M.D.
Miss M. F. Lyon, Ph.D.
F. I. MacLean, M.A.
H. S. Micklem, B.A.
R. J. Munson, Ph.D.
G. J. Neary, Ph.D.
Miss R. J. S. Phillips, B.Sc.
J. St. L. Philpot, M.A., B.Sc.
C. E. Purdom, Ph.D.
Mrs. L. M. W. Purdom, B.Sc.
J. R. K. Savage, Ph.D.
D. Scott, B.Sc.
A. G. Searle, Ph.D.
M. J. Ashwood Smith, M.Sc.
Miss J. E. Stanier, D. Phil.
S. R. Stitch, Ph.D.
L. A. Stocken, D.Phil., F.R.I.C. (*part-time*)
A. M. Thomas, M.B.
Miss S. M. Tonkinson, B.Sc.
O. A. Trowell, M.D.
D. R. Westgarth, M.Sc. (*until Sept.*, 1959)
J. Whittle, B.Sc.
Mrs. M. E. Williams, Ph.D. (*until June*, 1959)
F. S. Williamson, M.A.

Attached and Visiting Workers

D. A. Barber, Ph.D. (*Agricultural Research Council staff*)
Lieut. Col. J. A. H. Brown, M.D., R.A.M.C.
J. A. G. Davids, M.Sc. (*Reactor Centrum Nederland*)
L. G. Ekman (*Royal Veterinary College, Stockholm*)
G. Prins, Ph.D. (*Reactor Centrum Nederland*)
R. J. Scothorne, M.D., B.Sc. (*University of Glasgow*)
Surg. Capt. G. D. Wedd, O.B.E., M.B., R.N.
A. E. Williams, B.Sc. (*Microbiological Research Unit, C.D.E.E., Porton*)

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

Summary of Research

1. Physical studies:

(1) The production and measurement of very low voltage X-rays and their application in radiobiology.

(2) The production of thick films of lithium-6 deuteride for use as targets for neutron production. (Dose rates of 5 rads/minute at 15 cm. from the target can be obtained).

(3) The applicability of the Harwell pile BEPO to permit the irradiation of large animals with fast neutrons or gamma radiation.

(4) Development of equipment for automatic irradiation of laboratory animals for investigation of time and dose-intensity factors in effects of whole-body irradiation.

(5) Liquid scintillation counting as a means of estimating radioactive carbon in organic material.

(6) Investigation of flame spectrophotometry in the estimation of calcium, strontium and magnesium in biological materials.

(7) Development of spectral centrifuge for fractionation of cell particles, e.g., nuclei.

2. Chemical studies:

(1) Biochemical features of cell-division, especially the processes leading to synthesis of DNA.

(2) Study of organic peroxide production as a possible cause of death of irradiated animals.

(3) Search for improved anti-radiation drugs and study of mode of action of known ones.

(4) Metabolism of isolated cell nuclei in relation to mutagenic effects of radiation.

(5) Hormone dependent tumours; the mechanism of oestrogen biosynthesis. Investigation of adrenal and other glands as the site of oestrogen production.

3. Clinical and physiological studies:

(1) The recovery factor in the effects of daily exposure of mice to whole-body irradiation by fast neutron and gamma radiations.

(2) Life-shortening in mice by chronic irradiation with fast neutron and gamma radiation. The hypothesis, previously examined that life-shortening due to chronic irradiation at low dose rates is an expression of premature ageing, has been re-examined with more exact and detailed statistical tests.

(3) Studies of delayed toxicity of limited exposures to gamma radiation and fast neutrons (GLEEP).

(4) Investigation of the late somatic effects (notably tumours and leukaemia) of irradiation of mice.

(5) Follow-up investigation to determine the late effects in surviving monkeys given ^{90}Sr in West Africa.

(6) Radiographic investigation of gastric emptying after irradiation and the administration of drugs capable of modifying the effects of radiation.

(7) The scoring of the delayed effects of irradiation of mice with β-rays.

(8) Quantitative assessment of population of cells in bone marrow during recovery from irradiation.

(9) Quantitative assessment of changes in number of cells of various organs by determination of DNA.

(10) Investigations on the immunological status of radiation-chimaeras.

(11) The distribution of radiostrontium and radioyttrium in the eye and in teeth (with W. Holgate, A. Pirie and J. M. Vaughan).

(12) The use of radiation chimaeras for study of:

(a) immunological reactions—host v. graft and graft v. host.

(b) haemopoiesis.

(c) ageing of cell-populations.

(13) Further essays on treatment of murine leukaemia.

(14) The renal discrimination between strontium and calcium in man.

(15) Continuing investigations of the turnover of dietary calcium and strontium in children, including the assay of the urinary and faecal excretion of single doses of natural strontium.

(16) Continuing investigations of the effect of dietary strontium on the retention of oral and intravenous doses of radioactive strontium in rats, with special reference to the replacement of skeletal calcium.

(17) Continuation of the study of the uptake of radioactive strontium in normal and microophthalmic mice.

(18) Further investigation of the relative retention of daily and single doses of radioactive strontium in rabbits.

(19) The local concentration and translocation of nitrosoruthenium compounds in the gastrointestinal tract of the rat.

(20) Cytogenetics of spontaneous and induced neoplasms in the mouse and the Chinese hamster.

(21) Cell-population studies in radiation chimaeras of the mouse.

(22) Study of the chromosomes in myeloid cells from leukaemic human patients.

(23) Study of the chromosomes of human patients with defects of sex development and other congenital abnormalities, using cells from the bone marrow and tissue cultures established from small skin explants.

(24) Effect of X-radiation on mouse retina (*in vivo*) at different ages. Quantitation of effects on the different retinal layers by cell counting. Correlation of radiosensitivity with: (a) mitotic activity, and (b) differentiation.

4. Fundamental studies:

(1) The relative biological efficiencies of fast neutrons and gamma rays in causing chromosome breakage, mitotic delay and inhibition of root growth of broad bean seedlings in the presence and absence of oxygen.

(2) A statistical analysis of the distribution of radiation-induced chromosome aberrations in cells, with a view to revealing whether there is a correlation between chromosome damage and mitotic delay.

(3) The possible influence of chromosome number on the frequency and distribution of chromosome aberrations induced by gamma radiation.

(4) The rejoining time of chromatid breaks induced by gamma radiation at temperatures just above 0°C—protraction and fractionation experiments.

(5) Effect of temperature on the action of colchicine and on the rate of progress of cells through the mitotic cycle.

(6) Observations on continuous cultures of *E. coli* including:
(a) the effect of cell density, temperature and gamma-radiation dose-rate on the length of cells.
(b) the relation between the length of cells and their X-ray sensitivity.
(c) factors influencing the rates of mutation in unirradiated and irradiated cultures.

(7) Effect of X-radiation on thymus (rat, *in vivo*). (Quantitative measurements by cell counting.)

(8) Effect of extracts of various organs on various organs cultured *in vitro*.

(9) Culture of pieces of adult rat liver *in vitro*.

(10) Effects of (a) culture *in vitro* and (b) radiation on reticulin in various organs (nil).

(11) Radiosensitivity of mouse retina cultured *in vitro*, preliminary experiments.

5. Genetics:

(1) Fitness and length of larval life in irradiated populations of *Drosophila melanogaster*.

(2) Effect of radiation intensity on induction of mutations in *Drosophila melanogaster*.

(3) Factors affecting growth and size of laboratory populations of mice.

(4) Methods for detecting and measuring mutation in mice.

(5) Induction of mutations in mice by chronic irradiation with γ-rays and acute irradiation with X-rays.

(6) Genetics and development of induced and spontaneously arisen mutants in mice.

(*Publications see pp.* 162–165)

RADIOTHERAPEUTIC RESEARCH UNIT

HAMMERSMITH HOSPITAL, DUCANE ROAD, LONDON W.12

(1941)

Director

Miss C. A. P. Wood, M.A., M.R.C.P., F.F.R.

Staff

D. K Bewley, B.A.
G. Burton, B.Sc.
T. J. Deeley, M.B., F.F.R. (*part-time*)
N. A. Dyson, Ph.D.
P. E. Francois. Ph.D. (*until Mar.*, 1959)
A. W. G. Goolden, M.B., D.M.R.T. (*part-time*) (*until July*, 1959)
R. L. Morgan, M.B., B.Sc., D.M.R.T.
R. Morrison, M.D., F.R.C.P.E., F.F.R. (*honorary*)
G. R. Newbery, B.Sc., F.Inst.P. (*until July*, 1959)
A. Scott, B.Sc. (*until Sept.*, 1959)
A. Sharp, B.Sc.
Miss J. A. Stevenson, B.Sc.
H. J. Swallow, Ph.D. (*until Mar.*, 1959)
Miss B. A. Tucker, B.Sc.
P. C. R. Turner, B.Sc.
J. J. Veit, Ph.D. (*until Aug.*, 1959)
D. D. Vonberg, B.Sc.

The aim of the Unit is to improve the radiation treatment of disease. Investigations are being made to assess the therapeutic value of different types of radiation.

Summary of Research

1. Clinical trials of supervoltage radiation with the 8 MeV linear accelerator in certain forms of cancer.
2. Investigation to compare the results of treatment by surgery and radiotherapy in cancer of the lung; respiratory function tests on patients treated by both methods to assess the late effects of the treatment.
3. Study of the value of 8 MeV X-rays in the treatment of cancer of the bladder.
4. X-ray and electron dosimetry associated with the therapeutic use of the 8 MeV linear accelerator, including the development of an absolute calorimetric method of measurement. A limited trial of electron therapy in superficial cancer is in progress.
5. Clinical use of radioactive isotopes:
   (1) Continuation of studies on changes in body fluids in polycythaemia by the use of radioactive bromine.
   (2) Development of a technique for the combined use of ^{51}Cr and ^{59}Fe in the investigation of blood disorders.
   (3) Development of a technique of ablation of the pituitary gland in advanced breast cancer by means of radioative seeds of ^{90}Y.
   (4) The use of cyclotron-produced ^{15}O (as oxygen and as carbon monoxide in the study of pulmonary function).
   (5) Value of positron emitting isotopes for localization purposes.
   (6) The use of ^{52}Fe in studies of iron uptake.
6. Preparation and dosimetry of cyclotron-produced isotopes.
7. Continued development of neutron dosimetry.
8. Extraction and measurement of the cyclotron beam for therapy and isotope production.

(*Publications see p.* 165–166)

EXPERIMENTAL RADIOPATHOLOGY RESEARCH UNIT

HAMMERSMITH HOSPITAL, DUCANE ROAD, LONDON, W.12

(1953)

Director
G. J. Popják, M.D., F.R.I.C.

Assistant Director
N. B. Myant, D.M., B.Sc.

Staff

Miss T. Alper, M.A., M.S.(Ed.), F.Inst.P.
R. B. Beechey, Ph.D. (*until Nov.*, 1958)
Miss B. M. Cullen, B.Sc.
M. Ebert, Dr.rer.nat.
N. T. S. Evans, Ph.D.
K. Fletcher, Ph.D.
N. E. Gillies, Ph.D.
Mrs. I. Gore, Ph.D.
Miss P. Hele, M.B., Ph.D.
Miss H. R. Hellig, B.Sc.
F. A. Holton, Ph.D.
Mrs. S. Hornsey, B.Sc.
P. Howard-Flanders, Ph.D. (*until July*, 1959)
R. H. Thomlinson, M.B.
D. D. Tyler, B.A.

Attached and Visiting Workers

E. H. Ahrens, Jr., B.S., M.D. (*Rockefeller Institute, New York*)
Miss N. L. R. Bucher, M.D. (*John Collins Warren Laboratory, Harvard University, Boston*)
J. P. Christophe, M.D. (*St. Pierre University Hospital Brussels*)
A. Cuaron, M.D. (*Health Deparment, Mexico City, Mexico*)
L. R. Finch, B.Sc. (*Melbourne*)
D. S. Goodman, M.D. (*National Heart Institute, Bethesda, Maryland*)
H. R. Levy, Ph.D. (*The Ben May Laboratory for Cancer Research, University of Chicago*)
C. Osorio, Dr. of Medicine (*Santiago, Spain*)
G. Silini, Dr. of Medicine and Surgery (*Comitato Nazionale per le Ricerche Nucleari, Rome*)

The aims of the Unit are to study the mechanism of action of ionizing radiations on living cells in relation to the radiotherapy of cancer, and to investigate the metabolic changes induced by radiation and encountered in various diseases. Emphasis is being given to studies of enzyme reactions in connexion with metabolic investigations.

Summary of Research

1. Studies on protection against total body irradiation by hypothermia: effects on fertility, longevity, cataract induction.
2. Effects of inert gases and anaesthetics on radiation induced damage in experimental tumours and other biological systems.
3. Biological efficiency of fast neutrons relative to X-rays in experimental tumours.
4. Radiation effects in tissue cultures.
5. Modification of radiation effects in micro-organisms by treatments after irradiation. Studies on micro-organisms of different radiosensitivity.
6. Radiation chemical experiments with cyclotron produced α-rays.
7. Effects of nitric oxide on the radiosensitivity of micro-organisms.
8. Radiation inactivation of bacteriophage.
9. Radiation treatment of experimental tumours *in vivo* during administration of oxygen at high pressure.
10. Studies on protein biosynthesis; the activation of amino-acids.
11. Intermediary metabolism of experimental tumours.
12. Thyroxine-binding substances in the serum of mother and foetus.
13. Intermediary stages of cholesterol biosynthesis; isolation of intermediates and enzymes.
14. Hormonal and other effects on cholesterol biosynthesis.
15. Studies on the biochemistry of respiration in subcellular particles.
16. Development of apparatus for gas-liquid chromatography of radio-active substances.

(*Publications see pp.* 166–167)

CLINICAL EFFECTS OF RADIATION RESEARCH UNIT

DEPARTMENT OF RADIOTHERAPY,
WESTERN GENERAL HOSPITAL, EDINBURGH, 4

(1956)

Director

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

Staff

A. G. Baikie, M.B., M.R.C.P.E.
Miss K. E. Buckton, B.Sc.
Miss P. A. Jacobs, B.Sc.
Miss M. J. King, M.B.
J. A. McBride, M.B.
Miss I. M. Tough, B.Sc.
Miss M. J. Wilson, B.Sc. (*until July*, 1959)

The work of the Unit is particularly concerned with the delayed effects of radiation exposure on man.

Summary of Research

1. The study of patients treated with X-rays for ankylosing spondylitis, with a view to :
   (1) Studying the acute effects of radiation on haemopoiesis, and the possible residual permanent damage to the haemopoietic system.
   (2) The delayed effects of radiation, particularly with induction of tumours.
2. The study of unirradiated patients with ankylosing spondylitis.
3. The incidence of leukaemia in children exposed to X-rays during foetal life.
4. The study of human chromosomes.

(*Publications see pp.* 167–168)

BETATRON RESEARCH UNIT

CHRISTIE HOSPITAL AND HOLT RADIUM INSTITUTE,
WITHINGTON, MANCHESTER, 20

(1953)

Honorary Director
Professor Ralston Paterson, C.B.E., M.C., M.D., F.R.C.S., F.F.R.
Honorary Assistant Director
J. L. Dobbie, M.B., F.F.R.

Staff

D. Greene, Ph.D., A.Inst.P.
L. A. Mackenzie, B.Sc.

The general aim of the Unit is to explore appropriate techniques for the clinical application of megavoltage radiations in the treatment of malignant disease, and to assess the therapeutic advantages, if any, of this agent.

Summary of Research

1. Completion and publication of the relative biological effect (R.B.E.) studies, contrasting 4 M.V. (Linear Accelerator) and 20 M.V. (Betatron).
2. Completion of final series of quantitative experiments on the oxidation of ferrous sulphate.
3. Improvements in methods of clinical application of the betatron to exploit techniques peculiarly appropriate to this level of megavoltage, including:
   (1) production of a special beam directing device;
   (2) production of a collimator for square fields and wedge filters.
4. Development of methods of application of 20 M.V. (Betatron) to the treatment of the deeper cancers, particularly those of the bladder and of the lung.
5. Continuation of controlled clinical trials in cancer contrasting Linear Accelerator treatment with deep therapy; these apply particularly to bladder cancer and cancers of the head and neck.

(*Publications see p.* 168)

BONE-SEEKING ISOTOPES RESEARCH UNIT

THE CHURCHILL HOSPITAL, HEADINGTON, OXFORD

(1959)

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

Staff

Mrs. J. Dearnaley, B.A.
Mrs. E. Downie, B.Sc. (*until Aug.*, 1959)
G. M. Herring, B.A.
Mrs. E. Lloyd, M.Sc.
Miss H. S. M. Macpherson, M.A.
Mrs. M. E. Owen, D.Phil
Mrs. E. N. Ramsden, Ph.D., D.Phil. (*part-time*)

The aim of the Unit is to study the effect of bone-seeking isotopes on the skeleton and bone marrow.

Summary of Research

1. The determination of the radiation dose received by the skeleton and teeth from ^{90}Sr and ^{226}Ra.
2. The relation of both dose-rate and total radiation dose to radiation damage.
3. To extract and purify the organic constituents of bone in the hope of finding one that binds yttrium and plutonium.
4. To study the behaviour of yttrium in body fluids and soft tissues as well as bone with a view to understanding how it is bound in the skeleton.

(*Publications see p.* 168)

ENVIRONMENTAL RADIATION RESEARCH UNIT

DEPARTMENT OF MEDICAL PHYSICS,
THE UNIVERSITY OF LEEDS, THE GENERAL INFIRMARY, LEEDS, 1
(1959)

Honorary Director
Professor F. W. Spiers, D.Sc.

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

Staff

D. Hughes, Ph.D., A.Inst.P., A.M.I.E.E.
J. C. Duggleby, B.Sc.

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

Summary of Research

1. Measurements of radioactivity in the human body.
2. Development of an apparatus for the continuous and semi-automatic measurement of external gamma-radiation at a fixed site.
3. Survey of external gamma-radiation with a portable monitor over large selected areas.
4. Development of an apparatus for the measurement of gamma-radioactivity in soil and biological specimens.
5. Theoretical studies of the dose-response relationship in radiation carcinogenesis.
6. Theoretical and experimental studies on the radiation dosimetry of radioactive materials deposited in bone.

(*Publications see p.* 168)

RADIOLOGICAL PROTECTION SERVICE

(Jointly with the Ministry of Health)

CLIFTON AVENUE, BELMONT, SUTTON, SURREY
(1953)

Director
W. Binks, M.Sc., F.Inst.P.

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

Staff

D. O. Bottrill, B.Sc., D.I.C.
J. F. B. Dealler, B.Sc.
M. J. Duggan, B.Sc.
C. D. Johnson, B.Sc.
B. E. Jones, B.Sc., A.Inst.P.
T. O. Marshall, B.Sc.
G. Maycock, B.Sc.
Mrs. M. P. Taylor, B.Sc., A.R.I.C.
J. Vennart, B.Sc., F.Inst.P.
M. E. Wise, Ph.D.

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

Summary of Activities

1. The collection and dissemination of information regarding protection against ionizing radiations, including:
   (1) The assessment of maximum permissible body burdens and of concentrations in air and in water for a number of radioactive substances.
   (2) Assistance to the Medical Research Council's Committee on Protection against Ionizing Radiations and to the Radioactive Substances Advisory Committee and its Panels, in the preparation of rules for the guidance of those concerned with miscellaneous problems arising from the use of ionizing radiations.
   (3) Continued participation in the varied activities of the International Commission on Radiological Protection.

2. Radiation monitoring and advisory services:
   (1) Operation of a personnel radiation-monitoring Service and of punch-card techniques for the recording, analyzing and processing of the results of large numbers of tests and of the cumulative totals of radiation exposure of individual workers.
   (2) Carrying out inspections of departments and sites where radiation hazards 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, including those arising during waste disposal.
   (4) The measurement of the amount of radioactive material deposited in the bodies of persons exposed to unsealed radioactive materials.
   (5) Tests of the efficiency of protective materials.
   (6) Identification and assay of low-level radioactive components in miscellaneous samples, for example, of luminous paints, air, drinking water, soil, sewage, dental fillings and deposits on surface aircraft.

3. Miscellaneous researches:
   (1) Studies to improve the accuracy of techniques for measuring external radiation received by workers.
   (2) Development of new techniques for assessing the amount of radioactive material deposited in the body, including whole-body measurements of radiation emitted, measurement of radon exhaled in the breath, and chemical tests of excreta.
   (3) Survey of radium body burdens of persons formerly engaged in the luminizing industry.
   (4) Studies of correlation of Cs-137 content of urine with the total body burden of that isotope.
   (5) Investigation of levels of Sr-90 and Cs-137 which have accumulated in the bodies of human beings, as a result of ' fall-out ' from test explosions with atomic bombs.
   (6) Investigation of the hazards from Ra-D foils used in gas chromatography detectors.
   (7) Evolution of more accurate methods of monitoring all types of ionizing radiations by means of photographic films.
   (8) Development and calibration of radiometric equipment for various purposes, including measurement of X-rays from television receivers.
   (9) Statistical and theoretical physical studies concerning the effects of radiation in inducing leukaemia and in shortening life span.
   (10) Derivation of mathematical approximations for computing dose rates at various points in space, for different geometrical configurations of protection shields.

(*Publications see p.* 168)

CLINICAL GENETICS RESEARCH UNIT

INSTITUTE OF CHILD HEALTH, THE HOSPITAL FOR SICK CHILDREN, GREAT ORMOND STREET, LONDON, W.C.1

(1957)

Director

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

Staff

C. O. Carter, B.M., M.R.C.P.
Miss M. I. Dunsdon, Ph.D.
R. M. C. Huntley, B.A., B.Ed.

The main work of the Unit falls under two heads: (1) the study of genetic and other factors in the causation of developmental abnormalities in man; and (2) the role of inheritance in the causation of common diseases with some parallel studies on normal human variation.

Summary of Research

1. Collection of a series of women who have had two children with major congenital defects of the central nervous system in order to determine the risk of abnormality in further children.
2. The genetics of some abnormalities, for example, Hirschsprung's disease, hare lip and cleft palate, coeliac disease, congenital pyloric stenosis, and congenital dislocation of the hip and other joint dislocations.
3. Mongolism: aetiological factors, in particular, family history and history of parental exposure to radiation.
4. Quantitative human variation: physical and mental measurements on a series of twins and their relatives to obtain estimates of degrees of resemblance.
5. Continuation of studies on the role of inheritance in hypertension and on associations between blood groups and disease.

(*Publications see p.* 169)

POPULATION GENETICS RESEARCH UNIT

OLD ROAD, HEADINGTON, OXFORD

(1958)

Director

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

Staff

A. Barr, M.Sc. (*part-time*)
J. H. Edwards, M.B., M.R.C.P.
D. T. Hughes, B.Sc.
J. H. Renwick, M.B., Ph.D., M.R.C.P. (*until Feb.*, 1959)
L. I. Woolf, Ph.D.

The Unit is concerned primarily with work designed to illuminate the genetical structure of populations. Much of the activity is concerned with harmful traits of medical and genetical interest. Biochemical and cytological investigations relating to human genetics are related to a considerable extent to the field work of the unit.

Summary of Research

1. Familial aggregation of cases of cancer.
2. Amino-acid excretion patterns in a mentally defective population.
3. Epidemiology of hydramnios and fate of pregnancies so complicated.
4. Cytology of chorion cells from abortions.
5. Analysis of segregation ratios of some specific traits and of certain blood group phenotypes.

(*Publications see p.* 169)

MUTAGENESIS RESEARCH UNIT

INSTITUTE OF ANIMAL GENETICS
WEST MAINS ROAD, EDINBURGH

(1958)

Honorary Director

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

Staff

B. M. Cattanach, Ph.D.
J. L. Reissig, Ph.D.
B. M. Slizynski, Ph.D.

The work of the Unit is aimed at analyzing the processes of spontaneous and induced mutation. For a study of the more fundamental aspects micro-organisms are being used, while mice form the material for the study of phenomena which may be important for man and farm animals.

Summary of Research

1. Neurospora:

   Systems for the study of delayed mutation, particularly mutation to canavanine resistance in an arginine requiring strain.

2. Mice:

   (1) Analysis of the genetical basis for the sterilizing action of TEM (triethylene melamine).

   (2) Study of the action of other chemical mutagens including the use of artificial insemination where marked systemic toxicity for example with nitrogenic mustard, precludes the injection of genetically effective doses into the animal.

   (3) Study of the possible protective action of cysteamine against genetical effects of X-rays.

(*Publication see p.* 169)

UNIT FOR EXPERIMENTAL RESEARCH IN INHERITED DISEASES

UNIVERSITY COLLEGE LONDON, W.C.1

(1955)

Honorary Director

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

Staff

M. S. Deol, Ph.D.
W. Kocher, Ph.D.
Miss G. M. Truslove, Ph.D.

Attached Workers

R. J. Berry, Ph.D. (*M.R.C. Scholar*)
M. S. Grewal, M.Sc.

The Unit is concerned with the study of inherited diseases in laboratory animals, with special reference to medicine. Investigations include the genetical analysis, both of the pathological conditions themselves and of the various genetical backgrounds on which they can manifest themselves; and the study of the pathology and development of these conditions.

Summary of Research

1. The genetics and development of various mutants affecting the skeleton of the mouse.
2. Uncomplicated deafness in the mouse, and the development of hearing tests for its detection.
3. The neuro-pathology of labyrinthine mutants in the mouse.
4. Search for inherited abnormalities of the eye in the mouse.
5. Microphthalkia in the mouse.
6. A sex-linked anaemia in the mouse.
7. The development of third molars in a mouse strain in which these teeth tend to be absent.
8. Minor skeletal variants in inbred strains of mice: a search for correlations.
9. Minor skeletal variants in wild populations of mice and other rodents.

(*Publications see p.* 169)

MICROBIAL GENETICS RESEARCH UNIT

HAMMERSMITH HOSPITAL, DUCANE ROAD, LONDON, W.12

(1957)

Director

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

Staff

R. C. Clowes, Ph.D.
K. W. Fisher, Ph.D.
S. W. Glover, Ph.D.
J. D. Gross, B.Sc.
R. H Pritchard, Ph.D.
N. D. Symonds, Ph.D.

Microorganisms, in recent years, have proved to be uniquely adapted to highly refined analyses of genetic structure, organization and function. The Unit aims at detailed study of the fine structure of genes and chromosomes, and the mechanisms of their replication and transfer to other cells (i.e. sexuality) among microorganisms. 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. Factors determining lysogenisation and transduction of the pathogenic bacterium *Salmonella typhimurium*, by temperate virus (bacteriophage).
2. Investigation of the genetic structure of the bacterium, *Escherichia coli*, by means of transduction, in relation to biochemical function.
3. The nature and function of the fertility factor determining maleness in *Escherichia coli*.
4. Isolation and analysis of the lytic principle associated with infection of *Escherichia coli* by virus λ.
5. Study of the conjugal transfer of colicinogeny, and other characters determined by episomal genes, among bacteria.
6. Genetic fine structure in the mould *Aspergillus* and its relation to general theories of recombination.

(*Publications see p.* 170)

BIOPHYSICS RESEARCH UNIT

KING'S COLLEGE, STRAND, LONDON, W.C.2

(1947)

Honorary Director

Professor J. T. Randall, D.Sc., F.R.S.

Deputy Director

M. H. F. Wilkins, Ph.D., F.R.S.

Honorary Biological Adviser

Miss H. B. Fell, D.Sc., F.R.S.

Staff

Mrs. A. V. W. Brown, Ph.D.
G. L. Brown, Ph.D.
H. G. Davies, Ph.D.
Miss E. J. Hanson, Ph.D.
Miss S. F. Jackson, Ph.D.*
J. Lowy, Ph.D.
S. R. Pelc, D.Phil.†
B. M. Richards, Ph.D.
M. Spencer, Ph.D.
M. R. Watson, M.Sc.
C. R. Worthington, Ph.D.

* On leave of absence in the U.S.A. until July, 1959—Helen Hay Whitney Foundation Research Fellowship, Harvard Medical School, Massachusetts General Hospital, Boston, and the Rockefeller Institute in New York.

Strangeways Research Laboratory, Cambridge, from July, 1959 (External Scientific Staff).

† On leave of absence, from Mar. 1959, as Visiting Research Fellow of American Cancer Society, at the Cancer Research Institute of the University of California, San Francisco.

Visiting and Attached Workers

J. R. Baker, Ph.D. (*supported by M.R.C. grant*)
R. Barton, Ph.D. (*Nuffield Fellow*)
W. Fuller, B.Sc. (*M.R.C. Scholar*)
J. Gordon, B.Sc. (*M.R.C. Scholar*)
D. A. Marvin, B.Sc. (*Yale*)
B. M. Millman, B.Sc. (*Carlton, Ottawa*)
A. Yusa, Ph.D. (*Urbana, Illinois*)
G. L. Zubay, Ph.D. (*Harvard*)

The Unit is mainly concerned with the part played by macro-molecules, particularly proteins and nucleic acids, in the functioning of cells and tissues. Many physical and biochemical techniques are employed and are being developed for the study of these biological systems; they include X-ray diffraction analysis, microscopical methods such as electron microscopy and interference microscopy, microspectrometry in various parts of the spectrum, and molecular fractionation procedures.

Summary of Research

1. Structure and function of nucleic acid (DNA) and nucleoprotein.
2. Physiological, structural and biochemical aspects of muscular contraction.
3. The fine structure of cells and tissues with some current emphasis on:
   (1) protozoa in relation to contractility, morphogenesis and differentiation;
   (2) kinetosomes, cilia and flagella.
4. Development and application of optical methods for use in cytochemistry and other aspects of cytological studies.

(*Publications see pp.* 170–171)

MOLECULAR BIOLOGY RESEARCH UNIT

CAVENDISH LABORATORY, FREE SCHOOL LANE, CAMBRIDGE

(1947)

Director
M. F. Perutz, Ph.D., F.R.S.

Deputy Director
J. C. Kendrew, Ph.D., F.R.S.

Honorary Adviser
Sir Lawrence Bragg, O.B.E., F.R.S.

Staff

Mrs. L. Barnett, B.Sc.
S. Brenner, M.B., D.Phil.
F. H. C. Crick, Ph.D., F.R.S.
Miss A. F. Cullis, M.A. (*until April*, 1959)
Miss A. L. V. Jury, B.A.
M. G. Rossmann, Ph.D.
Mrs. A. Stockell Hartree, Ph.D.
B. E. Strandberg, F. M. (*Sweden*)

Attached and Visiting Workers

A. Aronson, Ph.D. (*Washington, D.C.*)
D. R. Davies, D.Phil. (*Washington, D.C.*)
R. E. Dickerson, Ph.D. (*Minneapolis, Min.*)
S. C. Glauser, Ph.D. (*Pennsylvania*)
J. A. Hunt, B.A. (*M.R.C. Scholar*)
L. S. Lerman, Ph.D. (*Colorado*)
Hilary Muirhead, B.A. (*Research Student*)
L. K. Steinrauf, Ph.D. (*Pasadena, Calif.*)

This Unit is devoted to the study of the structure and function of large molecules of biological interest. The structure of proteins is analyzed by a combination of physical and chemical methods and especially by X-ray diffraction, a method which has helped to elucidate the arrangement of the atoms in many simpler substances. During the year under review members of the Unit made some notable advances in the X-ray analysis of crystalline proteins, in the chemistry of the human haemoglobins and in the structure and genetics of viruses.

1. Calculation of a three-dimensional Fourier of myoglobin at 2 Å resolution. This is now being used to build an atomic model of the myoglobin molecule. First results show that long stretches of the polypeptide chain are α-helices.
2. Calculation of a three-dimensional Fourier of haemoglogin at 5·5 Å resolution. This shows that haemoglobin consists of four-sub-units arranged at the corners of a tetrahedron, and that each sub-unit resembles Kendrew's model of whale myoglobin.
3. Chemical studies of human haemoglobin showed that the glutamic acid residue which is replaced by valine in sickle cell anaemia occupies the sixth position from the N-terminal end in one of the pairs of chains (the β-pair).
4. In haemoglobin E a glutamic acid residue is replaced by lysine, as in haemoglobin C, but the change lies in a different part of the molecule.
5. Human foetal haemoglobin, like adult, consists of four polypeptide chains. One of these, the pair of α-chains, has now been found to be identical in the two proteins. The differences are confined to the other pair.
6. A new staining method has been developed for the high resolution electron microscopy of viruses and applied to the study of adenovirus, type 5. The results show the virus to be an icosahedron of 700 Å diameter, with faces covered by 252 protein sub-units of identical size.
7. Discovery of the gene controlling the head protein of bacteriophage has opened the way to a study of the relation between the fine structure of that gene and the sequence of amino-acids in the protein.
8. In a study of the genetic effects of chemical mutagens in T4 bacteriophage, the genetic fine structure of mutations induced by proflavin was found to have a different pattern from that produced by 5-bromo-uracil. This experiment shows the complexicity of the genetic fine structure of the virus.

(*Publications see p.* 171)

CELL METABOLISM RESEARCH UNIT

DEPARTMENT OF BIOCHEMISTRY, UNIVERSITY OF OXFORD

(1945)

Honorary Director

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

Staff

W. Bartley, Ph.D.
K. Burton, Ph.D.
G. H. Dixon, Ph.D.
D. E. Hughes, Ph.D.
H. L. Kornberg, Ph.D.
J. R. Quayle, Ph.D.
A. Rodgers, Ph.D.
Mrs. K. Rodgers, B.Sc. (*part-time*)
R. Whittam, Ph.D.

Attached Workers

J. E. Amoore, D.Phil. (*Christopher Welch Scholar*)
D. Bellamy, B.Sc. (*M.R.C. Scholar*)
A. L. Biran, B.Sc. (*Colonial Medical Research Student*)
L. M. Birt, Ph.D. (*Melbourne*) (1851 *Overseas Scholar*)
L. Fessler, Ph. D. (*Wisconsin*) (*U.S. Public Health Service Fellow*)
A. M. Gotto, B.A. (Vanderbilt University) (*Rhodes Scholar*)
D. B. Keech, Ph.D. (*C.S.I.R.O. Scholar (Australia)*)
A. Muhammed, D.Phil. (*Pakistan Govt. Overseas Scholar*)
D. Peel, B.Sc. (*M.R.C. Scholar*).
G. B. Petersen, D.Phil. (*D.Phil. Student*)
W. T. Riley, B.A. (*M.R.C. Scholar*)
J. R. Sadler, B.A. (*Rhodes Scholar*)
A. B. Stone, B.Sc. (M.R.C. Scholar)

The Unit is concerned with the study of metabolic processes in which energy is produced or consumed, with special reference to the mechanism of energy transmission. In addition, the properties of various enzymes are being investigated.

Summary of Research

1. Metabolic processes:
   (1) Rate controlling factors in respiration.
   (2) The exchange between cells and environment of inorganic and organic ions.
   (3) Secretory activity of mitochondria.
   (4) The absorption of vitamins by laboratory animals.
   (5) Metabolism of C_1- and C_2- compounds in micro-organisms.
   (6) Fat and phospholipid distribution within the cell; comparative biochemistry of mitochondria.
   (7) Biochemistry of phage multiplication.
   (8) Metabolism of phosphate polymers in bacteria.
2. Enzymes
   (1) Hydroxylation of nicotinic acid.
   (2) Malate synthetase, glyoxylic carboligase, glyceric dehydrogenase, glyceric acid kinase.
   (3) Carboxylation of ribulase diphosphate.
   (4) Bacterial polymetaphosphatase.
3. Techniques
   (1) The development of methods for breaking up bacterial and other microbial cells and for extracting enzymes and other cell constituents.
   (2) Ultramicro-analytical techniques, with special reference to the analysis of the fluids of the inner ear.
   (3) Study of degradation methods for determining the structure of DNA.
   (4) Application of the glass electrode to the measurement of sodium.

(*Publications see pp.* 172–173)

CHEMICAL MICROBIOLOGY RESEARCH UNIT

DEPARTMENT OF BIOCHEMISTRY, UNIVERSITY OF CAMBRIDGE

(1944)

Director

E. F. Gale, Sc.D., F.R.S.

Staff

R. Davies, Ph.D.
D. Kerridge, Ph.D.
B. A. Newton, Ph.D.
C. J. Shepherd, Ph.D. (*until Nov.*, 1958)

M.R.C. Scholars working under supervision of staff

J. M. Field, B.A.
M. T. Heydeman, B.A.
J. T. O. Kirk, B.A.
R. E. Monro, B.A.

Micro-organisms provide admirable material for the study of the synthesis of proteins and their organization as enzymes within the living cell. The investigations in this Unit are mainly concerned with the biochemistry of these processes in various micro-organisms, and the ways in which such processes can be inhibited by antimicrobial drugs.

Summary of Research

1. Assimilation and metabolism of amino-acids by bacteria, yeasts, fungi and protozoa; mechanism of protein and nucleic acid synthesis in these micro-organisms.
2. Functional organization of the bacterial cell.
3. Factors controlling the inheritance of enzymic activities and their adaptive capacity in micro-organisms.
4. Points of interference in anabolic processes by various chemotherapeutic agents, with special reference to the mode of action of antibiotics.

(*Publications see p.* 173)

CHEMOTHERAPY RESEARCH UNIT

MOLTENO INSTITUTE, DOWNING STREET, CAMBRIDGE

(1942)

Director

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

Staff

Miss E. W. McConnachie, Ph.D.

This Unit is studying the biology of protozoa, with special reference to the mechanism of the development of drug resistance in malaria parasites, and the effect of environmental factors upon the growth and life-cycle of parasitic protozoa.

Summary of Research

1. The effect of the size of the inoculum upon the rate of development of resistance to proguanil (paludrine) in *Plasmodium gallinaceum*, a malaria parasite of birds.
2. The effect of inorganic ions upon the *in vitro* development of the gametes of *P. gallinaceum*.
3. Investigations on the nutritional requirements and encystation of *Entamoeba invadens* in axenic cultures, and on the encystation and excystation of entamoebae in cultures containing bacteria.
4. The cultivation of certain parasitic ciliates and coprozoic flagellates.

(*Publications see p.* 173)

ANTIBIOTICS RESEARCH STATION

4, ELTON ROAD, CLEVEDON, SOMERSET

(1949)

Director

B. K. Kelly, B.A.

Staff

Miss J. M. Bond, Ph.D.
R. C. Codner, B.Sc.
J. J. Gordon, Ph.D., A.R.I.C.
C. W. Hale, A.R.I.C.
R. W. Harrison, Ph.D.
G. A. Miller
B. C. Platt, Ph.D., A.R.I.C.

Antibiotic fermentations and extractions are undergoing development with a view to producing sufficient quantities to enable their clinical possibilities to be established. Assistance is also given to other Council workers and University departments by carrying out fermentations and extractions on a scale larger than is convenient in the ordinary laboratory.

Summary of Research

1. Development of production of cephalosporin C and study of its derivatives.
2. Production of cephalosporin P for chemical studies.
3. Production by fermentation and extraction of actitriin.
4. Study of the monamycin fermentation.
5. Production and chemical studies of the antibiotic actinonin.
6. Production of carotenoid-producing bacteria.
7. Study of carotenoids produced by cephalosporium.
8. Production of nitrosomonas.
9. Continuous culture of bacteria.
10. Production of L-phenylalanine decarboxylase by streptococcus faecalis.

(*Publications see p.* 174)

EXPERIMENTAL VIRUS RESEARCH UNIT

DEPARTMENT OF VIROLOGY, THE UNIVERSITY, GLASGOW, W.2

(1959)

Honorary Director
Professor M. G. P. Stoker, M.D.

Assistant Director
N. P. L. Wildy, M.B.

Staff
I. A. MacPherson, Ph.D.

The Unit's aim is to study the interaction between viruses and cells, under controlled laboratory conditions, with particular reference to viruses which cause latent infections, such as the tumour viruses and herpes simplex virus. Special attention will be paid to the possibility of inherited abnormalities in cell function which such viruses might produce.

Summary of Research

1. Subunit structure of herpes virus studied by electromicroscopy and chemical analysis. Assembly of the virus particle. Effect of herpes virus on the physiology of cells in culture.
2. Interaction between fowl lymphoma virus and cultured chick cells, and between BP virus (a polyoma-like virus) and cultured mouse and hamster cells.
3. Methods of obtaining clones of differentiated cells direct from tissues.

VIRUS RESEARCH UNIT

MEDICAL RESEARCH COUNCIL LABORATORIES, WOODMANSTERNE ROAD, CARSHALTON, SURREY

(1955)

Director
F. Kingsley Sanders, D.Phil.

Staff
A. J. D. Bellett, M.Sc.
A. T. H. Burness, Ph.D.
A. D. Vizoso, Ph.D.

The work of the Unit is concerned with elucidating the mechanism of cellular infection by viruses. Tissue culture systems, where the behaviour of the infected cells can be studied chemically as well as virologically, are being used to study details of the behaviour of viruses within the cells they infect.

Summary of Research

1. The kinetics of the growth of a virus in tumour cells, using for investigation mouse ascites tumour cells kept alive outside the bodies of their hosts, either in liquid suspension or in agar layers, and monolayer cultures prepared from solid tumours.
2. Isolation and study of the properties of mutant virus strains capable of growing in mouse tumour cells naturally resistant to infection by naturally occurring strains of the virus.
3. Characterization of the material carrying virus properties in nucleic acid preparations made from virus infected cells at various stages of infection, and study of its effect upon susceptible cells.

(*Publications see p.* 174)

VIRUS CULTURE LABORATORY

MEDICAL RESEARCH COUNCIL LABORATORIES, WOODMANSTERNE ROAD, CARSHALTON, SURREY

(1956)

Director

P. D. Cooper, Ph.D.

Staff

Mrs. A. M. Burt, B.Sc.
M. L. Fenwick, Ph.D.
J. N. Wilson, M.Sc.

The aims of the Unit are to study in detail the growth in cell culture of one particular virus (poliomyelitis) as a model of the mechanisms of cell and virus growth, and to provide purified virus preparations, and other materials required on a large scale for virus research.

Summary of Research

1. Continuous suspended culture of animal cells and the further study of cell growth with this method.
2. Improved methods for plaque virus assay and for bulk virus growth, concentration and purification; a method for cup-plate assay of neutralizing antibody and its reacting antigen.
3. Characteristics of one-step virus growth in cell suspensions; virus eclipse mechanisms; 'shortened latency'; virus release and the cell surface; virus interference.
4. Interference and other microscopy of living and fixed infected and normal cells.
5. Purification of isotopically labelled virus, and the use of isotopes in the study of virus growth.

(*Publications see p.* 174)

HUMAN NUTRITION RESEARCH UNIT

NUTRITION BUILDING, NATIONAL INSTITUTE FOR MEDICAL RESEARCH, THE RIDGEWAY, MILL HILL, LONDON, N.W.7

(1944)

Director

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

Staff

Miss P. M. Carroll, B.Sc.
K. O. Godwin, Ph.D.
C. R. C. Heard, D.Phil.
D. J. Naismith, Ph.D.
P. R. Payne, B.Sc.
P. L. Pellett, Ph.D., A.R.I.C.

Attached and Visiting Workers

S. M. Ali, M.Sc.(*Pakistan*)
I. S. Dema, B.Sc. (*Nigeria*)
G. Donoso, M.D. (*Chile*)
Miss H. C. Fox, B.Sc. (*Jamaica—Colonial Medical Research Student*)
W. M. Frankul, B.A. (*Baghdad*)
T. Guminski, M.D. (*Poland*)
H. Hedayat, M.D. (*Iran*)
O. A. M. Lewis, M.Sc. (*S. Africa*)
C. C. Liang, B.Sc. (*Hong Kong*)
Mrs. D. Milétic, Mr.Ph. (*Yugoslavia*)
D. S. Miller, B.Sc. (*London—Rockefeller grant*)
G. Pampiglione, M.D., M.R.C.P. (*Hospital for Sick Children, Gt. Ormond St.*)
R. U. Qureshi, M.Sc. (*Pakistan*)

(*At the London School of Hygiene and Tropical Medicine—Department of Human Nutrition*)

G. R. Wadsworth, M.D. (*Senior Lecturer*)

The main study of the Unit has been the malnutrition of people in colonial territories; the investigations are now being extended to include the nutritional problems of other tropical and sub-tropical countries. 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 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. Study of the various forms and manifestations of malnutrition especially of the effects in man and animals of low-protein high carbohydrate diets:
   (1) Inter-relationships of dietary and endocrine factors.
   (2) Effects on the reproductive system, on the foetus and infant, on the development and function of the mammary gland, in the nervous system, alimentary canal and skin and on bone growth.
   (3) Biochemical changes in tissues, body fluids and secretions including milk.
   (4) Inter-relationships of malnutrition and the effects of zymotic disease including malaria and worm infestations.
2. Nutritional value of proteins determined by biological and chemical methods in foods, dishes, meals and dietaries.
3. Technology of food processing in relation to nutritional values of the processed product.

(*Publications see pp.* 174–175)

DUNN NUTRITIONAL LABORATORY

MILTON ROAD, CAMBRIDGE

(1926)

Director
L. J. Harris, Sc.D., F.R.I.C.

Deputy Director
T. Moore, Sc.D.

Staff

Miss E. M. Cruickshank, Ph.D.
A. N. Howard, Ph.D.
R. E. Hughes, Ph.D. (*until Sept.*, 1959)
E. H. Kodicek, M.D., Ph.D.
I. M. Sharman, Ph.D., F.R.I.C.
R. J. Ward, Ph.D., A.R.I.C. (*until Mar.*, 1959)

Attached Worker
V. H. Booth, Ph.D. (*Agricultural Research Council*)

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

Summary of Research

1. Factors influencing the relationship between minimum and optimum requirements for various nutrients.
2. Vitamin-C studies, in relation to: blood picture, adrenal structure, coagulation factors, metabolism of mucopolysaccharides and of folic acid and iron, urinary excretion.
3. ' Bound ' nicotinic acid in cereals.
4. Vitamin A: effects of deficiency; blood levels in human subjects; significance for farm animals; characterization of carotenoids.
5. Vitamin-E studies in relation to: human nutrition, ' haemolysis ' test, redox dyes, selenium, methods of determination, biological and anti-oxidative functions, kidney degeneration, cod-liver oil (pro- and anti-vitamin), distribution and function in leaves.
6. Studies on the distribution of vitamin D in rat tissues; metabolism of ^{14}C-labelled D_3 in infants and rats.

7. Various investigations on:

(1) Fat from moulds.

(2) Biosynthesis of isoprenoid compounds.

(3) Blood volumes.

(4) Food consumption as influenced by deficiency disease and the administration of toxic substances.

(*Publications see p.* 176)

MEDICAL RESEARCH COUNCIL LABORATORIES, GAMBIA
(1953)

Director

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

Staff

R. D. Foord, M.B., D.T.M. & H.
H. M. J. Gilles, M.D., B.Sc., D.T.M. & H. (*until Nov.*, 1958)
M. E. C. Giglioli, Ph.D.
M. C. D. Hurly, M.B. (*until Nov.*, 1958)
D. H. Murphy, B.Sc.

Visiting Workers

A. D. Berrie, B.Sc. (*M.R.C. External Staff*)
M. J. Gillies, F.R.C.S. (*Sussex Eye Hospital, Brighton*)
B. Hubendick, D.Sc. (*Naturhistoriska Museet Göteborg, Sweden*)
A. M. Thomson, M.B., B.Sc., D.P.H. (*Obstetric Medicine Research Unit*)

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 (p. 113) has a permanent field station at the Gambia Laboratories.

Summary of Research

Staff:

1. The effects of repeated parasitic infections on the health of a rural village community.
2. The effects of heavy and repeated malaria infections in Gambian infants and young children.
3. The effect on health and mortality of elimination of malaria in a rural community.
4. Chemical and electrophoretic studies of the blood protein patterns of Gambians of all ages.
5. The incidence and aetiology of anaemia in a rural African population.
6. The importance of the role of hookworm infections in the production of anaemia in rural populations.
7. The value of diethylcarbamazine (Hetrazan) in the field control of Bancroftian filariasis.
8. The antibody production in African children following administration of specific therapeutic vaccines.
9. The bionomics of mosquitoes of the *A. gambiae* complex.
10. The behaviour of prevalent Culicoides populations.
11. The anatomy of the mosquito ovariole.
12. Changes in the physiological age structure of *A. gambiae* vectors in relation to the characteristic periodicity of this mosquito in and beyond its breeding places.

Visitors:

1. Study of prevalent nutritional conditions in the Gambia and their effect on physique and health. (A. M. Thomson.)
2. Study of maternity and lactation in the Gambia. (A. M. Thomson.)
3. Study of the schistosome vector snails and their habitat. (B. Hubendick and A. D. Berrie.)

(*Publications see p.* 176)

TROPICAL METABOLISM RESEARCH UNIT

UNIVERSITY COLLEGE OF THE WEST INDIES, MONA, ST. ANDREW, JAMAICA

(1955)

Director

Professor J. C. Waterlow, M. D.

Staff

R. D. Montgomery, M.B., M.R.C.P.
D. Picou, B.M.
L. Rathbone, Ph.D.
R. Smith, M.B. (*until July*, 1959)
Miss J. M. L. Stephen, Ph.D. (*working at University College Hospital Medical School, London*)
Miss V. G. Wills, M.B., M.R.C.P., D.C.H. (*until April*, 1959)

Attached Worker

C. B. Mendes, B.Sc. (*Jamaica*)

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

The Unit collaborates with the Department of Medicine, University College of the West Indies, in research on diabetes, megaloblastic anaemia and peripheral neuropathy, and with the Government of Jamaica in the study of practical nutritional problems.

Summary of Research

1. Studies in malnourished infants:
   (1) Body composition and total body water.
   (2) Measurement of total exchangeable potassium.
   (3) Nitrogen, phosphorus and electrolyte balances.
   (4) Respiratory metabolism and oxygen uptake.
   (5) Protein turnover with radioactive methionine and iodinated albumin.
   (6) Mitochondrial enzyme systems of the liver.
   (7) Serum phospholipids.
   (8) Muscle composition: protein, nucleic acids, electrolytes and magnesium.
   (9) Excretion of formiminoglutamic acid in folic acid deficiency. (In collaboration with Dr. Luhby of New York.)
   (10) Feeding trials with human milk.
2. Studies in adults:
   (1) Oxidative phosphorylation in the liver in diabetes.
   (2) Serum biochemistry in peripheral neuropathy.
3. Experimental studies in rats fed on Jamaican diets:
   (1) Changes in the amount, type and rate of synthesis of muscle proteins.
   (2) Tests of mitochondrial damage in the liver.
4. Clinical nutritional surveys in the field.

(*Publications see p.* 177)

INFANTILE MALNUTRITION RESEARCH UNIT

MULAGO HOSPITAL, KAMPALA, UGANDA

(1953)

Director

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

Staff

Miss F. M. Bisset-Smith, M.B., M.R.C.P.E., D.C.H.
Miss K. M. Clegg, Ph.D. (*until July*, 1959)
Miss A. P. Farmer, B.Sc.
P. R. Murrell Jones, M.S.R.
Miss C. E. Matthew, B.A.
R. G. Whitehead, Ph.D.

Visting Workers

Dr. Marcelle Geber (*Paris*)
Professor W. W. Greulich (*Stanford University, U.S.A.*)

Summary of Research

1. Investigation of the biochemical abnormalities that may be due to malnutrition.
2. The utilization of locally produced foods for the prevention and treatment of nutritional disease.
3. Studies of psychomotor and somatic development. The techniques used include Gesell tests, the detailed measurement of bone growth, and somatotype-photography.
4. Studies of the home environment of the malnourished child and of the after-effects of an episode of malnutrition.

(*Publications see p.* 177)

BILHARZIA RESEARCH UNIT

WINCHES FARM, HATFIELD ROAD, ST. ALBANS

(1947)

Director

J. Newsome, M.D., D.T.M. & H.

Staff

A. Davis, M.B., M.R.C.P.E.*
D. L. H. Robinson, Ph.D.
G. A. T. Targett, B.Sc.

The Unit is working on schistosome metabolism, immunity in schistosomiasis, chemotherapy and the mode of action of schistosomicides.

Summary of Research

1. Physiology and metabolism of young and adult flukes.
2. Mechanisms of immunity to schistosomiasis.
3. Comparative biochemistry of vector and non-vector snails.
4. Changes in carbohydrate and protein metabolism of flukes due to drug action.
5. Trials in animals and man of old and new schistosomicides.

(*Publications see p.* 177)

* Working in East and Central Africa, based at Nairobi.

SOCIAL PSYCHIATRY RESEARCH UNIT

INSTITUTE OF PSYCHIATRY, MAUDSLEY HOSPITAL, DENMARK HILL, LONDON, S.E.

(1948)

Honorary Director

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

Assistant Director

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

Staff

G. W. Brown, B.A.
Mrs. B. Hermelin, Ph.D.
Miss E. M. Kirwan, B.A.
J. Loudon, M.B., Dip. Anthrop.‡
N. O'Connor, Ph.D.
K. Rawnsley, M.B., M.R.C.P., D.P.M.‡
J. Tizard, Ph.D.
P. H. Venables, Ph.D.
J. K. Wing, M.B., D.P.M.

Attached Workers

G. Berkson, M.S., Ph.D.
C. Fraser, M.A. (*M.R.C. Scholar*)
J. W. Moss, Ph.D.

The Unit studies the influence of social factors on the occurrence, continuance, and outcome of mental illness. Special attention is given to analysis of the psychological and social handicaps of the mentally ill and of mentally defective persons, and to exploring methods of overcoming these handicaps.

Summary of Research

1. Experimental studies of conceptual processes in imbecile children.
2. Studies in the education and management of imbecile children.
3. Learning and conditioning in chronic psychotics and in mental defectives.
4. Performance of chronic psychotic patients under specific experimental conditions, in the psychological laboratory and in industrial workshops.
5. Psychological change and subsequent performance at work of psychiatric patients passing through an Industrial Rehabilitation Unit.
6. Social factors in the rehabilitation of chronic psychotic patients discharged from hospital.
7. Social structure and attitudes in two defined populations in South Wales.
8. Attitudes to chronic mental and physical disability, in the same two populations. (The last two studies are in collaboration with the Pneumoconiosis Research Unit.)

(*Publications see pp.* 177–178)

NEUROPSYCHIATRIC RESEARCH UNIT†

WHITCHURCH HOSPITAL, CARDIFF

(1957)

Director

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

Staff

R. Balazs, M.D., Ph.D.
A. W. Brown, B.Sc.
G. B. David, B.Sc.
J. G. Ingham, Ph.D.
T. J. McDermott, M.Sc.
J. O. Robinson, M.Sc.

* Dr. Carstairs has been appointed Director of a new Unit the Council have set up to study the epidemiology of mental disorders.

† Shortly transferring to Medical Research Council Laboratories, Woodmansterne Road, Carshalton, Surrey.

‡ Based on Pneumoconiosis Research Unit, Penarth, Glam.

Attached Workers

H. Backer, L.S.A. (*Prague*)
G. Gardos, Ph.D. (*Budapest*)
M. R. Joshi, Ph.D. (*Bombay*)
J. R. Lagnado, Ph.D. (*Montreal*) (*Kathleen Schlesinger Fellow*)

The Unit is developing basic and clinical research in problems related to the causes and treatment of mental illness.

Summary of Research

1. The biochemistry of the brain in normal subjects and in mental hospital patients.
2. The metabolic changes associated with maturation and with functional activity of the brain.
3. The action of drugs and of electrical shock treatment on the brain.
4. The protein metabolism of schizophrenic patients.
5. Changes in the nerve cell as a result of injury.
6. The electrical activity of the brain in normal subjects and in patients.
7. The interaction between sensory stimuli in the brain.
8. The distribution of personality characteristics in the community.

(*Publications see p.* 178)

NEUROPHARMACOLOGY RESEARCH UNIT

DEPARTMENT OF EXPERIMENTAL PSYCHIATRY, THE MEDICAL SCHOOL, BIRMINGHAM, 15

(1958)

Honorary Director

P. B. Bradley, D.Sc.

Staff

B. J. Key, Ph.D.

Attached Worker

A. N. Nicholson, M.B. (*M.R.C. Scholar*)

The Unit is studying the action of drugs on the central nervous system with particular reference to the correlation between electro-physiological and behavioural effects. The drugs used are those with known effects on mental function and also certain drugs in use in psychiatry.

Summary of Research

1. The effects of drugs on sensory generalization and sensory discrimination in animals.
2. The effects of drugs on conditioned arousal responses produced by sensory stimuli, in relation to lesions localized at different levels of the afferent pathways.
3. The effect of drugs on the electrical activity of the hippocampus and the effect of lesions in this structure in relation to modifications of behaviour produced by drugs.

CLINICAL PSYCHIATRY RESEARCH UNIT

GRAYLINGWELL HOSPITAL, CHICHESTER, SUSSEX

(1957)

Director

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

Staff

Miss J. C. Grad, Ph.D.
J. B. Knowles, B.Sc., Dip.Psych.
C. J. Lucas, M.B., M.R.C.P., D.P.M. (*until Sept.*, 1959)
J. W. T. Redfearn, M.D., D.P.M.
J. C. Shaw, B.Sc.

The purpose of the Unit is to investigate clinical problems in psychiatry.

Studies are therefore being planned in conjunction with members of the hospital staff. In addition, the Unit has selected two main subjects for study: (1) factors in the social and family environment of mentally ill patients which may be related to their breakdown and admission to hospital, and (2) investigations into psychosomatic symptoms and the mechanisms underlying them.

Summary of Research

1. Clinical studies undertaken in conjunction with hospital staff:
   (1) Therapeutic trials with special reference to the problems of method and the placebo effect.
   (2) Clinical, social and environmental factors determining admission to mental hospital.
2. Social studies:
   (1) Social factors in the mental illnesses of patients referred from a New Town.
   (2) The social and familial factors in the genesis of schizophrenic delusions.
3. Psychosomatic and physiological studies:
   (1) A survey, classified by diagnosis, of neuroticism among all out-patients attending the different clinics in a general hospital.
   (2) Measurement of the effects of tranquillizing drugs on movement and muscle tension.
   (3) Investigations of some physiological concomitants of psychiatric illness, particularly tremor.

(*Publications see pp.* 178–179)

APPLIED PSYCHOLOGY RESEARCH UNIT

15, CHAUCER ROAD, CAMBRIDGE

(1944)

Director

D. E. Broadbent, M.A.

Assistant Directors

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

Staff

A. D. Baddeley, M.A.
I. D. Brown
A. Carpenter, M.B.
E. G. Chambers, M.A.
W. P. Colquhoun, Ph.D.
D. W. J. Corcoran, B.Sc.
H. C. A. Dale, B.Sc.
G. G. Denton, A.M.(SA)I.E.E.
C. B. Gibbs, B.Sc. (*until Oct.*, 1959)
S. D. Holmqvist, Lic.Eng. (*until Dec.*, 1959)
I. M. Hughes, M.A.
J. A. Leonard, Ph.D.
M. Stone, Ph.D.
R. T. Wilkinson, Ph.D.
Miss M. M. Woodhead

Attached and Visiting Workers

R. Davidon, Ph.D. (*Bryn Mawr, Penn.*)
R. M. Warren, Ph.D. (*Brown Univ. Rhode Is.*)
J. C. Webster, Ph.D. (*N.E.L., San Diego*)

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

Summary of Research

1. Perception:
   (1) Alertness during prolonged visual inspection.
   (2) Visual discrimination.
   (3) Simultaneous use of sight and touch for assessing surfaces.
   (4) Development of visual displays.
   (5) Presentation of technical information.
   (6) The effect of context on sensory judgments.
   (7) Factors affecting the intelligibility of speech.
   (8) Reaction times to speech.
2. Thinking:
   (1) Information theory research.
   (2) Subjective probability estimates and location of faults in electronic and other systems.
   (3) Design of keyboards.
   (4) Human limits in decision taking: speed and load stress in a variety of skilled performances.
   (5) Coding of information.
3. Moving:
   (1) Equipment design of manual controls.
   (2) Studies of the effects of lag and quickening on the integration of visual and proprioceptive data.
   (3) Efficiency of tracking various types of input signal.
   (4) Experiments on car driving performance.
4. Working Conditions:
   (1) Achievement after lack of sleep.
   (2) High intensity noise effects.
   (3) Effects of alcohol.
   (4) Length and arrangement of work shifts.
5. Learning:
   (1) Factors affecting immediate memory, especially in serial tasks.
   (2) Training of skills.
6. Personality:
   (1) Relation of individual differences to skilled performance.
7. Statistics:
   (1) Methods of assessing degree of confidence in experimental results.
   (2) Mathematical models for human performance.

(*Publications see p.* 179)

INDUSTRIAL PSYCHOLOGY RESEARCH UNIT

UNIVERSITY COLLEGE, LONDON, W.C.1

(1918)

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

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

Assistant Director
R. Marriott, M.Sc.

Staff

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

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

Summary of Research

1. Motivation and performance:
   (1) The merits and defects of incentive payment systems, including merit rating.
   (2) The relation between group structure and productivity.
   (3) The effects of alcohol and drugs on skilled performance.
   (4) Experimental studies of memory for spatial position.
2. Absence:
   (1) Studies of attendance, absence and sickness absence in various industries.
   (2) The relation between individual absence, overtime, financial responsibility and group membership.
3. Communication:
   (1) Administrative efficiency with reference to the flow of information in industry.
   (2) The validity and reliability of subjective measures of technical writing.
   (3) Comparative studies of the information value of direction signs.
4. Thinking:
   (1) Elimination in inductive thinking.
   (2) Response to negative information.
   (3) Thought processes involved in the comprehension of rules.

(*Publications see pp.* 179–180)

UNIT FOR THE EXPERIMENTAL INVESTIGATION OF BEHAVIOUR

UNIVERSITY COLLEGE, LONDON, W.C.1

(1955)

Honorary Director

Professor G. C. Drew, M.A.

Staff

P. H. Glow, Ph.D.
Miss M. Khaïry, Ph.D.
R. H. J. Watson, Ph.D.

Attached Workers

R. J. Audley, Ph.D. (*University College London*)
R. S. Lanterman, M.A. (*University College London*)
N. Mrosovsky, B.A. (*M.R.C. Scholar*)

The aim of the Unit is to study the relationship between body chemistry and behaviour. The research has practical applications in the fixing of industrial and similar toxicity standards, and in the treatment of certain behaviour disorders in man.

Summary of Research

1. Behaviour changes induced by the administration of pharmacological agents, including ' tranquillizers ', ' hallucinogens ', and nervous system poisons.
2. The relationship between behaviour differences and normal individual variations in body chemistry, particularly in cholinesterase and adrenaline-noradrenaline.
3. Electrophysiological changes accompanying changes in body chemistry.
4. Effects of reduced body temperature on biochemical systems and behaviour.
5. Effects of specific brain lesions on body chemistry and behaviour.
6. The development of improved techniques for the quantitative measurement of behaviour, especially those forms of behaviour found to be closely related to particular biochemical systems.

(*Publications see p.* 180)

UNIT FOR RESEARCH ON OCCUPATIONAL ASPECTS OF AGEING

DEPARTMENT OF PSYCHOLOGY, UNIVERSITY OF LIVERPOOL

(1955)

Director
Alastair Heron, Ph.D.

Honorary Scientific Adviser
Professor L. S. Hearnshaw, M.A.

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

Staff

Mrs. S. M. Chown, Ph.D.
Mrs. C. M. Cunningham, B.A.
T. Farrimond, B.Sc.
M. S. Featherstone, B.A.
Mrs. R. V. J. Stevens, B.A.
D. J. Stewart, B.A. (*until Aug.*, 1959)

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

Summary of Research

1. Experimental studies of the psychological concomitants of normal changes with age in perceptual standards, the present emphasis being on vision and hearing.
2. Studies of various aspects of psychological 'rigidity' including the examination of both intellectual and emotional aspects of this problem, and of its relevance to occupational training and re-training procedures.
3. Investigation of attitudes towards ageing and its consequences, adopted by ageing persons and by other groups of persons of various ages and occupational status.

(*Publication see p.* 180)

SOCIAL MEDICINE RESEARCH UNIT

THE LONDON HOSPITAL RESEARCH LABORATORIES, ASHFIELD STREET, LONDON, E.1.

(1948)

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

Staff

Mrs. M. D. Crawford, M.D. (*part-time*)
Miss E. M. Goldberg
J. A. Heady, M.A.
A. R. Kagan, M.B., M.R.C.P., D.P.H.
J. A. H. Lee, M.D., B.Sc., D.P.H.
S. L. Morrison, M.B., D.P.H.

Visiting Worker
K. L. White, M.D. (*North Carolina*)

The Unit is investigating the influence that social factors may have upon health and sickness, and the relation of social to other factors. Studies are made of populations and groups, and their environments; and individuals are studied in relation to these. Epidemiological and clinical case methods are used.

Summary of Research

1. Coronary artery disease and ischaemic heart disease in relation to nature of occupation and to other factors including physique, blood pressure, blood lipids, and smoking. Follow-up of ' coronary ' patients discharged from the London Hospital.
2. Familial and environmental factors in hypertension.
3. Techniques of individual dietary survey in adults.
4. Appendicitis: social and geographical distribution of morbidity and mortality from appendicitis. Use of national data to identify clinical syndromes.
5. Mental disease: clinical study of the families of young men admitted to local mental hospitals —the occupational history over three generations, family structure and relationships, and the family history of admission to mental hospitals. Study of the social class distribution of national samples of patients and their fathers (jointly with the General Register Office).
6. Operational research on the working of health services: case-fatality in teaching and non-teaching hospitals; variations of prescribing rates in general practice.

(*Publications see pp.* 180–181)

STATISTICAL RESEARCH UNIT

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE, LONDON, W.C.1

(1926)

Honorary Director

Professor A. Bradford Hill, C.B.E., D.Sc., F.R.S.

Deputy Director

W. R. S. Doll, O.B.E., M.D., D.Sc., F.R.C.P.

Staff

P. Armitage, Ph.D.
J. T. Boyd, M.D., D.P.H. (*part-time*)
A. S. Fairbairn, M.B.
Mrs. E. L. I. Hanington, M.B.
J. O. Irwin, Sc.D., D.Sc.
Miss J. M. Kennedy, M.B. (*until March*, 1959)
Miss B. J. Kinsley, B.Sc.
J. Knowelden, M.D., D.P.H. (*part-time*)
W. J. Martin, D.Sc.
Professor D. D. Reid, M.D., D.Sc., M.R.C.P. (*honorary*)
I. Sutherland, D.Phil.

The Unit is concerned with the development and application of statistical methods in medicine and in its associated sciences, including research into the epidemiology and aetiology of disease, the promotion and analysis of vital statistics, the design and analysis of therapeutic trials of new drugs and other agents, the design and analysis of field trials of prophylactic agents, the application of mathematical-statistical techniques to the solution of laboratory problems and the development of methods of biological assay. The investigations listed in the summary of research include not only the individual researches of members of the Unit's staff but also the main items of collaborative work with the Council and with other scientific workers.

Summary of Research

1. The epidemiology and aetiology of disease :
   (1) Aetiology of cancer of the lung, with particular reference to smoking, air pollution and industry.
   (2) The incidence and causes of fractures in the elderly.
   (3) Atmospheric pollution and respiratory disease.
   (4) The hazards of occupational exposure to ionizing radiations.
   (5) The dose to the gonads in diagnostic X-ray procedures.
   (6) Ankylosing spondylitis in relation to therapeutic irradiation.
   (7) Pelvimetry in relation to leukaemia.
   (8) Blood groups and gastro-duodenal diseases.
   (9) Epidemiological features of mortality from leukaemia and specific forms of cancer.

2. Therapeutic trials :
   (1) Drugs in respiratory tuberculosis in this country and abroad.
   (2) Cortisone, ACTH and related substances in rheumatic fever and in chronic rheumatic diseases.
   (3) Gamma globulin in hypogammaglobulinaemia.
   (4) Prolonged anticoagulant therapy in myocardial infarct.
   (5) Development of ' sequential ' methods in clinical trials.
   (6) Clinical trials of the treatment of various forms of cancer.
3. Field trials of prophylactic agents :
   (1) BCG and vole bacillus vaccine in the prevention of tuberculosis in adolescents.
   (2) Influenza vaccines in chronic bronchitics.
   (3) Problems of immunization in childhood.
4. Problems of railway accidents.

(*Publications see p.* 181)

DEPARTMENT FOR RESEARCH IN INDUSTRIAL MEDICINE

THE LONDON HOSPITAL RESEARCH LABORATORIES,
ASHFIELD STREET, LONDON, E.1
(1943)

Physician-in-Charge

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

Staff

R. G. Drew, B.Sc.
G. Kazantzis, M.B., Ph.D., F.R.C.S.
E. King, B.Sc.
D. J. Lawford, B.Sc.
A. I. G. McLaughlin, M.D., F.R.C.P. (*part-time*)

The Department investigates the effects upon the health of workmen of potentially dangerous substances and processes used in industry and agriculture. Investigations include the study of the clinical manifestations in patients with symptoms and signs of poisoning, and the assessment of the risk in particular occupations by means of clinical and enviromental studies.

Summary of Research

1. Cadmium:
   (1) Clinical investigation of chronic poisoning.
   (2) Follow-up investigation of men examined in a survey undertaken in 1953.
   (3) Experiments to study the distribution in tissues; the nature of the renal lesion, and of the unusual protein which appears in the urine.
   (4) A study of the efficacy of various chelating agents, and of the modifying effect of certain metals on the distribution and excretion of cadmium.
2. Clinical, environmental and experimental survey of the effects on the lungs and skin of oils used in industry.
3. Clinical and environmental survey of boiler scalers (with the Factory Department, Ministry of Labour, and Dr. W. M. MacLeod of Southampton).
4. The effects on the lungs of talc used in various industries..
5. Clinical, environmental and biochemical survey of the relative value of the various methods of estimating lead absorption and poisoning.
6. Pulmonary function studies in subjects with various industrial lung diseases, both in the laboratory and in field surveys.

7. Investigation of the possible carcinogenic properties of metals such as nickel, cobalt, chromium and iron, and, in particular, the study of patients and animals with implants of these metals or their alloys.
8. Monitoring of industrial premises for atmospheric mercury and the estimation of mercury excretion values in periodic specimens of urine from patients exposed to this hazard.
9. Investigation of patients with suspected poisoning of industrial origin.
10. Clinical and environmental aspects of cases of poisoning due to toxic chemical substances used in agriculture or horticulture.

(*Publications see p.* 182)

INDUSTRIAL INJURIES AND BURNS RESEARCH UNIT

BIRMINGHAM ACCIDENT HOSPITAL, BATH ROW, BIRMINGHAM, 15

(1952)

Director

J. P. Bull, M.D.

Staff

Miss S. Baar, F.R.I.C.
Mrs. S. A. Brooks, Ph.D.
J. W. L. Davies, Ph.D.
Mrs. M. R. Davies, M.B. (*part-time*) (*until Mar.*, 1959)
D. MacG. Jackson, M.D., F.R.C.S. (*part-time*)
J. C. Lawrence, Ph.D.
E. J. L. Lowbury, D.M.
W. M. McKernan, Ph.D. (*until Feb.*, 1959)
C. R. Ricketts, D.Sc.
S. Sevitt, M.D., M.Sc., F.R.C.P.I., D.P.H. (*part-time*)
E. Topley, M.D.

Visiting Worker

L. Colebrook, M.B., D.Sc., F.R.S.

The studies of the Unit are concerned with the causes, local and general pathology, complications and treatment of accidental injuries, including burns and scalds. The Unit works in close liaison with the staff of the Birmingham Accident Hospital.

Summary of Research

1. The types, causes and prevention of common industrial and domestic injuries. Social implications of burning injuries in children.
2. Studies of the shock stage following burns :
   (1) Controlled trial of primary excision of extensive burns and study of the associated bleeding diathesis.
   (2) Correlation of red cell and blood volume changes and colloid, electrolyte and fluid therapy with clinical signs and mortality.
   (3) Critical evaluation of red cell replacement by blood transfusion.
3. Investigation of red cell disappearance following burns; experimental studies of the fate of radioactively labelled red cells, surface counting in burned patients following injection of ^{51}Cr labelled red cells; study of abnormal haemoglobin demonstrated by alkaline denaturation curve.
4. Assessment of validity of various techniques for studying red cell and plasma volume during early stages following trauma. Development of radioactive techniques for measurement of plasma volume and cardiac output.
5. A study of blood loss and blood transfusion management following severe injuries, including a controlled trial of the adequacy of two levels of blood transfusion.
6. Studies of protein and nitrogen metabolism following injury using ^{131}I-labelled plasma proteins. Investigation of the labelling reaction.
7. The effect of various substrates, therapeutic agents and thermal damage on the metabolism of skin cells; studies of phosphate ester metabolism and the formation of intracellular sulphated polysaccharides.

8. Studies of the hexokinases of yeast, skin and red blood cells.
9. Pulmonary thrombo-embolism and deep vein thrombosis; primary sites of thrombosis; a controlled prophylactic clinical trial of anticoagulant therapy.
10. Further investigation of dextran; the preparation of some basic derivatives of dextran and exploration of their biological properties.
11. Studies on the growth of bacteria in serum and other body fluids. Contribution of bacterial infection to the pyrexia, blood changes, antibody formation and other general effects of burns.
12. Development of methods for identification of anaerobic flora, and their application in the bacteriological study of wounds and burns.
13. Epidemiology and effects 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.
14. Controlled trials of local chemotherapy and chemoprophylaxis in burns and open wounds. Studies of the use of various methods of skin disinfection.
15. Pathology and pathogenesis of renal failure after burning and injury, with special reference to the morphological changes, glomerular filtration and tubular function in oliguric and non-oliguric forms of uraemia.
16. Healing of fractures, normal and abnormal union; ischaemic necrosis following fracture; degeneration of new connective tissue as a cause of non-union.
17. General and special pathology after burning and injury.

(*Publications see p.* 182)

TOXICOLOGY RESEARCH UNIT

MEDICAL RESEARCH COUNCIL LABORATORIES, WOODMANSTERNE ROAD, CARSHALTON, SURREY

(1947)

Director

J. M. Barnes, M.B.

Staff

W. N. Aldridge, Ph.D.
Miss J. Cremer, B.Sc.*
D. F. Heath, D.Phil.
M. K. Johnson, B.Sc.
P. N. Magee, M.B.
A. R. Mattocks, Ph.D.
V. H. Parker, B.Sc.
B. J. Parsons, Ph.D.
Miss R. Schoental, D.Sc.
Miss M. M. Stewart, B.A.
H. B. Stoner, M.D., B.Sc.
C. J. Threlfall, B.Sc.

Visiting Worker

V. Popovic (*Zagreb*)

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.

Summary of Research

1. Toxic substances being investigated include: alkyl lead, mercury and tin compounds; dimethylnitrosamine and related compounds, nitrated phenols, barbiturates, acrylamide, DDT and dieldrin, pyrrolizidine alkaloids. The standard physical injury is tourniquet shock.
2. Studies include:
   (1) The metabolic responses of tissue slices and cell fractions both poisoned *in vitro* and taken from poisoned or injured animals.
   (2) The metabolism of toxic substances in the intact animal.
   (3) Biochemical mechanisms in liver cell damage.
   (4) Formation of cerebro-spinal fluid.

* French Exchange Scholar for 1958–59.

(5) Oxygen consumption, organ blood flow and tissue oxygen tension in unanaesthetized animals after poisoning or injury.
(6) The metabolism of carbohydrate after physical injury.
(7) Metabolism of nucleotides and related compounds after poisoning and injury.
(8) The isolation and identification of pyrrolizidine alkaloids. The synthesis of analogues.

(*Publications see pp.* 182–183)

ENVIRONMENTAL HYGIENE RESEARCH UNIT*

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE, KEPPEL STREET, LONDON, W.C.1, AND MEDICAL RESEARCH COUNCIL LABORATORIES, HOLLY HILL, HAMPSTEAD, LONDON, N.W.3

(1950)

Director

T. Bedford, O.B.E., D.Sc.

Staff

F. A. Chrenko, B.Sc.
C. N. Davies, D.Sc., F.Inst.P.
J. McK. Ellison, Ph.D. (*until Dec.*, 1958)
Mrs. I. Greenleaves, B.Sc.
F. E. E. Smith, M.B.E.
G. W. Spicer, M.Sc.
Miss B. E. Tredre, B.Sc.

Visiting Worker

J. R. Hodkinson, B.Sc., A.Inst.P.
(*Safety in Mines Research Establishment*)

The Unit's work is concerned with various factors of the atmospheric and thermal environment which may affect health, comfort and efficiency.

Summary of Research

1. Heating and ventilation:
   (1) Effects of the intensity and wave-length of radiant heat on sensations of warmth.
   (2) Comparison of methods of measuring radiation from the surroundings.
   (3) Estimation of the solar radiation received by man.
   (4) Measurement of spectral reflectance and transmission of polar clothing.
   (5) Development of remote-recording anemometers for use in conduits in buildings.
   (6) Survey of thermal conditions in railway signal boxes.
   (7) Study of the physical principles of design for the housing of livestock.

2. Naval hygiene:
   (1) Incidence of sickness in H.M. ships in relation to climate.
   (2) Environmental conditions in H.M. ships when closed down at sea, with special reference to the development of ventilated suits.

3. Aerosols:
   (1) Motion of dust particles in air.
   (2) Deposition of particles in lungs.
   (3) Optical properties of dust. Computation of light scattering by opaque particles, as an aid to the interpretation of optical measurements on mixed coal and rock dusts.
   (4) Deposition of atmospheric pollution. Review of the various mechanisms of deposition, and the study of deposition from a turbulent atmosphere.

(*Publications see pp.* 183–184)

* This Unit was disbanded on Dr. Bedford's retirement in September, 1959.

CLIMATE AND WORKING EFFICIENCY RESEARCH UNIT

DEPARTMENT OF HUMAN ANATOMY, SOUTH PARKS ROAD, OXFORD

(1948)

Honorary Director

Professor Sir Wilfrid Le Gros Clark, M.D., D.Sc., F.R.C.S., F.R.S.

Honorary Assistant Director

J. S. Weiner, Ph.D., M.R.C.S.

Staff

K. J. Collins, B.Sc.
Miss P. Cullingham, B.A. (*until Feb.*, 1959)
K. G. Foster, B.Sc.
R. F. Hellon, D.Phil.
Miss R. J. Morton, M.A.
K. A. Provins, Ph.D.
R. J. Whitney, Ph.D.

Attached Workers

G. W. Crockford, B.Sc. (*British Iron & Steel Research Assocation Bursar*)
P. W. Humphreys, B.Sc. (*National Coal Board*)
A. R. Lind, D.Phil. (*National Coal Board*)

The investigations of the Unit on the locomotor system of man are concerned with anatomical and physiological problems arising in his working environment. Climatic studies are in progress on working capacity and physical adaptation at high temperatures and on the effect of cold on muscle action.

Summary of Research

1. The pattern of forces and of postural changes associated with complex tasks, particularly the lifting and handling of heavy loads.
2. Effects of heavy muscular work and static effort on the peripheral circulation in different environmental conditions.
3. Determination of the sensory control of voluntary limb movements in normal and in cooled limbs.
4. Anatomical and physiological factors involved in turning rotatory manual controls, such as cranks and hand wheels, against heavy loads.
5. Effect of cold on muscle action and muscle strength.
6. 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.
7. Functioning and histochemistry of sweat glands in man and animals.
8. Growth and heat tolerance of animals at high temperatures.
9. *Ad hoc* problems :
   (1) Reduction of fatigue in the manual lifting of heavy loads as encountered in industry and the Services.
   (2) Limits of work in coal mining, steel works and other industries in relation to environmental conditions.
   (3) Design of seats and other supports, and of control equipment for the Services, and in industry and agriculture.
   (4) Analysis of photogrammetric records for anthropometric purposes, in particular for the design of seats and supports in vehicles, laboratory and hospital furniture, and Service equipment.

(*Publications see p.* 184)

PNEUMOCONIOSIS RESEARCH UNIT

LLANDOUGH HOSPITAL, PENARTH, GLAMORGAN

(1945)

Director

J. C. Gilson, O.B.E., M.B., F.R.C.P.

Staff

R. G. H. B. Boddy, Ph.D.
W. G. Clarke, M.S.R.
A. L. Cochrane, M.B.E., M.B., D.P.H.*
J. E. Cotes, B.M., M.R.C.P.
I. Davies, M.D., M.R.C.P., D.P.H. (*part-time*)
I. T. T. Higgins, M.D., M.R.C.P.
R. S. Jones, M.D., M.R.C.P. (*until Feb.*, 1959)
S. R. Kamat, M.B. (*part-time*)
Mrs. M. McDermott, B.Sc.
C. B. McKerrow, M.D., M.R.C.P.
W. E. Miall, M.B.
T. G. Morris, Ph.D., D.I.C.
P. D. Oldham, M.A.
D. Rivers, L.M.S.S.A.
C. E. Rossiter, B.A.
D. Segall, M.B.
J. Thomas, M.A.
V. Timbrell, Ph.D., D.I.C.

The Unit is investigating the effects of environment and heredity on prevalence and natural history of a number of common diseases. The research includes long-term epidemiological investigations in mining, urban, and agricultural communities in the United Kingdom and overseas. Work is also in progress with the aim of defining stages in the development of respiratory disability and the prognostic value of different patterns of disordered lung function.

Summary of Research

1. Epidemiological studies:
   (1) Tuberculosis—investigation of factors affecting attack and break-down rates in elderly males.
   (2) Pneumoconiosis—factors affecting the attack and progression rates of complicated pneumoconiosis in coalworkers.
   (3) Ischaemic heart disease—prevalence and attack rate in mining and agricultural groups, and its relation to occupation, heredity, and other factors (in collaboration with Dr. A. J. Thomas, Llandough Hospital; and the Council's Social Medicine Research Unit).
   (4) Arterial blood pressure and its relation to heredity, age, weight, and environmental factors. The studies have recently been extended to population samples in Jamaica.
   (5) The prevalence and attack rate of respiratory symptoms, bronchitis, and disability related to age, environment, occupation, and smoking. Studies have been extended to a population sample in Bornholm (Denmark).
   (6) Auditory acuity in relation to age, otological disease, and environment in agricultural and mining communities (in collaboration with the Council's Wernher Research Unit on Deafness).
   (7) Attitude to chronic ill-health in contrasting communities (in collaboration with members of the staff of the Council's Social Psychiatry Research Unit).
2. Studies in dust sampling and analysis:
   (1) Dust concentrations and composition in cotton mills and ginneries in relation to byssinosis (in conjunction with Dr. R. S. F. Schilling of the Occupational Health Department, London School of Hygiene and Tropical Medicine).
   (2) Testing of new instruments used for monitoring purposes, and gravimetric and compositional analyses of airborne dust.
3. Physiological studies:
   (1) Studies of the ventilation perfusion relationships and pulmonary diffusing capacity in severely disabled subjects.
   (2) Studies of the effect of temperature on the performance of athletes, and of the maximum diffusing capacity of their lungs.

* Dr. Cochrane has recently been appointed to the David Davies Chair of Tuberculosis in the Welsh National School of Medicine and the Council have agreed to set up a Research Unit under his honorary direction at Sully Chest Hospital, Penarth.

(3) Studies of factors affecting the efficiency of walking.
(4) Studies of the mechanism responsible for changes in pulmonary ventilation produced by breathing oxygen.
(5) Investigation of the acute effects of cotton and other dusts on pulmonary function.
(6) Studies of the effect of temperature, humidity, and other atmospheric factors on pulmonary ventilatory capacity.

4. Experimental and general pathology:
(1) The quantitative relationship between duration and concentration of dust exposure and the retained dust in the lung.
(2) Biological assay of the fibrogenic properties of respirable airborne dust by collagen production in the liver of mice.
(3) Relation of radiological appearance of the chest film to lung pathology; the quantities and composition of the dust in the lung and past industrial exposure to dust.

5. Other studies:
(1) Development of statistical methods for analysis of X-ray readings of simple pneumoconiosis.
(2) Development of physical instruments for analysis of respiratory gases.
(3) Preparation of material for sets of standard films demonstrating the new International Classification of Pneumoconiosis.
(4) Testing the value of antibiotics in the prophylactic and curative treatment of bronchitis and the common cold.

(*Publications see p.* 185)

AIR POLLUTION RESEARCH UNIT

DUNN LABORATORIES, ST. BARTHOLOMEW'S HOSPITAL, LONDON, E.C.1

(1955)

Director

P. J. Lawther, M.B., M.R.C.P.

Staff

B. T. Commins, M.Sc., A.R.I.C.
Miss M. M. Henderson, M.B., D.P.H.
J. McK. Ellison, Ph.D.
T. Nash, M.A., B.Sc., A.R.I.C.
R. E. Waller, B.Sc.

Visiting Worker

Professor A. Candeli (*Perugia*)

The Group is concerned primarily with the investigation of the clinical aspects of air pollution as it affects the general population. Studies are being made on the physical and chemical characteristics of pollutants and on the significance of polluted air especially in relation to lung cancer and chronic bronchitis.

Summary of Research

1. Physical characteristics of particulate pollution; minute structure of particles as shown by the electron microscope; chemical nature of solid, liquid and gaseous air pollutants and the reactions which occur between them, especially during temperature inversions.
2. Development of analytical techniques in determination of pollutants in the extreme dilutions occurring in urban atmospheres.
3. The possible adsorption of sulphur dioxide on particles and its oxidation to sulphuric acid.
4. Determination of carcinogenic substances in town air.
5. Health hazards of emissions from motor vehicles, with special attention to polycyclic hydrocarbons and carbon monoxide.
6. The effects of pollutants on pulmonary function.
7. Variations in the clinical condition of patients with chronic bronchitis and emphysema in relation to daily changes in weather and air pollution.
8. Clinical trials of smog masks and other protective devices.

(*Publication see p.* 185)

GROUP FOR EPIDEMIOLOGICAL RESEARCH ON RESPIRATORY DISEASES (AIR POLLUTION)*

UNIVERSITY OF SHEFFIELD, 10

(1956)

Honorary Director

Professor C. H. Stuart-Harris, M.D., F.R.C.P.

Staff

Miss M. Clifton, M.D.
D. Kerridge, B.Sc.
Miss W. Moulds, B.Sc.

The aim of the Group is to investigate the epidemiology of respiratory disease, with special reference to bronchitis and air pollution.

Summary of Research

1. The health and sickness absence of children entering school in 1956 in areas of contrasting air pollution.
2. Survey of all deaths in Sheffield in relation to air pollution.
3. Study of National Insurance certificates of incapacity ascribed to bronchitis, pneumonia and influenza in Sheffield.
4. Survey of patients with bronchitis, and others with arthritis, to relate chest symptoms to changes in air pollution.
5. Distribution of air pollution both by time and extent, and its relation to geographical and meteorological conditions.

(*Publication see p.* 186)

CARCINOGENIC SUBSTANCES RESEARCH UNIT

WASHINGTON SINGER LABORATORIES, UNIVERSITY OF EXETER

(1956)

Honorary Director

J. W. Cook, D.Sc., F.R.S.

Staff

W. Carruthers, Ph.D.
A. G. Douglas, B.Sc.
R. A. W. Johnstone, Ph.D.
G. W. J. Matthews, B.Sc.
J. R. Plimmer, Ph.D. (*until April*, 1959)
B. L. Tonge, Ph.D.
D. A. M. Watkins, Ph.D.

The Unit is investigating the chemistry of tobacco smoke and of certain high-boiling fractions of petroleum with reference to the cancer producing activity of these materials.

Direct experimental evidence is being sought for the possible role of cigarette smoke in the causation of lung cancer, by chemical analysis of the smoke and identification of any carcinogenic substances which may be present. Factors which may influence the composition of the smoke and hence possibly its biological activity are also being studied.

The work on high-boiling petroleum fractions is being carried out in collaboration with other members of the Council's Committee on the Carcinogenic Action of Mineral Oils, and has as its object the isolation and identification of the substances responsible for the carcinogenic activity of selected oils.

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* Group now disbanded although pollution measurements are being continued in Sheffield under auspices of Council's Air Pollution Research Unit, St. Bartholomew's Hospital, London.

Summary of Research

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1. Tobacco Smoke
   (1) Chemical investigation of smoke produced by smoking cigarettes in a machine, and isolation and identification of pure constituents.
   (2) Preparation of fractions of smoke condensate for biological testing.
   (3) Study of efficiency of filter materials and of the effect of certain additives on the temperature of combustion of cigarettes.
   (4) Investigation of the constituents of green and cured tobacco leaf.
2. Mineral Oils
   (1) Chemical examination of carcinogenic fractions distilled from selected crude oils, and isolation and identification of pure constituents from them.
   (2) Synthetic preparation of larger samples of these pure constituents for biological test.

(*Publications see p.* 186)

LABORATORY ANIMALS CENTRE

MEDICAL RESEARCH COUNCIL LABORATORIES, WOODMANSTERNE ROAD, CARSHALTON, SURREY

(1947)

Director

W. Lane-Petter, M.B.

Staff

Miss A. M. Brown, Ph.D.
Miss M. J. Cook, B.Sc.
G. Porter
A. A. Tuffery, M.Sc.*

The Centre exists 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, including their supply, breeding, feeding, general management, hygiene, and housing, and to maintain liaison with comparable organizations in other countries; (2) to maintain a selection centre for special strains, mainly of mice; (3) to conduct research relevant to the provision of animals of high quality; (4) to train staff, especially technicians, engaged in this field.

Summary of Activities

1. Preparation of news letters, catalogues and other material for distribution to laboratories; administration of an accreditation scheme for breeders of guinea-pigs, mice and rabbits.
2. Maintenance of 15 inbred and one non-inbred strains of mice; testing and comparison of their specific responses.
3. Investigations:
   (1) Methods of large scale production of animals, mainly mice, of specified quality through the provision of breeding nuclei.
   (2) Spread and control of infections in laboratory animals.
   (3) Raising productivity of animals through intensive breeding and selection.
   (4) Usefulness of new compound diets.
4. Organization of annual congresses for animal technicians, and of symposia on laboratory animals.

(*Publications see p.* 186)

* Salary financed in part by grants from pharmaceutical firms.

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NEUROLOGICAL RESEARCH UNIT

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UNIT FOR RESEARCH ON DRUG SENSITIVITY IN TUBERCULOSIS

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External Scientific Staff

Places of Work and Summaries of Research

Birmingham

QUEEN ELIZABETH HOSPITAL

Department of Medicine

J. M. FRENCH, M.D., Ph.D., M.R.C.P., D.T.M. & H.

1. The aetiology of coeliac disease and sprue.
2. Stercobilin and stercobilinogen excretion in steatorrhoea.
3. Faecal porphyrin excretion in steatorrhoea.
4. Duodenal and jejunal mucosal biopsy in steatorrhoea.
5. Protein absorption in normal human subjects and in patients with gastro-intestinal disease using ^{15}N labelled protein.

UNIVERSITY

Bacteriology Department

G. H. G. DAVIS, Ph.D.

The diagnosis and natural relationships of oral filamentous bacteria, including the application of cell-wall analysis techniques to these and other oral groups.

School of Dental Surgery

S. L. ROWLES, D.Phil.

1. Biochemistry of saliva and dental calculus in animals and man.
2. Chemical changes associated with the early stages of dental caries.
3. Certain natural and synthetic calcium phosphates.

Bristol

UNIVERSITY

Dental School

M. V. STACK, Ph.D.

1. Biometry of developing deciduous dentitions.
2. Chromatography of neonatal enamel proteins.

Cambridge

STRANGEWAYS RESEARCH LABORATORY

M. WEBB, D.Sc.
J. A. LUCY, Ph.D.

1. Studies on the chemical composition, growth, metabolism and biosynthetic activities of organized and unorganized tissues cultivated *in vitro* under different conditions.
2. Continuation of work on the function of folinic acid co-enzymes in the utilization of pyruvic and α-keto-isovaleric acids for the biosynthesis of leucine in *Aerobacter aerogenes*.

UNIVERSITY

Biochemistry Department

F. SANGER, Ph.D., F.R.S.
J. I. HARRIS, Ph.D.
L. F. SMITH, Ph.D.

1. Methods for the determination of amino-acid sequences in proteins using isotopic techniques.
2. Studies on the structure of bacteriophage proteins and its relation to genetic changes.
3. Relationship between chemical structure and biological activity in pituitary hormones.
4. Studies on the structure of turnip yellow mosaic virus, flagellin, bacterial cytochromes and phosvitin.
5. Chemical studies on the active centres of proteolytic enzymes.

Molteno Institute

H. LASER, M.D., Sc.D.

Continued studies on the biochemical phenomena underlying the biological effects of ionizing radiation, especially in relation to:

(1) changes in cellular metabolism and enzyme activity;
(2) induction of phage in lysogenic bacteria;
(3) characteristics of a highly radiation resistant bacterium (*micrococcus radiodurans*);
(4) the influence of heavy water on radiosensitivity of bacteria;
(5) relation between radiosensitivity and variations in oxygen tension.

Psychological Laboratory

W. E. HICK, M.A., M.D.

1. Study of skill with special reference to machine (including vehicle, aircraft, etc.) control and supervision.
2. Development of usable mathematical (including logical) methods, and application of them to the above and to other psycho-physiological problems.

Miss A. W. HEIM, Ph.D.
Miss M. A. VINCE, B.A.
Miss K. P. WATTS.
I. M. HUGHES, M.A.

1. Mental tests and personality assessment:
   (1) Exploration of a new verbal test to assess reasoning ability and other aspects of intellectual capacity.
   (2) Development of new vocabulary tests covering the range from secondary modern school-children to university graduates. Comparison of the test results with independent assessments of intelligence and personality.
2. Comparative studies of maturation and learning:
   (1) The development behaviour in the great tit (*parus major*), and Chinese painted quail (*Excalfactoria chinensis*,) with special reference to changes in learning capacity during the first year of life.
   (2) Developmental studies of changes of food intake and taste preference in the great tit and Chinese painted quail.
   (3) Experimental studies of human perceptual discrimination, with special reference to problems of measurement.

   (This work is under the direction of Professor O. L. Zangwill.)

Edinburgh

UNIVERSITY

Organic Chemistry Department

I. D. E. STOREY, Ph.D.

1. Biochemical studies on uronic acids, with particular reference to glucuronide metabolism in animal tissues.
2. The formation of glycosidic bonds as mediated by nucleotides.
3. Acid-soluble nucleotides of tissues.

Institute of Animal Genetics

B. M. SLIZYNSKI, Ph.D. (*until April*, 1959)*

Cytological studies of mutagenesis (under the direction of Professor C. H. Waddington).

Pharmacology Department

B. L. GINSBORG, Ph.D.
Neuromuscular transmission and contracture in avian muscle.

Surgical Science Department

E. J. DELORME, M.D., F.R.C.S.(C).

1. Prevention of gastro-intestinal injury following whole body irradiation.
2. Storage and transplantation of tissues and organs.
3. The special role of the lymphocyte in restoring haematopoietic activity following irradiation.
4. Further investigations into modification of the immune response in inbred rat and mouse strains.

* Now attached to Mutagenesis Research Unit.

Elstree

THE LISTER INSTITUTE OF PREVENTIVE MEDICINE

Mrs. J. M. DOLBY, Ph.D.

Bordetella pertussis infections in lungs and brains of mice and the two types of protection conferred by antisera.

Miss M. E. MACKAY, Ph.D.

1. A study of proteolytic enzymes in human plasma.
2. The study of physiologically active globulin in human plasma.

Englefield Green

ROYAL HOLLOWAY COLLEGE

Zoology Department

W. A. GAUNT, M.Sc.

1. Relationship between the blood supply to the deciduous and permanent teeth.
2. Vascularization of the pulp of mammalian teeth in relation to the disposition of their roots.
3. Histochemical aspects of root formation.

Farnborough

INSTITUTE OF AVIATION MEDICINE

G. MELVILL JONES, M.B.

1. Applied problems associated with maintenance of orientation in man-controlled flight.
2. Development of technique for measurement of angular velocity of the eye about its optic axis.
3. Quantitative relation between vestibular signals derived from rotational stimuli about three orthogonal axes.
4. Vertigo associated with sudden pressure changes in the middle ear.
5. Human tolerance to oscillatory motion in flight.

Hendon, Middlesex

WEST HENDON HOSPITAL

Institute of Orthopaedics Poliomyelitis Centre

A. B. KINNIER WILSON, M.B., M.R.C.P., D.P.M.
R. P. J. G. MCWILLIAM, B.A.

1. Rehabilitation of patients after respiratory poliomyelitis.
2. Analysis of flow characteristics of sputum.
3. Study of mechanics of obstructed breathing in poliomyelitis and other infectious diseases.
4. Study of carbon dioxide exhalation in patients with poliomyelitis and others in breathing machines.
5. Development of engineered equipment to aid those disabled from poliomyelitis and allied diseases.
6. Development of servo and other devices for assisting limb movement (with Mr. D. Dalrymple).

(This work is being carried out in collaboration with the Committee for Research on Apparatus for the Disabled.)

Leeds

UNIVERSITY

Medical Physics Department

J. B. DAWSON, Ph.D.

1. A comparative study of the estimation of calcium and magnesium in biological materials by chemical and spectro-chemical methods.
2. Development of a direct reading spectrophotometer for the simultaneous estimation of several elements.

(This work is being carried out in collaboration with the Metabolic Disturbances in Surgery Research Unit.)

Liverpool

SCHOOL OF TROPICAL MEDICINE

Miss W. A. F. WEBBER, Ph.D.

Studies on the morphology and taxonomy of:

(1) filarial worms of the genus *Loa* as found in man and monkeys in the Kumba area of the British Cameroons;

(2) filarial worms of the genus *Onchocerca*, as found in cattle in North Wales.

London

BRITISH MUSEUM (NATURAL HISTORY)

D. J. LEWIS, Sc.D.

1. *Simulium neavei* complex at Amani in Tanganyika.
2. Biting cycle of *S. damnosum* in the Cameroons and Liberia.
3. Distribution of Phlebotominae in Nigeria and Gambia (with Dr. B. McMillan and Mr. D. H. Murphy).
4. Age changes in *Chrysops bicolor* in Tanganyika.

GUY'S HOSPITAL MEDICAL SCHOOL

Chemical Pathology Department

B. MCARDLE, M.D., F.R.C.P., D.C.H.

1. Continued studies of the electrolyte metabolism of patients with the type of hereditary periodic paralysis due to a rise in plasma potassium, and of methods of preventing attacks.
2. The action of snake venom, lysolecithin and other lytic agents on rat brain.
3. Search for possible lytic agents in the blood and cerebrospinal fluid of cases of multiple sclerosis.
4. Development of methods for the colorimetric and chromatographic determination of catechol amines in urine and tissues.

Pathology Department

A. N. DAVISON, Ph.D.

1. Biochemical studies on the incorporation and persistence of radioactive isotopes in myelin lipids of the developing central nervous system of rats.
2. Comparison of cerebral lipid metabolism in developing and mature rats.
3. Development of chromatographic techniques for the separation and analysis of lipids from normal and diseased nervous tissue.
4. Metabolism of the proteolipids or neurokeratin of the brain of young and adult rats.

INSTITUTE OF PSYCHIATRY, MAUDSLEY HOSPITAL

Neuropathology Department

F. B. BYROM, M.D., F.R.C.P.

Production, mechanism and effects of experimental hypertension.

Miss S. J. STRICH, D.M.

1. Pathology of severe head injuries with long survival.
2. Pathology of acute head injuries.
3. Investigation of some congenital abnormalities of the nervous system.

LEWISHAM HOSPITAL

P. WOLF, M.D.

Isolation and examination of human blood coagulation factors and their clinical application.

MIDDLESEX HOSPITAL MEDICAL SCHOOL

J. COLOVER, M.D., M.R.C.P. (*part-time*)

1. Investigation of cerebrospinal fluid in multiple sclerosis by immunochemical methods, and a study of the relationship of the findings to the clinical condition of the patients examined.
2. Skin reactions and associated immunological changes in relation to the mechanism of production of allergic encephalomyelitis in guinea pigs.

NATIONAL HOSPITAL FOR NERVOUS DISEASES

A. ELITHORN, M.D., M.R.C.P., D.P.M. (*part-time*)*
Mrs. M. KERR, B.A. (Econ.) (*part-time*)

Clinical and psychological investigations into the relationship between anxiety and depression.

POSTGRADUATE MEDICAL SCHOOL OF LONDON

Department of Medicine

P. HUGH-JONES, M.A., M.D., F.R.C.P. (*part-time*)
Miss M. H. MACLEISH, B.Sc.
J. D. SINCLAIR, M.D., M.R.A.C.P., B.Med.Sc. (*until June*, 1959)
J. B. WEST, M.D.

1. Applications of rapid gas analysis of a single breath for three gases simultaneously by means of the mass spectrometer. Other tests of lung function in a variety of medical and surgical problems.
2. Introduction of mass spectrometer sampling tube into different lobes or segments of the lung to measure regional variations of gas- and blood-flow, both experimentally in animals and during routine diagnostic bronchoscopy in man.
3. Co-operation with the Radiotherapeutic Research Unit in the use of cyclotron-produced short-lived radioactive gases for studying regional lung function without intubation of patients.

J. P. SHILLINGFORD, M.D., F.R.C.P. (*part-time*)

1. The study of the circulation by dye dilution curves, including the localization and estimation of the size of intracardiac shunts and the measurement of coronary blood flow.
2. The direct measurement of the velocity of blood flow in man and its application to the study of resistance to blood flow in the pulmonary blood vessels and of ventricular function.
3. Studies of the blood pressure in man by continuous peripheral recording.
4. The use of the intracardiac microphone to localize shunts and analyze heart sounds.

Chemical Pathology Department

J. G. KRAAN, B.Sc.

Studies in experimental pneumoconiosis with particular reference to the metabolism of acid mucopolysaccharides in developing fibrous tissue.

(This work is being carried out under the direction of Professor E. J. King.)

Steroid Reference Collection

Miss M. MCENTEE, Ph.D. (*until Feb.*, 1959)†

1. Preparation of compounds for the Council's Steroid Reference Collection.
2. Studies on side-chain substituted steroids.

(This work is being carried out under the direction of Dr. W. Klyne.)

THE ROYAL INSTITUTION

Davy Faraday Research Laboratory

D. W. GREEN, Ph.D.
A. C. T. NORTH, Ph.D.

1. X-ray crystallographic investigation of the structure of haemoglobin.

* Now working mainly at the Royal Free Hospital, North Western Branch, Lawn Rd., N.W.3.

† Transferred to the National Institute for Medical Research.

2. The binding of heavy-metal ions by proteins.
3. Development of electronic computer programmes to carry out crystallographic calculations.
4. Measurement of anomalous dispersion of the absolute scale of intensities of X-ray diffraction spectra of haemoglobin.

(This work is being carried out under the direction of Sir Lawrence Bragg.)

ROYAL NATIONAL ORTHOPAEDIC HOSPITAL

A. McPHERSON, M.B., M.R.C.P.

1. The facilitation and inhibition of mono- and polysynaptic, hindlimb reflexes produced by electrical stimulation of the splanchnic, hypogastric, pelvic and vagus nerves and the sympathetic chain and by distension of the bladder.
2. The effects of visceral distension on the activity of abdominal and hindlimb muscles, measured myographically.

(With Dr. M. H. Evans.)

ROYAL VETERINARY COLLEGE

Surgery Department

Miss B. H. BILLING, Ph.D.*

Studies in bile pigment metabolism:

1. Extra-hepatic conjugation of bilirubin.
2. Factors controlling excretion of conjugated bilirubin.

ST. ANN'S GENERAL HOSPITAL, TOTTENHAM

Miss J. WRIGHT, D.M. (*until June*, 1959)

Cultivation of measles virus in various tissue culture systems.

UNIVERSITY COLLEGE

Biophysics Department

H. E. HUXLEY, M.B.E., Ph.D., F.R.S.

1. Physical and chemical structure of striated muscle in relation to the mechanism of muscular contraction.
2. Development of techniques for the examination of biological materials in the electron-microscope at very high resolution.
3. Electron-microscopy of nucleic-acid-containing structures (in collaboration with Dr. G. Zubay).

Galton Laboratory

Mrs. S. D. LAWLER, M.D.
Miss R. MARSHALL, B.Sc.

1. The use of human blood group systems as chromosome markers in searching for genetical linkages.
2. Study of the genetic interaction of Lewis, ABO and secretor systems in family material from different populations. Study of the developmental aspects of the Lewis system in samples collected from infants throughout the first year of life.
3. Investigation of the Gm serum groups in man serologically and genetically.

Miss U. MITTWOCH, Ph.D.

1. The leucocytes in mongolism.
2. Abnormal inclusions of the lymphocytes in gargoylism, amaurotic idiocy and Niemann-Pick's disease.
3. A study of human chromosomes.
4. A study of sex chromatin.

* From October, 1959, at the Royal Free Hospital School of Medicine and transferred to the school's staff in March, 1960.

Miss E. B. ROBSON, Ph.D. (Mrs. MacBeth)

Electrophoresis of serum proteins in starch gels:

1. Genetics and geographical distribution of haptoglobin types and transferrin variants in man.
2. Investigation of an unusual, genetically determined protein related to albumin.
3. Examination of animal sera.
4. Examination of pathological material.

Physiology Department

H. DAVSON, D.Sc.

1. The effects of lowered body temperature on the physiology of the ocular and cerebrospinal fluids.
2. *In vivo* and *in vitro* studies on the blood-brain barrier.

A. R. NESS, B.Sc., L.D.S.

1. The distribution of cells and of cell division in the continuously-erupting rabbit incisor.
2. The development and inheritance of malocclusion of the incisors of the rabbit.

Manchester

CHRISTIE HOSPITAL AND HOLT RADIUM INSTITUTE

Biochemistry Department

W. M. DALE, M.D., D.Sc.

1. The results of experiments on the isolation and identification of the irradiation products from aqueous thiourea solutions have been concluded and published.
2. *In vivo* experiments on the possible protective properties of some of the irradiation products.
3. Continued experiments on the oxidation of ferrous ions by ionizing radiations with particular emphasis on the statistical limits of accuracy of the G values of this reaction.
4. Investigations into the effect of radiation on bacterial metabolism; in particular, on the radiation resistance of the hydrogen-producing system during carbohydrate breakdown.
5. Determination of the relative biological efficiency of 20 MeV (Betatron) X-rays and 4 MeV (Linear Accelerator) X-rays using *E. coli* as the test object.

Experimental Chemotherapy Department

H. JACKSON, M.B., Ph.D.

1. Comparative effects of radiomimetic drugs and radiation on fertility.
2. Metabolism and mode of action of alkylating agents; the relation between chemical structure and biological activity.
3. The development of resistance in experimental tumours to radiomimetic drugs.
4. Thyroid function:
   (1) The iodinated components and comparative effects of different thyroglobulins.
   (2) The iodinated components of the plasma of patients treated with radioactive iodine.

Radiobiology Department

Mrs. EDITH PATERSON, M.B., F.R.C.P.E.

1. Completion of tests on the Relative Biological Efficiency of 4 MeV and 20 MeV X-irradiation. The criteria used have been the LD 50 of mice and the loss of organ weight.
2. Continuation of study of calcium metabolism using ^{45}Ca in normal, malignant, and irradiated cells.
3. Study of the fate of red cells after whole body irradiation of the Rhesus monkey.

UNITED MANCHESTER HOSPITALS

Dental Hospital

S. A. LEACH, Ph.D.

The chemical dynamics of calcification of bones, teeth and connective tissues (under the direction of Professor H. G. Radden).

THE CHURCHILL HOSPITAL

Central Workshop

F. D. STOTT, D.Phil.

1. Instrumentation for whole-body plethysmography.
2. Instruments for cardiac resuscitation.
3. Development of improved methods of arterial and venous flow and pressure measurement.
4. Measurement and control of temperature during hypothermia.

Radiotherapy Department

L. G. Lajtha, M.D., D.Phil.

1. The mechanism of radiation effects at the cellular level.
2. Kinetics of cell differentiation in the bone marrow.
3. Metabolism of normal and leukaemic bone marrow cells.

NUFFIELD ORTHOPAEDIC CENTRE

Nuffield Department of Orthopaedic Surgery

Miss K. LITTLE, D.Phil.

Examination X-ray diffraction and electron microscopy of teeth, bone and other tissues.

THE RADCLIFFE INFIRMARY

Mrs. E. BIDWELL, Ph.D. (*until April*, 1959)*

1. The clinical use of animal antihaemophilic globulin.
2. The antigenicity of animal antihaemophilic globulin.
3. The nature of the inhibition of blood coagulation by circulating anticoagulants.

UNIVERSITY

Biochemistry Department

Miss J. Lascelles, D.Phil.

1. The adaptive formation of tetrapyrrole and carotenoid pigments in photosynthetic bacteria.
2. The effect of environment on the intracellular level of tricarboxylic acid cycle intermediates in bacteria.

Sir William Dunn School of Pathology

G. G. F. NEWTON, M.C., D.Phil.

1. The chemical structure and biochemical properties of the antibiotic cephalosporin C and its derivatives.
2. Further purification of the hormone secretin and investigations on its chemical structure.
3. The mode of action of the penicillins, cephalosporin C and bacitracin.

D. S. ROBINSON, Ph.D.
Miss P. M. HARRIS, B.A.

1. Lipid transport and the heparin clearing reaction.
2. The effect of ethionine on the plasma lipids.
3. The effect of diet on hypercholesterolemia in animals.

A. M. WOODIN, Ph.D.

1. Purification and properties of the F component of leucocidin.
2. Purification and properties of the S component of leucocidin.

* Transferred to Blood Coagulation Research Unit, Churchill Hospital.

Department of the Regius Professor of Medicine
I. E. BUSH, M.B., Ph.D.

Steroids:
1. Oxidation—reduction of 11-oxygen functions in adrenal steroids, studied in liver homogenates in order to elucidate the substrate specificity of this enzyme system.
2. Bio-assay of anti-inflammatory and glycogenic steroids.

Social Medicine Department
Mrs. J. W. WEBB, M.B., D.P.H., D.I.H.

1. Work on the influence of pre-onset illness and treatment in childhood leukaemia.
2. Continued investigation into the etiology of mongolism in relation to leukaemia.

THE WARNEFORD HOSPITAL

R. W. PARNELL, D.M., M.R.C.P.

1. The relationship between normal and abnormal physique and behaviour. Survey of 4,000 mental hospital admissions.
2. The establishment of standards for somatotyping children to compare the physique of mental defectives and children at E.S.N. schools.
3. The relationship of physical types within the family and their correlation with emotional factors.

Stockholm, Sweden

THE STATE MUSEUM OF NATURAL HISTORY

Invertebrate Department
A. D. BERRIE, B.Sc.

1. Studies on freshwater gastropods in relation to their role as intermediate hosts of trematode parasites.
2. Survey in the Gambia and in Sierra Leone on the snail hosts of bilharziasis.
(This work is under the supervision of Dr. Bengt Hubendick.)

Stoke-on-Trent

CITY GENERAL HOSPITAL

Respiratory Physiology Department
M. C. S. KENNEDY, B.A., M.R.C.S. (*part-time*)

1. Studies on the natural history of the chronic bronchitis-asthma-emphysema syndrome.
2. Interrelation of cardiac and pulmonary factors in causing dyspnoea in patients with valvular disease of the heart, in collaboration with Dr. J. P. P. Stock, Cardiologist to the Stoke-on-Trent Group.

Publications

BIRMINGHAM

University

BAIRD-PARKER, A. C. and DAVIS, G. H. G. The morphology of *Leptotrichia* species. *J. gen. Microbiol.*, 1958, **19**, 446.

DAVIS, G. H. G. Morphology and bacterial taxonomy. *Lab. Pract.*, 1959, **8**, 161.

DAVIS, G. H. G. and BAIRD-PARKER, A. C. Cell-wall composition of *Leptotrichia* spp. *Nature, Lond.*, 1959, **183**, 1206.

ROWLES, S. L. On the occurrence of whitlockite in dental calculus. [Abstract.] *J. dent. Res.*, 1958, **37**, 749.

BRISTOL

University

STACK, M. V. Études biométriques du développement osseux et dentaire au cours de la vie foetale et post-foetale. *Biotypologie*, 1958, **19**, 113.

Differential growth of deciduous incisors. [Abstract.] *J. dent. Res.*, 1958, **37**, 760.

CAMBRIDGE

Strangeways Research Laboratory

BIGGERS, J. D. and WEBB, M. A factorial experiment to study factors which reverse aminopterin inhibition. Addendum to: Aminopterin inhibition in *Aerobacter aerogenes*, by M. Webb. *Biochem. J.*, 1958, **70**, 487.

BOSS, J. M. N. The contribution of the chromosomes to the early telophase nucleus in cells of the crested newt *Triturus cristatus carnifex*. *Proc. XV int. Congr. Zool.*, London, 1958, p. 741.

WEBB, M. Aminopterin inhibition in *Aerobacter aerogenes*: alanine and valine accumulation during the inhibition and their utilization on recovery. *Biochem. J.*, 1958, **70**, 472.

Unbalanced growth in bacterial cultures. In: *Biochemistry of morphogenesis: Proc. IV int. Congr. Biochem.*, Vienna, 1958. Edited by W. J. Nickerson. London (Pergamon Press) 1959, **6**, pp. 71–76.

WEBB, M. and BIGGERS, J. D. The utilization of ^{14}C-labelled glucose by embryonic chick bones cultivated *in vitro* in chemically defined media. In: *Biochemistry of morphogenesis: Proc. IV int. Congr. Biochem.*, Vienna, 1958. Edited by W. J. Nickerson. London (Pergamon Press) 1959, **6**, pp. 30–32.

University

HARRIS, J. I. Studies on pituitary polypeptide hormones. 3. The structure of α-melanocyte-stimulating hormone from pig pituitary glands. *Biochem. J.*, 1959, **71**, 451.

HARRIS, J. I. and ROOS, P. Studies on pituitary polypeptide hormones. 1. The structure of β-melanocyte-stimulating hormone from pig pituitary glands. *Biochem. J.*, 1959, **71**, 434.

2. The action of pepsin and subtilisin on β-melanocyte-stimulating hormone. *ibid.*, 1959, **71**, 445.

LASER, H. Irradiation of *Escherichia coli* B in heavy water. *Abstr. Pap. int. Congr. radiat. Res.*, Burlington, Vermont, 1958. *Radiat. Res.*, 1958, **9**, 142.

SANGER, F. The chemistry of insulin. Nobel Lecture. *Chem. & Ind.*, 1959, p. 104.

Chemistry of insulin. *Science*, 1959, **129**, 1340.

VINCE, M. A. Effects of age and experience on the establishment of internal inhibition in finches. *Brit. J. Psychol.*, 1959, **50**, 136.

WILLIAMS, J. and SANGER, F. The grouping of serine phosphate residues in phosvitin and casein. *Biochim. biophys. Acta*, 1959, **33**, 294.

ELSTREE

Lister Institute of Preventive Medicine

DOLBY, J. M. The separation of the histamine-sensitizing factor from the protective antigens of *Bordetella pertussis*. *Immunology*, 1958, **1**, 328.

FARNBOROUGH

Institute of Aviation Medicine

JONES, G. M. Disorientation in flight. *Air Ministry*, 1958, FPRC/Memo 96.

Pressure changes in the middle ear after flight. *ibid.*, 1958, FPRC 1059.

Vestibular interference with vision in flight. Contribution to: Discussion on new concepts of eye movement. [Abridged.] *Proc. R. Soc. Med.*, 1959, **52**, 185.

Disorientation due to rapid rotation in flight: (a cause of unexplained aircraft accident?) In: *Medical aspects of flight safety: (the unexplained aircraft accident)*. Edited by E. Evrard, P. Bergeret and P. M. van Wulfften Palthe. London (Pergamon Press) 1959, pp. 92–101.

Western Infirmary

KAY, A. W. and FORREST, A. P. M. The inhibitory action of locally applied antihistamine on the gastric secretion of acid and pepsin induced by mean and insulin in dogs. *Brit. J. Surg.*, 1958, **46**, 282.

LONDON

British Museum (Natural History)

GARNHAM, P. C. C. and LEWIS, D. J. Parasites of British Honduras with special reference to leishmaniasis. *Trans. R. Soc. trop. Med. Hyg.*, 1959, **53**, 12.

LEWIS, D. J. *Simulium damnosum* in the Tonkolili Valley, Sierra Leone. *Proc. X int. Congr. Ent.*, Montreal, 1956, **3**, 541.

The recognition of nulliparous and parous *Anopheles gambiae* by examining the ovarioles. *Trans. R. Soc. trop. Med. Hyg.*, 1958, **52**, 456.

Observations on *Simulium damnosum* Theobald at Lokoja in Northern Nigeria. *Ann. trop. Med. Parasit.*, 1958, **52**, 216.

Some observations on Ceratopogonidae and Simuliidae (Diptera) in Jamaica. *Ann. Mag. nat. Hist.*, Ser. 13, 1958, **i**, 721.

Simulium flies: pest of man and beast. *Span*, 1959, **2**, 31.

LEWIS, D. J. and GARNHAM, P. C. C. The species of *Phlebotomus* (diptera: psychodidae) in British Honduras. *Proc. roy. Ent. Soc. Lond.*, B, 1959, **28**, 79.

Guy's Hospital Medical School

ADAMS, C. W. M. and DAVISON, A. N. The histochemical indentification of myelin phosphoglycerides by their ferric hydroxamates. *J. Neurochem.*, 1959, **3**, 347.

DAVISON, A. N. Inhibition of brain monoamine oxidase. *Bull. Soc. Chim. biol., Paris*, 1958, **40**, 1737.

The irreversible inhibition of monoamine oxidase *in vivo*. *Arch. Biochem.*, 1958, **77**, 368.

Physiological role of monoamine oxidase. *Physiol. Rev.*, 1958, **38**, 729.

DAVISON, A. N. and DOBBING, J. Relative stability of brain lipids. *Lancet*, 1958, **ii**, 1158.

DAVISON, A. N., DOBBING, J., MORGAN, R. S. and WRIGHT, G. P. The deposition and disposal of (4-^{14}C) cholesterol in the brain of growing chickens. *J. Neurochem.*, 1958, **3**, 89.

Metabolism of myelin: the persistence of (4-^{14}C) cholesterol in the mammalian central nervous system. *Lancet*, 1959, **i**, 658.

DAVISON, A. N. and WAJDA, M. Persistence of cholesterol-4-^{14}C in the central nervous system. *Nature, Lond.*, 1959, **183**, 1606.

MCARDLE, B. Potassium paresis. In: *Clinical effects of electrolyte disturbances; proc. confr.*, London, 1959. Edited by E. J. Ross. London (Pitman Medical Publishing Co.) 1959, pp. 104–112.

O'BRIEN, R. D. and DAVISON, A. N. Antagonists to schradan poisoning in mice. *Canad. J. Biochem.*, 1958, **36**, 1203.

Hampstead

HOLLOWAY, P. J., MELLANBY, M. and STEWART, R. J. C. The effect of acid drinks on the molar teeth of rats. [Abstract.] *J. dent. Res.*, 1958, **37**, 752.

MELLANBY, M. Some effects of vitamin A on the growth and development of jaws and teeth. [Abstract.] *J. dent. Res.*, 1958, **37**, 752.

MELLANBY, M., MARTIN, W. J. and BARNES, D. Teeth of 5-year-old London schoolchildren (1957), with a comparison of the results obtained from 1929 to 1957. *Brit. med. J.*, 1958, **ii**, 1441.

Institute of Psychiatry

BYROM, F. B. and PRATT, O. E. Oxytocin and renal cortical necrosis. *Lancet*, 1959, **i**, 753.

Lewisham Hospital

WOLF, P. Studies of temperature and pH stability of human antihaemophilic factor (AHF) in plasma and in a concentrate. *Brit. J. Haemat.*, 1959, **5**, 169.

Middlesex Hospital Medical School

AYRES, P. J., PEARLMAN, W. H., TAIT, J. F. and TAIT, S. A. S. The biosynthetic preparation of [16-^{3}H] aldosterone and [16-^{3}H] corticosterone. *Biochem. J.*, 1958, **70**, 230.

COLOVER, J. Experimental allergic encephalomyelitis and its immunochemistry. *Proc. R. Soc. Med.*, 1958, **51**, 745.

Contributions to: *'Allergic' encephalomyelitis; proc. symp.*, Bethesda, 1957. Edited by M. W. Kies and E. C. Alvord, Jr. Springfield, Ill. (C. C. Thomas) 1959.

National Hospital for Nervous Diseases

ELITHORN, A. Prefrontal leucotomy and depression. Contribution to: Discussion on psychosurgery. *Proc. R. Soc. Med.*, 1959, **52**, 203.

ELITHORN, A., GLITHERO, E. and SLATER, E. Leucotomy for pain. *J. Neurol. Psychiat.*, 1958, **21**, 249.

Postgraduate Medical School of London

HUGH-JONES, P. Dyspnoea. *Trans. med. Soc. Lond.*, 1958, **74**, 59.

Management of tracheostomies. Contribution to: Discussion: Tracheostomy to-day. *Proc. R. Soc. Med.*, 1959, **52**, 412.

HUGH-JONES, P. and WEST, J. B. A hollow cast for the upper bronchial tree for studying the mode of gas flow. *J. Physiol.*, 1959, **146**, 30P.

The effects of bronchial and arterial constriction on the alveolar gas concentration in a lobe of the dog's lung. *ibid.*, 1959, **146**, 49P.

Patterns of gas flow in the upper bronchial tree. *ibid.*, 1959, **146**, 50P.

KLYNE, W. and PALMER, S. Urinary steroids and related compounds. Part II. 11:17-Disubstituted androstanes carrying no substituent at position 3. *J. chem. Soc.*, 1958, p. 4545.

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The Council assumed the major responsibility for the Institute of Cancer Research from the beginning of the financial year 1951–52, but the Institute has continued to receive substantial support from the British Empire Cancer Campaign. The work of the Institute consists of that of the Chester Beatty Research Institute and of the research activities of the Departments of Physics and Radiotherapy, which are joint departments of the Institute of Cancer Research and the Royal Marsden Hospital. Formerly a school of the University of London, the Institute still retains a similar association through its recognition as an Institute of the British Postgraduate Medical Federation. The subjects under study at the Chester Beatty Research Institute include the mechanism of action of carcinogenic and mutagenic chemical agents, cytology and cytogenetics, control mechanisms in normal growth, the study of tumour viruses, and experimental chemotherapy. In the Physics Department (Fulham Road Branch) investigations are mainly related to the physical aspects of the clinical use of radioactive isotopes and high energy radiations; at the new laboratories at Sutton the work is of a longer term character and is devoted to various aspects of carcinogenesis by radiations including studies of environmental contamination. In the Radiotherapy Department the programme of research includes clinical studies of malignant disease and the results of treatment, the use of radioactive isotopes for therapy and investigation, and other radiobiological researches.

Summary of Research

CHESTER BEATTY RESEARCH INSTITUTE

1. Experimental chemotherapy:
   (1) Phenylalanine Derivatives.
   (2) Serine and Threonine Mustards.
   (3) Modified Proteins.
   (4) Bis-[*p*-di-(2-chloroethyl)aminophenoxy]alkanes.
   (5) Polyol Dimesylates.
   (6) Amino Acid Antagonists.
   (7) Hydantoins related to Amino Acid Mustards.
   (8) Sulphydryl Group Reactors.
   (9) Potential Antipurines.
   (10) Bis-purinyl Alkanes.
   (11) Potential Inhibitors of DPN Synthesis.
   (12) Styryl Compounds.
   (13) Inhibition of Mouse Ascites Tumour by Cells various Chemotherapeutic Agents.

2. Actions of the Alkylating Agents:
   (1) Chemical Reactivity of Alkylating Agents.
   (2) Action of Nitrogen Mustards and other Alkylating Agents on Nucleo-protein.
   (3) Biological Alkylating Agents and the Alkylation of Purines.
   (4) Further studies of the Action of Alkylating Agents on Nucleic Acids and Nucleotides.
   (5) Action of Alkylating Agents on Bacteriophage Systems.
   (6) Comparison of the Physiological Response to Radiation and to Radiomimetic Agents.

3. Deoxyribonucleic Acids and Deoxyribonucleoproteins:
   (1) Characterization of Deoxyribonucleic Acids.
   (2) Deoxyribonucleic Acids.
   (3) Synthesis of Nucleic Acids in *B. Megaterium*.
   (4) Crosslinking of DNA in Nucleoproteins by Alkylating Agents.
   (5) Action of Deoxyribonuclease and Proteolytic Enzymes on Deoxyribonucleoproteins.

4. Ribonucleic Acids:
   (1) Ribonucleic Acids.
   (2) Fractionation of Ribonucleic Acids.
   (3) Metabolism of Ribonucleic Acid and Ribonucleotides in Normal Liver.
   (4) Metabolism of Ribonucleic Acid and Ribonucleotides in Liver Tumours.
   (5) Cytoplasmic Ribonucleases.

5. Amino acids, Histones and Proteins:
   (1) Avidity of Tumours for Amino Acids.
   (2) Possible Incorporation of *p*-di-(2-hydroxy-[1:2-^{14}C]ethyl)amino-L-phenylalanine into Protein.
   (3) Histones of Calf Thymus and other Tissues.
   (4) Protein Synthesis in Rat Liver—Role of the Microsomes.
   (5) Protein Synthesis in *B. Megaterium.*

6. Enzymes and Trace Elements:
   (1) Xanthine Oxidase.
   (2) Pyridoxal Phosphate-Vanadium (Pyrvanal) and Cysteine Metabolism.
   (3) Succinic Dehydrogenase Activity in Precancerous Livers and Hepatoma of August Rats, maintained on a 5 per cent. Protein Diet plus 0·06 per cent. 4-dimethylamino-azobenzene.
   (4) Substrate-induced Enzyme Adaptation in the Developing Chick Embryo.
   (5) Trace Elements.

7. Radiation Effects:
   (1) Effect of Ultra-violet Light on DNA.
   (2) Crosslinking of DNA in Nucleoproteins by Ionizing Radiations.
   (3) Irradiation of DNA *in vivo.*
   (4) Irradiation of Proteins and Other Substances with X- and α-rays.
   (5) Direct and Indirect Action of Radiation on Chymotrypsin.
   (6) Shortening of Life-span by Irradiation and by Radiomimetic Chemicals.

8. Physico-chemical Studies:
   (1) The Photochemistry of Nucleic Acid Constituents and of other Polyelectrolytes.
   (2) Physico-chemical and Biophysical Studies of Styrylquinoline Derivatives.

9. Carcinogenesis:
   (1) Carcinogenic action of iron-dextran in the mouse and rat.
   (2) Carcinogenesis by Cholesterol.
   (3) Influence of Cholesterol on Hydrocarbon-carcinogenesis.
   (4) Sarcomas Induced by a Carcinogen of Steroid Type.
   (5) Endocrine Carcinogenesis.
   (6) Carcinogenicity of Vegetable Tannins.
   (7) Induction of Tumours following Subcutaneous Implantation of Plastic Films.
   (8) The Solubilization of Benzopyrene by Caffeine.
   (9) Ferrocene.
   (10) Cigarette Smoke and Cancer of the Lung.
   (11) Problems of Air Pollution.

10. Leukaemogenesis:
   (1) Influence of Thymectomy on Leukaemogenesis by Ak Leukaemic Cell-free Extracts.
   (2) Leukaemogenesis in Ak-tolerant C3H Mice.

11. Metabolic Studies:
   (1) The Metabolism of Myleran in the Rat.
   (2) The Metabolism of Alkyl Alkanesulphonates and Related Compounds.
   (3) Biochemical Studies with Growth Inhibiting Alkylating Agents.
   (4) The Metabolism of Naphthalene.
   (5) The Metabolism of 2-Naphthylamine.
   (6) The Hydrolysis of Metabolites of 2-Naphthylamine by Enzymes of Human Urine.

(7) Enzymic Hydroxylation.
(8) The Estimation of Free and Conjugated 3-Hydroxyanthranilic Acid using Spectrofluorimetry.
(9) The Metabolism of 4-Amino-2[1]:3-dimethyldiphenyl in relation to the Induction of Intestinal Cancer.
(10) Mechanism of Action of Urethane.

12. Endocrine Effects:
(1) The Inhibition of Skin Pigmentation by the Administration of Stilboestrol in Hamsters treated with 8-Methoxypsoralen.
(2) The Effects of Nitrofurazone on the Male Accessory Sex Organs of Rats bearing the Walker Tumour.

13. Cytology:
(1) Chromosomes of Solid and Ascitic Tumours.
(2) Cytological Action of Ionizing Radiations.
(3) Cytology and Protein Synthesis.
(4) The Nucleus and Dividing Cells.

14. Mutagenicity:
(1) The Mutagenicity of Mesyloxy-esters with Special Reference to Mannitol-Myleran.
(2) Analysis of the ' Visible ' Loci on the X-Chromosome.
(3) Centres of Alkylation in Relation to Mutagenicity.

15. Immmunology:
(1) Radiation-induced Immunological Neutrality.
(2) Experimental Alteration of Immunological Reactions in Mice.

16. Other Aspects of Tumour Growth:
(1) Serum Mucoprotein associated with Tissue Growth.
(2) Tumour-stimulating Effects of Thiols.
(3) Pregnancy-responsive Mammary Tumours of Mice.

17. The Cell Surface:
(1) Nature of the Tumour Cell Surface.
(2) Surface-active Agents.

18. Microscopy:
(1) Interference Microscopy of Normal and Tumour Cells.
(2) Differential Fluorescent Staining of DNA/RNA by Acridine Orange.
(3) Microscopical Investigations of the Cytoplasm in Ascites Tumour Cells.
(4) Cell Membranes and Intercellular Contact.
(5) Electron Microscopy of Macromolecules.

19. Clinical and Chemotherapeutic Studies:
(1) Clinical Trials of Di-2-chloroethylamine (nor-HN2).
(2) Amino-chlorambucil.
(3) Melphalan.
(4) The Use of Busulphan (Myleran) in Polycythaemia Vera.
(5) The Action of Chlorambucil and Busulphan on the Haemopoietic Organs of the Rat.
(6) Vitamin B_{12} and Neuroblastoma.
(7) The Treatment of Cancer of the Bladder with Glucosaccharo:1—4:lactone.

20. Statistics and Demography:
(1) Cancer Statistics and Demography.
(2) Occupation and Social History in Cancer of the Bladder.

21. Differentiation Theory:
An Electronic Model for Morphogenesis.

PHYSICS DEPARTMENT

1. Problems of low level radioactivity identification and measurement:
   (1) Application of low level alpha-counting techniques in studies of natural radioactivity in a wide range of biological materials, foods and other substances.
   (2) Further development of chemical procedures for separation of radionuclides in biological materials.
   (3) Distribution of radionuclides in the body:
      (a) Chemical and alpha-counting methods of measuring activities of individual nuclides in bone and other tissues.
      (b) Physico-chemical studies of the binding of metal ions by tissue components. Refinement of methods of fractionating tissue components, particularly organic bone components.
   (4) Development of low background beta-counting equipment and its application to the measurement of fission products in foods and human tissues.
   (5) Investigation of fission products in the atmosphere and analysis of the radioactivity in human lung and lymph node tissue.
   (6) Investigation of various types of sample counters for low background measurements including development of special types of 4 π counters.
   (7) Low background NaI scintillation counting applied to the characterization of gamma-emitting isotopes, including ^{137}Cs and short-lived fission products, in various biological materials.
   (8) Construction of 100-channel analyzers for use in alpha, beta and gamma radiation measurements.

2. Clinical Applications of Radiation Physics:

   Therapeutic and diagnostic applications:

   (1) Development of diagnostic techniques using ^{131}I and ^{132}I and in studies with ^{47}Ca.
   (2) Improvements in automatic scintillation scanning system.
   (3) Development of ^{192}Ir grains for use in permanent implants.
   (4) Improvements in the design of beta-particle emitting applicators for ophthalmic work.
   (5) Application of low voltage gamma rays from ^{170}Tm to trigger the X-ray tube in certain types of diagnostic examinations.
   (6) Further design work on a ^{137}Cs treatment unit for use in the head and neck regions.
   (7) Measurement of doses to gonads in radiography—contribution to survey directed by the Adrian Committee.
   (8) Investigation of the distribution of radiation dose in treatment of the cervix uteri with radium.

   Experimental studies:

   (1) Development of liquid scintillation counting equipment for measurement of ^{3}H and ^{14}C in biological material.
   (2) Development of method for separating ^{111}Ag from irradiated palladium by ion exchange.
   (3) Study of short-lived radioactive isotopes, including ^{11}C and ^{43}K, produced by X-rays from the 30 MeV synchrotron.
   (4) Problems of radioactive isotope standardization, including gas counting techniques for the measurement of ^{35}S and ^{14}C.
   (5) Development of photographic methods for the measurement of dosage of high energy X-radiation.
   (6) Development of new rubber-like ' phantom ' material which can be adjusted to simulate tissues.
   (7) Application of calorimetric methods in the measurement of absolute intensity and absorbed dose from X-ray and gamma-ray beams.

3. Experimental biological and physiological investigations:
   (1) Radiation response of bone of the growing rat, with particular relation to bone tumour production, following:
      (a) internal administration of radioactive materials,
      (b) localized external irradiation.

   Application of histological, radiographic and autoradiographic techniques.

(2) Effects of protraction and of fractionation of radiation on the response of various tissues, particularly the blood-forming organs, the bone and the small intestine.

(3) Studies of the life span of blood cells in normal and irradiated animals.

(4) Comparison of mode of action of radiation and various anti-leukaemic drugs (in collaboration with the Chester Beatty Research Institute).

(5) Investigation of the excretion and turnover in the rat of the alkaline earth metals using ^{45}Ca, ^{85}Sr and $^{140}Ba+^{140}La$, and also of the trace element metabolism of zinc and cobalt.

RADIOTHERAPY DEPARTMENT

1. Clinical studies on factors influencing the development of malignant disease, natural history, prognosis, and results of treatment particularly in the bladder, brain, breast, eye, larynx and pharynx, lung, oesophagus, skin, testicle, thyroid and uterus, with similar work in relation to leukaemia, polycythaemia and the lymphomas.

2. Radioactive isotopes:

   Therapy:

   (1) ^{131}I for investigation and treatment of thyroid carcinoma.
   (2) ^{32}P for polycythaemia and certain generalized radio-sensitive diseases.
   (3) ^{198}Au colloid for malignant pleural and peritoneal effusions and some bladder tumours.
   (4) ^{182}Ta for interstitial implantation.
   (5) ^{198}Au and ^{90}Y in small sources (grains) for interstitial implantation.
   (6) ^{90}Sr for beta-ray plaques for eye lesions.
   (7) ^{137}Cs for beam therapy.

   Investigations:

   (1) ^{59}Fe for the study of haemopoiesis in various abnormal states and of marrow transplants.
   (2) ^{51}Cr for estimating red cell volumes (mostly in polycythaemia) and for red cell survival.
   (3) ^{60}Co and ^{58}Co-labelled vitamin B_{12} for studies of the macrocytic anaemias and of vitamin B_{12} metabolism.
   (4) DF^{32}P for platelet survival studies in diseases of the haematopoietic system.
   (5) ^{45}Ca and ^{47}Ca turnover in bones, in malignant disease and under the influence of hormones and irradiation.
   (6) A study of the metabolism of ^{14}C-stilboestrol and its phosphorylated ester in normal hamsters and in hamsters with human prostatic carcinoma explants.
   (7) The application of techniques with radioactive isotopes to certain histochemical methods.

3. Long-term effects of irradiation:

   (1) on the bone marrow and blood;
   (2) in the production of tumours;
   (3) on the eye.

4. Short-term effects of irradiation:

   (1) on connective tissue, with special reference to collagen;
   (2) on collagen formed in tissue cultures;
   (3) as modified by steroid hormones and actinomycin D.

5. ^{3}H-Thymidine.

   Studies of the uptake of ^{3}H-Thymidine by human leukaemic cells using autoradiographic techniques.

6. Measurements of changes in bone density.

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From the beginning of the financial year 1957–58 the Council assumed substantial financial responsibility for the Cancer Research Department at the Royal Beatson Memorial Hospital, Glasgow. The Department was previously supported by funds provided by the Glasgow Western Hospitals Board of Management, by an annual grant from the Department of Health for Scotland's Research Vote, and from unofficial sources. It continues to receive support from the British Empire Cancer Campaign, and also from private donations.

Summary of Research

The current programme of work includes research on the aetiology of cancer in fowls and mice. It has been found that tumours can be induced either by viruses or by synthetic chemical carcinogens under conditions which preclude the introduction of viruses, and comparative studies are now being made of both types of tumours by biological, biochemical and morphological techniques.

Research is also being undertaken on the mechanisms of carcinogenesis with a view to the development of preventive measures and on the role of free radicals in biological mechanisms by means of physio-chemical studies of chemical carcinogens. Other subjects under study are the influence of hormones on mammary tumour incidence in mice after endocrine ablation operations, and the distribution and absolute quantity of DNA in the nucleus in several species of mice. Investigations of the morphological relationship of DNA to RNA in intermitotic nuclei have thrown new light on the sex differences in the distribution of nuclear DNA. Research is also in progress on the relationship between lung cancer and atmospheric pollution and on the carcinogenicity of tobacco smoke; for example, quantitative estimations have been made of the arsenic content in the hair of smokers and non-smokers by the technique of activation analysis.

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Miss J. A. Knowlden, B.Sc.

National Collection of Type Cultures, Colindale

S. T. Cowan, M.D., D.Sc., Dip.Bact. (*Curator*)
Miss J. Midgley, B.Sc. (*M.R.C. External Staff*)
Miss J. E. Rippon, Ph.D., A.R.C.S., Dip.Bact. (*until April*, 1959)
Miss H. E. Ross, B.Sc.
K. J. Steel, B.Pharm., Ph.D.

Standards Laboratory for Serological Reagents, Colindale

Mrs. C. M. P. Bradstreet, M.B., Dip.Bact. (*Director*)
Miss E. M. Bailey, B.Sc.
Mrs. J. M. B. Edwards, M.B. (*part-time*)
Miss M. W. Hully, B.Sc.
Miss A. J. Tannahill, B.Sc.

BACTERIOLOGISTS SECONDED TO DIPLOMA IN BACTERIOLOGY COURSE, 1958–59

A. L. Furniss, M.D. ..
M. H. Hambling, M.B. .. } London School of Hygiene and Tropical Medicine
D. M. Jones, M.B. ..

JUNIOR BACTERIOLOGISTS IN TRAINING (UNALLOCATED)

P. Chadwick, M.B., Dip.Bact. (*Seconded to London School of Hygiene and Tropical Medicine from Jan.*, 1958)
T. A. E. C. Lorenzen, M.B.
J. W. G. Smith, M.B.
J. F. Archer, M.B.
J. R. Bennett, M.B.
E. J. G. Glencross, M.B.
W. C. Harris, M.B.
Miss F. E. Maurice-Williams, M.B.
R. B. F. Smith, M.R.C.S.
W. G. Strawbridge, M.D.

The Public Health Laboratory Service in England and Wales has been administered by the Council on behalf of the Ministry of Health, through which the necessary funds were provided. Originally introduced as a war-time emergency service, it was established on a permanent basis under the National Health Service Act, 1946. The new arrangements for its administration are described earlier in this Report (p. 13).

In addition to eight regional, fifty-one area laboratories, and sixteen recognized laboratories, there are nine reference laboratories and six special laboratories, most of which are housed at the main Central Laboratory at Colindale. Some of the reference and special laboratories also serve workers in the British Commonwealth and in other countries.

Investigations are undertaken not only on immediate problems of public health but also on fundamental problems of epidemiology and preventive medicine. The constitution of the Service is well adapted to the organization of group research—a particularly valuable method when information representative of the country as a whole may have to be collected rapidly. Moreover, by virtue of its close association with local medical officers, the Service is in a favourable position for carrying out controlled field trials of prophylactic agents.

Summary of Main Researches

INFECTIOUS DISEASES

1. Acute Respiratory Infections, including Influenza and the Common Cold:
   (1) Field trials of influenza vaccine in boys' schools and in patients suffering from chronic bronchitis; measurement of response to vaccine or infection by haem-agglutination-inhibition test.
   (2) Study of the growth of influenza viruses in tissue culture.
   (3) Studies of the nucleotide composition of influenza virus ribonucleic acid, with special reference to apparent variations in composition at different times of the year.
   (4) Determination of the amino-acid composition of the protein components of influenza virus.
   (5) Survey of acute respiratory infections in Portsmouth Naval Command, in R.A.F. recruits, and in other sections of the population, with particular reference to adeno-viruses and to Coe and para-influenza viruses; field trial of a trivalent adenovirus vaccine in R.A.F. recruits.
   (6) Serological, bacteriological and virological investigation of early cases of chronic bronchitis, and of asthma.
   (7) Study of virus infections associated with radiological lung shadows in patients attending a Mass X-ray unit.
   (8) Study of acute respiratory diseases in children admitted to hospital, especially those suffering from chronic bronchitis.
   (9) Investigation of Eaton's atypical pneumonia virus.
   (10) The common cold: field studies of epidemiology; prevention by means of autogenous vaccines; treatment by small doses of antibiotics; trial of bacterial vaccines in flying personnel in the R.A.F.

2. Dysentery:
   (1) The typing of strains of *Shigella sonnei* on the basis of colicine production.
   (2) Study of the antibiotic sensitivity of shigellae.
   (3) A controlled trial of neomycin and phthalylsulphathiazole in the treatment of clinical dysentery.

3. Enteric Fever:
   (1) Continued investigation of cellular and viral nucleic acids by fluorescence microscopy.
   (2) Investigation of the special properties of a number of lysogenic systems.

4. Food Poisoning: (see also *Salmonella* Infections):
   Continued study of the reported incidence of food poisoning in England and Wales.

5. Hospital Cross-Infection: (see also Staphylococcal Infections):
   (1) A survey of surgical wound infection.
   (2) Continued study of the mode of spread of staphylococcal infection in both surgical and medical patients.
   (3) The sterilization of bedding and apparatus in hospitals, especially by means of hypochlorite, formaldehyde vapour, ethylene oxide, and gamma radiation.
   (4) The design and ventilation of surgical operating theatres (on behalf of Newcastle-on-Tyne Regional Hospital Board).
   (5) Measurement of the numbers of staphylococci di[illegible]ed into the air by patients under various conditions.

6. Infantile Enteritis (see also *Salmonella* infections):
   (1) Development of phage-typing systems for strains of *Escherichia coli* responsible for infantile diarrhoea.
   (2) Continued study of the antigenic structure of serotypes of *E. coli*, with particular reference to the pathogenicity of different sub-types.
   (3) The use of ligated loops of rabbit gut to determine the pathogenicity of *E. coli*, salmonellae, and *Sh. sonnei*.

7. Malaria:
   (1) Preservation in a sealed desiccator of unstained and unfixed blood films of malaria and other blood parasites.
   (2) The infectivity of patients to anopheles mosquitoes at various stages of *P. vivax* infection: estimation of the percentage of an infective population.

8. Mycological Infections:
   (1) The control of fungal infection in swimming baths.
   (2) Study of the saprophytic life of *Madurella mycetomi* under various conditions.
   (3) Study of soils for the presence of pathogenic fungi.

9. Poliomyelitis (see also Virology):
   (1) Continued survey of the incidence of poliovirus in the faeces of normal children under five years of age.
   (2) Study of the incidence of poliomyelitis in persons vaccinated against the disease; investigation of the strains causing the disease.
   (3) Study of the effect of poliomyelitis vaccination in preventing provocation paralysis.
   (4) Study of the complement-fixing antibody response of persons receiving one, two and three doses of poliomyelitis vaccine; and (in collaboration with Professor Wilson Smith) a comparison of the response with neutralizing, precipitating, and flocculating antibodies.
   (5) Standardization of poliomyelitis neutralization tests and measurement of standard sera.
   (6) The structure and intracellular formation of poliovirus seen with the electron microscope (in collaboration with R. W. Horne of the Cavendish Laboratory, Cambridge).

10. Salmonella Infection (see also Food Poisoning, Infantile Enteritis, and Food Hygiene):
    (1) Extension of the phage-typing of *Salmonella typhi-murium*; development of phage-typing systems for a number of the more common salmonellae.
    (2) Study of the chlortetracycline sensitivity of strains of *Salm. typhi-murium* isolated from various sources from 1947 onwards.
    (3) Application of transduction to the routine identification of salmonellae deficient in flagellar antigens.
    (4) The incidence of salmonellae, shigellae, and pathogenic coliform organisms in the faeces of normal children under five years of age.
    (5) Investigation of animal feeding stuffs and fertilizers as a possible source of salmonella infection.
    (6) Continued inquiry into the contamination of home-produced and imported foods, especially meat and processed egg, with salmonella organisms.
    (7) The survival of *Salm. typhi-murium* in soil.

11. Staphylococcal Infections (see also Hospital Cross-Infection):
    (1) Further study of the extent to which lysogenicity determines phage type in staphylococci.
    (2) Experimental staphylococcal infections in guinea-pigs.
    (3) The distribution of *Staphylococcus aureus* in different groups of the population, with a study of their phage types, resistance to antibiotics, and relation to lesions.
    (4) Study of antibiotic resistance and egg-yolk reactions in staphylococci from epidemics and from sporadic infections in hospitals.
    (5) Investigation of some characteristics of staphylococci causing impetigo.
    (6) Investigation of factors affecting staphylococcal infection in maternity homes; the incidence of sepsis and of drug-resistant staphylococci in babies born in hospital compared with those born at home.

12. Streptococcal Infections:
    (1) The production and characterization of streptococcal protoplasts.
    (2) The production of L forms of streptococci; study of methods for their propagation in subculture.
    (3) The chemical composition and immunological properties of the streptococcal cell wall.
    (4) Further study of antistreptolysin reaction and of other streptococcal antibodies in human sera.
    (5) The use of fluorescent antibody for the rapid diagnosis of streptococcal infection.
    (6) The type distribution of *Streptococcus pyogenes* in England and Wales.
    (7) The frequency of rheumatic, nephritic and other complications of haemolytic streptococcal infection.

13. Tuberculosis:
    (1) Continued study of the part played by the ambulant infectious case of tuberculosis in spreading the disease (in collaboration with the M.O.H. and chest physicians of Gateshead).
    (2) Determination of the duration of the lag phase and the initial generation time of mycobacteria growing in any liquid or semi-solid medium.
    (3) Continued investigation of long-term chemotherapy in tuberculosis (in association with the Council's trials).
    (4) Chemotherapy of experimental silico-tuberculosis in mice.
    (5) Study of unusual acid-fast bacilli associated with lesions of the lung.

14. Venereal Disease:
    (1) An evaluation of the Reiter protein complement-fixation test in comparison with the treponemal immobilization test and the treponemal Wassermann reaction.
    (2) A clinical evaluation of the treponemal Wassermann reaction in normal persons and in patients with syphilis.
    (3) Estimation of the sensitivity of gonococci to penicillin, with a view to the detection of partially resistant strains.
    (4) Cultural and serological tests for pleuropneumonia-like organisms in patients with genital infections and in normal controls.

15. Virology (see also Acute Respiratory Infections, Poliomyelitis, and Miscellaneous):
    (1) Continued investigation of factors necessary to support growth of cells in tissue culture, particularly suspended cell cultures.
    (2) The incidence of enteric viruses in the faeces of sick and healthy children.
    (3) Virological investigation of cases of sudden death in infancy.
    (4) Study of the eclipse phase of adenovirus and poliovirus.
    (5) Serological relationship between mumps and glandular fever.
    (6) Study of the incidence of virus infections in Portsmouth Naval Command.

16. Whooping Cough:
    (1) A study of the vaccination state and family circumstances of children who die from whooping cough.

SANITARY BACTERIOLOGY

1. Air Hygiene:
    (1) Estimation of numbers of viable bacteria in air-borne particles, and in artificial dust particles, by use of electron bombardment.
    (2) Study of the survival of bacteria in the environment under various conditions.
    (3) Continued study of disinfection by the use of formaldehyde vapour and ethylene oxide.

2. Food Hygiene:
    (1) The effect of addition of chlortetracycline to feeding stuffs for chickens, and to dips for dressed poultry, on the survival and growth of *Salm. typhi-murium* in and on the carcasses (in collaboration with Houghton Poultry Research Station and the Low Temperature Research Station, Cambridge).
    (2) The effect of pasteurization on the bacterial content of frozen whole egg.
    (3) The effect of gamma-rays on the bacterial content of frozen whole egg; feeding experiments on rats (in collaboration with the Low Temperature Research Station, Cambridge, the Atomic Energy Research Establishment, Harwell, and with Dr. C. R. Murdock, Belfast).
    (4) Study of the survival and growth of bacteria in wine and in non-alcoholic drinks.

3. Water:
    (1) Study of the sewage pollution of bathing beaches, including an epidemiological inquiry into cases of poliomyelitis, typhoid fever and paratyphoid fever in bathers and non-bathers.
    (2) Development of a synthetic formate lactose glutamate medium for the examination of water.

MISCELLANEOUS

1. Gamma globulin:
    (1) Therapeutic trial of gamma globulin in hypogammaglobulinaemia (in association with the Council's working party on the subject).
    (2) Examination of sera for antibodies to poliovirus in patients with agammaglobulinaemia under treatment and after inoculation of poliomyelitis vaccines (in association with the Council's working party on the subject).
    (3) Examination of sera for antibodies to poliomyelitis and other viruses in hypogammaglobulinaemia patients under treatment with gamma globulin and in response to injections of influenza and poliomyelitis vaccines (in association with the Council's working party on the subject).
    (4) Continued study of the value of gamma globulin in the prevention of rubella in pregnant women.

2. The clinical, bacteriological and epidemiological features of acute gastro-intestinal illness in a group general practice at St. Paul's Cray, Kent.

3. Clinical and serological investigation of infections in early pregnancy in relation to abortion, stillbirth, and congenital defect (in collaboration with the Society of Medical Officers of Health and with the obstetric departments of certain hospitals).

4. Attack rates of infectious diseases: an analysis of information collected during the pertussis vaccine trials of secondary attack rates of different diseases in children exposed to infection in their own homes.

5. Investigation into the presence of circulating antibodies to bovine milk proteins in the serum of pregnant women.
6. Continued long-term experiments on the preservation of bacteria by freeze-drying.
7. The preparation and standardization of virus antigens, and of neutralizing and diagnostic sera for the typing of viruses.
8. Further study of the complement-fixation test for hydatid disease.
9. A new medium inhibitory to *Proteus* and to many aerobic spore-bearing bacilli.
10. The use of filter paper for separating different members of the Enterobacteriaceae.

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Investigations of staphylococcal infection acquired in Great Britain's hospitals. *Publ. Hlth. Rep., Wash.*, 1958, **73**, 961.

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Research Work Aided By Grants

During the period covered by this Report the Council have continued to make, from the public and private funds at their disposal, research grants to individual workers in aid of an extensive programme of clinical and laboratory investigations. A list of these grants, arranged according to the geographical location of the institutions in which they have been held, is given below:

Aberdeen

UNIVERSITY

Biological Chemistry Department

ROBERTSON, Dr. H. A.—assistance by Mr. I. R. Falconer, and expenses: determination of ^{131}I content of sheep thyroid arising as a consequence of fall-out from nuclear explosions, and its distribution in relation to geographic and climatic environment.

SIMKIN, Dr. J. L.—assistance by Mr. C. R. Sutton, and expenses: role of the microsome material in protein biosynthesis in mammalian cells.

Obstetric Medicine Research Unit

HERRIOT, Dr. A.—personal: relationship of (a) uterine blood flow to the oxygenation of the foetus, and (b) the rate of turnover and composition of the liquor amnii to the composition of maternal blood and the bearing of these factors on the well-being of the foetus.

Surgery Department

MURRAY, Mr. J. G.—assistance by Dr. J. H. Wyllie: distribution of pharmacologically active substances in the walls of the stomach of man and animals, and their relation to gastric function.

Ascot, Berks.

HEATHERWOOD ORTHOPAEDIC HOSPITAL

ARDEN, Mr. G. P.—expenses: comparison of injuries suffered in road accidents with the damage to the vehicle.

Belfast

THE QUEEN'S UNIVERSITY

Biochemistry Department

LESLIE, Dr. I.—assistance by Mr. J. J. Childs, and expenses: coupling of energy metabolism and synthetic reactions occurring in tissue cultures of normal and malignant human cells.

Microbiology Department

DICK, Professor G. W. A.—assistance by Mr. P. J. Campbell, and expenses: inactivation of penicillinase by the enzyme papain, and its possible clinical applications.

Psychology Department

SETH, Professor G.—assistance by Dr. Halla Beloff: problems of language and thinking in cases of brain injury and in schizophrenia.

Department of Social and Preventive Medicine

PEMBERTON, Professor J.—expenses: air pollution and mortality data from county boroughs.

Orthodontic Department

SMITH, Mr. G. E.—expenses: prevalence of malocclusion in West Africa.

Birmingham

BIRMINGHAM ACCIDENT HOSPITAL AND REHABILITATION CENTRE

CLARKE, Mr. A. Ruscoe—assistance by Dr. I. G. Graber, and expenses: illness of trauma.

BIRMINGHAM GENERAL HOSPITAL AND QUEEN ELIZABETH HOSPITAL

COX, Dr. E. V.—expenses (partly from the Peel Memorial Trust fund): gastro-enterology.

FAIRBURN, Dr. E. A.—personal: blood flow in skin lesions.

BIRMINGHAM AND MIDLAND HOSPITAL FOR WOMEN

Clinical Endocrinology Department

CROOKE, Dr. A. C.—(1) assistance by Mr. J. H. Michell : production *in vitro* of steroids by gonadal tissue under the influence of gonadotrophins ; (2) expenses: immunological investigation of human gonadotrophin.

LEYTON, Dr. G. B.—assistance by Dr. A. F. Cheyne, and expenses: therapeutic trial of 5-hydroxytryptophan in schizophrenia.

UNIVERSITY

Anatomy Department

ZUCKERMAN, Professor Sir Solly—(1) expenses: oogenesis; (2) expenses: (i) posture, (ii) dimensions and growth of the craniomandibular apparatus.

Bacteriology Department

PERRY, Professor S. V.—assistance by Mr. S. C. Bondy, and expenses: nitrogen metabolism of brain.

BISSET, Dr. K. A.—assistance by Mr. A. C. Baird-Parker and Mr. E. B. Pike, and expenses: bacteriology of dental caries.

Chemistry Department

STACEY, Professor M.—(1) assistance by Mr. G. Fuller, and expenses: preparation of a range of fluorocarbon compounds for test as anaesthetic agents; (2) assistance by Mr. R. J. German, and expenses: structure of the polysaccharides of mycobacteria.

Department of Medicine

CRANE, Dr. C. W.—personal: the fate of orally administered ^{15}N labelled protein in normal subjects and patients with malabsorption.

STANLEY, Mrs. M.—personal: carbohydrate metabolism under conditions of hypoxia.

Medical Biochemistry and Pharmacology Department

FRAZER, Professor A. C.—(1) expenses: metabolic research; (2) assistance by Dr. G. Hübscher: synthesis of glycerides and phospholipids in intestinal cells; (3) assistance by Mr. R. R. A. Dils: the intracellular enzymes concerned in lipid metabolism.

Microbiology Department

PEACOCKE, Dr. A. R.—assistance by Mr. B. N. Preston: the denaturation and degradation of nucleic acids and nucleoproteins by ionizing radiation and other physical agents.

Experimental Pathology Department

SQUIRE, Professor J. R.—(1) expenses: hypogammaglobulinaemia; (2) expenses: the nephrotic syndrome.

BLAINEY, Dr. J. D.—personal: protein metabolism in relation to the natural history of the nephrotic syndrome and other hypoproteinaemic states.

Pathology Department, Cancer Research Laboratories

WOODHOUSE, Dr. D. L.—expenses: (1) work on behalf of the Committee on the Carcinogenic Action of Mineral Oils; (2) (from the Tobacco Manufacturers' Benefaction): carcinogenicity of tobacco smoke tar.

Department of Social Medicine

MCKEOWN, Professor T.—assistance by Dr. I. M. Leck: environmental influences on the aetiology of congenital malformations.

School of Dental Surgery

HARDWICK, Dr. J. L.—expenses: uptake, release, and exchange of fluorides at the tooth surface.

MACGREGOR, Professor A. B.—expenses: treatment of teeth by root filling.

Public Health Laboratory

JAMESON, Dr. J. E.—expenses: factors determining the growth of various pathogenic organisms in different media.

Bristol

UNIVERSITY

Bacteriology Department

COOPER, Professor K. E.—(1) assistance by Mr. P. J. Chapple: features differentiating strains of *E. coli* from epidemic gastroenteritis in man and animals, with special reference to phages and colicines; (2) assistance by Mr. L. B. Quesnel: early phases of growth of a bacterial inoculum in continuous micro-culture, and the effect thereon of low concentration of streptomycin sulphate.

Dental School

DARLING, Professor A. I.—assistance by Mr. A. W. Brooks and Mr. K. V. Mortimer: (a) pathology of the carious lesion in enamel; (b) structural abnormalities of teeth.

POOLE, Dr. D. F. G.—personal: fine structure of normal and carious human enamel.

Engineering Department

PHILLIPS, Mr. C. I.—personal: glaucoma.

Organic Chemistry Department

BATTERSBY, Dr. A. R.—assistance by Mr. H. F. Hodson: structure of the alkaloids of Strychnos toxifera.

HOUGH, Dr. L.—assistance by Dr. J. R. Clamp: the egg mucoproteins ovomucoid and ovalbumin.

Pharmacology Department

HELLER, Professor H.—(1) assistance by Mr. A. M. J. N. Blair: (i) effect of diuretics and hormones on the water metabolism of protein-deficient animals; (ii) estimations of vasopressin and oxytocin in the body fluids of infants and adults under various experimental conditions; (2) assistance by Mr. K. Lederis: maturation of hypothalamo-neurohypophyseal system.

Psychology Department

DREW, Professor G. C.—assistance by Miss H. A. Long, and expenses: effects of alcohol on perceptual and skilled performance.

Bucksburn

ROWETT RESEARCH INSTITUTE

Enzymology Department

LEVVY, Dr. G. A.—assistance by Miss J. Findlay, and expenses: enzymology of mucopolysaccharides.

Callington, Cornwall

STAINES, Dr. F. H.—expenses: farmer's lung.

Cambridge

STRANGEWAYS RESEARCH LABORATORY

FELL, Dr. Honor B.—assistance by Miss J. M. Allen: tissue culture of tubercle bacilli (in collaboration with Dr. E. M. Brieger).

HUGHES, Mrs. Shirley—personal and expenses: development of mammalian dental tissues in culture.

UNIVERSITY

Anatomy School

HUGHES, Dr. A. F. W.—expenses: development of the nerve cell within vertebrate embryos.

MILLEN, Dr. J. W. and WOOLLAM, Dr. D. H. M.—expenses: congenital malformation in mammals.

HORN, Dr. G.—expenses: experimental neurological studies of attention.

Sir William Dunn School of Biochemistry

YOUNG, Professor F. G.—(1) expenses: influence of pituitary hormones on metabolism; (2) assistance by Mr. K. L. Manchester: influence of hormones on protein metabolism; (3) assistance by Dr. N. Powers, and expenses: aetiology of diabetic ketosis, with special reference to dietary influence.

DIXON, Dr. H. B. F.—expenses: chemistry of corticotrophin and the melanophore-stimulating hormone.

GREVILLE, Dr. G. D.—assistance by Mr. P. K. Tubbs: metabolism in animal tissues of D- and L-lactic acids, with particular reference to their inter-conversion.

NEEDHAM, Dr. Dorothy—assistance by Miss J. M. Cawkwell and expenses: mechanism of protein synthesis and related problems.

PERRY, Dr. S. V.—expenses: intracellular components of skeletal muscle.

RANDLE, Dr. P. J.—expenses: chemical and biochemical studies of diabetes mellitus.

SANGER, Dr. F.—assistance by Dr. J. Williams: the structure of phosvitin and other egg yolk proteins.

Colloid Science Department

ROUGHTON, Professor F. J. W.—expenses: rapid chemical processes of biological and medical interest (in collaboration with Professor Q. H. Gibson, University of Sheffield).

ROUGHTON, Professor F. J. W. and SCHULMAN, Dr. J. H.—assistance by Mr. L. O'Rourke and expenses: preparation and investigation of yeast cell protoplasts.

CHADWICK, Dr. C. S.—personal: physico-chemical and immunological investigations using proteins labelled with fluorescent dyes.

JOHNSON, Dr. Paley—(1) assistance by Mr. A. Feinstein: physico-chemical examination of aqueous extracts from grass pollens; (2) assistance by Mr. E. G. Richards: changes in the physical and chemical properties of well-defined protein molecules; (3) assistance by Mr. A. J. Rowe, and expenses: physico-chemical study of the proteins of the muscle fibril.

OTTEWILL, Dr. R. H.—assistance by Mr. W. M. McKernan: interaction between dextran derivatives and proteins.

Human Ecology Department, and University Health Service

DAVY, Dr. B. W.—assistance by Mrs. M. Sisson and Miss V. L. Worthington: personal and environmental factors which influence academic performance.

PICKLES, Dr. V. R.—personal: fundamental properties of the menstrual stimulant, and antagonists of possible value in the treatment of dysmenorrhoea.

Pathology Department

MARRACK, Professor J. R.—personal, assistance by Mr. C. B. Richards, and expenses: physical chemistry of reactions between antigens and antibodies (in association with Dr. Paley Johnson, Colloid Science Department).

NEWTON, Mrs. A. A.—personal and expenses: the nature of the virus-cell complex.

Physiological Laboratory

RUSHTON, Dr. W. A. H.—expenses: measurements of visual pigments in the eye.

MERTON, Dr. P. A.—expenses: central nervous pathways for impulses from muscle sense organs; the central mechanism of the stretch reflex and of tendon reflexes.

Psychological Laboratory

GREGORY, Mr. R. L.—assistance by Miss J. G. Wallace, and expenses: differential auditory and visual sensitivity.

Radiotherapeutics Department

MITCHELL, Professor J. S.—(1) assistance by Mr. P. Fawcett, and expenses: potential hazard to health of ^{90}Sr.; (2) expenses (from special funds at the Council's disposal): clinical and laboratory studies, using the linear accelerator, of the therapeutic applications of 15 MeV X-rays; (3) assistance by Miss A. R. Fisher: application of the techniques of tissue culture to the study of the effects of ionizing radiations and chemical agents upon proliferating normal and malignant cells.

HEARD, Dr. Dorothy—assistance by Mr. G. M. W. Cook: surface structure of tissue cells.

HEMINGWAY, Dr. J. T.—personal and expenses: natural inhibitors of normal and tumour cells.

HOLMES, Dr. Barbara E.—assistance by Miss E. Whittle: formation of the nucleic acids during the growth of the cell, and the effect of irradiation upon it.

Zoology Department

HINDE, Dr. R. A.—assistance by Mrs. T. Rowell: primate behaviour.

ROTHSCHILD, The Lord—expenses: problems of fertilization and the physiology of spermatozoa.

Cardiff

UNIVERSITY COLLEGE OF SOUTH WALES AND MONMOUTHSHIRE

Biochemistry Department

DODGSON, Dr. K. S.—assistance by Miss G. M. Powell: function of the aryl-sulphatases.

WELSH NATIONAL SCHOOL OF MEDICINE

Pathology and Bacteriology Department

GOUGH, Professor J.—expenses: pathology of pneumoconiosis.

SHUSTER, Dr. S.—expenses: (i) factors influencing corticotrophin release in man; (ii) cortisol metabolism in wasting diseases.

WHITCHURCH HOSPITAL

Neuropsychiatric Research Unit

RICHTER, Dr. D.—assistance by Mr. D. M. Robertson: metabolic activity of different protein fractions of the brain.

Carshalton

MEDICAL RESEARCH COUNCIL LABORATORIES

Toxicology Research Unit

STEWART, Dr. G. T.—personal, and expenses (from Dulverton Trust funds): role of blood lipids in the pathogenesis of atherosclerosis and related disorders.

CLEGG, Dr. E. J.—expenses: blood sampling.

Colwyn Bay

STOCKS, Dr. P.—personal, and expenses (from the Tobacco Manufacturers' Benefaction): relationship between air pollution and death rates from gastro-intestinal cancer and between pulmonary infection and cancer.

Dundee

QUEEN'S COLLEGE, UNIVERSITY OF ST. ANDREWS

Dental School

HITCHIN, Professor A. D.—expenses: inheritance of geminated composite odontome in the dog.

Pharmacology Department

HUNTER, Professor R. B.—assistance by Dr. A. C. Brownie and expenses: adrenal inhibitors.

MARSHALL, Dr. P. B.—assistance by Miss J. D. Reid, and expenses: problems associated with histamine and 5-hydroxytryptamine.

Physiology and Biochemistry Department

BELL, Professor G. H.—assistance by Dr. Olive M. J. Dunbar, and expenses: (1) physical properties of bone in experimental lathyrism in rats, and in osteoporosis in man; (2) statistical survey of the incidence and sites of fractures in elderly people.

DUTTON, Dr. G. J. F.—(1) expenses: metabolism of glucuronic acid in tissues, with reference to conjugation in liver and connective tissues (normal and tumorous); (2) assistance by Mr. I. H. Stevenson and expenses: mechanism and significance of extra-hepatic glucuronide synthesis.

Edinburgh

NORTHERN GENERAL HOSPITAL

Rheumatic Diseases Unit

DUTHIE, Dr. J. J. R.—assistance by Miss I. Bett and Dr. W. R. M. Alexander, and expenses: pathogenesis of rheumatoid arthritis.

ROYAL INFIRMARY

Bacteriology Department

BOWIE, Dr. J. H.—expenses: pressure-steam sterilizers.

WESTERN GENERAL HOSPITAL

Gastro-Intestinal Unit

CREAN, Dr. G. P.—personal: effects of anterior pituitary and adrenocortical hormones on gastric structure and function.

UNIVERSITY

Chemistry in relation to Medicine Department

GRANT, Dr. J. K.—expenses: metabolism of the steroid hormones.

Institute of Animal Genetics

WADDINGTON, Professor C. H.—(1) expenses: analysis of *Drosophila* populations with increased rates of genetic mutation: (2) assistance by Mr. A. A. Frohlich: immunological study of the ontogeny, distribution and changes in quantity of specific proteins in the early development of mice and amphibia.

ALDERSON, Dr. T.—personal: (1) mutagenic activity of various anti-tumour agents in *Drosophila melanogaster*; (2) mutagenic activity of urethane in the mouse.

BEALE, Dr. G. H.—assistance by Mr. J. O. Bishop and expenses: genetical and immunological studies with *Paramecium.*

Department of Medicine

DONALD, Professor K. W.—assistance by Dr. J. Macnamara and expenses: cardio-pulmonary research.

Pathology Department

MONTGOMERY, Professor G. L.—expenses (from Dulverton Trust funds): coronary arterial disease.

Pharmacology Department

VOGT, Dr. Marthe L.—(1) expenses: factors controlling the release of hormones from the adrenal cortex; (2) assistance by Mr. D. F. Sharman: adrenaline and noradrenaline levels in mental patients.

Physiology Department

DEWAR, Dr. A. D.—expenses: physiology of pregnancy in the mouse.

PASSMORE, Dr. R. and MEIKLEJOHN, Dr. A. P.—expenses: human metabolism in relation to diet.

Social Medicine Department

DOUGLAS, Dr. J. W. B.—assistance by Mr. D. G. Mulligan and expenses: prevalence and social concomitants of maladjustment and delinquency in school children.

Surgical Science Department

WOODRUFF, Professor M. F. A.—expenses: immunological tolerance of homologous tissue.

Zoology Department

MITCHISON, Dr. N. A.—expenses: transplantation and explantation of antibody producing cells.

WALKER, Dr. P. M. B.—assistance by Miss B. Mobbs: chemical control mechanisms of cell division and cell growth.

Epsom

HORTON HOSPITAL, EPSOM, AND ST. BERNARD'S HOSPITAL, SOUTHALL

MACSORLEY, Dr. Kate—personal, and expenses: fertility in mentally ill patients.

Exeter

UNIVERSITY

Washington Singer Laboratories

SCHOFIELD, Dr. K.—assistance by Mr. F. Comstock: chemical synthesis and biological properties of bi- and tri-cyclic tropolones analogous to colchicine.

Zoology Department

HARVEY, Mrs. C. Clare—assistance by Mrs. R. A. Linn: problems relating to human fertility.

TYLER, Dr. Christine—personal and expenses: occurrence of the oxytocic and vasopressor activities of the neurohypophysis in a variety of species.

ROYAL HOSPITAL FOR SICK CHILDREN

Department of Child Health

GRAHAM, Professor S. and LENIHAN, Dr. J. M. A.—assistance by Miss J. M. Warren, and expenses: strontium content of human tissue.

Pathology Department

SIMPSON, Dr. H. W.—personal and expenses: daily rhythm of the adrenal cortex.

UNIVERSITY

Anatomy Department

SCOTHORNE, Dr. R. J.—assistance by Mrs. I. Nagy: application of the method of organ culture to the study of the reactions between lymph node and homologous tissue.

Biochemistry Department

DAVIDSON, Professor J. N.—expenses: biochemistry of tissue growth, with particular reference to tissue nucleic acids.

MUNRO, Dr. H. N.—(1) expenses: biochemistry of protein synthesis; (2) assistance by Mr. D. Mukerji: influence of dietary amino-acid supply on the metabolism of proteins and nucleic acids, with particular reference to the action of glycine.

CROSBIE, Dr. G. W.—expenses: studies in pyrimidine biosynthesis using radio-active compounds.

DAWES, Dr. E. A.—expenses: (i) carbohydrate and fatty acid metabolism of *Sarcina lutea*; (ii) energetics of anaerobic citric acid metabolism of *Aerobacter aerogenes*.

Department of Medicine

DAVIS, Professor L. J.—expenses (from Dulverton Trust funds): problems of blood coagulation.

Institute of Physiology

DURNIN, Dr. J. V. G. A.—(1) assistance by Miss E. C. Blake and Miss K. Allan, and expenses: food intake and energy expenditure of adolescents and elderly people; (2) assistance by Dr. Anna Ferro-Luzzi, and expenses: digestibility factors for protein, fat and carbohydrate of present-day British diets.

Surgery Department

ILLINGWORTH, Professor C. F. W.—expenses: hormonal aspects of breast cancer.

BURNETT, Dr. W.—assistance by Miss C. Gordon, and expenses: origin of metabolic gall stones.

Zoology Department

BARNETT, Mr. S. A.—assistance by Miss E. Coleman, and expenses: physiological adaptation of mice living at low temperatures.

WESTERN INFIRMARY

Department of Medicine

NORDIN, Dr. B. E. C.—assistance by Mr. J. McGregor, and expenses: behaviour of living bone in a Warburg apparatus.

Surgery Department

KAY, Mr. A. W.—assistance by Dr. I. E. Gillespie: physiology of the pyloric antrum.

Harefield

HAREFIELD HOSPITAL

HOUGHTON, Dr. L. E.—assistance by Dr. Angela Lehane, and expenses: trial of corticosteroids in combination with chemotherapy in the treatment of pulmonary tuberculosis.

Pathology Department

SIMMONDS, Dr. F. A. H.—expenses: major surgery in pulmonary tuberculosis.

Hull

UNIVERSITY

Botany Department

CROMWELL, Dr. B. T.—assistance by Mr. K. Rothwell: biosynthesis of the alkaloids of hemlock (*Conium maculatum L.*) and pomegranate (*Punica granatum L.*).

Hunza, Pakistan

WARBURTON, Dr. K.—expenses: blood samples from remote populations in northern Pakistan.

Ibadan, Nigeria

UNIVERSITY COLLEGE

Physiology Department

GRAYSON, Professor J.—expenses: use of internal calorimetry in the determination of blood flow in solid organs.

Keele

UNIVERSITY COLLEGE OF NORTH STAFFORDSHIRE

Electronics Department

INGRAM, Dr. D. J. E.—assistance by Mr. G. A. Helcké: study of different haemoglobin derivatives by electron resonance.

Kenya

MEDICAL RESEARCH LABORATORY, NAIROBI

MINTER, Mr. D. M.—personal: the biology of sandflies.

Leeds

GENERAL INFIRMARY

Anaesthesia Department

HARBORD, Dr. R. P.—expenses: pulmonary ventilation problems in patients under anaesthesia.

Dermatology Department

INGRAM, Dr. J. T.—assistance by Dr. A. MacLennan: epidermal mitotic activity and metabolism in psoriasis.

UNIVERSITY

Bacteriology Department

OAKLEY, Professor C. L.—(1) assistance by Mr. G. Gowland: the degree of specificity of immunological tolerance of mammalian serum proteins; (2) assistance by Mr. P. D. Walker: serological examination of the spore antigens of members of the genus *Clostridium.*

Biochemistry Department

CHATTAWAY, Dr. F. W.—assistance by Mr. R. V. Brunt, and expenses: susceptibility to dermatophyte infection.

DAGLEY, Dr. S.—assistance by Mr. J. Sykes: enzyme activities of cell-free extracts.

KENNY, Dr. A. J.—expenses: (i) assay of glucagon in circulating blood: (ii) exopeptidases in liver.

Biomolecular Structure Department

PAUTARD, Dr. F. G. E.—personal: formation of hydroxyapatite by the flagella of unicellular algae and by the ciliate *Spirostomum ambiguum.*

School of Dentistry

WEATHERELL, Mr. J. A.—personal: organic matrix of skeletal and dental structures in connection with problems of calcification.

WEIDMANN, Dr. S. M.—assistance by Mr. R. G. Whitehead, and expenses: effects of fluorine on the development of teeth, alveolar bone and organic matrix formation in cartilage.

Department of Medicine

SHUCKSMITH, Mr. H. S.—expenses: effect of fibrinolytic activity on thrombosis.

WATKINSON, Dr. G.—expenses: gastric secretion.

Medical Physics Department

SPIERS, Professor F. W.—(1) assistance by Mr. M. J. McHugh, and expenses: development of a portable high pressure ionization chamber apparatus for testing of local gamma-ray backgrounds; (2) assistance by Mr. J. C. Duggleby, and expenses: development of a differential high pressure ionization chamber apparatus for continuous recording of background radiation.

Chemical Pathology Department

LATHE, Professor G. H.—assistance by Dr. Marjorie Flint, and expenses: bile pigment metabolism in the newborn infant.

Experimental Pathology and Cancer Research Department

GREEN, Professor H. N.—(1) assistance by Miss M. R. Anderson, and expenses: work on behalf of the Committee on the Carcinogenic Action of Mineral Oils; (2) expenses: nucleotide metabolism.

DAY, Dr. T. D.—expenses (from the Tobacco Manufacturers' Benefaction): experimental production of lung cancer by means of an inhalation technique and the testing of possible carcinogenic fractions from tobacco tar.

LAWS, Dr. J. O.—expenses (from the Tobacco Manufacturers' Benefaction): screening test for carcinogens.

Liverpool

UNIVERSITY

Anaesthesia Department

GEDDES, Dr. I. C.—expenses: metabolism of lidocaine ^{14}C and carbocaine ^{14}C.

Anatomy Department

HARRISON, Professor R. G.—expenses: functional control of the vascularization of the adrenal gland in the rabbit.

BOWSHER, Dr. D. R.—expenses: secondary sensory neurones in primates.

Department of Child Health

JONES, Dr. R. S.—personal and expenses: measurement of pulmonary blood flow in infants and young children.

Department of Medicine

MCCONNELL, Dr. R. B.—personal: possible genetic factors in duodenal ulcer and other common diseases.

Surgery Department

WELLS, Professor C. A.—expenses: sterilization of gloves.

EDWARDS, Mr. F. R.—assistance by Mr. C. Miller: development of the Lillehei De Wall heart-lung pump oxygenator.

School of Tropical Medicine

GORDON, Professor R. M.—assistance by Mr. G. Dickerson: filariasis.

KERSHAW, Professor W. E.—assistance by Mr. R. G. A. Stretch, and expenses: the effect of parasitism on animal intelligence.

WALTON HOSPITAL

Ear Nose and Throat Department

TUMARKIN, Mr. A.—(1) expenses (from Alexander Piggott Wernher Memorial Trust funds): nature and function of the accessory air spaces of the middle ear; (2) expenses: insert receivers for hearing aids.

London

BEDFORD COLLEGE

Zoology Department

MILLOTT, Professor N.—assistance by Mr. M. Yoshida, and expenses: sensitivity to light in eyeless animals.

CENTRAL MIDDLESEX HOSPITAL

Gastro-Enterology Department

JONES, Dr. F. Avery—(1) assistance by Miss B. White, and expenses: peptic ulceration; (2) expenses: (i) steatorrhoea; (ii) gastro-intestinal blood loss.

AVERY JONES, Dr. F. and ROWLANDS, Dr. E. N.—assistance by Dr. A. D. Cameron: measurement of gastro-intestinal blood loss using Cr^{51}.

DOLL, Dr. W. R. S.—assistance by Mrs. H. M. Drane: blood group substances and gastro-duodenal disease.

ROWLANDS, Dr. E. N.—expenses (i) steatorrhoea, using labelled fat; (ii) proteolytic enzymes in peptic ulcer.

SHINER, Dr. Margot—personal: development of the technique of small intestine biopsy.

TODD, Mr. I. P. and ROWLANDS, Dr. E. N.—assistance by Dr. A. M. Connell: normal and abnormal function in the colon.

Physiology Department

BURNS, Professor W.—assistance by Dr. R. P. Gannon: physiological basis of temporary and permanent noise-induced hearing loss.

STEVENS, Mr. A. J.—expenses: human responses to heat (to be undertaken during an expedition to Morocco).

GUY'S HOSPITAL MEDICAL SCHOOL

Anaesthetics Department

BURNS, Dr. T. H. S.—personal: development of non-explosive anaesthetic agents (in collaboration with Dr. J. M. Hall).

HALL, Dr. J. M.—personal: development of non-explosive anaesthetic agents (in collaboration with Dr. T. H. S. Burns).

Bacteriology Department

KNOX, Professor R. —(1) expenses: testing of cyano-acetic acid hydrazide and other compounds as anti-tuberculosis drugs; (2) assistance by Mr. N. A. Dickinson, and expenses: work on steam pressure sterilizers on behalf of the Working Party on Steam Pressure Sterilizers.

GORRILL, Dr. R. H.—assistance by Mr. B. E. B. Moseley: factors responsible for the production of a lysogenic state following infection of bacteria with a temperate phage.

Biochemistry and Chemistry Department

BROOKSBANK, Dr. B. W. L.—personal, and expenses: estimation of androst-16-en-3α-ol in human urine.

Dental Medicine Department

RUSHTON, Professor M. A.—expenses: histology of radiation damage in the teeth, following the administration of ^{90}Sr.

Experimental Medicine Department

BUTTERFIELD, Professor W. J. H.—assistance by Miss M. J. Whichelow: radio-active tracer studies of pyruvate levels in diabetic blood and tissue biopsy specimens.

Pathology Department

DAVISON. Dr. A. N.—assistance by Miss M. Wajda: experimental myelination.

Chemical Pathology Department

THOMPSON, Professor R. H. S.—assistance by Miss E. A. Marples and expenses: biochemistry and cytology of the brain with special reference to multiple sclerosis.

Pharmacology Department

ROBSON, Professor J. M.—(1) expenses: chemotherapy of tuberculosis and leprosy; (2) assistance by Miss E. Poulson: action of various drugs, including nucleotoxic drugs, on pregnancy.

Physiology Department

GRANT, Dr. R. T.—personal and expenses: release of vasoactive substances from tissues.

MACDONALD, Dr. I.—expenses: hepatic changes in rabbits maintained on deficient diets.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

Chemistry Department

OWEN, Dr. L. N.—assistance by Dr. R. Houghton, and expenses: development of a drug to promote the excretion of strontium (in collaboration with Professsor J. M. Danielli, King's College, University of London, and Professor G. Wilkinson, Imperial College of Science and Technology).

Physics Department

HOPKINS, Dr. H. H.—assistance by Mr. B. Cymerman, and expenses: design of an optical system for a cystoscopic camera (in association with Mr. J. G. Gow of Liverpool).

Chester Beatty Research Institute

ANDERSON, Dr. W.—expenses (from the Tobacco Manufacturers' Benefaction): atmospheric radio-activity in relation to lung cancer.

PASSEY, Professor R. D.—(1) expenses: carcinogenic properties of cigarette tars; (2) assistance by Mrs. P. A. Lewis: possible effects on respiratory epithelium of modification of diet resulting from cigarette-smoking, and its relation to the development of lung cancer. (Both from the Tobacco Manufacturers' Benefaction.)

INSTITUTE OF CHILD HEALTH

LUCAS, Dr. B. G. B. and WATERSTON, Dr. D. J.—expenses: design of pump oxygenator for use in endocardiac surgery in children.

TANNER, Dr. J. M.—expenses: steroid excretion and physique in adults and children.

TIZARD, Dr. J. P. M.—assistance by Dr. Ruth Harris, and expenses: electrical activity in the cerebral cortex of infants.

INSTITUTE OF DERMATOLOGY

PORTER, Dr. A. D.—expenses: effect of light on (i) normal skins, (ii) abnormal skins, and its relation to biochemical changes.

INSTITUTE OF DISEASES OF THE CHEST

REID, Dr. Lynne M.—expenses (from the Tobacco Manufacturers' Benefaction): certain aspects of mucus secretion in the bronchial tree.

INSTITUTE OF NEUROLOGY

ETTLINGER, Dr. E. G.—expenses: inter-relationship of the cerebral hemispheres, and their control of complex behaviour in the monkey.

MARSHALL, Dr. J.—expenses: long-term effects of passive ventilation on the output of electrolytes by the body.

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY

BROWNE, Professor J. C. McClure—expenses: changes in total exchangeable sodium and total body water in normal pregnancy and pre-eclampsia.

INSTITUTE OF OPHTHALMOLOGY

ASHTON, Professor N. H.—(1) expenses: pathology of retrolental fibroplasia: (2) assistance by Mr. C. N. Graymore and expenses: retinal metabolism.

INSTITUTE OF ORTHOPAEDICS

SISSONS, Dr. H. A.—(1) expenses: fate of experimental bone grafts in relation to the type of bone used; (2) assistance by Miss B. L. Stewart and expenses: (i) the structure and chemistry of normal bone; (ii) the behaviour of bone grafts in dogs; (3) assistance by Miss J. Jowsey; mechanism of osteoporosis.

INSTITUTE OF PSYCHIATRY

Biochemistry Department

MCILWAIN, Professor H. and RODNIGHT, Mr. R. B.—assistance by Dr. H. H. Hillman and Dr. C. G. Thomson, and expenses: identification of substances exchanged between the brain and the bloodstream.

Genetics Unit

SLATER, Dr. E. T. O.—assistance by Miss M. Malherbe: investigation of a series of systematically ascertained psychiatric twins.

Neuroendocrinology Department

HARRIS, Professor G. W.—assistance by Dr. J. F. Christ: effect of localized unilateral hypothalamic lesions and hypothalamic electrical stimulation on neurosecretory material.

Neuropathology Department

BYROM, Dr. F. B.—expenses: causes and effects of renal hypertension.

Psychology Department

EYSENCK, Professor H. J.—assistance by Mr. J. D. Sylvester and Mr. H. C. Holland, and expenses: personality, conditioning and perception.

SHAPIRO, Dr. M. B.—assistance by Mrs. B. Fox and expenses: measurement and investigation of fluctuations in the clinically relevant aspects of depressive illness.

Surgery Department

FALCONER, Mr. M. A.—assistance by Dr. I. P. James, and expenses: temporal lobe epilepsy and its relief by surgery.

INSTITUTE OF UROLOGY

FERGUSSON, Dr. J. D.—assistance by Mr. P. L. Grover and expenses: variations in the urinary enzymes glucuronidase and sulphatase in conditions of renal failure and in cases of bladder tumour.

KING'S COLLEGE

Anatomy Department

NICOL, Professor T.—assistance by Miss C. G. Druce: effect of chemical substances on the activity of the reticulo-endothelial system with regard to its function as a defence mechanism.

Biophysics Research Unit

BAKER, Dr. J. R.—personal: electron microscope studies on protozoa.

Chemistry Department

REES, Dr. C. W.—assistance by Mr. T. R. Emerson: N-oxides as chemotherapeutic agents.

Physiology Department

WIDDAS, Dr. W. F.—assistance by Dr. J. Stubbs: hexose transfer in muscle.

Zoology Department

DANIELLI, Professor J. F.—(1) assistance by Mr. R. J. Cole: streptomycin resistance in amoebae; (2) assistance by Mr. M. S. Bingley, and expenses: separate effects of background irradiation on the cell nucleus and cytoplasm and the effect of such irradiation on life span.

BARNARD, Dr. E. A.—assistance by Mr. J. Marbrook and expenses: isotopic labelling of specific reagents and antibodies as a quantitative cytochemical method.

KING'S COLLEGE HOSPITAL MEDICAL SCHOOL

Bacteriology Department

JACKSON, Dr. F. L.—assistance by Miss V. D. Lawton and expenses: action of a streptomycin antagonist.

Chemical Pathology Department

GRAY, Professor C. H.—assistance by Mrs. A. Kulczycka and expenses: synthesis of stercobilin.

HOLNESS, Dr. N. J.—personal and expenses: metabolism of cortisol.

SMITH, Dr. M. J. H.—assistance by Mr. A. K. Huggins, and expenses: effects of salicylate on the incorporation of C^{14} from C^{14} labelled substrates into the metabolic intermediates of preparations of animal tissues.

LEWISHAM GENERAL HOSPITAL

STAFFURTH, Dr. J. S.—personal and expenses: plasma volume and total body water in various conditions.

LISTER INSTITUTE OF PREVENTIVE MEDICINE

ASHESHOV, Dr. I. N.—personal: viral antibiotics and the development of *rutilantin*.

KEKWICK, Dr. R. A.—assistance by Mr. P. L. Walton: isolation and purification of proteins involved in the clotting mechanism in human plasma.

LONDON HOSPITAL MEDICAL COLLEGE

ROE, Dr. F. J. C.—expenses (from the Tobacco Manufacturers' Benefaction): production and testing of tobacco tar and its fractions, with special reference to the detection of incomplete carcinogens.

Dental Pathology Department

MILES, Professor A. E. W.—expenses: innervation of dentine and electron microscopy of dental tissues.

Pharmacology Department

WEATHERALL, Professor M.—assistance by Miss M. Waddell: effect of cardiac glycosides on the cationic exchanges of erythrocytes and of isolated uteri.

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE

Bacteriology and Immunology Department

SPOONER, Professor E. T. C.—assistance by Dr. I. G. Murray, and expenses: mycetoma.

Occupational Health Unit

SHILLING, Dr. R. S. F. —(1) assistance by Miss A. Davenport (working under the direction of Professor W. D. M. Paton in the Department of Pharmacology, Royal College of Surgeons of England) and expenses: the causal agents of byssinosis; (2) expenses: development of the Conicycle.

Applied Physiology Department

THOMSON, Dr. M. L.—expenses: development of tests for the survey of human lung function in the home and in industry.

MIDDLESEX HOSPITAL MEDICAL SCHOOL

Barnato Joel Laboratories

ROBERTS, Professor J. E.—assistance by Mr. G. Hems: (i) mechanism of action of radiation on solutions of adenine nucleotides; (ii) dependence of radiation action on reaction velocity in enzyme-coupled nucleotide system *in vitro*; (iii) velocity dependence *in vivo*.

Courtauld Institute of Biochemistry

DODDS, Sir Charles—assistance by Mrs. E. B. Smith, and expenses (from Dulverton Trust funds): physical characteristics of plasma lipoproteins and their relation to ischaemic heart disease.

ROITT, Dr. I. M.—assistance by Dr. Elizabeth Wilson : biochemical aspects of thyroid auto-immunity.

Ferens Institute of Oto-Laryngology

MONKHOUSE, Mr. J. P., NEGUS, Sir Victor, SEYMOUR, Dr. J. C. and TAPPIN, Mr. J. W.—expenses (from Alexander Pigott Wernher Memorial Trust funds): problems of oto-laryngology.

Institute of Clinical Research

GILLIATT, Dr. R. W.—expenses: electro-physiological studies of peripheral nerve function in patients with isolated peripheral nerve lesions and polyneuritis.

NABARRO, Dr. J. D. N.—assistance by Dr. Clara Youngday: insulin assay, using the epididymis fat pad method, and its application to endocrinological problems.

Department of Medicine

FURNASS, Dr. S. B.—personal: metabolism in relation to body weight.

NATIONAL HOSPITAL FOR NERVOUS DISEASES

Neurological Research Unit

ELITHORN, Dr. A.—expenses: (i) central inhibition of the psychological refractory period; (ii) maze test research; (iii) clinical studies on leucotomy.

Psychology Department

ZANGWILL, Professor O. L.—assistance by Mrs. E. Warrington: perceptual phenomena associated with visual field defects.

NATIONAL INSTITUTE FOR MEDICAL RESEARCH

Department of Human Physiology

BLACK, Dr. S.—personal: effect of hypnosis on blood flow.

Physiology and Pharmacology Department

KOVACS, Dr. B. A.—personal: anti-histamine substance in leucocytes.

NEW END HOSPITAL

Endocrine Research Unit

SCHRIRE, Dr. I.—personal: creatine metabolism in myasthenia gravis.

POSTGRADUATE MEDICAL SCHOOL OF LONDON AND HAMMERSMITH HOSPITAL

Morbid Anatomy Department

DONIACH, Dr. I.—assistance by Dr. E. D. Williams: neo-natal thyroid growth, and repair of autografts, in rats.

Bacteriology Department

BARBER, Dr. Mary—assistance by Miss M. Beard: an experimental antibiotic policy.

Haematology Department

DACIE, Professor J. V. —(1) assistance by Dr. Barbara Macgibbon: human anti-haemophilic globulin; (2) assistance by Miss M. Low and expenses: carbohydrate metabolism of erythrocytes in hereditary haemolytic anaemias.

ELMES, Dr. P. C.—expenses (from the Tobacco Manufacturers' Benefaction): (i) the effect of infections and irritants on animals with an abnormal bronchial mucosa produced by exposure to chlorine (in association with Dr. Lynne Reid, Institute of Diseases of the Chest, London): (ii) the biochemical analysis of respiratory mucus.

MOLLIN, Dr. D. L.—assistance by Miss B. Anderson and expenses: metabolism of vitamin B^{12} using a method of microbiological assay with *Euglena gracilis.*

Department of Medicine

COPE, Dr. C. L.—assistance by Dr. G. Nicolis: aldosterone metabolism.

DIXON, Dr. A. St. J.—assistance by Dr. I. H. Porter: relationship of gastro-intestinal bleeding to orally administered drugs.

FLETCHER, Dr. C. M.—assistance by Dr. C. M. Tinker and expenses: natural history of chronic bronchitis. (Half the grant provided from the Tobacco Manufacturers' Benefaction.)

LAIDLAW, Dr. J. P.—personal, assistance by Mr. S. A. Cang and expenses: significance of electroencephalographic abnormalities in general medical conditions.

READ, Dr. A. E.—personal: (i) anti-tissue antibodies in patients with juvenile cirrhosis; (ii) effects of morphia in patients with cirrhosis.

SHERLOCK, Dr. Sheila—assistance by Miss J. McLaren: pathogenesis of hepatic coma with respect to altered nitrogen metabolism.

SHILLINGFORD, Dr. J. P.—assistance by Dr. I. T. Gabe and expenses: estimation of valvular incompetence.

Chemical Pathology Department

MACINTYRE, Dr. I.—assistance by Miss N. W. Alcock: experimental magnesium deficiency in the rat.

Pathology Department

PEARSE, Dr. A. G. E.—assistance by Miss S. Brown and expenses: histochemical changes in enzyme content of neoplastic and non-neoplastic cells.

Radio-Diagnostic Department

STEINER, Dr. R. E.—expenses: treatment of malignant disease by pituitary ablation.

Department of Surgery

AIRD, Professor I.—expenses: exchangeable albumins in surgical patients.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

Pharmacology Department

PATON, Professor W. D. M.—expenses: decompression sickness.

ROYAL EYE HOSPITAL

SORSBY, Professor A.—expenses (from Alexander Pigott Wernher Memorial Trust funds): variations in the components of refraction during growth.

ROYAL FREE HOSPITAL SCHOOL OF MEDICINE

Pharmacology Department

HODGES, Dr. J. R.—expenses: control of secretion of anterior pituitary hormones.

ZAIMIS, Professor Eleanor J.—(1) expenses: mechanism of neuromuscular transmission: (2) assistance by Miss J. Maclagan : influence of lowered body temperature on the effects of some drugs.

Physiology Department

KILLICK, Professor Esther M.—assistance by Miss J. M. Marchant and expenses: carbon monoxide poisoning in dogs (on behalf of the Committee for Research on Breathing Apparatus for Protection against Dangerous Fumes and Gases).

DOWNMAN, Dr. C. B. B.—assistance by Miss M. A. Alderson and expenses: functional topography of the brain stem reticular formation in small mammals.

ROYAL HOLLOWAY COLLEGE

Zoology Department

BUTLER, Dr. P. M.—asistance by Miss P. M. Aldridge, and expenses: ontogenetic basis of molar occlusion.

GAUNT, Mr. W. A.—expenses: relationship between the blood vessels supplying the pulp of mammalian teeth, and the disposition of their roots.

ROYAL MARSDEN HOSPITAL

Clinical Pathology Department

KAY, Dr. H. E. M.—assistance by Dr. G. Barraclough and expenses: collection and preservation of foetal tissues.

ROYAL VETERINARY COLLEGE

Physiology Department

AMOROSO, Professor E. C.—assistance by Miss S. Heyner and expenses: low temperature effects on avian and mammalian cartilage.

DEMPSTER Mr. W. J.—expenses: (ii) transplantation of the ureter; (ii) the production of portal and pulmonary hypertension.

ST. BARTHOLOMEW'S HOSPITAL MEDICAL COLLEGE

Pathology Department

BLACKLOCK, Professor J. W. S.—expenses (from the Tobacco Manufacturers' Benefaction): carcinogenic activity of compounds fractionated from cigarette smoke and air conditioning filters.

LEHMANN, Dr. H.—expenses: abnormal haemoglobin.

SHOOTER, Dr. R. A.—assistance by Mr. J. A. Girling and expenses: cross-infection in hospital wards.

Physics and Physiology Departments

ROTBLAT, Professor J. and LINDOP, Dr. P. J.—assistance by Miss J. Hazzledine and expenses: long-term effects of radiation, with particular reference to dependence on age at the time of irradiation.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL

Bacteriology Department

ELEK, Professor S. D.—assistance by Dr. T. Rees: comparative immunology.

Chemical Pathology Department

MARTIN, Professor N. H.—assistance by Mr. L. I. Irons, and expenses: interaction of metallic ions with human proteins and peptides.

ST. MARY'S HOSPITAL MEDICAL SCHOOL

Medical Unit

ACKROYD, Dr. J. F.—(1) expenses: hypersensitivity; (2) assistance by Dr. N. Pride (from Dulverton Trust funds); control of coumarin therapy.

Pathology and Bacteriology Department

PORTER, Dr. K. A.—expenses: immunological study of X-irradiated animals with marrow transplants.

Chemical Pathology Department

NEUBERGER, Professor A.—assistance by Miss W. Thompson: biosynthesis of porphyrins.

Pharmacology Department

ANDREWS, Dr. W. H.—assistance by Dr. I del Rio Lozano: excretion of substances into bile, and the production of hepatic lymph.

Physics Department

ROWLANDS, Dr. S.—expenses: regulation of the circulation in anaesthetized animals.

Physiology Department

HUGGETT, Professor A. St. G.—expenses: foetal and placental physiology.

CROSS, Dr. K. W.—assistance by Dr. June Hill and expenses: neonatal metabolism with particular reference to cooling and low oxygen consumption.

HOLTON, Dr. Pamela M.—expenses: chemical transmitters at nerve endings.

Wright-Fleming Institute of Microbiology

HAMILTON, Dr. Elizabeth D.—personal: the role of fungus spores as allergic excitants.

ROWLEY Dr. D.—assistance by Mr. Waquar Ali and expenses: factors affecting the natural immunity of animals to infection by gram-negative organisms.

ST. THOMAS'S HOSPITAL MEDICAL SCHOOL

Bacteriology Department

MEYNELL, Dr. G. G.—expenses: aetiology of fatal infections in partially immune hosts.

Chemical Pathology Department

PRUNTY, Professor F. T. G.—expenses: experimental endocrinology.

Radiotherapy Department

CHURCHILL-DAVIDSON, Dr. I.—assistance by Dr. M. G. Paine, Dr. N. T. S. Evans and Dr. C. A. Foster: use of high-pressure oxygen in the radiotherapy of malignant tumours.

SIR JOHN CASS COLLEGE

Chemistry and Biology Department

LINDSEY, Dr. A. J.—expenses (from the Tobacco Manufacturers' Benefaction): chemical and physical nature of smoke.

UNIVERSITY COLLEGE

Biochemistry Department

ASHBY, Dr. J. H.—personal: construction of a micro reaction calorimeter for the determination of the heats of reaction of antibodies with antigens.

DATTA, Dr. S. P.—assistance by Mr. G. Margetts and expenses: metabolism of orotic acid in man and its effect on the urinary nitrogen distribution.

Botany Department

LEWIS, Professor D.—expenses: gene structure and function through the colour mutants of spore pigments in *Aspergillus nidulans.*

Chemistry Department

NYHOLM, Professor R. S.—assistance by Dr. L. F. Larkworthy: (i) preparation of oxygenated iron-indigo and cobalt complexes; (ii) study of their structure by chemical and physical techniques.

Phonetics Department

EISLER, Dr. Frieda—personal: the nature of thinking as revealed through the speech process.

Physiology Department

BROWN, Professor Sir Lindor—(1) assistance by Mrs. L. M. Brown: distribution of acetylcholine in sympathetic ganglia; (2) assistance by Mr. C. B. Ferry: effect of neuronal rest on the output of sympathetic transmitter from the spleen of the cat.

DAWSON, Dr. G. D.—expenses: the nature of epilepsy.

DIAMOND, Dr. J.—expenses; characteristics of regenerating nerve terminals.

HILL, Professor A. V.—assistance by Mr. J. V. Howarth: heat production of nerve.

HARKNESS, Dr. R. D.—assistance by Mrs. M. L. R. Harkness and Miss B. M. Cullen: the physiology of connective tissues.

PASCOE, Mr. J. E.—assistance by Dr. K. Diete-Spiff: central control of motor neurones.

Psychology Department

DREW, Professor G. C.—assistance by Mrs. B. S. Boydell, and expenses: inductive and deductive thinking.

The Student Health Association

MALLESON, Dr. N.—expenses: medical and social factors in relation to academic performance.

Zoology Department

MAYNARD-SMITH, Mr. J.—assistance by Mrs. J. Trent: physiology of ageing in *drosophila*.

UNIVERSITY COLLEGE HOSPITAL

Medical Unit

TROTTER, Dr. W. R.—expenses: effect of triiodothyroacetic acid on the basal metabolic rate and blood cholesterol.

UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL

Bacteriology Department

SMITH, Professor Wilson—expenses: the influenza group of viruses.

Biochemistry Department

DENT, Professor C. E.—(1) expenses: amino-acid metabolism in normal subjects and in patients with inborn errors of metabolism; (2) assistance by Dr. G. A. Rose: calcium fractions of plasma in hyper- and hypo-parathyroidism and other metabolic disorders.

Clinical Research Department

SHALOM, Dr. E. S.—personal: normal and abnormal iodine metabolism.

Dermatology Department

SPEARMAN, Mr. R. I. C.—personal and expenses: factors affecting epidermal activity in the tail skin of ichthyotic and normal mice.

Medical Unit

ROSS, Dr. E. J.—assistance by Dr. Elizabeth K. McLean: isolation of aldosterone stimulating hormone from urine.

Morbid Anatomy Department

CAMERON, Sir Roy.—expenses: recovery from chronic disease, with particular reference to liver fibrosis following chronic biliary obstruction and α-naphthyl-iso-thiocyanate administration.

Pathology Department

SPECTOR, Dr. W. G.—expenses: mechanics of increased capillary permeability.

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MELLANBY, Lady—expenses: structure of teeth.

MILES, Professor A. A. (Lister Institute of Preventive Medicine), KING, Mr. Ambrose J. (London Hospital) and MCELLIGOTT, Dr. G. L. M. (St. Mary's Hospital)—assistance and expenses (from funds provided by the United States Public Health Service): aetiology and treatment of non-specific urethritis, on behalf of the Working Party on Non-Specific Urethritis.

LUSH, Dr. B. S.—expenses: investigation into convulsive disorders, for the Committee for Research in General Practice.

Loughton

WYKEHAM-BALME, Dr. H.—expenses: protein bound iodine and thyroid function.

Manchester

THE ROYAL INFIRMARY

WILKINSON, Dr. J. F.—expenses: purification and assay of animal anti-haemophilic globulin.

UNIVERSITY

Anatomy Department

TORR, Dr. J. B. D.—expenses: nuclear sex.

Bacteriology Department

MAITLAND, Professor H. B.—assistance by Dr. D. J. Lea: *H. pertussis* antigen.

Chemistry Department

BU'LOCK, Dr. J. D.—expenses: metabolism of simple unsaturated fatty acids.

Department of Education of the Deaf

EWING, Sir Alexander—assistance by Mr. D. Saunders, Miss J. C. Hunt and Miss B. R. Chadwick, and expenses (all from Alexander Pigott Wernher Memorial Trust funds): educational treatment of deafness in children.

Chemical Engineering Department

MORTON, Professor F.—assistance by Mr. M. J. Ray and Mr. P. I. F. Niem, and expenses: separation of hydrocarbons in petroleum.

Pathology Department

GOWENLOCK, Dr. A. H.—assistance by Miss A. M. Hartley: adrenal secretion rates of aldosterone in man under physiological and pathological conditions.

KENCH, Dr. J. E.—(1) assistance by Mrs. A. R. Wells: metabolism of the porphyrins, with particular reference to the effects of heavy metal poisoning; (2) assistance by Mr. J. C. Smith: nature and source of the urinary protein observed in cadmium poisoning.

Physiology Department

MILLS, Dr. J. N.—expenses: effect of adrenal cortical hormones upon phosphate distribution and renal function.

Nepal

JACKSON, Dr. F. S.—expenses: (i) effect on the electrocardiogram of prolonged exertion at high altitude; (ii) nature and incidence of heart disease among communities living at high altitudes.

Newcastle-upon-Tyne

UNIVERSITY OF DURHAM (KING'S COLLEGE)

Chemistry Department

BADDILEY, Professor J.—assistance by Mr. U. Raj Bhandary, and expenses: nucleotides and related compounds in micro-organisms.

Nuffield Department of Industrial Health

BROWNE, Professor R. C.—assistance by Mr. R. Graham, and expenses (from the Tobacco Manufacturers' Benefaction): vandium pentoxide in exhaust gases and in the atmosphere.

Physiology Department

JENKINS, Mr. G. N.—expenses: mechanism of the anti-caries action of fluoride.

TAYLOR, Dr. W.—assistance by Mr. B. A. Cooke and expenses: *in vitro* and *in vivo* metabolism of progesterone.

ROYAL VICTORIA INFIRMARY AND KING'S COLLEGE MEDICAL SCHOOL

Department of Psychological Medicine

ROTH, Professor M.—assistance by Miss S. O. Allison and expenses: (i) electrical activity in the cerebral cortex of patients with depressive states: (ii) incidence of mental disorders in old age according to social class.

VALLANCE-OWEN, Dr. J.—assistance by Miss M. D. Lilley: the nature of the inhibition to insulin action in *Diabetes mellitus*.

Mickley-on-Tyne

CLEMO, Professor G. R.—expenses (from the Tobacco Manufacturers' Benefaction): chemical constituents of cigarette smoke.

Northampton

PUBLIC HEALTH LABORATORY

HOYLE, Dr. L.—(1) expenses: influenza; (2) assistance by Mrs. Sheila Davies: chemical structure of influenza virus.

THE CHURCHILL HOSPITAL

Radiotherapy Department

LAJTHA, Dr. L. G.—assistance by Mrs. E. Hell, and expenses: mechanism of growth and differentiation of cells.

THE RADCLIFFE INFIRMARY

Clinical Biochemistry Department

TAYLOR, Dr. W. H.—expenses: gastric proteolytic enzymes obtained from normal subjects and from patients with gastric disease.

Clinical Medicine Department

WITTS, Professor L. J.—expenses: pernicious anaemia and other diseases of the blood.

TRUELOVE, Dr. S. C. —(1) expenses: trials of cortisone in the treatment of ulcerative colitis; (2) expenses: the aetiology and treatment of ulcerative colitis.

Neurology Department

SPALDING, Dr. J. M. K.—personal: artificial respiration in paralysed patients.

Pathology Department

MACFARLANE, Dr. R. G.—expenses: purification and assay of animal anti-haemophilic globulin.

UNIVERSITY

Biochemistry Department

WILLIAMSON, Mr. J. R.—personal: measurement of oxygen uptake of perfused rat hearts.

WILSON, Dr. Dagmar C.—expenses: study of goitre in an endemic area of East Sussex.

Chemical Crystallography Laboratory

HODGKIN, Mrs. Dorothy—assistance by Mrs. C. Kennedy: insulin and related structures.

YOUNG, Dr. G. T.—assistance by Dr. Margaret Clubb: synthesis of arginine-vasopressin.

Inorganic Chemistry Laboratory

IRVING, Dr. H.—assistance by Dr. Otto Weber: chelating agents of possible use for the removal of radioactive substances from the body.

Genetics Laboratory

MCWHIRTER, Dr. K. G.—personal and expenses: (i) human polymorphism and its bearing on specific disease; (ii) control of mammalian sex ratio; (iii) inherited polyhedral virus; (iv) rapid evolution and high selection pressures in *Maniola jurtina.*

Human Anatomy Department

POWELL, Mr. T. P. S. and COWAN, Dr. W. M.—expenses: connections of the nuclei of the thalamus and corpus striatum.

Department of Medicine

BUSH, Dr. I. E.—(1) assistance by Miss M. Gale and expenses: steroids ; (2) assistance by Mr. D. J. Short and expenses: humoral physiology and pathology with a possible relation to mental disease.

Nuffield Institute for Medical Research

BORN, Dr. G. V. R.—assistance by Mr. M. P. Esnouf (from Dulverton Trust funds): chemical changes associated with blood clotting.

Nuffield Laboratory of Ophthalmology

PIRIE, Dr. Antoinette—expenses: effect of irradiation on the metabolism of the lens.

Sir William Dunn School of Pathology

FLOREY, Professor Sir Howard—expenses (from Dulverton Trust funds): disposal of dietary fat.

DAY, Dr. A. J.—personal: metabolism of lipids by the reticulo-endothelial system, and its importance in atherosclerosis.

GOWANS, Dr. J. L.—personal: fate and function of the mammalian lymphocyte.

VAN HEYINGEN, Dr. W. E.—expenses: bacterial toxins of the aerobic sporing bacilli.

Pharmacology Department

BURN, Professor J. H.—expenses: the testing of new anaesthetics, on behalf of the Committee on Non-explosive Anaesthetic Agents.

Physiology Department

GLEES, Dr. P.—assistance by Mr. J. W. Cole and Dr. M. Fillenz, and expenses: effects of hypothermia and tranquillizers in monkeys and cats.

MARRIOTT, Dr. F. H. C.—personal: nervous summation and inhibition and quantum effects in the visual system of man and of animals.

MORRIS, Dr. Valerie—personal: measurement of visual thresholds.

Institute of Experimental Psychology

OLDFIELD, Professor R. C.—assistance by Dr. M. Treisman, and expenses: retinal interaction effects of short exposures to light.

DEUTSCH, Mr. J. A.—(1) assistance by Mr. J. K. Clarkson: the mechanism of vocal control; (2) expenses: the role of hypothalamic and other central mechanisms in satiation and reward.

KAY, Dr. H.—(1) assistance by Mr. J. Annett: conditions influencing the rate of learning of paced and unpaced motor tasks; (2) assistance by Mr. M. E. Sime, and expenses: discrimination reversal learning.

Social Medicine Department

STEWART, Dr. Alice—expenses: the Oxford Child Health Survey.

THE WARNEFORD HOSPITAL

PARNELL, Dr. R. W.—assistance by Mr. H. C. A. Somerset: relationship between physique and behaviour: and physique in families.

Penzance

WILLIS, Professor R. A.—(1) personal and expenses: embryological aspects of pathology and related problems; (2) personal and assistance by Mr. Hou Lee-Tsun, and expenses (from the Tobacco Manufacturers' Benefaction): carcinogenic properties of cigarette products.

Portsmouth

CENTRAL LABORATORY

O'BRIEN, Dr. J. R.—expenses (from Dulverton Trust funds): blood coagulation in relation to lipaemia.

Reading

UNIVERSITY

Psychology Department

VERNON, Professor M. D.—assistance by Mrs. C. Hutt: relation of perception to motivation.

Redcar

HODGKIN, Dr. G. K. H.—expenses: records of age, diagnoses and morbidity in a general practice.

St. Andrews

UNIVERSITY

Biochemistry Department

GOODLAD, Dr. G. A. J.—assistance by Mrs. C. M. Goodlad, and expenses: mechanism of action of hormones and tumours on protein metabolism in the animal body.

Sheffield

THE CHILDREN'S HOSPITAL

Pathology Department

EMERY, Dr. J. L.—assistance by Dr. A. Mithal and expenses: normal structure of organs during the later stages of intra-uterine life and in infancy.

Bacteriology Department

BEATTIE, Professor C. P.—expenses: aetiology and treatment of toxoplasmosis.

Biochemistry Department

GIBSON, Professor Q. H.—assistance by Mr. D. Gilbert: DPNH oxidase activity of flavoproteins.

DALZIEL, Dr. K.—expenses: biological kinetics.

HARRISON, Mrs. P. M.—personal: structure and function of ferritin.

Department of Medicine

STUART-HARRIS, Professor C. H.—assistance by Dr. D. Hobson, and expenses: virus diseases and respiratory infections.

SINGER, Dr. Bertha—assistance by Dr. J. R. Cox and Mr. P. J. Leonard, and expenses: (i) aldosterone secretion in the rat; (ii) the urinary excretion of aldosterone in pulmonary heart disease.

Pharmacology and Therapeutics Department

GREEN, Dr. M.—personal: hazards of I^{131} therapy of thyrotoxicosis.

Physiology Department

SMYTH, Professor D. H.—expenses: the active transport of nutrient substances in physiological preparations.

Slough

SLOUGH INDUSTRIAL HEALTH SERVICE

Occupational Hygiene Laboratories

HICKISH, Mr. D. E.—expenses: occupational hearing loss in industry.

Southampton

UNIVERSITY

Chemistry Department

COOKSON, Professor R. C.—assistance by Mr. R. G. Lingard, and expenses: conversion of triterpenes into analogues of steroidal hormones.

Zoology Department

MUNDAY, Dr. K. A.—assistance by Miss M. R. Edwards, and expenses: paramagnetic resonance of metallo-protein compounds.

Southend

WILLIAMS, Dr. R. E. O.—expenses: staphylococcal epidemiology.

Stanmore

INSTITUTE OF ORTHOPAEDICS

MCPHERSON, Dr. A.—expenses: influence of sensory factors on the recovery of motor function and on the pathogenesis of disease of the nervous system.

Biomechanics and Surgical Materials Department

SCALES, Dr. J. T.—(1) expenses: the use of plastic and other materials in orthopaedics; (2) expenses: the development of porous dressings.

Biochemistry Department

WALKER, Dr. P. G.—assistance by Mr. C. G. Grieg and expenses: studies of β-glucosaminidase, and the amino-sugar sulphates.

Stoke-on-Trent

CITY GENERAL HOSPITAL

Respiratory Physiology Department

KENNEDY, Dr. M. C. S.—expenses: the natural history of the asthma-bronchitis-emphysema syndrome.

Sunderland

GENERAL HOSPITAL, RESEARCH UNIT

Geriatric Medicine Department

WILLIAMS, Dr. E. Woodford—expenses: red cell longevity in the aged.

Taplow

CANADIAN RED CROSS MEMORIAL HOSPITAL

Rheumatism Research Unit

BYWATERS, Professor E. G. L.—assistance by Dr. G. L. Asherson: auto-antibody mechanism.

COLOVER, Dr. J.—personal: experimental allergic encephalitis.

Wickford

RUNWELL HOSPITAL

CORSELLIS, Dr. J. A. N.—expenses: clinico-pathological analysis of post-mortem findings at Runwell Hospital, with particular reference to the incidence of pathological changes related to the process of ageing.

Psychology Department

FOULDS, Dr. G. A.—assistance by Miss P. Robinson and Miss B. Bishop and expenses: schizophrenic and paranoid states.

Publications by Grantholders and Others

ABERDEEN

University

MURRAY, J. G. The consequences of injury and disease of nervous tissue: recent advances in knowledge. (A Sir David Wilkie Lecture). *J. R. Coll. Surg. Edinb.*, 1959, **4**, 199.

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The Queen's University

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Birmingham Accident Hospital and Rehabilitation Centre

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University

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University

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CARDIFF

Central Tuberculosis Laboratory

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University College of South Wales

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DUNDEE

Queen's College, University of St. Andrews

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Research Fellowships and Scholarships

FELLOWSHIPS

ROCKEFELLER TRAVELLING FELLOWSHIPS IN MEDICINE

The Rockefeller Foundation have continued to make generous provision for the award of medical travelling fellowships by the Council. These fellowships are intended for medical or scientific graduates resident in this country who have had some training in research work in clinical medicine, surgery, or medical science, and who would benefit by a year's work at a centre in the United States of America or elsewhere abroad, before taking up higher teaching or research appointments in the United Kingdom.

The following appointments were made by the Council for the academic year 1958–59:

Dr. G. Burnstock (University of Oxford)—to study electro-physiology of smooth muscle using Amphiuma, at the University of Illinois, Chicago, under the supervision of Professor C. L. Prosser.

Dr. P. J. Holloway (National Institute for Medical Research)—to study nutrition and resistance to dental caries, at the Harvard School of Dental Medicine, Boston (Professor J. H. Shaw).

Mr. W. B. Jennett (University of Manchester)—to study physiological consequences of brain stem distortion in compression, at the University of California Medical Center, Los Angeles (Dr. H. W. Magoun).

Dr. A. P. Mathias (University College, London)—to study growth factors and inhibitors for *in vitro* culture of mouse leukaemia lymphoblasts, at the Yale University School of Medicine (Professor A. D. Welch).

Dr. R. P. Michael (Maudsley Hospital, London)—to study neurophysiological and biochemical correlates of patterns of behaviour, at the National Institute of Mental Health, Bethesda, Maryland (Dr. S. Kety).

Dr. P. H. A. Sneath (National Institute for Medical Research)—to study bacterial genetics, at the School of Medicine, University of Wisconsin (Professor J. Lederberg).

LEDERLE TRAVELLING FELLOWSHIP IN MEDICINE

The Lederle Laboratories Division of the American Cyanamid Company again placed a Travelling Fellowship at the Council's disposal. The following appointment was made for the academic year 1958–59:

Dr. R. J. Linden (University of Leeds)—to study cardiovascular physiology and blood flow, at the National Heart Institute, Bethesda (Dr. S. J. Sarnoff).

LILLY FOREIGN FELLOWSHIPS

After nomination by the Council the following appointments were made by Eli Lilly and Company, Indianapolis, U.S.A., to Lilly Foreign Fellowships for the academic year 1958–59:

Mr. J. D. Griffiths (St. Bartholomew's Hospital, London)—to study methods of preventing dissemination of carcinoma, at the University of Illinois, Chicago (Dr. W. H. Cole).

Dr. C. W. M. Wilson (University of Liverpool)—to study sedative and analeptic drugs and changes in pharmacologically active amines in the central nervous system, at the National Heart Institute, Bethesda (Dr. B. B. Brodie).

UNITED STATES PUBLIC HEALTH SERVICE FELLOWSHIPS

In 1958 the National Institutes of Health of the United States Public Health Service, inaugurated a programme of research fellowships for European scientists and invited the Council to nominate candidates from the United Kingdom. The Fellowships are open to medical or scientific graduates, and preference is given to candidates who have completed a doctoral degree in one of the medical sciences and have shown outstanding research ability. After nomination by the Council, the following candidates were elected by the United States Public Health Service to fellowships for 1958–59:

Dr. B. S. Hartley (University of Cambridge)—to study amino-acid sequence in the large β chain of oxidized α-chymotrypsin, at the University of Washington, Seattle (Professor H. Neurath).

Dr. K. W. Cross (St. Mary's Hospital Medical School, London)—to study respiratory physiology research methods, at the University of California Medical Center, San Francisco (Dr. J. H. Comroe, Jr.).

Dr. A. Doig (Royal Infirmary, Edinburgh)—to study intestinal function in uraemia, and absorption and excretion of cholesterol in the nephrotic syndrome, at the University of Illinois, Chicago (Dr. R. M. Kark).

DOROTHY TEMPLE CROSS RESEARCH TRAVELLING FELLOWSHIPS IN TUBERCULOSIS

These fellowships, provided from an endowment by the late Mrs. Odo Cross, are awarded to suitably qualified British graduates who intend ultimately to devote themselves ' to the advancement by teaching or research of the curative or preventive treatment of tuberculosis in any of its forms'. No award was made for the academic year 1958–59.

ALEXANDER PIGOTT WERNHER MEMORIAL TRUST

TRAVELLING FELLOWSHIPS IN OPHTHALMOLOGY AND OTOLOGY

These awards are provided from a special fund placed at the disposal of the Council by the trustees of the late Lady Ludlow under the terms of a bequest in memory of her son, to be used ' towards the prevention and cure of blindness and deafness in the United Kingdom and the British Empire, and in particular research in connexion 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. 112, 115, 116, 243, 244, 248) 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 appointment was made for the academic year 1958–59:

Dr. G. B. Arden (Institute of Ophthalmology, London)—to study neurophysiology at the Nobel Institute, Stockholm (Professor Granit).

KATHLEEN SCHLESINGER RESEARCH FELLOWSHIP

This fellowship is provided from an endowment by the late Mr. and Mrs. Eugen M. Schlesinger in memory of their daughter and is intended for research in the field of neuro-pathology. On the advice of the Fellowship Advisory Committee, preference has been given in recent years to candidates proposing to investigate mechanisms underlying degenerative processes affecting the brain.

In May, 1957, Dr. J. R. Lagnado (Allan Memorial Institute of Psychiatry, Montreal) was appointed to the fellowship for work on the regulation of carbohydrate metabolism in nervous tissue, under the supervision of Dr. D. Richter at the Neuropsychiatric Research Unit, Whitchurch Hospital, Cardiff; and has continued to work at this centre.

MAPOTHER BEQUEST RESEARCH FELLOWSHIP

This fellowship is provided from a benefaction by the late Dr. and Mrs. Edward Mapother for research in psychiatry. Miss N. M. Goodman was appointed to the Fellowship in March, 1956, for work on the relationship between proneness to mental disorders and age of mother at birth, and she has continued to work at the Institute of Psychiatry, Maudsley Hospital, London.

PEEL MEDICAL RESEARCH TRUST

A donation placed at the Council's disposal by the Dowager Countess Eleanor Peel Memorial Trust may be used for research on high blood pressure; and also for the travelling expenses of senior British research workers who wish to study any medical subject at a centre abroad.

In the year 1958–1959 the following travel grants were made from this Trust:

Dr. J. T. Scales (Royal National Orthopaedic Hospital, Stanmore, Middlesex)—for the expenses of a visit to the United States in connexion with work on the fate of metal implants and the use of porous plastic dressings.

Dr. E. V. Cox (General Hospital, Birmingham)—to take up a Research Fellowship in the Department of Gastroenterology at the Johns Hopkins Hospital, Baltimore.

CLINICAL RESEARCH FELLOWSHIPS

These fellowships are offered to suitably qualified medical graduates who wish to prepare for careers in clinical research. It is intended that each Fellow appointed should have the opportunity, as part of his training, of studying methods of research in the basic subjects most relevant to his particular clinical interest, and that this training should preferably be given in departments other than his own.

The following appointments were made for the academic year 1958–59:

Third year Fellows

Dr. E. H. Cooper (St. Mary's Hospital, London)—to the Department of Biochemistry, Oxford University (Dr. L. A. Stocken).

Dr. E. Marley (Maudsley Hospital, London)—to the Department of Pharmacology, Royal College of Surgeons, London (Professor W. D. M. Paton).

Dr. G. F. M. Russell (Edinburgh University)—to the Institute of Psychiatry, Maudsley Hospital, London (Professor Sir Aubrey Lewis).

Second year Fellows

Dr. J. H. Adams (Glasgow University)—to the Department of Neuropathology, Maudsley Hospital, London (Professor P. M. Daniel).

Dr. R. N. P. Sutton (Duchess of York Hospital for Babies, Manchester)—to the Department of Medicine, University of Sheffield (Professor C. H. Stuart-Harris).

First year Fellows

Dr. G. Harris (Stobhill General Hospital, Glasgow)—to the Nuffield Department of Clinical Medicine, University of Oxford (Professor L. J. Witts).

Dr. C. R. Rizza (Queen's College, Dundee)—to the Radcliffe Infirmary, Oxford (Dr. R. G. Macfarlane).

Miss Barbara F. Smith (King's College Hospital, London)—to the Department of Neuropathology, Institute of Psychiatry, The Maudsley Hospital, London (Professor P. M. Daniel).

Mr. L. Symon (Department of Surgery, University of Aberdeen)—to the National Institute for Medical Research, London (Dr. W. Feldberg).

Mr. F. C. Walker (The Royal Infirmary, Glasgow)—to the Department of Experimental Pathology, University of Birmingham (Professor J. R. Squire).

Publications by Holders of Fellowships

ABERCROMBIE, M., EVANS, D. H. L. and MURRAY, J. G. Nuclear multiplication and cell migration in degenerating unmyelinated nerves. *J. Anat., Lond.*, 1959, **93**, 9.

ASHMORE, J. and MAHLER, R. F. CO_2 fixation in hepatic gluconeogenesis. *Fed. Proc.*, 1959, **18**, 183.

BARGER, A. C., LIEBOWITZ, M. R. and MULDOWNEY, F. P. The role of the kidney in the homeostatic adjustments of congestive heart failure. *J. chron. Dis.*, 1959, **9**, 571.

BARTHOLOMEW, A. A., BOURNE, G. L. and MARLEY, E. Distribution of methylpentynol and methylpentynol carbamate in human body fluids. *Clin. Sci.*, 1958, **17**, 629.

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COWIE, V. A. and SLATER, E. T. O. Psychiatric genetics. *Recent Progr. Psychiat.*, 1959, **3**, 1.

DOUGHERTY, E. C., HANSEN, E. L., NICHOLAS, W. L., MOLLETT, J. A. and YARWOOD, E. A. Axenic cultivation of *Caenorhabditis briggsae* (nematoda: rhabditidae) with unsupplemented and supplemented chemically defined media. *Ann. N.Y. Acad. Sci.*, 1959, **77**, 176.

FOLCH, J., WEBSTER, G. R. and LEES, M. The preparation of proteolipides. *Fed. Proc.*, 1959, **18**, 228.

KNOX, E. G. Genotypic frequencies among close relatives of propositi with conditions determined by X-recessive genes. *Brit. J. prev. soc. Med.*, 1958, **12**, 183.

On the nature of the determinants of congenital pyloric stenosis. *ibid.*, 1958, **12**, 188.

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KNOX, E. G. and MACKINTOSH, J. Post-neonatal infant mortality in Birmingham between 1947 and 1956. *Brit. J. prev. soc. Med.*, 1958, **12**, 131.

LEAF, A., ANDERSON, J. and PAGE, L. B. Active sodium transport by the isolated toad bladder. *J. gen. Physiol.*, 1958, **41**, 657.

MCNEILL, R. S., RANKIN, J. and FORSTER, R. E. The diffusing capacity of the pulmonary membrane and the pulmonary capillary blood volume in cardiopulmonary disease. *Clin. Sci.*, 1958, **17**, 465.

MARLEY, E. Pharmacology of methylpentynol and methylpentynol carbamate. *Brit. J. Pharmacol.*, 1959, **14**, 284.

MARLEY, E. and PATON, W. D. M. The effect of methylpentynol and methylpentynol carbamate on the perfused superior cervical ganglion of the cat. *Brit. J. Pharmacol.*, 1959, **14**, 303.

MELTZER, J. I., WHEELER, H. O. and CRANSTON, W. I. Metabolism of sulfobromophthalein sodium (BSP) in dog and man. *Proc. Soc. exp. Biol., N.Y.*, 1959, **100**, 174.

NICHOLAS, W. L. The cultural and nutritional requirements of free-living nematodes of the genus Rhabditis and related genera. *Tech. Bull. Minist. Agric., Lond.*, 1959, No. 7, p. 161.

NICHOLAS, W. L., DOUGHERTY, E. C. and HANSEN, E. L. Axenic cultivation of *Caenorhabditis briggsae* (nematoda: rhabditidae) with chemically undefined supplements; comparative studies with related nematodes. *Ann. N.Y. Acad. Sci.*, 1959, **77**, 218.

SHOEMAKER, W. C., MAHLER, R. F. and ASHMORE, J. The effect of insulin on hepatic glucose metabolism in the unanesthetized dog. *Metabolism*, 1959, **8**, 494.

SPEAKMAN, J. S. Aqueous outflow channels in the trabecular meshwork in man. *Brit. J. Ophthal.*, 1959 **43**, 129.

Endothelial cell vacuolation in the cornea. *ibid.*, 1959, **43**, 139.

WHEELER, H. O., CRANSTON, W. I. and MELTZER, J. I. Hepatic uptake and biliary excretion of indocyanine green in the dog. *Proc. Soc. exp. Biol., N.Y.* 1958, **99**, 11.

SCHOLARSHIPS

FRENCH EXCHANGE SCHOLARSHIPS IN MEDICAL SCIENCE

These awards are made in collaboration with the Centre National de la Recherche Scientifique, and allow for the exchange of two workers from each country if the award is held for a full academic year.

The following scholars were nominated by the C.N.R.S. for the academic year 1958–59:

Mlle. Marie Cécile Jendrot (Laboratoire de Pharmacie Chimique de la Faculté de Pharmacie de Paris)—to study the synthesis of analogues of lignocaine, in the Department of Pharmacology, University of Manchester (Dr. K. Bullock).

Mme. L. Peyrin (Stagiaire de Recherches au C.N.R.S., Laboratoire de Physiologie de la Faculté de Médecine de Lyon)—to study the techniques of estimating catecholamines at Runwell Hospital, Wickford, Essex (Dr. J. Dawson and Mr. A. D. Bone).

The following British scholars were nominated by the Council for awards to be held in France during the academic year 1958-59:

Miss Suzanne Reiman (Department of Psychology, Institute of Psychiatry, Maudsley Hospital, London)—to study language and thought development in children at the Hôpital Ste. Anne, Paris (Professor Pichot), and the Hôpital Lariboisière, Paris (Dr. Le Beau).

Miss Jill Cremer (Toxicology Research Unit)—to study biochemical action of narcotic drugs on brain cell metabolism, at the Institut de Biologie Physico-Chimique, Paris (Dr. A. J. Rosenberg).

SCHOLARSHIPS FOR TRAINING IN RESEARCH METHODS

These scholarships are awarded to recent medical, dental, or scientific graduates of special promise who wish to be trained in research techniques in order to make their career in medical research.

Forty-five new appointments were made for the academic year 1958–59 and the total number of scholars under instruction during that academic year was 104. The numbers of scholars according to subject studied were: internal medicine (4), radiation (2), genetics (10) biophysics (2), biochemistry (23), nutrition (3), tropical medicine (1), microbiology (10), psychology (9), psychiatry, including neuropharmacology and neuroendocrinology (6), chemistry, including physical chemistry (5), pathology, including immunology and haematology (4), pharmacology (7), physiology (15), biology, including zoology and embryology (3).

Scholarships were held at the following centres:

Aberdeen University	2
Belfast: Queen's University	1
Birmingham University	1
Bristol University	1
Cambridge University	26
Cardiff: University College of South Wales and Monmouthshire	3
Whitchurch Hospital	1
Dundee: Queen's College	2
Glasgow University	3
Leeds University	1
London University: King's College	3
Queen Elizabeth College	1
Guy's Hospital Medical School	1
Royal Free Hospital School of Medicine	1
St. Mary's Hospital Medical School	1
School of Pharmacy	1
University College	18
British Postgraduate Medical Federation: Institute of Psychiatry	4
Manchester University	3
Oxford University	24
Sheffield University	5
Swansea: University College	1

Publications by Holders of Scholarships

BAKER, R. V. Observations on the localization of 5-hydroxytryptamine. *J. Physiol.*, 1958, **142**, 563.

The intracellular localization of 5-hydroxytryptamine (5-HT) in relation to mitochondrial enzymes. *ibid.*, 1958, **143**, 80P.

Mitochondria and storage granules for 5-hydroxytryptamine. *ibid.*, 1959, **145**, 473.

BAYLEY, C. R. and JONES, A. S. Nucleotide sequence: the oxidation of DNA with potassium permanganate. *Trans. Faraday Soc.*, 1959, **55**, 492.

BISCHITZ, P. G. and SNELL, R. S. A study of the melanocytes and melanin in the skin of the male guinea-pig. *J. Anat., Lond.*, 1959, **93**, 233.

BRENT, L., BROWN, J. B. and MEDAWAR, P. B. Skin transplantation immunity in relation to hypersensitivity. *Lancet*, 1958, ii, 561.

CRAWFORD, L. V. Nucleic acid metabolism in *Escherichia coli* infected with phage T5. *Virology*, 1959, **7**, 359.

EDWARDS, A. W. F. and FRACCARO, M. The sex distribution in the offspring of 5,477 Swedish ministers of religion, 1585–1920. *Hereditas*, 1958, **44**, 447.

GILES, C. H., HASSAN, A. S. A., LAIDLAW, M. and SUBRAMANIAN, R. V. R. Adsorption at organic surfaces. III. Some observations on the constitution of chitin and on its adsorption of inorganic and organic acids from aqueous solution. *J. Soc. Dy. Col.*, 1958, **74**, 647.

GILL, E. W. and ING, H. R. Furan and tetrahydrofuran compounds analogous to ganglion-blocking agents of the 3-oxapentane-1:5-bistrialkylammonium series. *J. chem. Soc.*, 1958, p. 4728.

GURDON, J. B., ELSDALE, T. R. and FISCHBERG, M. Sexually mature individuals of *Xenopus laevis* from the transplantation of single somatic nuclei. *Nature, Lond.*, 1958, **182**, 64.

HAWKINS, D. F. and ROSA, L. Some observations on the release of a substance active on the rat's uterus from guinea-pig lung during anaphylactic shock. *Int. Arch. Allergy, N.Y.*, 1959, **14**, 312.

HEMINGWAY, J. T. Corticosteroids and the radiation effect in regenerating liver of the rat. *Experientia*, 1959, **15**, 189.

KEILIN, D. and NICHOLLS, P. Reactions of catalase with hydrogen peroxide and hydrogen donors. *Biochim. biophys. Acta*, 1958, **29**, 302.

KERRIDGE, D. The effect of actidione and other antifungal agents on nucleic acid and protein synthesis in *Saccharomyces carlsbergensis*. *J. gen. Microbiol.*, 1958, **19**, 497.

MORAY, N. Attention in dichotic listening: affective cues and the influence of instructions. *Quart. J. exp. Psychol.*, 1959, **11**, 56.

RICHMOND, M. H. Formation of a lytic enzyme by a strain of *Bacillus subtilis*. *Biochim. biophys. Acta*, 1959, **33**, 78.

Properties of a lytic enzyme produced by a strain of *Bacillus subtilis*. *ibid.*, 1959, **33**, 92.

ROBSON, J. G. An instantaneous frequency meter for nerve impulse recording. *J. Physiol.*, 1958, **143**, 34P.

SWALLOW, D. L. and ABRAHAM, E. P. Formation of ε-(aminosuccinyl)-lysine from ε-aspartyl-lysine from bacitracin A, and from the cell walls of lactobacilli. *Biochem. J.*, 1958, **70**, 364.

The amide and carboxyl groups of bacitracin A. *ibid.*, 1959, **72**, 326.

SWALLOW, D. L., LOCKHART, I. M. and ABRAHAM, E. P. Synthesis of ε-aspartyl-lysines and of *iso*hexylamides of aspartic acid. *Biochem. J.*, 1958, **70**, 359.

WORK, C. E. The action of a lytic enzyme from Bacillus spores on other species of bacteria. *IV int. Congr. Biochem.*, Vienna, 1958. *Int. Abstr. biol. Sci.*, 1958, **10**, Suppl., p. 129.

List of Members of the Council's Principal Committees

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Medulloblastoma
Leukaemia
Bone Sarcoma
Neuroblastoma

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Animal Anti-haemophilic Globulin

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J. G. Scadding, M.D., F.R.C.P.
Professor Clifford Wilson, D.M., F.R.C.P.
Mary Barber, M.D. (*Secretary*)

Working Party:
Trials of Chemotherapy in Early Chronic Bronchitis

Chemotherapy

Sir Charles Harington, Sc.D., F.R.S. (*Chairman*)
E. P. Abraham, D.Phil.
Mary Barber, M.D.
Ann Bishop, Sc.D., F.R.S.
J. D. Fulton, M.B., Ph.D., D.T.M.
E. F. Gale, Sc.D., F.R.S.
P. M. D'Arcy Hart, C.B.E., M.D., F.R.C.P.
F. Hawking, D.M., M.R.C.P., D.T.M.
A. Isaacs, M.D.
D. R. Laurence, M.D., M.R.C.P.
Professor G. Pontecorvo, Ph.D., F.R.S.
M. R. J. Salton, Ph.D.
J. Walker, D.Sc.
Professor D. D. Woods, Ph.D., F.R.S.
M. R. Pollock, M.B. (*Secretary*)

Working Party on Resistance of Gonococci to Penicillin

R. W. Fairbrother, M.D., F.R.C.P. (*Chairman*)
Professor R. Cruickshank, M.D., F.R.C.P., D.P.H.
F. R. Curtis, M.Sc., M.B.
E. H. Gillespie, M.B.
Miss R. I. Hutchinson, M.D., D.P.H., D.T.M.
A. J. King, M.B., F.R.C.S.
L. A. Little, M.B., Dip. Bact.
Elisabeth Rees, M.D.
Professor D. T. Robinson, M.Sc., M.R.C.S., Dip. Bact.
B. R. Sandiford, M.D.
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Tuberculosis Chemotherapy Trials

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Professor J. W. Crofton, M.D., F.R.C.P.
Professor R. Cruickshank, M.D., F.R.C.P., D.P.H.
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Tuberculosis Vaccines Clinical Trials

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Clinical Trials of Corticotropin A
Clinical Trials of Growth Hormone
Tritiated Steroids

Anterior Pituitary Hormone Standards

D. G. Evans, D.Sc., F.R.S. (*Chairman*)
S. J. Folley, Ph.D., F.R.S.
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Therapeutic Trials in Chronic Rheumatic Diseases

(Jointly with the Nuffield Foundation)

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J. C. Beavan }

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Professor S. G. Graham, M.D., F.R.C.P.E.
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Professor J. Knowelden, M.D., D.P.H.
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Control of Cross Infection

Professor A. A. Miles, C.B.E., M.D., F.R.C.P. (*Chairman*)
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Lt.-Col. P. D. Stewart, M.B., R.A.M.C.
Brigadier J. D. Welch (*retd.*)
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Virus Diseases in the Tropics

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Jacqueline Walker, Ph.D.
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C. J. La Touche, M.Sc., L.A.H. (*Secretary*)

Aetiology of Chronic Bronchitis

Professor C. H. Stuart-Harris, M.D., F.R.C.P. (*Chairman*)
Professor J. W. Crofton, M.D., F.R.C.P.
W. R. S. Doll, O.B.E., M.D., D.Sc., F.R.C.P.
J. C. Gilson, O.B.E., M.B., F.R.C.P.
Professor J. Gough, M.D.
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R. E. O. Williams, M.D., B.Sc., M.R.C.P.
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Working Party on Acute Respiratory Virus Infection

Professor C. H. Stuart-Harris, M.D., F.R.C.P. (*Chairman*)
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B. E. Andrews, M.R.C.S., Dip. Bact.
A. J. Beale, M.D., Dip. Bact.
R. S. Gardner, M.B., Dip. Bact.
N. R. Grist, M.B., B.Sc., F.R.C.P.
J. C. McDonald, M.D., D.I.H., D.P.H.
H. G. Pereira, Dr.Med.
Marguerite S. Pereira, M.B.
A. T. Roden, M.D., D.P.H.
R. E. Hope Simpson, M.R.C.S.
D. A. J. Tyrrell, M.D., M.R.C.P. (*Secretary*)

Influenza and other Respiratory Virus Vaccines

Professor C. H. Stuart-Harris, M.D., F.R.C.P. (*Chairman*)
C. H. Andrewes, M.D., F.R.C.P., F.R.S.
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W. J. Martin, D.Sc.
A. T. Roden, M.D., D.P.H.
D. A. J. Tyrrell, M.D., M.R.C.P.
J. C. McDonald, M.D., D.I.H., D.P.H. (*Secretary*)

Poliomyelitis : Vaccines

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Sir Wilfred Sheldon, K.C.V.O., M.D., F.R.C.P.
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Poliomyelitis : Safety Tests for Vaccines

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J. O'H. Tobin, B.M., Dip.Bact.
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Working Party on Electro-therapy for Muscle Stimulation

Professor A. E. Ritchie, M.D., B.Sc. (*Chairman*)
P. Bauwens, M.R.C.P.
R. Brennand, A.M.Brit.I.R.E.
D. M. Brooks, M.B., F.R.C.S.I.
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W. G. S. Stephens, B.Sc.
W. S. Tegner, B.M., F.R.C.P.
Squadron Leader C. B. Wynn-Parry, C.B., M.B.E., D.M.

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Preservation of Pathological Mutants in the Mouse

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Mass Miniature Radiography

Research in General Practice

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G. I. Watson, M.D., D.T.M. & H.
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Research on Atmospheric Pollution

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Subcommittee:
Constituents of Atmospheric Pollution and Means of Protection against it

Working Party on Fractures in the Elderly

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J. M. Rogan, M.D., F.R.C.P.E., D.P.H.
R. S. F. Schilling, M.D., M.R.C.P., D.P.H., D.I.H.
J. Watkins-Pitchford, M.D., D.P.H., D.I.H.
P. J. Chapman, M.B. (*Secretary*)

Subcommittee :
Chronic Cadmium Poisoning

Industrial Pulmonary Diseases

Professor W. M. Arnott, T.D., M.D., F.R.C.P., F.R.C.P.E. (*Chairman*)
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W. R. S. Doll, O.B.E., M.D., D.Sc., F.R.C.P.
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P. D'Arcy Hart, C.B.E., M.D., F.R.C.P.
Professor E. J. King, D.Sc.
A. Meiklejohn, M.D., D.P.H.
E. R. A. Merewether, C.B., C.B.E., M.D., F.R.C.P., D.I.H.
G. Nagelschmidt, Ph.D.
J. M. Rogan, M.D., F.R.C.P.E., D.P.H.
J. G. Scadding, M.D., F.R.C.P.
Alice Stewart, M.D., F.R.C.P.
C. L. Sutherland, C.B.E., M.D., D.P.H.
P. J. Chapman, M.B. (*Secretary*)

Subcommittees :
Dust—with Panels on
(1) Sampling Methods
(2) Chemical and Physical Analyses of Dust
(3) Biological Activity of Dust
(4) Field Surveys Concerned with the Relationship between Dust and Pulmonary Disease

Toxicology

Professor E. J. King, D.Sc. (*Chairman*)
J. H. Gaddum, Sc.D., M.R.C.S., F.R.S.
D. Hunter, C.B.E., M.D., F.R.C.P.
A. Thelwall Jones, M.D., M.R.C.P., D.P.H.
E. R. A. Merewether, C.B., C.B.E., M.D., F.R.C.P., D.I.H.
Professor W. D. M. Paton, D.M., F.R.S.
Sir Rudolph Peters, M.C., M.D., F.R.C.P., F.R.S.
G. Samuel, M.Sc.
Professor J. R. Squire, M.D., F.R.C.P.
J. Walker, D.Sc.
Professor R. T. Williams, D.Sc.
Professor Andrew Wilson, M.D., Ph.D., F.R.F.P.S.G.
J. M. Barnes, M.B. (*Secretary*)

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Professor M. A. Rushton, C.B.E., M.D., F.D.S. (*Chairman*)
Professor R. Bradlaw, C.B.E., D.D.Sc., F.R.C.S.
Professor A. I. Darling, M.R.C.S., F.D.S.
Professor A. D. Hitchin, D.D.Sc.
G. N. Jenkins, Ph.D.
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Professor A. B. MacGregor, M.D., F.D.S.R.C.S.
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Professor G. L. Montgomery, C.B.E., T.D., M.D., Ph.D., F.R.F.P.S.G.
Professor H. G. Radden, D.D.Sc., F.D.S.
Professor B. Cohen, D.D.S., M.S.D., H.D.D. (*Secretary*)

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Professor A. Bradford Hill, C.B.E., D.Sc., F.R.S. (*Chairman*)
E. A. Cheeseman, Ph.D.
Professor L. T. Hogben, D.Sc., F.R.S.
J. O. Irwin, Sc.D., D.Sc.
W. P. D. Logan, M.D., Ph.D., D.P.H.
P. L. McKinlay, M.D., D.P.H.
Sir George Maddex, K.B.E., F.I.A.
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P. Stocks, C.M.G., M.D., F.R.C.P., D.P.H.
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Sir John Cowley, K.B.E., C.B., A.M.
Professor G. C. Drew, M.A.
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O. G. Edholm, M.B., B.Sc.
W. B. Littler, C.B., Ph.D., A.I.C.
Lt.-Gen. Sir Harold Pyman, K.C.B., C.B.E., D.S.O.
Professor M. L. Rosenheim, C.B.E., M.D., F.R.C.P.
H. A. Sargeaunt, O.B.E., B.A.
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F. E. E. Smith, M.B.E. (*Assistant Secretary*)

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Captain T. T. Lewin, D.S.C., R.N.
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N. A. B. Wilson, O.B.E., Ph.D.
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C. H. Wyndham, M.B., M.R.C.P.
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Subcommittee :

Nomenclature of Heat Illness (*Jointly with the Advisory Committee on Medical Nomenclature and Statistics of the General Register Office*)

Clinical Psychiatry

Professor Sir George Pickering, M.D., F.R.C.P., F.R.S. (*Chairman*)
E. J. M. Bowlby, M.D.
Professor A. L. Cochrane, M.B.E., M.B., D.P.H.
D. Curran, M.B. F.R.C.P., D.P.M.
Professor G. R. Hargreaves, O.B.E., M.Sc., M.R.C.S.
Professor A. Bradford Hill, C.B.E., D.Sc., F.R.S.
Denis Hill, M.B., F.R.C.P., D.P.M.
Professor Sir Aubrey Lewis, M.D., F.R.C.P.
The Hon. W. S. Maclay, C.B., O.B.E., M.D., F.R.C.P., D.P.M.
A. B. Monro, M.D., Ph.D., D.P.M.
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E. T. O. Slater, M.D., F.R.C.P.
Professor E. J. Wayne, M.D., Ph.D., F.R.C.P.
Professor O. L. Zangwill, M.A.
P. Sainsbury, M.D., D.P.M. (*Secretary*)

Subcommittees:

Clinical Trials (Drugs in Psychiatry)
Psychopathic Personality
National Statistics of Mental Disorder

Epidemiology of Mental Disorders

Professor Sir Aubrey Lewis, M.D., F.R.C.P. (*Chairman*)
G. M. Carstairs, M.B., M.R.C.P.E., D.P.M.
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Professor R. W. Firth, Ph.D.
Professor D. V. Glass, Ph.D.
W. D. P. Logan, M.D., Ph.D., D.P.H.
Professor W. M. Millar, M.D., Dip.Psych.E.
Professor J. N. Morris, M.A., F.R.C.P., D.P.H., D.C.H.
Professor Sir George Pickering, M.D., F.R.C.P., F.R.S.
Professor D. D. Reid, M.D., D.Sc., M.R.C.P.
P. Sainsbury, M.D., D.P.M.
Professor C. H. Stuart-Harris, M.D., F.R.C.P.
J. Tizard, Ph.D.
K. Rawnsley, M.B., M.R.C.P., D.P.M. (*Secretary*)

Human Factor in Railway Accidents

Professor G. C. Drew, M.A. (*Chairman*)
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D. E. Broadbent, M.A.
D. Russell Davis, M.D., M.R.C.P., D.P.M.
O. G. Edholm, M.B., B.Sc.
Professor A. Bradford Hill, C.B.E., D.Sc., F.R.S.
Alistair Heron, Ph.D.
Professor H. Kay, Ph.D.
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H. C. Weston, O.B.E., F.I.E.S.
J. W. Whitfield, M.A.
Professor W. D. Wright, D.Sc., D.I.C.
P. J. Chapman, M.B. } (*Joint Secretaries*)
A. S. Fairbairn, M.B. }

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Professor Sir Lindor Brown, C.B.E., M.B., M.Sc., F.R.C.P., F.R.S.
Professor J. R. Squire, M.D., F.R.C.P.
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(*Jointly with the Colonial Office*)

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Professor P. C. C. Garnham, M.D., D.Sc., D.P.H.
Professor R. M. Gordon, O.B.E., M.D., Sc.D., F.R.C.P., D.P.H., D.T.M.
F. Hawking, D.M., M.R.C.P., D.T.M.
Professor W. E. Kershaw, M.B., D.T.M. & H.
Professor G. Macdonald, C.M.G., M.D., F.R.C.P., D.P.H., D.T.M.
Professor B. G. Maegraith, M.B., D.Phil., F.R.C.P.
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R. Lewthwaite, C.M.G., O.B.E., D.M., F.R.C.P. (*Secretary*)

Subcommittees:
Helminthiasis
Malaria
Personnel
Leprosy
Mollusc-Borne Diseases

Working Party:
Sickle-Cell Trait and Sickle-Cell Anaemia

Biological (Non-Medical) Problems of Nuclear Physics

(*Jointly with the Agricultural Research Council and the Development Commission*)

Sir James Denby Roberts, M.A. (*Chairman*)
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H. R. Barnell, Ph.D.
Professor G. E. Briggs, M.A., F.R.S.
R. F. Glascock, Ph.D.
Professor J. E. Harris, Ph.D., F.R.S.
A. W. Kenny, M.A., B.Sc., F.R.I.C.
J. F. Loutit, C.B.E., D.M., F.R.C.P.
A. S. McLean, M.B., D.I.H.
W. G. Marley, O.B.E., Ph.D.
R. Scott Russell, Ph.D.
Professor H. G. Sanders, Ph.D.
A. W. Stableforth, D.Sc., M.R.C.V.S., D.V.S.M.
E. B. Worthington, Ph.D.
H. B. Fawcett (*Secretary*)

Subcommittees:
Aquatic Hazards
Managing Subcommittee on Monitoring
Radiobiological Research Panel

U.K. National Committee of the British Commonwealth Collections of Micro-organisms

(*Jointly with the Department of Scientific and Industrial Research and the Agricultural Research Council*)

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Professor R. E. Glover, M.A., F.R.C.V.S.
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G. G. Samuel, M.Sc.
H. G. Thornton, D.Sc., F.R.S.
J. M. Shewan, Ph.D., F.R.I.C.
S. T. Cowan, M.D., Dip.Bact. (*Secretary*)

Lighting and Vision

(*Jointly with the Building Research Board of the Department of Scientific and Industrial Research*)

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Professor R. C. Oldfield, M.A.
A. Pott, A.R.I.B.A.
R. A. Weale, D.Sc.
H. C. Weston, O.B.E., F.I.E.S.
Professor W. D. Wright, D.Sc., A.R.C.S., D.I.C.
J. B. Collins, B.Sc., A.M.I.E.E. } (*Joint Secretaries*)
H. W. Bunjé, M.D., M.R.C.P. }

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H. C. Weston, O.B.E., F.I.E.S.
J. W. Whitfield, M.A.
R. L. Moore, M.Sc., A.Inst.P. (*Secretary*)

Panel:

Medical Questions of Driving Licence Forms

Publications

DEPARTMENT OF SCIENTIFIC AND INDUSTRIAL RESEARCH AND MEDICAL RESEARCH COUNCIL. *Final report of the Joint Committee on Human Relations in Industry 1954–57 and report of the Joint Committee on Individual Efficiency in Industry, 1953–57.* London (H.M.S.O.) 1958.

MEDICAL RESEARCH COUNCIL COMMITTEE ON PROTECTION AGAINST IONIZING RADIATIONS. Maximum permissible dietary contamination after the accidental release of radioactive material from a nuclear reactor; a report. *Brit. med. J.*, 1959, i, 967.

MEDICAL RESEARCH COUNCIL NERVE INJURIES SUBCOMMITTEE. Electrodiagnostic stimulators; a report. *Brit. med. J.*, 1958, ii, 714.

MEDICAL RESEARCH COUNCIL WHOOPING-COUGH IMMUNIZATION COMMITTEE. Vaccination against whooping-cough; final report. *Brit. med. J.*, 1959, i, 994.

MEDICAL RESEARCH COUNCIL WORKING PARTY ON ANTICOAGULANT THERAPY IN CORONARY THROMBOSIS. An assessment of long-term anticoagulant administration after cardiac infarction; a report. *Brit. med. J.*, 1959, i, 803.

MEDICAL RESEARCH COUNCIL WORKING PARTY ON PRESSURE-STEAM STERILISERS. Sterilisation by steam under increased pressure; a report. *Lancet*, 1959, i, 425.

Council Publications

Report to Parliament

Report of the Medical Research Council for the year 1957–1958. (1959.) Cmnd. 792.

Current Medical Research—A reprint of the articles in the Report of the Medical Research Council for the year 1957-58.

Benefactions

During the period covered in this Report, the Council have received the following funds from private sources:

	GRANTS	
Rockefeller Foundation, New York	$35,000	For travelling fellowships in medicine
Alexander Pigott Wernher Memorial Trust	£32,000	For research in blindness and deafness
National Fund for Poliomyelitis	£12,500	For research in poliomyelitis and other crippling diseases
A group of British Tobacco Manufacturers	£35,715	For research in lung cancer
The Trust instituted by the late Lord Dulverton	£18,000	For research in coronary thrombosis
Wellcome Trust	£15,000	For research in trachoma
	PAYMENTS ON ACCOUNT OF BEQUESTS	
The late Lady Wadia	£51,575	For research in the University of Cambridge
The late Mrs. Mabel J. Shilp	£900	For research in epilepsy and nervous disorders
The late Frederic Saunders	£300	For research in cancer
The late Mrs. E. M. E. Dale	£33	For the general purposes of research in medicine
	DONATIONS	
The late Miss Daisy E. Norriss	£1,800	For research in cancer
The late Miss R. Rashleigh	£750	For research in osteoarthritis
Amounts under £50		
Dr. R. F. A. Dean, Kampala (further donations); Miss Freda Sumpter, Eastbourne: an Anonymous donation		For the general purposes of research in medicine
Mr. A. J. Campbell for group of people in Catford; Victor Gollancz Ltd. (further donations)		For research in cancer
Dr. D. J. Batterham, Newton Abbot		For research in lung cancer
Chaffcombe Women's Institute; Wellingborough High School for Girls (further donations); Burnley High School for Girls (further donations)		For research in poliomyelitis
Mrs. E. Woodward, Deane, Bolton; Mrs. A. Bright, Ellesmere, friends and relatives		For research in coronary thrombosis
I.C.I. Staff Committee; Mr. J. Cowley, Walthamstow & District Football Charity Competition (further donations); Welwyn Garden City; Mrs. Mary Reece, Cradley		For research in tuberculosis
Mrs. A. J. Dods, Tunbridge Wells (further donations)		For research in rheumatism
Mr. and Mrs. L. Tarrant, Stanmore (further donations)		For research in meningitis

Amounts under £50—contd.

Mrs. and Miss Heath, Weybridge; The Thirty Club, Kingston; The Society of Civil Service Authors; The Guild of St. Lawrence, Effingham.	For research in mongolism (Richard Harrison Memorial Fund)
Mrs. C. Dengiz, a visitor from Istanbul; Mr. Y. Kiriscisghi, a visitor from Turkey; Miss A. Andonian, a visitor from Iraq	For research in radiotherapy
Christ Church School, Wolverhampton ..	For research in leukaemia
Central Newcastle High School for Girls ..	For research into the common cold
Miss C. A. Proctor, London; Mr. E. J. Proctor, London; Mr. J. D. Proctor, Crowthorne (further donation); Miss M. D. Proctor, London (further donation)	For research in psychiatry
Friends of Mr. R. Harper, Kendal	For research in children's diseases
Mr. H. C. Long, Deeping Gate	For research in rheumatic fever
Mr. D. W. Turner, Nottingham	For research in virus diseases

INDEXES

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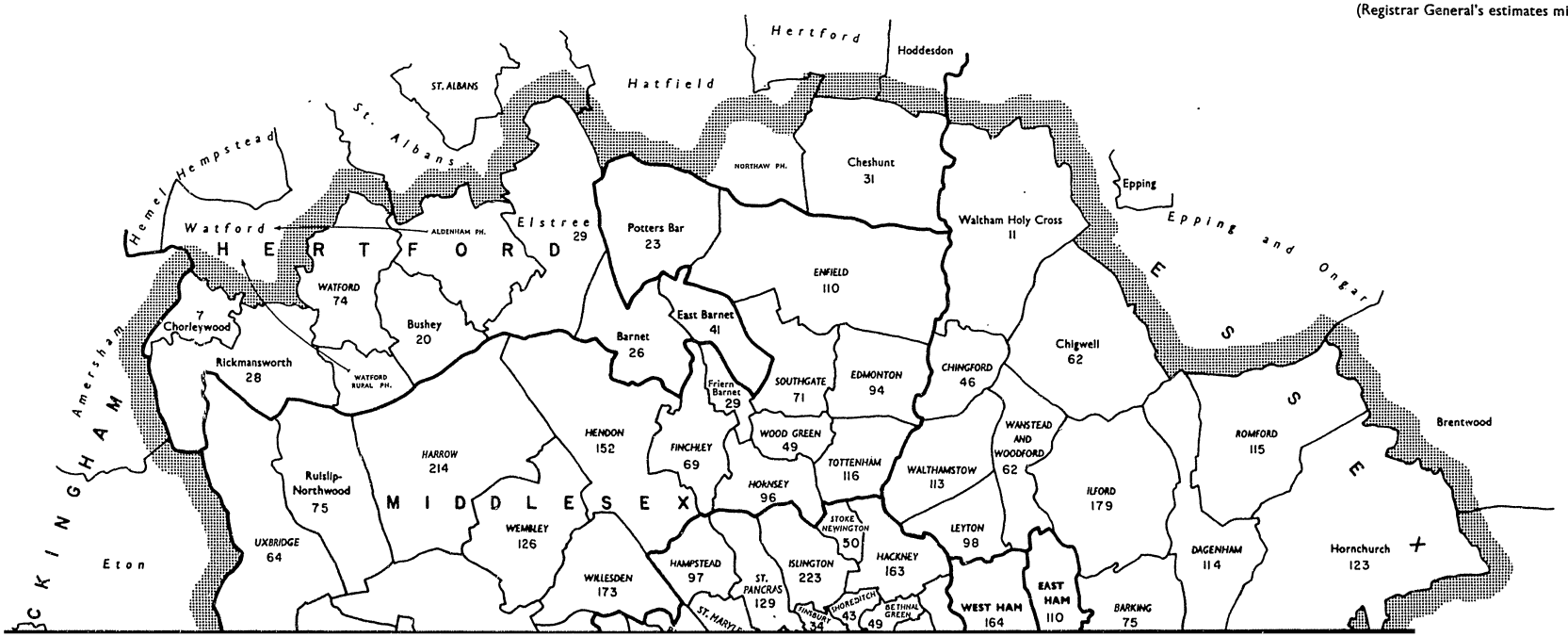
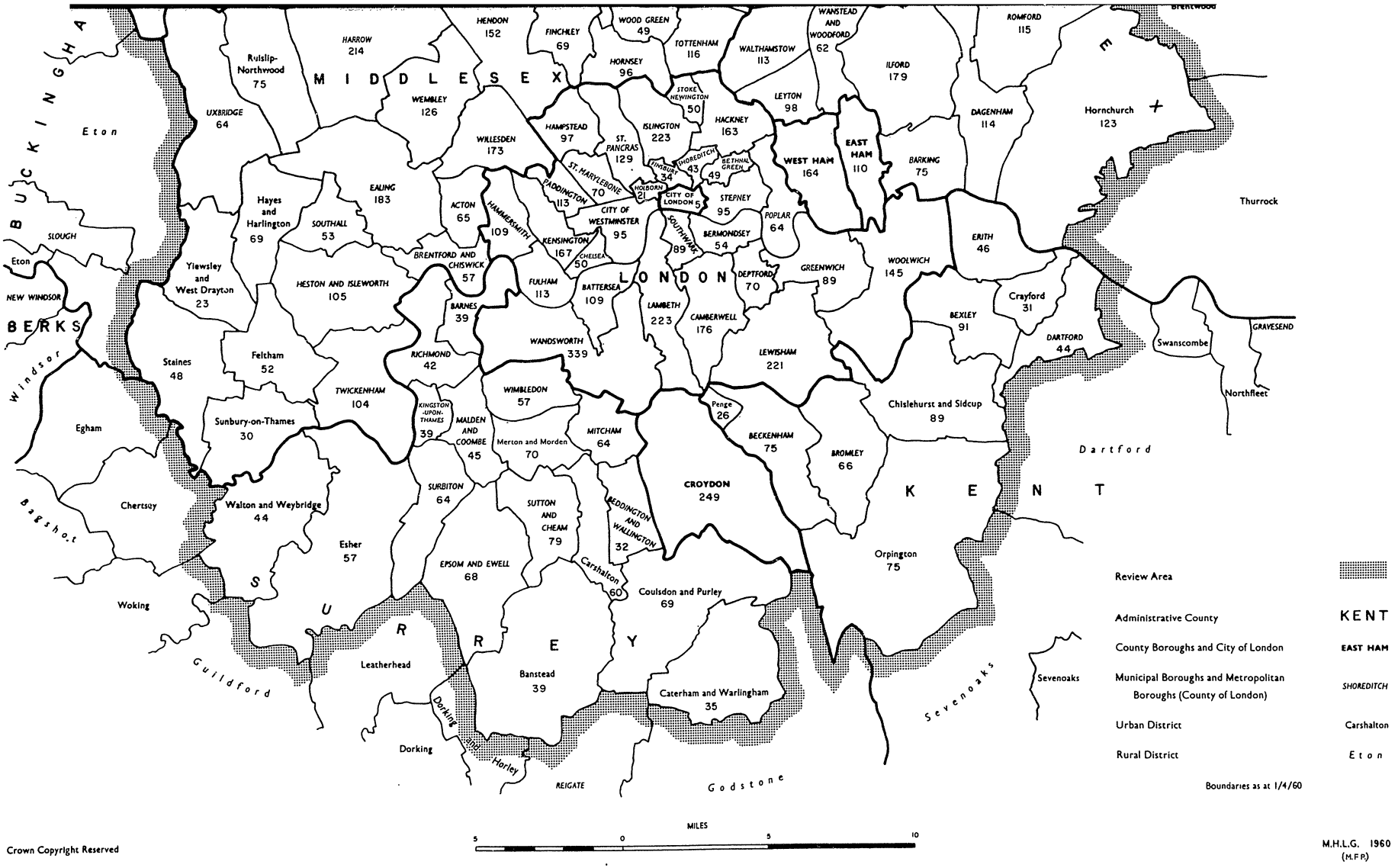
ROYAL COMMISSION ON LOCAL GOVERNMENT IN GREATER LONDON

THE REVIEW AREA

Figures represent population in thousands

(Registrar General's estimates mid-1959)

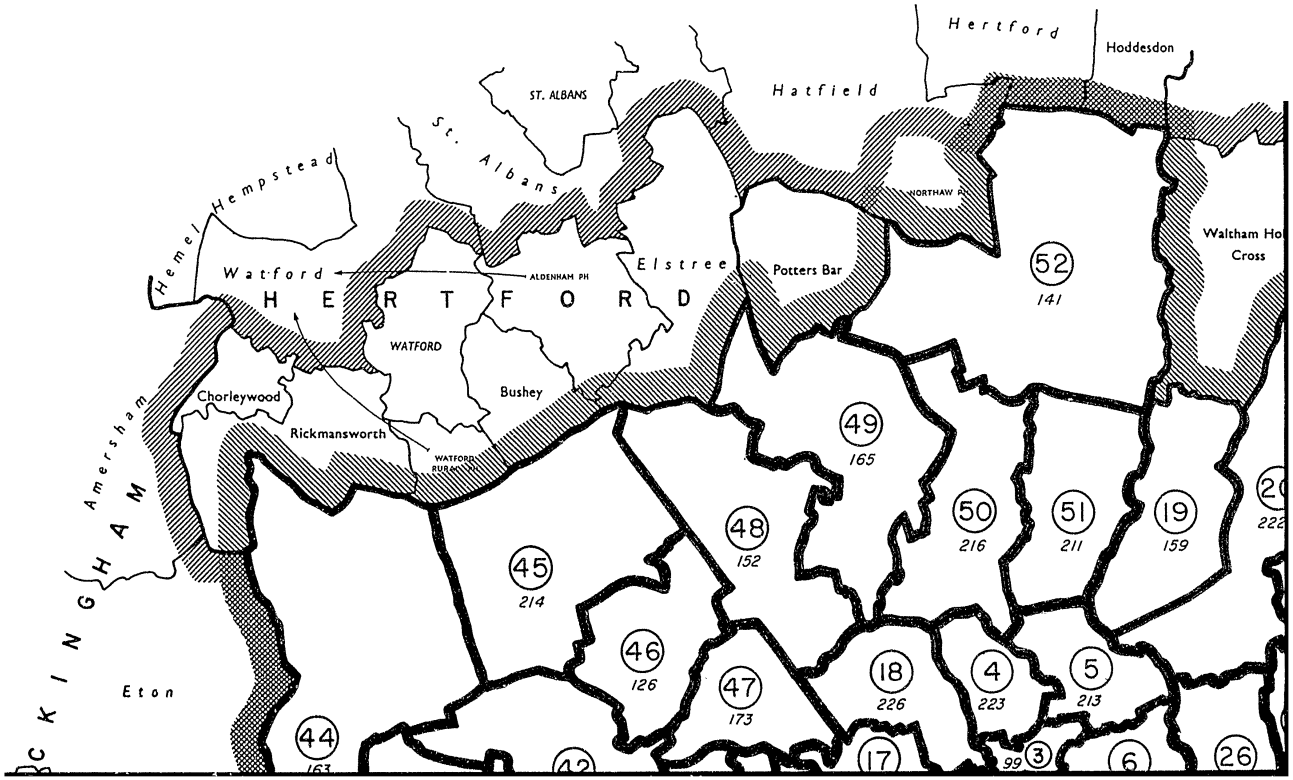




1 CITY OF LONDON
2 CITY OF WESTMINSTER
3 FINSBURY
HOLBORN
SHOREDITCH
4 ISLINGTON
5 HACKNEY
STOKE NEWINGTON
6 BETHNAL GREEN
POPLAR
STEPNEY
7 WOOLWICH
8 DEPTFORD
GREENWICH
9 LEWISHAM
10 CAMBERWELL
11 BERMONDSEY
SOUTHWARK
12 LAMBETH
13 WANDSWORTH (part)
14 BATTERSEA
WANDSWORTH (part)
15 FULHAM
HAMMERSMITH
16 CHELSEA
KENSINGTON
17 PADDINGTON
ST. MARYLEBONE
18 HAMPSTEAD
ST. PANCRAS
19 CHINGFORD
WALTHAMSTOW
20 Chigwell
LEYTON
WANSTEAD AND WOODFORD
21 ILFORD
22 ROMFORD
23 Hornchurch
24 BARKING
DAGENHAM
25 EAST HAM
26 WEST HAM
27 BEXLEY
Crayford
ERITH
28 Chislehurst and Sidcup
Orpington
29 BECKENHAM
BROMLEY
Penge
30 CROYDON
31 Caterham and Warlingham
Coulsdon and Purley
32 Banstead
EPSOM AND EWELL
33 BEDDINGTON AND WALLINGTON
Carshalton
SUTTON AND CHEAM
34 Merton and Morden
MITCHAM
WIMBLEDON
35 BARNES
RICHMOND
36 KINGSTON-UPON-THAMES
MALDEN AND COOMBE
SURBITON
37 Esher
Walton and Weybridge
38 Feltham
Staines
Sunbury-on-Thames
39 TWICKENHAM
40 HESTON AND ISLEWORTH
41 ACTON
BRENTFORD AND CHISWICK
42 EALING
43 Hayes and Harlington
SOUTHALL
44 Ruislip — Northwood
UXBRIDGE
Yiewsley and West Drayton
45 HARROW
46 WEMBLEY
47 WILLESDEN
48 HENDON
49 Barnet
East Barnet
FINCHLEY
Friern Barnet
50 HORNSEY
SOUTHGATE
WOOD GREEN
51 EDMONTON
TOTTENHAM
52 Cheshunt
ENFIELD

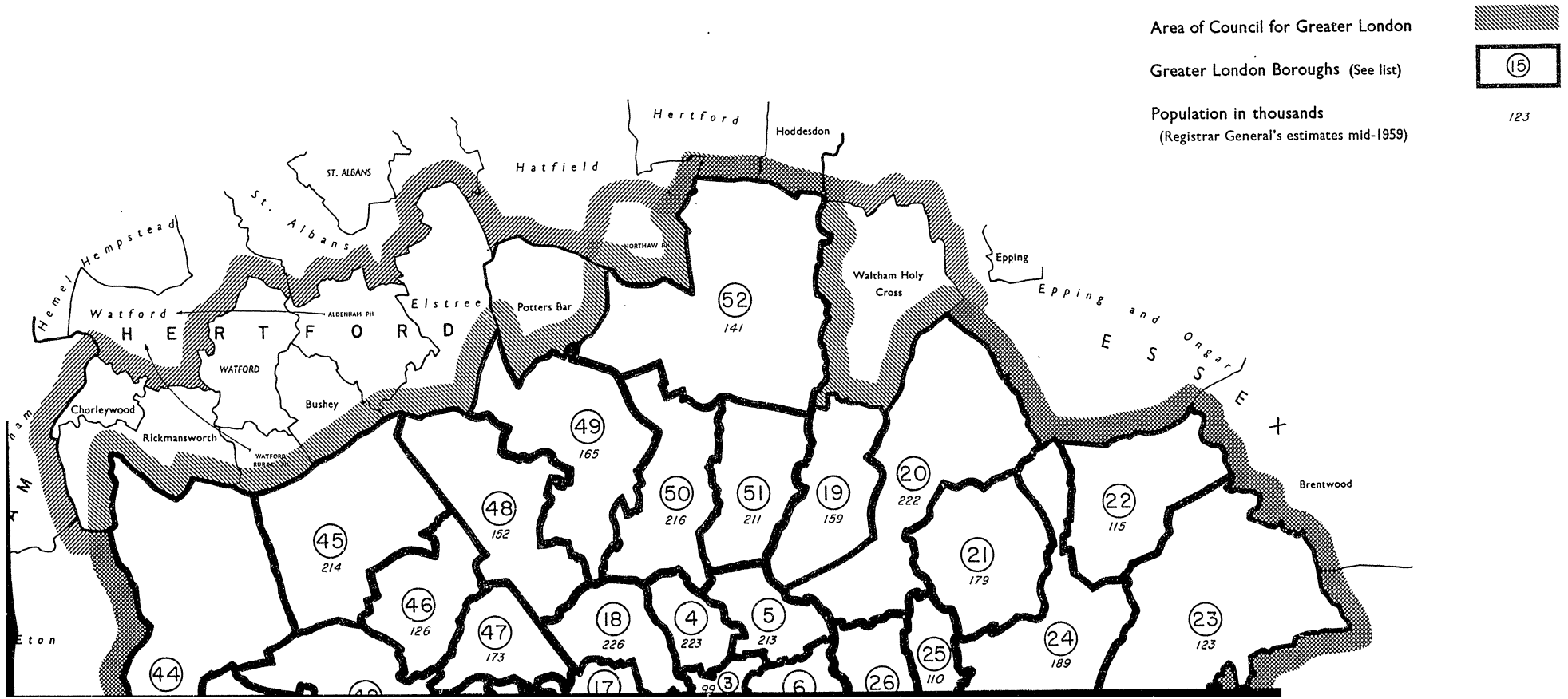
ROYAL COMMISSION ON LOCAL GOVERNMENT IN G

PROPOSALS FOR REORGA



ROYAL COMMISSION ON LOCAL GOVERNMENT IN GREATER LONDON

PROPOSALS FOR REORGANISATION

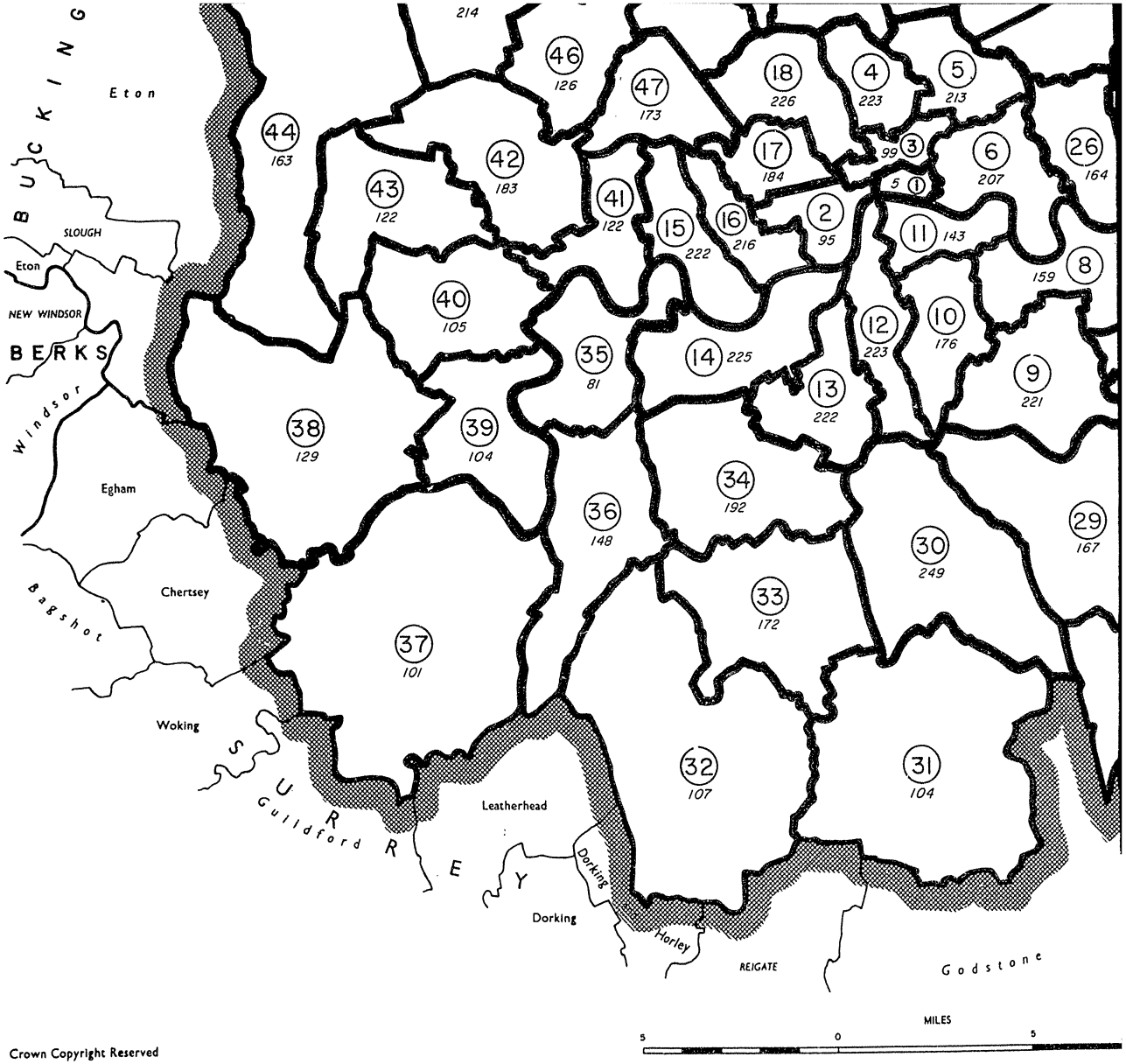


ERITH

28 Chislehurst and Sidcup
Orpington

51 TOTTENHAM

52 Cheshunt
ENFIELD



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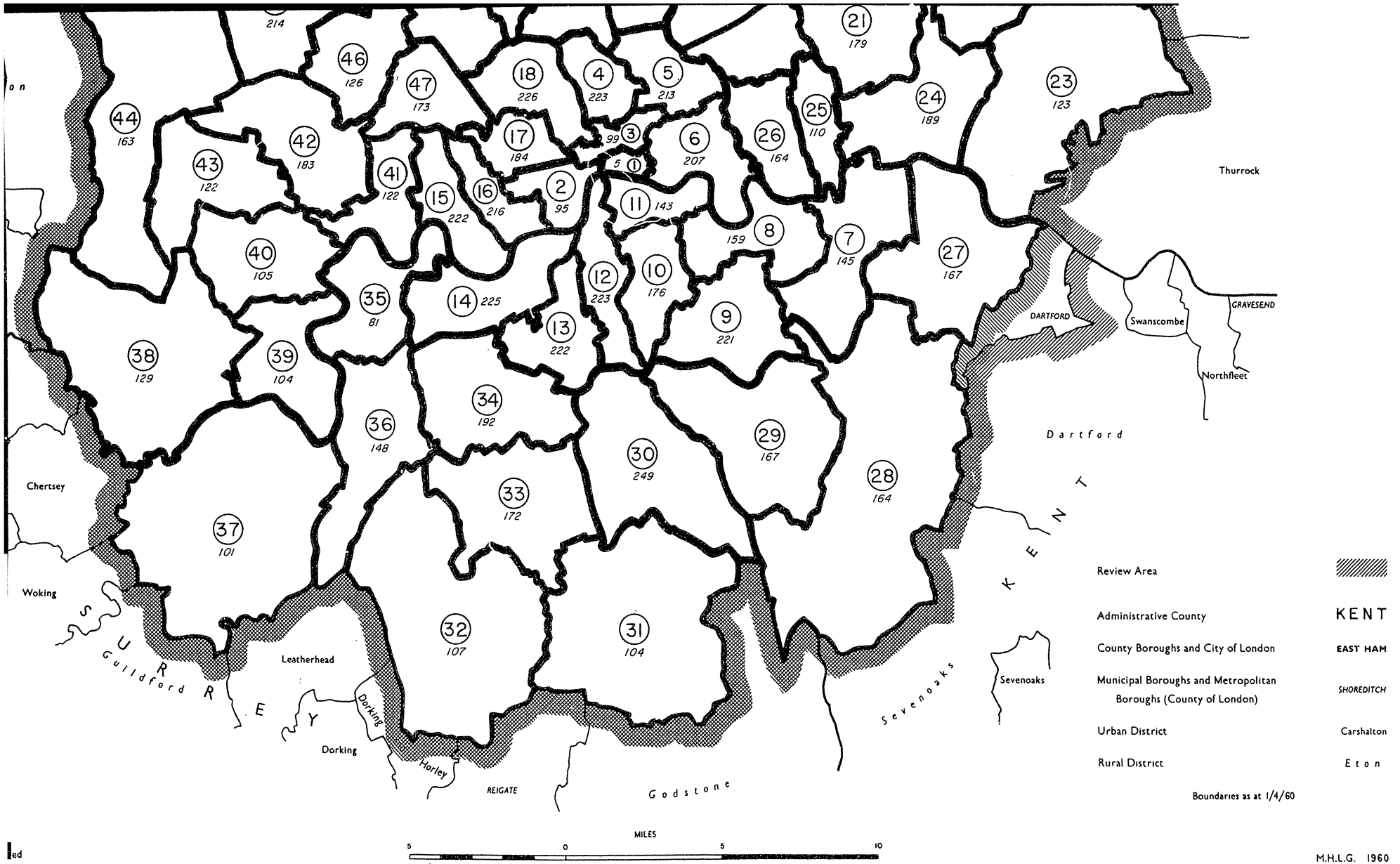
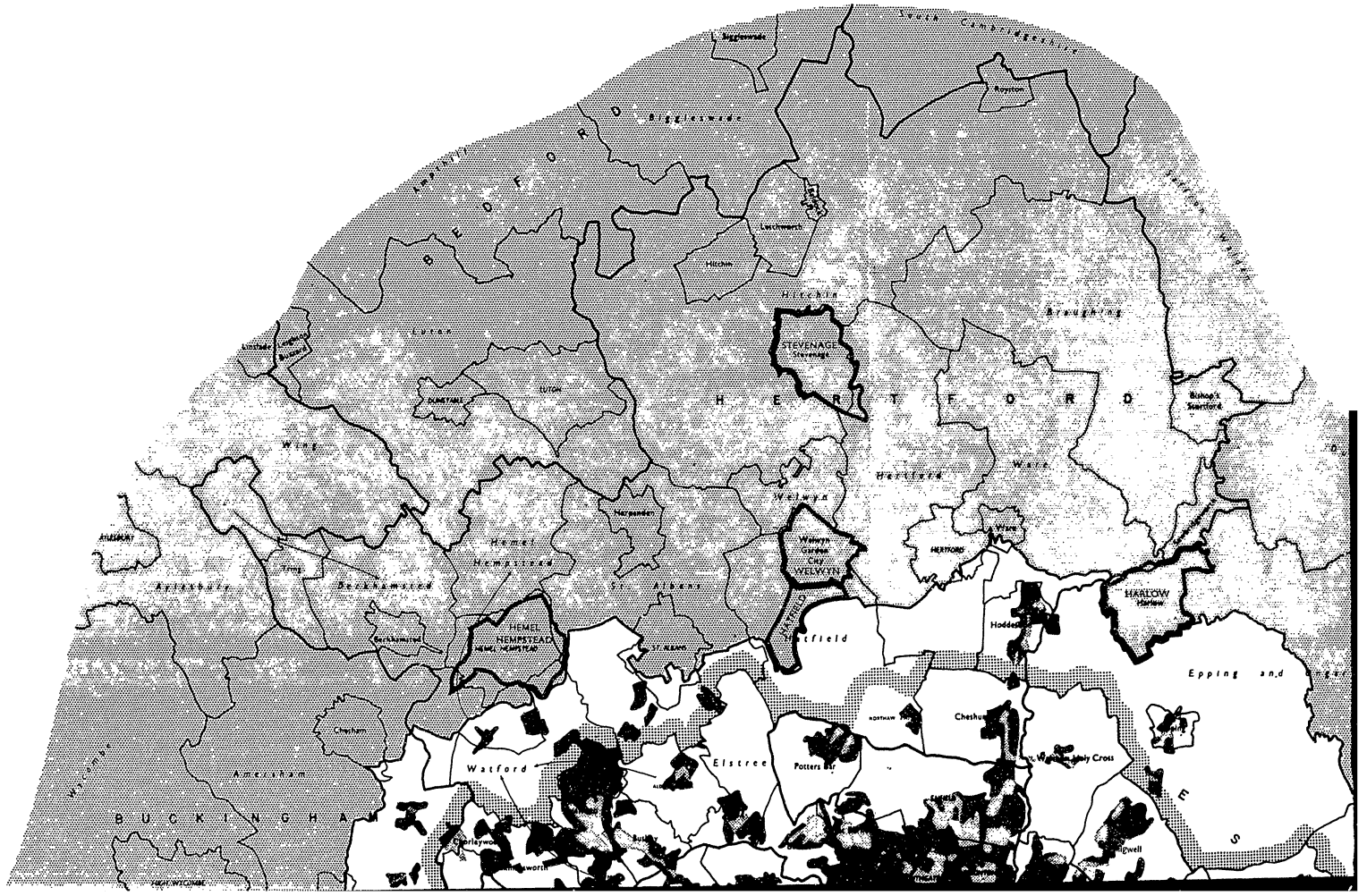


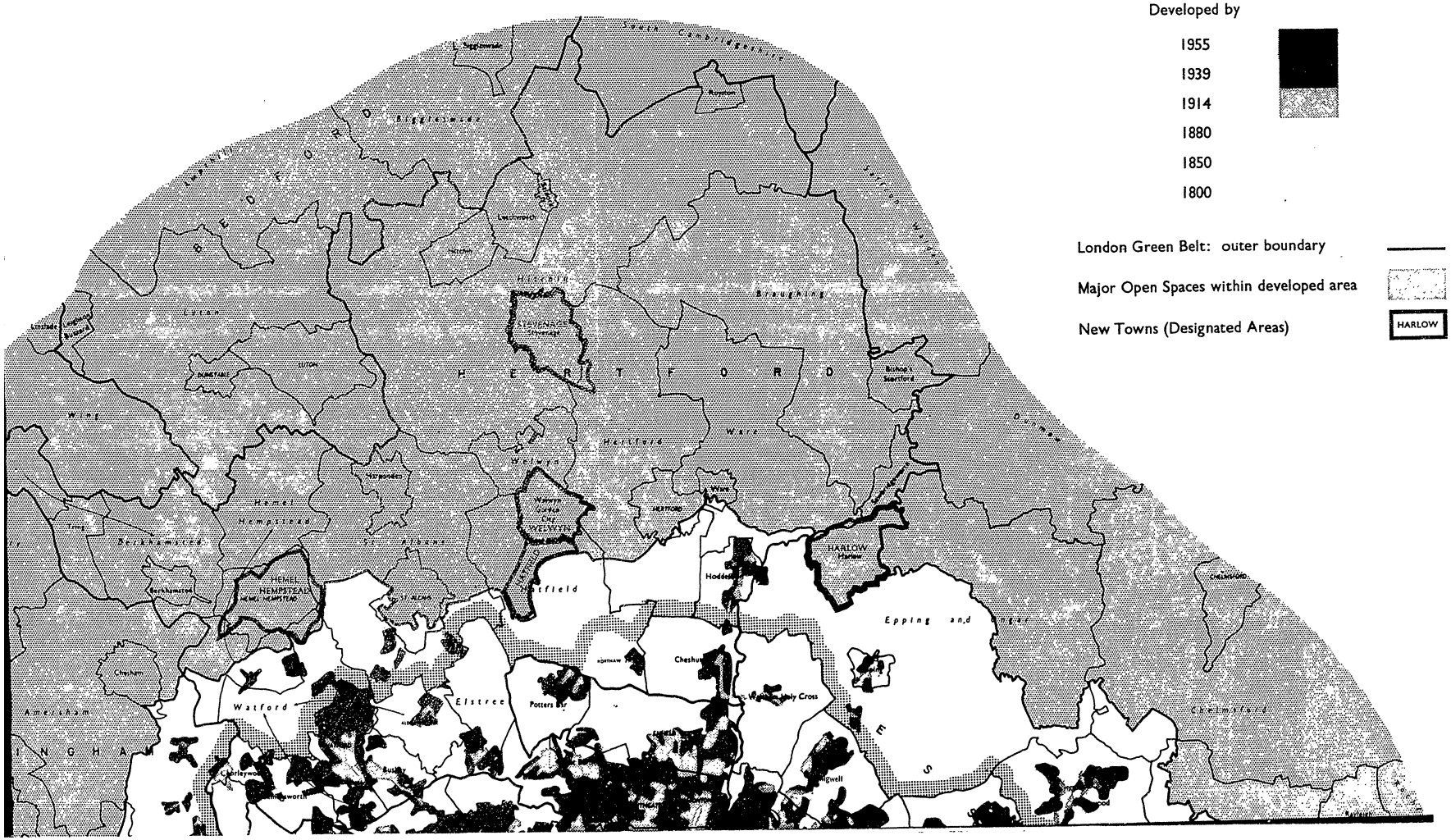
ROYAL COMMISSION ON LOCAL GOVERNMENT IN GREATER LONDON

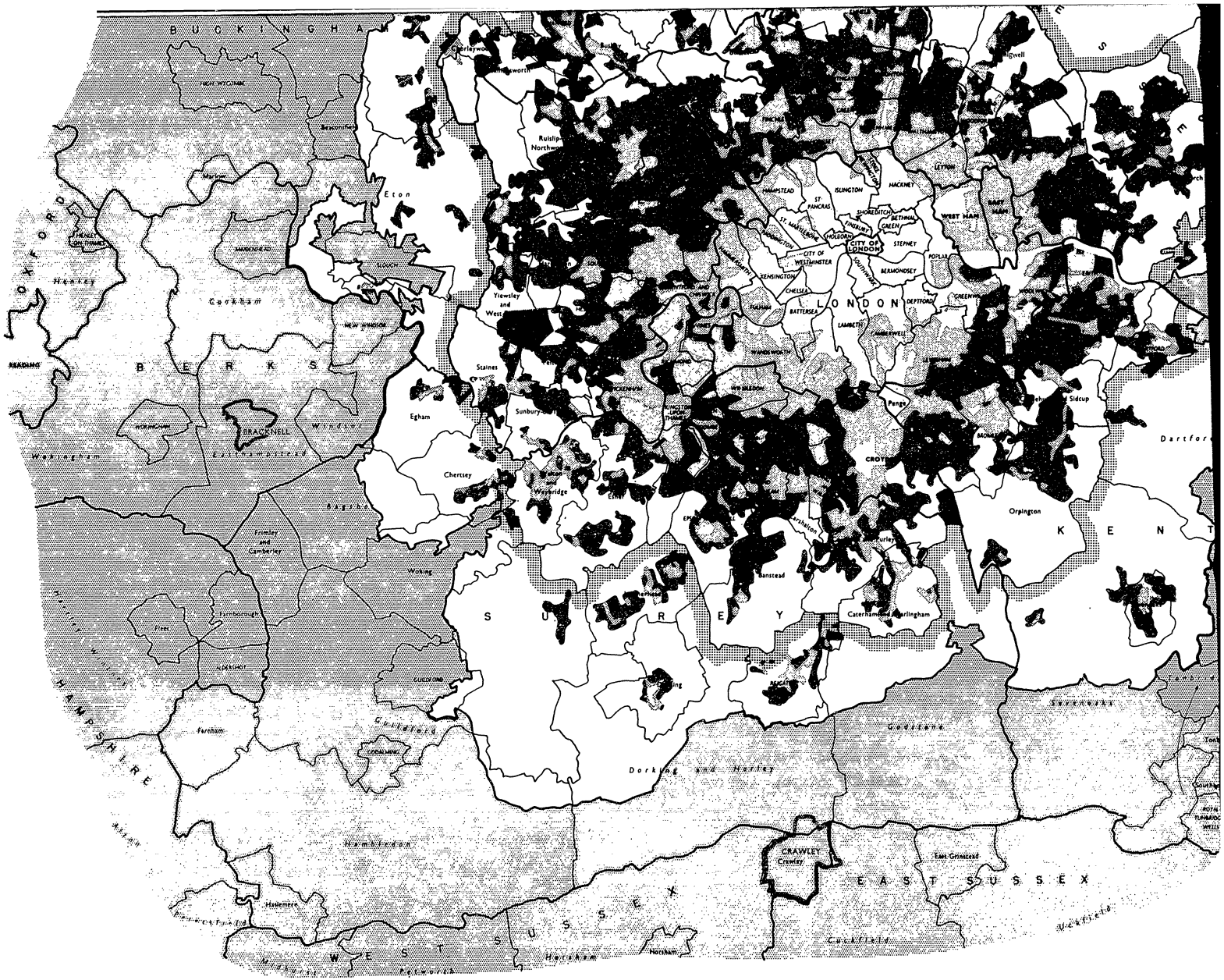
THE GROWTH OF LONDON

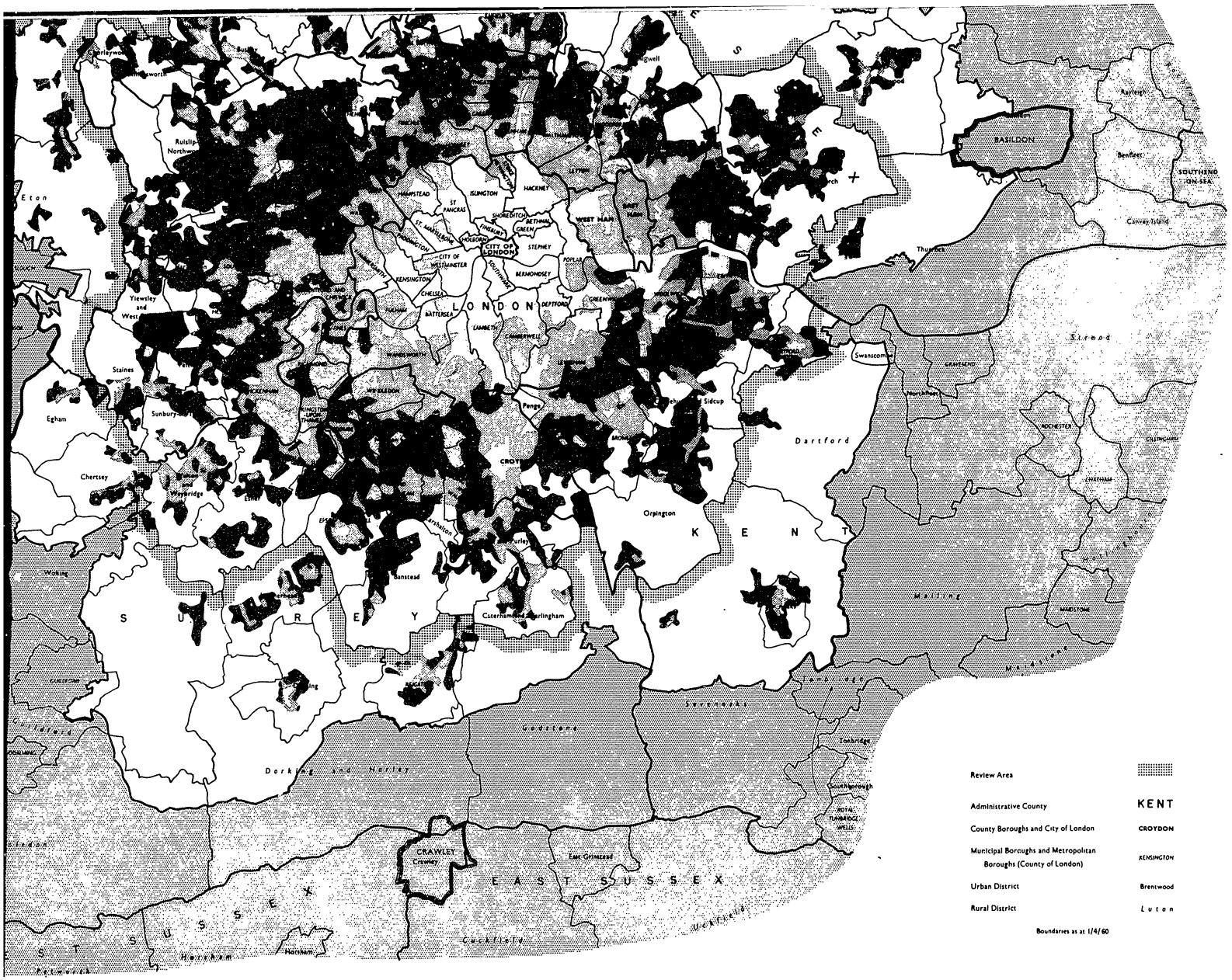


ROYAL COMMISSION ON LOCAL GOVERNMENT IN GREATER LONDON

THE GROWTH OF LONDON

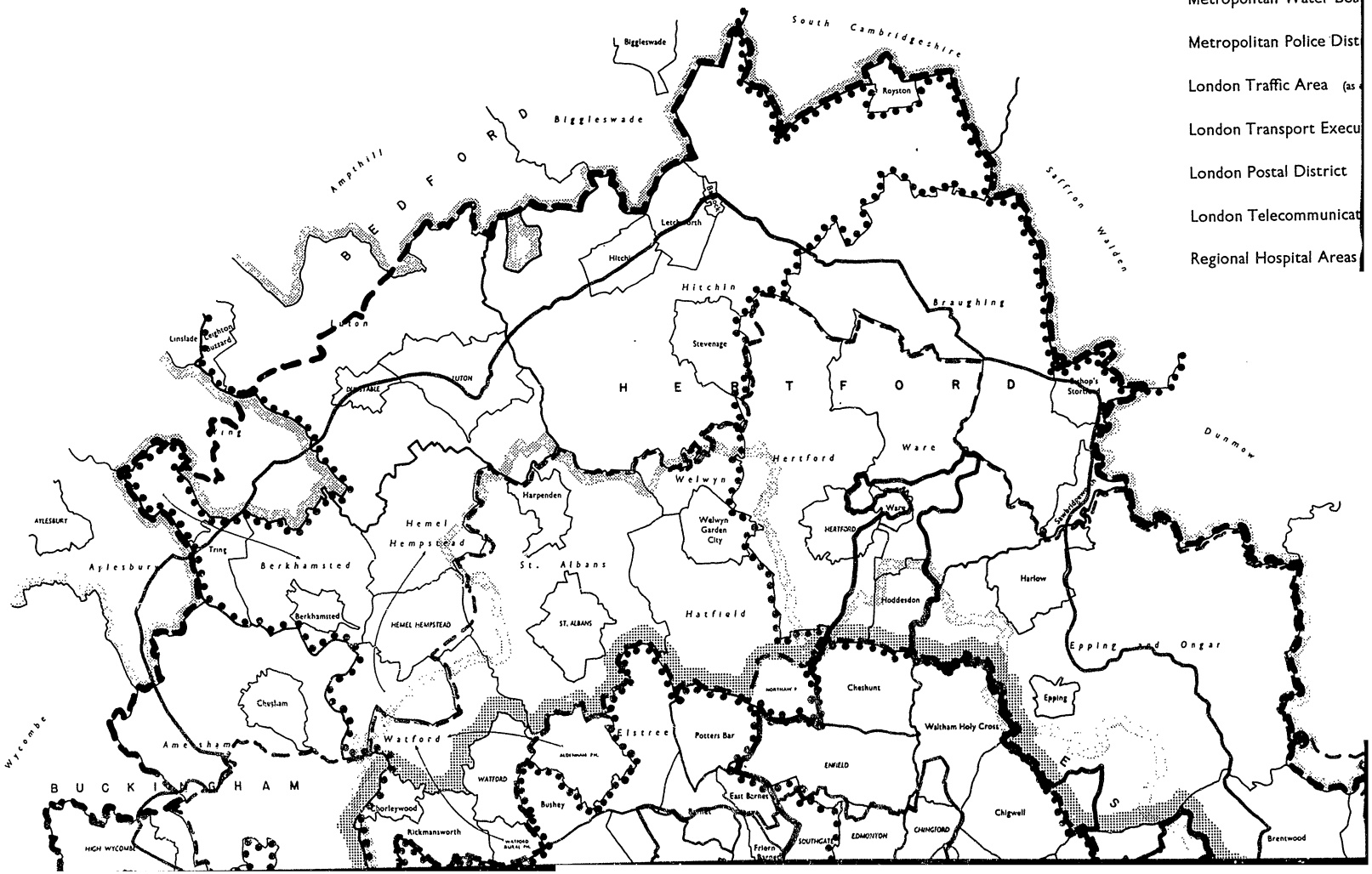






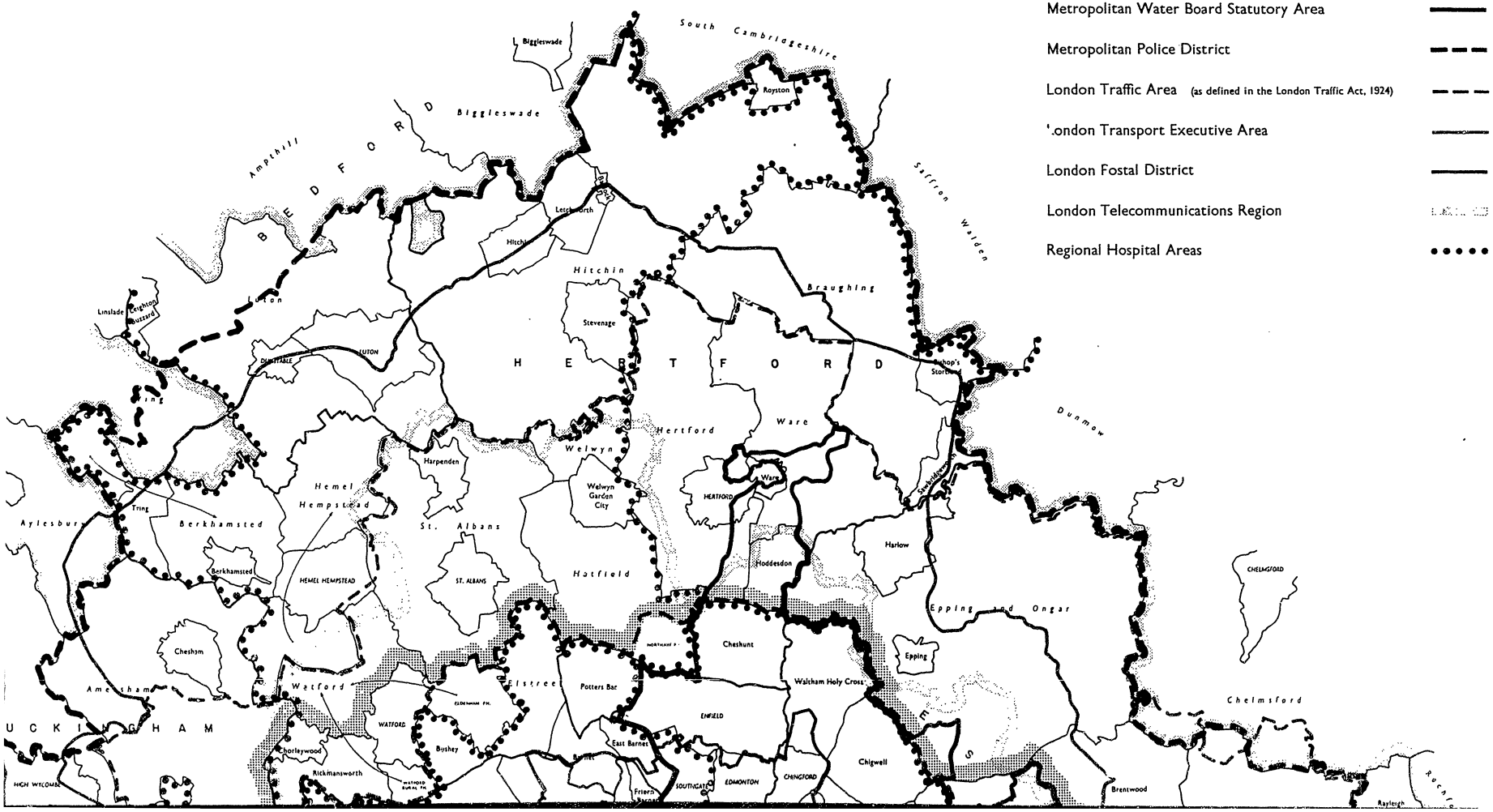
M.H.L.G. 1960
(H F P)

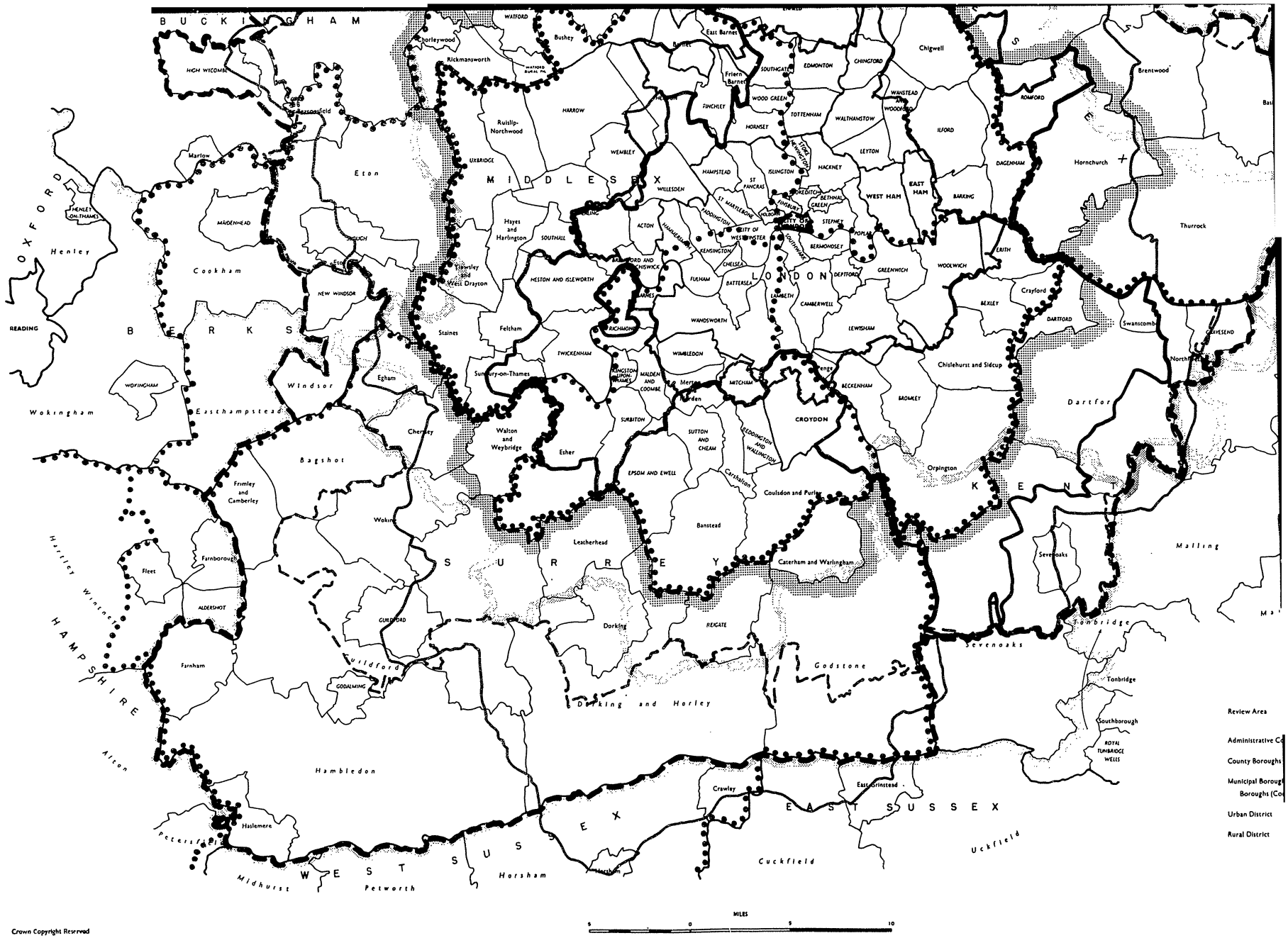
ROYAL COMMISSION ON LOCAL GOVERNMENT IN GREATER LONDON

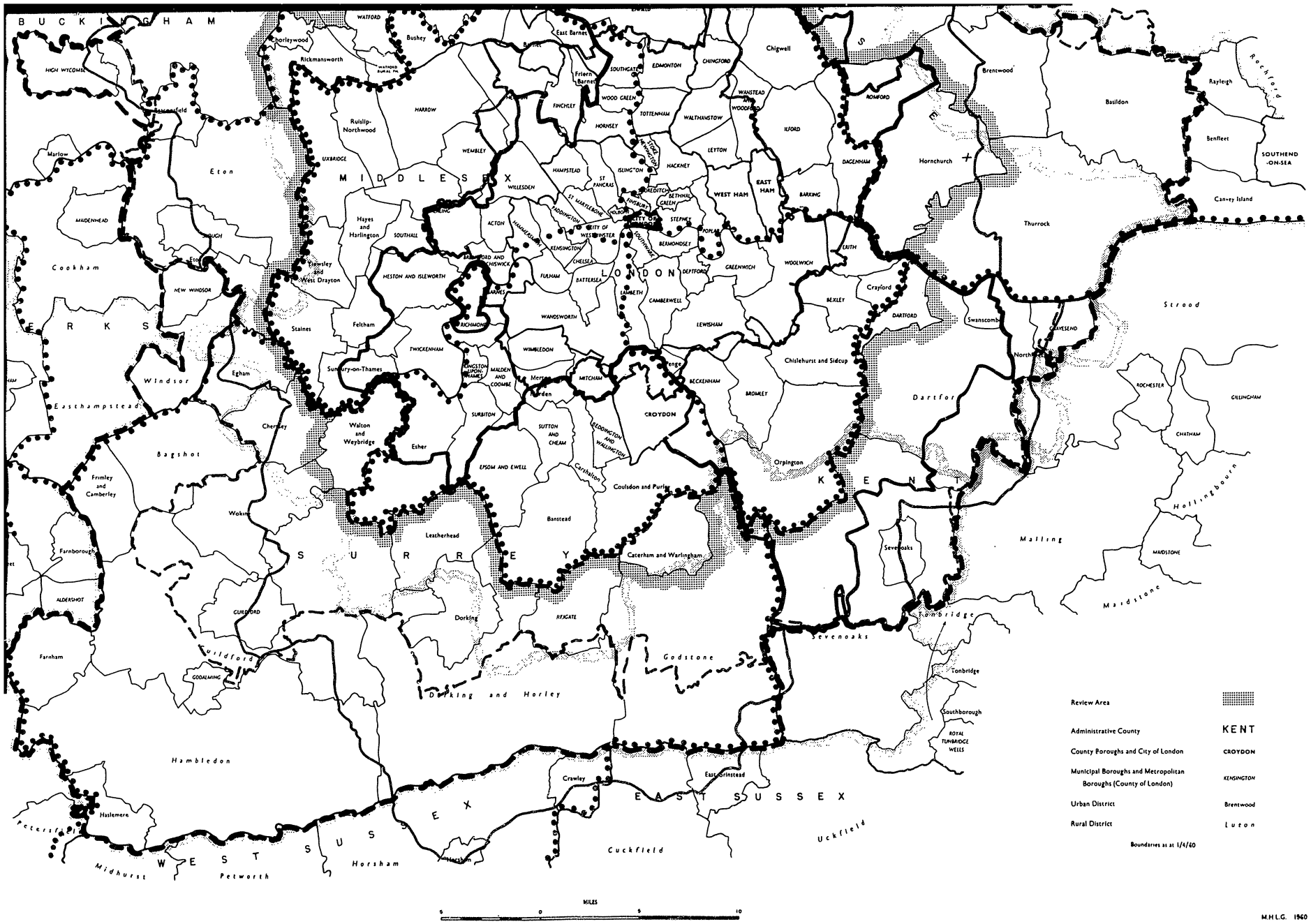


ROYAL COMMISSION ON LOCAL GOVERNMENT IN GREATER LONDON

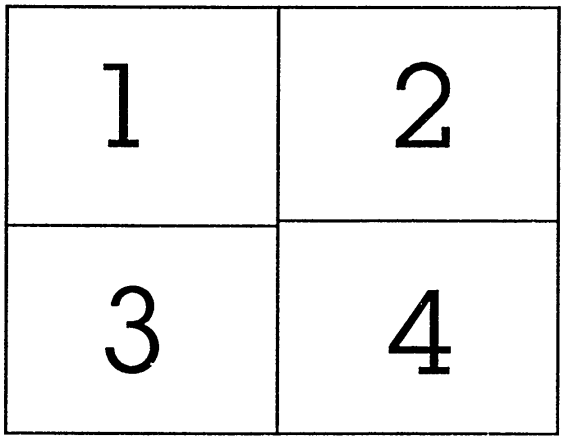
MAP 4





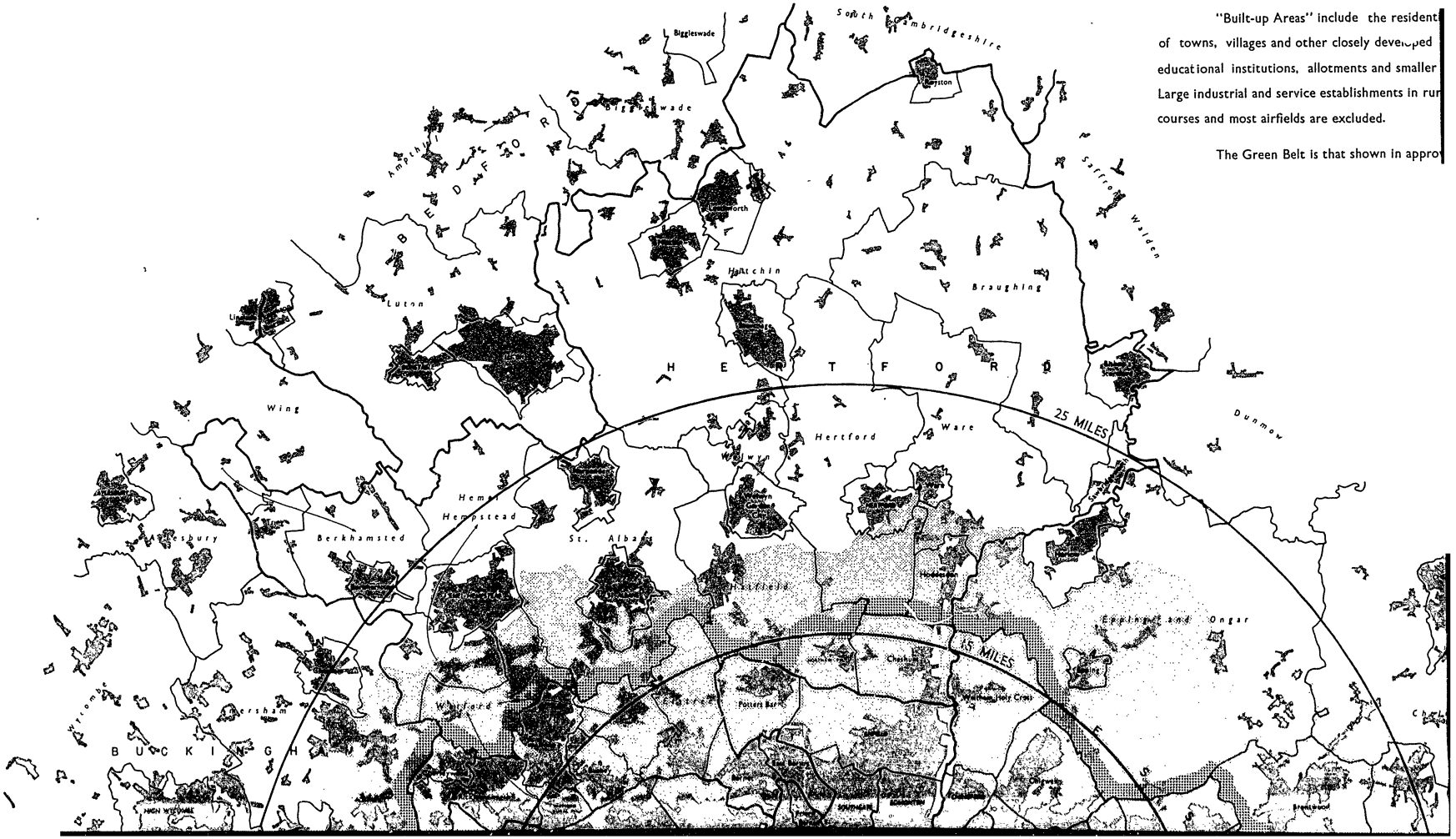


The following item is a foldout and has been filmed in sections. Please see the diagram below which indicates the filming pattern.



ROYAL COMMISSION ON LOCAL GOVERNMENT IN GREATER LONDON

BUILT-UP AREAS 1958
AND
LONDON GREEN BELT



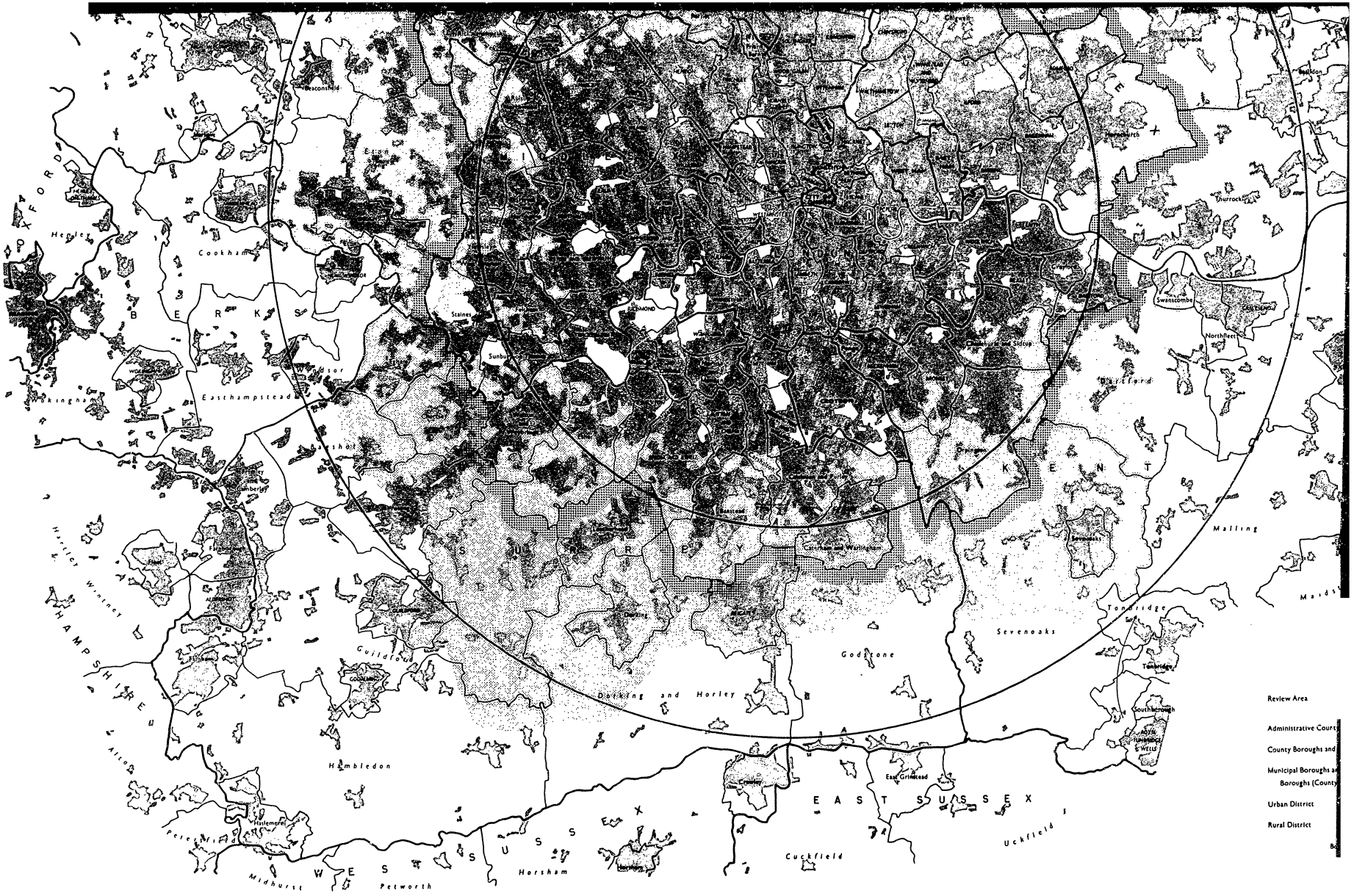
"Built-up Areas" include the resident
of towns, villages and other closely deve
educational institutions, allotments and smaller
Large industrial and service establishments in rur
courses and most airfields are excluded.

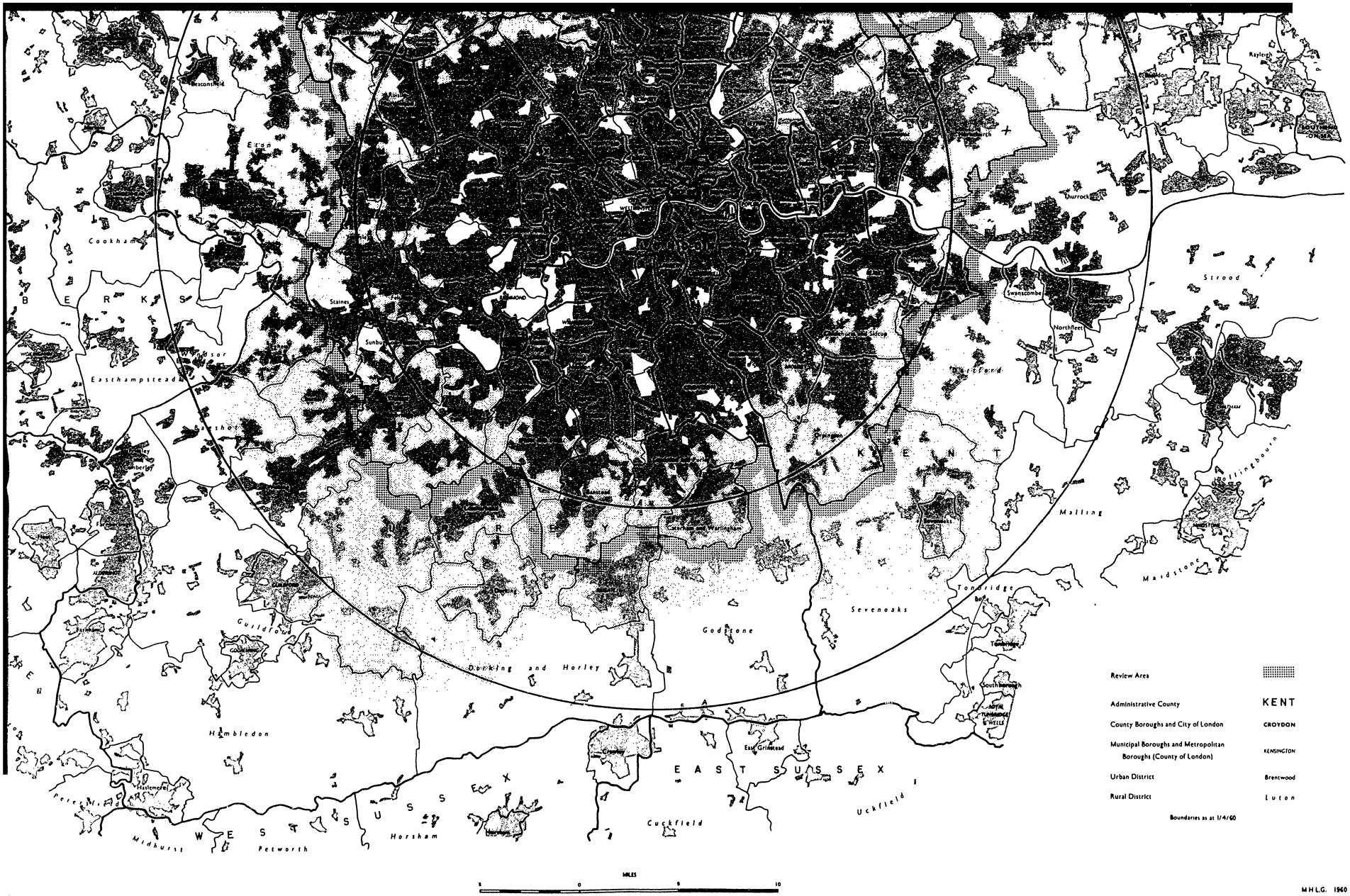
The Green Belt is that shown in appro

BUILT-UP AREAS 1958
AND
LONDON GREEN BELT

"Built-up Areas" include the residential, industrial and business areas of towns, villages and other closely developed settlements, together with the educational institutions, allotments and smaller open spaces which they envelop. Large industrial and service establishments in rural areas are also included. Golf courses and most airfields are excluded.

The Green Belt is that shown in approved Development Plans at 1/1/60.



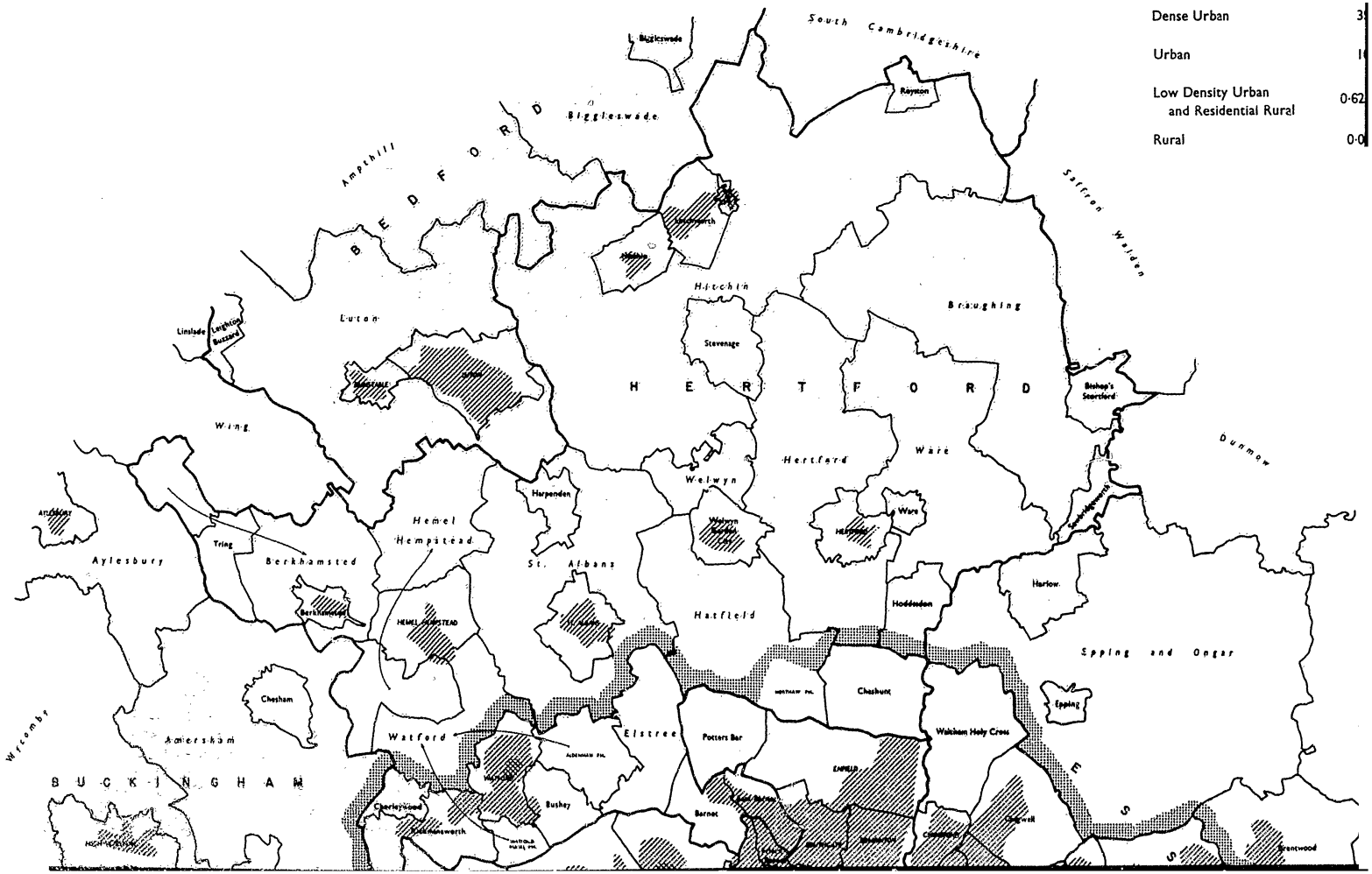


MHLG. 1960
(M.F.P.)

ROYAL COMMISSION ON LOCAL GOVERNMENT IN GREATER LONDON

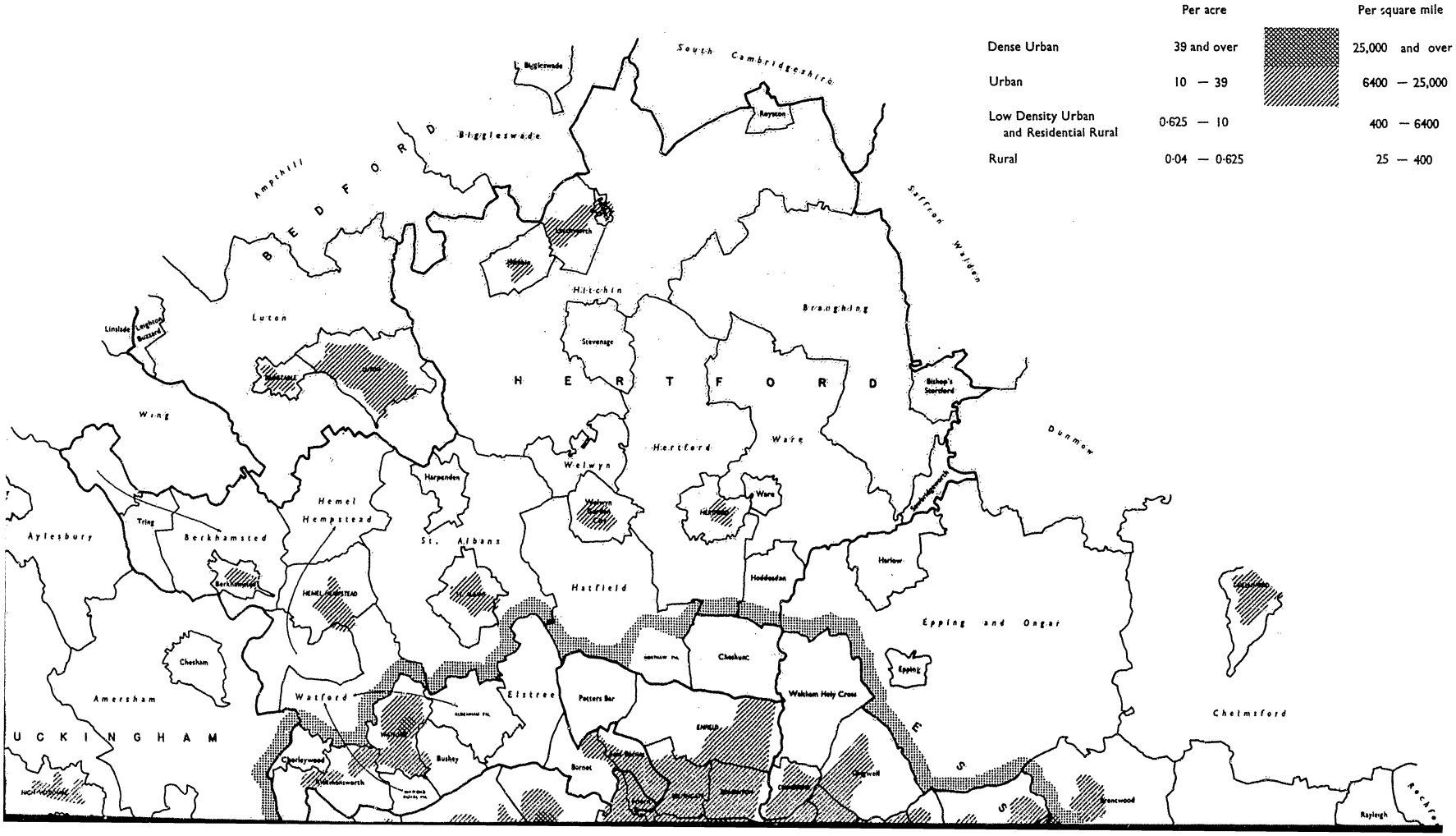
POPULATION DENSITY 1951

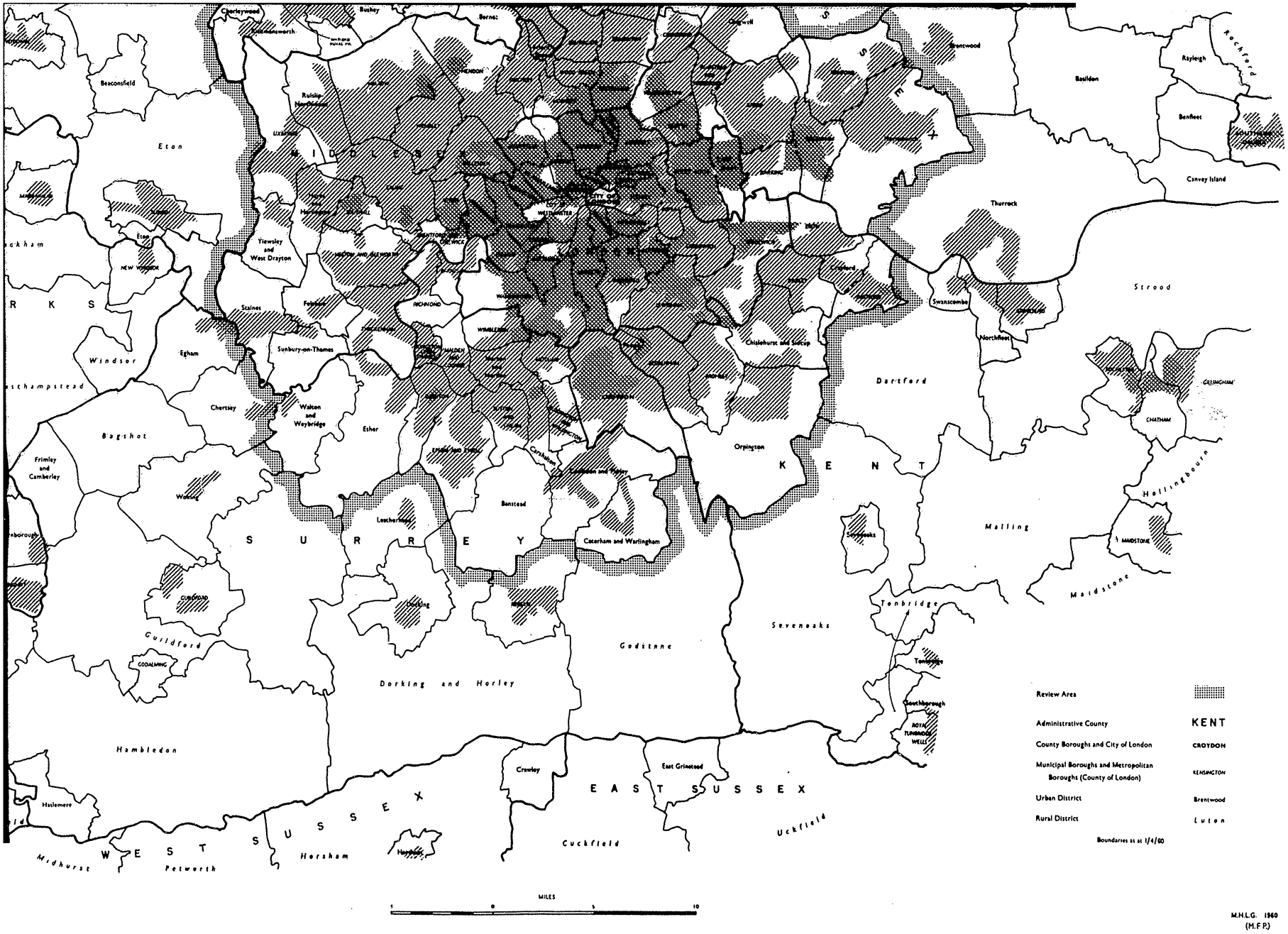
Compiled from the County Reports of the 1951 Census



POPULATION DENSITY 1951

Compiled from the County Reports of the 1951 Census

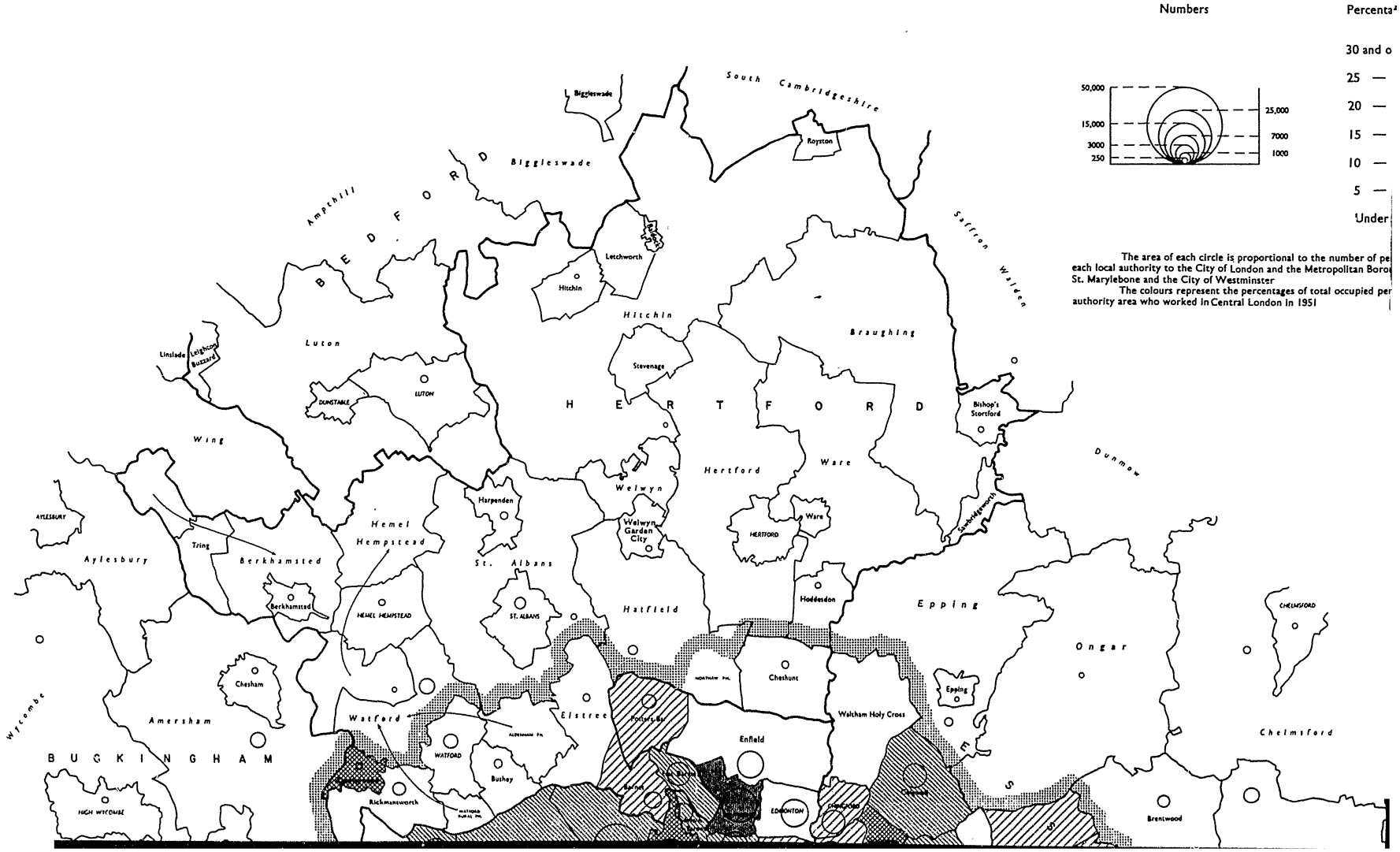




ROYAL COMMISSION ON LOCAL GOVERNMENT IN GREATER LONDON

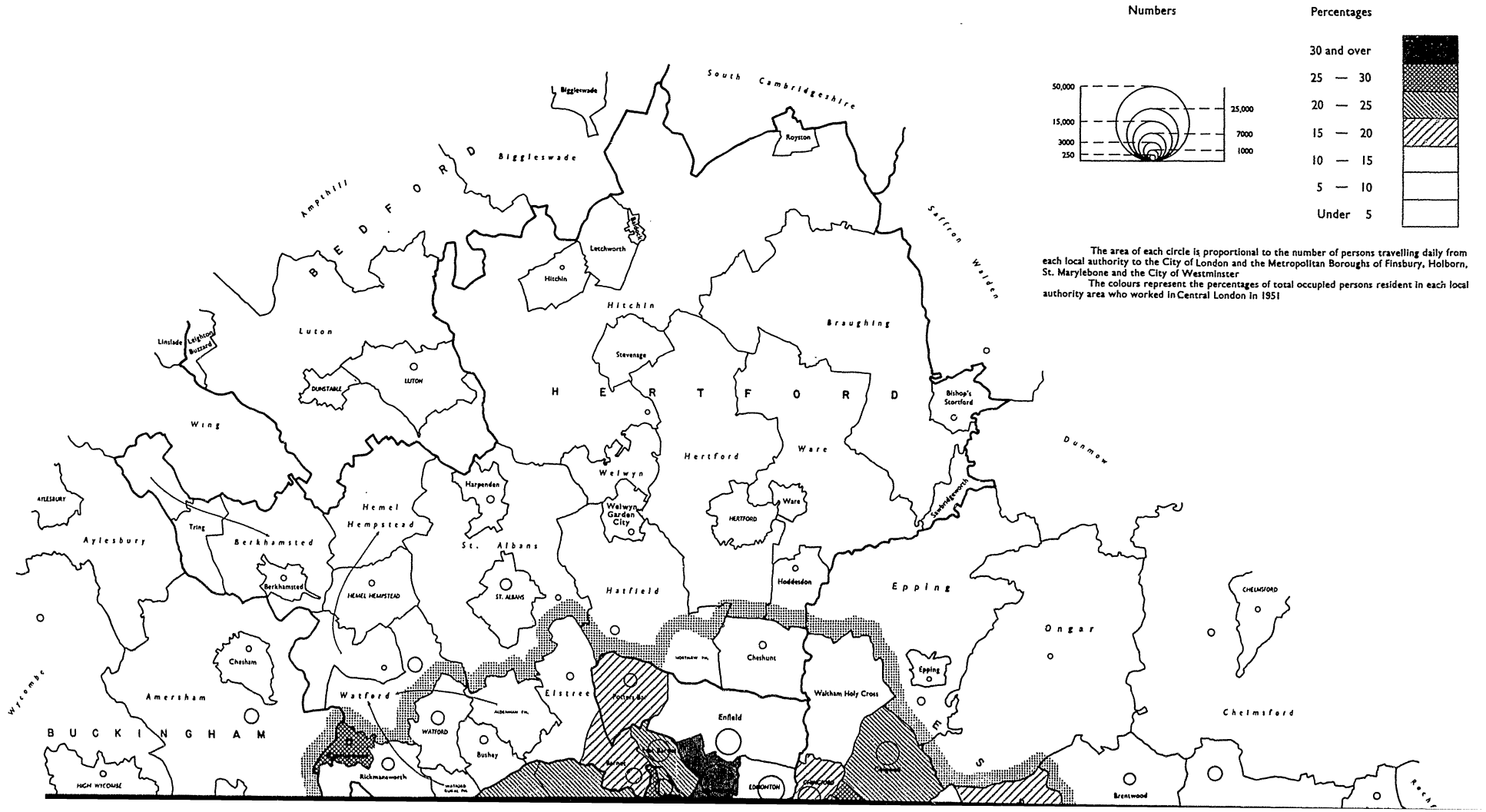
TRAVEL TO WORK INTO CENTRAL LONDON

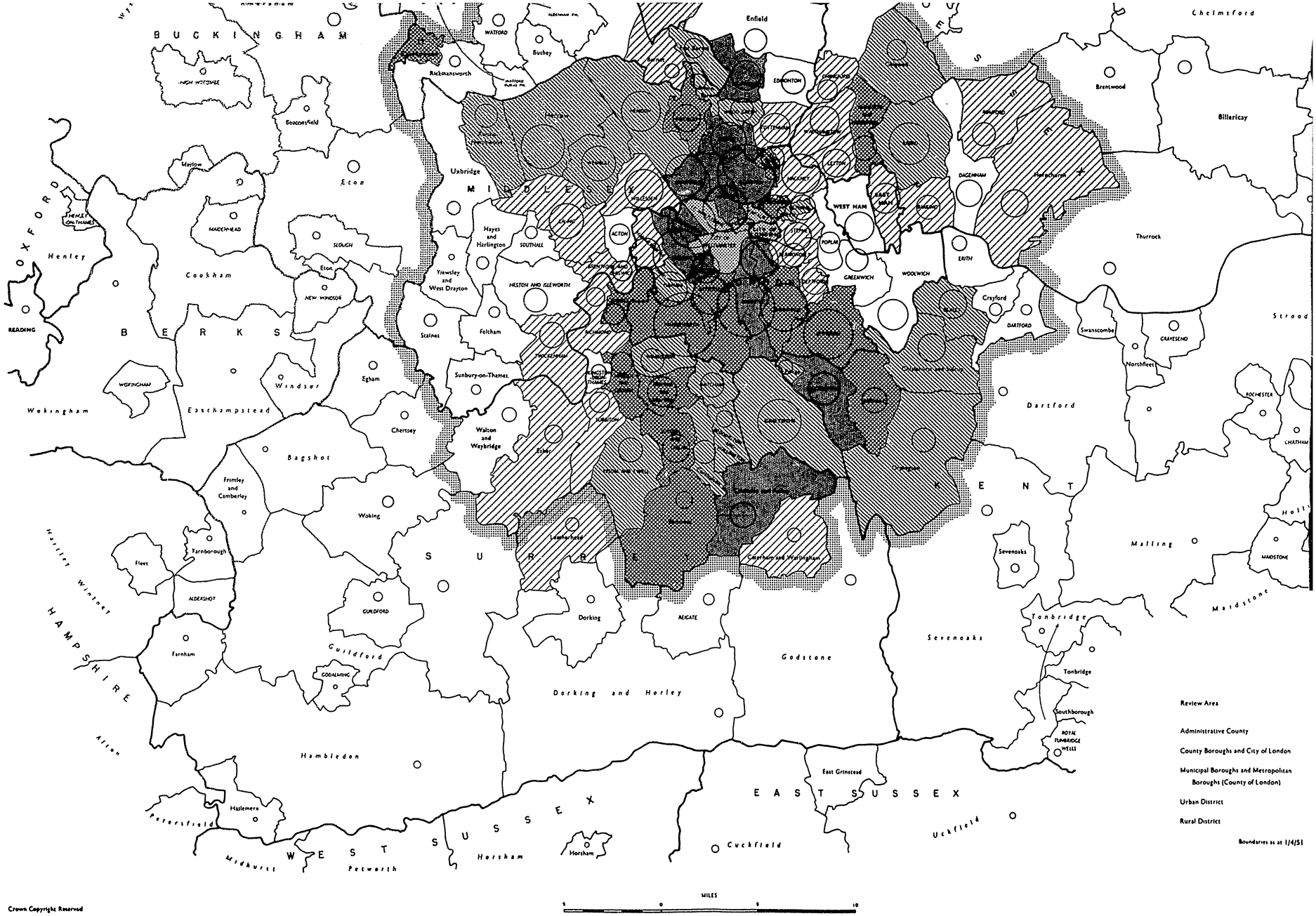
1951 Census: Report on Usual Residence and Workplace



TRAVEL TO WORK INTO CENTRAL LONDON

1951 Census: Report on Usual Residence and Workplace





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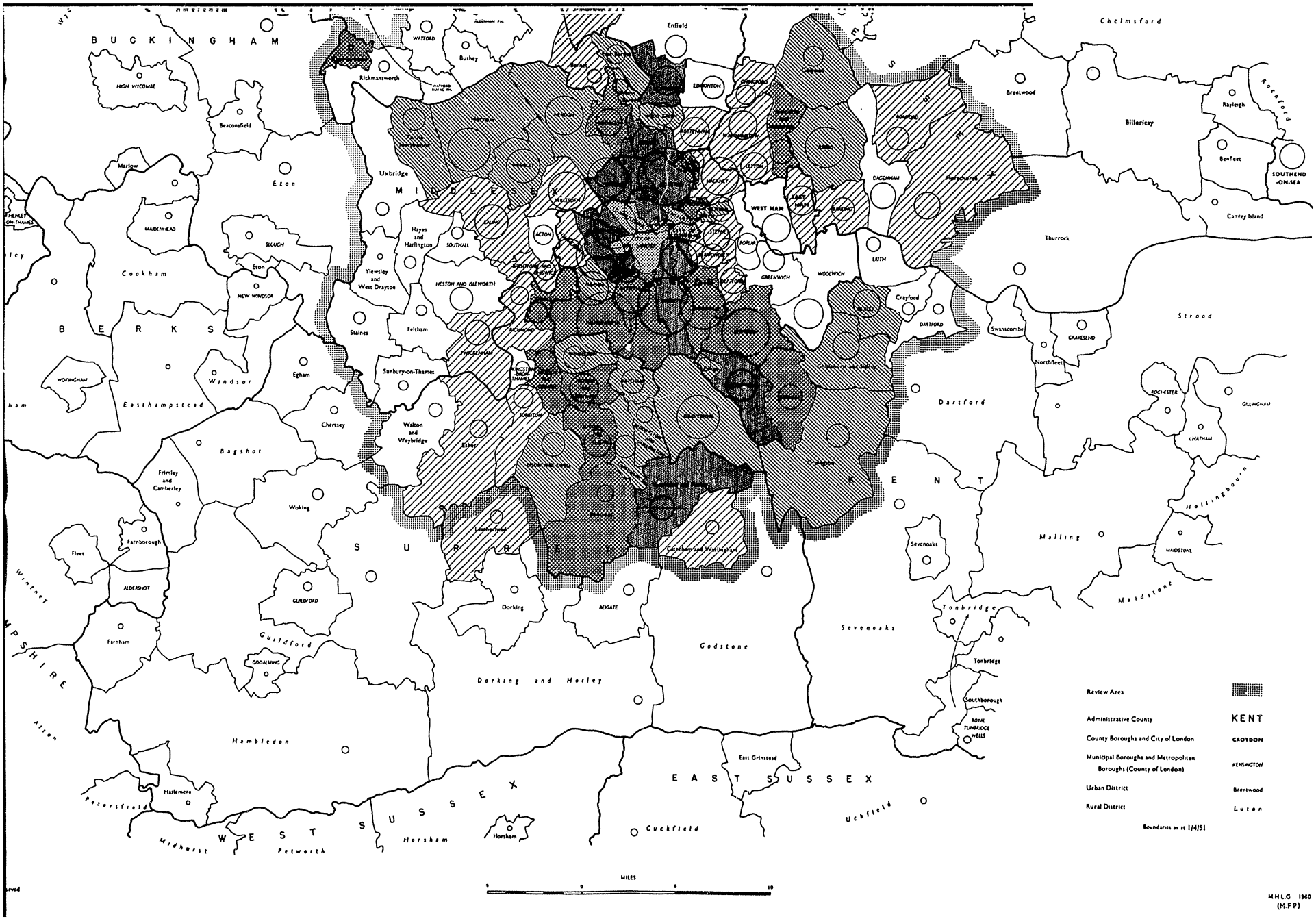
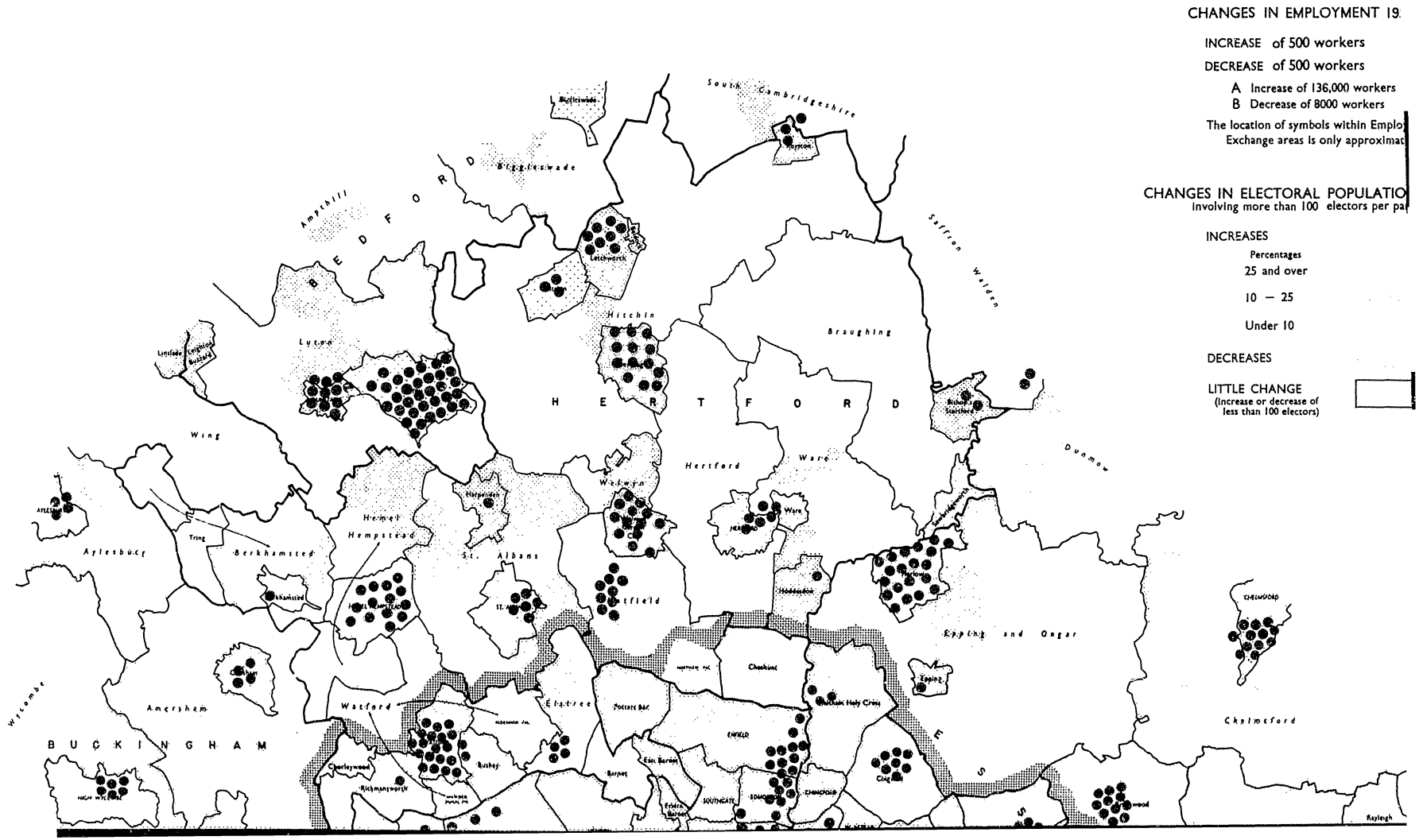
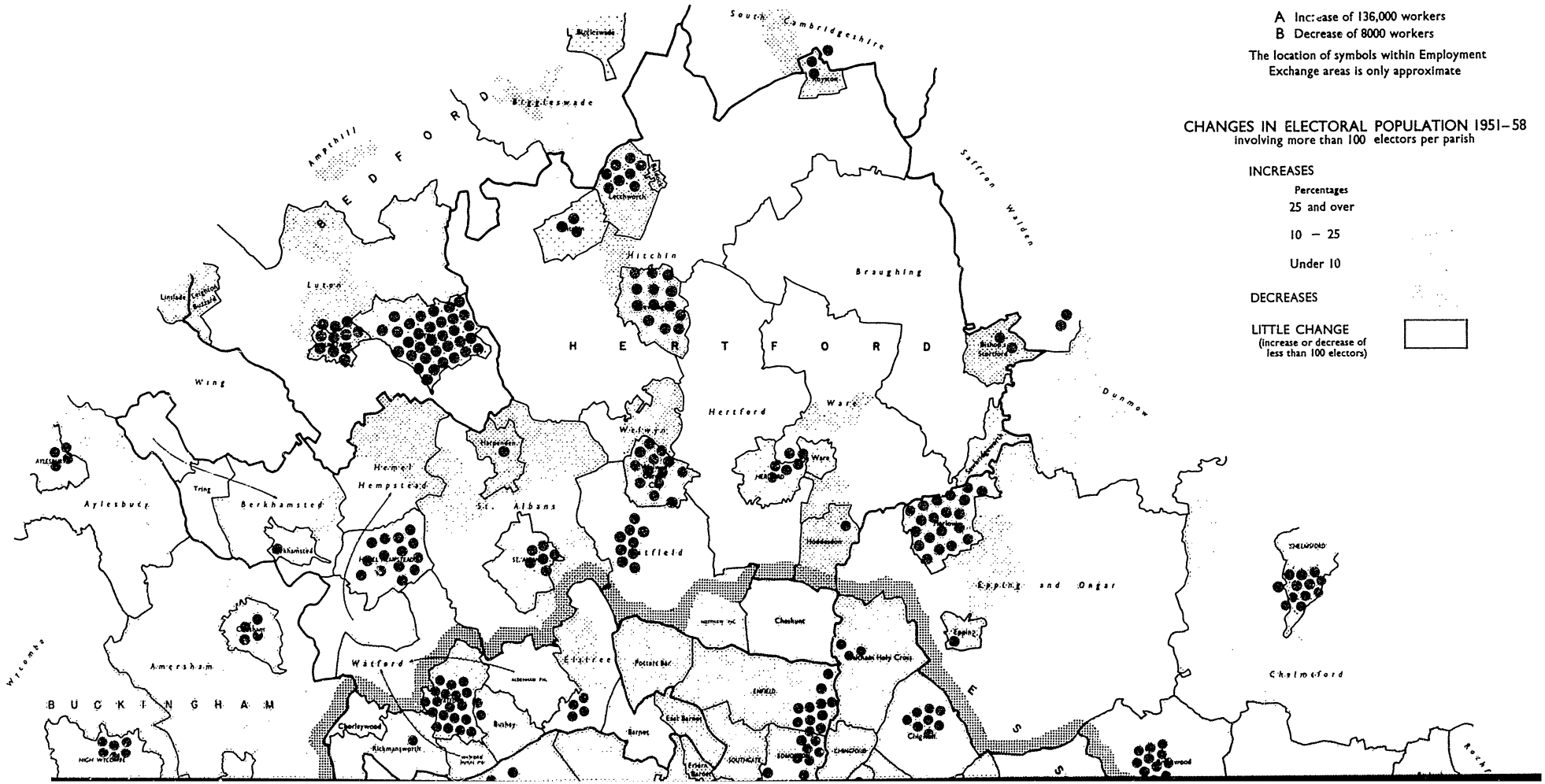


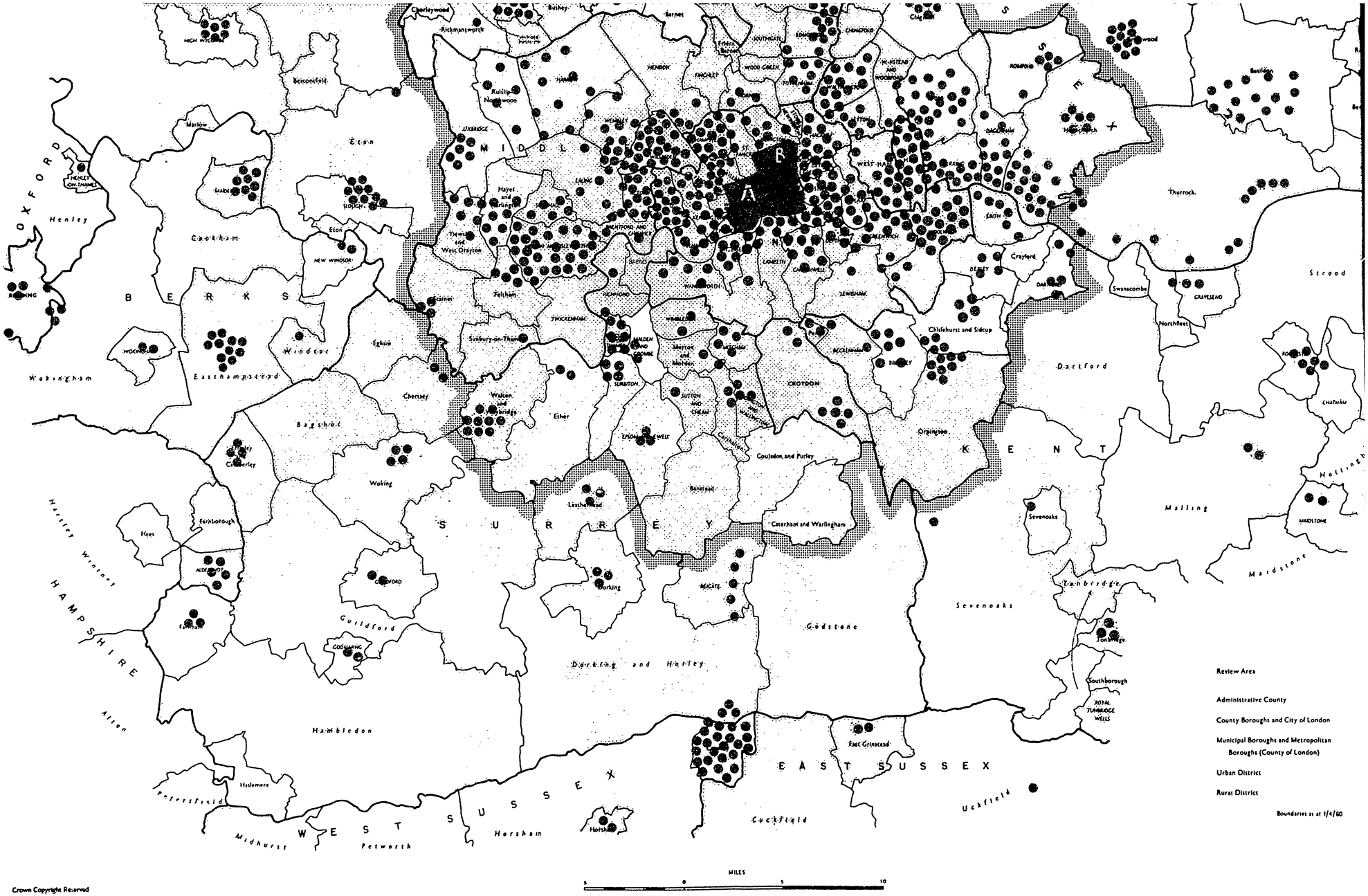
ROYAL COMMISSION ON LOCAL GOVERNMENT IN GREATER LONDON

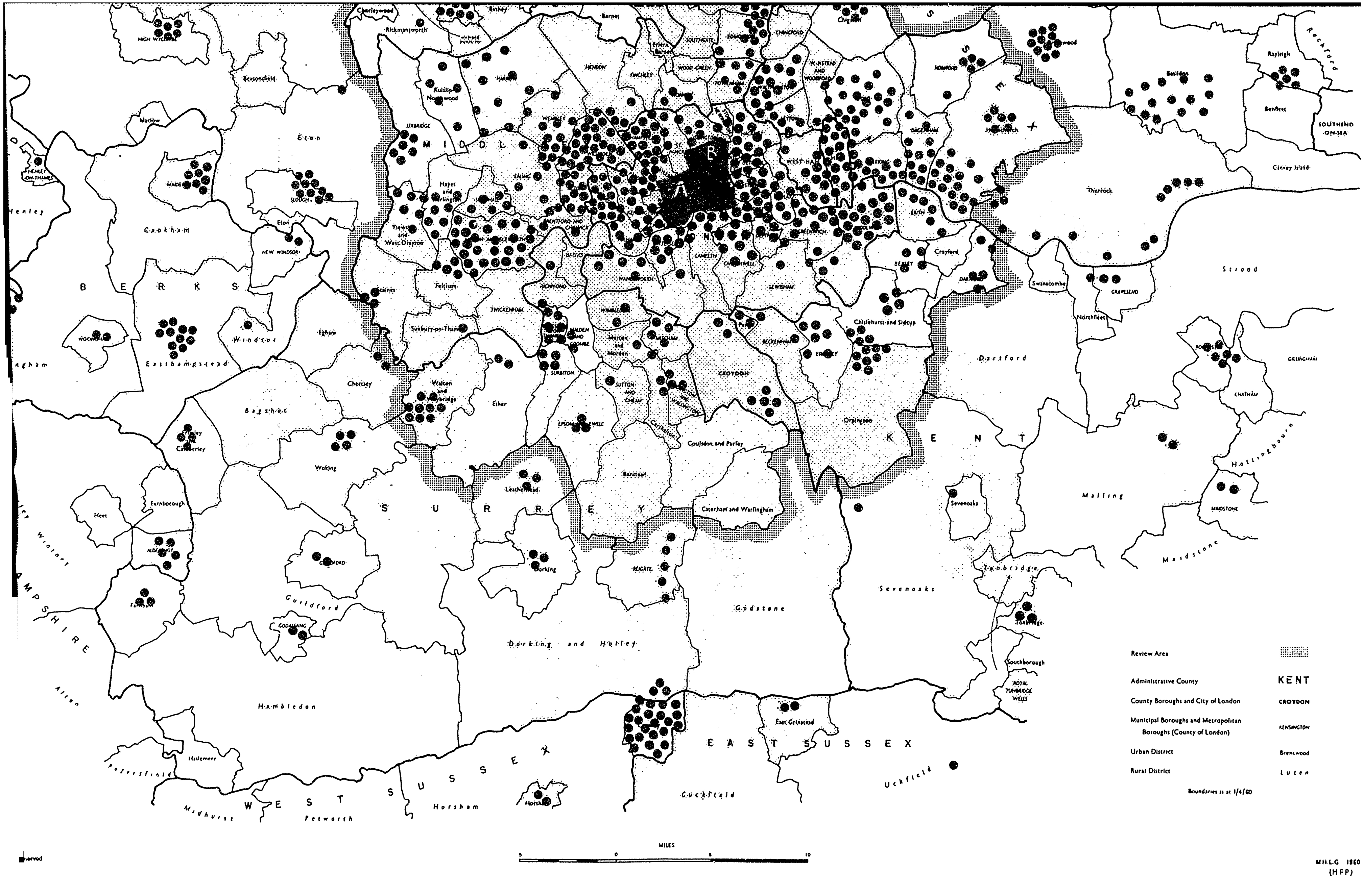
CHANGES IN POPULATION AND EMPLOYMENT



CHANGES IN POPULATION AND EMPLOYMENT



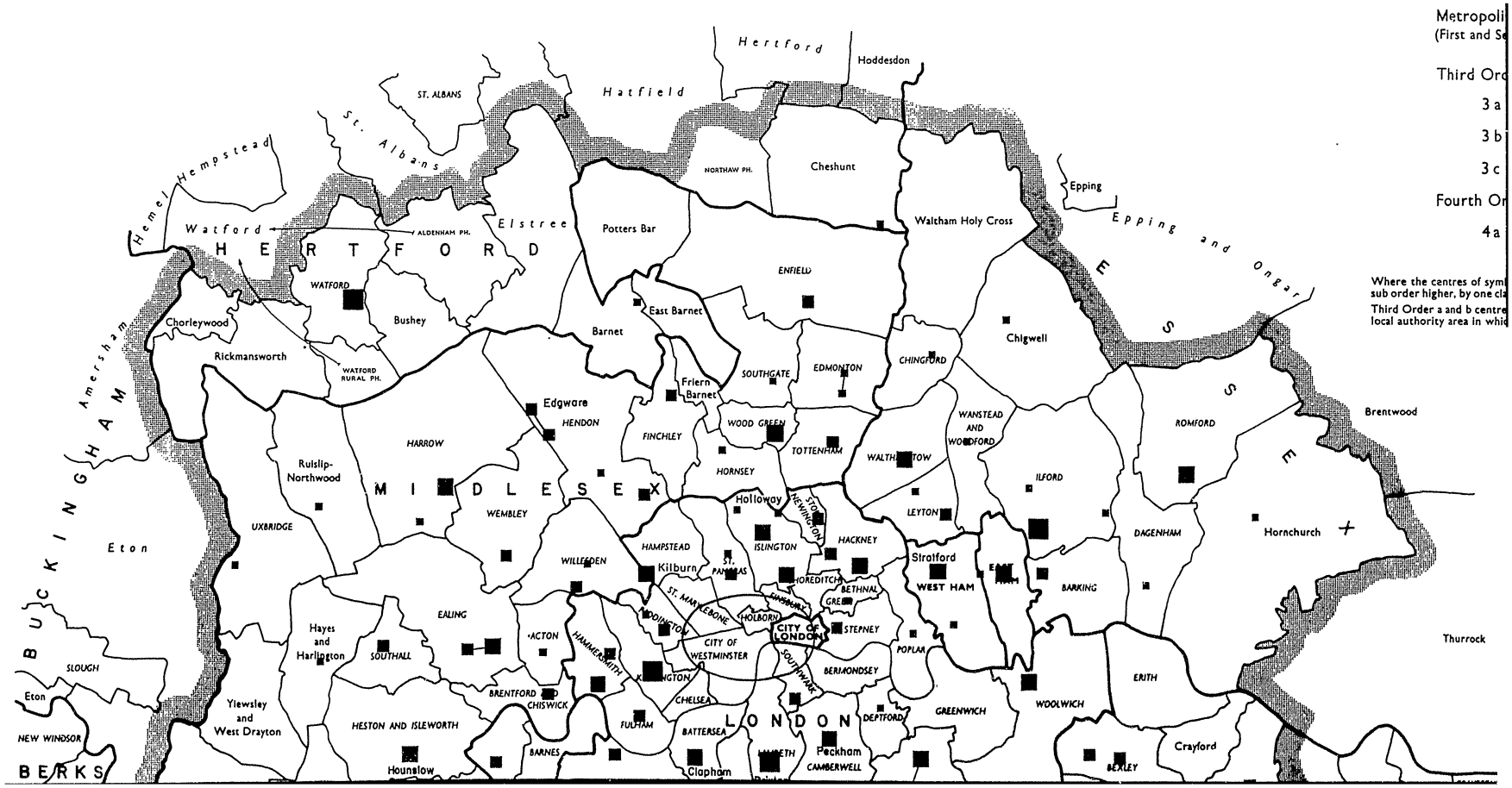




ROYAL COMMISSION ON LOCAL GOVERNMENT IN GREATER LONDON

CLASSIFICATION OF SERVICE CENTRES

as determined by the intensity of provision and use of selected "central area" facilities



CLASSIFICATION OF SERVICE CENTRES

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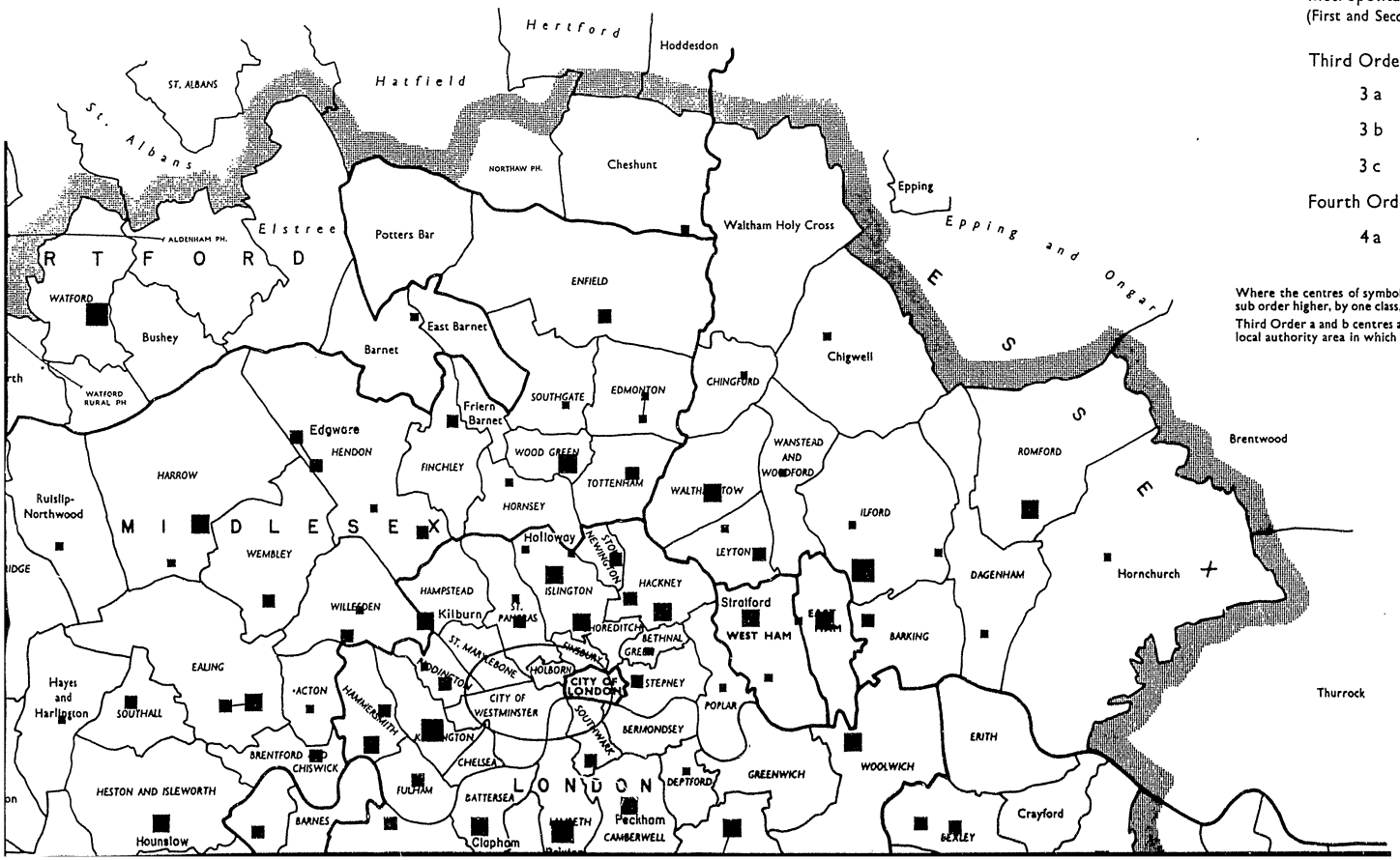


Metropolitan Centre
(First and Second Order)

Third Order Centres

3 a

3 b

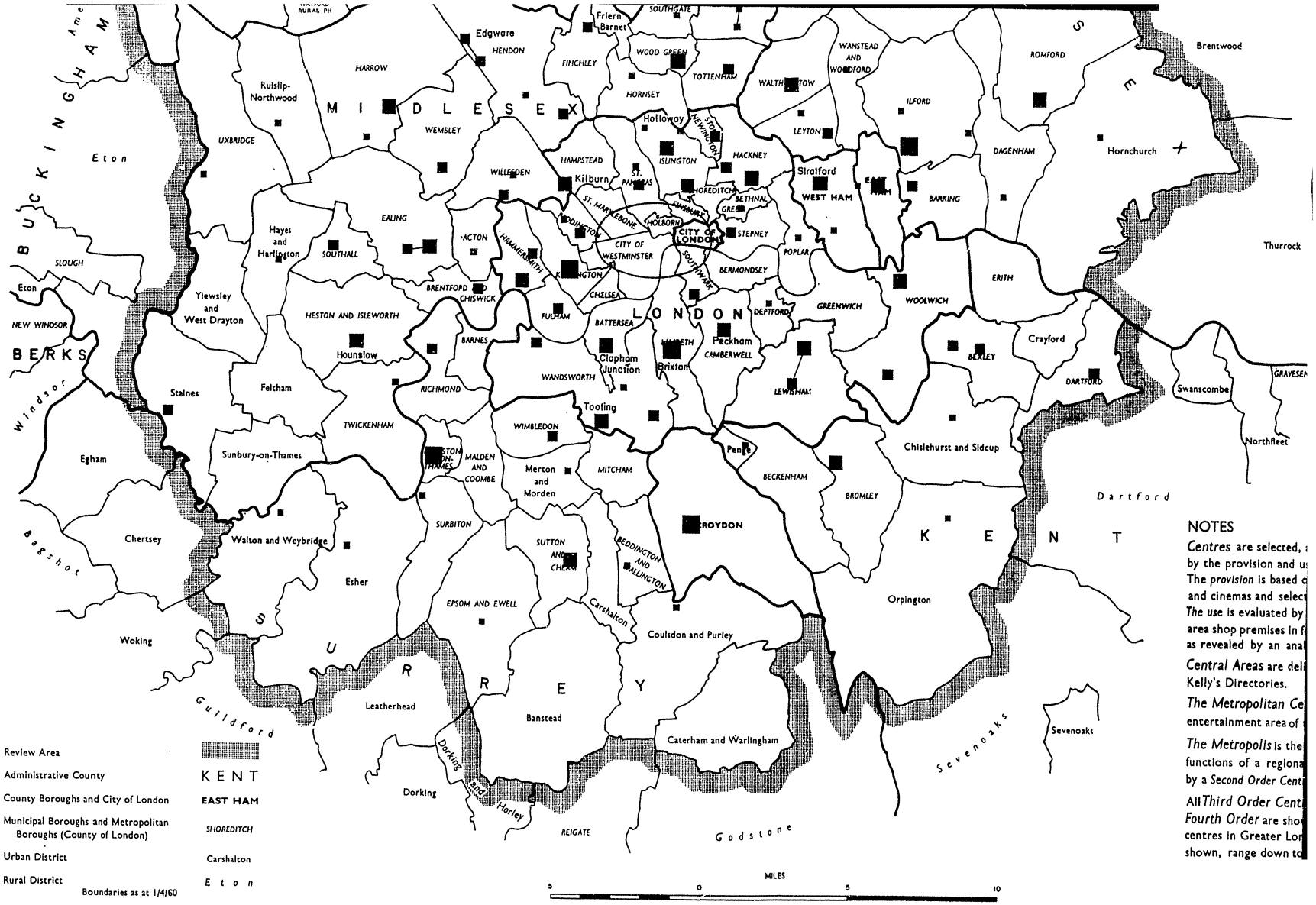
3 c

Fourth Order Centres

4 a

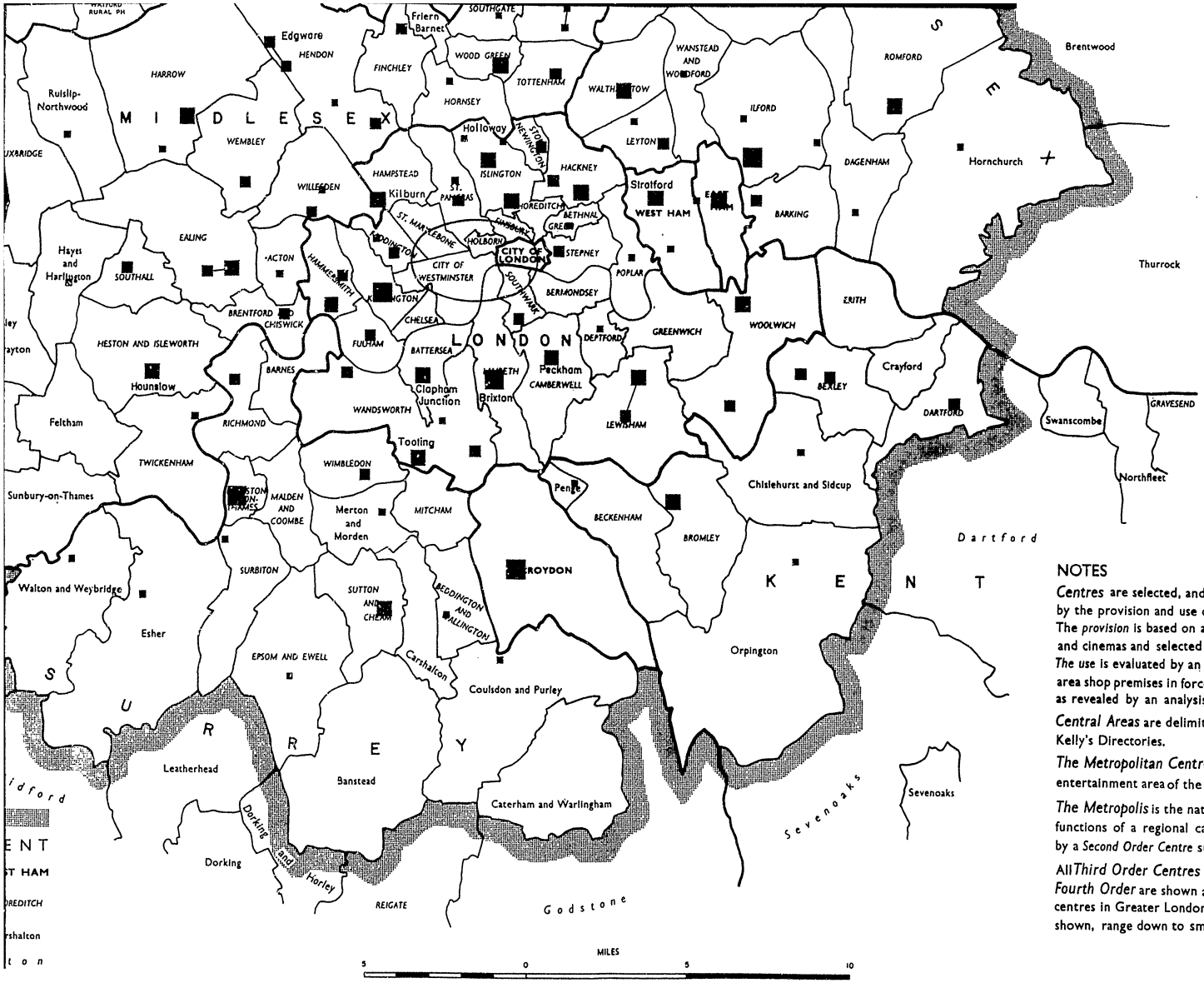
Where the centres of symbols are linked, the status of the "twin" is that of a sub order higher, by one class, than that of its components or higher component.

Third Order a and b centres are named where the name differs from that of the local authority area in which they are situated.



NOTES

Centres are selected, by the provision and u
The *provision* is based o and cinemas and selec
The use is evaluated by area shop premises in f as revealed by an anal
Central Areas are del Kelly's Directories.
The Metropolitan Ce entertainment area of
The Metropolis is the functions of a regiona by a *Second Order Cent*
All *Third Order Cent* *Fourth Order* are sho centres in Greater Lo shown, range down t



NOTES

Centres are selected, and classified according to status, as indicated by the provision and use of central area facilities.

The *provision* is based on a quantitative evaluation of banks, theatres and cinemas and selected classes of shops, as in 1958.

The use is evaluated by an examination of the rateable values of central area shop premises in force in 1959 and of the nodality of the centres as revealed by an analysis of the 9·30 a.m. to 4·0 p.m. bus services.

Central Areas are delimited by reference to Development Plans and Kelly's Directories.

The Metropolitan Centre is here taken to include the shopping and entertainment area of the West End, City, Victoria and Knightsbridge.

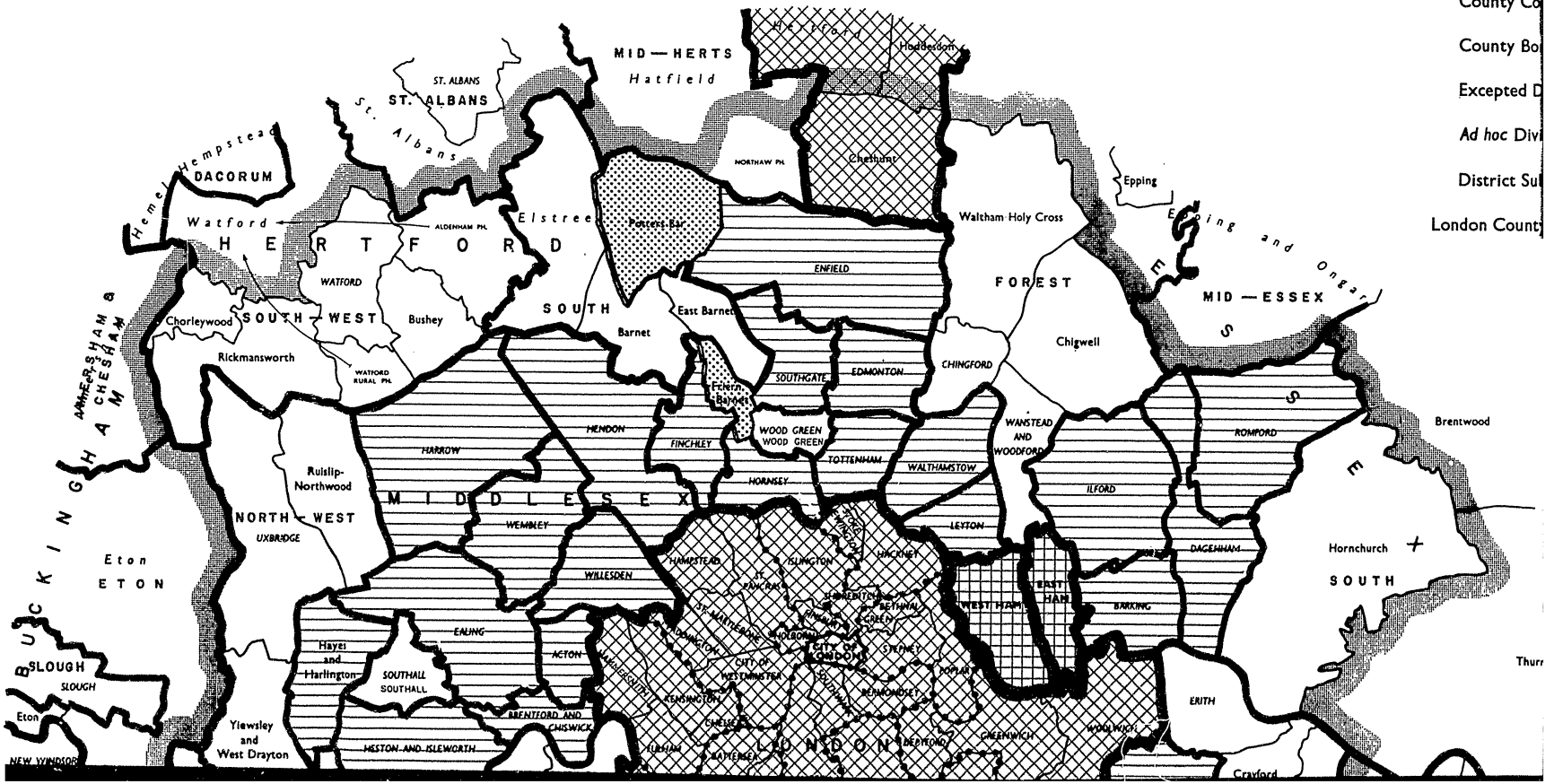
The Metropolis is the national *First Order Centre* and also has the functions of a regional capital fulfilled in other parts of the country by a *Second Order Centre* such as Birmingham or Bristol.

All *Third Order Centres* and Centres in the upper division of the *Fourth Order* are shown and together include the 98 most significant centres in Greater London. Other service centres, which are not shown, range down to small groups of a few shops.

ROYAL COMMISSION ON LOCAL GOVERNMENT IN GREATER LONDON

EDUCATIONAL ADMINISTRATION

as at 1/4/60



Areas administ
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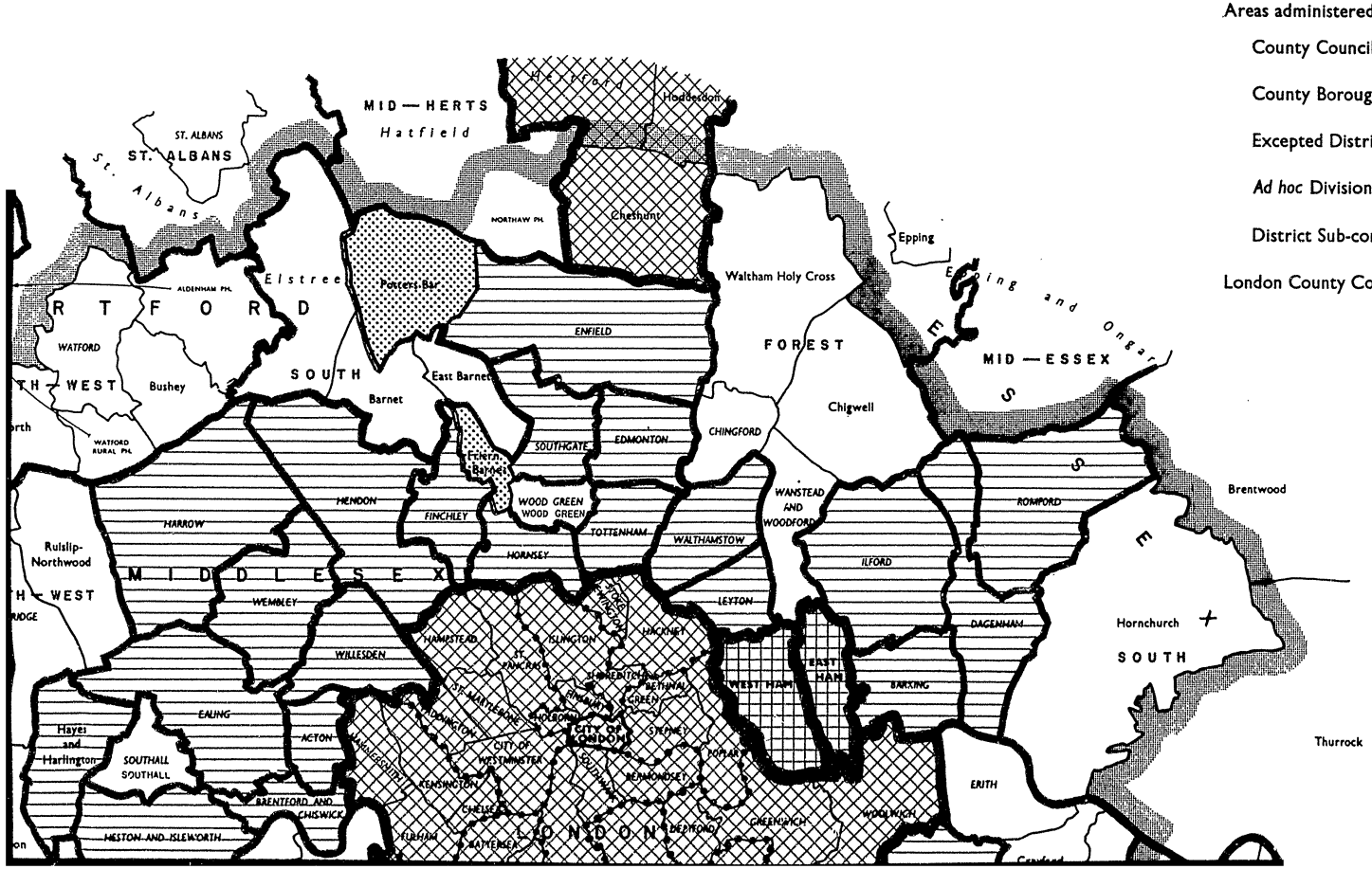
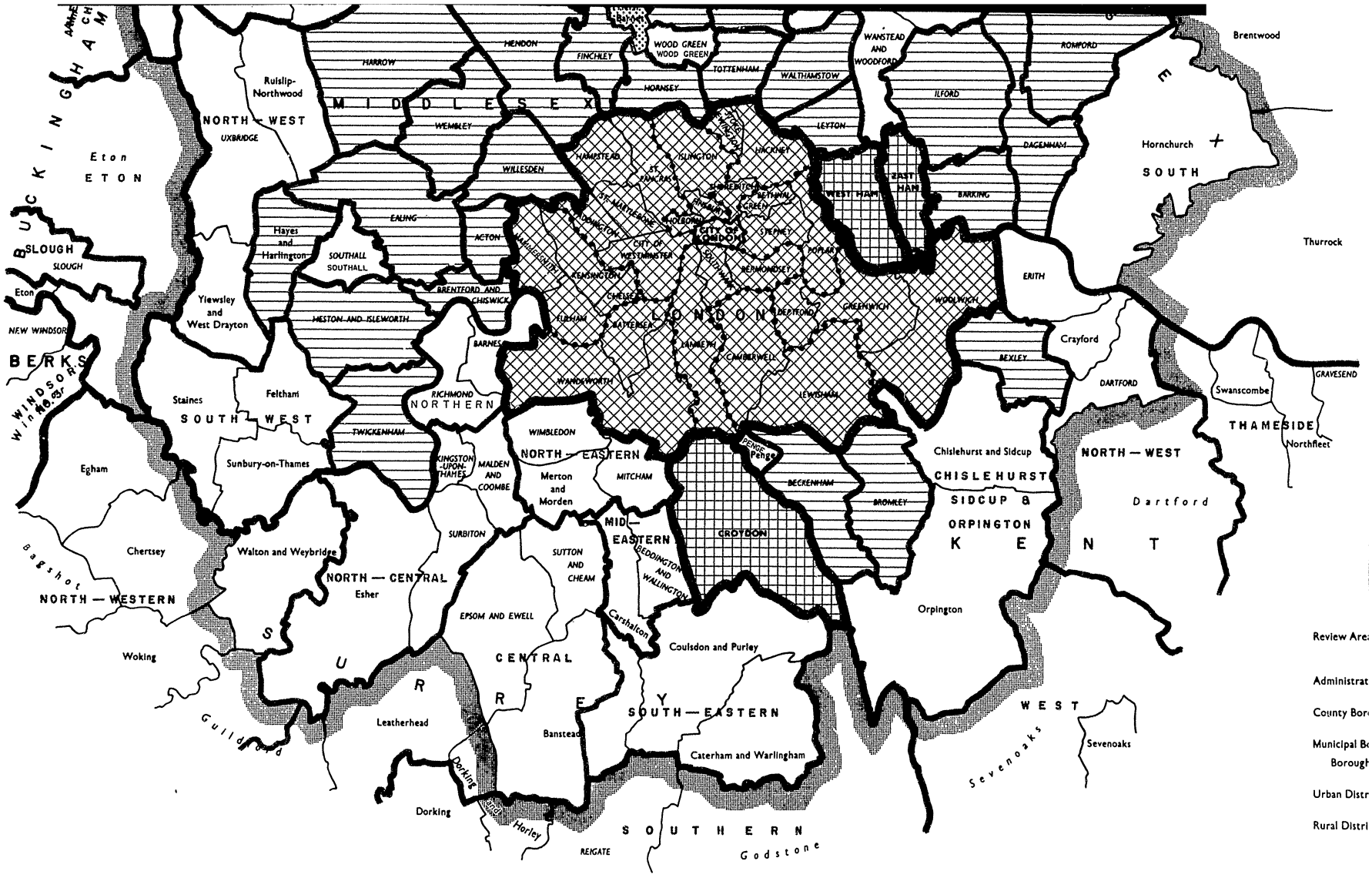
Ad hoc Divi
District Su
London Count

EDUCATIONAL ADMINISTRATION

as at 1/4/60





Review Are:

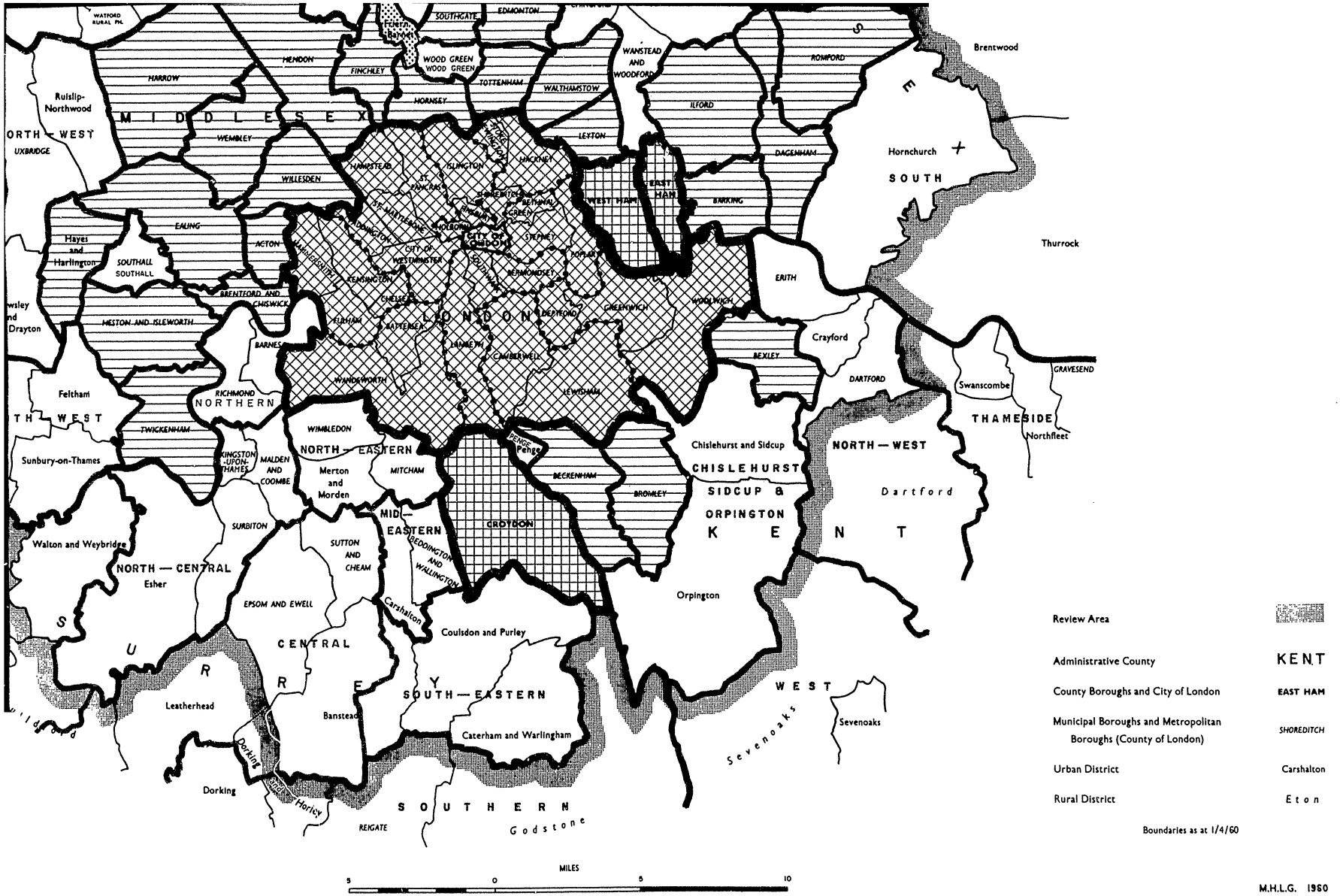
Administrat

County Bor

Municipal B
Borough

Urban Distr

Rural Distri



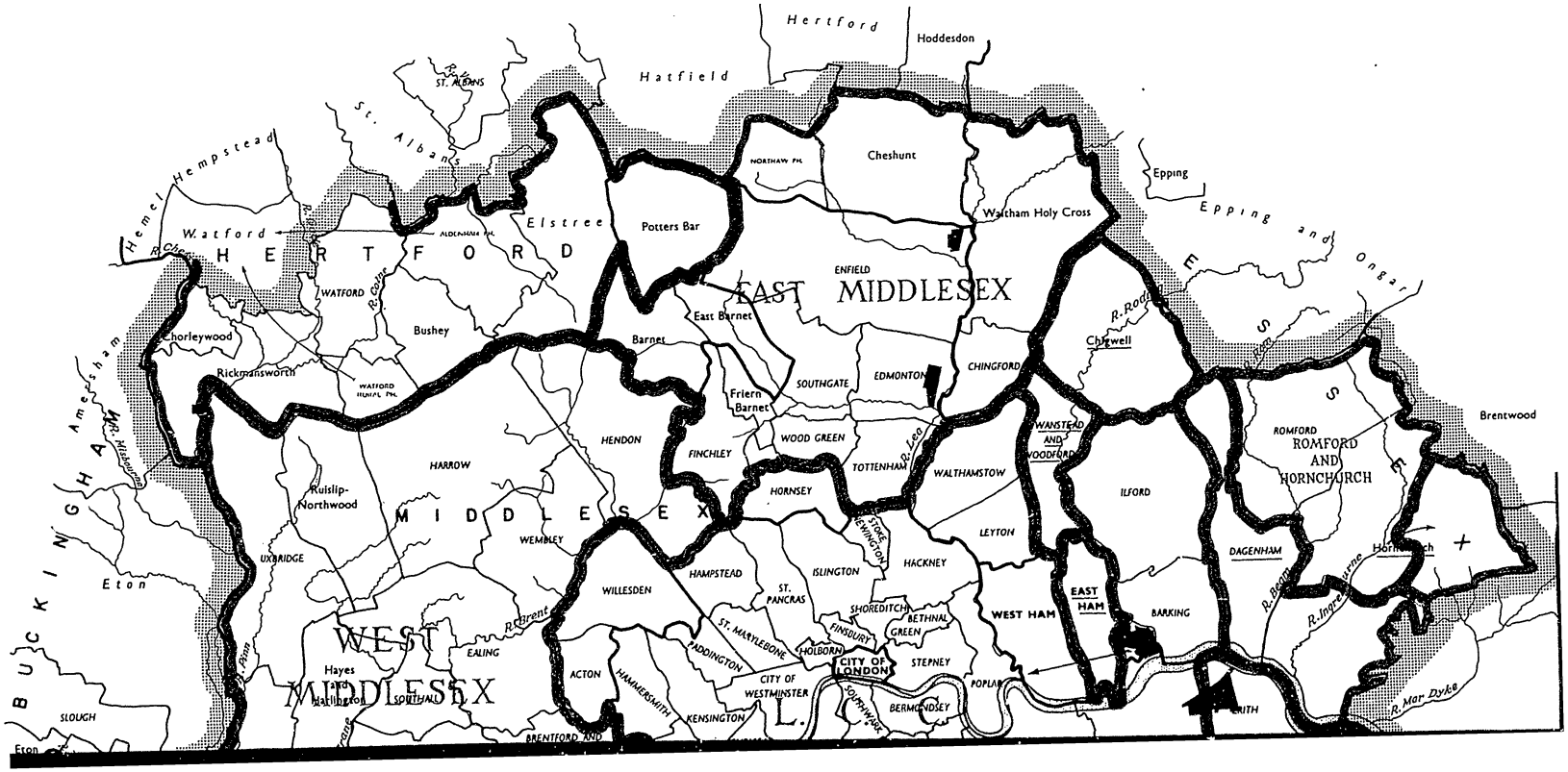
Review Area	
Administrative County	KENT
County Boroughs and City of London	EAST HAM
Municipal Boroughs and Metropolitan Boroughs (County of London)	SHOREDITCH
Urban District	Carshalton
Rural District	Eton

Boundaries as at 1/4/60

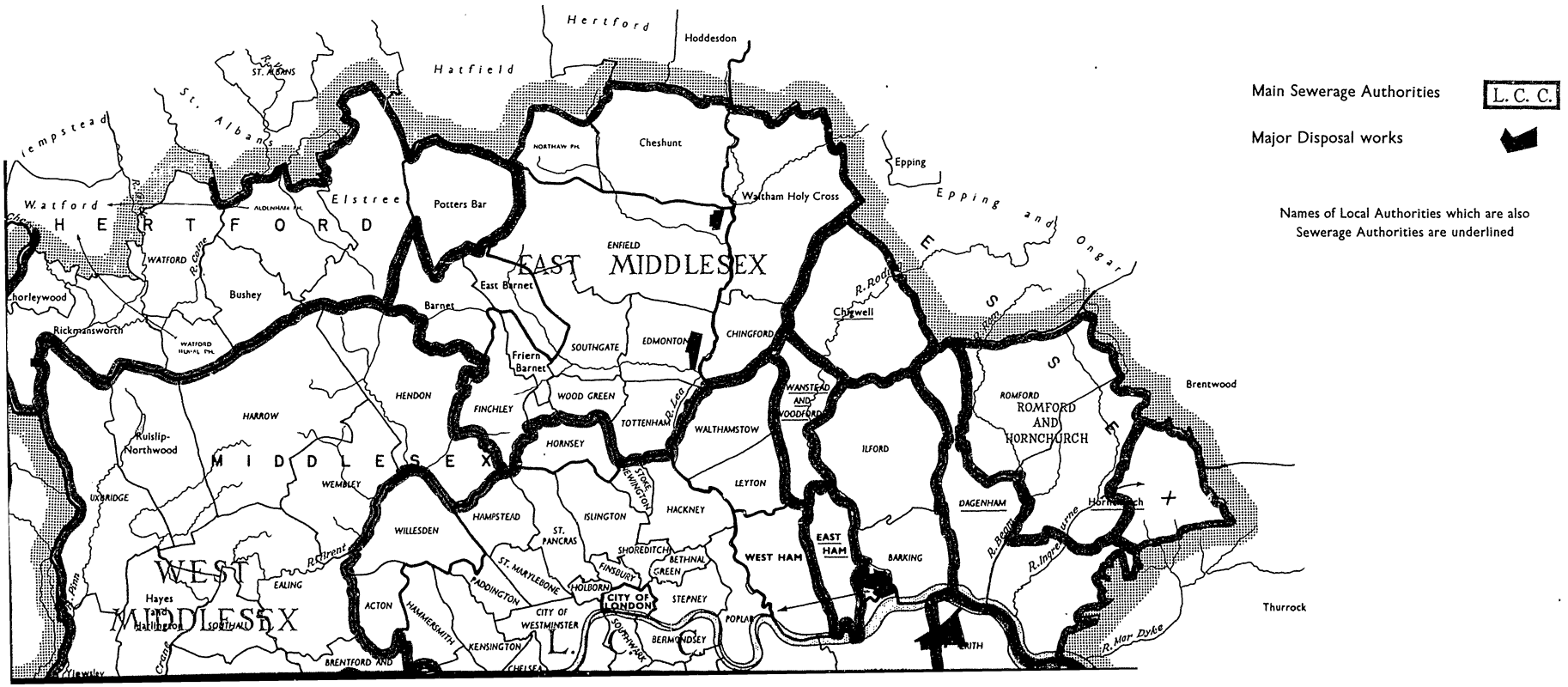
M.H.L.G. 1960
(M.F.P.)

ROYAL COMMISSION ON LOCAL GOVERNMENT IN GREATER LONDON

SEWERAGE AND SEWAGE DISPOSAL



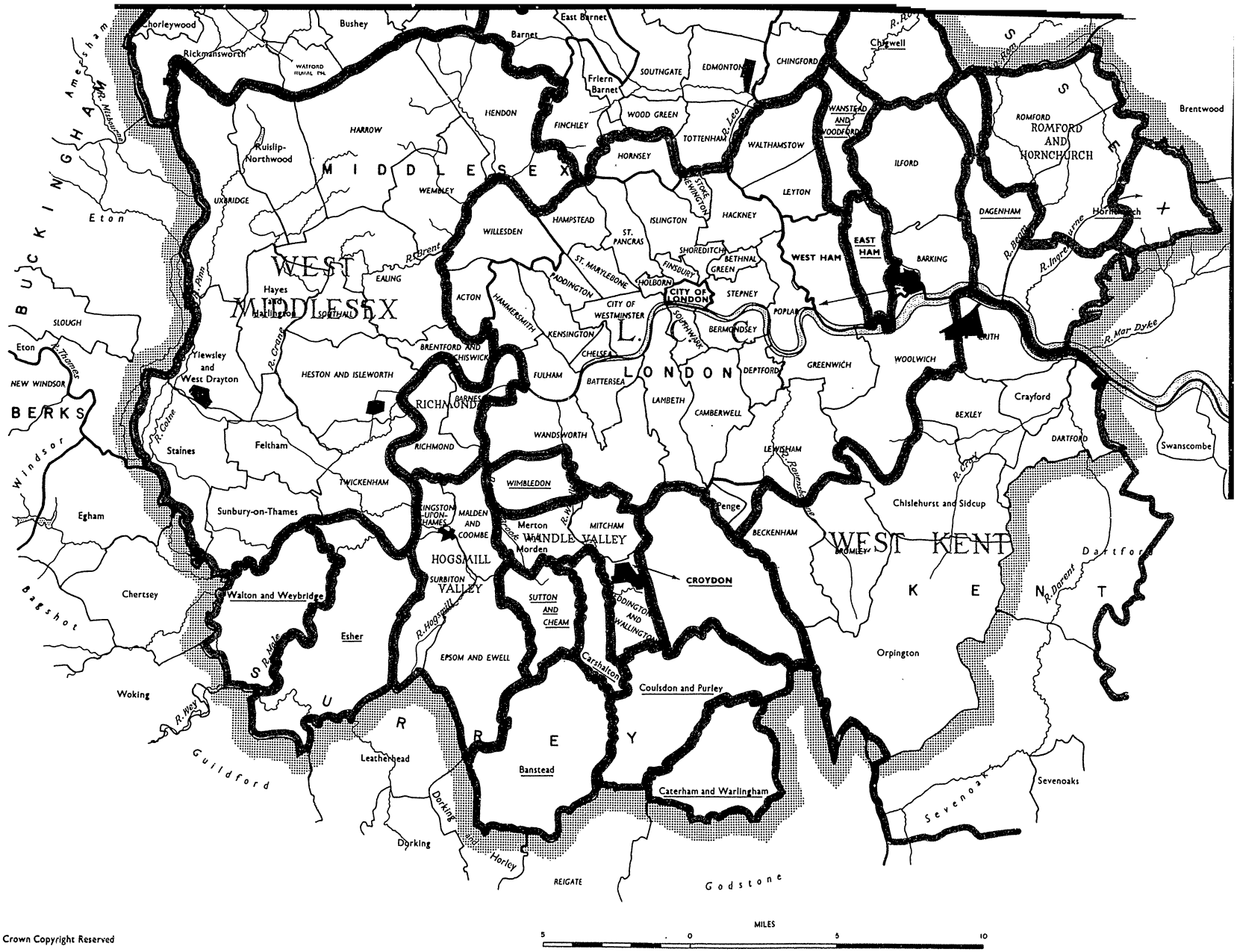
SEWERAGE AND SEWAGE DISPOSAL

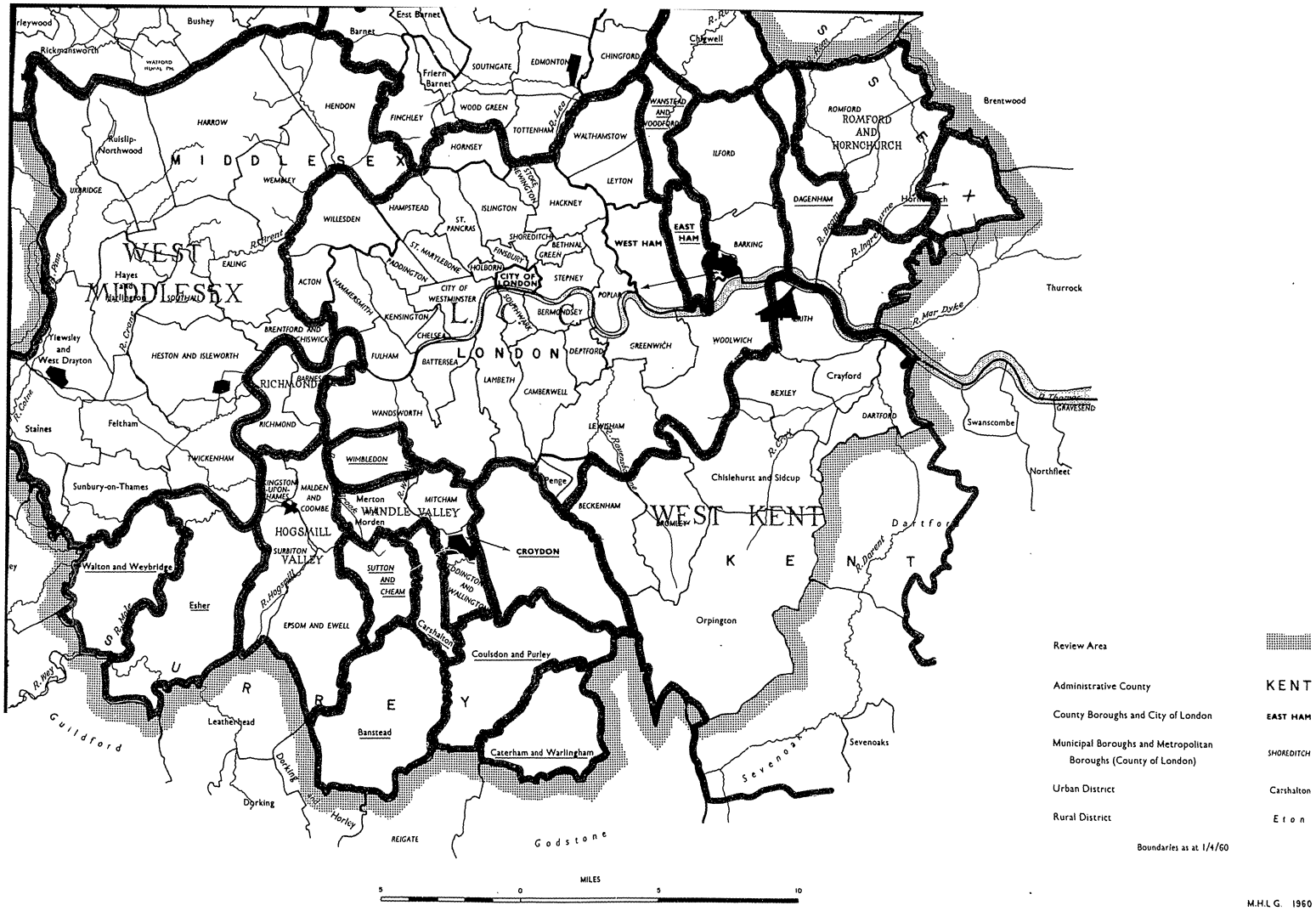


Main Sewerage Authorities L. C. C.

Major Disposal works

Names of Local Authorities which are also Sewerage Authorities are underlined





ROYAL COMMISSION ON LOCAL GOVERNMENT IN GREATER LONDON

CENTRAL AREAS

London Transport Central Area

London Transport Road Service Census Points
(south of the river)

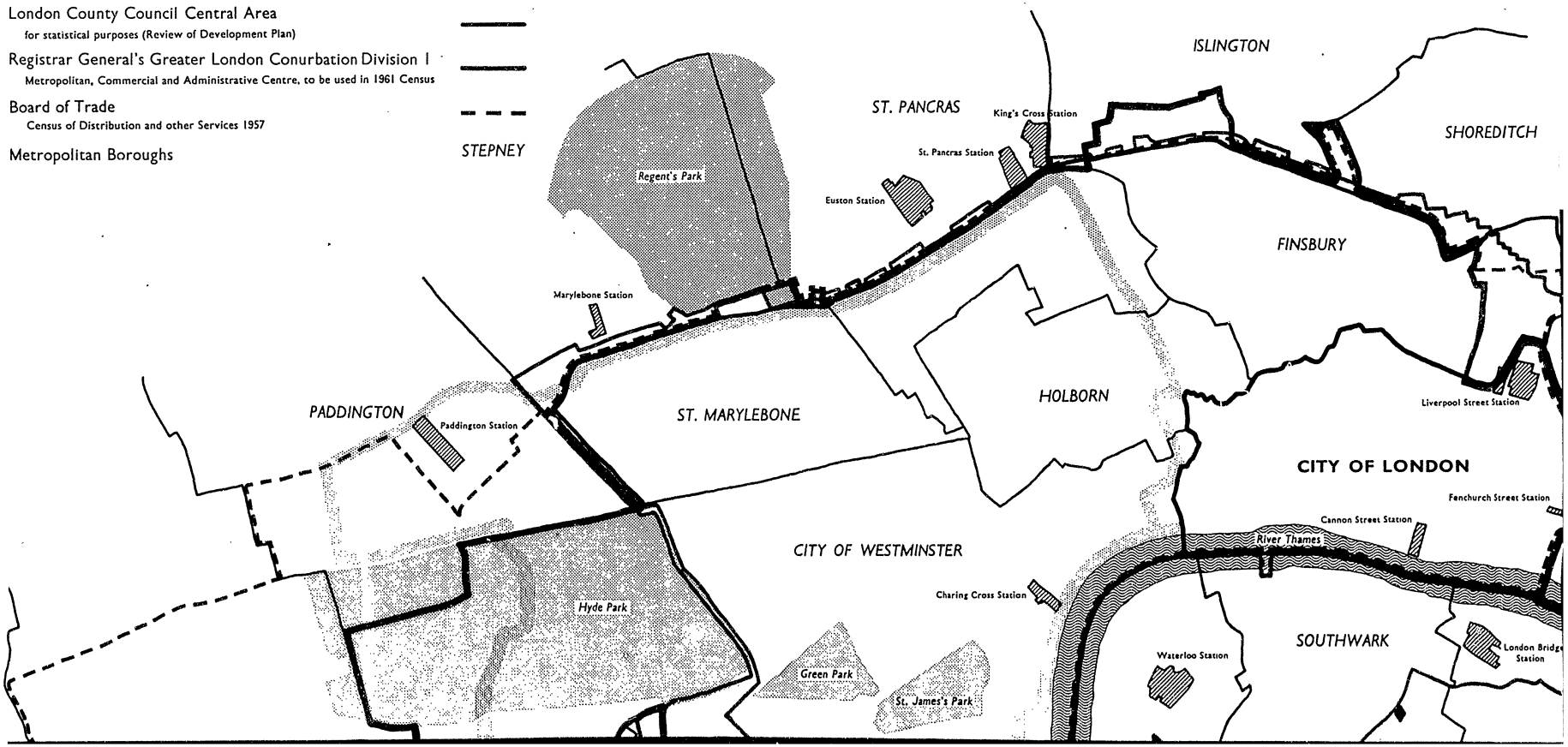
Metropolitan Police Central Traffic Area

London County Council Central Area
for statistical purposes (Review of Development Plan)

Registrar General's Greater London Conurbation Division I
Metropolitan, Commercial and Administrative Centre, to be used in 1961 Census

Board of Trade
Census of Distribution and other Services 1957

Metropolitan Boroughs



ROYAL COMMISSION ON LOCAL GOVERNMENT IN GREATER LONDON

MAP 12

CENTRAL AREAS

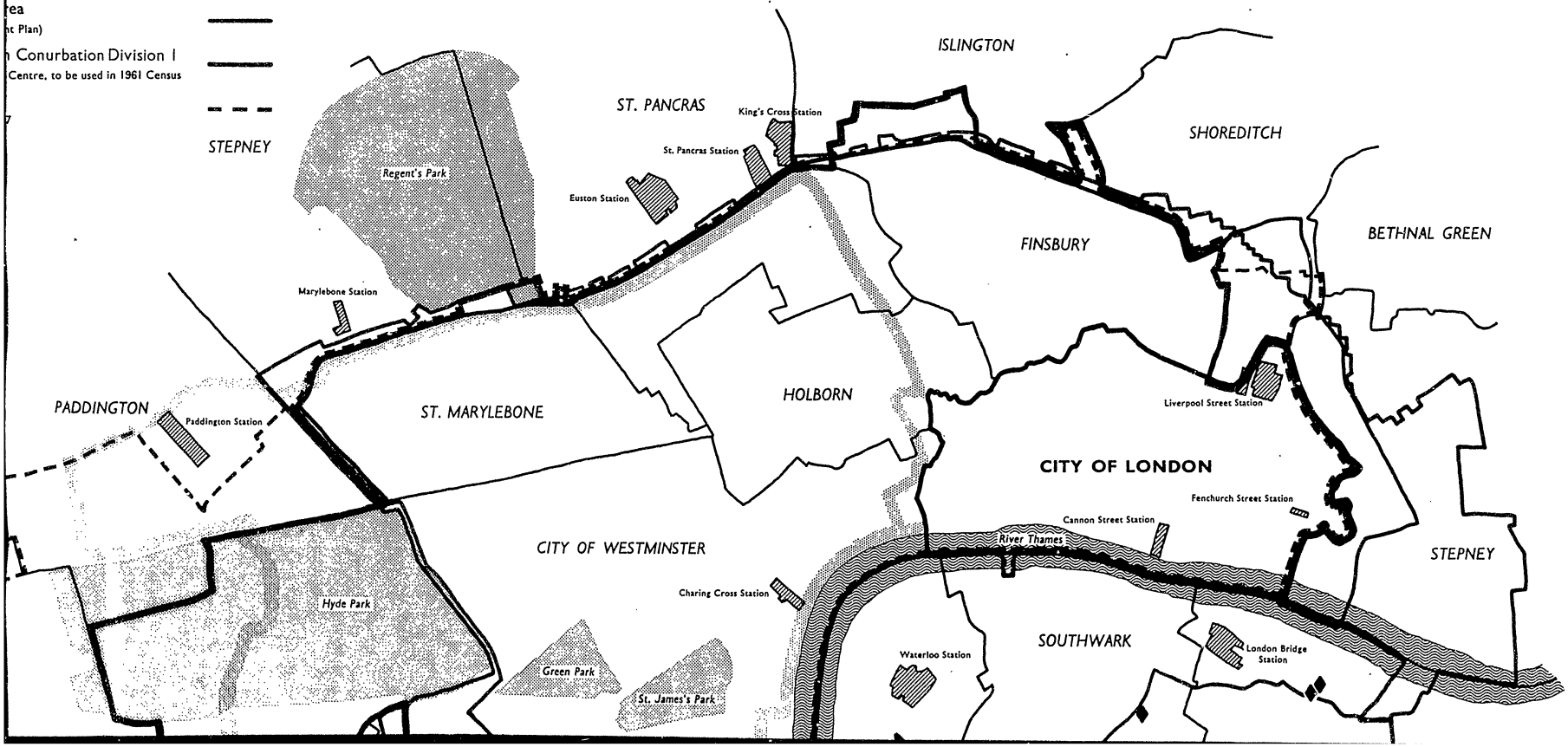
nsus Points

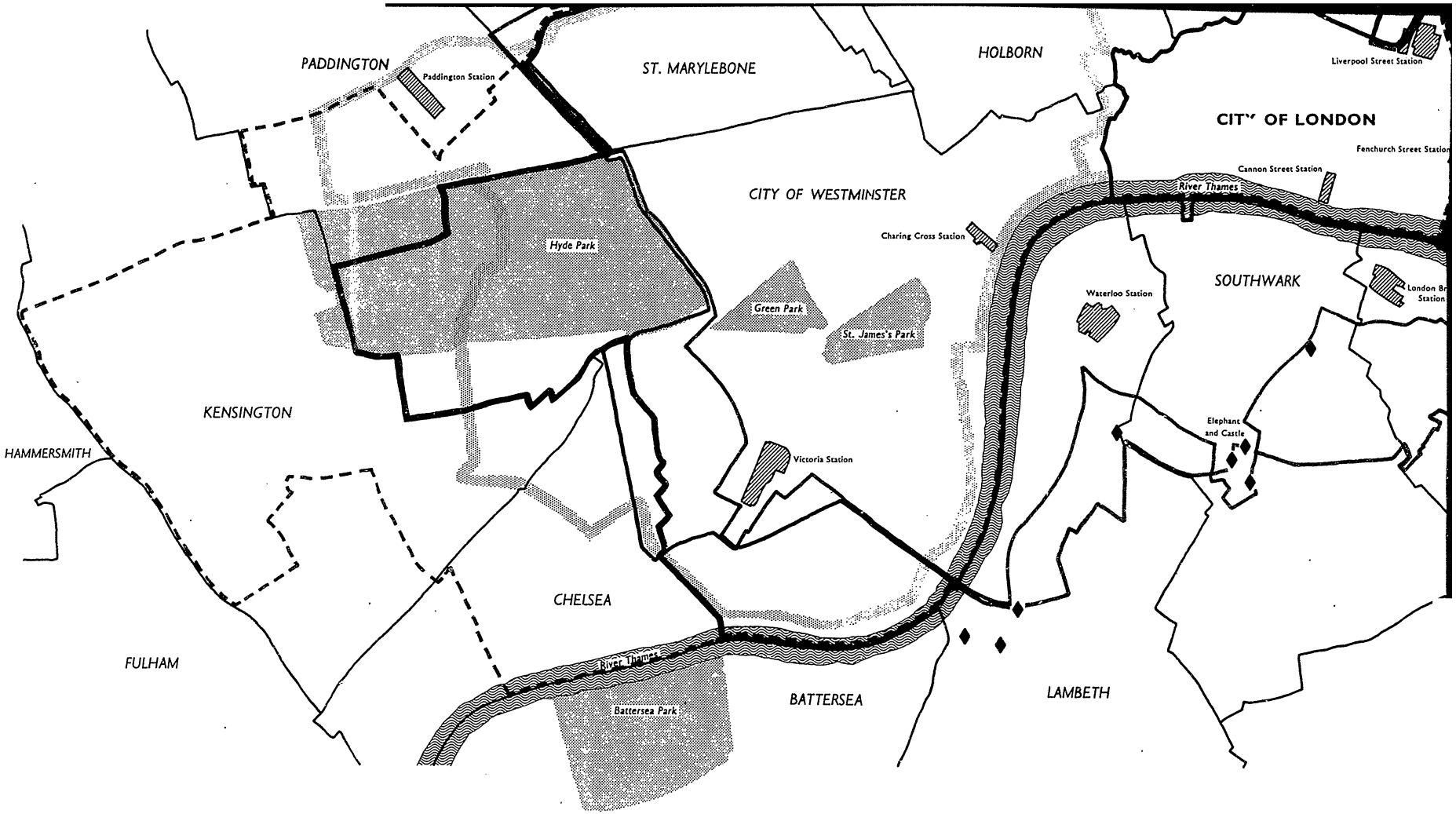
Area

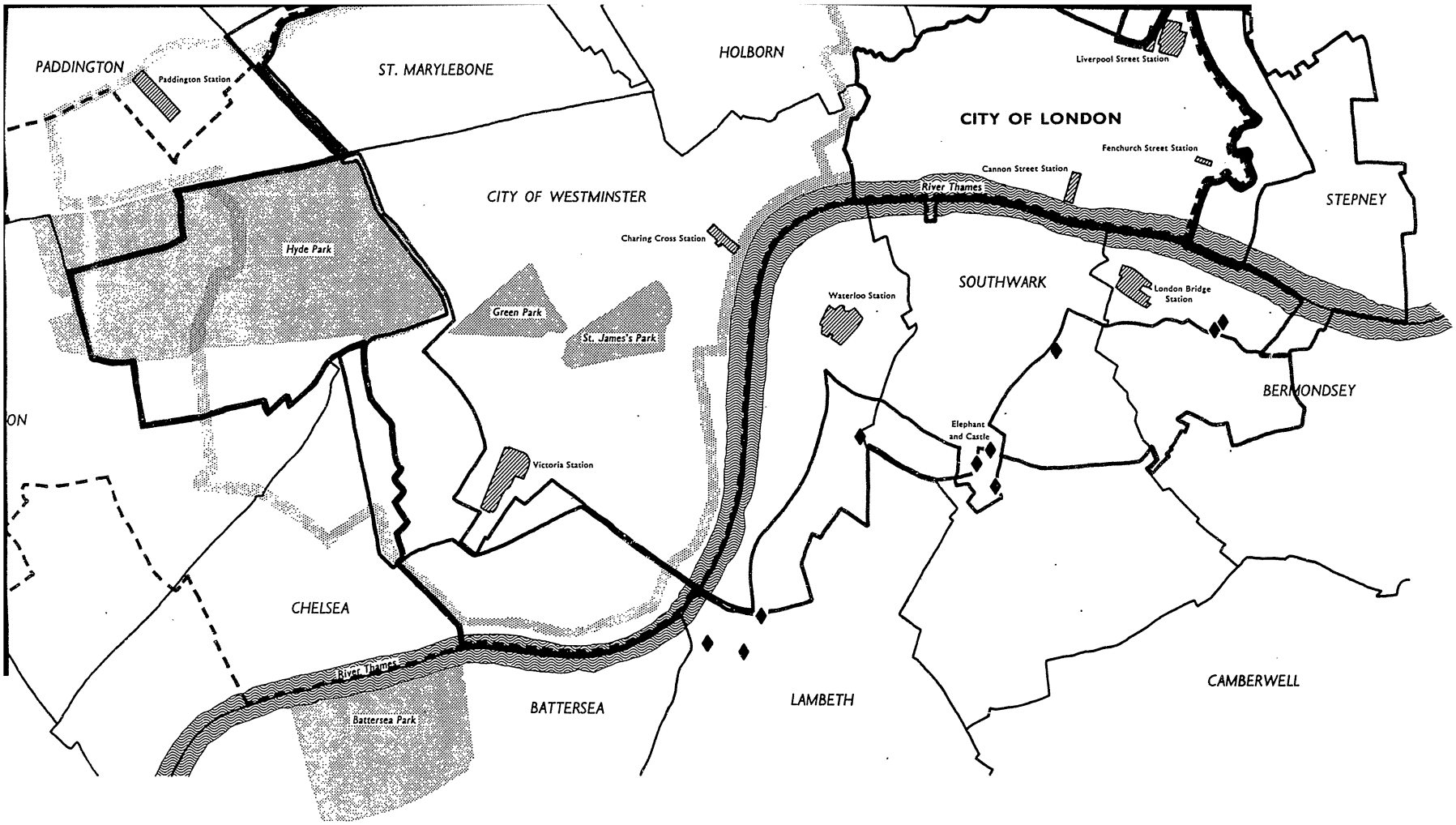
ea
t Plan)

Conurbation Division I
Centre, to be used in 1961 Census

7







M.H.L.G. 1960
(M F.P)