1939-40 [Cmd. 6163] **Committee of the Privy Council for Medical Research. Report of the Medical Research Council for the year 1938-1939**

COMMITTEE OF THE PRIVY COUNCIL
FOR MEDICAL RESEARCH

REPORT OF THE MEDICAL RESEARCH COUNCIL FOR THE YEAR 1938–1939

Presented by the Lord President of the Council to Parliament
by Command of His Majesty
January 1940

LONDON
HIS MAJESTY'S STATIONERY OFFICE
1940

Cmd. 6163

THE COMMITTEE OF THE PRIVY COUNCIL FOR MEDICAL RESEARCH

(Ex Officiis)

THE LORD PRESIDENT OF THE COUNCIL (*Chairman*).
THE MINISTER OF HEALTH (*Vice-Chairman*).
THE SECRETARY OF STATE FOR SCOTLAND.
THE SECRETARY OF STATE FOR HOME AFFAIRS.
THE SECRETARY OF STATE FOR DOMINION AFFAIRS.
THE SECRETARY OF STATE FOR THE COLONIES.
THE SECRETARY OF THE MEDICAL RESEARCH COUNCIL (*Secretary*).

THE MEDICAL RESEARCH COUNCIL

The Rt. Hon. LORD BALFOUR OF BURLEIGH (*Chairman*).
W. M. GOODENOUGH, D.L. (*Treasurer*).
R. K. LAW, M.P.
Professor M. J. STEWART, M.B., F.R.C.P.
Professor G. E. GASK, C.M.G., D.S.O., F.R.C.S.
Professor L. J. WITTS, M.D., F.R.C.P.
Professor C. R. HARINGTON, Ph.D., F.R.S.
Professor W. W. C. TOPLEY, M.D., F.R.C.P., F.R.S.
*Professor A. J. CLARK, M.C., M.D., F.R.C.P., F.R.S.
*Professor T. R. ELLIOTT, C.B.E., D.S.O., M.D., F.R.C.P., F.R.S.
*Professor E. D. ADRIAN, M.D., F.R.C.P., F.R.S.
Sir EDWARD MELLANBY, K.C.B., M.D., F.R.C.P., F.R.S., K.H.P. (*Secretary*).

* Appointed at or after the close of the period covered by this report to succeed :—

Professor H. S. Raper, C.B.E., D.Sc., M.B., F.R.C.P., F.R.S.
Professor J. A. Ryle, M.D., F.R.C.P.
Professor J. Mellanby, M.D., F.R.S. (*died 15th July*, 1939).

TABLE OF CONTENTS

THE REPORT OF THE COMMITTEE OF THE PRIVY COUNCIL FOR MEDICAL RESEARCH

THE REPORT OF THE MEDICAL RESEARCH COUNCIL

I. INTRODUCTION

II. THE NATIONAL INSTITUTE FOR MEDICAL RESEARCH

III. THE DETERMINATION OF BIOLOGICAL STANDARDS AND THE METHODS OF BIOLOGICAL ASSAY AND MEASUREMENT

IV. CLINICAL RESEARCH UNITS

V. EXTERNAL SCIENTIFIC STAFF

VI. RESEARCH WORK AIDED BY GRANTS

VII. RESEARCH IN TROPICAL MEDICINE

VIII. INDUSTRIAL HEALTH RESEARCH

IX. TRAVELLING FELLOWSHIPS

X. PERSONNEL AND REPRESENTATION

Note.—A cross classification of the contents of the Report, based wholly on scientific subjects instead of largely on administrative arrangement, will be found at p. 158.

REPORT

OF THE

COMMITTEE OF THE PRIVY COUNCIL FOR MEDICAL RESEARCH

FOR THE YEAR 1938–1939

TO THE KING'S MOST EXCELLENT MAJESTY IN COUNCIL

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 ended on 30th September, 1939.

1. A grant-in-aid of £265,000 was provided by Parliament for the expenditure of the Medical Research Council during the present financial year. This was made up of provision of the same amount as in the year before for current purposes, with the addition of £70,000 specially provided towards the cost of the new buildings for the National Institute for Medical Research.

2. The estimates of the Medical Research Council for the present financial year are being met by our provisional allocation of funds under the following heads :

For administration, including expenses of the Council, of the administrative offices and staff, and of travelling, we have allocated £10,000.

For the expenses of the National Institute for Medical Research at Hampstead and of the farm laboratories at Mill Hill in association with it, for the salaries of the scientific staff and the expenses of research work done by them or by other workers temporarily attached, we have allocated £60,000.

For the salaries and expenses of scientific staff working elsewhere, including those in the units for clinical research maintained by the Council in certain hospitals, those attached to various universities and other institutions, and those engaged in statistical inquiries or in work under the Industrial Health Research Board, we have allocated in all £40,000.

For temporary research grants, both for personal remuneration and for expenses, to workers engaged in investigations at universities, hospitals, and other centres in the United Kingdom, for postgraduate studentships and research fellowships in clinical science and experimental pathology, and for research fellowships in tropical medicine, we have allocated in all £55,000.

For research in chemotherapy, at present partly in respect of the cost of the new buildings required, we have provided £30,000.

For the new buildings which are being erected at Mill Hill we have allocated—in addition to the amounts previously set aside for this purpose—£70,000.

3. In accordance with the provision of the Royal Charter, as amended in 1926, we determined by an Order dated 25th July, 1939, that Henry Stanley Raper, C.B.E., D.Sc., M.B., F.R.C.P., F.R.S. (Brackenbury Professor of Physiology in the University of Manchester), and John Alfred Ryle, M.D., F.R.C.P. (Regius Professor of Physic in the University of Cambridge), should be the members of the Medical Research Council to retire on 30th September, 1939.

By the same Order, after statutory consultations with the Medical Research Council and with the President of the Royal Society, we appointed Alfred Joseph Clark, M.C., M.D., F.R.C.P., F.R.S. (Professor of Materia Medica in the University of Edinburgh), and Thomas Renton Elliott, C.B.E., D.S.O., M.D., F.R.C.P., F.R.S. (Professor Emeritus of Medicine in the University of London and Consulting Physician to University College Hospital), to be members of the Medical Research Council from 1st October, 1939.

4. Since the end of the period under report, by an Order made on 9th November, 1939, after statutory consultations as aforesaid, we have appointed Edgar Douglas Adrian, M.D., F.R.C.P., F.R.S. (Professor of Physiology in the University of Cambridge), to be a member of the Medical Research Council in the vacancy caused by the death of John Mellanby, M.D., F.R.S. (Waynflete Professor of Physiology in the University of Oxford) on 15th July, 1939.

5. 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, 1939. This is the twenty-fifth annual report upon the research work falling now to their duty and formerly to that of their predecessors, the Medical Research Committee.

6. The public moneys available for the work of the Medical Research Council have again received important augmentations from other sources. Funds for the promotion of particular schemes of research have been provided by the Dental Board of the United Kingdom, the British Empire Cancer Campaign, the Trustees of the late Viscount Leverhulme, the Sir Halley Stewart Trust, the Rockefeller Foundation of New York, and the Miners' Welfare Fund. The assistance given by the Rockefeller Foundation was substantially increased during the year, and for this further generous act of co-operation special thanks are due. The parts of the Council's programme which have been aided in this way are mentioned under the appropriate heads in the report. Benefactions from private sources have included a donation by Mr. James Weir towards the cost of research on the radium treatment of cancer. Income from endowments received in earlier periods has also been available.

7. The Medical Research Council have continued to maintain close contact, at relevant points in their work, with the chief administrative Government Departments concerned with questions of health. They have in particular, as in previous years, co-operated with the Ministry of Health and the Department of Health for Scotland: as regards the health of industrial workers they have kept in touch with the Home Office and the Mines Department, while in problems of tropical medicine they have acted in consultation with the Colonial Office. In addition, the Council have assisted various other Departments which have from time to time referred problems of health to them for advice or investigation. The Council have again, also, been closely concerned with international health work under the League of Nations—especially in questions of nutrition and of biological standards, upon the commissions dealing with which they are directly represented.

8. During the past year the Medical Research Council and their officers have been increasingly called upon for assistance in framing plans for emergency medical services of various kinds which would be required in the event of war. Since the outbreak of hostilities they have had the responsibility of administering certain of these services which were placed under their direct control: the expenditure involved is being met from funds specially provided for the purpose. They have also been called upon by the Defence Services and Government Departments for advice as to the application of new knowledge in many directions. As the war proceeds, the Medical Research Council will be required to undertake the investigation of special medical problems as these arise: some of them can be foreseen, and steps which have already been taken to promote new researches are mentioned in the following Report.

9. Effective consultation on questions of common interest has been maintained between the Medical Research Council, the Department of Scientific and Industrial Research, and the Agricultural Research Council, acting under their respective Committees of the Privy Council. The Medical Research Council have also continued to correspond with research organisations and institutions overseas, especially in the Dominions and in India, having scientific interests equivalent to their own.

STANHOPE,
Lord President.

EDWARD MELLANBY,
Secretary to the Committee of the Privy Council for Medical Research.

23rd January, 1940.

MEDICAL RESEARCH COUNCIL

Temporary Office: c/o London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.

Headquarters Staff

Sir EDWARD MELLANBY, K.C.B., M.D., F.R.C.P., F.R.S., K.H.P. (*Secretary*).

A. LANDSBOROUGH THOMSON, C.B., O.B.E., D.Sc. (*Principal Assistant Secretary*).

F. H. K. GREEN, M.D., M.R.C.P.

D. V. T. FAIRRIE, B.A., A.C.A. (*Finance Officer*).

D. K. M. CHALMERS, M.D., D.P.H. (*see also p.* 37).

F. J. C. HERRALD, M.B., M.R.C.P.E.

Air Vice-Marshal Sir DAVID MUNRO, K.C.B., C.I.E., M.B., F.R.C.S.E. (*Secretary, Industrial Health Research Board*).

REPORT

OF THE

MEDICAL RESEARCH COUNCIL

FOR THE YEAR 1938-1939

TO THE LORDS OF THE COMMITTEE OF THE 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 year from 1st October 1938 to 30th September 1939.

I. INTRODUCTION

The Council offer as usual, by way of Introduction, some general observations on matters of current importance or special interest. These will be followed, in subsequent sections, by more systematic accounts of the research work done during the past year, either directly for the Council or with their assistance. This work includes that of the Council's staff, whether in their own laboratories at the National Institute for Medical Research, in the clinical units which they have established in various hospitals, or elsewhere. It also includes, although the reference has necessarily to be brief, the numerous researches which are aided by grants from the Council in universities, hospitals, and other institutions throughout the country.

Medical Research and the War

During the past year the work of the Medical Research Council has gone steadily forward and, except in the case of their administrative staff, the continuous state of war expectancy affected it but little until the late summer. The policy of the Council has been to encourage their research staff and grantees to continue their investigations as under normal conditions. On the outbreak of war this policy has been maintained, although some research workers have had to respond to special calls—to join the Defence Services, to take part in emergency schemes, or to undertake special investigations suggested by war conditions.

It cannot be denied that the disturbed political atmosphere of the past year has brought increased difficulties to those whose work depends so greatly upon concentration of thought and action, and upon freedom from worry. At the same time, perusal of this Annual Report, and especially the account of the work done at the National Institute for Medical Research and at other special centres throughout the country, will show that a harvest of discovery has been procured in spite of the unrestful situation.

The Council foresaw that the work at the National Institute would be at least as important in time of war as in time of peace, and took

action to provide protection for the staff at Hampstead. Since the outbreak of hostilities, therefore, the staff of the National Institute have been able to proceed with their work. It cannot be expected, however, that medical research either there or elsewhere can remain unaffected by war. Apart from changes and possibly some reduction in personnel, the natural desire of many investigators is to leave their peace-time problems and direct their attention to subjects of immediate war interest. The presentation of new war problems requiring investigation is therefore usually received with enthusiasm by the research worker. The danger, in fact, is not that of failure to investigate such problems but rather that, by switching over to other objectives of immediate practical interest, the fruits of promising research unrelated to war should be lost. It is the intention of the Council, so far as they are able, to prevent such losses to important knowledge.

At the same time, it is recognised that war conditions in themselves offer special opportunities for the acquisition of knowledge which is by no means of emergency interest only. It will be remembered, for instance, that the Medical Research Council (then Committee) came into being immediately before the last war, and during their early years directed most of their attention and energy to the solution of problems presented and made urgent by the emergency. In the words of the Annual Report for 1917–18, " the needs of war have given stimulus to enquiries upon many sides, and out of the circumstances of the time some unusual opportunities and facilities have come to scientific workers ". The history of work done during the years 1914–18 is a remarkable one, and a perusal of the records of the Medical Research Committee of those years cannot but excite admiration both for the success with which the opportunities offered were seized by workers in this field and for the inspiring energy with which the Secretary, Sir Walter Fletcher, carried out the general policy. It was the first time in the history of this country that organised scientific endeavour in medical research ever had a chance of justifying itself, and right well did it respond.

While it is impossible to detail all the problems studied and the knowledge gained during the last war, by investigations initiated by the Medical Research Committee, an idea of these activities can be obtained by the mere mention of the special committees set up at that time. These included committees for the study of (1) surgical shock and allied conditions, under the chairmanship of the late Sir William Bayliss ; (2) chemical warfare medical investigations, under the chairmanship of the late Professor A. R. Cushny ; (3) anaerobic bacteria and infections, with Professor William Bulloch as chairman ; (4) air medical investigations, with Sir Henry Head as chairman ; (5) amoebic and bacillary dysentery, with the late Sir William Leishman as chairman. Memories of important contributions to knowledge will also be recalled by mention of the war-time investigations concerned with the treatment of infected wounds by saline solutions and by new antiseptics such as eusol, Dakin's

solution and acriflavine ; with infections, including those of typhoid, paratyphoid and cerebrospinal fever ; with trench (war) nephritis ; and with gunshot wounds of the chest. Advances were made in the treatment of surgical shock and allied conditions, in work on " gassed " patients, and in investigation of nerve injuries. Important enquiries were initiated in the then new field of the physiological problems of flying. Difficulties arising at home, especially in industry among munition factories, owing to bad environmental conditions of labour working under abnormal pressure, were met by the setting up of the Industrial Fatigue (now Health) Research Board. Special problems, such as the poisoning of industrial workers by trinitrotoluene, also demanded and received the attention of the scientific investigator.

The Medical Research Committee undertook for the Army Council the large enterprise of compilation and analysis of medical records. This was maintained by their Statistical Department, housed for the time in the British Museum. The results thus obtained formed the main record available for the adjudication of future pension claims, as well as providing the data upon which statistical analysis of injuries or diseases could be made. The magnitude of this undertaking can be realised by the fact that at the end of the war the Statistical Department of the Medical Research Committee was receiving inquiries from the Ministry of Pensions at the rate of 1,500 a month. In addition, health and injury records were extracted and handed over to the corresponding authorities in Canada, Australia and New Zealand.

It may also be well to recall that the research on war problems promoted by the Medical Research Committee at that time was greatly helped by the close working arrangements between the Committee and the Army. In particular, the appointment of Professor T. R. Elliott as consultant physician in France allowed the early transmission of information on the special problems urgently needing enquiry from the Army Medical Service to the Medical Research Committee, so that the attention of investigators at home could be quickly directed to the subjects requiring study.

Most of the research initiated and controlled during the years 1914–18 was directed to the immediate problems of war ; but it is worth recording that, among what were then regarded as more academic problems, the subject of nutrition received substantial support by the Medical Research Committee from the outset of their work. Before the end of the war, nutritional questions had become matters of major importance, both for the Services and the civilian population. These investigations became, therefore, of great value in giving practical guidance in feeding both the forces in the field and the civilians at home. It will be remembered that, immediately following the war, knowledge of the feeding of children was greatly changed by this work. The high incidence of nutritional disease, and especially that of rickets among the children of former enemy countries, was combated most effectually by knowledge gained in this country during the war period.

It will be asked what contribution medical investigation can make in the present war. At the moment this question is almost impossible to answer. Although substantial knowledge has been gained in the twenty years that have elapsed since the last war, it is quite certain that many of the old problems of shock, of wound infection and of the hygiene of warfare will again claim great attention. In the case of wound shock, modern work has made it clearer that injury to the tissues brings into play factors which disorganise both the nervous system and the normal chemical reactions of the body. One of the main objects of research must be to find out how these " insults " to the nervous system are related to the liberation of toxic chemical factors. As regards the treatment of shock, modern research has continued to emphasise the great importance of increasing the fluid in the general circulation. It is at least certain that the more recent developments of blood transfusion, together with a well organised service for allowing this to be carried out on a large scale, will lead to results far better than those obtained by the transfusion of gum acacia solution introduced in the later part of the war of 1914–18 through the work of the Committee on Shock.

In the case of wound infection, probably the largest single cause of death among wounded men reaching hospital in the last war, it can be safely predicted that modern discovery in the chemotherapeutic treatment of bacterial infection will be one of the outstanding beneficial factors. Where the infection is due to haemolytic streptococci, it may be hoped that the established curative effect of the sulphanilamide group of compounds will be as successful in wounded men as it has proved in puerperal sepsis and septicaemia. The evidence of the curative effect of these compounds in gas-gangrene infection is not so certain, but what evidence there is suggests that in this case also they will be life saving. It will be necessary as soon as possible to get evidence on this point, and especially to evaluate the relative curative effects of the sulphanilamide compounds and gas-gangrene antitoxin. Although the use of gas-gangrene antitoxin still receives wide support, its beneficial effects have never been established with certainty. Needless to say, however useful the new chemotherapeutic compounds will prove, it is not likely that the need for proper surgery in the treatment of wounds will diminish.

Another matter which presses for early solution is the possible prophylactic effects of the sulphanilamide derivatives, apart from their curative action. Arrangements have already been made by the Army Medical Service to determine whether the administration of these compounds immediately following injury will prevent subsequent infection by the more common pathogenic micro-organisms. There will be, no doubt, many minor problems arising out of the extension of this knowledge to the present war, but generally speaking it would appear probable that the back of the enormous problem of bacterial infection of wounds had been broken before the war began, and it only remains to see that the best skill is directed to the application of this knowledge.

In pneumococcal pneumonia, also, it can be predicted with assurance that the use of sulphapyridine will effect a substantial reduction in the death rate and in the time spent in hospital. It will indeed be a great triumph if published results on the treatment of pneumonia in civil life can be repeated under war conditions. How great may be the saving of life in pneumonia by this new treatment can be seen in the reduction of mortality rate reported by Gaisford among patients under fifty years of age. In cases treated with sulphapyridine the death rate was 1·6 per cent., while among those not receiving this drug 17 per cent. died. Other published results of the curative effects of this drug in gonorrhoea and cerebrospinal meningitis indicate that these diseases also will not now cause the serious damage which they did in the last war. For instance, those with great experience in the treatment of gonorrhoea claim that nearly 90 per cent. of cases can now be cured within a week, whereas previous curative treatment often required five or more months. The case mortality in untreated cerebrospinal meningitis has varied from 37 per cent. to about 90 per cent. In a recent series of 72 cases of this disease treated with sulphanilamide and sulphapyridine by Dr. Banks, there was only one death, giving a mortality rate of 1·4 per cent. It will be necessary to establish the best methods for avoiding or minimising the harmful effects these drugs are also capable of producing.

In time of war, or when war is prominent in men's minds, it is common to read and to hear the accusation that modern science is wholly given over to the promotion of instruments of destruction. Little can those who make such statements know of the discoveries of medical science and their effect on war. It is probably true to say that, up to the present century, more wars were decided by the incidence of disease than by military prowess and equipment. In other words, every army in the field had to fight disease—a more powerful enemy than its immediate human adversary. Plague, typhus, dysentery and other infections, often acting in association with nutritional deficiency, were the main arbiters of war. The power of Napoleon himself was probably more broken by the disease of his troops than by military opposition. This was notably so in his retreat from Moscow. Of his later army of 500,000 men raised in 1813, only 170,000 remained to fight the allies at Leipzig, 105,000 having been lost in previous battles and 219,000 through disease. As late in history as 1856, during the Crimean War, the French lost 20,356 by wounds, but 49,815 died of disease, while the British lost 4,947 by wounds and 17,225 by disease. In the South African War of 1899–1902 the British lost many more men through enteric fever than were killed in battle or died of wounds. On the other hand, medical science had advanced sufficiently by this time to eliminate such diseases as typhus and plague. In the war of 1914–18 enteric fever had become preventable by inoculation, and the incidence of this disease was almost negligible among the troops of western countries.

With assured protection against most diseases contracted under war conditions, the outcome of military action in the last war depended more on the weight and efficiency of machines of destruction, although nature was even then prepared to give a demonstration of the relative destructive capacity of military weapons and disease. The influenza pandemic of 1918–19 killed ten million people in the course of a few months, as compared with the seven million men killed during the four years of the war.

In the last war, however, military arms were much aided in their destructive effects by the inability of medical men to control the deadly results caused by the invasion of wounds by pathogenic micro-organisms, and it is quite certain that, had such infection been preventable, the total list of deaths would have been tremendously reduced—some authorities guess by at least 50 per cent. Medical science at an early stage in the war won an important battle against wound infection by giving every wounded man a protective dose of tetanus antitoxin. As pointed out on page 27, it is hoped that a further advance in knowledge of the prevention of tetanus will reduce the incidence of the disease in the present war almost to the point of elimination. In addition, as mentioned above, there are now hopes that the two types of bacteria previously mainly responsible for wound infection and death, namely haemolytic streptococci and the bacilli of gas-gangrene, can now be much more successfully combated than ever before. In other words, medical science has approached the point where most wounded men who escape the immediate lethal shattering of military weapons, and who receive early attention, can be expected to survive their injuries. In the dance of death, war will receive less help from death-bringing micro-organisms.

The history of war is, in one sense, largely a race between the development of instruments of physical destruction and the advancement of medical knowledge for saving the life of wounded and sick men. The destructive power of arms will indeed have increased immensely since 1918 if it overshadows the advances in knowledge for the saving of life which modern discovery has placed at the disposal of medical men. If a strict comparison were made between what science has done to increase war mortality and what medical science has done to lessen these lethal effects, there is good reason to believe that the latter would be an easy winner. No man with any knowledge of the history of disease in relation to war would ever say that science is wholly given to the forging of instruments of destruction.

However great may have been the effect of progress in medical knowledge on war mortality, this is only a part of its much greater beneficial effect on disease in general. Two hundred years ago, 74 per cent. of all children born in London died before reaching the age of five. Now the corresponding figure is probably less than 10 per cent. In the last fifty years, expectation of life for a newborn child has increased by sixteen years.

There can be no doubt that the essential factor in this revolutionary change in health has been increase in knowledge; and that even greater success may be expected in the future if this growth in knowledge is allowed to proceed without hindrance. However great the size and however fine the equipment of hospitals, however numerous and skilful doctors and nurses may be, success in their efforts must depend primarily on knowledge of the means for the prevention and cure of disease. Knowledge comes by investigation, made usually by those trained in research, although it is true that important discoveries have been made by men in the ordinary course of medical practice. This was, of course, frequently the case during the years when the advance of medicine depended mainly on the direct observation of sick people; but, since the opening of the experimental era, it is possible to attack medical problems from so many angles that a research worker versed in several different techniques is more likely to deal successfully with these questions. Cases innumerable can be quoted, and many instances have been given in these Annual Reports, where the finest medical care has failed until new knowledge of a preventable cause, or of a new drug, or of some other form of treatment has been made available by research. And yet, although the truth of these statements is self-evident, many people would be prepared to give unlimited endowment to hospital buildings and equipment, and still hesitate over the provision of a minute fraction of such expenditure for medical research. It ought to require but little wisdom and foresight to realise the enormous return in terms of health, physique and prolongation of life that has followed the relatively small expenditure of public and private funds on medical research during the present century.

War Emergency Services

During the two years preceding the war the Medical Research Council were entrusted with a number of responsibilities, on behalf of H.M. Government, for the preparation of various emergency medical services. The nature of these was briefly indicated in the last Report, and they can now be more fully described. The actual outbreak of war has involved the Council in further responsibility in giving effect to the arrangements which had been made, and other tasks have since been added. This work has occupied much of the time of the administrative staff and of certain technical advisers. Except where the work has been definitely of a research nature, the cost of it has, of course, not been met out of the funds available for medical research, but has been specially provided through the different Departments to which the assistance has been given—the Ministry of Health, the Department of Health for Scotland, the Home Office, the Admiralty, the War Office, and the Air Ministry.

Medical Supplies

One of the first things of the kind which the Council were asked to undertake was the organisation and supply of certain antitoxins to be held in readiness for war purposes. These were, in particular,

tetanus antitoxin and gas-gangrene antitoxin. It was clear that these materials would be required on a scale out of all proportion to normal stocks and rate of production. It was also necessary to co-ordinate the supply for the Defence Services on the one hand and for the civilian hospital organisation on the other. Arrangements were accordingly made for increased production by British laboratories and for the accumulation of reserve stocks. The Council are similarly dealing with the question of further supplies required during the war. They are not responsible for the distribution of these materials in detail, but they control a pool upon which the Services and Departments concerned are able to draw as occasion arises.

In addition to these antitoxins required for casualties, some provision was also made of various vaccines and sera which might be needed in dealing with outbreaks of epidemic disease. The object in this instance was to form a special reserve stock to supplement supplies ordinarily available.

Although the Council had no direct responsibility for other medical supplies in time of war, they were represented on the official Committee dealing with the subject, and their officers made various inquiries on behalf of that body. Since the beginning of the war they have taken an active part in arranging for the rapid production in this country of important drugs previously obtainable only from abroad; this work has involved the co-operation of manufacturing firms, chemists, pharmacologists and clinicians.

In consultation with the Ministry of Health, a special committee has been invited by the Council to consider the subject of essential drugs to be used under war conditions, and to give guidance to those responsible for large scale purchase and supply.

Specialist Personnel

The ordinary work of the Council places them in a unique position as regards contact with those who have special knowledge of different branches of medical science and allied subjects. They have thus, both before and since the outbreak of war, been able to assist in finding men possessing the highly specialised qualifications required for various items of emergency work which have arisen.

On a wider basis, they have accepted responsibility for the registration of all pathologists and medical bacteriologists, and of experienced technicians in the same subjects, as it was evident that large numbers of these would be required both by the Services and for civilian work. This register has served as a source of information where emergency posts have had to be filled; and it has at the same time helped to prevent the removal of essential personnel from work which would continue to be important in war-time. This activity has been closely co-ordinated with the similar functions undertaken by the Central Emergency Committee of the British Medical Association on the one hand, and by the Royal Society and the Ministry of Labour and National Service on the other.

Emergency Public Health Laboratory Service

The chief task specially entrusted to the Council—outside the scope of their ordinary functions—was the organisation of an emergency laboratory service, to operate under their own direction in augmentation of existing facilities. It was considered desirable to provide against the increased danger of epidemic disease resulting from evacuation schemes and other movements of the population, and from disorganisation of normal arrangements. The laboratory services available for public health purposes in many parts of the country unfortunately left much to be desired in ordinary circumstances, and were incapable of dealing with any great increase of work: in areas well served in this respect, no attempt was made to supplant existing laboratories which were able to continue functioning in a satisfactory manner.

The emergency service was mobilised at the outset of the war. It consisted of three central and sixteen subsidiary laboratories, in different parts of England and Wales, under the direct control of the Council. In addition, arrangements were made for ten subsidiary laboratories on the outskirts of London to be administered as part of the Emergency Hospital Service for the area; six University laboratories in the Midlands and North of England were also associated with the scheme. Similar arrangements were made by the Department of Health for Scotland in consultation with the Council.

A great deal of organising work was naturally involved in developing this scheme. Accommodation which could be used for laboratory purposes had to be found at suitable places, and for the most part this was done by arrangement with universities and public schools where this was possible without seriously interfering with the teaching of science. Provision had to be made for the supply of bacteriological apparatus as soon as it should be required, and for each laboratory a staff of pathologists and technicians had to be chosen. On the outbreak of war the equipment previously accumulated was distributed and the appointed personnel went directly to their posts. The Council have been greatly impressed by the efficiency with which all arrangements were made, and they wish to acknowledge the excellent assistance which they received, both in framing the plans and in carrying them out, from the bacteriologists and pathologists of the country.

Blood Transfusion Depots

The Council also undertook the organisation of four depots for the collection, storage and supply of blood for transfusion purposes. These are situated in the Home Counties and are intended—in addition to serving their own immediate neighbourhoods—to augment the arrangements made by the hospitals in London itself. Although the Council's direct responsibility was restricted to these four depots, they also assisted in co-ordinating the work of the hospitals in London and in providing them with apparatus. Advice was likewise

given, when requested, to those locally responsible for blood transfusion schemes in other parts of the country.

These depots were mobilised at the beginning of the war, and have since been maintained in a state of readiness. Although primarily for civilian needs, blood from some of the depots has already been supplied to the Army. New uses have been found for blood which has been stored for transfusion purposes for its maximum period without being required.

In particular, part of the blood is being recovered for use as a prophylactic against measles, in view of the fact that the serum of most adults (in a community exposed to the infection) has some power of conferring resistance against the disease. The availability of this prophylactic in unusually large quantities is likely to be useful in dealing with the epidemics which are to be expected during the winter, as the limiting factor in the past has been the relative inadequacy of supplies in the early stages of an outbreak. In this regard particular attention is being paid to evacuated children in reception areas.

Nutrition in Time of War

During the last war knowledge of human nutrition which was then new proved to be of great value in dealing with questions of the nation's food supply under conditions of restriction. It is no less vital that this knowledge should be applied now, if similar conditions recur. In the meantime, however, the facts have become more widely known, and the importance of the qualitative as well as the quantitative aspect of rationing is generally realised. The special need of milk and other protective foods, which had previously to be pointed out by experts, is now appreciated by the public.

Nevertheless, there have been many further additions to knowledge of this subject in the interval. It therefore remains true that scientific guidance is essential in all measures affecting the food supply either of the armed forces or of the population at large, if the best results are to be obtained. Among other things, the great use which is necessarily made of tinned foodstuffs in Service rations raises questions as to whether the processes used involve any destruction of vitamins, and in that event whether the deficiency can be remedied. The Council have for some time been concerning themselves with this matter at the request of the War Office, and various points relating to Army rations have been investigated by members of their staff working at the Lister Institute and at Cambridge. Similar work of wider scope is now being undertaken by the Council at the request of the Department of Scientific and Industrial Research in relation to its own investigations into methods for the preservation of food during transport and storage.

Industrial Health under War Conditions

One of the lessons of the last war was that " the country cannot afford the extravagance of paying for work done during incapacity from fatigue ". This statement was made in the Interim Report

(1917) of the Health of Munition Workers Committee. To that body the Industrial Fatigue (now Health) Research Board was the direct successor, and it has for twenty years formed a part of the Council's organisation. The stimulus to production in industry now is similar to that which occurred in the last war, when experience showed that unduly long hours, especially in heavy work, resulted in a reduction of output which more than counterbalanced the additional time available for production. This conclusion, reached empirically by the Health of Munition Workers Committee, has since been confirmed by evidence collected in the course of scientific investigations directed by the Board. Other researches have dealt with optimum length of spell, the effect of rest pauses, the influence of various environmental conditions, the physiology and psychology of work, accident proneness, vocational selection, and labour wastage. Of the resulting knowledge much is capable of practical application, and has indeed already been widely applied in factories during normal times: some of it acquires added importance owing to the war—for instance, in relation to the "black-out", knowledge about optimum conditions of lighting, heating and ventilation.

The need at the moment is for more application of this previously gained knowledge rather than for new researches, although the war is in time likely to raise fresh problems for investigation. In this matter the assistance of the Industrial Health Research Board is being sought by Government Departments engaged in promoting the production of war material, and also in selecting personnel for special or skilled training either in industry or in the Services. The Council and their Board have of course no executive responsibility in this regard, but it is gratifying that the scientific advice which they are able to offer has been utilised at an early stage in the present emergency.

Research on War Problems

Most of the emergency measures described above involve applications of existing knowledge rather than research for new knowledge. The question of actual research work in relation to war has already been generally discussed, but a few special investigations may be briefly mentioned. Some of the medical problems presented by the war are old ones for which no complete solution had been found. Among these is the question of shock occurring after serious wounds or severe operations. The Council have appointed a special committee to review this problem in the light of present day knowledge, and to organise both laboratory and clinical studies in the subject. Related to this is the question of blood transfusion, with regard to which various investigations are in progress.

Other subjects have taken on fresh aspects under changed conditions. For example, the physiological problems of aviation present themselves in new forms in relation to the flying of modern war machines. In this field the Council have been assisting the Royal Air Force, and their Secretary is Chairman of the special committee set up by the Air Ministry.

There are also new problems. As already mentioned, the recent great development of chemotherapy in dealing with bacterial infections gives hope of great success in treating sepsis in war wounds. The new methods will, however, need to be carefully controlled at first so that their results may be evaluated and the best conditions for their use determined. The Council have released the member of their scientific staff who has been most closely concerned with work on this subject, in order that he might accept appointment as Consulting Pathologist with the British Expeditionary Force. Colonel Colebrook will have the co-operation at home of a special laboratory unit which the Council have set up by arrangement with the Ministry of Health to investigate streptococcal infections of wounds, including of course civilian as well as military casualties.

Further problems will doubtless arise, of kinds which have not yet been foreseen. These will in their turn call for the services of the scientific personnel and equipment best suited for each particular purpose.

Research in Preventive Medicine

In the last Report attention was drawn to the remarkable contrast between the rapid adoption of new knowledge in curative medicine and the tardy acceptance of new methods of preventing disease and maintaining good health. Nobody doubts that in relative value to the community the latter kind of information is of much greater importance, and one of the major problems of public health administration must be to find means of quickening the adoption of methods shown to be capable of preventing disease and of promoting health.

The Council reviewed this problem with the object of seeing how they could best stimulate increased interest and activity in the prevention of disease by "fertilising it with the research spirit". To this end they appointed a Committee on Preventive Medicine, the constitution of which is given at page 149. It will be seen that the members, under the chairmanship of Sir Wilson Jameson, include well-known Medical Officers of Health selected from London, the Provinces, Wales and Scotland, with two officers of the Ministry of Health and one of the Department of Health for Scotland, and also individual experts in immunology, nutrition, statistics and clinical medicine. It has been agreed that the Medical Officers of Health on the Committee shall serve for a limited period, so that the representation of this field may be kept as fluid and wide as possible: others will be members of sub-committees on particular subjects. The Council have indeed reason to be grateful for the ready response that has been given to their request for special help in this matter.

From the outset it was clear that the Committee had an enormous field in which to work, and it was necessary to focus attention in the first place on a few specific subjects. These included the study of methods of immunisation against diseases such as diphtheria and whooping cough, with a view to evaluating their efficiency and

determining the best technique; inquiry into the problem of cross infection in hospital wards; field studies in nutrition, especially as regards children; and investigations into the causes of the high mortality rates due to broncho-pneumonia, to enteritis in children, and to respiratory diseases during winter. Although the new Committee began work only a few months ago, the Council have already been able to initiate investigations on their advice into certain of these important health problems, in particular cross infection in wards. At the beginning of the war they were in consultation with the London County Council, who proposed to establish a special research unit to study the problem of epidemic diarrhoea and vomiting in children. Help was also given to the health authorities of Jersey in their campaign against diphtheria by compulsory preventive inoculation.

Cross Infection in Hospital Wards

To enter a hospital for relief of one disease and to die of another contracted there constitutes a tragedy which has long troubled civilised man. In the nineteenth century, and especially in its earlier part, the situation in this respect was often appalling; and instances have been known where the mortality rate in children's wards has reached 50 or even 100 per cent. It will be remembered, too, that the maternity wards in Vienna at one time earned the name of "*seminarium mortis*". With the general improvement in hygiene, and the development of bacteriological science, there resulted a steady decline in the mortality rates due to cross infection, particularly those due to gastro-intestinal and wound infections. The work of Pasteur, Lister and Semmelweiss caused a revolutionary reduction in hospital infection; by making first the antiseptic and then the aseptic technique possible, it eliminated the great mass of infection and opened the door to modern surgery.

The problem of cross infection in hospital is, however, by no means solved: among paediatricians especially, it has on a number of occasions in late years been the chief subject of discussion at national and international meetings. Generally speaking, nevertheless, medical men have been slow until recently to grasp its true significance, and although interest has been awakened in cases where broncho-pneumonia or gastro-intestinal affections have swept through wards, such events have not often been appreciated to the extent of rousing action or even study.

Cross infection in hospital wards, however, is not always as obvious as in these instances. More difficult has it been to understand how infection is acquired in the rarer cases where women die of puerperal infection with haemolytic streptococci, or where patients develop middle-ear disease after admission to hospital. The difficulty in the way of tracing the source of infection was that haemolytic streptococci are present in the throats of many normal persons, so that it was generally impossible to decide from which

person, if any, of those with whom the patient had come in contact, a particular infection had been derived. A method of attacking this problem was provided by the work of Griffith and of Lancefield; they showed that, by agglutination and precipitation reactions, it was possible to recognise a multiplicity of different types of haemolytic streptococci. Using this technique, the passage of a particular type of haemolytic streptococcus from one case to another, or from an apparently healthy person to a case, can now be determined.

The first practical problem successfully attacked along these lines was that of the residuum of puerperal sepsis. The studies of Smith and of D. Colebrook showed clearly that the majority of such cases were due to infection of the patient by some person in attendance on her, or by the carriage of infection from her own throat to her own genital tract. It followed that the customary nursing technique needed improvement.

The next problem on which light was thrown was the frequency of cross infections in surgical wards devoted to the treatment of diseases of the ear, nose and throat. Okell and Elliott described fourteen outbreaks in which they were able to demonstrate the passage of a particular type of haemolytic streptococcus from one case to another: altogether, 68 patients were infected during their stay in hospital, many were seriously ill, and two died. Such cross infections are not confined to surgical wards, but have been shown to occur in medical wards as well, particularly in children, leading to such infections as tonsillitis, otitis media, broncho-pneumonia and scarlet fever. Keevil and Camps have described 42 cases in which patients were proved to have been infected in hospital, four of them dying as a result. Dr. W. H. Bradley, working for the Council in an observation of 120 medical beds in a general hospital, demonstrated 50 instances of ward infection with haemolytic streptococci, including two deaths. Such cross infections are not, of course, confined to haemolytic streptococci. Pneumococci can also be differentiated into a number of different serological types, and in one investigation in the United States fifteen ward infections of pneumonia, developing in a general hospital and leading to six deaths, were described.

As would be expected, such cross infections are particularly common in fever hospitals, and here—in addition to the actual harm done to many of those affected—there is an economic consequence that cannot be neglected. It is customary to retain cases of diphtheria in hospital until they no longer harbour diphtheria bacilli in the throat. Glass and Wright found that 36·6 per cent. of 246 cases of diphtheria under treatment in a fever hospital in Liverpool were still carrying diphtheria bacilli, not because they had retained the particular type of bacillus with which they had been admitted, but because they had been infected with another type while in the ward. The cost of this increase in the length of stay in hospital is a serious one. In the hospital studied by Senior and Wright it amounted to at least £600 a year, and probably much more.

These and other similar studies have shown quite clearly that our present system of controlling the spread of infection in hospital wards is inadequate, and that it must be revised. Such revision, if it is to be effective and economical, must be based on planned experiments; for until these have been made we cannot tell what changes are required to produce the desired results. There is a wide range of possible methods, varying from the ordinary open ward system to the isolation of individual patients in separate cubicles. A compromise between these extremes is the method known as "bed isolation", in which a wider spacing of beds in an open ward is combined with a stricter nursing technique. The efficiency of any established measure will clearly depend on the discovery of the process or processes whereby the passage of infecting organisms from one person to another takes place. In some cases they may be conveyed in the larger droplets discharged in spray during coughing or loud speaking, in other cases in finer droplets which remain suspended in the air for long periods, in others by infected dust, and so on. Such evidence as at present exists would suggest that aerial transmission of infection cannot be disregarded. Brown and Allison found haemolytic streptococci widely distributed in the air of four large scarlet fever wards, and R. Cruickshank obtained similar results in wards occupied by patients with infected burns. In another instance it was found that the dust of 27 single-bed wards housing patients infected with haemolytic streptococci was constantly contaminated with these organisms, and that in most cases the strain isolated from the dust was of the same type as that infecting the patient.

Within the last year the Council, advised by their new Committee on Preventive Medicine, had arranged for controlled trials of different methods of preventing cross infection in fever hospitals. These were to be made under the direction of Professor Hedley Wright in Liverpool and by Dr. Joyce Wright in one of the fever hospitals of the London County Council. Both these enquiries have unfortunately had to be suspended owing to the war. That at Liverpool had not proceeded beyond the initial stage of planning; but preliminary results obtained by Dr. Joyce Wright suggest that bed isolation, in its usual form, is not an effective method of preventing cross-infection in scarlet fever wards.

Infective Enteritis and Diarrhoea in Children

Since about 1914 there has been a great reduction in the incidence of summer diarrhoea and vomiting, and also in the number of deaths from this cause. No definite reason is known for the virtual disappearance of this disorder, which used to appear in epidemic form in most summers and be particularly virulent when the temperature was high. Some have ascribed the change to the great reduction in house-flies which has accompanied the displacement of horses by motor cars, others to the better feeding of children. Whatever the cause, the benefit to child-life can hardly be exaggerated.

This gain tends to mask the fact that enteritis remains the greatest cause of death among infants. Although the summer and autumn peaks of very high incidence of mortality have been levelled out, the residuum of deaths occurring at a constant rate throughout the year still presents a challenge to medical research. In 1937 there were 4,925 deaths in this country due to diarrhoea and enteritis, and most of these cases occurred in children under two years of age.

Particularly distressing are the cases of gastro-enteritis which develop in epidemic form in children's hospitals and institutions, and these form an important part of the problem of cross infection considered in the previous section. Infections of this type may be divided broadly into two main categories—acute ileo-colitis of a dysenteric type, which tends to attack children over one year of age; and acute gastro-enteritis, which tends to attack infants under one year and particularly new-born infants during the first few weeks of life.

Among cases of the former type of disease, rather over half appear to be due to infection with one or other of the recognised species of dysentery bacilli. In this country the species mainly concerned are *Bact. flexneri* and *Bact. sonnei*; the latter has been identified with increasing frequency during recent years, and it shows a marked tendency to cause hospital epidemics of a kind which our present nursing methods fail to control. The case mortality of this type of infection is low in adults, but considerably higher in young children; Blacklock records a case fatality rate of 18·4 per cent. among 215 cases in a children's hospital in Glasgow. In nearly half the cases of the ileo-colitis type, however, the infecting organism is not determined, and in not a few instances hospital epidemics of considerable size may occur without any of the generally recognised pathogenic bacteria being identified.

The position as regards gastro-enteritis in infants is still more disquieting. In the last decade, and particularly since 1934, there have been increasingly numerous reports of institutional epidemics with a high case fatality rate: these attack new-born infants within the first few weeks of life, usually before the end of the third week. The most fully documented accounts have come from New York, but similar outbreaks have been reported in this country and elsewhere. These outbreaks present very striking and constant features, including the fact that susceptibility seems to be sharply limited to the first few weeks of life. In nurseries attached to maternity hospitals the disease spreads rapidly among new-born infants; but if infants are attacked after leaving hospital and are re-admitted to an ordinary children's ward, the infection does not spread. The disease has a high fatality rate, and in institutions that are affected it is a major cause of infant mortality. In various maternity hospitals and nursing institutions in New York, during the years 1934 to 1937, 5,082 babies were born: of these 750 developed gastro-enteritis and 356 died—a mortality rate among all live births of 7 per cent., and among those attacked of 47·5 per

cent. In spite of extensive and detailed bacteriological investigations, the cause of this disease remains quite unknown.

While in most of these cases of gastro-enteritis and diarrhoea, infection is undoubtedly the prime causative factor, it would be wrong to study this feature alone in investigations made to elucidate their true nature. Improper diet and malnutrition in its widest sense are often a crucial feature in the development of the infections, and more especially in the death of the affected children. Breast-fed infants not only have a much lower incidence of gastro-intestinal infections than artificially fed infants, but when attacked are much less likely to die: even partial breast-feeding has a large protective influence in both respects. Clearly, breast-feeding must lower the opportunities of infection, but apart from this it undoubtedly raises the resistance of the child against the lethal effect of gastro-enteritis. In older children, also, proper feeding along lines of modern knowledge of nutrition reduces the virulence of these infections of the alimentary canal and gives a greater chance of survival to those affected.

These intestinal infections in children constitute a major problem of preventive medicine, and one of the first tasks of the new Committee on that subject is to assist the Council in instituting an intensive study of outbreaks of this kind. Here again, the progress of the work may be delayed as a result of the war; but since such outbreaks may well become more frequent rather than less frequent under war conditions, every effort will be made to investigate them as fully as circumstances permit. In particular, as mentioned above, the London County Council are fully alive to this problem and intend to institute an intensive study of its nature. Needless to say, the Medical Research Council will gladly give all assistance in their power to aid this work.

Advances in Immunisation against Infectious Diseases

Active and Passive Immunity

No aspect of medicine is more important at the present time than that of inducing or reinforcing resistance to infectious disease. In the case of some such diseases, recovery is accompanied by the development of an immunity sufficiently great to protect the individual against further attacks for the rest of his life; while in other instances only a transient immunity results. As is well known, medical science has found means of artificially raising the immunity against certain diseases independently of an actual attack, and the methods used are constantly being improved.

Active Immunity.—Two methods have been used for evoking or reinforcing a resistance of the type which is naturally acquired during recovery from an attack. The older method, and the most effective when it can be applied, is the " active " immunisation of the subject by inoculating the infective agent after it has been rendered inactive or attenuated in virulence. In Jennerian vaccination the virus of small-pox had been naturally modified by passage through the less

susceptible bovine host ; in Pasteur's method of protecting sheep against anthrax, the culture of the bacillus was attenuated by growth at an unfavourable temperature ; in the inoculation against typhoid fever, now used throughout the world, the inoculum is made from a killed culture of the specific bacillus.

In some infectious diseases, instead of injecting the actual infective agents, it is possible to obtain specific products ("antigens") from the latter, and by injecting these to evoke protective reactions, which induce a state of resistance. Recent developments give promise that purified antigens, extracted from the bacteria by chemical treatment, may be effectively used in preventive inoculation against some diseases: it is even possible that greater knowledge of the chemistry of some of these substances may eventually lead to their synthetic production. The soluble toxins which some bacteria produce in culture can be changed, by simple chemical means, so that they are rendered harmless but are still capable of producing antitoxins on injection, and thus of increasing immunity to the corresponding specific infections. These modified bacterial toxins are called toxoids.

Active immunity can, therefore, be produced by a number of methods, ranging from an attack of the disease itself down to the injection of harmless antigens prepared from the causal micro-organism. Such immunity is of relatively long duration, being due to stimulation of the natural defensive mechanism of the body; when this mechanism is thus called into action by one or more inoculations, it may continue for years to produce the protective antibodies, even without further stimulus.

Passive Immunity.—The alternative "passive" method of immunisation depends on the transfer to the patient of protective substances (antibodies) which have been produced in the body of another man or animal and are present in the blood serum. They may have been formed in the human body during recovery from an attack, or in successful resistance to the infection ; protection can thus be given against measles by injecting blood serum from patients convalescent from the disease, or even from any adult members of a community in which exposure to the infection is frequent. Another method of conferring such passive immunity depends on the use of blood serum from an animal, such as a horse, in which a high concentration of the specific antibodies has been produced in response to a long series of graded injections of the infective organism or its products. The antitoxins for diphtheria and bacillary dysentery, as well as antisera of other types such as those directed against the organisms of pneumonia, have found their chief and immensely important applications in the treatment of the corresponding infections, when these have already produced their characteristic diseases.

Tetanus

As an immediate preventive measure passive immunisation is also highly effective. During the last war, the early injection of

tetanus antitoxin into wounded men became an established routine and prevented in unnumbered cases the danger of tetanus, which had been so terribly prevalent in the Franco-Prussian war of 1871. Thus, following the introduction of the use of tetanus antitoxin as a prophylactic agent in October, 1914, the incidence of tetanus dropped from 9 per 1,000 wounded to less than 1 per 1,000 in 1915. This passive immunity, however, though rapidly established, is brief in duration, since it lacks the factor of spontaneous renewal by which an active immunity is maintained. When the antitoxin is obtained from a different species, usually a horse, the evanescence of its effect is further accentuated by an immunity reaction of the patient's system against the serum itself, as a foreign protein substance.

Although the production of active immunity against tetanus by use of an analogous toxoid prepared from tetanus toxin was discovered earlier, its practical application in human preventive medicine is a more recent development, but one which gives promise of at least as great a success. In another section of the Report mention is made of an investigation in which Dr. Hartley has co-operated with Dr. Ciuca of Bucharest, in evaluating the immunising effects of such preventive inoculation with tetanus toxoid. Investigations of a similar type have been made by other workers in this and several other countries. An important feature of these results is the demonstration that, as in other active immunisations, a primary inoculation of tetanus toxoid will leave a basal immunity lasting for years, as measured by the antitoxin content of the blood serum. There is no need to emphasise the importance of the fact that such detailed knowledge of the practical possibilities of this method has come in time for use at the outset of another great war, and that its protective value is available to any member of the fighting services who will accept it. To what extent tetanus toxoid will ultimately replace tetanus antitoxin cannot yet be foretold. Until prophylactic inoculation by toxoid is more extensively adopted to give active immunity against tetanus, it can be regarded only as a supplement to the use of antitoxin as a means of conferring temporary passive immunity on casualties.

Measles

The relative practical value of each method can be well illustrated by the treatment of measles. Under the age of three years an attack of measles is very dangerous to the life of a child ; when a child of this age has been exposed to measles infection, it is therefore desirable to inject sufficient immune serum to suppress the disease completely. This is an instance of passive immunisation : no lasting immunity is produced, and the child may be again attacked if later exposed to infection. In an older child, when the danger from an attack of measles is not so great, it is better to give a smaller injection of immune serum at a longer interval after exposure to infection. This mitigates the disease, but does not completely suppress it : the mild

attack of measles stimulates active immunity and the child becomes resistant to further infection for its lifetime.

Diphtheria

It is obviously desirable to replace passive immunisation by an active immunisation where possible. The earliest success in this direction was obtained by using diphtheria toxin with a small addition of antitoxin, just sufficient to neutralise it almost completely. Such an inoculum had the drawback, for production on a large scale, that the margin of adjustment between dangerous toxicity and ineffectiveness was so narrow as to require exact control and supervision. Important advances were made by depriving a toxin of its toxicity by treatment with formaldehyde; by the use of floccules from a neutral mixture of "toxoid" with antitoxin; and, finally, by precipitating the toxoid with alum. These details of the rapid improvement in the reagents available for producing activity immunity to diphtheria deserve mention, if only to emphasise the fact that most of them were due to discoveries made and first published in this country. On the other hand, the practical extinction of diphtheria by their application, and the removal thereby of one of the major threats to the life of children in large communities, has been the achievement of other countries, as pointed out in the Council's Report for 1937–38.

Prevention and Treatment

It will be seen that, so far as the prevention of infective disease is concerned, active immunisation with vaccines, toxoids, or similar reagents has great advantages over temporary passive immunisation with specific antisera. In regard to the treatment of disease which is already established, the specific antitoxins are likely to maintain their position as essential therapeutic agents. There are other specific antisera which act not on bacterial toxins but on the bacteria themselves, assisting the body to dispose of them in a variety of ways: among such are the antisera commonly used in the treatment of pneumonia and of cerebrospinal meningitis. The recent discovery of the therapeutic value of sulphanilamide, and of various related compounds such as sulphapyridine, has provided a new and highly effective weapon against the two diseases just mentioned, and against many other bacterial infections—notably those caused by haemolytic streptococci. Whether chemotherapy will entirely replace serum treatment in infections of this type it is too early to say; but it is at least possible that such antibacterial sera, as contrasted with the antitoxic sera, may become of secondary importance. It is in the prevention of disease that immunological methods play, and will continue to play, their major role.

Artificial Induction of Fertility

The rapid advance made by physiologists during recent years in knowledge of the anterior pituitary lobe, and analogous principles controlling sexual functions, has not been attended by an equally

rapid advance in their scientific use in practical medicine. It is true that preparations of such hormones have been extensively prescribed by medical men, but such treatment has only too often been completely empirical and indiscriminate, possibly doing harm rather than giving benefit to individual patients. More recent research, however, has given promise of a great advance in practical use: although much more information must be obtained by animal experiments before the methods can be safely applied to man, it seems probable that stock breeding at least will profit greatly by the work in the near future. In this particular case, the great increase in knowledge of the factors controlling the reproductive cycle in mammals forms the basis of the new developments.

Among the many hormones that have been detected in the anterior lobe of the pituitary gland, two are recognised which directly influence the ovary—they are said to have a gonadotrophic effect. One of these substances stimulates the growth and ripening of ovarian follicles; the second causes bursting of the ripe follicles and a change (luteinization) of their walls after the escape of the ova. For the promotion of fertility in the female it is probable that the production of the ripe follicles is of primary importance, although Russian investigators claim to have produced an increase of fertility in ewes by the injection of the second or luteinizing hormone, as found in the urine of pregnancy.

Elsewhere in this Report (p. 48) an account is given of work, at the National Institute for Medical Research and the Middlesex Hospital, in which it was shown that extracts of the anterior pituitary lobes of horse and man contain the two gonadotrophic hormones in effective proportion: injection into rats deprived of their pituitary glands induces the development of ovarian follicles, which grow to maturity, ovulate and form true *corpora lutea*. On the other hand, extracts from the anterior pituitary lobes of oxen, sheep and pigs produce precocious luteinization in immature ovarian follicles.

Dr. A. S. Parkes, at the National Institute, developed this subject by studying the effect of horse pituitary extracts on fertility in rabbits. At a later stage Dr. J. Hammond extended the experiments to immature and anoestrous ewes, and this work is being actively pursued. In rabbits, Dr. Parkes found it possible to produce such an abnormal number of ripe follicles that mating resulted in a pregnancy with as many as forty embryos.

The experiments on sheep were made by Dr. Hammond with the collaboration of Dr. Parkes at the Animal Nutrition Institute at Cambridge—the longer experiments on a small flock of sheep maintained there, and the shorter ones on animals made available a few days before slaughter. Experiments were made to see whether extract of horse pituitary gland rich in follicle-stimulating hormone, if injected three to five days before the expected time of oestrus and followed by normal mating, would result in the implantation of a supernormal number of embryos in the uterus. Other experiments

were made to see whether fertility could be induced during anoestrus, when sexual activity is normally in abeyance.

As regards the first question, five foetuses were found on one occasion when the ewe was killed during the third month of pregnancy. More work is needed to obtain adequate control over the ovaries of animals so treated, but it is likely that, in the case of those sheep which usually produce only a single lamb at a birth, a useful increase in productivity may be obtained by this method.

In the second part of the work, the induction of fertility during anoestrus, the results are clearer. This is obviously a matter of great agricultural significance, because the breeding season of the chief breeds of sheep kept in the British Isles for the production of meat and wool extends only from August to February and only one crop of lambs can be produced in a year. It has been found that a single injection of horse pituitary extract creates a remarkable response of the quiescent ovary of the anoestrous sheep, causing follicular maturation and ovulation. The number of ripe follicles produced by a single injection of anterior pituitary extract depends on the dosage given, and large ovaries containing several dozen follicles can be produced by a big dose. In contrast, the number of the ripe follicles which burst and liberate their ova is not correlated with the dosage and is usually between one and three, which is normal for sheep. In other words, if a small dose of extract is given, producing only a few ripe follicles, then all may ovulate ; but if a large dose is given, only perhaps one in ten of the follicles may ovulate. It is evident, therefore, that the act of ovulation is not itself caused by the administered exogenous hormone : it is almost certainly due to an endogenous hormone produced by the anoestrous animal's own pituitary under the influence of the events (follicular maturation) occurring in the artificially stimulated ovary. This fact seems to increase greatly the practical applicability of the results, since a fairly wide range of dosage produces the same end result : breed and individual variations in sensitivity can be largely discounted.

Ovulation thus induced in ewes is peculiar in not being accompanied, at least on the first occasion, by willingness to accept the ram. The reason for this is not clear, but the fact that a large proportion of ewes will mate after a second ovulation, induced sixteen days after a first, suggests that the presence of an old *corpus luteum* in the ovary may be necessary for the appearance of sexual receptivity. This difficulty can be overcome by artificial insemination at the time of the first induced ovulation, or by repetition of the treatment some two weeks later in the anticipation that normal mating will probably take place on the second occasion. Several pregnancies were produced by the latter method in a small group of anoestrous ewes in June and July 1939, the lambs being born in November and December.

It is clear that the practical possibilities of stimulating and controlling the reproductive powers of sheep, as suggested by the

investigations of Dr. Parkes and Dr. Hammond, are great. Not only may it be possible to obtain three sets of offspring in the course of two years, where at present two are obtained, but the number of lambs born may be increased at each pregnancy. In addition, it may be possible to induce a first pregnancy in sheep at an earlier time in their life than the usual age of eighteen months.

The work is now being extended on a much larger scale, using whole flocks of sheep as experimental units. More intensive work on a laboratory scale is also being continued, and the information so obtained may ultimately allow the extension of the method to stimulate fertility in women. The interest of man has too often been engaged in the development of scientific methods for preventing fertility, and only last year the Council reported the production of a new oestrogenic compound which had the property of counteracting the effect of a hormone of the ovary and ending pregnancy. It is satisfactory to observe that research in this field is also producing knowledge of the means of increasing fertility rather than suppressing it, and the work described above suggests that such knowledge is approaching the stage of practical application.

Chemistry of Brain Reaction

It has been a common experience in medical research during the past fifty years that, when once investigation has been able to correlate chemical change with function, advance in knowledge has been rapid.

Recently, this stage of investigation seems to have been reached in the case of the brain and nervous system generally, and there is ground for the hope that a new chapter concerning the chemical basis of nerve reaction, with all its peculiar manifestations, is about to be opened up. It will be obvious that, in the case of the nervous system, the evidence of its activity is quite different from that of other systems of the body. In an organ such as the pancreas or kidney, activity can be measured by the amount and nature of its secretion; in a muscle, by its contraction; and in a ductless gland by its content of active principles or by the effect of these on other organs. When an indication of the activity of the brain is sought, however, only too often has reliance to be placed on unco-ordinated or peculiar movement, or on such intangible characteristics as consciousness, emotion, memory, judgment and other psychological qualities. Yet it is obvious that, if it were possible to correlate these functional activities of nervous tissue with specific chemical change, a new world of study would be at hand. Not only would such information be of great importance from the point of view of understanding brain activity, but it might well help towards the elucidation and control of many phenomena in the field of psychiatry, including abnormal thought, action and emotion, which form at present such an enormous social problem. It cannot be said that the newer knowledge has even approached this position, but there is now a distinct possibility of this stage being ultimately attained. From the point of view of psychiatry, most of the progress leading to increased practical control

has depended on advances in psychology ; and, however great these may have been, an enormous territory in the field of prevention and cure of mental abnormality is still outside medical control.

It has long been known that the nervous system is peculiarly susceptible to drug action, often in a surprisingly specific way. Such instances as the action of caffein or benzedrine in dispersing mental fatigue, of potassium bromide and luminal in relieving epilepsy, of cocaine in stimulating and then depressing cerebration, and of morphine and aspirin in alleviating pain, show how different functions of the central nervous system can be specifically affected by particular chemical groupings. Even more perplexing has been the recent discovery that " shock " effects produced by insulin and cardiazol are often followed by improvement in the mental condition of schizophrenics.

It is also well established that substances normally present in the body have specific functions to perform in relation to the nervous system : the simplest example of this is the dependence of the activity of the respiratory centre of the brain on carbon dioxide tension. Another example is the relation of the development and functioning of the brain to secretion of the active principle of the thyroid gland. In its absence the brain of an infant ceases to develop and a cretin results ; while a deficiency of thyroid secretion in the adult produces the sluggish cerebration associated with myxoedema. Recently, a particularly striking instance of chemical control by a normal constituent of the body over a specific brain function has been suggested by the experimental work of Sir Charles Martin, Dr. Harriette Chick and their colleagues. These workers have shown that when pigs are reared on diets deficient in vitamin B_6 they suffer from epileptic fits identical in appearance with those seen in human epilepsy. If the vitamin is then added to the food the fits cease. It would thus appear that the normal activity of the motor cells of the cerebral cortex is dependent on a proper supply of vitamin B_6, which is now known to be 2-methyl-3 hydroxy-4 : 5-di (hydroxymethyl) pyridine.

All these instances have emphasised the importance of chemical change and reaction in the brain and nervous system in relation to function ; but their essential significance has remained obscure, because knowledge of the actual chemical changes normally associated with nervous function has been lacking. Recent research on brain chemistry is beginning to dissipate this ignorance.

One of the outstanding facts established by investigations on brain chemistry is the key position held by glucose as the main fuel of nervous tissue. Anything which interferes with its supply or use puts the brain and nervous system rapidly out of action. The simplest case of this deprivation of glucose is the result of an overdose of insulin, when the sugar in the blood may be so reduced that a number of characteristic nerve disorders develop, ranging from subjective feelings of weakness and impaired vision to the more serious conditions of convulsions, unconsciousness and even death.

Complete and immediate recovery can usually be obtained in such cases by injecting glucose directly into the bloodstream and so supplying the nervous system with its main fuel. But the ability to use sugar depends, not only on the presence of this substance in the brain cells, but also on a sufficiency of other chemical substances necessary for its oxidation, including oxygen itself. The effects of a deficient oxygen supply to the brain are well known and are often seen in mountaineering and in flying at high altitudes. The first effects of mental instability, loss of judgment and fatigue may quickly pass to the stage of unconsciousness; but, if oxygen is supplied in proper quantity, recovery may be equally rapid. The problem of sufficiency of oxygen supply to the brain, in order to maintain full mental activity, is one of great importance in aviation at the present time.

The complicated nature of the process of sugar oxidation by the brain cells has been emphasised by modern biochemical investigation. There may be sufficient sugar and oxygen in the nervous system, and yet the mechanism breaks down for other reasons. Probably the best instance of this is seen in the results of the interesting work of Professor R. A. Peters and his colleagues at Oxford. These workers started from the older observation that, when vitamin B_1 is deficient in the diet, both animals and man develop characteristic abnormalities of the nervous system: they were then able to show that the chemical changes of avitaminous brain tissue, as determined in the laboratory, were fundamentally abnormal. Further, if the vitamin was added to the solution containing the avitaminous brain tissue under study, the chemical actions were largely restored. By this means it was possible to demonstrate that vitamin B_1 played a controlling part in the oxidation of sugar (glucose) by the cells of the brain. If vitamin B_1 were absent from these cells they could not make proper use of glucose as a food, because the normally complete oxidation of this substance was arrested at an intermediate stage. The addition of vitamin B_1 to the avitaminous brain tissue *in vitro* restored the power to oxidise glucose completely, just as the injection of this vitamin at once restored the nervous system of the avitaminous animal to its normal activity. Thus we now know that some and probably most of the defects in function of the nervous system in men suffering from beri-beri are due to inability to use glucose because of the absence of a controlling factor in the oxidative mechanism, namely vitamin B_1.

The interference with the oxidation of glucose caused by absence of vitamin B_1 leads to accumulation, both in the brain and in other tissues of the body, of the intermediate oxidation product, pyruvic acid; it has in fact been shown, particularly by the work of Dr. B. S. Platt on patients suffering from beri-beri, that estimation of the pyruvic acid content of the blood gives a useful indication of the degree of deficiency of vitamin B_1 and is also valuable in following the results of treatment with the vitamin.

Even when the supplies of oxygen, glucose and vitamin B_1 are adequate the actual process of oxidation of glucose may be

diminished or suppressed by the action of certain chemical substances; this point is of practical importance since the group of compounds which exhibit such an inhibitory action includes most of the common anaesthetics and narcotics. Thus it appears that alcohol and such drugs as ether and the barbiturates produce their effects of drowsiness and ultimate unconsciousness by suppressing the oxidation of glucose in the brain.

The interesting generalisation may therefore be made that such different events as narcosis, oxygen deprivation, insulin shock and deficiency of vitamin B_1 all have one result in common, namely the diminution of oxidation of glucose in the nervous system.

Reference has been made in previous Reports to the importance of acetylcholine in the transmission of nervous impulses, since the discovery of this phenomenon has depended so greatly on the investigations of Sir Henry Dale and his colleagues at the National Institute for Medical Research. Acetylcholine has actually been isolated from the brain by Dr. E. Stedman at Edinburgh, and reality is thus given to the conception that it plays an essential part in the transmission of excitation at certain junctions in this part of the nervous system, as had already been shown to be the case in ganglia and at most peripheral nerve endings. The actual process of formation of acetylcholine by brain tissue *in vitro* has been studied at the City Mental Hospital, Cardiff, by Dr. J. H. Quastel and his colleagues, who have shown that the synthesis of this essential substance can take place only in presence of glucose or certain of its metabolic products (lactate or pyruvate) and with a free supply of oxygen; furthermore, Dr. F. C. MacIntosh, working at the National Institute, has found that peripheral ganglia, previously exhausted of their acetylcholine, are able to regenerate this compound only when glucose or one of its possible metabolic products is supplied. It is true that in the intact animal neither extreme deprivation of glucose (produced by overdosage with insulin) nor deficiency of vitamin B_1 is sufficient to lower the acetylcholine content of the brain, although in both these conditions cerebral function is impaired; nevertheless, in spite of this failure to demonstrate in the living animal that formation of acetylcholine depends on normal oxidation of glucose, the experiments of Dr. Quastel and Dr. MacIntosh suggest that such a dependence does indeed exist. If this suggestion is confirmed, we may have here the beginning of an explanation of the reason why the oxidation of glucose is so essential to the normal function of the nervous system.

It has further been revealed by the studies of Dr. Quastel that the acetylcholine which is contained in brain tissue is present both in the free state (in which alone it is physiologically active) and in a combined form, the equilibrium between these two forms being controlled by chemical substances. In particular, the liberation of free acetylcholine from the inactive combined form is greatly favoured by increase in the concentration of potassium salts, and this is of special interest in view of the close relationship—mentioned in a previous Report—between attacks of familial periodic paralysis and

a low potassium content of the blood; it will be recalled that this condition is immediately cured by the administration of potassium salts. In this connection it will also be remembered that Dr. Brown and Dr. Feldberg had earlier shown, at the National Institute, that an excess of potassium ions liberates acetylcholine in a living ganglion. Dr. MacIntosh and Dr. Harvey have now found that such liberation does not take place in the absence of calcium ions.

It is obvious that much further work will be required before the part played by acetylcholine in relation to other chemical reactions and to brain function can be properly assigned. Starting, however, with the simple fact that sugar oxidation is essential for brain and other nerve activity, the complicated means whereby this is brought about, and the detailed sequence of chemical events which accompany the change, are gradually being unfolded. At different stages in this process it has been possible to correlate failure of interaction with abnormality in function of the nervous system. There must be many facts still to be elucidated concerning this oxidative mechanism and other chemical changes in the brain, but the knowledge already obtained gives promise of a fine future of discovery in this field, and possibly even of a scientific basis for interpreting physiological and pathological reactions of the nervous system.

"Breathing Machines"

Under their more striking but less accurate description as "iron lungs", these machines have become a subject of widespread interest during the past few years, because of certain reported cases where they have maintained the life of individuals who otherwise would have died at once. Before the subject received the increased newspaper publicity that followed the generous offer of a certain type of breathing machine to all parts of the Empire by Lord Nuffield, the Council had already formed a Committee to study the various types of machine available, and to consider this matter not only from the point of physiological efficiency but also with regard to cost and distribution. The immediate stimulus to this action was a request to the Council from the Ministry of Health for guidance regarding the supply of these machines. The Ministry sought advice in view of the number of cases in which this apparatus was shown to be useful in the epidemic of poliomyelitis (infantile paralysis) in 1938. This epidemic, although small in comparison with some of those occurring in other countries, was nevertheless attended by a number of cases of respiratory paralysis sufficient to demand serious attention.

Artificial respiration is a procedure needed in many other conditions than poliomyelitis. For instance, another disease occasionally demanding treatment of this kind is diphtheria, when the respiratory muscles may be temporarily paralysed. The commonest occasions are those of asphyxia associated with drowning and coal-gas poisoning, and artificial respiration can then usually be given by hand. If spontaneous breathing remains in abeyance for long, however, the manual method becomes not only tedious but wholly impracticable; some form of machine is then necessary.

When the Committee started work, under the chairmanship of Professor L. J. Witts, the problem to be studied appeared relatively easy, for most medical men were familiar only with two types of breathing machine—the Drinker apparatus or "iron lung", and the Bragg-Paul "pulsator". These represented two different principles of maintaining the action of the lungs, which might be briefly described as negative and positive pressure methods of mechanical artificial respiration. Further consideration, however, revealed that the problem was one of great complexity. Instead of two, there were many types of apparatus to be considered; and the best type of machine for one disease was not the best for another disease. Again, cost had to be considered, and also the degree of skill and amount of attention required for efficient working of any machine. On such points as these, moreover, rested the decision as to the best means of maintaining a service that would work effectively throughout the country. All these questions and many others have been considered by the Committee. They have described in their report, recently published by the Council, most or all of the machines available. They have discussed the advantages and disadvantages of these, the relative cost, the kind of assistance necessary for operation, and the policy to be adopted in order to meet sudden demands for supply.

The Committee point out in their report how limited is the usefulness of any breathing machine, and how much more important it is for all members of the community to be familiar with manual methods of artificial respiration. The application of artificial respiration by hand must never be postponed in an emergency through the mistaken idea that a patient can be better treated with a machine. Paralysis of respiration of sufficient degree and duration to demand treatment in a breathing machine is evidence of a very profound disturbance of the organism; and, if a patient is really ill enough to require such treatment, he is very likely to die whatever is done. It is estimated that, even in a peak year, the annual incidence in Great Britain and Ireland of all forms of respiratory paralysis likely to benefit from treatment by breathing machines will not exceed 600, and only in a few of these cases will the treatment be truly life-saving.

In view of the relative ease of transport of patients with respiratory failure, the small number of cases, the necessity for highly skilled medical supervision and nursing, and the desirability of progressive improvement in design of the instruments used, the Committee strongly recommended that the treatment of protracted respiratory failure should be concentrated in the smallest possible number of hospitals. Fully equipped units for the treatment of acute anterior poliomyelitis might appropriately be created in each regional area, and other units might usefully be placed at one or more large hospitals in each area.

The Council consider the report to be of great importance, not only because it brings together all the known facts regarding the many kinds of breathing machine available, but because it allows a true perspective to be obtained of the whole subject.

II. THE NATIONAL INSTITUTE FOR MEDICAL RESEARCH

Hampstead and Mill Hill, London

PHYSIOLOGY, PHARMACOLOGY, and BIOCHEMISTRY

Staff—

Sir Henry H. Dale, C.B.E., M.D., F.R.C.P., F.R.S. (*Director of the Institute*).
R. B. Bourdillon, M.C., A.F.C., D.M.
G. L. Brown, M.Sc., M.B.
J. Argyll Campbell, D.Sc., M.D.
H. King, D.Sc., F.R.S.
H. P. Marks, B.Sc.
C. Rimington, Ph.D.
Winifred I. Strangeways, Ph.D.
T. A. Webster, A.I.C.
F. G. Young, Ph.D., D.Sc.

Attached workers—

F. C. MacIntosh, Ph.D.
O. Rosenheim, D.Sc., F.R.S.
J. Walker, B.Sc., Ph.D.
L. L. Ware, B.Sc., Ph.D.
T. S. Work, Ph.D.

Endocrinology

Staff—

A. S. Parkes, Sc.D., F.R.S.
R. K. Callow, M.A., D.Phil.
I. W. Rowlands, M.Sc., Ph.D.

Attached workers—

Ruth Deanesly, D.Sc. (Mrs. Parkes).
C. W. Emmens, M.Sc., Ph.D.
Nancy H. Callow, B.A.
Margaret H. Warwick, B.Sc.

EXPERIMENTAL PATHOLOGY and BACTERIOLOGY

Staff—

Sir Patrick P. Laidlaw, B.Ch., F.R.C.P., F.R.S. (*Deputy Director of the Institute*).
C. H. Andrewes, M.D., F.R.C.P., F.R.S.
W. J. Elford, B.Sc., Ph.D.
R. E. Glover, B.Sc., F.R.C.V.S. (*Veterinary Officer*).
J. R. Perdrau, M.B. (*d. 29th May*, 1939).
W. J. Purdy, M.B.
Wilson Smith, M.D.
P. Bruce White, B.Sc.

Attached workers—

D. G. ff. Edward, M.D.
I. A. Galloway, D.Sc., M.R.C.V.S.
C. H. Stuart-Harris, M.D.
M. van den Ende, M.B.

Protistology

Staff—

Clifford Dobell, M.A., F.R.S.

Microscopy and Physical Methods

Staff—

J. E. Barnard, F.R.S. (*Hon. Director*).
John Smiles, A.R.C.S.

BIOLOGICAL STANDARDS

Staff—

Percival Hartley, C.B.E., M.C., D.Sc., F.R.S. (*Director of Biological Standards*).

Margaret Llewellyn Smith, M.Sc., Ph.D. (*With the co-operation of others named above*).

ADMINISTRATION

Medical Administrative Officer—
D. K. M. Chalmers, M.D., D.P.H.

Librarian—
Kathleen Baverstock.

Designer and supervisor of apparatus—
E. J. H. Schuster, D.Sc. (*part-time*).

VISITING WORKERS

Dr. T. Bradshaw, Dublin.
Dr. J. P. Chu, Hankow.
Dr. J. H. Comroe, Philadelphia.
Dr. F. B. Gordon, Chicago.
Mr. M. E. Griffiths, Sydney.
Dr. A. M. Harvey, Baltimore.
Dr. M. Hermann-Fischer, Zagreb.
Professor O. Loewi, Graz.
Miss K. M. Lundevall, Stockholm.
Dr. W. d'A. Maycock, Montreal.
Dr. L. Mesrobeanu, Bucharest.
Dr. A. Pop, Bucharest.
Dr. E. Singer, Prague.

Summary of Research Work

The following is a summary of the work done during the past academic year by members of the Council's staff and others in the Institute at Hampstead, and in the associated Farm Laboratories at Mill Hill. The proposed concentration of the whole of these activities at the Mill Hill site will inevitably be delayed by the war, but good progress has already been made with the new buildings there. Some of the ancillary buildings are ready for occupation, and the shell of the main building is nearing completion.

The Institute has suffered a severe loss by the sudden death of Dr. J. R. Perdrau, at the age of 56. A native of Mauritius, he had spent his working life in this country and joined the staff at Hampstead in 1926. He had specialized in neuropathology, and his name will be particularly associated with advances in knowledge of virus diseases of the central nervous system.

At the end of the period under review, Dr. Wilson Smith resigned from the staff, which he joined in 1927, to take up the appointment of Professor of Bacteriology in the University of Sheffield. Mr. I. A. Galloway, who had for thirteen years been attached to the Institute as a worker on behalf of the Foot-and-Mouth Disease Research Committee of the Ministry of Agriculture and Fisheries, has left to become Scientific Superintendent of the Ministry's own research station in this subject.

Virus Diseases

Influenza : epidemic studies.—From January to April, 1939, a disease recognized clinically as influenza appeared in the form of a series of outbreaks limited to particular cities or districts, or even to schools and institutions, but occurring within those limits with an incidence sometimes rising as high as fifty per cent. There was no general epidemic sweeping in a wave over the country, as in the case of those which occurred in the early months of 1933 and 1937. In 1939, although there was some general increase in the prevalence of influenza and respiratory catarrh, it was only in certain localities that this attained epidemic proportions. It was only locally, again, that the pneumonia rate showed the sharp rise characteristically associated with epidemic influenza. The opportunity was taken for investigating further the association of the disease with the now well-known virus.

Dr. Stuart-Harris, working in association with the Institute as a Foulerton Research Fellow of the Royal Society, studied the clinical conditions in a number of successive outbreaks, and collected material from representative cases for laboratory investigation by Dr. Andrewes and Dr. Wilson Smith. In contrast with the uniform clinical picture observed in the more typical and generalized epidemic of 1937, the outbreaks in 1939 presented a mixture of clinical types, many being such as to suggest a diagnosis of nasopharyngitis or bronchial cold, while others had all the characters previously

regarded as typical of influenza. Even with material from typical cases, all attempts to transmit a virus infection to ferrets and mice were unsuccessful in the early stages, and it was not until the middle of February that evidence of a connexion of influenza virus with the outbreak was obtained. From that time onwards the virus was recovered from a proportion of the cases in each outbreak visited; and additional cases gave evidence of its presence in the increase of neutralizing antibodies observed in samples of blood serum taken during and after the attack.

Altogether, of the throat-washings obtained from different outbreaks only 7, out of 59 tested, yielded virus infecting ferrets. Some of these strains appeared to be of low virulence for the test animals, though all showed antigenic relationship with some of the strains obtained in the more typical epidemics of earlier years. Of 63 patients from whom serum samples were tested, 20 showed a clear increase of antibodies neutralizing one of the stock strains of virus. It was noteworthy, however, that such evidence of the presence of influenza virus, whether direct or serological, had no relation to the clinical type of the disease; it was not obtained in a significantly greater proportion of the cases regarded as typical of influenza, than of those which would have been classed as "febrile catarrh". The presence of virus, again, was not associated with a greater severity of the symptoms; on the contrary, as judged by duration of fever or by involvement of the chest, the attacks had a somewhat greater average severity in the cases in which virus was not detected. The outbreak, as a whole, appears to have been one in which the known influenza virus, transmissible to ferrets and mice, played a subordinate part. The possibility that other strains of virus may have been concerned, antigenically distinct from those known and without significant virulence for the test animals, cannot be excluded by the methods available. In any event, it seems to be clear that, between the well defined epidemics of influenza associated with the transmissible virus, less typical and milder outbreaks may occur, in which other causal agents—whether viral or bacterial—predominate; and that, in such a relatively mild outbreak, the previously recognized clinical distinction between the true influenza yielding transmissible virus on the one hand, and febrile catarrhs due to other types of infection on the other, does not hold good.

Experimental vaccination against influenza.—The Council's Report for 1936–37 described an attempt made to vaccinate groups of volunteers with a formaldehyde-treated preparation of the influenza virus which had been isolated in the 1933 epidemic. The fact that the 1937 epidemic began before the planned vaccination had been completed, and the subsequent discovery that the strains of virus concerned in it were antigenically different from that used in preparing the vaccine, made the experiment inconclusive. The result showed, however, that the procedure was completely innocuous, and gave useful indications for a further trial under conditions eliminating some of the factors which had complicated this first

attempt. In the expectation of a possible epidemic in the corresponding months of 1939, preparations were accordingly made well in advance. In addition to a vaccine similar to that used in the earlier trial, another was prepared with wider antigenic constitution from a mixture of virus strains.

By the courtesy of the Medical Director-General of the Navy and the officers in direct control, the trial was made on volunteers in the Royal Naval Training Establishment at Shotley. Of these 483 were vaccinated, each receiving 1, 2 and 3 doses of one or other of the two vaccines under test. An approximately equal number, chosen to correspond with those vaccinated in all relevant respects, were listed as controls and kept under similar observation as regards the incidence of influenza or like conditions. The vaccination was completed before the end of 1938; and, since Shotley was one of the last institutions to be affected by the 1939 outbreak, there was no question in this instance of an inadequate interval for the vaccine to produce its immunizing effect. If the outbreak had proved to be a typical one clearly associated with the virus, the test of this method of vaccination would have been a good one. In fact, it was a mild example of the outbreaks above described, affecting less than eight per cent. of the boys on the strength of the establishment, and having the variable character and doubtful association with the virus characterizing the outbreaks elsewhere in the same season. The results showed no significant difference, in the incidence of the respiratory infections which occurred, between the vaccinated and the control groups; but unfortunately, for the reasons stated, they cannot be regarded as giving any decision for or against the value of such vaccination against influenza in the typical, epidemic form.

Meanwhile Dr. Andrewes and Dr. Wilson Smith have continued their experimental inquiry into the factors influencing the immunizing effect of the influenza vaccine. They find that, as in the case of vaccination against dog distemper (which was in some sense the starting-point of the researches on influenza), the presence of proteins of a foreign species hinders the immunizing effect of the influenza virus when this has been inactivated with formaldehyde. The results suggest that the success of immunization may depend on the perfecting of methods for freeing the virus from the constituents of non-human tissues, in which it must be cultivated for use in human vaccination, or on the use of the virus in living condition, still capable presumably of a limited multiplication in the body. The latter method has already been tried, apparently with greater promise of success and with no evidence of danger, especially in the United States of America.

The fact that strains of the influenza virus with new antigenic properties appear to arise in the human organism, even in the course of an epidemic, had led Dr. Wilson Smith to make a systematic attempt to produce such variant strains under laboratory conditions of propagation, but so far without success.

Dimensions and properties of viruses.—In collaboration with Dr. T. F. McNair Scott at the Wellcome Research Institution, Dr. Elford has applied his methods of ultrafiltration and differential centrifugation to determining the dimensions of the infective units of lymphocytic chorio-meningitis; this is a virus disease affecting the brain membranes of mice, and has in more than one laboratory been accidentally found to be transmissible to man. The diameters of the units, as determined by these independent methods, showed excellent agreement, the calculated average values being 50 and 46 millimicrons respectively (a millimicron being a millionth of a millimetre). At the time of the death of Dr. Perdrau, Dr. Elford was collaborating with him in a dimensional comparison of the virus from the outbreak of encephalitis which occurred some years ago at St. Louis, U.S.A., with that from a more recent outbreak in Japan of a disease in many respects similar. The work has been completed in collaboration with Dr. F. B. Gordon, of Chicago, working at the Institute with a Travelling Fellowship from the Rockefeller Foundation.

Further studies on purified bacteriophages have been made by Dr. Elford, with regard to their stability over a range of acidities and temperatures, and with regard to their adsorption on strains of organisms sensitive and resistant to their lytic actions. With Dr. Andrewes, he has also been investigating the nature of their reactions with the specifically neutralizing antibodies obtained by the artificial immunization of rabbits. These latter studies, made with virus-like agents of which the actions can be measured with quantitative precision and without the uncertainties and complications of experiments on animals, may give important clues to some factors in the immunity to typical viruses.

Louping-ill.—The virus of louping-ill is responsible for that important disease in sheep, but is apparently transmissible to man only by relatively rare accident. It offers special opportunities for studying the conditions of infection by neurotropic viruses, and of immunity to them, on account of the readiness with which it can be transmitted to small rodents. Burnet had shown that when this virus is instilled into the nasal passages of rats, although it produces no signs of the characteristic cerebral infection, it can for some time be recovered from the olfactory bulbs as well as from the nasal mucosa. When the rat had acquired immunity as the result of earlier instillations, however, no virus could be detected in the olfactory bulbs after a further similar application by the nostrils. Dr. Gordon has now made further experiments, from which it seems clear that this active immunity involves some factor of tissue immunity or resistance in the cells of the mucosa: the resistance apparently extends to the olfactory bulbs as well, since virus was found to disappear from the latter even after it had been directly inoculated into them. Dr. Gordon has also found that the virus, after nasal instillation into normal rats, is found in the cervical lymph glands and the lungs, as well as in the nasal mucosa and

olfactory bulbs, but not in the rest of the brain, the blood, or other organs ; when directly injected into the olfactory bulbs, on the other hand, it reached other parts of the brain.

Immunology

Reversed anaphylaxis.—Dr. van den Ende has completed an investigation, which he had undertaken at Cambridge, on the phenomenon termed " reversed anaphylaxis ". It was known that if an antiserum to guinea-pig serum was prepared by a course of injections into a rabbit, the serum of the immunized rabbit evoked in a normal guinea-pig a train of symptoms closely resembling that observed in the ordinary anaphylactic shock. The result had been attributed to the union of the injected antibody with the antigens of the guinea-pig's serum, and the consequent production of a circulating poison. Dr. van den Ende has found, however, that the isolated and blood-free plain muscle of the normal guinea-pig gives a reaction to this antibody for guinea-pig's serum closely similar to that which plain muscle from an anaphylactic guinea-pig gives to the sensitizing antigen. The phenomenon thus appears to represent a " reversed anaphylaxis", in the strict sense that it is due to an antibody reacting with a tissue-fixed antigen, instead of an antigen with a tissue-fixed antibody. This raised the question whether a cellular fixation of a foreign antigen could be produced, corresponding to the fixation of a foreign antibody in passive anaphylaxis. The completion of the experiments has been deferred by the incidental discovery that the antibody globulin, from the serum of a rabbit immunized against pneumococcus (type I), is a distinct antigen from the corresponding globulin of normal rabbit's serum—a point of interest at least as great as that which led to the experiment.

Tissue fixation of antibodies.—Last year's Report mentioned investigations by Dr. Hartley on the specific acceptability of antibodies from the sera of different species by the plain-muscle cells of the guinea-pig, as demonstrated by passive sensitization of the isolated muscle of the uterus *in vitro*. A further technical advance has been made in the method, by the discovery that this sensitizing fixation of antibodies—producing a condition of passive anaphylaxis—does not require the maintenance of the organ in a state of physiological activity at body temperature. If the excised horn of the uterus is immersed in a suitable dilution of the antibody in cold Locke's solution, and left in the ice-box overnight or longer, fixation of the antibody occurs readily. If the preparation is then washed, and restored to normal activity by suspension in oxygenated Locke's solution at body temperature, its acquisition of specific sensitiveness to the corresponding antigen can be demonstrated ; and this is entirely comparable with that observed in passive sensitization of the living animal. The procedure has obvious analogies with the long-known fixation of haemolytic antibodies by blood corpuscles at a low temperature ; and it should greatly

extend the range and convenience of the test, on the isolated organ, for the production of passive anaphylaxis.

Bacterial antigens.—Much interest has been aroused in recent years by the demonstration, given by several groups of workers using different methods, of the possibility of obtaining—from a number of pathogenic bacteria—soluble and relatively stable antigens capable of evoking a high degree of immunity to infection by the corresponding organisms. Dr. Elford has initiated a physico-chemical study of the molecular dimensions of these antigens, and of the polysaccharide haptenes which can be dissociated from them. A visit to the Institute by Dr. Mesrobeanu, of Bucharest, gave the opportunity of investigating a series of antigens produced by the method due to Boivin and Mesrobeanu, from the food-poisoning bacilli (Aertrycke and Gärtner), the typhoid bacillus and the dysentery bacilli of Shiga and of Flexner. Similar studies are being made, in collaboration with Professor W. W. C. Topley, on the analogous antigen preparations produced by the different method devised by Topley and Raistrick.

Leprosy

Sir Patrick Laidlaw has made experiments which have an interesting bearing on the relation between human leprosy and that occurring in the rat. The rat disease, which is caused by an organism very similar to that found in the leprous lesions of man, is relatively rapid in development and is transmitted without difficulty from rat to rat; but there was only one previous record of a successful attempt to transmit leprosy to the rat by material from a case of leprosy in man. During the past year material from cases of human leprosy in the Belgian Congo had been sent by air-mail to Dr. A. Dubois of Antwerp; and this had been used to inoculate Syrian hamsters, following the description of the transmission of human leprosy to that species by Professor S. Adler of Jerusalem. One of the hamsters showed typical bacilli in a number of its organs when killed for examination, and pieces of tissue from this animal were transmitted to the Institute through Dr. E. Muir of the British Empire Leprosy Relief Association.

With this material Sir Patrick Laidlaw found it remarkably easy to transfer a rapidly spreading infection, not only to hamsters but also to white rats: it appeared to be innocuous for guinea-pigs. The readiness with which the infection was transmitted to rats as well as hamsters, and the observations made on the tissues of these animals after death, suggested to Sir Patrick Laidlaw that the human lesions from which the material was originally obtained were due to infection with the organism of rat leprosy, and not with the organism of the usual human type. This opinion has been confirmed by Dr. Dubois and also by Professor Adler, to whom microscopic preparations and descriptions of the findings were submitted. In the one previous case on record, mentioned above, the infection of man by rat leprosy was also suspected; but the clinical condition in the case

now under discussion had, apparently, aroused no suspicion of such an origin. The question naturally arises whether human leprosy, in general, may have originated by infection from the more rapidly spreading and more widely prevalent rat disease, the bacilli subsequently losing their pathogenicity for the rat with adaptation to the human tissues.

With regard to the infection of hamsters with the bacillus of typical human leprosy, it is important to distinguish mere survival of organisms at the site of inoculation from active multiplication and infective spread to other tissues. Sir Patrick Laidlaw has accordingly studied the behaviour of a number of other mycobacteria, including a few from the National Collection of Type Cultures listed as "associated with leprous lesions". Such organisms differ from true leprosy bacilli in being capable of growth on artificial media. In most cases they could be recovered from the sites of inoculation in hamsters as long as six months after injection; but the survival was strictly local, no organisms being found in the lymph glands, spleen, liver, or other organs. A mycobacterium obtained from butter survived for months in this restricted manner, as well as those which had originally been found in association with leprous lesions.

Protistology

By the methods which had already proved so fruitful in the study of the life-cycles of *Entamoeba histolytica* and *Entamoeba coli*, Mr. Dobell has now worked out a large part of the life-cycle of *Endolimax nana*, a small amoeba also inhabiting the intestines of man and monkeys. He has made further progress with the study of the intestinal flagellates of these hosts, and the knowledge of them required for practical purposes is now nearly complete. Attention has also been given to the flagellate commonly found in the human mouth, with a view to deciding the proper nomenclature of this organism.

Authentic strains of a number of the intestinal protozoa of man and monkeys have still been maintained in culture and have been made available to other workers in this country and abroad. It is noteworthy that the oldest strain of *Entamoeba histolytica* in Mr. Dobell's possession has now been maintained continuously in artificial culture for fifteen years, and all stages in its life-history reproduced at will. Cultures of this strain have been successfully sent to workers in America, France, Belgium, and other countries.

Chemotherapy and Pharmacology

Antimalarial compounds.—Dr. T. S. Work and Dr. J. Walker have now joined the staff of the Institute, with a view to the extension of the programme of chemotherapy. The former is investigating further the possibility of producing synthetic compounds related in structure to quinine and possessing antimalarial actions, in continuation of the work of Dr. Ainley and Dr. King. Incidentally, he has obtained a substance possessing strong activity as a local anaesthetic, and the properties of this are being further explored.

Alkaloids.—Dr. King, following an indication given by Dr. Harvey's work mentioned elsewhere, has prepared a quaternary ammonium base having a powerful curare-like action, even when given by the mouth. He has also made progress in identifying the alkaloids of the different types of curare and tracing them to their botanical sources. With Dr. Ware, he has made further investigations on the alkaloids of belladonna root, using larger quantities of the raw material. The former finding that l-hyoscyamine is the only alkaloid present of its type has been confirmed; but evidence has been obtained of the presence, in very small proportion, of a simpler and as yet unidentified base.

Porphyrin excretion and methaemoglobinaemia.—Dr. Rimington has continued his investigation into the production of porphyrinuria by the action of drugs of the sulphanilamide group, and has extended it to a number of other relatively simple substances. Dr. Goldblatt, medical officer to the British Dye-Stuffs Corporation, co-operated in the examination of industrial workers dealing with aniline, nitrobenzene and other substances recognized as capable of producing this type of toxic effect. The further results confirm the recognized association between increased porphyrin excretion and the formation of methaemoglobin in the blood corpuscles; but the excess of porphyrins in the urine could be detected even in workers exposed to such substances, but exhibiting no cyanosis indicative of methaemoglobinaemia, and no symptoms of other toxic action. It is intended to continue the inquiry, with the object of determining whether porphyrinuria can be used as an index of susceptibility among those exposed, and especially whether it gives warning of a liability to the bladder tumours which occur in a significant proportion of workers long exposed to contact with certain aromatic amines. It is in this group that the substances producing methaemoglobinaemia and porphyrinuria are chiefly to be found.

Dr. Rimington has also co-operated in investigations on blackwater fever by Dr. N. Hamilton Fairley, of the Hospital for Tropical Diseases, and Mr. H. Foy, of the Wellcome Trust Research Laboratory at Thessaloniki. Dr. Fairley had shown that the substance usually supposed to be methaemoglobin, occurring in the blood plasma in blackwater fever, was in fact a different though related substance. It has proved to be a compound of haematin with the serum albumin of the blood, and, at Dr. Rimington's suggestion, has been named "methaemalbumin." There would appear to be a normally quite subsidiary path for the degradation of haemoglobin, leading to porphyrin as the excretory end product. Haemolysis, poisoning by aromatic amines, infections and impaired liver function may all play a part in giving abnormal prominence to this alternative metabolism, in which the formation of methaemalbumin may figure as a stage. It contrasts with the normally predominant process, in which the liver produces bilirubin as the end product from the haemoglobin of effete red corpuscles.

Resistance to Low Tensions of Oxygen

Dr. Campbell has carried further his investigation, arising from the unexpected observation that rats fed on carrots alone will survive exposure for an hour to a tension of oxygen so low as to be rapidly fatal to rats receiving a normal mixed diet. Such an effect of diet had an obvious potential importance in relation to the physiological problems of flying at high altitudes, and a systematic effort has been made to identify more clearly the dietary constituents which thus favour, or on the contrary depress, resistance to oxygen deficiency. A high protein content of the diet has been found to be generally unfavourable to resistance, an exception being the zein of maize, which has a protective effect. On the other hand, no adverse effect was detected as the result of adding to the diet the particular amino-acids in which zein is lacking. The main conclusion which seems to be justifiable is that resistance is promoted by decreasing the proportion of protein and increasing that of carbohydrates, and particularly of vegetable and fruit fibre, in the diet. It was thought that the effect of indigestible fibre might be due to its adsorbent effect on substances produced by bacterial action in the intestine; and charcoal, paper pulp and kaolin in suitable proportions were found, indeed, to be favourable to resistance. Altogether, the effect appears to be a complex one; a diet which increases resistance probably promotes a preponderance of relatively harmless bacteria in the intestinal flora, and also provides adsorbents which restrict the absorption of such toxic substances as are produced.

Endocrinology

Slow absorption of hormones.—Reference has been made in earlier Reports to work by Dr. Deanesly and Dr. Parkes on the administration of different hormones by subcutaneous implantation of solid pellets of the pure substances, with the object of producing continuity of the action of a hormone circulating in low concentration and thereby approaching the conditions associated with normal function. The method has now been shown to give good results experimentally in the case of progesterone, and it seems likely to have practical application in securing the continuous action of this hormone often required in therapy, as it has already had in the cases of oestradiol and testosterone.

Corticosterone is a hormone in which such continuity of administration would seem to be especially desirable in therapeutics, but the free sterone is absorbed too rapidly from a subcutaneous depot to produce the desired effect. In desoxy-corticosterone acetate, however, a compound has been found which is absorbed with appropriate slowness, and in a manner likely to favour a continuous and unwasteful application in therapeutics. The principle involved is evidently one which may apply to the administration of a number of hormones. Where slow, continuous action is required, the advantages of chemical isolation and artificial production by synthesis are apt to be offset by loss of

effectiveness, due to too rapid absorption and excretion. Practical success may, therefore, depend on the discovery in each such case of a suitable ester, allowing the hormone to be absorbed from an artificial depot at the optimum rate.

Esters of the artificial oestrogen, diethylstilboestrol, are now being studied by Dr. Emmens, in order to find one acting optimally with tablet implantation. The free stilboestrol is absorbed from such a tablet very rapidly, but its esters with aliphatic acids show decreasing rates of absorption with increasing length of the esterifying radicle. It may be expected that, with some of these hormones and similarly acting substances, different esters will be appropriate for different therapeutic applications, requiring different degrees of speed and duration of effect.

Multiple activities of hormones.—Reference has been made in earlier reports to indications that the steroid principles of the gonads and the suprarenal cortex show other actions than those which characterize their recognized activities as hormones. This multiplicity of action is even more prominent in some of the numerous derivatives which have now been obtained from these hormones, either as natural secretory products or by artificial synthetic modification of their structure. In some cases it is not possible to classify a particular substance simply as "androgenic" or "progestational", for example, since its action under different conditions may be predominantly either the one or the other. In addition to this multiplicity of primary or direct actions, the steroid hormones and their derivatives exhibit a complex of antagonisms and synergisms with other hormones. The effect of an androgen such as testosterone, in restoring the growth and turgescence of the comb of a capon, is depressed by the antagonistic action of an oestrogen simultaneously administered: on the other hand, an oestrogen may under appropriate conditions appear to reinforce the effect of the androgen in promoting the growth of the accessory sexual apparatus in the castrated rat. Apart from such direct antagonisms and synergisms, injections of oestrogens and of some androgens strongly depress the endocrine activity of the anterior pituitary lobe, and may thus secondarily depress the activity, and even cause atrophy, of the gonads in which the injected hormones are naturally formed.

It is clear that in practical therapeutics, with a view to the replacement of a pathological deficiency, it would often be very desirable to use a substance producing the required activity, without an associated danger of antagonizing the effect of another hormone or of depressing the activity of an important endocrine organ. It might thus be of great practical value to have a substance available with a potent oestrogenic or androgenic action, but with no depressant action on anterior pituitary function; on the other hand, there might well be use for a substance which would depress the endocrine action of the anterior pituitary lobe without at the same time directly exciting a sexual function. With such possibilities in view,

Dr. Emmens has been making a preliminary survey of natural and artificial derivatives from the androgenic, oestrogenic and progestational compounds, and has already obtained evidence of wide variations in the proportions in which these multiple activities are represented in the actions of different members of these groups.

Artificial induction of fertility.—In the Introduction (p. 28), some account has already been given of work on this subject by Dr. Parkes, partly in collaboration with Dr. J. Hammond of the Animal Nutrition Institute, University of Cambridge.

Analysis of gonadotrophic effects.—As indicated above, gonadotrophic preparations of different kinds exhibit a wide range of differences as regards the proportion in which they produce the two phases of the complete gonadotrophic effect—firstly, growth and ripening of follicles; secondly, ovulation with ensuing development of *corpora lutea.* The investigation of these effects has been further complicated by the unknown degree of the participation of the hormones of the animal under experiment, in the total effect following the artificial injection of any such extract. An extract which by itself would induce only one of the phases, might appear to produce the complete effect when complemented by the animal's own pituitary activity. With the co-operation of Dr. R. L. Noble and Mr. P. C. Williams of the Middlesex Hospital, Dr. Rowlands and Mrs. Warwick have accordingly tested the effects of a series of such extracts on rats from which the pituitary gland had been removed completely. Under such conditions the gonadotrophic extract from human urine of pregnancy caused only the luteinizing effect; and extracts from the anterior pituitary lobes of oxen, sheep and pigs showed a predominant induction of this phase. Only the extracts of the anterior pituitary lobes of the horse and of man showed a production of both phases in due proportion, follicles being induced which grew to maturity, ovulated and produced true *corpora lutea.* Similar experiments, under these uncomplicated conditions, showed that the increased amount of gonadotrophic hormone obtainable from the human pituitary body late in life, after sexual functions have ceased, consists of the follicle-stimulating hormone only.

The depressant action of an oestrogen on hormone production by the anterior pituitary lobe, already recognized in animals, has also been shown to occur in human subjects. Dr. Rowlands has tested extracts from the anterior pituitary lobes of women, dying after the menopause, who had received treatment with oestradiol benzoate—the material being obtained through Dr. E. Sharpey-Schafer of the British Postgraduate Medical School. The pituitary glands of a woman at that age should normally give a high yield of gonadotrophic hormone; but, as the result of the oestradiol treatment, the extract was found to contain a reduced amount of the hormone, or none at all.

Antihormones.—Further work has been done on the nature of the so-called " antihormones ", appearing in the sera of animals which have received a series of injections of certain hormone-containing

extracts, especially those derived from animals of a different species. Since the phenomenon was originally described by Collip and his co-workers in Montreal, there has been much discussion as to the nature of these antagonistic substances in relation to the true antibodies known in pathology. Dr. Rowlands has made further studies, with Dr. A. W. Spence of St. Bartholomew's Hospital, of the antihormone appearing in the serum of patients treated with the gonadotrophic extract from the serum of pregnant mares. After four to six weeks of such treatment, whether the injections were given daily or twice weekly, the serum of these patients was found to have a strong antagonistic action to the effect of this gonadotrophin, as tested on the ovaries of immature rats, but did not affect the activities of the gonadotrophin from human pituitary gland or from the urine of human pregnancy. For long-continued treatment with a gonadotrophin in the human patient, it is clear that a preparation of human origin should be used, such as the extract from human urine of pregnancy, which provokes no formation of an antihormone in man.

New light has also been thrown on the puzzling phenomenon of an apparent augmentor activity, acquired by the serum of an animal receiving an intensive course of injections with gonadotrophic extracts from the pituitary body of its own and certain other species. Dr. Rowlands has found that this augmentation of the gonadotrophic effect is not present when the test is carried out on rats from which the pituitary glands have been removed. Apparently, therefore, the peculiar action of such a serum is due not to a direct augmentation of the effect of the injected extract, but probably to stimulation of the pituitary gland of the animal to an increased output of its natural gonadotrophic hormone.

Several other investigations have been designed directly to answer the question whether the antihormones have the nature of true immune antibodies. Dr. van den Ende, Dr. Rimington, Dr. Rowlands, Dr. Young and Miss Strangeways have taken part in different aspects of this work.

Dr. van den Ende has used the familiar precipitin and anaphylactic reactions in investigating the nature of the interactions between gonadotrophic principles and the sera neutralizing their effects. The gonadotrophic extract from urine of pregnancy was found to contain a complex of antigenic substances, present also in normal urine and unconnected with the gonadotrophic activity, so that the reactions of the preparation with the antiserum were extremely complicated. The reactions of the gonadotrophic preparation from pregnant mares' serum have given much clearer results. The antiserum neutralizing the activity of this extract gives no immunological reactions with the separated globulins and albumin of normal horse serum, but definite ones with the complete, untreated serum, as well as with the gonadotrophic extract itself. The factor concerned has now been identified as the subsidiary protein of normal serum known as " seroglycoid "—a non-coagulable protein containing a large proportion of carbohydrate. It remains

to be determined whether the seroglycoid, as seems probable, is merely concentrated in the gonadotrophic fraction as an accidental result of its preparation, or is somehow linked with the gonadotrophic principle itself to form a complex antigen. Dr. Rimington is co-operating in that aspect of the work which is concerned with the further study and identification of the subsidiary proteins of normal serum.

Hormone assays on human material.—A full account was given last year of work by Dr. and Mrs. Callow, with Dr. Emmens, on the androgenic and oestrogenic substances excreted in human urine: the difficulties created by the lack of exact chemical knowledge concerning the constituents of the fraction producing a particular effect were there discussed. By further application of chemical and physico-chemical methods of separation, Dr. and Mrs. Callow have now succeeded in identifying some of the constituents of the enriched androgenic fraction obtained from the urine of a patient under treatment with injections of testosterone. The substances recognized as constituents of this fraction, and as excreted in excess during testosterone treatment, were androsterone and its isomer, known only by the chemical name "*epi*aetiocholanolone." Further investigation then showed, however, that both these substances occur in the androgenic fraction from the urine of normal men. Their presence there might have been attributed to their formation from the testosterone of normal testicular origin; such a simple interpretation, however, is excluded by the further observation that both these substances are also present in the urine of normal women and even in that of eunuchs. Certain of the hormones are so closely related to each other in chemical structure, and particularly the androgens to the hormone of the suprarenal cortex, that it is not surprising that some of them should yield a common group of excretory end-products. The difficulty of diagnosing hormonal abnormalities from estimates of such products is obvious.

Diabetes produced by pituitary injections.—Dr. Young and Mr. Marks have continued their investigation of the permanent diabetes in dogs which follows a course of progressive injections of an extract from the pituitary anterior lobe, and have compared the condition in detail with the long familiar diabetes produced in the dog by removal of the pancreas. It has been established that the diabetes produced by pituitary injections may be more severe, as Best and his collaborators in Toronto have also observed, in the sense that a larger dose of insulin is required to reduce the blood sugar nearly to the normal level, and to abolish glycosuria, than in the dog deprived of its pancreas. From one dog, in which the pituitary diabetes and the insulin requirement had remained nearly constant for about a year, the pancreas was removed, with the result that a new and somewhat lower level of insulin requirement was established, though still higher than that of a previously normal dog deprived of its pancreas. It appears, therefore, that the permanent effect produced by the pituitary injections is not wholly due to the

degenerative changes produced in the islets of Langerhans, or to the suppression of insulin production in them. Further evidence of these effects on the islets, however, has been obtained by Dr. K. C. Richardson's histological studies of the pancreas from dogs in which the pituitary diabetes had existed for varying periods. The results show all stages of degeneration.

Pancreotropic effect.—Dr. Richardson and Dr. Young had previously obtained evidence of hypertrophy in the pancreatic islets of rats receiving injections of an anterior pituitary extract, using a laborious method of quantitative histological measurement. Dr. Young and Mr. Marks have now found that this increase of islet tissue is accompanied by a pronounced increase of the insulin which can be extracted from such a pancreas, as measured by the ordinary biological test. This more rapid method has enabled a study to be made of the nature of the constituent in anterior pituitary extracts responsible for the effect. In particular, it was of importance to test the possibility that the principle causing this islet hypertrophy in the rat might be the same as that which causes islet degeneration and permanent diabetes in the dog, since both these contrasted effects are obtainable with the same fresh extract. The new evidence seems definitely to exclude such identity.

Fractionation of anterior pituitary extracts.—Dr. Young has continued his attempts to separate the different hormones or active principles which the extract from perfectly fresh pituitary anterior lobe presents in such bewildering complexity. Some, such as the diabetogenic factor, are obtainable only from perfectly fresh material by the most conservative methods, and tend to disappear rapidly from the extracts. Others can be prepared from material dried and stored under various conditions; and one at least, the so-called "glycotropic" principle rendering an animal refractory to insulin, resists heating to boiling point in a moderately alkaline solution. Other separations have been made by fractional precipitation of the euglobulin, pseudoglobulin and albumin fractions of certain extracts: experiments on the ketogenic action of these have been made in collaboration with Dr. C. H. Gray of King's College Hospital, London. Prolactin fractions, obtained free from thyrotropic action, have been given a practical test with the collaboration of Dr. S. J. Folley, of the National Institute for Research in Dairying, and have caused an increase in the volume and fat content of cow's milk.

The whole problem of these anterior pituitary principles is one of great complexity, and will probably entail the expenditure of much labour and material in many laboratories. The clear tendency of present progress is in the direction of showing that the different activities which have been recognized are due to chemically separable principles, and are not different aspects of the action of one or a few. Meanwhile the scientific and safe application of anterior pituitary preparations in medicine, for the production of particular effects, must await further progress in this difficult field of laboratory research.

Neuromuscular Physiology

Most of the work in this field during the past year has been concerned with the mechanism by which the excitatory process is transmitted from motor nerve endings to voluntary muscles, and with the responses of such muscles under normal and pathological conditions.

Action of quinine.—The action of quinine on the activity of voluntary muscles has acquired practical interest from the discovery of its effect in relieving the symptoms of myotonia congenita in man, as well as of a closely similar condition found in goats. Dr. Harvey of Baltimore, continuing his work here with a Travelling Fellowship from the Rockefeller Foundation, has completed a systematic experimental analysis of the complex effect of quinine on the responses of a normal mammalian muscle, using the methods which have been evolved in the Institute during recent years. Quinine was found to have the curious effect of increasing the tension of a single twitch, while depressing that of a tetanus. In this depression two actions of quinine are concerned—a slowing of the contraction wave and lengthening of the refractory period, which appears to be the effect also responsible for increasing the tension of the single twitch ; and, in addition, a relatively weak action of the curare type. Since both these effects are concerned in depressing and shortening the response of the normal muscle to an artificial tetanizing stimulus applied to the nerve, it is probable that both play a part in the therapeutic action of quinine, in correcting the involuntary persistence of voluntary contractions which characterizes the behaviour of the muscles of a sufferer from myotonia. The curare-like action of quinine can be greatly enhanced by methylation to form a quarternary ammonium base, as in work by Dr. King already mentioned, so that this becomes the outstanding action on the response of voluntary muscle. Dr. Harvey found that a suitable dose of this base given by the mouth could produce a complete curariform paralysis lasting for some hours, but without other appreciable effects if artificial respiration were maintained ; recovery was complete, and without after effects, as the paralysis disappeared. Such a substance has obvious therapeutic possibilities, in suitably regulated doses.

Myotonia congenita in goats.—With the kind co-operation of colleagues in the United States, Dr. Harvey arranged for the transport to this country of several pairs of goats from a local strain, in which all the offspring from affected parents early show symptoms of a condition closely similar to those typical of the human disorder myotonia congenita, or Thomsen's disease. Dr. Brown and Dr. Harvey have made a thorough experimental study of the abnormal muscular response in these goats, and have shown that it is not due to an abnormality of the mechanism of neuromuscular transmission, but to an abnormal response of the fibres of the muscle itself to any kind of stimulus, mechanical or electrical. These muscles respond by a prolonged tetanus to a single induction shock or to a sharp tap on the surface ; and the muscle gives similar

responses to such stimuli when it has been fully curarized, or when its motor nerve has been cut and allowed to degenerate. The principal abnormality of such a muscle, in response to chemical stimuli, is its remarkably high sensitiveness to potassium ions. The strain of these goats has now been established at the Farm Laboratories at Mill Hill, and the animals will be available for further investigation. It is of interest to note the rapidity with which the nature of a human abnormality has been made practically certain by taking advantage of the unusual occurrence of an apparently identical congenital defect of function in a lower animal species, so that a direct experimental analysis of the condition could be undertaken.

Local tetanus.—It has long been known that the toxin of the tetanus bacillus, injected locally in small dose into a muscle, will evoke a persistent state of contraction in that muscle, and in neighbouring ones to which the toxin has penetrated. This was formerly attributed to passage of the toxin up the motor nerve fibres to the corresponding cells in the spinal cord. The late Professor Abel and his co-workers in Baltimore had shown, however, that the local tetanus involved a peripheral effect, and that the tetanus produced by action of the toxin on the motor nerve cells was of a different, spasmodic type. On the other hand it was well established that integrity of the nerve to the muscle was in some way essential to the production, or the persistence, of the local tetanus. Dr. Harvey has obtained clear evidence that the local tetanus is due to an effect on the motor nerve endings, and that it is the integrity of these, and not of the connexion with the nerve centres, which is necessary for its production.

An analysis of the effect on the nerve endings has given results which can be interpreted on the theory attributing neuromuscular transmission to the liberation of acetylcholine at the nerve endings. Under the action of tetanus toxin, acetylcholine apparently leaks continually from the depots at the nerve endings, while the cholinesterase disappears from the same region. The muscle is accordingly kept in a state of persistent irregular tetanus, while a nerve volley—liberating diminished charges of acetylcholine from partly depleted depots—causes only a weak twitch. The condition is abolished by curarine, as was to be expected, or by degeneration of the motor nerve after section. There can be little doubt that this effect on the motor nerve endings plays a part in the spastic phenomena, such as the familiar lock-jaw, of general tetanus following infection, together with the long recognized effect on the excitability of the motor cells of the nerve centres.

Effects of calcium deficiency.—Dr. Harvey and Dr. MacIntosh have studied the effects of perfusing the superior cervical sympathetic ganglion with a Locke's solution partly or entirely deficient in calcium. Other workers had shown that in such deficiency the excitability of nerve fibres is increased, and this appears to hold good also for the cells of the ganglion, which exhibit a spontaneous and

long continued output of post-ganglionic impulses. In this condition the cells are abnormally sensitive to the stimulus of potassium ions, while their response to acetylcholine is somewhat reduced. The most striking effect, however, is the rapid abolition of the transmission across the synapses of the excitatory effect of preganglionic impulses, and the concurrent failure of the liberation of acetylcholine into the perfusion fluid; both are promptly and simultaneously restored by the addition of a trace of a calcium salt to the perfusion, and the spontaneous activity of the ganglion cells is also brought to an end. The presence of calcium ions appears, therefore, to be a necessary condition of the liberation of acetylcholine by impulses reaching preganglionic nerve endings, and of the synaptic transmission of their effect. Dr. Brown and Dr. Harvey have examined the responses, to motor nerve impulses, of the muscles of goats fed on a diet deficient in calcium and having a low calcium content in the blood. The responses were, again, of a type to suggest a deficient release of acetylcholine by the impulses reaching the motor nerve endings, the second response of a pair in quick succession involving many more muscle fibres than the first.

Natural synthesis of acetylcholine.—Dr. MacIntosh has completed his work, with Dr. Kahlson of Lund, on the necessity of glucose, lactate, or pyruvate for the synthetic replacement of acetylcholine at ganglionic synapses, from which it had been exhausted by stimulation in the absence of such substances. He has found that mannose is the only sugar which has an effect in producing this restorative synthesis, comparable to that of glucose and its natural metabolites. Mannose was already known as the only sugar which could effectively replace glucose, with intravenous injection, in relieving the convulsions of hypoglycaemia due to excess of insulin. The question arose whether these convulsions might be associated with a defective replacement of acetylcholine at synapses, owing to the hypoglycaemia. To test this possibility, determinations were made of the acetylcholine which could be extracted from the brains of animals killed during the nearest approach to complete aglycaemia which insulin could produce. The quantity obtained, however, did not differ from that yielded by normal brains with similar extraction.

An analogous possibility was tested on animals under severe deficiency of Vitamin B_1 (aneurin). The work of Peters and his collaborators had shown that, in this condition, the brain tissue is deficient in the power of carrying the oxidative metabolism of glucose beyond the stage of pyruvic acid; and it seemed possible that this oxidation might be concerned in the normal synthesis of acetylcholine. Here again, however, the brains and the sympathetic ganglia gave normal yields of acetylcholine. It thus appears that neither the glucose content of the brain nor its pyruvic acid metabolism (if that be indeed involved) can be reduced by such means below the very small minimum required for acetylcholine synthesis; and it is clear that

exhaustion of synaptic acetylcholine is not concerned in the defects of nervous function in either case.

The observation of normal acetylcholine synthesis in the absence of Vitamin B_1 is in conformity with simultaneous observations by Mr. Webster, who has examined the effect of a deficiency of Vitamin B_1 on the acetylation of substances artificially introduced into the body. He has found that in rats with varying degrees of deficiency of Vitamin B_1 the acetylation of such substances as *p*-aminobenzoic acid, sulphanilamide and 2-sulphanilaminopyridine, is carried out with the same efficiency as in normal rats.

Control of vascular tone.—A large amount of study has been devoted in recent years, particularly in the Department of Physiology of Harvard University, to the control and variation of the tone of the blood vessels, and the maintenance of an efficient circulation, after the whole of the sympathetic nerve chains have been removed and all known connexions with the vasomotor centres thereby eliminated. Even after the suprarenal medulla has also been extirpated, the animals exhibit but little deficiency of circulation, except for the absence of the normal acceleration of the heart with exercise. Dr. Brown and Dr. Maycock have made further studies of the factors controlling the circulation under these conditions. The rise of blood pressure, with which ordinary decerebrated animals respond to stimulation of sensory nerves, is replaced in these by a fall; but this is found to be due to the vasodilatation engendered by some chemical change accompanying muscular activity. On the other hand, maintenance of the blood pressure in the absence of such activity is not wholly due to spontaneous tone of the blood vessels, but appears to involve the action of some nerve centre in the lower brain. Even when muscular movement has been eliminated by curare, section of the spinal cord in the neck is followed by a large fall in the vascular tone. The nervous pathway through which such a centre produces its effects, in the complete absence of the normal sympathetic connexions, is still unknown.

Library

During the year, 535 bound volumes, mainly periodicals, have been added to the library and seven withdrawn. The total number of volumes belonging to the library is approximately 15,670.

The Library Committee are glad to receive offers of books and periodicals, and the librarian will forward on request a list of desiderata. Approved persons interested in medical research are allowed to consult books in the library by arrangement with the librarian.

Lady Murphy has continued to work voluntarily in the library, and the Council are again glad to record their appreciation and thanks. The Council also wish to record their thanks to those who have contributed to the usefulness of the library by giving books and periodicals.

Publications during the year from the National Institute or by members of the staff

C. H. Andrewes—
Control of the common fevers. Epidemic influenza. *Lancet*, 11th March, 1939.
The occurrence of neutralising antibodies for Rous sarcoma virus in the sera of young "normal" chicks. *J. Path. Bact.*, 1939, **48**, 225.
Immunity in influenza: the bearing of recent research work. *Proc. R. Soc. Med.*, 1939, **32**, 145.

C. H. Andrewes and R. E. Glover—
A case of neurolymphomatosis in a turkey. *Vet. Rec.*, 29th July, 1939.

C. H. Andrewes and Wilson Smith—
The effect of foreign tissue extracts on the efficacy of influenza virus vaccines. *Brit. J. exp. Path.*, 1939, **20**, 305.

J. E. Barnard—
Presidential Address: Towards the smallest living things. *J.R. micr. Soc.*, 1939, **59**, 1.

C. I. Bliss and H. P. Marks—
The biological assay of insulin. I—Some general considerations directed to increasing the precision of the curve relating to dosage and graded response. *Quart. J. Pharm.*, 1939, **12**, 82. II—The estimation of drug potency from a graded response. *Ibid.*, 1939, **12**, 182.

G. L. Brown and A. M. Harvey—
Congenital myotonia in the goat. *J. Physiol.*, 1939, **96**, 11P.

G. L. Brown and H. S. MacIntosh—
Discharge in nerve fibres produced by potassium ions. *J. Physiol.*, 1939, **96**, 10P.

J. B. Buxton and R. E. Glover—
Experiments in calves on immunity conferred by single and double injections of BCG in an oily excipient. *J. comp. Path.* 1939, **52**, 47.
Tuberculin tests in cattle. Observations on the intradermal tuberculin test in cattle, with special reference to the use of synthetic medium tuberculin. *Agric. Res. Coun. Rep. Ser., Lond.*, No. 4, 1939.

N. H. Callow—
The isolation of two transformation products of testosterone from urine. *Biochem. J.*, 1939, **33**, 559.

N. H. Callow and R. K. Callow—
The isolation of androsterone and *trans*dehydroandrosterone from the urine of normal women. *Biochem. J.*, 1938, **32**, 1759.
The isolation of 17-ketosteroids from the urine of normal women. *Ibid.*, 1939, **33**, 931.

N. H. Callow, R. K. Callow and C. W. Emmens—
Preliminary observations on the metabolism of androgenic substances. *Chemistry and Industry*, 1939, **58**, 147.
The effect of the administration of testosterone propionate on the urinary excretion of compounds allied to the steroid hormones. *J. Endocr.*, 1939, **1**, 99.

N. H. Callow, R. K. Callow, C. W. Emmens and S. W. Stroud—
Methods of extracting compounds related to the steroid hormones from human urine. *J. Endocr.*, 1939, **1**, 76.

R. K. Callow—
Organic chemistry. Steroids. *Ann. Rep. chem. Soc.*, 1938, **35**, 281.

J. Argyll Campbell—
Resistance to oxygen want. *J. Physiol.*, 1939, **95**, 1P.
Protein and resistance to oxygen want. *Ibid.*, 1939, **95**, 28P.
Zein and resistance to oxygen want. *Ibid.*, 1939, **96**, 33P.

J. Argyll Campbell—

An inclusion body in the liver cells of the mouse. *J. Path. Bact.*, 1939, **48**, 223.

Increase of resistance to oxygen want in animals on certain diets. *Quart. J. exp. Physiol.*, 1938, **28**, 231.

Diet and resistance to oxygen want. *Ibid.*, 1939, **29**, 259.

Carcinogenic agents present in the atmosphere and incidence of primary lung tumours in mice. *Brit. J. exp. Path.*, 1939, **20**, 122.

The last thousand feet on Everest: possible bacterial factor. *Nature, Lond.*, 15th July, 1939.

A. C. Crooke and R. K. Callow—

The differential diagnosis of forms of basophilism (Cushing's syndrome), particularly by the estimation of urinary androgens. *Quart. J. Med.*, 1939, n.s. **8**, 233.

H. H. Dale—

Chemical mediation in the peripheral nervous system and its relation to endocrine organs. *III-Internat. Neurol.-Kongr.*, Copenhagen, 21–25th August, 1939.

Biological standardisation. *Analyst*, 1939, **64**, 553.

R. Deanesly—

Depression of hypophyseal activity by the implantation of tablets of oestrone and oestradiol. *J. Endocr.*, 1939, **1**, 36.

R. Deanesly and T. Warwick—

Observations on pregnancy in the common bat (*Pipistrellus pipistrellus*). *Proc. zool. Soc. Lond.*, A, 1939, **109**, 57.

C. Dobell—

The common flagellate from the human mouth, *Trichomonas tenax* (O.F.M.): its discovery and its nomenclature. *Parasitology*, 1939, **31**, 138.

On "Teranympha" and other monstrous Latin parasites. *Ibid.*, 1939, **31**, 255.

C. W. Emmens—

Reports on Biological Standards. V—Variables affecting the estimation of androgenic and oestrogenic activity. *Spec. Rep. Ser. Med. Res. Coun., Lond.*, No. 234, 1939.

The oral activity of certain androgens, oestrogens and augmenting substances. *J. Physiol.*, 1938, **94**, 22P.

The effect of prolonged dosage with oestrogens on the adult Brown Leghorn cock. *Ibid.*, 1939, **95**, 379.

Time-to-time variation in the response of ovariectomized mice to oestrone. *Nature, Lond.*, 18th March, 1939.

The duration of action of certain natural and synthetic oestrogens when administered orally or by injection. *J. Endocr.*, 1939, **1**, 142.

C. W. Emmens and A. S. Parkes—

Multiple activities of anhydro-oxy-progesterone. (Letter.) *Nature, Lond.*, 24th June, 1939.

E. C. Fieller, J. O. Irwin, H. P. Marks and E. A. G. Shrimpton—

The dosage-response relation in the cross-over rabbit test for insulin. Parts I and II. *Quart. J. Pharm.*, 1939, **12**, 206 and 724.

S. J. Folley and F. G. Young—

The effect of continued treatment with anterior pituitary extracts on milk volume and milk-fat production in the lactating cow. *Biochem. J.*, 1939, **33**, 192.

P. J. J. Fourie and C. Rimington—

A further case of congenital porphyrinuria (pink tooth) in a living grade Friesland cow in South Africa. (Cedara case.) *Onderstepoort J. vet. Sci.*, 1938, **10**, 431.

I. A. Galloway—

Pituitary extracts and the virus of foot-and-mouth disease. The effect on the virus of certain chemical methods employed in their preparation. *J. Hyg., Camb.*, 1939, **39**, 597.

R. E. Glover—

Immunisation of birds against fowl pox and pigeon pox respectively with viruses propagated on the chorio-allantoic membrane of the developing egg. *J. comp. Path.*, 1939, **52**, 29.

Cultivation of the virus of Aujeszky's disease on the chorio-allantoic membrane of the developing egg. *Brit. J. exp. Path.*, 1939, **20**, 150.

A. M. Harvey—

The mechanism of action of quinine in myotonia and myasthenia. *J. Amer. med. Ass.*, 1939, **112**, 1562.

The actions of procaine on neuromuscular transmission. *Johns Hopk. Hosp. Bull.*, 1939, **65**, 223.

The action of tetanus toxin on skeletal muscle. *J. Physiol.*, 1939, **95**, 30P.

The actions of quinine on skeletal muscle. *Ibid.*, 1939, **95**, 45.

The peripheral action of tetanus toxin. *Ibid.*, 1939, **96**, 348.

G. Kahlson and F. C. MacIntosh—

Acetylcholine synthesis in a sympathetic ganglion. *J. Physiol.*, 1939, **96**, 277.

H. King—

Curare alkaloids. Part IV.—Bebeerine and tubocurarine. Orientation of phenolic groups. *J. chem. Soc.*, 1939, p. 1157.

Synthesis of diphenyl ethers containing methoxy- and ethoxy-groups. *Ibid.*, 1939, p. 1165.

Amphiporine, an active base from the marine worm *Amphiporus lactifloreus*. *Ibid.*, 1939, p. 1365.

H. King and L. L. Ware—

4-Thiopyridone and derived substances. *J. chem. Soc.*, 1939, p. 873.

H. King and E. V. Wright—

Some guanyl- and guanido-naphthalenes. Group migration in cyano-naphthalenes. *J. chem. Soc.*, 1939, p. 253.

Phthalic esters as alkylating agents. *Ibid.*, 1939, p. 1168.

F. C. MacIntosh—

L'effet de la section des fibres préganglionnaires sur la teneur en acétylcholine du ganglion sympathique. *Arch. int. Physiol.*, 1938, **47**, 321.

The effect of insulin hypoglycaemia and B_1-avitaminosis on the acetylcholine content of brain. *J. Physiol.*, 1939, **96**, 6P.

H. P. Marks and F. G. Young—

The "pancreotropic" action of anterior pituitary extracts. *Chemistry and Industry*, 1939, **58**, 652.

R. L. Noble, I. W. Rowlands, M. H. Warwick and P. C. Williams—

Comparative effects of certain gonadotrophic extracts on the ovaries of normal and hypophysectomized rats. *J. Endocr.*, 1939, **1**, 22.

A. S. Parkes—

Oral activity of derivatives of testosterone. *Chemistry and Industry*, 1938, **57**, 1110.

A. S. Parkes and F. G. Young—

The influence of the subcutaneous implantation of tablets of solid insulin on the blood sugar level of the rabbit. *J. Endocr.*, 1939, **1**, 108.

J. R. Perdrau—

Persistence of the virus of herpes in rabbits immunised with living virus. *J. Path. Bact.*, 1938, **47**, 447.

Ammonium molybdate as a mordant for Mann's stain and the Weigert-Pal method. *Ibid.*, 1939, **48**, 609.

C. Rimington—

A reinvestigation of turacin, the copper porphyrin pigment of certain birds belonging to the Musophagidae. *Proc. Roy. Soc.*, B., 1939, **127**, 106.

Über das Vorkommen von Koproporphyrin III. *Hoppe-Seyl. Z.*, 1939, **259**, 45.

Disturbances of pigment metabolism following administration of drugs of the sulphonamide series and simpler related substances. *Proc. R. Soc. Med.*, 1939, **32**, 351.

Porphyrins and their relation to the metabolism of blood pigments. *Ibid.*, 1939, **32**, 1268.

C. Rimington and P. J. J. Fourie—

A rapid phase test for distinguishing between carotinoid and bile staining of fat in carcasses. *Onderstepoort J. vet. Sci.*, 1938, **10**, 439.

C. Rimington and A. W. Hemmings—

Porphyrinuric action of drugs related to sulphanilamide. Comparison with reported toxicity, therapeutic efficiency and causation of methaemoglobinaemia. Definition of the structure responsible for porphyrinuric action. *Biochem. J.*, 1939, **33**, 960.

C. Rimington, G. C. S. Roets and P. J. J. Fourie—

Quantitative studies upon porphyrin excretion in bovine congenital porphyrinuria (pink tooth) No. 1. *Onderstepoort J. vet. Sci.*, 1938, **10**, 421.

I. W. Rowlands—

Preliminary note on the reproductive cycle of the red squirrel (*Sciurus vulgaris*). *Proc. zool. Soc. Lond.*, A, 1938, **108**, 441.

The rate of appearance of anti-luteinizing activity in the serum of rabbits injected with extract of ox pituitary gland. *J. Endocr.*, 1939, **1**, 172.

Further observations on the pro-gonadotrophic and antithyrotrophic activity of antisera to extracts of the anterior pituitary gland. *Ibid.*, 1939, **1**, 177.

I. W. Rowlands and A. W. Spence—

Production of antigonadotrophic activity in man by injection of extract of pregnant mares' serum. *Brit. med. J.*, 11th Nov., 1939.

I. W. Rowlands and F. G. Young—

The capacity of pituitary preparations containing the thyrotrophic hormone to induce the formation of antisera. *J. Physiol.*, 1939, **95**, 410.

T. F. McNair Scott and W. J. Elford—

The size of the virus of lymphocytic choriomeningitis as determined by ultrafiltration and ultracentrifugation. *Brit. J. exp. Path.*, 1939, **20**, 182.

M. Llewellyn Smith—

The standardisation of tetanus antitoxin : factors influencing the assay. *Bull. Hlth Org. L. o. N.*, 1938, **7**, 739.

M. Llewellyn Smith and S. A. Price—

Staphylococcus β haemolysin. *J. Path. Bact.*, 1938, **47**, 361.

Staphylococcus γ haemolysin. *Ibid.*, 1938, **47**, 379.

Wilson Smith—

The action of bile salts on viruses. *J. Path. Bact.*, 1939, **48**, 557.

The prevention and control of virus diseases. *St. Mary's Hosp. Gaz.*, 1939, **45**, 126.

C. H. Stuart-Harris—

A neurotropic strain of human influenza virus. *Lancet*, 4th March, 1939.

M. van den Ende—

Some observations on reversed anaphylaxis. *J. Hyg., Camb.*, 1939, **39**, 471.

Precipitins in antigonadotrophic sera. *J. Endocr.*, 1939, **1**, 156.

F. G. Young—

The preparation and properties of insulin-inhibiting extracts of the pituitary gland. *Chemistry and Industry*, 1938, **57**, 1190.

Carbohydrates as constituents of proteins. *J. Amer. Med. Ass.*, 1939, **113**, 876.

The relation of the anterior pituitary gland to carbohydrate metabolism. *Brit. med. J.*, 19th Aug., 1939.

The anterior pituitary gland and diabetes mellitus. *New Engl. J. Med.*, 1939, **221**, 635.

F. G. Young, E. T. Waters, J. Markowitz and C. H. Best—

The effect of administration of some carbohydrate derivates on the hypoglycaemic symptoms of the hepatectomized dog. *Amer. J. Physiol.*, 1938, **124**, 295.

III. THE DETERMINATION OF BIOLOGICAL STANDARDS AND THE METHODS OF BIOLOGICAL ASSAY AND MEASUREMENT

Work upon Biological Standards at the National Institute for Medical Research

(*For Staff see p.* 37)

In addition to the work involved in the maintenance and distribution of the various standards already issued, in fulfilment of national, imperial and international obligations, three new standards, or new forms of issue, have been adopted and made available during the year.

Chorionic Gonadotrophin.—Four international standards for anterior pituitary hormones and analogous principles were recommended in 1938 by a conference held at Geneva at the invitation of the League of Nations Health Organization. Of these, that relating to the gonadotrophic substance extracted from human urine of pregnancy ("chorionic gonadotrophin") has now been prepared and issued. For the large amount of valuable material required, and for the final preparation of the mixed product in the form of convenient tablets packed and sealed in dry nitrogen, thanks are due to leading industrial organizations in five countries. Adequate supplies of this new standard have been sent to the national control centres in countries in which these have been established, and individual issues have also been made to research workers. The preparation of other standards of this group is well advanced.

Gas-gangrene Antitoxin (histolyticus).—A British standard for a further antitoxin of the gas-gangrene group, against the so-called "histolyticus" toxin, has now been made available. Part of the material forming the international standard was kindly provided for the purpose by the State Serum Institute, Copenhagen. The standard has now been distributed to all requiring it for use under the Therapeutic Substances Act or the British Pharmacopoeia.

Diphtheria Antitoxin.—The British standard for diphtheria antitoxin has now been placed on regular issue in the form of a solution suitable for determinations by the flocculation method, as well as in the ordinary form suitable for use in animal tests.

Tuberculin.—The international standard for tuberculin hitherto in use, which was constituted from a portion of the material prepared for the British standard, represents the relatively crude "old tuberculin" in use at the time of its adoption. There has in recent years been a progressive tendency to use tuberculin obtained from cultures of the tubercle bacillus on media containing only pure chemical constituents in known proportions. Work done largely in the United States of America, principally by Long and Seibert, has made it possible to obtain from such tuberculin a solid material representing the active substance in a relatively pure and uniform

state. This so-called P.P.D. (purified protein derivative) from tuberculin is being used on the American Continent, in Denmark, and in this country, for organized investigations into the prevalence and progress of tuberculosis; and it seems likely that it will replace "old tuberculin" in its crude form. Arrangements are in train for the adoption of a new international standard for tuberculin on this basis. It will, in the first instance, be additional to that already in use, in terms of which its specific activity will be accurately determined; but it is probable that the solid, dry standard, consisting of this relatively pure and reproducible material, will eventually supersede the one at present recognized. The Wellcome Foundation has generously presented a quantity of a representative P.P.D. preparation to the Institute, sufficient to enable Dr. Hartley to investigate its properties, with a view to its eventual use in constituting the British standard of this type.

It may be hoped that one result of this movement, for the production of a more satisfactory standard for the tuberculin used in human medicine, will be the creation of a more stable basis for the standardization of the tuberculin preparations used in veterinary diagnosis. The need for a true standardization, by which uniformity in action could be ensured for this essential reagent in the diagnosis of bovine tuberculosis, has been widely recognized in recent years. It has obvious importance, not merely for the dairy farmer but also for the health of the human community.

Tetanus Toxoid.—The value of this detoxicated preparation of tetanus toxin, in producing active immunity in man and animals against tetanus, has rapidly gained recognition. Its importance at the present time, in protecting troops against one of the major secondary risks of warfare, needs no emphasis. Before its issue could be authorized under the Therapeutic Substances Act, it was necessary to lay down in full detail the tests necessary to ensure that every batch so issued has been freed from the specific toxicity of the parent toxin, has retained adequate potency as an immunizing antigen, and is perfectly sterile. Dr. Hartley has been responsible for the investigations at the Institute required for the information and advice of the Authority administering the Therapeutic Substances Act, to enable a schedule of appropriate and effective regulations to be framed and adopted. In co-operation with Professor Ciuca, of Bucharest, Dr. Hartley has determined the tetanus antitoxin present in the sera of a large number of subjects who had received immunizing injections of the tetanus toxoid, under a variety of conditions as regards the dosage employed and the time intervals between successive injections. The results of this inquiry confirm those obtained in other countries, in showing that the toxoid is a very efficient immunizing antigen, and that it can be given in combined injection with a bacterial vaccine, such as the widely used anti-enteric vaccine T.A.B., without any impairment of its immunizing efficiency. Of particular practical importance is the fact that, when a basal immunity has once been established

by a primary immunization with the toxoid, a small injection given after an interval of as long as two years will produce a rapid and large increase in the tetanus antitoxin circulating in the blood.

Tetanus Antitoxin.—In continuation of the experiments reported last year, as part of the international investigation into certain discrepancies in the standardization of tetanus antitoxin, Miss Llewellyn Smith has now obtained definite evidence of the presence in tetanus toxin of more than one lethal factor. Five samples of the toxin were tested on mice, guinea-pigs and rabbits. The ratio between the lethal dose for guinea-pigs and that for mice was the same in the case of all the five toxins, within the limits of accuracy of the determinations. Between the lethal doses for rabbits and mice, on the other hand, expressed in both cases as doses per unit of weight, ratios varying from 85 to 0·5 were obtained with the different toxins. Such a variation appears to be inexplicable, except on the assumption that a lethal factor is concerned in the effect on rabbits, additional to that responsible for the effects observed in guinea-pigs and mice.

Gas-gangrene Antitoxin (perfringens).—Earlier experience had suggested that a test based on the haemolytic action of the perfringens toxin could be used, as an alternative to that based on its lethal action on animals, in comparing a sample of the corresponding antitoxin with the standard preparation; and that the results obtained by the two methods would be practically identical. Miss Llewellyn Smith has co-operated with Dr. Sordelli of Buenos Aires, and Dr. Ipsen of Copenhagen, in experiments which have shown that some samples of the authentic perfringens toxin contain two haemolysins, only one of which is identical with the lethal factor. The necessity is indicated of choosing a toxin which is free from this source of discrepancy, if the method based on haemolysis is to be used in the practical standardization of this antitoxin.

Stability of an antitoxin.—To provide data for a monograph in preparation by the British Pharmacopoeia Commission, defining the properties of staphylococcus antitoxin, Miss Llewellyn Smith has made a systematic study of the rate at which this antitoxin loses potency during storage at different temperatures. No difference in this respect was detected between the natural and the purified product. The deterioration—accelerated by keeping the antitoxin at the abnormal temperature of 35° C—was found to follow the course of a unimolecular reaction, falling thus to about 60 per cent. of the initial value in about eighteen months, and then to proceed at a slower rate. The stability of the antitoxin at ordinary temperatures was found to be good.

Desiccation of antisera.—Dr. Hartley has applied the method of desiccation *in vacuo* to produce stable preparations of agglutinating sera for use in diagnosis, at the request of Professor Gardner and Colonel Bridges of the Standards Laboratory for serological diagnostic materials at Oxford. One of these is an agglutinating antityphoid

serum, for use in an international investigation into the serological diagnosis of typhoid fever. Dr. Hartley has also co-operated with Dr. R. I. N. Greaves, of Cambridge, on the large-scale desiccation of antitoxins in the frozen condition by the method recently described by Dr. Greaves and Mrs. Adair.

Vitamins.—In preparation for a further international Conference on Vitamin Standards, which had been planned for the autumn of 1939, the Institute has given assistance in arrangements for the preliminary investigations. Two of the principal subjects in view for discussion were the possibility of adopting a standard preparation of a pure Vitamin A of animal origin to replace the β-carotin standard ; and the adoption of a standard for Vitamin E in the form of α-tocopherol acetate, a supply of which was available through the generosity of the Hoffmann-La Roche Company of Basel. Mr. Webster has co-operated in the preparation of solutions of known concentration, and these have been distributed to workers in different countries for trial, in accordance with plans made by the Accessory Food Factors Committee.

Insulin.—Mr. Marks has been associated with Mr. C. I. Bliss, who has dealt with the statistical theory involved, in two papers dealing with the planning of tests on rabbits for the assay of insulin in comparison with the international standard, and with the interpretation of the results of such tests. For the information of the British Pharmacopoeia Commission, who desire to indicate the limits of the error to which the biological assays of insulin are liable, Mr. Marks has collaborated with Mr. Fieller, Dr. Irwin and Mr. Shrimpton, in an investigation of the accuracy of the available methods. A paper on the slope of the dose-response curve, characteristic for the blood-sugar changes caused in rabbits by different doses of insulin, has been published ; the data dealt with are obtained partly from the records of Mr. Marks's own assays, and also from records provided by the commercial laboratories in which this method of testing is employed. Mr. Marks has further investigations in hand, also in association with a committee of the British Pharmacopoeia Commission, on anomalies and suggested improvements in the methods available for the assay of insulin in the form of its complex with protamine and zinc, and for the measurement of the desired retardation of the action of insulin which this form of combination is designed to produce.

Sex Hormones.—Dr. Emmens has made a very thorough investigation of the sources of error which complicate the assay, in comparison with the accepted standards, of different preparations now available of androgens and oestrogens—the hormones and analogous substances primarily concerned with male and female characteristics respectively. Some of the sources of error are such as are generally inherent in methods of biological standardization, but there are others specifically related to the application of such methods to the biological assay of the sex hormones in question. The results of Dr. Emmens's survey have been published in the Council's series.

The National Collection of Type Cultures of Micro-organisms

Staff—
R. St. John-Brooks, M.D. (*Curator*).
Mabel Rhodes (*Assistant Curator*).
Rosamund E. E. Barnes, B.Sc. (*Technical assistant*).

The National Collection of Type Cultures of micro-organisms continues to be accommodated at the Lister Institute of Preventive Medicine, London, by the courtesy of the Governing Body. The Curator and his assistants are in the whole-time service of the Council.

The number of cultures of bacteria and micro-fungi distributed to workers at home and abroad again exceeded six thousand in the year under review, and over four hundred new strains were deposited for maintenance or identification.

Among the types added to the Collection were the following :—

Collection of micro-organisms isolated from rotten eggs —from Dr. R. B. Haines, Low Temperature Research Station, Cambridge.

Flexner-like dysentery organisms—from Colonel J. S. K. Boyd, R.A.M.C.

English type strains of *Diplococcus pneumoniae* (Types I to XXXII)—from Dr. M. Y. Young and Prof. A. Fleming, St. Mary's Hospital, London.

Collection of micro-fungi and bacterial types—from Sir Aldo Castellani, London.

Cladosarum olivaceum n. sp.—from Mr. J. L. Yuill, New Earswick, York.

Collection of New Zealand strains of *Aspergillus* and *Penicillium* spp.—from Mr. J. C. O'Neil, Plant Research Bureau, Palmerston North, N.Z.

Streptococcus sp. used in sulphanilamide work—from Dr. Leonard Colebrook, Queen Charlotte's Hospital, London.

Dolman and Wilson's strains of *Staphylococcus*—from Dr. F. Griffith, Ministry of Health, London.

Strains of *Bacillus megatherium* and allied species—from Mr. T. Gibson, Edinburgh and East of Scotland College of Agriculture.

Autotrophic " Iron " Bacteria (*Leptothrix* Kützing), isolated by Prof. A. Sordelli, Buenos Aires—from Prof. G. S. Wilson, London School of Hygiene and Tropical Medicine.

Phytopathogenic bacteria—from Dr. W. J. Dowson, Botany School, Cambridge, and Imperial Mycological Institute, Kew.

Strains of *Corynebacterium equi*—from Prof. H. Magnusson, Malmö, Sweden.

Strains of pathogenic fungi—from Dr. J. T. Duncan, London School of Hygiene and Tropical Medicine, Mrs. E. Silver Keeping, and Prof. P. Redaelli, University of Pavia, Italy.

Collection of *Staphylococcus* types producing alpha, beta and gamma toxins—from Miss M. Llewellyn Smith, National Institute for Medical Research, London.

Organisms causing " Sarcina sickness " in beer—from Dr. J. L. Shimwell, Cork, Eire.

Clostridium botulinum Type E—from Department of Health, New York State.

Mycobacterium sp. from voles (*Microtus agrestis*)—from Dr. A. Q. Wells, University of Oxford.

Fungi isolated from diseased tea plants—from Dr. C. H. Gadd, Tea Research Institute of Ceylon.

Types of British Pyrenomyces—from Dr. C. G. C. Chesters, Birmingham University.

Type cultures of Mucorales isolated from soil—from Dr. Marie E. Campbell, University of Edinburgh.

Mycobacterium tuberculosis " B.C.G." and " Vallée " strains—from Dr. A Stanley Griffith, Field Laboratories, Cambridge.

Complete type collection of one hundred *Salmonella* strains—from Dr. F. Kauffmann, Statens Seruminstitut, Copenhagen.

Phytopathogenic fungi from Prof. Dr. J. Westerdijk and *Margarinomyces* spp, isolated from butter—from Dr. F. H. van Beyma thoe Kingma, Centraalbureau voor Schimmelcultures, Baarn, Holland.

Human strain of *Bacterium pseudotuberculosis rodentium*—from Dr. N. H Topping, U.S. Public Health Service, Washington, D.C.

Cultures of *Leptospira canicola*—from Major H. C. Brown, Wellcome Research Institution, London.

Yeast cultures—from Dr. T. Castelli, University of Perugia, Italy.

Strains of *Actinomyces bovis* (Wolff and Israel)—from Dr. L. P. Garrod, St. Bartholomew's Hospital, London.

Strains of *Vibrio fetus*—from Prof. T. Dalling, Cambridge University, and Dr. W. S. Gordon, Animal Diseases Research Association, Midlothian.

Strain of *Bact. proteus* (which agglutinates with an anti-brucella serum) - from Prof. Dr. Reiner Müller, Cologne University, Germany.

New *Moraxella* spp.—from Dr. A. Lwoff, Institut Pasteur, Paris.

For all these donations the Council desire to express their thanks.

A new and revised report on the genus *Salmonella* has been prepared by the Salmonella Sub-Committee of the Nomenclature Committee of the International Association of Microbiologists, of which the Curator is Secretary. This report was presented to the Nomenclature Committee at the Third International Congress for Microbiology which took place in New York in September, 1939.

The Standards Laboratory for Serological Reagents, Oxford

Staff—

Lieut.-Col. R. F. Bridges, M.B., R.A.M.C. (*ret.*)
Edith F. Stubington, B.Sc.

The work of producing, standardizing and distributing bacterial suspensions and sera for the diagnosis of enteric, dysenteric, *Brucella* and meningococcal infections has been continued at the Standards Laboratory in the School of Pathology at Oxford. The demand for these materials has been well maintained during the year and new clients have been added to the list of recipients. Colonel Bridges and Miss Stubington give whole-time service to the Council: Professor A. D. Gardner acts as honorary Consulting Director.

The drying of agglutinating sera has been actively pursued during the year. Several batches of sera have been dried at the National Institute for Medical Research, by the kindness of Dr. Hartley, and the Standards Laboratory is now in a position to do much of this work itself. As pointed out in last year's Report,

the method will not only lead to economy in working, but will also enable the Standards Laboratory to provide a wider range of service than has been possible hitherto.

As a result of publications by Dr. A. Felix and others on the recently discovered Vi antigen of *Bact. typhosum*, many applications have been made to the Standards Laboratory for a suitable suspension for Vi test. Most of the early work on this antigen had been done with living suspensions, which are obviously unsuitable for distribution. The preparation of a killed suspension of high initial sensitivity, and capable of retaining this property unimpaired over a reasonable period, presented problems which have engaged the attention of the Standards Laboratory during the year. In this work co-operation has been given by the staff of the Mental Hospitals Department of the London County Council: they have supplied many sera for test, both of carriers and non-carriers, and have carried out parallel tests themselves with suspensions provided by the Standards Laboratory.

The danger which may arise to the community through the employment of typhoid carriers among water-duty personnel or those who handle food has long been recognized, but there has been no simple test by which these dangerous individuals can be recognized. Serum tests with H and O antigens have been tried, but have not been successful. It is hoped that the Vi antigen may prove to be a more valuable reagent for this test, since it is believed that the presence of Vi agglutinin in the blood is evidence that the individual concerned is harbouring living and virulent typhoid bacilli in his body. The authorities of the Metropolitan Water Board are interested in this matter and are proposing to test all their employees, numbering several hundreds, by this method. Suspensions will be supplied by the Standards Laboratory for the purpose.

Researches by Boyd on the antigenic structure of the Flexner group of dysentery bacilli have recently been published and are of particular importance to the Standards Laboratory. It has been shown that during artificial culture these organisms undergo changes which result in the gradual, or in some cases rapid, acquisition of group characteristics. These changes materially affect the question of agglutinability standards, and must be taken into account during the preparation of suspensions and sera from the Flexner bacilli.

Two recently discovered organisms, known at present as types 103 and P119, have been added to the list of suspensions and sera prepared in the Standards Laboratory. These organisms have been shown by Boyd to be members of the Flexner group, and they are known to be a cause of dysentery both in England and abroad. These additions necessitate some modification in the arrangements for the supply of materials prepared from the bacilli of the Flexner group: a leaflet is being prepared and will be distributed to all concerned.

Another organism from which suspensions and sera are now being prepared is *Bact. dysenteriae* Schmitz. This bacillus has been

incriminated as a cause of dysentery in India for some years past, but has received little recognition from bacteriologists in this country. Recent outbreaks of dysentery in a mental hospital in North Wales were shown to be due to this organism, and it is probable that it occurs more often than has been thought. The failure to recognize it may be due to the fact that agglutinating serum must be prepared from recently isolated strains, or at least from strains which have retained in culture their original antigens. The majority of stock cultures maintained in laboratories are of little use for this purpose.

IV. CLINICAL RESEARCH UNITS

The Department of Clinical Research, University College Hospital, London

Staff—
Sir Thomas Lewis, C.B.E., M.D., F.R.C.P., F.R.S. (*Director*).
G. W. Pickering, M.B., F.R.C.P.
E. E. Pochin, M.B., M.R.C.P.

Visiting worker—
Dr. M. Mendlowitz, New York.

Attached workers—
R. G. Bickford, M.B.
Janet Hill.
J. H. Kellgren, M.B., M.R.C.P., F.R.C.S.
J. R. Squire, M.B.

The post of Director has been permanently endowed by the Rockefeller Foundation, but this department is otherwise staffed and supported by the Council. Dr. Pickering left the staff at the end of the period under review to take up the appointment of Professor of Medicine at St. Mary's Hospital, London.

Dr. Kellgren has continued his investigation of referred pain from deep-lying somatic structures. He found it possible to map out many segmental areas of pain by stimulating the individual interspinous ligaments of the vertebral column, using as the stimulus a small injection of 6 per cent. saline. These pain areas differ from Foerster's dermatomes and from Head's areas of skin tenderness.

An extensive investigation of deep-lying structures—fasciae, periosteum, tendons, joints, and muscles—has led him to conclude that the pain derived from these differs much in its diffusion. It may be confined to a spot or diffused over the full segmental distribution ; whether it is local or segmental in distribution appears to depend more upon the depth at which the stimulated tissue lies than upon its nature.

Sir Thomas Lewis and Dr. Kellgren recognised that the observations upon referred pain from deep somatic structures would be given a wider significance if they could be related with certain other phenomena, and especially if the underlying mechanism could be correlated with that underlying the referred manifestation of visceral disease. When deliberate search was made from this standpoint, they found that stimulation of the interspinous ligaments gave rise not only to segmental pain but to superficial areas of skin tenderness and to characteristic muscular rigidities. It was found possible, by injecting saline into various ligaments of the back, to reproduce pain having not only the segmental distribution recognised as characteristic of visceral disease, but simultaneously such superficial and deep tenderness and such muscular rigidity as are usually associated in the corresponding visceral diseases (the so-called viscero-sensory and viscero-motor reflexes). It would appear, from these and other observations, that there is no feature of visceral pain

and no associated phenomenon which may not be derived from stimulation of somatic structures. To compare in detail reflex muscular rigidity produced by stimulating somatic and visceral structures, the decapitated cat has been used and a close comparison made of the reflexes from such structures as the muscles of the back and such organs as the pancreas. They do not differ in any substantial feature, provided that appropriate and similar methods of stimulation are used. The reflex induced from the somatic structures is propagated through somatic nerves, and that induced from the viscus through nerves of the anatomical sympathetic system. Reasons have been advanced for the belief that the fibres of the splanchnic nerves which form the afferent channel are sensory. It is concluded that deep somatic and certain visceral structures are supplied by a common set of afferent nerves, stimulation of which produces similar pain and many similar reflex phenomena ; and that this common system is responsible for all the pain and referred phenomena of visceral disease. The relation of these observations and conclusions to past theories of visceral pain—with associated tenderness and rigidity—has been discussed in the published account.

Dr. Pickering has continued to work on renin and its possible relation to hypertension, further assays being made on the kidneys of normal rabbits and of rabbits with experimental hypertension. With Dr. Butler, attempts are being made to isolate the substance. Dr. Pickering has found that the purest preparations yet obtained produce in the unanaesthetised rabbit a transient fall followed by a pronounced rise in the rate of urine flow ; the antidiuretic phase is accompanied by a decrease in the rate of glomerular filtration, the diuretic phase by a large increase in sodium chloride excretion.

One of the difficulties standing in the way of the hypothesis that renin is the effective agent in any type of persistent hypertension is that, in the anaesthetised animal, successive injections produce diminishing responses. Miss Hill and Dr. Pickering have found that in the unanaesthetised rabbit the blood pressure may be kept elevated for at least four hours by infusing into an ear vein a solution of renin at a suitable rate. If the rate is too great, the arterial pressure rises at first to a high level and falls progressively from this as the infusion continues, the final value being but little above the normal level.

Dr. Pochin has investigated the effects of stimulating the sympathetic nerves in man, and compared them with the abnormalities of the eyes in Graves's disease. He concludes that neither the protrusion of the eyes nor the retracted staring position of the upper eye-lids in this condition should be ascribed, as is usually done, to over-activity of the sympathetic nervous system. The retraction of the upper lid appears to be due to spasm of the striated muscle of the lid ; the cause of the protrusion is now being investigated.

Dr. Bickford has investigated itching such as follows puncture of histamine into the skin, and other appropriate forms of stimulation, on the lines previously adopted in this laboratory for the investigation of local skin tenderness. He finds that, in addition to spontaneous

itching, an independent condition of itchy skin develops around the lesion. Evidence is brought to show that this itchy skin arises through a local nervous (axonic) pathway. The sensation of spontaneous itch and that derived from rubbing itchy skin appear to be carried by different sensory nerve fibres; thus, asphyxia abolishes the latter while leaving the former intact.

Dr. Mendlowitz has made a careful investigation of local circulation in forms of finger clubbing. He brings evidence to show that the maximal heat elimination—and hence the bloodflow—of the distal phalanges of clubbed fingers, secondary to lung or congenital heart disease, is usually increased. The digital arterial pressure is increased, and the brachial-digital pressure gradient decreased, in these forms of clubbed fingers; but in hereditary clubbing these pressures and gradients are normal.

R. G. Bickford—
Experiments relating to the itch sensation, its peripheral mechanism and central pathways. *Clin. Sci.*, 1938, **3**, 377.
J. H. Kellgren—
On the distribution of pain arising from deep somatic structures, with charts of segmental pain areas. *Clin. Sci.*, 1939, **4**, 35.
T. Lewis and J. H. Kellgren—
Observations relating to referred pain, viscero-motor reflexes and other associated phenomena. *Clin. Sci.*, 1939, **4**, 47.
M. Mendlowitz—
Some observations on clubbed fingers. *Clin. Sci.*, 1938, **3**, 387.
G. W. Pickering—
The problem of high blood pressure in man. (Hertzstein lecture, abstract.) *Brit. med. J.*, 7th Jan., 1939.
Experimental observations on headache. (Hanna lecture.) *Ibid.*, 6th May, 1939.
G. W. Pickering and M. Prinzmetal—
Experimental hypertension of renal origin in the rabbit. *Clin. Sci.*, 1938, **3**, 357.
E. E. Pochin—
Ocular effects of sympathetic stimulation in man. *Clin. Sci.*, 1939, **4**, 79.
The mechanism of lid retraction in Graves' disease. *Ibid.*, 1939, **4**, 91.

The Clinical Research Unit, Guy's Hospital, London

Staff—
R. T. Grant, M.D., M.R.C.P., F.R.S. (*Director*).
Attached worker—
H. E. Holling, M.Sc., M.B., M.R.C.P.

Visiting Worker—
M. A. Wachstein, M.D.

The Director is in the whole-time service of the Council, and has the honorary status of Assistant Physician to the Hospital, with charge of eight beds and an out-patient clinic. Dr. Holling received a personal grant.

During the year observations have been made on patients displaying fever, with a view to obtaining clearer insight into the mechanism of the changes in body temperature. The work has led to refinements towards greater accuracy and sensitivity in thermo-electric methods of measuring both deep and superficial body temperature, and also to further observations on the control of body

temperature in the normal subject. It has been found that, in fever, a conspicuous diminution in skin blood flow not only accompanies but precedes—and is the chief factor producing—the rise of rectal temperature. An outpouring of adrenaline, which in the past has been thought to be a cause of the vasoconstriction, can hardly be held responsible for this, since not only is cutaneous blood flow diminished, but that to the limb muscles shows no evidence of any increase during the onset or subsidence of the fever. The observations emphasize the importance of the physical in contrast to the chemical regulation of body temperature, and especially the large part played by the circulation through the hands and feet in maintaining body temperature at normal levels under ordinary conditions.

Attention has been directed to the variability of the effect of small doses of adrenaline introduced into the blood stream. It has been found both in patients and in normal subjects that, in circumstances not yet understood, minute doses which ordinarily cause no material circulatory change (beyond an increase in muscle blood flow) may cause intense pallor of the skin and unpleasant subjective sensations.

The plethysmographic method of measuring blood flow through voluntary muscle, referred to last year, has opened a way for more direct study of certain aspects of the metabolism of muscle in the human subject. Observations have been made on both the oxygen and sugar metabolism of the limb muscles. The results show that, as with blood flow, the oxygen consumption of resting human muscle is lower and more constant than is found in animal experiment. The observations have given an explanation for the great variations in the oxygen content of venous blood removed from a forearm vein, and have made it clear that a change in the arterio-venous oxygen difference cannot be regarded as indicative of a change in the oxygen metabolism of the limb unless the actual blood flow is also taken into account. A study of the metabolism of the forearm muscles in hyperthyroidism has suggested new aspects of the nature of the thyreotoxic state. Although blood flow through resting muscle in hyperthyroid patients is increased considerably beyond the normal, yet the oxygen used by the muscle is not appreciably increased ; nor is it affected by thyroidectomy as is the total oxygen consumption of the patient. This suggests the presence, in hyperthyroidism, of a circulatory stimulant other than the increased metabolism.

Further observations have been made on the blood flow to the limbs of patients with unilateral peripheral vascular disease and intermittent claudication, in order to test the efficacy of certain remedies thought to increase the circulation to diseased limbs. In such patients, although the blood flow to the muscles increases after a standard exercise, the increase does not reach such high levels as normally and takes much longer to subside. The observations indicate that, in the investigation of remedies to be used in the treatment of intermittent claudication, an increase in the blood

flow to resting muscle is of little account and that the remedies must be shown to have a beneficial effect on the hyperaemia associated with exercise. Of the remedies tested, none has been found to have any material effect even on resting muscle blood flow; and, so far, exercise remains the most potent factor in provoking increased blood flow to the limb muscles. In this regard, an attempt was made to apply thermo-electric methods for estimating muscle blood flow at the bedside, to replace the more complicated plethysmographic method now used. It was previously shown that exercise of muscle after a period of rest caused a conspicuous rise of muscle temperature, due mainly to increased blood flow through the muscle. It was found, however, that although the rate of temperature rise in muscles with deficient circulation is slower than in normal limbs, yet the rate of rise is so influenced by other factors not readily controlled that the method seems impracticable for the purpose.

Observations have been made on cases of so called primary pulmonary hypertension; also on the aetiology of vascular symptoms due to cervical rib, and on the improvement in limb circulation resulting from removal of the rib.

The Neurological Research Unit, National Hospital for Diseases of the Nervous System, Queen Square, London

Staff—
E. Arnold Carmichael, M.B., F.R.C.P. (*Director*).

Halley Stewart Fellow—
W. M. Honeyman, M.D., M.R.C.P.

Attached workers—
Beryl Bolton, M.R.C.S.
W. K. Stewart, B.Sc., M.B.

Visiting workers—
A. M. Barry, M.B.
Professor G. S. Melvin, M.D., Kingston, Ontario.
Dr. T. Lidz, Baltimore.
Dr. L. C. Kolb, Baltimore.
Dr. T. Lindquist, Uppsala.
Dr. H. Lax, Budapest.
Dr. W. K. Smith, Rochester, Minnesota.

The work of the Unit has been directed mainly to a study of the autonomic nervous system in man. Following upon the detailed study of the vasomotor responses made last year, Professor Melvin, Dr. Barry and Dr. Wilbur Smith—with Dr. Carmichael—investigated the time difference, following a given stimulus, in the onset of the response as recorded from the toes and fingers. As a longer period of latency was found for the response because of the interference of the pulse beat, a number of experiments were made with the circulation occluded. From the results obtained it became evident that the vessels of the toe constricted from 1·2 to 3·0 seconds after the vessels in the fingers. With Dr. Honeyman, Dr. Kolb and Dr. Stewart, investigations were undertaken to determine if changes in skin resistance, following a given stimulus, were of sufficient intensity and abruptness to permit of a more close determination of the time difference. It was early found that an analysis of the phenomena responsible for changes in skin resistance required further study. Thereupon, it was first shown that the response was associated with either vasomotor activity or sweating or both.

Fatigue materially altered the character of the response. It was further found that comparable results could be obtained only with the parts under observation at like temperatures and in a state of vasodilation produced by warming the body. After the ideal conditions for obtaining the response had been determined, a study was made to find out the conduction rate in the peripheral sympathetic system in man. By comparing the time of onset of the reflex change at two sites in one dermatome of the trunk, a conduction rate of about two metres per second, and a similar rate for the sympathetic fibres to the arm and face, were found. In the leg, however, the conduction rate was considerably slower.

The work on intestinal motility with Professor McSwiney has been elaborated, and a study of changes in blood pressure and of vasomotor activity has been undertaken, following distension of the duodenum, jejunum and rectum. It has been found that vasomotor responses, frequently unassociated with any conscious sensation, occur after rapid small distensions of these hollow viscera. Changes in blood pressure have been produced though no digital vasomotor activity took place. Careful note has also been made of any sensation caused by the distension. Similar methods have been used to investigate subjects in whom the splanchnic nerves have been removed at operation : this has been made possible by the kindness of Mr. P. B. Ascroft of the Middlesex Hospital.

Dr. Lindquist and Dr. Lax have undertaken a study of the reaction of the larger blood-vessels of man to rapid occlusion. By recording blood pressure and pulse wave, distal to the occluding cuff, they have obtained evidence that in healthy subjects a large artery, such as the brachial artery, has the ability to constrict, while in older subjects this ability is greatly reduced. Dr. Lindquist has begun an investigation of tremor in association with the changes of potential from the cerebral cortex. By altering the rhythm of potential changes, through over-ventilation and by other methods, it has been possible to dissociate the two rhythms entirely. The effects of lesions at different levels of the nervous system, as well as fatigue in this tremor, are now being investigated.

Dr. Kolb and Dr. Bolton have studied, in animals, the effect of injection of heterologous serum sensitised to kidney or to brain. No changes have been found in the nervous system, although with kidney-sensitised serum changes in the kidney were easily provoked. This work was a preliminary to further studies on the possible cause of certain demyelinating diseases such as disseminated sclerosis.

Dr. Lidz has made a close study of a subject before and after right frontal lobectomy. A variety of tests of a psychological character, including intelligence and temperament tests, were given to the patient. It was found that the complete removal of the right frontal lobe in this right-handed subject resulted in no demonstrable change in the ability to perform the tests. As a method of determining the functional capacity of the frontal lobes, these tests are thus shown to be of dubious value.

Dr. Bolton has completed and published her work on the blood supply of the human spinal cord. A careful mapping of the blood supply of the medulla oblongata, pons and mid-brain is now being undertaken, and several new points of interest have emerged.

Dr. Carmichael and Dr. J. N. Cumings, biochemist to the hospital, have undertaken a metabolic study of a case of hyperparathyroidism with marked muscular weakness. Dr. Cumings has made determinations of the potassium content of the muscle, before, immediately after, and several months after operation for removal of the enlarged parathyroid. Marked deviation from the normal potassium content of the muscle and blood were found before the operation; and the relationship of this alteration in potassium to the muscular weakness was studied. Further investigations in cases of myxoedema and hyperthyroidism are being undertaken to find whether there is any disturbance of potassium balance associated with the disturbance of muscle function in such cases.

B. Bolton—
The blood supply of the human spinal cord. *J. Neurol. Psychiat.*, 1939, **2**, 137.

E. A. Carmichael, J. Doupe, A. A. Harper and B. A. McSwiney—
Vasomotor reflexes in man following duodenal distension. *J. Physiol.*, 1939, **95**, 276.

J. Doupe, W. E. Miller and W. K. Keller—
Vasomotor reactions in the hypnotic state. *J. Neurol. Psychiat.*, 1939, **2**, 97.

J. Doupe, H. W. Newman and R. W. Wilkins—
A method for the continuous recording of systolic arterial pressure in man. *J. Physiol.*, 1939, **95**, 239.
The effect of peripheral vasomotor activity on systolic arterial pressure in the extremities of man. *J. Physiol.*, 1939, **95**, 244.

T. Lidz—
A study of the effect of right frontal lobectomy on intelligence and temperament. *J. Neurol. Psychiat.*, 1939, **2**, 211.

H. W. Newman, J. Doupe and R. W. Wilkins—
Some observations on the nature of vibratory sensibility. *Brain*, 1939, **62**, 31.

R. W. Wilkins, J. Doupe and H. W. Newman—
The rate of blood flow in normal fingers. *Clin. Sci.*, 1938, **3**, 403.

The Unit for Clinical Research in Surgery, Edinburgh

Staff—
W. C. Wilson, M.B., F.R.C.S.E. (*Director*).
Attached and visiting workers—
Alexander Brown, M.B.
R. A. McKail, M.B. (Houldsworth Scholar).
H. M. Adam, M.B. (Leckie-Mactier Fellow).
A. G. Ross Lowdon, M.B., F.R.C.S.E. (Vans Dunlop Scholar).
J. Harold Kay, M.D., San Francisco.
H. N. Harkins, M.D., Chicago.
A. W. Wilkinson, M.B.
Ian Aird, M.B., Ch.M., F.R.C.S.E.
A. B. Wallace, M.B., F.R.C.S.E.
T. I. Wilson, M.B., F.R.C.S.E.

The Unit is situated at the Royal Infirmary and the Royal Hospital for Sick Children, Edinburgh, with laboratory facilities in the Wilkie

Surgical Research Laboratory of the University. Mr. Wilson gave whole-time service to the Council as Director, but left at the end of the year to become Professor of Surgery at Aberdeen.

Mr. Wilson and Dr. McKail have continued the investigation, mentioned in last year's Report, into the excitability of the cerebral motor cortex, and particularly the effect of anticholinesterases on cortical excitability. The complicated responses of the cortex are being analysed in experiments in which the blood vessels of the brain are perfused.

Extending the study of the clinical course of extensive burns, Mr. Wilson and Dr. C. P. Stewart found characteristic changes in the chemical constituents of the blood and of other extracellular fluids, notably in sodium, potassium, non-protein nitrogen and chlorides. Simultaneously the action of desoxycorticosterone (a synthetic hormone of the suprarenal cortex) was tested in burns and other surgical conditions associated with circulatory failure. In some conditions, e.g. shock, the synthetic hormone rapidly restored the blood chemistry levels to normal and it also exerted an occasional beneficial action on the circulation. These observations on patients were confirmed and extended by experiments in which Dr. McKail, Mr. Ross Lowdon and Mr. S. L. Rae collaborated. More recently a similar investigation has been begun by Mr. Lowdon, Dr. Stewart and Mr. Wilson on blood chemistry changes in patients subjected to heavy X-radiation in the treatment of malignant disease, while Dr. Adam and Dr. J. Harold Kay have carried on the investigation of the actions of desoxycorticosterone, especially its action on metabolism. Another aspect of the subject of burns, namely the toxic properties of oedema fluid, was studied by Dr. Harkins: he confirmed and amplified previous work done in the laboratory of the Unit.

Dr. Alexander Brown completed the construction of an apparatus for the measurement, by a new method, of the water loss from the human skin. This method he is using to study the relation of water loss to alterations in the circulation of blood through the skin. Mr. T. I. Wilson has observed the changes in agglutinins and agglutinogens in human blood which has been stored for long periods at a low temperature.

At the Royal Hospital for Sick Children, Dr. Wilkinson and Dr. G. P. Thomson applied the laevulose tolerance test of liver function to surgical conditions in childhood. They found that the normal standards in children were in some degree different from those in adults, and that liver function was impaired by certain diseases and injuries, by anaesthesia, and by some drugs frequently employed in therapeutics. Their results have been prepared for publication.

A. G. Ross Lowdon, R. A. McKail, S. L. Rae, C. P. Stewart and W. C. Wilson—
Changes in sodium and in other constituents of blood and extracellular fluids following scalds. *J. Physiol.*, 1939, **96**, 27 P.

W. C. Wilson and C. P. Stewart—
Changes in blood chemistry after burning injuries and in other grave surgical conditions; with some reference to treatment by desoxycorticosterone acetate. *Trans. med-chir. Soc. Edinb.*, 1939, **118**, 153.

V. EXTERNAL SCIENTIFIC STAFF

Investigations by Members of the Staff and Co-Workers

It continues to be part of the Council's policy to maintain an external staff to undertake researches elsewhere than in their own central institute. The work of some members of this staff has already been noticed in the two preceding sections, under the headings of Biological Standards and Clinical Research Units. Investigations by the staff working under the Industrial Health Research Board are mentioned separately at p. 141. The present section gives an account of the work of most of the remaining members of the external scientific staff: the work of two members who are taking part in research in chemotherapy at Liverpool, of one who is engaged in the investigation into pulmonary disease among coal-miners in South Wales, and of another who is making nutritional studies in the tropics, is mentioned at pp. 133, 140, and 139, respectively.

Diseases of Children

Queen's Hospital for Children, London

Medical Research Council staff (part-time)—
Helen M. M. Mackay, M.D., F.R.C.P.

Dr. Mackay has been investigating problems relating to nutritional anaemia in young children. She has, for example, been examining the question whether small doses of iron salts which by themselves are ineffective in treatment can be made effective by giving copper in addition. She has also been seeking evidence as to the possible persistence and availability of an iron store after iron treatment.

Dr. Mackay has shown that babies getting a mixture of equal parts of soya flour and dried milk grow nearly, if not quite, as well as babies wholly on a dried milk diet. They have a similar morbidity rate, and they have a higher haemoglobin level than babies given unmedicated dried milk. Tests of a roller-process dried milk showed that this provided a sufficient quantity of vitamin A to meet the needs of infants under six months who had no other source of the vitamin.

H. M. M. Mackay—
Vitamin A requirements of infants. *Arch. Dis. Childh.*, 1939, **14**, 245.

Growth and Development

Institute of Anatomy, University College, London

Medical Research Council staff—
Matthew Young, M.D., D.Sc.

During the year Dr. Young continued to collect observations for a combined radiological and clinical investigation of the influence which minor variations in the form of the pelvis have on foetal presentation and labour. The work is being done in co-operation with Dr. J. G. Hastings Ince of the Obstetric Unit, University College

Hospital, and has now been completed, after some delay caused by an extension of the original scope of the inquiry. The analysis of the data, with the assistance of Miss Irene Allen, has also been completed for publication. In this paper are recorded the results of a detailed study of the architecture of the pelvis, as revealed by radiography in a consecutive series of fully 500 women attending the ante-natal clinic, and of an attempt to correlate variations in the pelvic size and shape with subsequent obstetric histories. One of the main conclusions is that the classification of pelvic form mainly from the shape of the inlet by subjective impressions, which has recently been strongly recommended by some, is not only unscientific but cumbersome and of no practical value. Minor variations in the form of the pelvis, on the obstetric importance of which much emphasis has been laid, were found to have little or no influence in determining the course of labour.

The radiological investigation, begun with the late Professor H. H. Woollard, into the skeletal appearances and growth of the hands and heads of some 200 children, from five to nine years of age, is now being continued with Dr. A. G. M. Weddell. Arrangements have kindly been made by Dr. R. P. Garrow, Medical Officer of Health for Hornsey, for the same children to be sent to University College for radiological and clinical examination at six-monthly intervals. Good progress is being made with the analysis of the data. The results have not fulfilled the early hope that they might provide a reliable index of nutrition, but they have given much useful information on growth and development. The consecutive radiographs of the children's heads enable the internal architectural features to be accurately measured; they also seem likely to yield valuable information regarding variation in facial growth in children with the jaws in normal and abnormal relationship, respectively.

The collection of records of normal spinal curvature and other data in children in the later stages of school life is being continued with Commander Geoffrey Whitehouse. An ingenious special instrument for tracing and recording the curvature with considerable exactitude has been constructed to a design by Commander Whitehouse. The instrument is easily manipulated and has greatly facilitated the process of recording curvatures. Besides increasing our knowledge of the variations in normal spinal curvature, it is hoped that the inquiry will throw some light on the development of adolescent kyphosis.

A joint report with Mr. W. T. Russell, on the results of an investigation of the available statistics of appendicitis, was published by the Council during the year. Some evidence was found to suggest that the actual incidence of appendicitis has increased in recent years, apart from any apparent increase that may be due to greater scientific knowledge and skill in diagnosis. There has been at the same time a great decline in the case fatality from the disease, and there is convincing evidence that early admission to hospital is one of the most potent factors in reducing the fatality. The mortality

rate from the disease varies greatly in the different social orders: in the highest social class it is at least two-and-a-half times that found in the lowest social class. The incidence of the mortality from the disease is heavier on spinsters than on married women.

M. Young and W. T. Russell—
Appendicitis. A statistical study. *Spec. Rep. Ser. Med. Res. Coun., Lond.*, No. 233, 1939.

Puerperal Infections

Queen Charlotte's Hospital, Hammersmith, London

Medical Research Council staff—
L. Colebrook, M.B.
Leverhulme Research Fellow—
Dora Colebrook, M.D.
Attached workers—
R. M. Fry, M.R.C.S.
A. T. Fuller, Ph.D.
E. D. Hoare. M.B
G. V. James, M.Sc.

The work of this unit receives support not only from the Council, but also from the Pilgrim Trust and from an anonymous donor—the latter having given £1,000 per annum during the past eight years.

Since the beginning of 1939, all puerperal fever patients infected by haemolytic streptococci (and also patients with *B. coli* urinary infections) have been treated by sulphapyridine (M and B 693) on behalf of the Therapeutic Trials Committee, for comparison with the results obtained in previous years by red prontosil and sulphanilamide. In addition to clinical observation, the absorption and excretion of this drug, and the changes undergone by it in the body, have been studied.

In regard to this drug and the other members of the sulphonamide group, particular attention has been directed in recent months to the danger of a harmful effect upon the blood-forming organs, resulting sometimes in a fatal agranulocytosis. Among nearly 600 patients treated at Queen Charlotte's Hospital during the past three-and-a-half years, this harmful effect has been detected four times—happily only once with a fatal result. For the better understanding of this danger and how it may be avoided, an attempt has been made to induce a similar effect upon the blood-forming system of animals: other experiments have been made to determine which of the sulphonamide preparations is least liable to exert this harmful effect, and whether the doses employed hitherto have been larger than are necessary.

The effect of simultaneous treatment by a specific serum and a sulphonamide preparation in streptococcus infections has also been studied in the mouse, to test the suggestion that this might give an even more striking result than treatment with the drug alone, and also the possibility that the dosage of the latter might thus be reduced.

Routine testing (*in vitro*) of a number of strains of streptococci isolated from puerperal infections has brought to light the interesting fact that patients who do not make the usual satisfactory response to treatment by sulphanilamide are in many instances infected by cocci which are demonstrably insensitive to the drug. It is hoped that a comparison of the biochemical properties of these strains with those of sensitive strains may help to explain how the drug affects the metabolism of these and other micro-organisms.

Other work directed to the same end has been in progress throughout the year—particularly the study of various substances which antagonise the action of sulphanilamide upon streptococci. Certain toxic degradation products formed from these drugs in the human body have also been under investigation.

Dr. Dora Colebrook has continued her study of the problems connected with the serological classification of haemolytic streptococci, seeking especially to recognise and to eliminate the cross reactions which occur in typing and grouping by agglutination and precipitation tests.

L. Colebrook—
Chemotherapy and the white cells. *Lancet*, 15th July, 1939.

A. T. Fuller, L. Colebrook and W. R. Maxted—
Factors which determine the fate of haemolytic streptococci (group A) in shed blood and in serum. *J. Path. Bact.*, 1939, **48**, 443.

A. T. Fuller and W. R. Maxted—
The production of haemolysin and peroxide by haemolytic streptococci in relation to the non-haemolytic variants of group A. *J. Path. Bact.*, 1939, **49**, 83.
A type of group A haemolytic streptococcus which fails to form peroxide. *Brit. J. exp. Path.*, 1939, **20**, 177.

E. D. Hoare—
The case for prophylaxis with sulphanilamide and M. & B. 693. *Lancet*, 14th Jan., 1939.
The suitability of "liquoid" for use in blood culture media, with particular reference to anaerobic streptococci. *J. Path. Bact.*, 1939, **48**, 573.

M. E. Sutherland—
Agranulocytosis following administration of M. & B. 693. *Lancet*, 27th May, 1939.

Inheritance and Disease

Galton Laboratory, University College, London

Medical Research Council staff—
Julia Bell, F.R.C.P.

During the past year, work on hereditary ataxia and spastic paraplegia has been completed, and a report has been published in collaboration with Dr. E. A. Carmichael (see page 73). Amongst many points of interest revealed by the material collected are those suggesting the short average duration of the disease. This appears to be independent of the age of onset of symptoms or the genetic type, and to bear no relationship to the normal expectation of life, whatever the age of onset. It is clearly of considerable practical

importance that such a feature of a chronic incurable disease should be established on more adequate data than can be obtained from study of so rare an example as hereditary ataxia.

Another point for the consideration of the geneticist and the neurologist lies in the fact that some thirty-five families have been shown to include cases of typical Friedreich's ataxia, and also cases of spastic ataxia. It is difficult to avoid the conclusion that the same gene can be responsible for the two clinical types of disease; moreover, little evidence can be produced from analysis of the clinical descriptions to suggest any fundamental differentiation in these two types of hereditary ataxia.

The analysis of nearly 100,000 consanguinity inquiry cards is proceeding. These were filled in by a number of general and special hospitals, with a primary view to determining the consanguinity rate in the parentage of the hospital population. The consanguinity rate is low—probably not higher than 0.8 per cent. in the general hospitals, or 0.6 per cent. if only first cousin marriages be considered. It is of importance to the geneticist to have this measure, and it should assist him to estimate the incidence of certain recessive hereditary diseases in the country. It was hoped also that this material would reveal the presence of a recessive character as the determinant of some rare diseases of obscure aetiology. A few pointers in this direction are of undoubted interest and will be followed up by other methods of investigation. The rarity of consanguineous marriage makes this mode of establishing the recessive character of a rare disease an unlikely event, but a considerable amount of negative evidence can be provided by it.

Other points of interest emerging from this material consist in the age distribution and sex incidence of specific diseases. It is of importance to obtain measurements of these factors, as they may have a very significant bearing upon the aetiology of a disease and its treatment. To give a few examples only, conditions diagnosed as rheumatism, rheumatic carditis, Sydenham's chorea, mitral stenosis and rheumatoid arthritis all occur in marked excess amongst females: a similar or even more striking excess occurs in cases of gall-stones, cholecystitis and diabetes. Amongst males it is difficult to explain the great preponderance in the incidence of peptic ulcer, particularly marked in duodenal ulcer; of papillomata, whether of the bladder or larynx, etc.; and of cancer of the tongue, lip, mouth, palate, larynx and thorax. An excess of males suffer from cancer of the oesophagus, bladder, rectum and stomach; whereas cancer of the colon occurs with a similar frequency in both sexes. Why should 85 out of 109 cases of congenital pyloric stenosis occur in males? It is perhaps understandable that 38 out of 45 cases of congenital dislocation of the hips should occur in females, but again why should 27 out of 34 cases of cervical rib be noted in females? Further, why should more than 70 per cent. of cases of inguinal hernia in children occur on the right side? Clinicians may be aware of many of these facts, some of which need to be verified on ampler

material, but it is important to obtain a measure of them: it is accordingly hoped that the many hospital workers who have contributed the material will feel that their labours have been of value.

Julia Bell and E. A. Carmichael—

On hereditary ataxia and spastic paraplegia. *Treasury of human Inheritance*, 1939, **4**, 141. Cambridge (University Press).

Mental Defect

Royal Eastern Counties' Institution, Colchester

Medical Research Council staff—
L. S. Penrose, M.D.

Attached workers—
T. A. Munro, M.B., D. Psych., F.R.C.P.E.
Caecilia E. M. Pugh, M.Sc., Ph.D.
J. C. Raven, M.Sc.

The investigations directed by Dr. Penrose are supported in part by the Council, and in part from funds provided by the Darwin Trust and by the Rockefeller Foundation, with facilities given by the Royal Eastern Counties' Institution itself. Dr. Penrose resigned last summer from the Council's staff, and from the directorship of this department, to take up an appointment in Canada.

Work this year has been chiefly on types of mental defect which are associated with gross physical abnormalities. Many family histories of patients with mongolism, microcephaly, hydrocephaly, anencephaly and spina bifida have been collected. Several general hospitals granted facilities for a similar investigation of other developmental abnormalities, such as placenta praevia and congenital pyloric stenosis. The relative importance of environmental and hereditary factors has been analysed in these diseases and anomalies. A positive association exists between maternal age and the incidence of mongolism, gross malformation of the nervous system and central placenta praevia. Primogeniture is likely to be a significant factor in the incidence of gross malformation of the nervous system and of congenital pyloric stenosis. Mongolism and some other malformations may have their origins in chromosome anomalies. The underlying cause of congenital pyloric stenosis seems to be a recessive diathesis.

Dr. Munro has again held a Beit Memorial Fellowship, with a grant for expenses from the Council. He has prepared for publication an analysis of the relationship between parental consanguinity and mental disorder. He has also examined nearly fifty families of defectives with phenylketonuria. The recessive inheritance of phenylketonuria is proved. The blood groups of these defectives, and those of most of their near relatives, have been determined by Dr. G. L. Taylor and his colleagues at the Galton Laboratory, in a search for possible genetic linkage.

Summaries of all the above researches were presented by Dr. Penrose, Dr. Taylor and Dr. Munro to the International Congress of Genetics at Edinburgh in August, 1939.

Dr. Pugh completed a biochemical examination of the metabolism of creatine and creatinine in about 500 patients with severe mental defect.

Mr. Raven, receiving grants from the Medical Research Council and from the Child Guidance Council, has standardised the series of perceptual tests, "Progressive Matrices", with the help of Mr. R. M. Woolner. These non-verbal tests are now published with norms for children between six and fourteen years of age.

M. Davidson—
Studies in the application of mental tests to psychotic patients. *Brit. J. med. Psychol.*, 1939, **18**, 44.

F. M. Miller and J. C. Raven—
The influence of positional factors on the choice of answers to perceptual intelligence tests. *Brit. J. med. Psychol.*, 1939, **18**, 35.

L. S. Penrose—
Intelligence test scores of mentally defective patients and their relatives. *Brit. J. Psychol.*, 1939, **30**, 1.
Maternal age and parity in placenta praevia. *J. Obstet. Gynaec.*, 1939, **46**, 645.
Is our national intelligence declining? The genetic aspect of the question. *Ment. Hyg.*, 1939, **5**, 7.
Eugenic prognosis with respect to mental deficiency. *Eugen. Rev.*, 1939, **31**, 35.
Maternal age, order of birth and developmental abnormalities. *J. ment. Sci.*, 1939, **85**, 1141.
Intelligence and birth rate. *Occup. Psychol.*, 1939, **13**, 110.
Peripheral nerve tumours in a case of phenylketonuria. *Lancet*, 11th March, 1939.
Mental disease and crime: outline of a comparative study of European statistics. *Brit. J. med. Psychol.*, 1939, **18**, 1.

L. S. Penrose and C. E. M. Pugh—
Creatinine in mentally defective patients. *J. ment. Sci.*, 1939, **85**, 1151.

J. C. Raven—
Progressive matrices. London (H. K. Lewis & Co.), 1938.
The R.E.C.I. series of perceptual tests: an experimental survey. *Brit. J. med. Psychol.*, 1939, **18**, 16.

J. C. Raven and A. Waite—
Experiments on physically and mentally defective children with perceptual tests. *Brit. J. med. Psychol.*, 1939, **18**, 40.

Physiology and Pathology of Vision

Department of Physiology, University College, London

Medical Research Council staff—
R. J. Lythgoe, M.D.
Attached workers—
Dr. E. E. Broda.
S. H. Hooper, B.Sc.
A. J. Marshall, Ph.D.
L. R. Phillips, Ph.D.

With the object of improving the efficiency of look-outs and others who have to see at low illuminations, Dr. Phillips has been working with Dr. Lythgoe on the individual variations in the night vision of normal persons. Part of this work has been done in the Department of Psychology at University College. In observers well supplied with vitamin A, the greatest single factor in determining the subsequent course of dark adaptation is the diameter of the

pupil in the preliminary period of light adaptation. In observers with large pupils the course of dark adaptation is slower than for observers with small pupils. There is some compensation for the possession of a large pupil in the light, however, since it predisposes to a comparatively large pupil in the dark. The power of dark adaptation was found to deteriorate rapidly with age, and there was some evidence that persons with a heavily pigmented fundus oculi became adapted relatively rapidly to darkness. In the absence of pathological conditions, it is possible to select persons who will probably have night vision above the average. Dr. Marshall has followed up this work with an investigation into the increase in visual acuity during dark adaptation.

Dr. Lythgoe and Dr. C. F. Goodeve have continued their work on the photochemistry of vision, for which expenses and assistance are provided by the Rockefeller Foundation. With Dr. Broda and others, they have continued their investigation into the effect of light on visual purple, the light sensitive substance found in the retina which is responsible for the process of dark adaptation. They find that when visual purple is bleached by light, it is transformed into an orange substance named " transient orange ", which, owing to its great instability, must be manipulated at temperatures around 0°C. It has been found that transient orange is converted quantitatively into indicator yellow without another intermediate stage.

The same workers have studied the sensitivity of visual purple to ultra-violet radiation, in an attempt to explain the much increased sensitivity of this region of the spectrum possessed by persons who have had their crystalline lenses removed on account of cataract. They have determined the iso-electric point of the protein visual purple, and find it to be exceptionally low for a protein.

E. E. Broda, C. F. Goodeve, R. J. Lythgoe and E. Victor—
Cataphoretic measurements on solutions of visual purple and indicator yellow. *Nature, Lond.*, 21st Oct., 1939.

R. J. Lythgoe and J. P. Quilliam—
The relation of transient orange to visual purple and indicator yellow. *J. Physiol.*, 1938, **94**, 399.

L. R. Phillips—
Some factors producing individual variations in dark adaptation. *Proc. Roy. Soc.*, B, 1939, **127**, 405.

E. E. Schneider, C. F. Goodeve and R. J. Lythgoe—
The spectral variation of the photosensitivity of visual purple. *Proc. Roy. Soc.*, A, 1939, **170**, 102.

Biological Effects of Radiation

Strangeways Research Laboratory, Cambridge

Medical Research Council staff—
F. G. Spear, M.D.

The following experiments are part of a larger investigation by a group at the Strangeways Research Laboratory, to which brief reference is made elsewhere (p. 116).

Dr. Spear left England in October, 1938, to spend some months at the Radiation Laboratory, University of California. Most of the time was devoted to experimental work at Berkeley on the biological effect of neutrons; but visits were also made to other research centres in California, with some of which future collaborative research has been planned.

The work on the biological effect of neutrons falls into two groups —experiments concerned with the mode of action of radiation; and quantitative observations on the response of mammalian and amphibian tissue exposed to a neutron beam of known intensity. The intensity of the neutron beam was first determined indirectly. A series of exposures was then made, keeping the intensity factor constant, in order to compare the biological efficiency of a neutron beam with that of gamma and X-radiation. The material is now being examined at Cambridge by Dr.A. Glücksmann, who is analysing it by the quantitative method which he worked out on normal tissues exposed to gamma radiation.

A report on the various biological and chemical investigations being done at Berkeley has been submitted to the Council, in view of the proposal to set up a cyclotron in England reserved for biological and medical research. There would seem to be enough biological problems awaiting solution to justify at least one cyclotron being set apart for such research.

Dr. Glücksmann is now engaged on a quantitative study of the reaction of squamous cell and basal cell carcinomata in man to carefully measured therapeutic doses of gamma rays. He is comparing these findings with those already obtained from normal material after comparable experimental doses. Hospitals in London, in the provinces and in California are contributing material for this investigation, which is yielding useful data on the relative efficiency of different radiation methods.

Dr. D. E. Lea has completed his work on the bactericidal action of radiations, and is studying the biological significance of alteration in the intensity and wave-length factors in irradiation. These experiments have given indications of the probable mode of action of radiations in the different types of biological response studied. Dr. Lea is collaborating with Dr. I. Lasnitzki in a comparison of the effect of physically equivalent doses of gamma and X-rays on tissue cultures.

A. Glücksmann—
Studies on bone mechanics *in vitro*. II. The role of tension and pressure in chondrogenesis. *Anat. Rec.*, 1939, **78**, 39.

A. Glücksmann and F. G. Spear—
The effect of gamma radiation on cells *in vivo*. Part II. *Brit. J. Radiol.*, 1939, n.s. **12**, 486.

D. E. Lea—
Devices for maintaining constant the output of X-ray tubes. *Brit. J. Radiol.*, 1939, n.s. **12**, 359.

F. G. Spear, L. H. Gray and J. Read—
Biological effect of fast neutrons. *Nature, Lond.*, 17th Dec., 1938.

Pathology of the Nervous System

Bernhard Baron Institute of Pathology, London Hospital

Medical Research Council staff—
Dorothy S. Russell, M.D.

Dr. Russell has continued her work in neurological pathology, special attention being directed to the tumours of the nervous system and to technical methods for the demonstration of their histology. Study of the morbid anatomy of chronic internal hydrocephalus has also been continued, and an examination of over sixty cases has shown great diversity in the pathological causes responsible for the condition: the mechanism of its production has been of a uniform character, namely obstruction at some point to the circulation of the cerebrospinal fluid. Thus, so-called "idiopathic" hydrocephalus does not appear to exist.

Two cases displaying an unusual complication of chronic internal hydrocephalus have been studied with Mr. D. W. C. Northfield. In these cases, which occurred in infants, a false diverticulum of one lateral ventricle was formed in the white matter of the cerebral hemisphere, apparently through rupture of the ependymal lining of the ventricle, and led to hemiplegia through interruption of the fibres of the motor cortex. Ventriculography was carried out in one of these cases, and produced curious appearances which are probably characteristic of the condition.

An opportunity has arisen for the study of the morbid anatomy of gargoylism, a disease of children characterised by mental deficiency, enlargement of the liver and spleen, skeletal deformities and grotesque face: the condition has been recognised only within recent years and has as yet been little studied. The investigation of this case, not yet complete, has so far revealed a strong similarity to family amaurotic idiocy, accompanied by widespread storage of a complex lipoid substance in other parts of the body.

An example of the Laurence-Moon-Biedl syndrome has also been the subject of special study.

D. W. C. Northfield and D. S. Russell—
False diverticulum of a lateral ventricle causing hemiplegia in chronic internal hydrocephalus. *Brain*, 1939, **62**, 311.

D. S. Russell—
Histological technique for intracranial tumours. London (Oxford University Press), 1939.
The pathology of intracranial tumours. *Postgrad. med. J.*, 1939, **15**, 150.

Experimental Pathology

Department of Pathology, University of Cambridge

Medical Research Council staff—
A. N. Drury, M.D., F.R.S.
Attached worker—
T. G. Armstrong, M.B., M.R.C.P.

Dr. Drury has continued his investigations upon cardiac hypertrophy produced experimentally. As a result of a change in procedure, considerable hypertrophy can now be obtained by

arterio-venous anastomosis, hearts of double the normal size being frequent. A detailed study has been made of the characteristics of this hypertrophy and of its cause. In addition, observations have been made to determine whether this hypertrophy is physiological, in that the heart returns to its normal size when the increased strain is removed. In most cases the heart does return to its normal size, but in some it remains hypertrophied, and the reasons for this are being investigated. By the method of arterio-venous anastomosis it is now possible to obtain hypertrophied and dilated hearts, hypertrophied hearts, and hearts which have returned to normal size after being hypertrophied and dilated. Dr. Drury has measured the refractory period in such hearts, and in all instances it is within normal limits. The functional disability of the hypertrophied and dilated heart is not reflected in any change in the refractory period.

With Miss G. Plaut, Dr. Drury has been investigating the rate of disappearance of particulate material from the blood stream, and the influence of changed circulatory conditions, drugs and poisons upon the rate. Up to the present none of these has been found to change the rate of disappearance.

Dr. Armstrong has been investigating the heart failure produced by the injection of irritants into the pericardium. The animals die of congestive cardiac failure characterised by hydrothorax, ascites, oedema and engorgement of the liver. The condition has its origin in heart failure, and a number of observations on the dynamics of the circulation and the protein content of the effusions have been made.

Observations have been made by Dr. Armstrong and Dr. T. D. Day on the histology of the liver in human cases of heart failure. Fibrosis of the liver occurs as a result of heart failure only when the venous pressure has been raised for a long period of time. Hepatic fibrosis is invariably found in constrictive pericarditis and is seen also in cases of very long-standing right-sided heart failure. On the clinical side, a special study has been made of constrictive pericarditis and of failure of the right side of the heart.

Bacteriology of Tuberculosis

University Field Laboratories, Cambridge

Medical Research Council staff—
A. Stanley Griffith, C.B.E., M.D., Ph.D.

Dr. Griffith has now completed his investigations of the bacteriological characteristics of tubercle bacilli occurring in the sputum of persons suffering from pulmonary tuberculosis. With Dr. J. Smith, Dr. Griffith has examined strains of tubercle bacilli from 969 cases from the city of Aberdeen and from neighbouring districts in the north-east of Scotland. Of the 433 city cases, 402 yielded eugonic human (including 5 atypical), 12 dysgonic human, 18 dysgonic bovine, and one a mixture of human and bovine strains. Of the

536 rural cases, 464 yielded eugonic human (including 9 slightly abnormal), 23 dysgonic human, 48 dysgonic bovine and one a mixture of human and bovine tubercle bacilli—making 9·1 per cent. of bovine infections.

In the centre and south of Scotland, Dr. W. T. Munro has examined the sputum of 1,104 cases of pulmonary tuberculosis and Dr. Griffith has examined 515 cases. Together, out of 1,619 cases, they have identified bovine bacilli in 85 instances, or 5·3 per cent. These were practically all rural cases, and the percentage of bovine infections for the centre and south was thus shown to be appreciably less than that for country districts in the north-east of Scotland. Dysgonic human strains occurred in the centre and south but were proportionately much less frequent than in north-east Scotland.

In the north and midlands of England, 1·8 per cent. of the 2,118 cases examined have yielded bovine tubercle bacilli. In Wales (203 cases) the percentage was 1·0, and in the south and south-east of England (985 cases) it was 0·6. There is thus a gradually decreasing frequency of bovine infections in pulmonary tuberculosis from north-east Scotland to south-east England.

The results of some experiments on the golden hamster and the field-vole with tubercle bacilli and the vole strain of acid-fast bacilli, have been published: further work with both species of animal has been done.

Dr. Griffith had prepared an important paper on "The problem of the virulence of the tubercle bacillus" for presentation at the meeting of the International Union against Tuberculosis which was to have been held at Berlin in September, 1939. This will be published later.

A. S. Griffith—

The susceptibility of the golden hamster (*Cricetus auratus*) to bovine, human and avian tubercle bacilli and to the vole strain of acid-fast bacillus (Wells). Histological observations by W. Pagel. *J. Hyg., Camb.*, 1939, **39**, 154.

The relative susceptibility of the field-vole to the bovine, human and avian types of tubercle bacilli and to the vole strain of acid-fast bacilli (Wells, 1937). *Ibid.*, 1939, **39**, 244.

Infections of wild animals with tubercle bacilli and other acid-fast bacilli. *Proc. R. Soc. Med.*, 1939, **32**, 1405.

A. S. Griffith and R. E. Glover—

Immunity experiments on guinea-pigs with killed tubercle bacilli and B.C.G. *J. comp. Path.*, 1939, **52**, 57.

Bacterial Chemistry

(a) *Bland-Sutton Institute of Pathology and Courtauld Institute of Biochemistry, Middlesex Hospital, London*

Medical Research Council staff—
P. G. Fildes, O.B.E., M.B., F.R.S.
Leverhulme Fellows—
G. P. Gladstone, M.B.
H. McIlwain, M.Sc., Ph.D.
Halley Stewart Fellow—
D. D. Woods, Ph.D.
Attached worker—
G. M. Hills, B.Sc.

In the last Report it was mentioned that two unknown nutritive factors for *Streptococcus haemolyticus* h l been demonstrated by Dr. Fildes and his colleagues. Furthe· vork has subdivided these into at least three, two of which have been determined. One of these has been shown to be glutamine. This substance is of special interest because, although it has been known for years to be present in vegetable root crops, it has not been recognised to have any metabolic significance. It has now, however, been recovered from meat and is in fact widely distributed in animal tissues. Dr. Fildes and Dr. Gladstone have found that glutamine is not only a growth factor for streptococci, but that a number of other organisms require it to a greater or less extent. It would appear that the mode of action of glutamine differs from that of other growth-promoting factors, in that the concentration of the latter determines the mass of growth, whereas with glutamine the minimum active dose produces a maximum effect.

The second unknown nutrient requirement of streptococci has been shown by Dr. McIlwain to be pantothenic acid. This substance was first described by Williams several years ago as a growth factor for yeast, and since by Evans (unpublished) for *C. diphtheriae:* a letter in the technical press indicates that its action on streptococci has also been discovered by Subbarow and Rane. It has been stated, further, that pantothenic acid is a constituent of the vitamin B complex active for rats and chicks. Should this be confirmed, it provides another instance of the value of spreading nutritional studies over a wide biological field.

The well-known stimulating action of agar on the production of haemolysin by staphylococci has been found by Dr. McIlwain to be due to the carbohydrate fraction : this was inactive, however, when the gelling power was lost. It might act by adsorbing metabolic products injurious to haemolysin production. Dr. McIlwain and Dr. G. M. Richardson, a former worker in the department, described a new method of synthesis of certain amino acids required in a state of purity for nutritional studies.

Dr. Gladstone has grown *B. anthracis* on a medium similar to that devised for staphylococci, and has found curious inter-relationships between certain of the constituent amino acids, namely toxicities of some counteracted by others with the production of a stimulatory mixture. An amino acid found to be "indispensable" was essential only as a detoxicant of another. If the latter was omitted the former was no longer indispensable.

During the year the department lost the services of Dr. B. C. J. G. Knight. He has been replaced by Dr. D. D. Woods from the School of Biochemistry, Cambridge. Dr. Woods has been exploring the nutrition of the gonococcus. Mr. G. M. Hills has joined as a whole-time worker for the Council, and is studying the metabolism of *Str. haemolyticus* in the light of present knowledge of its nutrition.

P. Fildes and G. P. Gladstone—
Glutamine and the growth of bacteria. *Brit. J. exp. Path.*, 1939, **20**, 334.
G. P. Gladstone—
Inter-relationships between amino-acids in the nutrition of *B. anthracis*. *Brit. J. exp. Path.*, 1939, **20**, 189.

H. McIlwain—
The effect of agar on the production of staphylococcal α-haemolysin. *Brit. J. exp. Path.*, 1938, **19**, 411.
Pantothenic acid and the growth of *Streptococcus haemolyticus*. *Ibid.*, 1939, **20**, 330.
H. McIlwain, P. Fildes, G. P. Gladstone and B. C. J. G. Knight—
Glutamine and the growth of *Streptococcus haemolyticus*. *Biochem. J.*, 1939, **33**, 223.
H. McIlwain and G. M. Richardson—
Preparation of α-amino-acids through α-oximino-esters. *Biochem. J.*, 1939, **33**, 44.

(*b*) *Institute of Biochemistry, University of Cambridge*

Medical Research Council staff—
Marjory Stephenson, Sc.D.
Attached worker—
E. F. Gale, B.Sc.

The studies made here of bacterial enzymes have been greatly helped by the use of the bacterial mill previously described. Hitherto it had been possible to make enzyme studies only by the use of bacterial suspensions, and so long as they were confined to material of this degree of complexity, much inevitably remained obscure. It is, for example, difficult to analyse systems into enzyme and co-enzyme and to be certain in the case of oxidising enzymes by what path the transfer of hydrogen to oxygen is attained.

The organism is grown in bulk and the cells fed into the crusher. The resulting material can be separated, by centrifuging and filtering, into a clear juice free from solid particles and a solid residue of insoluble material of varying degrees of particle size. Certain enzymes are found in the juice and others are obstinately attached to the solid particles. The juice can be fractionated by the usual methods employed in enzyme chemistry.

Two enzyme systems of the juice have been studied in detail. In the case of the malic dehydrogenase, it was found possible to split the system into three components. These are analogous to the three components of the corresponding animal enzyme, and each component of the bacterial system is able to replace its opposite number in the animal system and *vice versa*. One other enzyme of the juice, aspartase II, has been worked out in detail.

The enzymes which adhere to the solid phase of the ground material are on the whole more difficult of attack. One of these—formic dehydrogenase—has been studied in detail. It has not been found possible to obtain it in a soluble state, but it has been purified by the removal of much adherent material by tryptic digestion and by autolysis. It has been found that it reacts with oxygen by means of cytochrome B, which also adheres to the solid phase of the cell. In the course of digestion with trypsin the cytochrome disappears and the dehydrogenase is then unable to oxidise formate by oxygen; the cytochrome B of the cell can, however, be replaced in the system by a preparation of animal cytochrome plus cytochrome oxidase from heart muscle.

The formic dehydrogenase itself is extremely sensitive to oxygen. Increasing oxygen tension during growth leads to a decreased formation of the enzyme and the purified enzyme is quickly inactivated by oxygen. *In vivo* cytochrome B protects the enzyme from the action of oxygen; *in vitro* this protective action can be imitated by other hydrogen acceptors.

It is possible, once the presence and action of a co-enzyme is demonstrated, to show whether its amount in the cell varies. It has been found in the case of co-enzyme I that its amount varies with the age of the culture but never attains sufficient concentration to permit malic dehydrogenase to function at its optimum rate. It also appears that the cell synthesises enzyme and co-enzyme at different rates and subsequently destroys the latter faster than the former: this presents another cause of the variation in enzymic activity with age of culture.

E. F. Gale—
Formic dehydrogenase of *Bacterium coli*: its inactivation by oxygen and its protection in the bacterial cell. *Biochem. J.*, 1939, **33**, 1012.
E. F. Gale and M. Stephenson—
l-Malic dehydrogenase and codehydrogenase of *Bacterium coli*. *Biochem. J.*, 1939, **33**, 1245.
M. Stephenson—
Bacterial metabolism. London (Longmans, Green & Co.), 2nd edition, 1939.

VITAMINS

(*a*) *Lister Institute of Preventive Medicine, London*

Medical Research Council staff—

(i) S. S. Zilva, Ph.D., D.Sc., F.I.C. (ii) E. Margaret Hume, M.A.

Attached workers—

C. L. Arcus, B.Sc., Ph.D. Hannah Henderson Smith.
G. A. Snow, M.Sc.

(i) Research into the natural occurrence and mode of action of vitamin C has been continued by Dr. Zilva and his assistants. The Department of Scientific and Industrial Research has again provided the cost of part of the work which has special interest for the Food Investigation Board.

Dr. Zilva has continued the investigation of the variable indophenol reducing capacity of the leucocytes under normal and pathological conditions. Whilst, as already reported, the reducing capacity of the leucocytes obtained by pathological stimulation from guinea pigs "saturated" with vitamin C was of the same order as that of muscle tissue, it is now found that when the leucocytes are obtained directly from the blood of such animals, their ascorbic acid content is considerably higher and reaches at times values usually observed in tissues which are outstanding for their ability to accumulate the vitamin. Dr. Zilva has also been examining the blood from leukaemic and other human subjects to ascertain whether the high reducing capacity of the leucocytes observed by Stephens and Hawley in leukaemic cases was due to the presence of ascorbic acid.

Continuing the inquiry into the relation of the intake of ascorbic acid to urinary output and to the storage of the vitamin in the body, Dr. Zilva and Dr. A. E. Kellie endeavoured to ascertain the minimum dosage required to maintain an adult " saturated " in respect of vitamin C. They have also studied the ascorbic acid content of the blood during the various stages of this inquiry. Comparison of this with the urinary excretion suggests that there is no constant renal threshold. There exists a competition for the ascorbic acid of the blood between the absorptive tendency of the tissues which varies with the degree of " saturation " and the excretory function of the kidney. Blood levels determined at random therefore do not by themselves indicate the degree of " saturation " of a subject.

Dr. Zilva and Dr. Kellie have recently shown that *l*-ascorbic acid was destroyed when exposed in aqueous solution to ultra-violet light in the absence of oxygen and sensitisers. The chemical nature of this anaerobic photolysis of the vitamin is now being studied with Dr. Arcus.

To facilitate investigation of the physiological function of ascorbic acid in metabolism, Dr. Zilva and Mr. Snow have re-examined the method for determining glutathione in tissues.

As the ascorbic acid content of King Edward potatoes reaches its highest level early in September and then falls off fairly rapidly, it was thought that if potatoes lifted about then were canned, the canned product would retain considerable quantities of the vitamin even if losses were incurred in the processing. Dr. Zilva and Mr. Morris of the Low Temperature Research Station, Cambridge, have therefore made experiments by canning potatoes in August, alone and in a meat and vegetable ration. Indophenol titrations indicated that a loss of only 7 per cent. was incurred in canning the meat and vegetable ration and 25 per cent. in canning the potatoes. This work is being pursued on a large scale under factory conditions.

The biological re-testing of apples to which ascorbic acid was added before canning revealed a loss of about 50 per cent. after three years' storage. These results suggest the desirability of adding synthetic ascorbic acid to canned products which naturally contain just sufficient quantities of the vitamin, but which will become inadequate in this respect after prolonged storage. In the hope of linking up the progressive change in the equilibrium between dehydroascorbic acid and ascorbic acid, previously observed by them during the development of the apple, with a definite physiological function, Dr. Zilva and Dr. C. West of the Ditton Laboratory are now investigating the influence of certain environmental factors on the relative content of the two forms of the vitamin.

In collaboration with Dr. J. Barker of the Low Temperature Research Station, Cambridge, Dr. Zilva is investigating the ascorbic acid content of potatoes lifted from the soil at various stages of their development, and the subsequent decline in the vitamin C concentration of the tubers during storage. The content of ascorbic acid was found to reach a maximum in the early part of September :

between this date and the final lifting in October there is a considerable drop in the vitamin concentration. On storage at 10°C. the potatoes lifted in October continued to lose the vitamin rapidly at first, but later the drop became gradual. On the other hand, the fall in samples lifted before October—the normal time of lifting—was much more striking. Biological tests have shown that although the greater part of the reduction of indophenol in these experiments was due to vitamin C, substances other than ascorbic acid might under certain conditions be responsible for this reduction in potatoes.

(ii) Miss Hume, with the assistance of Miss Henderson Smith, has continued to collaborate with Dr. I. Smedley-Maclean and Mr. L. C. A. Nunn in studying the deficiency of the essential unsaturated fatty acid in rats. The results previously reported, showed that methyl linoleate and linolenate were both effective in the treatment of the deficiency, but that the latter had only about one-sixth of the potency of the former. The study has now been extended to include an investigation of the efficacy of methyl arachidonate to function as the essential unsaturated fatty acid, a point on which conflicting results have been reported. This substance was prepared from adrenal glands and liver, and was found to have about twice the potency of methyl linoleate for promoting weight increase, but its curative effect on skin lesions did not appear to be any greater than that of methyl linoleate.

Miss Hume is also joint secretary, with Dr. H. Chick, of the International Conferences on Vitamin Standardisation under the Health Organisation of the League of Nations; and she has been much occupied in preparing material for the meeting, which was to have been held at the end of 1939. The meeting has now been indefinitely postponed, but the collaborative experimental work which was already in train is being completed as far as possible. This is concerned with the proposed new standard for vitamin E, already mentioned at p. 64, and with the value for the factor converting the results of spectroscopic estimations of vitamin A into international units. For the latter purpose a solid preparation of vitamin A 2-naphthoate has been made by Dr. T. H. Mead, of the British Drug Houses, Ltd. By the courtesy of the firm, a sufficient supply of this has been made available. Spectroscopic tests, biological tests, and tests of stability on the feeding solutions, have been organised in the same way as was done previously with a preparation of halibut liver oil and the U.S. Pharmacopoeia reference cod-liver oil.

E. M. Hume—
Estimation of vitamin A. *Nature, Lond.*, 7th Jan., 1939.

E. M. Hume, R. Burbank and V. Korenchevsky—
Some effects of the administration of oestrogens on the organs of castrated and non-castrated male rats partially deprived of vitamin A. *J. Path. Bact.*, 1939, **49**, 291.

E. M. Hume, L. C. A. Nunn, I. Smedley-Maclean and H. H. Smith—
Studies of the essential unsaturated fatty acids in their relation to the fat-deficiency disease of rats. *Biochem. J.*, 1939, **32**, 2162.
A. E. Kellie and S. S. Zilva—
The vitamin C requirements of man. *Biochem. J.*, 1939, **33**, 153.
G. A. Snow and S. S. Zilva—
The non-specificity of the ascorbic acid oxidase. *Biochem. J.*, 1938, **32**, 1926.
S. S. Zilva, F. Kidd and C. West—
Ascorbic acid in the metabolism of the apple fruit. *New Phytologist*, 1938, **37**, 345.

(b) *Dunn Nutritional Laboratory, Cambridge*

Medical Research Council Staff—
L. J. Harris, Sc.D., Ph.D., D.Sc.
T. Moore, D.Sc., Ph.D.
Visiting workers—
G. G. Banerji, B.Sc., Calcutta.
E. Kodicek, M.D., Prague.
K. Rajagopal, M.B., Coonoor, India.
Y. L. Wang, B.Sc., Nanking, China.
J. Yudkin, M.B., Ph.D.

In addition to the workers listed above, Dr. R. C. Burgess from the Federated Malay States, Dr. F. M. Purcell from the Gold Coast, and Dr. W. D. Raymond from Tanganyika, have spent short periods in the laboratory studying methods to be used in nutritional surveys in the Colonies (see p. 139).

Further progress has been made by Dr. Harris and his colleagues in elaborating tests to assess the level of nutrition in human beings. With Mr. Wang, a simple chemical procedure has now been devised for detecting partial deficiency of vitamin B_1, and it has been shown that this can safely be used in place of the equally accurate but more laborious biological method. An interesting finding was the frequency of low reserves of the vitamin during pregnancy, and the occurrence of a state of "conditioned deficiency" (so-called "secondary polyneuritis") occasioned by diseases in which absorption and utilisation are defective or appetite is impaired. With Mr. Banerji, the possibility has been investigated of detecting lowered reserves of this same vitamin by an alternative procedure, based on measurements of abnormalities in carbohydrate metabolism.

With Dr. Raymond, a method has been perfected for measuring the excretion of nicotinic acid, the anti-pellagra factor. The amount excreted by volunteers kept on restricted diets was found to vary according to their intake, and rose after the administration of test doses. Low values were found in pellagra and with anorexia; and hence it seems likely that this method will be of use for diagnostic purposes.

Dr. Harris has investigated further certain differences seen between species in their reactions to various vitamin deficiencies. Thus it is well known that a deficiency of vitamin B_1 causes in man an increased rate of heart beat, whereas a slowing of the rate results when rats are used as the experimental animal. Other species have been examined during the past year to ascertain whether

they resemble rats or human beings in this respect. In pigeons a slowing of the heart was found to result from uncomplicated deficiency of vitamin B_1; and this is distinct from the bradycardia and 'heart block' earlier recorded by Carter and Drury in pigeons kept on a diet of polished rice. In cats, a low heart rate has been observed in long-standing chronic deficiency of vitamin B_1.

Another example of species difference is seen in the requirements for nicotinic acid. Whereas it has long been known that a regimen of maize gives rise to pellagra in man and to the corresponding disease ('blacktongue') in dogs, in rats on the contrary no ill effects are apparent. Dr. Harris has found that rats kept on a maize diet may continue to excrete nicotinic acid, and this suggests that these animals possess some power of synthesising the vitamin. Previously Dr. Harris had shown that monkeys resemble human beings and dogs, and apparently differ from rats, in requiring nicotinic acid; and new experiments have now indicated that pigeons and guinea-pigs also need nicotinic acid under the conditions studied.

Dr. Moore has continued his examination of the abnormalities produced by a deficiency of vitamin E in the rat. He has found that the lesions in the uterus and in the kidneys, previously described in collaboration with Dr. A. J. P. Martin, can be prevented by administration of synthetic *dl*-α-tocopherol. Final proof is forthcoming, therefore, that these ill effects are due to a lack specifically of vitamin E and not of some associated substance in the concentrates hitherto employed. Dr. Moore has also observed that vitamin E deficiency in the rat may diminish the reserves of vitamin A in the tissues. With Dr. Rajagopal, the distribution of vitamin E in the body has been studied by the spectrographic method. The absorption band characteristic of vitamin E has been detected in the storage fat of rats which had been given large amounts of wheat germ, but not in other tissues. A study of the isomerism of polyethylenic fatty acids in the cow has been concluded in collaboration with Dr. Kon, Mr. Cotton and Mr. Houston of the National Institute for Research in Dairying. Similar work with the chicken has been done with Mr. Houston and with Miss E. M. Cruickshank of the School of Agriculture, Cambridge.

Dr. Moore and Mr. A. W. Davies have examined the vitamin A content of cheese, and found it to be roughly parallel with the amount of milk fat. With Dr. M. K. Maitra, similar results were obtained with the so-called "light-white" casein. Tests by Dr. Moore and Dr. C. A. Baumann failed to confirm any antagonistic action between vitamin A and overdoses of thyroxin.

Dr. Kodicek, with a grant from the Society for the Protection of Science and Learning, has developed the method for estimating nicotinic acid in foodstuffs and animal tissues. Measurements have been made of the nicotinic acid in the organs of normal as compared with deficient animals, of its distribution in yeast extracts and certain other foodstuffs, and of the effect of storage under varying conditions.

Mr. Wang has worked out a modification of the thiochrome test suitable for use in the estimation of vitamin B_1 in foodstuffs. The process involves a preliminary hydrolysis for converting the ester of vitamin B_1, co-carboxylase, into the free vitamin. Comparisons are in progress of the results of this method with those obtained by biological tests.

Dr. Yudkin has begun an investigation to assess the possible rôle of vitamins in the causation of certain obscure symptoms in a number of diseases, paying particular regard to the suggested incrimination of vitamin A in several disorders associated with degeneration of the nerves, and of vitamin B_1 in cardiac and neurological symptoms of unknown origin. He has been unable to confirm a claim that a deficiency of vitamin B_1 is of importance in many types of cardiac disorder. On the other hand, in a few isolated cases of oedema of clinically obscure aetiology, he was able to establish definitely that there was a deficiency of vitamin B_1. With Mr. Banerji and Mr. Wang, studies have been completed upon the metabolism of vitamin B_1 in volunteers kept on a beriberi-producing diet.

During the period under review, work on the standardisation of vitamins on behalf of official sub-committees, and on the examination of foodstuffs for government departments, has formed a major proportion of the laboratory's activities. Acknowledgment is made of the generous help given by Bayer Products Limited, Messrs. Lever Brothers Limited, Messrs. Eli Lilly and Company Limited, and Roche Products Limited, in providing free supplies of materials.

B. Ahmad and L. J. Harris—
Assessment of the level of nutrition. Vitamin-A : further observations with the dark-adaptation test. *Chemistry and Industry*, 1938, **57**, 1190.
Assessment of the level of nutrition. Vitamin-C. *Ibid.*, 1938, **57**, 1190.

G. G. Banerji and L. J. Harris—
Methods for assessing the level of nutrition. A carbohydrate tolerance test for vitamin B_1. I. Experiments with rats. *Biochem. J.*, 1939, **33**, 1346.

C. A. Baumann and T. Moore—
Thyroxin and hypervitaminosis-A. *Biochem. J.*, 1939, **33**, 1639.

E. M. Cruickshank, J. Houston and T. Moore—
Spectroscopic changes in fatty acids. V. The effect of the dietary fat on the body fat and egg fat of the hen. *Biochem. J.*, 1939, **33**, 1630.

A. W. Davies and T. Moore—
The vitamin-A content of cheese. *Biochem. J.*, 1939, **33**, 1645.
Determination of vitamin A and carotene in organs. *Z. Vitaminforsch.*, 1939, **9**, 254.

L. J. Harris—
Vitamins and vitamin deficiencies. Vol. I. Historical and introductory. Vitamin B_1 and beriberi. London (J. & A. Churchill, Ltd.), 1938.
The vitamin-B_2 complex. Part IX. Nicotinic acid as a dietary essential for pigeons and guinea-pigs. *Chemistry and Industry*, 1939, **58**, 471.
Vitamin-B_1 deficiency and bradycardia in pigeons and kittens. *Ibid.*, 1939, **58**, 472.

L. J. Harris and W. D. Raymond—
Assessment of the level of nutrition. Estimation of nicotinic acid in urine. *Chemistry and Industry*, 1939, **58**, 652.

J. Houston, A. G. Cotton, S. K. Kon and T. Moore—
Spectroscopic changes in fatty acids. IV. Acids from specimens of butter fat from cows under different nutritional treatments. *Biochem. J.*, 1939, **33**, 1626.

P. C. Leong—
Vitamin B_1 in the animal organism. III. The maximum storage of vitamin B_1 in various species. *Biochem. J.*, 1939, **33**, 1394.
Effect of soil treatment on the vitamin B_1 content of wheat and barley. *Ibid* 1939, **33**, 1397.

M. K. Maitra and T. Moore—
The vitamin A content of "light white" casein. *Biochem. J.*, 1939, **33**, 1648.

A. J. P. Martin and T. Moore—
Some effects of prolonged vitamin E deficiency in the rat. *J. Hyg. Camb.*, 1939, **39**, 643.

T. Moore—
Vitamin-E deficiency in the rat. (1) The prevention of uterine, discoloration and kidney degeneration by dl-α-tocopherol. (2) Vitamin E and the storage of vitamin A. *Chemistry and Industry*, 1939, **58**, 651.
Spectroscopic changes in fatty acids. VI. General. *Biochem. J.*, 1939, **33**, 1635.

T. Moore, A. J. P. Martin and K. R. Rajagopal—
Some aspects of the physiological action of vitamin E. *Vitamin E: a symposium held under the auspices of the Food Group, Society of Chemical Industry*, 1939, p. 41.

Y. L. Wang and L. J. Harris—
Methods for assessing the level of nutrition of the human subject. Estimation of vitamin B_1 in urine by the thiochrome test. *Biochem. J.*, 1939, **33**, 1356.

J. Yudkin—
A case of beri-beri occurring in London. *Lancet*, 10th Dec., 1938.

Vital Statistics

London School of Hygiene and Tropical Medicine

Statistical Committee—

Professor M. Greenwood, D.Sc., F.R.C.P., F.R.S. (*Chairman*).
L. Isserlis, D.Sc. (*Vice-Chairman*).

Medical Research Council Staff—

A. Bradford Hill, D.Sc., Ph.D. (*part-time*).
J. O. Irwin, D.Sc., Sc.D.
W. T. Russell.
E. Lewis-Faning, B.Sc., Ph.D.
W. J. Martin, B.Sc., Ph.D.
E. A. Cheeseman, B.Sc.

The staff named above work under the direction of the Statistical Committee (p. 153) and in the department of Epidemiology and Vital Statistics of which the Chairman is the head. The Committee and staff also serve the Ministry of Health in the field of medical statistics. As will appear from the appended list of publications, the staff have applied statistical methods in many fields of medical work, and here reference will simply be made to typical investigations of different types.

When it is desired to measure the contamination of water or milk with a particular organism, it is evident that the smaller the volume of fluid which need be used to obtain a growth of the organism, the greater must be the contamination: the plan of testing a suspected fluid in increasing dilution has therefore long been in use. Some relation must exist between the proportions of sterile tubes at different dilutions and the actual density of organisms in the original fluid; and so long ago as 1915 McCrady suggested a quantitative method based on the assumption of a perfectly random distribution of organisms. Two years later Greenwood and Yule independently suggested a similar method, and provided numerical aids to workers. Since then many writers have dealt with the problem, often from the standpoint of water testing, and various tables have been prepared. Legislation dealing with the purity of milk required the adoption of standardised methods, and those in use have been based upon these statistical principles. Mr. H. Barkworth and Dr. Irwin have now re-investigated the subject and made improvements in the statistical technique. Each of three workers made seventeen tests, and each test consisted of fivefold inoculations into lactose-bile-salt-peptone at four levels (1 in 10, 1 in 50, 1 in 250, and 1 in 1,250). Except for three slightly anomalous results, the data were found to be consistent with the hypothesis that the chance of a tube remaining sterile is constant for all tubes inoculated from the same sample of milk at any one dilution. It appeared that the statistical assumption upon which the earlier investigations had been based was adequate to give a good idea of the order of magnitude of the number of bacteria in unit volume. There was, however, some tendency (more evident in the tests made in the autumn than in those made in the spring) for the estimated count to rise at higher dilutions, a result which might plausibly be attributed to the breaking up of clumps. This is an example of collaboration between experimental and statistical investigators in the study of a practically important problem in which a careful technique is essential.

A different field of investigation is illustrated by work which Professor Greenwood and Dr. Irwin have done on the bio-statistics of senility. The data of human experience seem to show that the rate of mortality increases with age at a slackening speed as age advances; at ages over 90 accurate data are comparatively scanty, but there seems no doubt that formulae which postulate a geometrical increase of the force of mortality with age overstate the facts. It is biologically possible that at extreme ages survivorship depends very directly upon factors which may perhaps be heritable. Professor Greenwood and Dr. Irwin show that the simple hypothesis of a continuous distribution of proneness to survive does describe the data fairly well. The results suggest that it might be of interest to study the physiology and pathology of senility in animals with a normal life span small compared with that of human beings.

Thirdly, the report by Dr. M. Young and Mr. Russell on the statistical history of appendicitis—already mentioned at p. 78—illustrates another type of research. At the beginning of this century the term appendicitis was sufficiently novel for fluctuations in the recorded death rate to be regarded as little more than changes of attribution, but for many years now the term has been part of common professional knowledge. The death rate from the disease shows no decided tendency to fall, but analysis of hospital records shows that case fatality rates have declined, and there is evidence that the technique of treatment—as well as a habit of earlier resort to treatment—has improved. The inference appears to be that the disease is becoming increasingly common, and this is supported by the fact that Scottish health insurance statistics record over a period of five years a definite increase of attack rates. The problem therefore arises whether any aetiological factors, perhaps dietetic, play a part. This is a subject which deserves further investigation : a merely statistical study can here point a way, but further data and other methods are needed to reach a conclusion.

In addition to undertaking statistical investigations of their own, the staff have continued to take part in the critical examination of research proposals and reports referred to the Committee by the Council and by the Industrial Health Research Board. All reports intended for publication by the Council are examined in this way if they include statistical data to an important extent, or make use of statistical methods.

H. Barkworth and J. O. Irwin—
Distribution of coliform organisms in milk and the accuracy of the presumptive coliform test. *J. Hyg., Camb.*, 1938, **38**, 446.

E. A. Cheeseman—
The effect of the war years upon mortality in childhood. *Human Biol.*, 1938, **10**, 537.

E. A. Cheeseman, W. J. Martin and W. T. Russell—
Disease and environment. *Biometrika*, 1939, **30**, 341.
Diphtheria. A suggested explanation of the relative change in age incidence. *J. Hyg., Camb.*, 1939, **39**, 181.

K. K. Conrad and A. B. Hill—
Mortality from cancer of the skin in relation to mortality from cancer of other sites. An analysis of occupational mortality statistics of England and Wales. *Amer. J. Cancer*, 1939, **36**, 83.

M. Greenwood—
The first life tables. *Notes Roy. Soc.*, 1938, **1**, 70.
Occupational and economic factors of mortality. *Brit. med. J.*, 29th April, 1939.

M. Greenwood, A. B. Hill, W. W. C. Topley and J. Wilson—
The effect of withdrawing mice from an infected herd at varying intervals. *J. Hyg., Camb.*, 1939, **39**, 109.

M. Greenwood and J. O. Irwin—
The biostatistics of senility. *Human Biol.*, 1939, **11**, 1.

W. Gunn and W. T. Russell—
A review of the measles epidemic 1935–36, including references to treatment and the preparation and use of immune measles sera. *L.C.C. Rep. med. Offr Hlth Measles Epidemic* 1935–36, p.19, 1938.

A. B. Hill—
Principles of medical statistics. London (Lancet Ltd.), 2nd edition, revised and enlarged, 1939.

A. B. Hill and M. G. Hyder—
Construction of an abridged life table. *Lancet*, 28th Jan., 1939.

A. B. Hill and H. E. Magee—
Some observations on the weight and length of infants in the first year of life. *Med. Off.*, 1938, **60**, 157 and 167.

A. B. Hill and B. M. Rao—
Mortality in childhood. *Rep. med. Offr Minist. Hlth, Lond., 1937*, p.23, 1938.

J. O. Irwin and E. A. Cheeseman—
On an approximate method of determining the median effective dose and its error, in the case of a quantal response. *J. Hyg., Camb.*, 1939, **39**, 471.

A. A. Miles, S. S. Misra and J. O. Irwin—
The estimation of the bactericidal power of the blood. *J. Hyg., Camb.*, 1938, **38**, 732.

VI. RESEARCH WORK AIDED BY GRANTS

Investigations in Specific Subjects

In previous years an account has been given, under general subject heads, of the numerous investigations assisted by the Council by means of research grants to workers in universities, medical schools, hospitals and other institutions throughout the country. It has been necessary to curtail the Report on this occasion, and to give only a list of grant-holders, with the main subject or subjects of research in each case. Reference is also made to the work done by holders of certain scholarships and fellowships, and to some other investigations, not involving grants, which have been directed by the Council's scientific committees. The publications listed at the end of each section include a few references to papers published by workers whose grants had ended before the beginning of the period under review.

During the past academic year the Rockefeller Foundation of New York has generously provided new funds, to be administered by the Council, for the support of work in the special fields of neurology, psychiatry and endocrinology. The grants made from this fund, and from other funds previously placed at the disposal of the Council, are specially indicated.

Clinical Medicine

The work of the special Clinical Research Units supported by the Council has already been mentioned at p. 69. An account of the inquiry, made by the special Committee named at p. 149, into the uses of different types of "breathing machines" for artificial respiration, has been given in the Introduction (p. 35).

Geoffrey Bourne, M.D., F.R.C.P. (St. Bartholomew's Hospital, London)—assistance by Courtenay Evans, M.D., M.R.C.P., and expenses: causes and treatment of different types of cardiac pain.

J. Crighton Bramwell, M.D., F.R.C.P. (University and Royal Infirmary, Manchester)—expenses: problems of heart disease in pregnancy (with Dr. R. W. Luxton and Dr. T. Holme); prognostic significance of various clinical manifestations of high blood pressure (with Dr. H. J. Wade).

I. G. W. Hill, M.B., F.R.C.P.E. (University and Royal Infirmary, Edinburgh)—personal: clinical and electrocardiographic studies of heart disease.

G. L. S. Konstam, M.D., F.R.C.P. (West London Hospital)—expenses: effects on the heart of alcoholism and other conditions leading to vitamin B_1 deficiency.

William Evans, M.D., F.R.C.P. (London Hospital)—personal: treatment of high blood pressure with various drugs (with Dr. O. Loughnan); comparative value of different preparations of digitalis in the treatment of acute and chronic heart failure.

Professor E. J. Wayne, M.Sc., Ph.D., M.D., F.R.C.P. (University of Sheffield)—expenses: relationship of cyanosis to the oxygen saturation of blood (with Dr. W. D. Wallace).

J. D. S. Cameron, M.D., F.R.C.P.E. (Royal Infirmary, Edinburgh) —expenses: follow-up study of cases of nephritis and high blood pressure (with Dr. D. M. F. Batty).

W. M. Arnott, B.Sc., M.D., F.R.C.P.E. (Royal Infirmary, Edinburgh)—expenses: treatment of obstructive vascular disease by intermittent venous occlusion (with Mr. J. J. M. Brown); effect of venous occlusion on skin and muscle blood flow (with Dr. J. D. Allen and Dr. J. J. R. Duthie).

The late E. P. Poulton, D.M., F.R.C.P. (Guy's Hospital, London) —expenses: local oxygen want in tissues, and treatment of cardiac and vascular diseases with oxygen.

E. A. Schott, M.D. (National Hospital for Diseases of the Heart, London)—expenses: effect of physical exercise on oxygen consumption and carbon dioxide output.

Professor L. S. P. Davidson, M.D., F.R.C.P.E. (University of Edinburgh)—expenses: pathology and bacteriology of acute and chronic rheumatic diseases and experimental arthritis (Dr. J. R. M. Innes, Dr. J. G. Sclater and Dr. Scott Thomson); mechanism of peripheral vascular control (Dr. J. J. R. Duthie and Dr. W. M. Arnott); treatment of gastric and duodenal ulcer, and problems of alkalosis (Dr. Bruce M. Nicol).

W. H. Bradley, D.M. (University of Cambridge)—personal and expenses: clinical and epidemiological features of haemolytic streptococcal infections; bacteriological studies of rheumatic fever (with Dr. G. H. Eagles); alterations in the constituents of the blood during rheumatic fever (with Dr. R. A. Kekwick and Dr. E. de Liee).

W. Goldie, M.B. (University of Leeds)—expenses: gold therapy in rheumatoid arthritis.

J. F. Wilkinson, M.Sc., Ph.D., M.D., F.R.C.P. (University and Royal Infirmary, Manchester)—assistance by B. R. S. Mainwaring, B.Sc., and F. X. Aylward, B.Sc., Ph.D., and expenses: chemistry of anti-anaemic principles of stomach and liver; studies of different types of anaemia (with Dr. M. C. G. Israëls); clinical tests of desoxycorticosterone-acetate in the treatment of Addison's disease (for the Therapeutic Trials Committee).

C. C. Ungley, M.D., F.R.C.P. (Royal Victoria Infirmary, Newcastle-on-Tyne)—assistance by W. Kelly, B.Sc., Ph.D., and expenses: nutritional deficiencies in relation to disease.

Professor N. Morris, D.Sc., M.D., M.R.C.P. (University of Glasgow) —expenses: relative efficiency of vitamins D_2 and D_3 in the treatment of rickets in infants (with Dr. Mary M. Stevenson); use of calcium in the treatment of cardiac failure (with Dr. A. S. Rogen).

R. D. Lawrence, M.D., F.R.C.P. (King's College Hospital, London) —expenses: clinical problems of diabetes.

L. Wislicki, M.D. (University of Manchester)—personal (from the Gertrude Nicholl bequest) : effects of certain vegetable extracts on the blood sugar level (under the direction of Professor A. D. Macdonald).

Mrs. K. Maunsell, M.D. (King's College Hospital, London)—personal : clinical problems of bronchial asthma.

S. Alstead—
Potassium iodide and ipecacuanha as expectorants. *Lancet*, 28th Oct., 1939.

W. M. Arnott and J. J. M. Brown—
The investigation and treatment of obstructive peripheral vascular disease. *Trans. med.-chir. Soc. Edinb.*, **118**, 41.

G. Bourne—
Angina of effort as the only symptom of coronary thrombosis. *Lancet*, 20th May, 1939.

G. Bourne and C. Evans—
The four-lead electrocardiogram in angina of effort. *Lancet*, 10th Dec., 1938.

W. H. Bradley—
The prevention of droplet infection with special reference to streptococcal disease. *J. R. sanit. Inst.*, 1939, **59**, 600.

L. S. P. Davidson—
The mechanism of megaloblastic blood formation. *Edinb. med. J.*, 1939, **46**, 474.

L. S. P. Davidson and J. Smith—
Weil's disease in the north east of Scotland. An account of 104 cases. *Brit. med. J.*, 14th Oct., 1939.

C. Evans—
Changes in the chest lead electrocardiogram in coronary thrombosis. *Brit. Heart J.*, 1939, **1**, 161.

W. Evans and O. Loughnan—
The drug treatment of hyperpiesia. *Brit. Heart J.*, 1939, **1**, 199.

S. J. Hartfall, H. G. Garland and W. Goldie—
Treatment of rheumatoid arthritis with a new gold salt. *Lancet*, 17th Dec., 1938.

A. M. Jones and C. Bramwell—
Alcoholic beri-beri heart. *Brit. Heart J.*, 1939, **1**, 187.

R. D. Lawrence—
Biochemical examinations in diabetes, and the general practitioner. *Practitioner*, 1939, **142**, 596.
The diabetic life. London (J. & A. Churchill, Ltd.), 11th edition, 1939.
The treatment of insulin cases by one daily injection. *Acta med. scand.*, 1938, Suppl. xc, p. 32.
Zinc-protamine-insulin in diabetes : treatment by one daily injection. *Brit. med. J.*, 27th May, 1939.

R. D. Lawrence and K. Madders—
The employment of diabetics. *Brit. med. J.*, 26th Nov., 1938.

J. R. Learmonth and W. M. Arnott—
Section on ' diseases of the blood vessels of the limbs ' in *Textbook of modern treatment* (Dunlop, Davidson and McNee). Edinburgh (E. & S. Livingstone), 1939.

A. Lyall and B. M. Nicol—
The gastric secretions in experimental hypochloraemia. *J. Physiol.*, 1939, **96**, 21.

A. D. Macdonald and L. Wislicki—
Effects of cabbage extracts on carbohydrate metabolism. *J. Physiol.*, 1938, **94**, 249.

N. Morris—
Deficiency diseases with special reference to their treatment. *Clin. J.*, 1939, **68**, 94 and 150.
The treatment of coeliac disease. *Med. Pr.*, 1938, **197**, 37.
N. Morris and M. M. Stevenson—
Vitamins D_2 and D_3 in infantile rickets : a comparison of their therapeutic efficiency. *Lancet*, 21st Oct., 1939.
B. M. Nicol—
Control of gastric acidity in peptic ulcer. *Lancet*, 21st Oct., 1939.
B. M. Nicol and A. Lyall—
Gastric secretions during pathological hypochloraemia. *Lancet*, 21st Jan., 1939.
E. P. Poulton—
Local tissue anoxia and its treatment, with special reference to rheumatic myocarditis. *Lancet*, 5th Aug., 1939.
Respirators (Poliomyelitis) Committee—
"Breathing machines" and their use in treatment. *Spec. Rep. Ser. Med. Res. Coun., Lond.*, No. 237, 1939.
C. C. Ungley—
The clinical manifestations of vitamin B_1 deficiency. *Newcastle med. J.*, 1939, **19**, 43.
A. Wilson—
Vitamin B_1 und Kohlehydratstoffwechsel. *Z. klin. Med.*, 1939, **136**, 77.

Postgraduate Studentships and Research Fellowships in Clinical Science and Experimental Pathology

These studentships and fellowships, which were instituted by the Council three years ago, are intended primarily to provide opportunities for training young clinicians and pathologists for research and academic posts.

1st year Fellows.

T. G. Armstrong, M.B., M.R.C.P. : clinical and experimental studies of pericarditis, under Professor J. A. Ryle and Dr. A. N. Drury at Cambridge (p. 86).

R. G. Bickford, M.B. : studies of the itch sensation, under Sir Thomas Lewis in the Department of Clinical Research, University College Hospital, London (p. 69).

D. A. K. Black, B.Sc., M.B., M.R.C.P. : blood volume and kidney function in alimentary bleeding, under Professor L. J. Witts at Oxford.

Miss J. M. Cass, M.D. : problems of nephritis, under Professor L. G. Parsons at Birmingham ; clinical and immunological aspects of neonatal sepsis, under Dr. J. C. Spence at Newcastle.

A. H. Cruickshank, M.B. : functions of the lymphocyte, under Professor H. W. Florey at Oxford.

W. K. Stewart, B.Sc., M.B. : functional activity of the autonomic nervous system, under Dr. E. A. Carmichael in the Neurological Research Unit, National Hospital, Queen Square, London (p. 73).

2nd year Fellows.

J. Hardman, M.B., F.R.C.S. : studies of the angio-architecture of cerebral tumours, under Mr. Geoffrey Jefferson at the Royal Infirmary, Manchester.

D. A. Jennings, B.M.: aetiology and pathology of peptic ulcer, under Professor H. W. Florey at Oxford.

W. D. Wallace, M.B.: mechanism of cyanosis and velocity of blood-flow in certain types of heart disease, under Professor E. J. Wayne at Sheffield.

Miss J. Wright, D.M.: epidemiology of haemolytic streptococcal infections, at University College Hospital Medical School and the Hendon Isolation Hospital (with Dr. W. S. Stalker and Dr. S. L. Wright).

The latter four fellows have completed the two years of tenure. Mr. Hardman has been appointed Neurological Surgeon to the Sheffield Royal Hospital and Infirmary, and Dr. Wright received a personal grant on the expiry of her fellowship (p. 129).

D. A. K. Black—
Urea clearance in haematemesis. *Lancet*, 11th Feb., 1939.

R. M. Calder—
Autoplastic splenic grafts: their use in the study of the growth of splenic tissue. *J. Path. Bact.*, 1939, **49**, 351.

J. M. Cass—
The ultimate prognosis of nephritis in childhood. *Arch. Dis. Childh.*, 1939, **14**, 137.

J. Hardman and G. Jefferson—
Cerebellopontine angle signs produced by ependymomata (cyst, tumour). *Zbl. Neurochir.*, 1938, **3**. 137.

Clinical Trials of New Remedies

The Therapeutic Trials Committee (p. 148) continue to receive applications from manufacturers for clinical trials of new products which seem likely, on the evidence of laboratory tests, to have value in the treatment of disease. Clinical tests of new remedies for venereal disease are arranged by a special sub-committee.

The publications listed below relate to tests completed under the Committee's authority during the year under review. The Council would here again express their thanks to all those clinicians who have generously given of their time and experience in testing new remedies on the Committee's behalf. (See also pp. 107, 108, 115.)

T. Anderson—
Sulphanilamide in the treatment of measles. *Brit. med. J.*, 8th April, 1939.

H. S. Banks—
Chemotherapy of meningococcal meningitis. *Lancet*, 28th Oct., 1939.

L. W. Harrison—
Solu-salvarsan: toxicological and therapeutic tests made on behalf of the Therapeutic Trials Committee of the Medical Research Council. *Brit. J. vener. Dis.*, 1939, **15**, 203.

R. J. Kellar and J. K. Sutherland—
Clinical experiences with a new synthetic oestrogen—'stilboestrol' (diethyl-stilboestrol). *J. Obstet. Gynaec.*, 1939, **46**, 1.

S. L. Simpson—
Recent developments in the treatment of Addison's disease. *Proc. R. Soc. Med.*, 1939, **32**, 685.

J. F. Wilkinson—
Recent developments in the treatment of Addison's disease. *Proc. R. Soc. Med.*, 1939, **32**, 689.

SURGERY

Work in this field by Mr. W. C. Wilson and his colleagues in the Surgical Research Unit, Royal Infirmary, Edinburgh, has been noticed at p. 75.

L. O'Shaughnessy, M.D., F.R.C.S. (Lambeth Cardiovascular Clinic, London and Buckston Browne Research Farm, Downe, Kent)—expenses (from the Sir Horace Plunkett bequest): clinical and experimental work on cardiac surgery (with Dr. H. E. Mansell and Dr. D. Slome); problems of thoracic surgery (with Dr. G. G. Kayne, Dr. W. Pagel and Mr. G. A. Mason).

A. B. Wallace, M.Sc., M.B., F.R.C.S.E. (University and Royal Infirmary, Edinburgh)—personal and expenses: lymphatic absorption from the pelvic organs.

Ian Aird, M.B., Ch.M., F.R.C.S.E. (University of Edinburgh)—personal and expenses: problems of intestinal obstruction.

P. R. Allison, M.B., Ch.M., F.R.C.S. (University and General Infirmary, Leeds)—personal and expenses: clinical and pathological studies of bronchiectasis.

D. P. Cuthbertson, M.D., D.Sc. (Royal Infirmary, Glasgow)—expenses: effects of injury on metabolism (with Mr. J. L. McGirr and Dr. J. S. M. Robertson).

J. Charnley, B.Sc., M.B., F.R.C.S. (King's College, London)—expenses: blood volume in experimental shock.

G. A. G. Mitchell, M.B., Ch.M. (University of Aberdeen)—expenses: anatomy of the peripheral autonomic nervous system; spread of peritoneal effusions.

O. V. Lloyd-Davies, M.S., F.R.C.S. (St. Mark's Hospital, London)—expenses: follow-up study of cases of rectal cancer.

A. H. Hunt, B.M., F.R.C.S. (St. Bartholomew's Hospital, London)—personal: effect of vitamin C on the healing of wounds.

D. Engel, M.D., F.R.C.S.E. (University and Royal Infirmary, Edinburgh)—expenses: permeability of joint tissues.

A. J. Helfet, B.Sc., M.D., M.Ch., F.R.C.S. (St. Thomas's Hospital, London)—personal and expenses: treatment of certain bone and joint diseases.

I. Aird—
The behaviour of the blood volume in intestinal obstruction and strangulation. *Brit. J. Surg.*, 1938, **26**, 418.

D. P. Cuthbertson, J. L. McGirr and J. S. M. Robertson—
The effect of fracture of bone on the metabolism of the rat. *Quart. J. exp. Physiol.*, 1939, **29**, 13.

G. A. G. Mitchell—
A specimen showing unusual arrangements of autonomic nerves. *J. Anat., Lond.*, 1939, **73**, 496.
The condition of the peritoneal vaginal processes at birth. *Ibid.*, 1939, **73**, 658.
Spread of retroperitoneal effusions arising in the renal regions. *Brit. med. J.*, 9th Nov., 1939.

L. O'Shaughnessy—
Future of cardiac surgery. *Lancet*, 4th Nov., 1939.

L. O'Shaughnessy, G. G. Kayne and W. Pagel—
Pulmonary tuberculosis : pathology, diagnosis, management and prevention. London (Oxford University Press), 1939.
L. O'Shaughnessy and G. Mason—
Thoracolysis : a conservative and selective operation for the treatment of certain cases of pulmonary tuberculosis. *Brit. med. J.*, 21st Jan., 1939.
L. O'Shaughnessy, D. Slome and F. Watson—
Surgical revascularisation of the heart : the experimental basis. *Lancet*, 18th March, 1939.
A. B. Wallace—
A method of demonstrating the posterior abdominal wall lymphatics and dye absorption thereby. *Brit. J. Urol.*, 1939, **11**, 117.

Anaesthetics

Research on problems of anaesthesia is directed by a Committee (p. 148) appointed jointly with the Section of Anaesthetics of the Royal Society of Medicine. The inquiry into the question of explosions in operating theatres, to which reference was made in the Report for 1937-38, has been extended, in consultation with the Institute of Electrical Engineers. The Committee have maintained their interest in the British manufacture of cyclopropane for anaesthetic purposes, and their advice has been sought by the Mercantile Marine Department of the Board of Trade, as to the best means of inducing anaesthesia or analgesia in cases of grave emergency arising on ships not carrying surgeons.

F. W. G. Smith, M.D., M.Ch. (East Ham Memorial and Ramsgate General Hospitals)—expenses : relationship of heat regulation to late ether convulsions.

T. A. B. Harris, M.B., D.A. (Guy's Hospital, London)—expenses : respiratory exchange during general anaesthesia.

H. J. Brennan, M.B., D.A. (Royal Infirmary, Manchester)—expenses : shock in prolonged neurosurgical and other operations.

Obstetrics and Gynaecology

Research on puerperal infections by Dr. Leonard Colebrook and his colleagues at Queen Charlotte's Hospital, London, has already been noticed (p. 79).

Mrs. E. C. Pillman-Williams, M.B.E., M.B. and Miss J. A. M. Moore, M.B., F.R.C.S., M.R.C.O.G. (Royal Free Hospital, London)—expenses : seasonal variations in gastric secretion in young women under normal conditions and during pregnancy.

E. M. Robertson, M.B., F.R.C.S.E., M.R.C.O.G. (University and Royal Infirmary, Edinburgh)—personal : motility of the human uterus and causes of uterine pain ; changes in electrical potential associated with ovulation.

C. P. Stewart, M.Sc., Ph.D. and T. N. MacGregor, M.D., F.R.C.S.E., M.R.C.O.G. (Royal Infirmary, Edinburgh)—expenses : hormone excretion in recurrent abortion, and treatment with progesterone and vitamin E (for the Therapeutic Trials Committee) ; causes and treatment of amenorrhoea and other disorders of menstruation (Dr. MacGregor).

R. J. Kellar, M.B., M.R.C.P.E., F.R.C.S.E., M.R.C.O.G. (British Postgraduate Medical School, London)—expenses: arterial hypertension in pregnancy (with Dr. J. K. Sutherland); clinical tests of synthetic oestrogenic agents (for the Therapeutic Trials Committee).

A. M. Sutherland, M.B., M.R.C.O.G. (Royal Maternity and Women's Hospital, Glasgow)—personal: pathological study of endocarditis in pregnancy (with Dr. H. L. Sheehan).

T. N. MacGregor and C. P. Stewart—
An investigation of cases of recurrent abortion and their treatment with progesterone. *J. Obstet. Gynaec.*, 1939, **46**, 857.

E. M. Robertson—
The effects of emotional stress on the contractions of the human uterus: preliminary report. *J. Obstet. Gynaec.*, 1939, **46**, 741.

H. L. Sheehan and A. M. Sutherland—
Sex and age factors in acute and chronic valvular disease. *Brit. Heart J.*, 1939, **1**, 303.

Paediatrics

Work in this field by Dr. Helen Mackay, of the Council's external scientific staff, has been mentioned at p. 77.

Professor L. G. Parsons, M.D., F.R.C.P. (Children's Hospital, Birmingham)—expenses and assistance by Miss Eva Tonks, M.Sc.: haemolytic anaemia (Dr. T. W. Lloyd and Dr. H. S. Baar); experimental anaemia (Dr. E. M. Hickmans); content of vitamins A and C in blood, and vitamin A content of liver (Miss Tonks); vitamin B_1 content of blood in patients with dropsy (Dr. C. G. Parsons).

Miss Winifred F. Young, M.B. (University of Cambridge and Children's Hospital, Birmingham)—personal: kidney function in gastro-enteritis in infancy (under the direction of Dr. R. A. McCance).

Professor G. B. Fleming, M.B.E., M.D. (University and Sick Children's Hospital, Glasgow)—expenses: absorption and utilization of carbohydrate (Dr. T. Crawford); biochemical studies of cerebro-spinal fluid in meningitis (Dr. Esther Hendry); iron metabolism in infancy (Dr. J. H. Hutchison); blood changes in nephritis (Dr. P. Macarthur).

T. Crawford—
A case of Morquio's disease. *Arch. Dis. Childh.*, 1939, **14**, 70.
The causation of the low blood-sugar curve in coeliac disease. *Quart. J. Med.*, 1939, n.s., **8**, 251.

E. Hendry—
The blood and spinal fluid sugar and chloride content in meningitis. *Arch. Dis. Childh.*, 1939, **14**, 159.

J. H. Hutchison—
Nutritional anaemia in an industrial district. *Arch. Dis. Childh.*, 1938, **13**, 355.

J. D. Keith and E. M. Hickmans—
Vitamin C excretion in children, with particular reference to rheumatic fever. *Arch. Dis. Childh.*, 1938, **13**, 125.

L. G. Parsons—
Some nutritional problems of childhood. (Dawson Williams Memorial Lecture.) *Brit. med. J.*, 5th Nov., 1938.
The haemolytic anaemias of childhood. (Schorstein lecture.) *Lancet*, 17th Dec., 1938.

C. W. Ross—
Intravenous and oral glucose curves as an indication of glucose tolerance. *Arch. Dis. Childh.*, 1938, **13**, 289.

NUTRITION

The Council are advised in this field generally by the Nutrition Committee (p. 149). An account of the nutritional survey in Nyasaland by Dr. B. S. Platt of the Council's staff is given at p. 139.

Professor E. P. Cathcart, C.B.E., D.Sc., M.D., F.R.S. (University of Glasgow)—assistance by Mrs. A. M. T. Murray, Ph.D., and expenses: studies of family diets.

R. A. McCance, Ph.D., M.D., F.R.C.P. (University of Cambridge)—assistance by Miss E. M. Widdowson, B.Sc., Ph.D., Miss M. H. Lee, M.Sc. and Miss M. E. Masters, B.Sc., Ph.D., and expenses: chemical composition of foods; food consumption of individual children; absorption and excretion of iron, calcium and magnesium; experimental salt deficiency (with Dr. B. M. Wilkinson); anaemia of pregnancy; clinical and biochemical studies of disordered renal function.

J. T. Irving, Ph.D., M.D. (Rowett Research Institute and Royal Infirmary, Aberdeen)—assistance by E. C. Owen, M.Sc., and expenses: calcium requirements and metabolism of elderly subjects (with Dr. A. Lyall).

Miss W. M. Clifford, M.Sc. (King's College of Household and Social Science, London)—expenses: effects of salts on enzyme action.

Miss M. Watson, M.D. (London School of Hygiene)—personal and expenses, and assistance by Miss F. M. Tucker, B.Sc.: experimental studies of the relation of diet to fertility, growth and resistance to infection (with Professor W. W. C. Topley).

E. P. Cathcart and A. M. T. Murray—
A note on the percentage loss of calories as waste on ordinary mixed diets. *J. Hyg., Camb.*, 1939, **39**, 45.

R. A. McCance—
The ionisable and available iron in foods. *Chemistry and Industry*, 1939, **58**, 528.

R. A. McCance and E. M. Widdowson—
The chemical composition of foods. *Spec. Rep. Ser. Med. Res. Coun., Lond.*, No. 235, 1939.
The fate of calcium and magnesium after intravenous administration to normal persons. *Biochem. J.*, 1939, **33**, 523.
Functional disorganization of the kidney in disease. *J. Physiol.*, 1939, **95**, 36.

M. Masters—
The determination of sulphur in biological material. *Biochem. J.*, 1939, **33**, 1313.

M. Masters and R. A. McCance—
The sulphur content of foods. *Biochem. J.*, 1939, **33**, 1304.

E. C. Owen—
The calcium requirement of older male subjects. *Biochem. J.*, 1939, **33**, 22.

E. M. Widdowson—
Iron administration and haemoglobin levels during pregnancy. *Lancet*, 16th Sept., 1939.

Vitamin studies

Research on vitamins is under the general direction of the Committee named at p. 150, appointed jointly with the Lister Institute of Preventive Medicine. Investigations relating to the maintenance of the international standard preparations of the individual vitamins are supervised by a series of sub-committees, and have been noticed at pp. 64 and 93. Investigations by members of the Council's external scientific staff and their co-workers are described at p. 91.

R. A. Morton, Ph.D., D.Sc. (University of Liverpool)—expenses: chemistry and spectroscopic examination of vitamins A and E; distribution of vitamins A and A_2 in the tissues of fish (with Dr. J. A. Lovern, of the Torry Research Station, Aberdeen).

Professor R. A. Peters, M.C., M.D., F.R.S. (University of Oxford)—assistance by C. Long, B.Sc., and H. W. Kinnersley, and expenses: chemical and experimental studies of the vitamin B complex.

Miss Harriette Chick, C.B.E., D.Sc. (Institute of Animal Pathology, Cambridge, and Lister Institute, London)—expenses: factors in the vitamin B complex necessary for the nutrition of pigs, and symptoms due to deficiency (with Sir Charles J. Martin, Dr. T. F. Macrae and Dr. A. J. P. Martin).

Miss Harriette Chick, C.B.E., D.Sc. and T. F. Macrae, D.Sc. (Lister Institute, London)—assistance by H. G. Hind, B.Sc.: isolation of the various factors of the vitamin B_2 complex.

Miss Lucy Wills, M.B. (London School of Hygiene and Tropical Medicine)—expenses: nature of the factor curative in tropical macrocytic anaemia (with Dr. T. F. Macrae and Mrs. Work).

Miss A. M. Copping, M.Sc. (Lister Institute, London)—personal: tests of various substances for vitamin E activity (under the direction of Professor R. Robison and Dr. Harriette Chick), in relation to chemical studies of the vitamin by Professor A. R. Todd, of Manchester.

D. E. Green, Ph.D. (University of Cambridge)—expenses: isolation of a new compound (flavoprotein) of vitamin B_2 from milk (with Dr. J. G. Dewan, Mr. H. S. Corran and Mr. A. H. Gordon).

Professor J. C. Drummond, D.Sc., and others (University College, London)—expenses: chemistry and physiological actions of vitamin E.

Sir Edward Mellanby, K.C.B., M.D., F.R.C.P., F.R.S. (Nutrition Laboratory, National Institute for Medical Research, Mill Hill)—expenses: phytic acid as the rachitogenic compound in cereals (with Professor D. C. Harrison, of Belfast): bone hyperplasia and nerve degeneration due to vitamin A deficiency.

I. Banga, S. Ochoa and R. A. Peters—
Pyruvate oxidation in brain. VI. The active form of vitamin B_1 and the role of C_4 dicarboxylic acids. *Biochem. J.*, 1939, **33**, 1109.

A. M. Copping and V. Korenchevsky—
The effect of vitamin E deficient diets on the weights of organs of male and female rats. *Vitamin E : a symposium held under the auspices of the Food Group, Society of Chemical Industry*, 1939, p. 44.

H. S. Corran, J. G. Dewan, A. H. Gordon and D. E. Green—
Xanthine oxidase and milk flavoprotein. *Biochem. J.*, 1939, **33**, 1694.

J. C. Drummond, C. H. Gray and N. E. G. Richardson—
The antirachitic value of human milk. *Brit. med. J.*, 14th Oct., 1939.

D. C. Harrison and E. Mellanby—
Phytic acid and the rickets-producing action of cereals. *Biochem. J.* 1939, **33**, 1660.

C. Long—
Pyruvate oxidation in brain. IV. The oxidation products of pyruvic acid. *Biochem. J.*, 1938, **32**, 1711.

C. Long, S. Ochoa and R. A. Peters—
Pyruvate oxidation in brain, not involving a succinate cycle. *J. Physiol.*, 1939, **96**, 7P.

C. Long and R. A. Peters—
Pyruvate oxidation in brain. V. Evidence derived from the metabolism of α-ketobutyric acid. *Biochem. J.*, 1939, **33**, 759.

J. A. Lovern, T. H. Mead and R. A. Morton—
Halibut intestinal oil. *Biochem. J.*, 1939, **33**, 338.

J. A. Lovern and R. A. Morton—
The distribution of vitamins A and A_2. III. *Biochem. J.*, 1939, **33**, 330.
The distribution of the fatty acids in halibut intestinal oil, with a note on the presence of free fatty acids in the intestines of fish. *Ibid.*, 1939, **33**, 1734.

J. A. Lovern, R. A. Morton and J. Ireland—
The distribution of vitamins A and A_2. II. *Biochem. J.*, 1939, **33**, 325.

T. F. Macrae, A. R. Todd, B. Lythgoe, C. E. Work, H. G. Hind and M. M. El Sadr—
Observations on the liver filtrate factor of the vitamin B_2 complex. *Biochem. J.*, 1939, **33**, 1681.

E. Mellanby—
The State and medical research. (Harveian oration, 1938.) Edinburgh (Oliver & Boyd), 1939.
Recent advances in medical science : a study of their social and economic implications. (Rede Lecture, 1939.) Cambridge (University Press).
The experimental method in the conquest of disease. (Stephen Paget Memorial Lecture, 1939.) *Fight ag. Dis.*, 1939, **27**, 14.
The experimental production of deafness in young animals by diet. *J. Physiol.*, 1938, **94**, 380.
Further observations on bone overgrowth and nerve degeneration produced by defective diet. *J. Physiol.*, 1939, **96**, 36P.

R. A. Morton and R. H. Creed—
The conversion of carotene to vitamin A_2 by some fresh-water fishes. *Biochem. J.*, 1939, **33**, 318.

A. R. Moss and J. C. Drummond—
A new method for the isolation of α- and β-tocopherols. *Biochem. J.*, 1938, **32**, 1953.

S. Ochoa—
Enzymic synthesis of co-carboxylase in animal tissues. *Biochem. J.*, 1939, **33**, 1262.

S. Ochoa, R. A. Peters and L. A. Stocken—
Acetylphosphate and pyruvate oxidation. *Nature, Lond.*, 28th Oct., 1939.

R. A. Peters—
The catatorulin test for vitamin B_1. *Biochem. J.*, 1938, **32**, 2031.

R. A. Peters and R. W. Wakelin—
The dissociating power of salts of fatty acids. Preliminary paper. *Biochem. J.*, 1938, **32**, 2290.

Dental Disease

The Dental Board of the United Kingdom contribute substantially to the cost of research in this subject, which is supervised by the Committee named at p. 150.

P. Pincus, D.D.Sc., L.D.S. (Royal Dental Hospital, London)—expenses: bacteriology of dental caries; studies of enamel protein and saliva.

Miss M. M. Murray, D.Sc. (Bedford College, London)—assistance by Miss G. E. Glock, M.Sc., and expenses: biochemical studies of dental caries; origin and significance of salivary phosphatase in relation to tartar formation (with Dr. P. Pincus); spectrographic analysis of dental materials (with Miss F. Lowater, of the Imperial College of Science and Technology).

J. Thewlis, M.Sc. (National Physical Laboratory, Teddington)—expenses (by arrangement with the Department of Scientific and Industrial Research): X-ray studies of tooth structure; (*a*) calcification of enamel and dentine; (*b*) submicroscopic structure of enamel.

Lady Mellanby, D.Sc. (Nutrition Laboratory, National Institute for Medical Research, Mill Hill)—expenses: further studies on the effect of diet on the development, structure and susceptibility to disease of the teeth and jaws.

J. D. King, Ph.D., L.D.S. (University Field Laboratories, Sheffield)—personal and expenses: *B. acidophilus* infection and dental caries in children, and influence of sweet eating on the activity of this process (with Dr. J. M. Croll); microscopic structure of dental enamel; dental conditions of children in rural and urban districts; experimental vitamin A deficiency.

R. Whyte, L.D.S. (University of St. Andrews Medical School, Dundee)—expenses: effect of carbohydrates on the *B. acidophilus* content of the mouth, in relation to dental caries.

E. W. Fish, D.Sc., M.D., L.D.S. (St. Mary's Hospital, London)—expenses: processes of repair in bone and dentine; experimental studies of the reaction of bone to infection.

W. S. Ross, L.D.S. (St. Mary's Hospital, London)—expenses: preservation of the dental pulp, and prevention of apical infection.

Miss S. Glasstone (Mrs. A. Hughes), L.D.S. (Strangeways Research Laboratory, Cambridge)—personal: development of teeth in artificial culture.

S. Wilson Charles, L.D.S. (Guy's Hospital, London)—personal and expenses: development of the jaws, and growth and eruption of teeth in animals.

Professor H. H. Stones, M.D., M.D.S. (University of Liverpool)—expenses: causes of pyorrhoea, and experimental studies of the disease.

Professor R. V. Bradlaw, M.R.C.S., L.D.S. (University of Durham)—expenses: nerve supply of the teeth and their supporting structures.

A. B. MacGregor, M.B., L.D.S. (St. Bartholomew's Hospital, London)—expenses: lymph flow in the teeth and jaws, and eruption and absorption of teeth; deposition of tartar, and its relation to pyorrhoea.

C. A. Mawson, M.Sc., Ph.D. (Royal Berkshire Hospital, Reading)—expenses: vitamin C deficiency in relation to pathological conditions of the mouth and gums.

E. W. Fish—
Calcified tissue of repair. *Proc. R. Soc. Med.*, 1939, **32**, 609.
Bone infection. *J. Amer. dent. Assoc.*, 1939, **26**, 691.

S. Glasstone—
A comparative study of the development *in vivo* and *in vitro* of rat and rabbit molars. *Proc. Roy. Soc.*, B., 1938, **126**, 315.

G. E. Glock and M. M. Murray—
A chemical investigation of salivary calculus. *J. dent. Res.*, 1938, **17**, 257.

G. E. Glock, M. M. Murray and P. Pincus—
The origin and significance of salivary phosphatase. *Biochem. J.*, 1938, **32**, 2096.

J. D. King—
A note on the microscopic structure of enamel. *J. Anat., Lond.*, 1939, **73**, 424.

J. D. King and J. M. Croll—
Dental caries, carbohydrates and *B. acidophilus*. *Brit. dent. J.*, 1939, **66**, 19.

M. M. Murray—
Caries and sugar: crude and refined sugars compared in respect of calcium and phosphorus content. *Brit. dent. J.*, 1939, **66**, 144.

M. M. Murray, G. E. Glock and F. Lowater—
Chemical and spectrographic determination of iron in tooth material. *Brit. dent. J.*, 1939, **66**, 345.

P. Pincus—
Enamel protein. *Proc. R. Soc. Med.*, 1939, **32**, 513.
Qualitative tests on human enamel protein. *Biochem. J.*, 1939, **33**, 694.
The study of caries: sterilisation of teeth. *Brit. dent. J.*, 1939, **66**, 350.

H. H. Stones—
Calculus: some notes on chemical solvents which have been advocated for its removal. *Dent. Rec.*, 1939, **59**, 247.
An histopathological study of the investing tissues of the teeth, the dentine and dental pulp. *Brit. dent. J.*, 1938, **65**, 737.

J. Thewlis—
Optical properties of dental enamel. *Nature, Lond.*, 22nd April, 1939.
The submicroscopic structure of dental enamel. *Proc. Roy. Soc.*, B., 1939, **127**, 211.

J. Thewlis, G. E. Glock and M. M. Murray—
Chemical and X-ray analysis of dental, mineral and synthetic apatites. *Trans. Faraday Soc.*, 1939, **35**, 358.

Neurology

The work of the Neurological Research Unit directed by Dr. E. A. Carmichael at the National Hospital, Queen Square, London, has been noticed at p. 73, and research in neuro-pathology by Dr. Dorothy S. Russell at p. 86; Dr. Carmichael and Dr. Russell are members of the Council's whole-time scientific staff.

N. M. Dott, M.B., F.R.C.S.E. (University of Edinburgh)—assistance by G. L. Alexander, B.Sc., M.B., F.R.C.S., and expenses (from fund provided by the Rockefeller Foundation): functions of the hypothalamic region of the brain, in relation to experimental diabetes insipidus.

J. G. M. Hamilton, M.B., F.R.C.P.E. (University of Edinburgh)—personal (from fund provided by the Rockefeller Foundation): electroencephalographic studies of epilepsy, and artificially induced fits in schizophrenia (with Dr. W. Ritchie Russell).

B. H. C. Matthews, Sc.D. (University of Cambridge)—expenses (from fund provided by the Rockefeller Foundation): relationship of electrical changes in the spinal cord to reflex activity (with Dr. D. H. Barron and Dr. Dunn).

W. E. Carnegie Dickson, M.D., F.R.C.P.E. (West End Hospital for Nervous Diseases, London)—personal and expenses: pathology of tumours of the brain and spinal cord.

Miss E. C. Eaves, M.D. (University of Sheffield)—expenses: pathology of "sleepy sickness" (encephalitis lethargica) and other nervous diseases.

Ivy Mackenzie, B.Sc., M.D. (Eastern District Hospital, Glasgow)—expenses: anatomy and pathology of the extra-pyramidal nervous system, and the visual pathways.

J. H. Biggart and G. L. Alexander—
Experimental diabetes insipidus. *J. Path. Bact.*, 1939, **48,** 405.

Kathleen Schlesinger Research Fellowship

This fellowship, endowed by the late Mr. Eugen M. Schlesinger and Mrs. Schlesinger in memory of their daughter, is intended for research on cysts of the brain and allied conditions. On the recommendation of the special Advisory Committee, the Council awarded the fellowship to Miss G. M. Griffiths, M.D., M.R.C.P., for work under the direction of Dr. J. G. Greenfield at the National Hospital, Queen Square, London, following the resignation of the first holder, K. Stern, M.D.

M. T. Moore and K. Stern—
Vascular lesions in the brain-stem and occipital lobe occurring in association with brain tumours. *Brain*, 1938, **61,** 70.

G. E. Smyth and K. Stern—
Tumours of the thalamus. A clinico-pathological study. *Brain*, 1938, **61,** 339.

K. Stern—
The pathology of apoplexy. Critical review. *J. Neurol. Psychiat.*, 1938, **1,** 26.

K. Stern—

Note on the nucleus ruber magnocellularis and its efferent pathway in man. *Brain*, 1938, **61**, 284.

Chemical study on fluids obtained from cerebral cysts. *Ibid.*, 1939, **62**, 88.

Severe dementia associated with bilateral symmetrical degeneration of the thalamus. *Ibid.*, 1939, **62**, 157.

Mental Disorders

The Committee named at p. 150 direct research in this subject. The inquiries into problems of mental deficiency by Dr. L. S. Penrose, of the Council's staff, and his colleagues at the Royal Eastern Counties' Institution, Colchester, have already been noticed at p. 82.

Professor F. L. Golla, B.M., F.R.C.P. (Maudsley Hospital, London, and Burden Neurological Institute, Bristol)—assistance by L. D. MacLeod, B.Sc., and expenses (from fund provided by the Rockefeller Foundation) : effect of various drugs and hormones on the metabolism of the central nervous system ; pharmacological properties of 'epanutin' ; electroencephalographic studies of epilepsy and other disorders of the nervous system (Mr. Grey Walter).

J. M. Blackburn, B.Sc., Ph.D. (Maudsley Hospital, London)—personal : disturbance of memory after treatment with convulsant drugs (with Dr. G. Tooth) ; tests of the clinical uses of isomyn and methylisomyn (for the Therapeutic Trials Committee).

E. T. Slater, M.B., M.R.C.P. (Maudsley Hospital, London)—expenses : incidence of different types of mental disorder among twins.

F. Warden Brown, D.M., M.R.C.P. (Maudsley Hospital, London)—personal : hereditary aspects of the common psychoneuroses.

J. H. Quastel, Ph.D., D.Sc. (City Mental Hospital, Cardiff)—expenses, and assistance by A. H. M. Wheatley, B.Sc., P. J. G. Mann, B.Sc., Ph.D., J. J. Gordon, B.Sc., Ph.D., D. M. Webley, B.Sc., and M. Tennenbaum, Ph.D. (in the last two cases from funds provided by the Rockefeller Foundation) : acetylcholine metabolism in the brain *in vitro* (with Dr. Mann and Dr. Tennenbaum) ; studies of vitamin B_1 in the nervous system (with Mr. Webley) ; interaction of organic arsenical compounds with tissue proteins (with Dr. Gordon) ; effect of benzedrine on amine oxidation in brain tissue (with Dr. Mann) ; hippuric acid excretion in schizophrenia (with Dr. W. T. Wales).

A. S. Paterson, M.D., M.R.C.P. (National Hospital, Queen Square, London)—expenses : mental changes in dystrophia myotonica (with Dr. O. Maas).

J. J. Gordon and J. H. Quastel—

Estimation of lactic acid in biological material by oxidation with ceric sulphate. *Biochem. J.*, 1939, **33**, 1332.

O. Maas and A. S. Paterson—

The identity of myotonia congenita (Thomsen's disease), dystrophia myotonica (myotonia atrophica) and paramyotonia. *Brain*, 1939, **62**, 198.

P. J. G. Mann, M. Tennenbaum and J. H. Quastel—
Acetylcholine metabolism in the central nervous system. The effects of potassium and other cations on acetylcholine liberation. *Biochem. J.*, 1939, **33**, 822.
Acetylcholine metabolism in the central nervous system. *Ibid.*, 1939, **33**, 1506.

J. H. Quastel—
Respiration in the central nervous system. *Physiol. Rev.*, 1939, **19**, 135.
The significance of anoxaemia in modern psychiatric treatment. *Proc. R. Soc. Med.*, 1939, **32**, 951.

J. H. Quastel and D. M. Webley—
Vitamin B_1 and acetate oxidation by bacteria. *Nature, Lond.*, 7th Oct., 1939.

G. Tooth and J. M. Blackburn—
Disturbance of memory after convulsion treatment. *Lancet*, 1st July, 1939.

Tuberculosis

Research in tuberculosis is directed by the Committee named at p. 150, appointed jointly with the Agricultural Research Council. Work by Dr. A. Stanley Griffith, of the Council's staff, has been noticed at p. 87. Reference to the Dorothy Temple Cross Research Fellowships in tuberculosis is made at p. 144.

Professor J. W. S. Blacklock, M.D. (Royal Infirmary, Glasgow)—expenses: nature and significance of acid-fast bacilli, other than tubercle bacilli, isolated from man; primary infection of tuberculosis in childhood; experimental study of effect of tuberculosis on iron metabolism (with Dr. S. L. Tompsett).

B. R. Clarke, M.D. (Forster Green Hospital, Belfast)—expenses: follow-up study of late results of institutional treatment of tuberculosis.

K. Robson, M.B., M.R.C.P. (Brompton Hospital, London)—expenses (provided from the Dorothy Temple Cross Research Fellowships Fund): follow-up investigation of cases of 'primary' pleurisy with effusion.

P. W. Edwards, M.B. (Cheshire Joint Sanatorium)—expenses (provided from the Dorothy Temple Cross Research Fellowships Fund): incidence of bovine infections in non-pulmonary tuberculosis.

Cell and Tissue Growth

Miss H. B. Fell, D.Sc., and colleagues (Strangeways Research Laboratory, Cambridge)—expenses: studies of bone mechanics, and the development of joint capsules, in artificial culture; embryology of the jaw (Dr. Fell and Dr. W. Jacobson); development of early rabbit embryos *in vitro*, and maintenance of functional activity of rabbit organs in nutrient media (Dr. P. Pincus); perfusion of organs with nutrient fluid under sterile conditions (Dr. A. F. W. Hughes); studies of the argentaffine cells of the alimentary tract, in relation to blood cell formation (Dr. W. Jacobson); phagocytic and tissue reactions to strains of *Monilia* isolated from man (Dr. N. A. Burges); evocation of tissues with chemical substances (Mr. M. Abercrombie).

Work at the Strangeways Research Laboratory on the biological effects of radiation by Dr. F. G. Spear, of the Council's staff, and Dr. A. Glücksmänn has already been noticed at p. 84.

E. M. H. Creech—
Carcinogenic and related non-carcinogenic hydrocarbons in tissue culture. I. *Amer. J. Cancer*, 1939, **35**, 191.

H. B. Fell—
The origin and developmental mechanics of the avian sternum. *Philos. Trans.*, B., 1939, **229**, 407.

W. Jacobson—
The argentaffine cells and pernicious anaemia. *J. Path. Bact.*, 1939, **49**, 1.

S. C. Shen—
A quantitative study of an amphibian neural tube induction with a water-soluble hydrocarbon. *J. exp. Biol.*, 1939, **16**, 143.

Malignant Disease

Some of the tissue-culture work noticed in the previous section has a direct bearing on problems of malignant disease, and reference to clinical studies in the radiotherapy of cancer is made in the following section.

Miss M. Gilmour, M.B. (Marie Curie Hospital, London)—personal: studies of the possible relationship of the female sex hormone, oestrone, to the process of carcinogenesis; relative effects of X and gamma rays on cancer cells; histology of breast cancer, and microscopic grading of tumours of the cervix uteri.

Radiology and Radiotherapy

The stock of radium held by the Council on behalf of H.M. Government is supplemented by further quantities provided by the British Empire Cancer Campaign and the National Radium Commission, the whole amount being distributed on loan to various centres in respect of a co-ordinated scheme of clinical and experimental research into the radium treatment of cancer and some other diseases. The Campaign contributes towards the working expenses of the 'radon centre' at the Middlesex Hospital, where an important fraction of the Government radium is kept in solution as a source of radium emanation; assistance by Miss D. Clephan in the radium work at the hospital is provided by the Council.

A summary of the reports received on research work with radium in 1938 has been prepared by the Radiology Committee (p. 151) and published. Nine of the following centres hold radium on loan from the Council, and they have all continued to co-operate in the clinical studies: the Middlesex Hospital, St. Bartholomew's Hospital, University College Hospital, King's College Hospital, the Royal Free Hospital, the Marie Curie Hospital, St. George's Hospital and St. Peter's Hospital, London; the General Hospital, Birmingham; the Royal Infirmary, Cardiff; the Royal Infirmary, Aberdeen; and the Irish Radium Committee, Dublin. A few additional institutions and research workers have shared in the facilities for the supply of radon. Radium has also been lent for experimental work to Dr. J. C. Mottram at the Mount Vernon Hospital, Northwood; to

Dr. W. V. Mayneord at the Royal Cancer Hospital, London; to Dr. Joan M. Ross at the Royal Free Hospital, London; to Professor F. L. Hopwood at St. Bartholomew's Hospital, London; to Professor Sidney Russ at the Middlesex Hospital, London; to Sir Leonard Hill and Dr. H. J. Taylor at the St. John Clinic, London; to the Strangeways Research Laboratory, Cambridge (p. 84); to Dr. J. Ralston Paterson and others at the Holt Radium Institute, Manchester; and to the Institute of Animal Genetics, Edinburgh.

Researches on the treatment of cancer by radium beam therapy at the Radium Institute, London, are directed by the Advisory Committee named at p. 151. This is appointed jointly by the Council and by the Department of Scientific and Industrial Research, with representatives of other bodies contributing to the cost of the scheme—the Royal College of Surgeons of England, the British Empire Cancer Campaign, and the Mount Vernon Hospital and Radium Institute—and of the National Radium Commission. A donation of £50 towards the expenses of the work was received during the year from Mr. James Weir, Glasgow, and is gratefully acknowledged. The greater part of the large quantity of radium used has been generously lent for the purpose by the Union Minière du Haut Katanga (Radium Belge). Personal grants to Miss C. A. P. Wood, M.R.C.S., D.M.R.E., T. A. Green, M.B., F.R.C.S., D.M.R.E., and L. G. Grimmett, B.Sc., assistance by M. W. L. Owen, M.B., J. A. V. Fairbrother, B.Sc., Ph.D. and F. I. Wright, B.Sc., and general expenses—including those of related pathological work by Professor J. McIntosh, of the Middlesex Hospital—have been provided in respect of this work.

J. S. Mitchell, M.B., Ph.D. (University of Cambridge)—personal and expenses: clinical and experimental work on the radiotherapy of malignant tumours.

Miss Joan M. Ross, M.D. (Royal Free Hospital, London)—expenses: studies of the carcinogenic action of radium.

Sir Leonard Hill, M.B., F.R.S. and H. J. Taylor, B.Sc., Ph.D. (St. John Clinic, London)—expenses: effects of infra-red radiation on the skin, subcutaneous tissues, and respiratory tract; studies of vascular tone.

C. B. Allsopp, Ph.D. (University of Cambridge)—personal and expenses: chemical effects of ultra-violet and gamma rays on substances of biological importance.

J. Forman (London Hospital)—personal (including contribution by the Department of Scientific and Industrial Research): development and application of apparatus for the treatment of disease by ultra-short high frequency waves (with Professor D. T. Harris).

L. Hill—
The penetration of rays through the skin and radiant energy for the treatment of wounds. *J. R. Soc. Arts*, 1939, **88**, 89.

J. Honeybourne, L. F. Lamerton, D. W. Smithers and W. V. Mayneord—
Symposium on three-dimensional radiation distributions. *Brit. J. Radiol.*, 1939, n.s., **12**, 269.

F. L. Hopwood and R. Phillips—
Polymerization of liquids by irradiation with neutrons and other rays. *Nature, Lond.*, 15th April, 1939.

W. V. Mayneord—
A dose contour projector and its application to three-dimensional radiation distributions. *Brit. J. Radiol.*, 1939, n.s., **12**, 262.

M. E. Nahmias, F. L. Hopwood, T. E. Banks, W. H. Rann and L. G. Grimmett—
Apparent existence of a very penetrating radiation from radium and (radium+beryllium). *Nature, Lond.*, 24th June, 1939.

Radiology Committee—
Medical uses of radium: summary of reports from research centres for 1938. *Spec. Rep. Ser. Med. Res. Coun., Lond.*, No. 236, 1939.

J. Read and J. C. Mottram—
'Tolerance concentration' of radon in atmosphere. *Brit. J. Radiol.*, 1939, n.s., **12**, 54.

Vision

The Committee named at p. 151 supervise research on physiological problems of vision and on diseases and abnormalities of the eye. The work of Dr. R. J. Lythgoe, of the Council's staff, has been mentioned at p. 83.

Miss M. D. Vernon, M.A. (University of Cambridge)—personal: visual perception and interpretation in normal and emotionally unstable children (under the general direction of Professor F. C. Bartlett).

K. J. W. Craik, M.A. (University of Cambridge)—expenses: factors determining subjective brightness (under the general direction of Professor F. C. Bartlett).

Sir W. Stewart Duke-Elder, M.D., Ph.D., D.Sc., F.R.C.S. (University College, London)—expenses: mechanism of formation of intra-ocular fluids, in relation to the pathology of glaucoma.

Mrs. M. C. Bourne, M.Sc. (University College, London)—personal and expenses: studies of 'retinitis pigmentosa' and the metabolism of the retina (with Dr. K. Tansley and Dr. M. Kerley).

W. D. Wright, Ph.D., D.Sc. (Imperial College of Science, London)—assistance by H. V. Walters, B.Sc., and expenses: studies of colour vision: (*a*) change in sensitivity of the retina after adaptation to coloured radiations; (*b*) difference between direct and indirect light adaptation.

M. C. Bourne and H. Grüneberg—
Degeneration of the retina and cataract: a new recessive gene in the rat (*Rattus norvegicus*). *J. Hered.*, 1939, **30**, 131.

W. D. Wright—
A colorimetric equipment for research on vision. *J. sci. Instrum.*, 1939, **16**, 10.
Light adaptation at the fovea for normal eyes. *Brit. J. Ophthal.*, 1939, **23**, 51.
The response of the eye to light in relation to the measurement of subjective brightness and contrast. *Trans. Illum. engng Soc., Lond.*, 1939, **4**, 1.
The perception of light. London (Blackie), 1938.

Hearing

The Committee named at p. 152 direct research on the physiology of hearing and on diseases of the ear.

C. S. Hallpike, M.B., F.R.C.S. (Middlesex Hospital, London)—expenses (partly from fund provided by the Rockefeller Foundation): experimental and embryological studies of inherited deafness (with Dr. H. Grüneberg and Dr. A. Ledoux, of Liège); pathology and clinical features of 'Ménière's disease' (with Mr. A. J. Wright, and Mr. T. E. Cawthorne); studies of endolymph and perilymph from the aural labyrinth (with Dr. Ledoux and Miss P. Aldred).

Mrs. P. M. T. Kerridge, M.Sc., Ph.D., M.R.C.P. (University College, London)—expenses: tests of hearing acuity of industrial employees working in noisy environments.

A. W. G. Ewing, Ph.D. (University of Manchester)—(*a*) expenses: relief of deafness through the use of hearing aids (with Dr. T. S. Littler)—(*b*) assistance by Miss D. Gandine-Stanton, M.Sc., Ph.D.: effects of deafness on mental capacity and scholastic attainment in school children.

Work at the National Physical Laboratory, Teddington—expenses (by arrangement with the Department of Scientific and Industrial Research): calibration of hearing aids.

J. H. Shaxby, D.Sc. (School of Medicine, Cardiff)—assistance by J. W. Hughes, B.Sc., Ph.D., and expenses: physical and physiological problems of hearing, including the interaction of notes applied ipsilaterally or contralaterally, and determination of the differential threshold for hearing.

R. S. Sturdy, M.A. (University of Cambridge)—personal (from fund provided by the Rockefeller Foundation): differential intensity threshold of the ear (under the general direction of Professor F. C. Bartlett).

G. Briggs, D. P. Choyce, J. Hill and P. M. T. Kerridge—
The acuity of hearing of left- and right-handed children. *J. Physiol.*, 1939, **96**, 48P.

D. B. Fry and P. M. T. Kerridge—
Tests for the hearing of speech by deaf people. *Lancet*, 14th Jan., 1939.

J. W. Hughes—
Binaural localization with two notes differing in phase by 180°. *Brit. J. Psychol.*, 1939, **30**, 52.

P. M. T. Kerridge—
Recent advances in hearing aids. *Practitioner*, 1938, **141**, 625.
Instrumental aids for defective hearing. *Phys. Soc. Rep. Prog. Phys.*, 1938, **5**, 150.
Hearing aids and social problems of the deaf. *Ulster med. J.*, 1939, **8**, 244.

P. M. T. Kerridge, G. Briggs, D. P. Choyce and J. Hill—
Defective hearing and nutrition in children. *Lancet*, 7th Oct., 1939.

General Physiological Researches

Sir Joseph Barcroft, C.B.E., F.R.S. (University of Cambridge)—expenses: physiology of foetal life, with special reference to the oxygen requirements of the foetus, and the development

of the nervous system (with Dr. D. H. Barron, Dr. K. J. Franklin, Mr. P. H. Forsham, Captain A. MacDonald and Mr. A. T. Cowie).

A. E. Barclay, O.B.E., D.M., M.R.C.P. (University of Oxford)—expenses: X-ray cinematographic studies of the time and manner of closure of the ductus arteriosus in the full-term foetus (with Sir Joseph Barcroft).

Professor D. M. Blair, D.Sc., M.B. (University of Glasgow) and Professor F. Davies, D.Sc., M.D. (University of Sheffield)—expenses: studies of the conducting system of the mammalian heart; and of the salamander heart (Professor Davies, with Dr. E. T. B. Francis).

W. d'A. Maycock, M.D. (St. Thomas's Hospital, London)—personal: studies of the abdominal autonomic nervous system, and of vasomotor reflexes (under the direction of Professor B. A. McSwiney).

Mrs. C. J. Jones, B.Sc., Ph.D. (Royal College of Surgeons, London)—personal and expenses: physiology of the abdominal autonomic nervous system (under the direction of Dr. J. Beattie).

G. W. Hayward, M.D., M.R.C.P. (St. Bartholomew's Hospital, London)—expenses: relation of pulmonary congestion to the vagal control of respiration (under the direction of Professor H. Hartridge).

Professor D. Burns, D.Sc. (King's College, Newcastle-on-Tyne)—expenses: nature of parathyroid tetany.

Professor G. A. Clark, M.D. (University of Sheffield)—expenses: mode of production of 'adrenaline shock'; origin of fluids in the inner ear (with Dr. G. Wilkinson); studies of anticoagulants (with Dr. R. T. Gaunt).

J. Secker, D.Sc., M.R.C.S. (King's College, Newcastle-on-Tyne)—expenses: relationship of the adrenal glands to the motor activities of sympathetic nerves.

Professor E. W. H. Cruickshank, Ph.D., D.Sc., M.D., M.R.C.P. and W. Burns, B.Sc., M.B. (University of Aberdeen)—expenses: carbohydrate metabolism and fatty acid utilization of the heart.

H. A. Krebs, M.D. (University of Sheffield)—assistance by W. A. Johnson, M.Sc., and expenses: intermediary metabolism of carbohydrates and amino acids.

H. W. Kosterlitz, Ph.D., M.D. (University of Aberdeen)—expenses: metabolism of galactose.

J. M. Peterson, D.Sc. (School of Medicine, Cardiff)—expenses: rôle of the liver in carbohydrate metabolism.

J. D. P. Graham, B.Sc., M.D. (University of Glasgow)—expenses: pharmacological actions and therapeutic properties of the fruits of the common hawthorn (under the direction of Professor E. P. Cathcart).

[1] S. D. Bacon, D. J. Bell and H. W. Kosterlitz—
Acyl migration in a derivative of galactose. *J. chem. Soc.*, 1939, p. 1248.

A. E. Barclay, J. Barcroft, D. H. Barron and K. J. Franklin—
X-ray studies of the closing of the ductus arteriosus. *Brit. J. Radiol.*, 1938, n.s., **11**, 570.
A radiographic demonstration of the circulation through the heart in the adult and in the foetus, and the identification of the ductus arteriosus. *Ibid.*, 1939, n.s., **12**, 505.
A. E. Barclay and K. J. Franklin—
The time of functional closure of the foramen ovale in the lamb. *J. Physiol.*, 1938, **94**, 256.
J. Barcroft—
The intra-uterine development of respiratory effort. *Brit. med. J.*, 18th Nov., 1939.
J. Barcroft and D. H. Barron—
The development of behavior in foetal sheep. *J. comp. Neur.*, 1939, **70**, 477.
Movement in the mammalian foetus. *Ergebn. Physiol.*, 1939, **42**, 107.
J. Barcroft, D. H. Barron, A. T. Cowie, P. H. Forsham and A. MacDonald—
The effect of asphyxia on inhibition of respiratory movement in the sheep's foetus. *J. Physiol.*, 1939, **96**, 12P.
J. Barcroft and J. A. Kennedy—
The distribution of blood between the foetus and the placenta in sheep. *J. Physiol.*, 1939, **95**, 173.
J. Barcroft, J. A. Kennedy and M. F. Mason—
The blood volume and kindred properties in pregnant sheep. *J. Physiol.*, 1939, **95**, 159.
The direct determination of the oxygen consumption of the foetal sheep. *Ibid.*, 1939, **95**, 269.
J. Barcroft, K. Kramer and G. A. Millikan—
The oxygen in the carotid blood at birth. *J. Physiol.*, 1939, **94**, 571.
D. M. Blair and F. Davies—
The conducting system in the human and in the calf heart. *J. Anat., Lond.*, 1939, **74**, 137.
B. Cavanagh and H. S. Raper—
A study of the passage of fatty acids of food into lipins and glycerides of the body using deuterium as an indicator. *Biochem. J.*, 1939, **33**, 17.
F. Davies and E. T. B. Francis—
The conducting (connecting) system of the heart of the salamander (*S. salamandra*). *J. Anat., Lond.*, 1939, **74**, 138.
T. Gotsev—
The blood volume in lambs. *J. Physiol.*, 1939, **94**, 539.
J. D. P. Graham—
Crataegus oxyacantha in hypertension. *Brit. med. J.*, 11th Nov., 1939.
W. A. Johnson—
Aconitase. *Biochem. J.*, 1939, **33**, 1046.
H. W. Kosterlitz—
Synthetic galactose-1-phosphoric acid. *Biochem. J.*, 1939, **33**, 1087.
Galactose-1-phosphoric acid in galactose metabolism. *Nature, Lond.*, 7th Oct., 1939.
H. A. Krebs and P. P. Cohen—
Glutamic acid as a hydrogen carrier in animal tissues. *Nature, Lond.*, 16th Sept., 1939.
H. A. Krebs and A. Örström—
Microdetermination of hypoxanthine and xanthine. *Biochem. J.*, 1939, **33**, 984.
A. Örström, M. Örström and H. A. Krebs—
The formation of hypoxanthine in pigeon liver. *Biochem. J.*, 1939, **33**, 990.
A. Örström, M. Örström, H. A. Krebs and L. V. Eggleston—
The synthesis of glutamine in pigeon liver. *Biochem. J.*, 1939, **33**, 995.
J. Secker—
A note on the suprarenal cortex and the transmission of the activity of the sympathetic nerves of the cat. *J. Physiol.*, 1939, **95**, 282.

Hormones

Research on prob'ms of endocrinology is directed by the Committee named at p. 152. Work in this field by members of the Council's staff has already been noticed at p. 46.

Professor E. C. Dodds, M.V.O., Ph.D., D.Sc., M.D., F.R.C.P. (Middlesex Hospital, London)—expenses, and assistance by F. W. Chattaway, B.Sc., S. W. Stroud, B.Sc., P. C. Williams, B.Sc., and N. R. Campbell, B.Sc. : chemistry and metabolism of synthetic oestrogenic agents (the former with Sir Robert Robinson, of Oxford) ; studies of pituitary hormones (with Dr. R. L. Noble, Dr. H. Rinderknecht, Dr. I. W. Rowlands and Mrs. M. H. Warwick) ; chemical studies of aqueous humour and other body fluids (with Dr. J. D. Robertson).

Professor G. F. Marrian, D.Sc. (University of Edinburgh)—expenses (from fund provided by the Rockefeller Foundation) : chemistry of oestrogens and other steroids in the urine.

D. Beall, Ph.D. (British Postgraduate Medical School, London)—expenses : chemistry of the steroids of the testis and adrenals, with special reference to the oestrogens in these glands.

Mrs. M. Boycott, B.Sc., M.B. (University College Hospital, London)—expenses : estimations of blood oestrone, in relation to uterine inertia ; effect of vitamin E therapy in pregnancy.

Miss A. M. Hain, Ph.D., D.Sc. (University of Edinburgh)—personal and expenses : studies of urinary pregnanediol excretion throughout normal pregnancy and labour, in cases of toxaemia of pregnancy, and during the menstrual cycle in sterile women.

Professor R. V. Christie, M.Sc., M.D., M.R.C.P. and E. F. Scowen, M.D., M.R.C.P. (St. Bartholomew's Hospital, London)—assistance by Mrs. J. S. Mallek, M.Sc., M.D., and expenses (from fund provided by the Rockefeller Foundation) : estimation of urinary pregnanediol, in relation to corpus luteum function.

J. M. Robson, M.D., D.Sc. (University of Edinburgh)—expenses : actions of oestrogens on the corpus luteum ; studies of gonadotrophic hormone prepared from horse pituitary (with Dr. P. Eggleton), and of synthetic oestrogens—in particular new active compounds of triphenylethylene (with Professor A. Schönberg).

S. Zuckerman, D.Sc., M.R.C.S. (University of Oxford)—expenses : sensitivity of the uterus to oestrogenic stimulation ; effect of sex hormones on water retention in organs and tissues ; studies of prostatic changes induced by endocrine stimulation, the morphogenesis of intersexuality, and the relation of brightness discrimination to pituitary stimulation.

Professor V. Korenchevsky (Lister Institute, London)—personal, and assistance by Miss K. Hall, Ph.D. : effects of androgenic and oestrogenic hormones, and of vitamin A deficiency, on the different organs of the body (with Mr. R. Burbank and Miss A. Ross).

A. W. Greenwood, Ph.D., D.Sc. (University of Edinburgh)—expenses: tests of the hormone activity of various synthetic compounds in capons (with Professor E. C. Dodds).

Professor L. T. Hogben, D.Sc., F.R.S. (University of Aberdeen)—expenses: mechanism of ovulation in Anura; hormonal mechanism underlying naturally occurring cortical changes in the mouse adrenal.

Professor T. Nicol, M.D., D.Sc., F.R.C.S.E. (King's College, London)—expenses: histological and endocrine studies relating to the preparation of the uterus for pregnancy and to the nutrition of the fertilised ovum (with Captain Weston and Dr. Munter).

G. H. Bell, B.Sc., M.B. (University of Glasgow)—expenses: X-ray studies of the activity of the pseudopregnant uterus; sensitivity of the uterus to oxytocin.

W. H. Newton, M.Sc., M.D. (University College, London)—expenses (from fund provided by the Rockefeller Foundation): metabolism of pregnancy, and criteria of placental activity.

C. W. Bellerby, M.A. (King's College, London)—expenses: control of the reproductive cycle by the anterior pituitary body, using *Xenopus laevis* as test animal; reproductive cycle of the domestic cat (with Dr. O. G. Edholm).

Professor A. W. M. Ellis, M.D., F.R.C.P. (London Hospital)—assistance by B. Cortis-Jones, B.Sc.: chemistry of the adrenotrophic hormone of the anterior pituitary lobe.

C. H. Gray, M.Sc., M.B. (King's College Hospital, London)—expenses: fractionation of the ketogenic factor of the anterior pituitary body (with Dr. F. G. Young).

E. G. Oastler, M.B., M.R.C.P. (University of Glasgow)—expenses: relation of the pituitary gland to growth and obesity, and (with Dr. A. B. Anderson) to the production of ketosis.

O. E. Aykroyd and S. Zuckerman—
The effect of sex hormones on the bulbo-urethral glands of rhesus monkeys. *J. Anat., Lond.*, 1938, **73**, 135.

D. Beall—
The isolation of progesterone and 3 : 20-*allo*pregnanolone from ox adrenals. *Biochem. J.*, 1938, **32**, 1957.
Isolation of oestrone from the adrenal gland. *Nature, Lond.*, 8th July, 1939.

D. Beall and T. Reichstein—
Isolation of progesterone and allopregnanolone from the adrenal. *Nature, Lond.*, 10th Sept., 1938.

G. H. Bell—
The movements of the unloaded rabbit uterus. *J. Physiol.*, 1939, **95**, 8P.

M. Boycott and J. M. Smiles—
Diagnosis of hydatidiform mole by biological assay. *Lancet*, 24th June, 1939.

J. B. Brooksby and W. H. Newton—
The effect of the placenta on the body weight of the mouse. *J. Physiol.*, 1938, **92**, 136.

N. R. Campbell, E. C. Dodds and W. Lawson—
Oestrogenic activity of anol; a highly active phenol isolated from the by-products. *Nature, Lond.*, 24th Dec., 1938.

N. R. Campbell, E. C. Dodds, W. Lawson and R. L. Noble—
Biological effects of the synthetic oestrogen hexoestrol 4 : 4′-dihydroxy-*y*: *d*-diphenyl-*n*-hexane. *Lancet*, 5th Aug., 1939.

W. E. Le Gros Clark, T. McKeown and S. Zuckerman—
Visual pathways concerned in gonadal stimulation in ferrets. *Proc. Roy. Soc.*, B., 1939, **126**, 449.

R. F. Dawson and J. M. Robson—
The pharmacological actions of diethyl-stilboestrol and other oestrogenic and non-oestrogenic substances. *J. Physiol.*, 1939, **95**, 420.
The effects of diethylstilboestrol on striped muscle. *Ibid.*, 1939, **96**, 23P.

E. C. Dodds, L. Golberg, W. Lawson and R. Robinson—
Synthetic oestrogenic compounds related to stilbene and diphenylethene. *Proc. Roy. Soc.*, B., 1939, **127**, 140.

D. Dow and S. Zuckerman—
Further observations on the vaginal pH of monkeys treated with oestrogenic substances. *Endocrinology*, 1939, **25**, 525.

P. Eggleton and J. M. Robson—
Gonadotrophin from horse pituitaries. *J. Physiol.*, 1939, **96**, 4P.

S. J. Folley, A. N. Guthkelch and S. Zuckerman—
The mammary gland of the rhesus monkey under normal and experimental conditions. *Proc. Roy. Soc.*, B., 1939, **126**, 469.

A. M. Hain—
Comb atrophy after adult castration (bantam cocks). *Quart. J. exp. Physiol.*, 1938, **28**, 349.
The effect of temperature on the response of bantam capons to androsterone. *Ibid.*, 1938, **28**, 353.
Oestrogenic and androgenic substances in advanced pregnancy. *Ibid.*, 1939, **29**, 139.
Triphenyl ethylene tested on capons. *Brit. med. J.*, 19th Nov., 1938.

A. M. Hain and E. M. Robertson—
Pregnanediol excretion in the menstrual cycle. *Brit. med. J.*, 17th June, 1939.

V. Korenchevsky—
The bisexual and other effects of pure male sexual hormones on females. *Ergebn. Vitamin-Hormonforsch.*, 1939, **2**, 418.

V. Korenchevsky, R. Burbank and K. Hall—
The action of the dipropionate and benzoate-butyrate of oestradiol on ovariectomized rats. *Biochem. J.*, 1939, **33**, 366.

V. Korenchevsky and K. Hall—
Prolonged injections of male sex hormones into normal and senile male rats. *Brit. med. J.*, 7th Jan., 1939.
Manifold effects of male and female sex hormones in both sexes. *Nature, Lond.*, 3rd Dec., 1938.

V. Korenchevsky, K. Hall and R. Burbank—
The manifold effects of prolonged administration of sex hormones to female rats. *Biochem. J.*, 1939, **33**, 372.

V. Korenchevsky, K. Hall, R. Burbank and A. Ross—
The manifold activity of testosterone dipropionate as compared with that of testosterone propionate in gonadectomized rats. *Biochem. J.*, 1939, **33**, 36.

V. Korenchevsky, K. Hall and M. A. Ross—
Prolonged administration of sex hormones to castrated rats. *Biochem. J.*, 1939, **33**, 213.

F. W. Landgrebe—
The maintenance of reproductive activity in *Xenopus laevis* for pregnancy diagnosis. *J. exp. Biol.*, 1939, **16**, 89.

A. M. MacDonald and J. M. Robson—
The production of vaginal mucification with the synthetic oestrogen, triphenyl ethylene. *J. Path. Bact.*, 1939, **48,** 95.

W. H. Newton and N. Beck—
Placental activity in the mouse in the absence of the pituitary gland. *J. Endocr.*, 1939, **1,** 65.

R. L. Noble, H. Rinderknecht and P. C. Williams—
The apparent augmentation of pituitary antidiuretic action by various retarding substances. *J. Physiol.*, 1939, **96,** 293.

E. G. Oastler and A. B. Anderson—
Ketosis in the hypophysectomized rat. *Biochem. J.*, 1939, **33,** 1094.

A. Palmer and S. Zuckerman—
Further observations on the similarity of stilboestrol and natural oestrogenic agents. *Lancet,* 22nd April, 1939.

H. Rinderknecht, R. L. Noble and P. C. Williams—
Preliminary extraction of gonadotrophic principle from pregnant mare serum. *Biochem. J.*, 1939, **33,** 381.

H. Rinderknecht and P. C. Williams—
Separation of follicle-stimulating fraction from pituitary gonadotrophin. *J. Endocr.*, 1939, **1,** 117.

J. D. Robertson and P. C. Williams—
The creatinine, sugar, and urea equilibrium between plasma and lymph, aqueous humour, cerebro-spinal fluid, and gastric secretion after a hypertonic injection of these solutions. *J. Physiol.*, 1939, **95,** 139.

J. M. Robson—
Failure to antagonize the action of oestradiol on the corpus luteum by progesterone or testosterone. *Quart. J. exp. Physiol.*, 1939, **29,** 159.
Maintenance of pregnancy in the hypophysectomized rabbit by the administration of oestrin. *J. Physiol.*, 1939, **95,** 83.
Comparison of the amounts of progesterone and of desoxycorticosterone acetate needed to produce certain progesterone-like actions. *Ibid.*, 1939, **96,** 21P.

J. M. Robson and G. M. Bonser—
Production of mammary carcinomas in mice of a susceptible strain by the synthetic oestrogen, triphenyl ethylene. *Nature, Lond.*, 5th Nov., 1938.

J. M. Robson, A. Schönberg and H. A. Fahim—
Duration of action of natural and synthetic oestrogens. *Nature, Lond.*, 13th Aug., 1938.

B. G. Shapiro—
Control of urinary secretion by the anterior pituitary. *Lancet,* 24th Dec., 1938.

S. W. Stroud—
Recovery of injected oestrogenic substances from rabbit urine. *J. Endocr.*, 1939, **1,** 201.

S. Zuckerman—
Water-retention in the reproductive organs of female monkeys. *J. Physiol.*, 1938, **94,** 3P.
The effect of sex hormones, cortin, and vasopressin on water-retention in the reproductive organs of monkeys. *J. Endocr.*, 1939, **1,** 147.

S. Zuckerman, A. Palmer and G. Bourne—
Changes in the water-content of organs and tissues as a result of stimulation by oestradiol. *Nature, Lond.*, 25th March, 1939.

S. Zuckerman and O. C. Sandys—
Further observations on the effects of sex hormones on the prostate and seminal vesicles of monkeys. *J. Anat., Lond.*, 1939, **73,** 597.

General Biochemical Researches

Sir Frederick G. Hopkins, O.M., D.Sc., M.B., F.R.C.P., F.R.S. (University of Cambridge)—expenses: properties of succinic dehydrogenase (with Mrs. Lutwak-Mann and Mr. E. J. Morgan).

R. P. Cook, B.Sc., Ph.D. (University of Cambridge)—expenses: cholesterol metabolism, in relation to atheroma of the arteries (with Dr. G. P. McCullagh).

Professor H. J. Channon, D.Sc. (University of Liverpool)—expenses: cause and control of fat deposition in the liver (with Dr. A. W. Beeston and Dr. A. P. Platt).

W. A. Bain, B.Sc., Ph.D. (University of Leeds)—assistance by Mrs. S. Dickinson, M.R.C.S., and expenses: kinetics of adrenaline inactivation by tissues *in vitro*.

Mrs. E. Stedman, M.Sc. (University of Edinburgh)—personal: genesis of acetylcholine in brain tissue (with Dr. E. Stedman).

J. St. L. Philpot, B.Sc. (University of Oxford)—personal and expenses: use of the Svedberg ultracentrifuge in studies of the physical chemistry of proteins (with Dr. A. G. Ogston).

J. H. Schulman, Ph.D. (University of Cambridge)—personal: molecular interactions in ' monolayer ' surface films.

A. W. Beeston and A. P. Platt—
The effect of supplements of tyrosine on the dietary fatty liver. *Chemistry and Industry*, 1939, **58**, 557.

E. G. Cockbain and J. H. Schulman—
Molecular interaction in monolayers. Association between amines and organic acids. *Trans. Faraday Soc.*, 1939, **35**, 6.

R. P. Cook and G. P. McCullagh—
A comparative study of cholesterol metabolism and its relation to fatty infiltration, with particular reference to experimental cholesterol atheroma. *Quart. J. exp. Physiol.*, 1939, **29**, 283.

F. G. Hopkins, E. J. Morgan and C. Lutwak-Mann—
The influence of thiol groups in the activity of dehydrogenases. II. With an addendum on the location of dehydrogenases in muscle. *Biochem. J.*, 1938, **32**, 1829.

E. J. Morgan and E. Friedmann—
S-cysteinosuccinic acid. *Biochem. J.*, 1938, **32**, 2296.

F. J. Philpot and J. St. L. Philpot—
The effect of calcium on the sedimentation constant of casein. *Proc. Roy. Soc.*, B., 1939, **127**, 21.

J. St. L. Philpot—
Examination in the ultracentrifuge. Addendum to an article by H. S. Corran and D. E. Green entitled ' The isolation of a flavoprotein from cow's milk.' *Biochem. J.*, 1938, **32**, 2240.

J. St. L. Philpot and P. A. Small—
A clue to the structure of pepsin. *Proc. Roy. Soc.*, A., 1939, **170**, 62.

A. P. Platt—
The dietary prevention of fatty livers. Compounds related to choline. *Biochem. J.*, 1939, **33**, 505.

E. K. Rideal and J. H. Schulman—
Reactions with monolayers and their biological analogies. *Nature, Lond.*, 15th July, 1939.

J. H. Schulman and E. Stenhagen—
Molecular interaction in monolayers. III. Complex formation in lipoid monolayers. *Proc. Roy. Soc.*, B., 1938, **126**, 356.

E. Stedman and E. Stedman—
The mechanism of the biological synthesis of acetylcholine. II. *Biochem. J.*, 1939, **33**, 811.

General Pathological Researches

Professor H. W. Florey, M.B., Ph.D. (University of Oxford)—expenses: effect of removal of lymphatic tissue (with Dr. A. G. Sanders); the substrate of lysozymes (Dr. L. A. Epstein).

J. G. Stephens, B.Sc., M.B. (University of Oxford)—personal: functions of the spleen in health and disease.

F. J. McLean, B.Sc. (University of Oxford)—personal: experimental renal hypertension.

N. G. Heatley, Ph.D. (University of Oxford)—personal: study of tumour metabolism with a microrespirometer (with Dr. I. Berenblum and Dr. E. Chain).

Professor H. N. Green, M.Sc., M.D. (University of Sheffield)—expenses: effect of bacterial toxins on tumours; nature of bactericidal action of sulphanilamide on *Brucella abortus*.

Professor D. F. Cappell, M.D. (Royal Infirmary, Dundee)—expenses: toxic absorption from wounds (with Dr. H. E. Hutchison).

F. B. Byrom, M.D., M.R.C.P. (London Hospital)—personal and expenses: experimental hypertension.

W. M. Arnott, B.Sc., M.D., F.R.C.P.E. (University of Edinburgh)—expenses: mechanism of arterial hypertension (with Dr. G. D. Matthew); blood complement in acute nephritis and eclamptic toxaemia (with Dr. Scott Thomson and Dr. Matthew).

G. L. Montgomery, M.B., Ph.D. (Royal Hospital for Sick Children, Glasgow)—expenses: experimental nephritis; pathological and experimental studies of bronchiectasis.

Miss J. M. Vaughan, D.M., F.R.C.P. (British Postgraduate Medical School, London)—(*a*) expenses: haemoglobin metabolism in chronic infections (with Dr. M. F. Saifi); maintenance doses of liver extract and iron in different types of anaemia—(*b*) expenses (from fund provided by the Rockefeller Foundation): red cell characteristics and inheritance of acholuric family jaundice (with Dr. G. L. Taylor, of the Galton Laboratory).

R. G. Macfarlane, M.D. (British Postgraduate Medical School, London)—expenses: problems of blood coagulation (with Dr. Trevan) and of fibrinolysis (with Dr. L. I. M. Castleden); conservation and administration of stored blood for transfusion purposes (with Dr. J. M. Vaughan and Dr. G. A. Elliott); clinical studies of various haemorrhagic diseases.

R. B. Scott, D.M., M.R.C.P. (St. Bartholomew's Hospital, London)—expenses: experimental studies of bone marrow transplants.

W. M. Arnott and G. D. Matthew—
The nature of the arteriolar hypertonicity in acute glomerulo-nephritis. *Quart. J. Med.*, 1939, n.s., **8**, 353.

I. Berenblum, E. Chain and N. G. Heatley—
The study of metabolic activities of small amounts of surviving tissues. *Biochem. J.*, 1939, **33**, 68.

G. M. Brown, F. J. McLean and B. G. Maegraith—
The pressor response of hypertensive rabbits to injections of tyramine and posterior pituitary extract. *J. Physiol.*, 1939, **96**, 46P.

G. A. Elliott, R. G. Macfarlane and J. M. Vaughan—
The use of stored blood for transfusion. *Lancet*, 18th Feb., 1939.

N. G. Heatley—
An easily made microburette. *Mikrochemie*, 1939, **26**, 147.

N. G. Heatley, I. Berenblum and E. Chain—
A new type of microrespirometer. *Biochem. J.*, 1939, **33**, 53.

R. G. Macfarlane—
A simple method of measuring clot retraction. *Lancet*, 27th May, 1939.

G. L. Montgomery—
Experimental acute perchloride intoxication. *Brit. J. exp. Path.*, 1939, **20**, 316.

R. B. Scott—
Sternal puncture in the diagnosis of diseases of the blood-forming organs. *Quart. J. Med.*, 1939, n.s, **8**, 127.

J. G. Stephens—
Concentration and sedimentation rates of blood from the splenic artery and vein. *J. Physiol.*, 1938, **94**, 411.
Prolongation of red cell life by the spleen. *Ibid.*, 1939, **95**, 92.
Size of the spleen in relation to blood sedimentation rate. *Ibid.*, 1939, **95**, 132.

S. Thomson, W. M. Arnott and G. D. Matthew—
Blood complement in acute glomerulo-nephritis and toxaemia of pregnancy. *Lancet*, 30th Sept., 1939.

C. Wilson and F. B. Byrom—
Renal changes in malignant hypertension. Experimental evidence. *Lancet*, 21st Jan., 1939.

J. M. Vaughan and C. V. Harrison—
Leuco-erythroblastic anaemia and myelosclerosis. *J. Path. Bact.*, 1939, **48**, 339.

J. M. Vaughan and M. F. Saifi—
Haemoglobin metabolism in chronic infections. *J. Path. Bact.*, 1939, **49**, 69.

Bacteriology, Bacterial Chemistry and Immunology

The Committee on Bacteriology (p. 152) advise the Council in these subjects. Research by investigators in the Council's whole-time service and their co-workers has been noticed under the headings of the National Institute (p. 38) and of the External Scientific Staff (p. 88).

Professor J. W. McLeod, O.B.E., M.B., F.R.S. (University of Leeds)—expenses: bacteriological and pathological studies of diphtheria, and of broncho-pneumonia in children (with Dr. J. W. Orr and Dr. H. E. de C. Woodcock); culture of diphtheria bacilli; streptococcal haemolysins; oxidation and reduction in bacterial cultures (Dr. K. I. Johnstone).

Professor H. D. Wright, M.D., D.Sc. (University of Liverpool)—expenses: cross-infection in diphtheria wards (with Dr. H. R. Shone).

Miss J. Wright, D.M. (University College Hospital Medical School, London)—personal: cross-infection in hospital wards.

Professor W. J. Tulloch, O.B.E., M.D. (University College, Dundee)—expenses: serological and experimental studies of influenza.

W. A. Oliver, M.D., M.R.C.P. (St. Bartholomew's Hospital, London)—expenses: bacteriology and chemotherapy of pneumonia.

A. Q. Wells, D.M. (University of Oxford)—personal and expenses: bacteriology of the mycobacterial diseases of wild voles.

W. Goldie, M.B., M.R.C.P. (University of Leeds)—expenses: pathology and bacteriology of arthritis in swine (with Dr. D. H. Collins).

C. E. van Rooyen, M.D. (University of Edinburgh)—expenses: morphology of elementary and inclusion bodies found in virus diseases.

G. H. Eagles, M.D. (Lister Institute, London)—expenses: bacteriological and serological studies of the rheumatic diseases (with Dr. W. H. Bradley).

A. G. Signy, M.B. (The Infants' Hospital, London)—expenses: bacteriology of rheumatic fever.

W. Levinthal, M.D. (Royal National Hospital for Rheumatic Diseases, Bath)—expenses: serological studies of chronic rheumatism.

C. E. Kellett, M.D., M.R.C.P. (King's College, Newcastle-on-Tyne)—expenses: complement titre of the blood in acute glomerulo-nephritis (with Dr. J. Greig Thomson).

R. A. Kekwick, M.Sc. (Lister Institute, London)—personal and expenses: ultracentrifugal and electrophoretic analyses of various types of sera in health and disease (with Dr. A. S. McFarlane, Dr. W. T. J. Morgan and Dr. W. H. Bradley).

Professor H. W. Florey, M.B., Ph.D. (University of Oxford)—assistance by R. V. G. Ewens, B.Sc.: nucleotidase of snake venom.

W. R. Wooldridge, M.Sc., Ph.D. (London School of Hygiene)—expenses: effect of bacterial toxins on the activity of tissue enzymes.

Professor M. E. Delafield, M.C., M.B. (London School of Hygiene)—expenses: changes in tissue glycogen and blood sugar brought about by non-protein chemical fractions derived from *Bact. aertrycke* (with Professor G. R. Cameron).

Professor C. R. Harington, Ph.D., F.R.S. (University College Hospital Medical School, London)—assistance by Mrs. M. E. Yuill, M.B.: immunological properties of artificial protein complexes.

Professor A. Wormall, D.Sc. (St. Bartholomew's Hospital Medical College, London)—assistance by J. C. Boursnell, B.Sc., and expenses: studies of the trypanocidal agent "Bayer 205"; immunological and chemical properties of certain protein compounds (with Dr. I. Berenblum and Dr. W. E. Gaunt).

Professor J. R. Marrack, D.S.O., M.C., M.D. (London Hospital)—assistance by Miss D. A. Duff, B.Sc., Ph.D., and expenses: studies of the relations between the specificity of immunological reactions and the chemical structure of the reacting substances; preparation of antigens and antibodies for the study of reactions in surface films.

J. Gordon, M.D., M.R.C.P. (University of Leeds)—expenses: artificial opsonification of bacteria (with Dr. W. R. Atkin); bactericidal power of normal serum (with Dr. K. I. Johnstone).

F. C. Happold, Ph.D., D.Sc. (University of Leeds)—expenses: nutrition of *C. diphtheriae* (with Dr. W. C. Evans and Dr. W. R. C. Handley).

Professor A. A. Miles, F.R.C.P. (University College Hospital Medical School, London)—assistance by E. M. Crook, M.Sc.: chemical and immunological studies of strains of *Proteus vulgaris*.

D. E. Green, Ph.D. and V. H. Booth, Ph.D. (University of Cambridge)—expenses: use of an improved design of wet-crushing mill in chemical and immunological studies of bacteria.

N. W. Abdalla and J. W. McLeod—
The antigenic properties of streptolysin. *Brit. J. exp. Path.*, 1939, **20**, 245.

I. Berenblum and A. Wormall—
The immunological properties of proteins treated with $\beta\beta'$-dichlorodiethylsulphide (mustard gas) and $\beta\beta'$-dichlorodiethylsulphone. *Biochem. J.*, 1939, **33**, 75.

J. C. Boursnell, W. G. Dangerfield and A. Wormall—
Studies on Bayer 205 (Germanin) and Antrypol. III. Further observations on the method of determination and on the retention of this drug in the animal body. *Biochem. J.*, 1939, **33**, 81.

J. C. Boursnell and A. Wormall—
Studies on Bayer 205 (Germanin) and Antrypol. IV. The retention of the drug in the animal body. *Biochem. J.*, 1939, **33**, 1191.

J. F. Danielli, M. Danielli and J. R. Marrack—
Surface films of antibodies and antigens. I. The effect of spreading on a water surface on the specific properties of pneumococcus (Type II) antibody and horse-serum globulin. *Brit. J. exp. Path.*, 1938, **19**, 393.

M. E. Delafield and H. A. Smith—
The influence of the pancreas and of pancreatic preparations used for the extraction of certain fractions from *Bact. aertrycke* on the oxygen uptake of brain and muscle suspensions. A correction. *Brit. J. exp. Path.*, 1939, **20**, 216.

G. H. Eagles and W. H. Bradley—
The agglutination of suspensions of virus-like particles prepared from exudates in acute rheumatic fever. *Quart. J. Med.*, 1939, n.s., **8**, 173.

W. C. Evans, F. C. Happold and W. R. C. Handley—
The nutrition of *C. diphtheriae* (types *mitis*, *gravis* and *intermediate*). *Brit. J. exp. Path.*, 1939, **20**, 41.

W. C. Evans, W. R. C. Handley and F. C. Happold—
The nutrition of *C. diphtheriae*. Pantothenic acid as an essential growth factor for certain strains of *C. diphtheriae gravis*: the synthesis of some physiologically active compounds by *C. diphtheriae* cultures in synthetic media. *Brit. J. exp. Path.*, 1939, **20**, 396.

W. E. Gaunt and A. Wormall—
Immunological and chemical properties of carbobenzyloxy-proteins. I. Serum globulin and egg albumin derivatives. II. Insulin derivatives. *Biochem. J.*, 1939, **33**, 908.

J. Gordon and W. R. Atkin—
Artificial opsonins: globin as an opsonin. *J. Path. Bact.*, 1939, **48**, 477.

R. A. Kekwick—
The electrophoretic analysis of normal human serum. *Biochem. J.*, 1939, **33**, 1122.

C. E. Kellett and J. G. Thomson—
Complementary activity of blood serum in nephritis. *J. Path. Bact.*, 1939, **48**, 519.

W. Levinthal—
The aetiological problem of rheumatism. *Ann. rheum. Dis.*, 1939, **1**, 67.

J. W. McLeod, J. W. Orr and H. E. de C. Woodcock—
The morbid anatomy of *gravis*, *intermedius* and *mitis* diphtheria: observations on a series of 51 post-mortem examinations. *J. Path. Bact.*, 1939, **48**, 99.

O. M. Telling and W. A. Oliver—
A case of massive pneumonia, Type III, with massive collapse, treated with 2-(*p*-aminobenzenesulphonamide) pyridine. *Lancet*, 18th June, 1938.

W. J. Tulloch—
Observations on the virus of influenza, with a view to elaborating a simple diagnostic test whereby its presence in the respiratory tract of man may be revealed. *Edinb. med. J.*, 1939, **46**, 117.

C. E. van Rooyen—
The chemical composition of the molluscum contagiosum inclusion body. *J. Path. Bact.*, 1939, **49**, 345.

W. R. Wooldridge and C. Higginbottom—
The effect of certain bacterial toxins upon some respiratory mechanisms of animal tissues. *Biochem. J.*, 1938, **32**, 1718.

Helminthology

Professor R. T. Leiper, M.D., D.Sc., F.R.C.P., F.R.S. (London School of Hygiene and Institute of Agricultural Parasitology, St. Albans)—assistance by Miss M. Young, B.Sc., and expenses: sub-clinical infection with parasitic worms.

V. D. van Someren—
The bone marrow in trichinosis of the rat. *J. Helminth.*, 1939, **17**, 13.
The treatment of experimental trichinosis in the rat with butolan. *Ibid.*, 1939, **17**, 65.
The treatment of trichinosis; a review of methods. *Brit. med. J.*, 25th Feb., 1939.

Medical Entomology

The Committee named at p. 152 have continued to direct investigations aimed at finding the safest and most efficient means of eradicating bed-bugs from dwelling-houses. The work has included a study of the biology of the bed-bug, toxicity tests of insecticides and field studies of the fumigants used. The following grants have been made in respect of this inquiry :—

Professor G. R. Cameron, M.B., D.Sc. (University College Hospital, London)—assistance by Miss C. R. Doniger, M.B., and M. M. R. Clarke, M.R.C.S., and expenses.

Professor P. A. Buxton, M.R.C.S. (London School of Hygiene)—assistance by C. G. Johnson, B.A., and expenses.

Professor J. W. Munro, D.Sc. (Imperial College of Science, London)—assistance by N. F. Sarsfield, B.Sc., H. Hurst, B.Sc., and R. G. Popple, B.Sc., and expenses.

S. A. Ashmore, B.Sc. (Government Laboratory, London)—expenses.

A. W. McKenny Hughes, D.I.C. (British Museum—Natural History)—expenses.

G. R. Cameron and C. R. Doniger—
The toxicity of indene. *J. Path. Bact.*, 1939, **49**, 529.
G. R. Cameron, C. R. Doniger and A. W. McKenny Hughes—
The toxicity of lauryl thiocyanate and *N*-butyl-carbitol-thiocyanate (lethane 384). *J. Path. Bact.*, 1939, **49**, 363.
C. G. Johnson and K. Mellanby—
Bed-bugs and cockroaches. *Proc. R. ent. Soc. Lond.*, (A), 1939, **14**, 50.
A. B. P. Page, O. F. Lubatti and F. P. Gloyns—
The ventilation of houses after fumigation with hydrogen cyanide. *J. Hyg., Camb.*, 1939, **39**, 12.

CHEMOTHERAPY

Research on problems of chemotherapy is directed by the Committee named at p. 153, including chemical representatives appointed by the Department of Scientific and Industrial Research. The investigation has comprised chemical studies and correlated biological tests of new trypanocidal agents, antimalarial and antibacterial drugs, and antiseptics. Grants in respect of this programme of work have been made as indicated below; in addition, Sir Gilbert Morgan and his successor, Dr. G. S. Whitby, and their colleagues at the Chemical Laboratory, Teddington, have continued to co-operate on the chemical side, by arrangement with the Department. Related work by Dr. J. D. Fulton and Sir Rickard Christophers is noticed below, and other investigations bearing on the subject are mentioned in the subsequent section dealing with Tropical Medicine. Research in chemotherapy also forms an increasing part of the work of the National Institute, and reference to investigations there has already been made at p. 44. An account of work in this field by Dr. Leonard Colebrook and his colleagues has been given at p. 79.

Chemical studies

Sir Robert Robinson, D.Sc., F.R.S. (University of Oxford)—assistance by W. L. Glen, B.Sc., and L. Golberg, M.Sc., D.Phil., and expenses: synthetic antimalarial drugs (biological tests by Professor D. Keilin). For other work see p. 123.

W. O. Kermack, D.Sc. (Royal College of Physicians, Edinburgh)—assistance by Miss A. P. Weatherhead, and expenses: synthetic antimalarial drugs; preparation of new sulphanilamide compounds (with Dr. W. Tebrich).

Professor G. R. Clemo, Ph.D., D.Sc., F.R.S. (King's College, Newcastle-on-Tyne)—expenses: synthetic antimalarial drugs.

J. D. Loudon, Ph.D., D.Sc. (University of Glasgow)—assistance by C. W. N. Holmes, B.Sc., and G. Newlands, B.Sc.: preparation of new compounds of the sulphanilamide group (in relation to biological studies in Professor C. H. Browning's department).

Biological studies

Professor Warrington Yorke, M.D., F.R.C.P., F.R.S. (Liverpool School of Tropical Medicine)—expenses: trypanocidal activity of guanidine and amidine compounds (with Dr. E. M. Lourie and Dr. J. Devine, who have been temporarily appointed to the Council's staff, and Dr. H. King, of the National Institute).

Professor C. H. Browning, M.D., F.R.S. (University of Glasgow)—assistance by Miss J. V. M. Robb, M.B., and expenses: trypanocidal and antiseptic properties of new chemical compounds prepared at the Chemical Laboratory, Teddington, and elsewhere; mode of action and therapeutic effect of different compounds of the sulphanilamide group in experimental infections with streptococci and pneumococci.

Professor D. Keilin, Sc.D., F.R.S. and Miss A. Bishop, M.Sc., Ph.D. (University of Cambridge)—personal (Miss Bishop) and expenses: tests of new synthetic compounds—including 'R. 63', prepared by Sir Robert Robinson—against avian malaria caused by *Plasmodium relictum.*

Lt.-Col. S. P. James, C.M.G., M.D., F.R.S. (University of Cambridge)—expenses: biological studies of *Plasmodium gallinaceum* and *Plasmodium relictum.*

The Malaria Research Unit at the London School of Hygiene and Tropical Medicine

J. D. Fulton, B.Sc., M.B., Ph.D.—Leverhulme Research Fellow: biochemical and experimental studies of isolated *P. knowlesi* parasites obtained from rhesus monkeys; tests of two new drugs against avian and monkey malaria; dissociation studies of plasmoquin.

Sir S. Rickard Christophers, formerly Director of the Unit, collaborated with Dr. Fulton during part of the year. In extension of previous arrangements, Dr. Fulton's fellowship and the expenses of the work have been provided from funds generously placed at the Council's disposal by the Leverhulme Trustees, and accommodation and facilities have been given by the School.

C. H. Browning—

The present position of chemotherapy by drugs of the sulphanilamide group. The bacteriological and experimental aspect. *Brit. med. J.*, 5th Aug., 1939.

C. H. Browning, P. Browning and J. V. M. Robb—

A note on antiseptic properties and trypanocidal action. *J. chem. Soc.*, 1939, p. 489. Note to article by W. L. Glen, M. M. J. Sutherland and F. J. Wilson entitled 'The preparation and therapeutic properties of certain 4-substituted quinoline derivatives.'

S. R. Christophers and J. D. Fulton—

Observations on the course of *P. knowlesi* infection in monkeys (*Macacus rhesus*) with notes on its treatment by (1) atebrin and (2) I : II normal undecane diamidine, together with a note on the action of the latter on bird malaria. *Ann. trop. Med. Parasit.*, 1938, **32**, 257.

Experiments with isolated malaria parasites (*P. knowlesi*) free from red cells. *Ibid.*, 1939, **33**, 161.

Respiratory metabolism of *T. rhodesiense* and *P. knowlesi* with observations on the inhibitive effect of various compounds on O_2 uptake by these organisms. *Acta Conventus Tertii de Tropicis atque Malariae Morbis*, Amsterdam, 1938, Pt. II, p. 509.

S. P. James—

The incidence of exo-erythrocytic schizogony in *Plasmodium gallinaceum* in relation to the mode of infection. *Trans. R. Soc. trop. Med. Hyg.*, 1939, **32**, 763.

S. P. James and M. Ciuca—
Species and races of human malaria parasites and a note on immunity. *Acta Conventus Tertii de Tropicis atque Malariae Morbis*, Amsterdam, 1938, Pt. II, p. 269.

W. O. Kermack, W. T. Spragg and W. Tebrich—
3-Nitro- and 3-amino-4-hydroxybenzenesulphonamide. *J. chem. Soc.*, 1939, p. 608.

W. O. Kermack and A. P. Weatherhead—
Nitration of derivatives of 4-hydroxyquinaldine. *J. chem. Soc.*, 1939, p. 563.

Epidemiology

Experimental Epidemiology

Professor W. W. C. Topley, M.D., F.R.C.P., F.R.S. (London School of Hygiene)—assistance by Mrs. J. Wilson, M.B., and expenses: experimental epidemics in populations of mice (with Professor M. Greenwood and Dr. A. Bradford Hill); (*a*) effect of periods of isolation in separate cages, and of varying the degree of contact, during long-continued epidemics; (*b*) methods of immunisation against enteric infection; (*c*) effect of diet on susceptibility to infection (with Dr. Marion Watson).

M. Greenwood, A. Bradford Hill, W. W. C. Topley and Joyce Wilson—
The effect of withdrawing mice from an infected herd at varying intervals. *J. Hyg., Camb.*, 1939, **39**, 109.

School Epidemics

The investigation of the incidence and spread of epidemics, to which reference was made in the last Report, has been continued under the direction of the Committee named at p. 153.

Human Genetics

Research in this field is directed by the Committee named at p. 154. Other related studies, undertaken primarily from the point of view of mental disorders, have been noticed at p. 115. The work of two members of the Council's external scientific staff, Dr. Julia Bell and Dr. L. S. Penrose, has already been described at pp. 80 and 82. The inquiries into the incidence of certain rare congenital defects among school children, and into the incidence of consanguineous parentage among hospital patients, have been extended under the direction of the Committee.

G. L. Taylor, Ph.D., M.D. (Galton Laboratory, University College, London)—personal, and assistance by R. R. Race, M.R.C.S., Miss A. M. Prior, M.Sc. and Miss E. W. Ikin, B.Sc. (from fund provided by the Rockefeller Foundation): serological aspects of human heredity (under the general direction of Professor R. A. Fisher), including studies of hereditary ataxia (with Dr. Julia Bell and Dr. E. A. Carmichael); of phenylketonuria (with Dr. L. S. Penrose and Dr. T. A. Munro); of acholuric jaundice (with Dr. Janet M. Vaughan); of Huntington's chorea (with Dr. E. Guttmann and Dr. L. Minski, of the Maudsley Hospital, London).

J. R. Mutch, M.D. (University of Aberdeen)—expenses: studies of familial corneal dystrophy.

D. G. Ferriman, D.M., M.R.C.P. (Westminster Hospital, London)—expenses: mode of inheritance in oxycephaly.

C. Gordon, M.Sc., Ph.D. (University of Aberdeen)—expenses: experimental work on the relation between the phenomena of penetrance and dominance.

G. L. Taylor and E. W. Ikin—

Observations on the performance of blood-group tests. *Brit. med. J.*, 20th May, 1939.

G. L. Taylor and A. M. Prior—

Blood groups in England. III. Discussion of the family material. *Ann. Eugen., Camb.*, 1939, **9**, 18.

The distribution of the M and N factors in random samples of different races. *Ibid.*, 1939, **9**, 97.

VII. RESEARCH IN TROPICAL MEDICINE

The programme of research work in the field of tropical medicine, inaugurated four years ago after consultation with the Colonial Office, has been maintained along the same general lines. In the award of Fellowships for training suitable men and sending them abroad, and of grants for investigations at home or overseas bearing on problems of tropical disease, the Council are advised and assisted by the Tropical Medical Research Committee, of which the composition is shown at p. 154.

Research Fellowships

The scheme of Research Fellowships in Tropical Medicine is now in its fourth year of operation. Junior Fellowships, tenable for three years, are awarded for the training of selected men. Senior Fellowships, which may be given to candidates who have either held Junior Fellowships or have acquired the necessary training in some other way, are awarded for sending workers abroad to undertake investigations into special problems arising in the tropics: these also are tenable for three years in the first instance.

Junior Fellows.—Dr. G. B. Ludlam has concluded his Fellowship at the end of its third year, after a period of work in Sierra Leone. Of the second-year group, Dr. I. W. MacKichan has taken up an appointment with the Sleeping Sickness Survey in Bechuanaland, and Dr. D. A. Cannon has joined the Nigerian Medical Service: Dr. J. L. Dales has continued to work at the Liverpool School of Tropical Medicine. Of the three Fellows appointed last year, Dr. S. G. Cowper and Dr. W. H. R. Lumsden have been studying in Liverpool and Dr. A. J. Haddow in London.

Senior Fellows.—Dr. C. J. Hackett has returned to England after his second period of work in Uganda, where he had been following up cases of yaws observed during his previous visit. He is now engaged in preparing a report on his investigations. Dr. F. Hawking has returned from Tanganyika by way of the Belgian and French Congo, in order to visit sleeping sickness centres there, and has also spent some time in Nigeria. The work of these two Fellows is described under subject heads below.

Investigations in Specific Subjects

Trypanosomiasis (Sleeping Sickness).—As has been mentioned above, Dr. F. Hawking is holding a Senior Fellowship and has been studying trypanosomiasis in Tanganyika Territory and in Nigeria. An investigation was made of the trypanocidal activity produced in the blood plasma by the intravenous injection of tryparsamide. The activity in the blood was found to be approximately similar in its extent and duration to that produced by tryparsamide in the cerebro-spinal fluid. Cultures of freshly isolated strains of *Trypanosoma*

gambiense were made in human blood; trypanosomes grew readily in the blood of patients who had recently recovered from sleeping sickness, and there was no evidence of trypanocidal antibodies.

As already mentioned at p. 130, Professor A. Wormall, of St. Bartholomew's Hospital Medical College, London, has continued investigations—undertaken at the Council's request—into the fate of "Bayer 205" and "Antrypol" in the body, with particular reference to their use as a prophylactic against sleeping sickness.

Dr. E. M. Lourie, working in the service of the Council at Liverpool, has recently gone to Sierra Leone to make practical trial of new compounds in the treatment of sleeping sickness. Other work on the chemotherapy of trypanosome infections is mentioned at p. 133.

Filariasis.—Dr. Hawking has also been investigating filariasis in Tanganyika. Further experiments were made by the transfusion of microfilariae into clean subjects, to determine in what organs of the body microfilariae are destroyed. Various experiments on the treatment of filariasis yielded only negative results. As shown in the list of publications given below, Dr. Hawking also studied other tropical conditions as opportunity arose.

Yaws.—Dr. C. J. Hackett, holding a Senior Fellowship, has erturned from his second visit to Uganda, where he continued his field work in the study of the bone lesions of yaws. Over two-thirds of the 350 cases observed during the previous year were traced and re-examined, so that there is now a good series of records. The analysis of this material is not yet complete, but already different types of bone lesions have been found associated with particular stages of the disease. There also appears to be a different reaction in the bones, during the stage in which the generalised eruption is present, according to the age at which the patient became infected; in children the predominant change is periosteal deposition, while in adults the most obvious change is focal rarefaction.

Among this material are cases indicating the development of "sabre tibiae". It would seem that this deformity may be the final stage of more than one earlier condition: probably the most frequent antecedent is an extensive periosteal deposition in early childhood. Further observations were made of the late yaws changes of the palms and soles: these changes are relatively frequent in the area where this study was carried out.

Malaria.—Experimental work on the chemotherapy of malaria, and on related aspects of that disease, is described at pp. 133, 134.

Yellow Fever.—Further results have been published, as shown below, of work at the Wellcome Research Institution, London, for which a grant was made last year for assistance to Dr. G. Marshall Findlay by Dr. F. O. MacCallum.

Leprosy.—Professor S. Adler, at the Hebrew University, Jerusalem, has continued to receive an expenses grant for experimental work on leprosy. Reference is made at p. 43 to research on this subject which is being done at the National Institute.

S. Adler and R. Ashbel—
Experimental human leprosy in the hamster. Resistance of leprosy bacilli to drying and to chaulmoogra. *Trans. R. Soc. trop. Med. Hyg.*, 1938, **32**, 4.

G. M. Findlay and F. O. MacCallum—
Spontaneous variation in the neurotropic strain of yellow fever virus. *Brit. J. exp. Path.*, 1938, **19**, 384.
The transmission of yellow fever virus to monkeys by mouth. *J. Path. Bact.*, 1939, **49**, 53.

F. Hawking—
Analysis of the trypanocidal action of trivalent arsenicals and acriflavine. *Ann. trop. Med. Parasit.*, 1938, **32**, 313.
A quantitative study of the photosensitivity induced in trypanosomes by acriflavine. *Ibid.*, 1938, **32**, 367.
A note on the trypanocidal action of atebrin in relation to its absorption by trypanosomes. *Ibid.*, 1938, **32**, 383.
The chemotherapeutic reactions of relapsing fever spirochaetes *in vitro*. *Ibid.*, 1939, **33**, 1.
The mode of action of Germanin (Bayer 205). *Ibid.*, 1939, **33**, 12.
A new focus of onchocerciasis occurring in Kenya colony. *Trans. R. Soc. trop. Med. Hyg.*, 1939, **33**, 95.
A case of acute primary suppurative gastritis. *Lancet*, 24th June, 1939

F. Hawking, T. J. Hennelly and W. T. Wales—
Trypanocidal activity and arsenic content of the cerebrospinal fluid after administration of arsenic compounds. II. *J. Pharmacol.*, 1938, **64**, 146.

Nutritional Surveys

In the last Report, an account was given of plans for a series of field surveys of nutritional problems affecting native populations within the Colonial Empire. The Council had been asked by the Colonial Office to assist this scheme, and they had agreed to appoint a small staff to undertake the scientific co-ordination of the surveys in different territories. The travelling and other special expenses of this staff were provided by a grant from the Colonial Development Fund.

In accordance with this arrangement, Dr. B. S. Platt was appointed by the Council and proceeded to Nyasaland. Throughout the past year he has been engaged there in directing inquiries into the dietetic, nutritional, agricultural, anthropological and social conditions of the country. In this work he has had the co-operation of the International Institute of African Languages, as well as of officers in various departments under the Nyasaland Government. The investigation has now reached the end of its first stage, and many interesting results have been obtained. It is hoped that a report on these will be available for publication soon after Dr. Platt's return to this country in the near future. In addition, Dr. Platt has visited centres in Tanganyika, Kenya, Uganda and Rhodesia, with the object of arranging for further nutritional investigations there.

VIII. INDUSTRIAL HEALTH RESEARCH

In the promotion of research into particular problems of industrial disease and industrial health, the Council are assisted by their Industrial Health Research Board, and by a number of special committees, the composition of which is shown in the Appendix.

Industrial Medicine

Industrial Pulmonary Disease

The first year's field work in the investigation into chronic pulmonary disease among South Wales coal-miners was described in the last Report. During the year under review a number of representative mines both in the anthracite and in the steam-coal areas of South Wales have been examined from the point of view of the medical condition of workers at the coal-face. In the light of the findings, analyses of various environmental conditions to which these men are exposed are being made. The object of this research is threefold—to determine the incidence of chronic pulmonary disease in various parts of the coal-field ; to elicit the causes of the excessive incidence of disabling disease certifiable as silicosis in the anthracite area ; and to discover whether other disabling industrial pulmonary conditions exist that do not come under the present definition of silicosis for purpose of certification. The medical side of the inquiry has been carried out by Dr. P. D'Arcy Hart, of the Council's staff, and Dr. E. A. Aslett, seconded from the Welsh National Memorial Association ; they have had the help of officials of the Mines Department and Inspectorate, and the willing co-operation of the mine-owners and mine-workers. Dr. A. Bradford Hill has continued to advise on statistical questions affecting the results.

The measurement of temperature, humidity and air-velocity, and the collection of atmospheric dust and assessment of its numerical concentration and size-distribution at the coal-face, have been done by Dr. T. Bedford and Dr. C. G. Warner of the staff of the Industrial Health Research Board, while Professor H. V. A. Briscoe and his assistants—Dr. N. L. Spoor and Mr. P. F. Holt—have been responsible for assessing the mass concentration and mineral content of the dust. Dr. A. Brammall and Major J. G. C. Leech have continued their petrological and petro-chemical examinations of the rock strata of the mines ; and Mr. J. I. Graham and Dr. Runnicles have made analyses of nitrous fumes at the coal-face. By arrangement with Dr. F. S. Sinnatt, assistance has been given by the staff of the Coal Survey Laboratory, Cardiff, who have sampled and analysed the seams and some of the associated strata, and have supplied representative samples to some of the other investigators.

All the suitable post-mortem material available in the South Wales coal-field is being examined chemically and histologically by Dr. E. J. King and Dr. T. H. Belt. Close co-operation with these

pathologists and with Professor Briscoe has been maintained by Dr. G. Nagelschmidt, who is using X-ray diffraction spectroscopy in the examination of mineral residues of pulmonary tissue, air-borne dust and rock samples.

The whole of this extensive investigation is under the direction of the Industrial Pulmonary Diseases Committee of the Council (p. 154), of which the chairman is Dr. C. G. Douglas, and the secretary, Dr. E. L. Middleton, of the Factory Department, Home Office.

E. A. Aslett, P. D'Arcy Hart and J. McMichael—
The lung volume and its subdivisions in normal males. *Proc. Roy. Soc.*, B., 1939, **126**, 502.

T. H. Belt—
Silicosis of the spleen : a study of the silicotic nodule. *J. Path. Bact.*, 1939, **49**, 39.

F. J. C. Herrald and J. McMichael—
Determination of lung volume. A simple constant volume modification of Christie's method. *Proc. Roy. Soc.*, B., 1939, **126**, 491.

E. J. King—
The biochemistry of silicic acid. VIII. The determination of silica. *Biochem. J.*, 1939, **33**, 944.

E. J. King and W. Roman—
The biochemistry of silicic acid. VII. Depression of the apparent solubility of silica in body fluids. *Biochem. J.*, 1938, **32**, 2283.

Toxicity of Industrial Solvents

Research into the toxicity of organic solvents used in industry is directed by the Committee named at p. 155. The chief investigator, Wing-Commander T. J. McClurkin, before returning to Royal Air Force duties at the outbreak of war, had been continuing research into solvents of the chlorinated group, and had almost completed an investigation of the toxic effects of ethylene dichloride. The work on this subject at the Chemical Defence Research Station is now temporarily in abeyance.

Occupation and Gastric Disease

The Council were represented at a number of conferences held at the Ministry of Labour to inquire into the circumstances attendant upon an admittedly high incidence of gastric disease in busmen, and to relate these, if possible, to occupational conditions. A report of the proceedings of these conferences was issued by the Ministry of Labour in November. Irregularity of meals and nervous strain were considered to be prominent factors.

Industrial Physiology and Psychology

Industrial Health Research Board Staff and Assistants

Sickness-absence and labour wastage : London School of Hygiene and Tropical Medicine.
May Smith, D.Sc.
Assistant : Margaret Leiper (Mrs. A. Gregory).

Vocational selection and accident proneness : University of Cambridge.
E. Farmer, M.A.
E. G. Chambers, M.A.
Assistants : W. H. N. Hotopf, B.A. ; Alice Heim.

Effects of monotony, fatigue and incentives : University of Manchester.
S. Wyatt, D.Sc. .
Assistants : F. G. L. Stock ; R. Marriott, B.Sc.
Heating and ventilation : London School of Hygiene and Tropical Medicine.
T. Bedford, Ph.D., D.Sc.
C. G. Warner, B.Sc., Ph.D.
Lighting and vision : Imperial College of Science, London.
H. C. Weston.

Special functions devolving on the Industrial Health Research Board during the war have been referred to in the Introduction at p. 18.

Previous to the outbreak of war, the Board had been continuing their investigations into the effects of conditions of work on the health and efficiency of industrial employees. For a fuller report of their work, reference may be made to their Annual Report issued separately.

Nineteenth Annual Report of the Industrial Health Research Board, H.M. Stationery Office, 1939.

Sickness-absence and Labour Wastage

In the London School of Hygiene and Tropical Medicine, Dr. May Smith and Mrs. Gregory, with the assistance and advice of Professor M. Greenwood and his staff, have collected and analysed records of sickness-absence and labour wastage in various industrial and other organisations. Variations found in the statistical data, together with a study of the medical diagnoses of recorded sickness, are being found more and more to give valuable information to employers on the state of health and contentment of their workers.

Conditions of Work, Vocational Aptitudes and Accidents

Dr. Wyatt, assisted by Mr. Marriott and Mr. Stock, has continued to study the physiological and psychological effects of mechanisation, mass-production, and " speeding-up ". In conveyor methods, for example, it is important to ascertain the optimum working conditions, as these depend on the speed, uniformity and continuity of the plant and supply of material. In mechanised industrial work, also, units and standards of performance are sometimes determined by time-studies of the industrial unit of operation without adequate regard to individual variations in physiological capacity.

Mr. Farmer and Mr. Chambers, with the assistance of Mr. Hotopf and Miss Heim, have extended their investigations into the human factors underlying accident causation and the value of tests for accident proneness. A report on accident proneness amongst motor drivers is being issued.

Mr. Farmer has also been in charge of an inquiry, initiated by the Cambridge University Appointments Board, into the value of University education as a preparation for business life.

The same investigators have continued to study problems of vocational guidance and selection, including the use of various tests. These problems have also been investigated by Miss M. D. Vernon,

working for the Council in the Psychological Laboratory at Cambridge University; and by Dr. May Smith and Mrs. Gregory, who continue to pay particular attention to psycho-neurotic symptoms in the industrial "misfit".

Under the direction of Professor F. C. Bartlett at Cambridge University, Mr. O. L. Zangwill (receiving a personal grant) has completed a study of the effects of incentives on human performance.

E. G. Chambers—
A preliminary inquiry into the part played by character and temperament in accident causation. *J. ment. Sci.*, 1939, **85**, 115.

A. Heim—
A preliminary note on a vocational investigation. *Brit. J. Psychol.*, 1939, **29**, 246.

M. D. Vernon—
Characteristic motivation in the activities of school-girls. *Brit. J. Psychol.*, 1939, **29**, 121.

Ventilation and Heating

At the London School of Hygiene and Tropical Medicine, Dr. Bedford and Dr. Warner have continued their researches on work at high temperatures; in these they have had the assistance of Mr. J. S. Weiner, receiving an expenses grant. They have also investigated the stimulating effects of air movement, with special reference to stagnation of air in cramped or crowded spaces, and have made further studies of the natural ventilation of houses.

T. Bedford and C. G. Warner—
Subjective impressions of freshness in relation to environmental conditions. *J. Hyg., Camb.*, 1939, **39**, 498.

Lighting and Vision

Mr. Weston has continued, at the National Physical Laboratory, to study the effects of variations in brightness contrast on the illumination needed for visual tasks requiring discrimination of fine detail. In collaboration with Mr. Graeme G. Talbot, he has completed an inquiry instituted at the request of the National Ophthalmic Treatment Board on the benefit to working health and efficiency of correcting errors of refraction. Their evidence is in favour of correcting small errors of refraction, particularly low degrees of hypermetropia.

H. C. Weston and E. Stroud—
The lighting of cinema auditoriums for visibility and safety. *Trans. illum. engng Soc., Lond.*, 1939, **4**, 2.

Noise and Deafness

Investigating noisy occupations, Dr. Phyllis M. T. Kerridge, of University College, London, has found deafness (as measured by an audiometer) to be only moderate in degree even after from twenty to thirty years' work; and to occur roughly in the same frequency ranges whatever the character of the noise, provided that it is of high intensity.

IX. TRAVELLING FELLOWSHIPS

Rockefeller Medical Fellowships

The Rockefeller Foundation of New York have continued generously to entrust the Council with the award in Great Britain of medical travelling fellowships. These fellowships, endowed by the Foundation, are intended for British graduates who have had some training in research work in clinical medicine or surgery or in some other branch of medical science, and who are likely to profit by a period of work in the United States, or elsewhere abroad, before taking up positions for higher teaching or research in the United Kingdom.

Fellowships for the academic year 1939–40 were awarded by the Council to the following :— Mr. Guy Blackburn, Demonstrator in Anatomy, St. Bartholomew's Hospital, London ; Dr. J. C. Dick, Assistant Pathologist, University of Glasgow and Glasgow Royal Infirmary ; Dr. J. L. Henderson, Assistant, Department of Child Life and Health, University of Edinburgh ; Dr. R. S. Illingworth, Resident Medical Assistant and Clinical Pathologist, Hospital for Sick Children, Great Ormond Street, London ; Dr. R. M. Kark, formerly Demonstrator in Pathology and Registrar to Medical Outpatients, Guy's Hospital, London ; Dr. E. P. Sharpey-Schafer, First Assistant, Department of Medicine, British Postgraduate Medical School, London. Arrangements had been made for these fellows to work at centres in the United States, but owing to the war the awards were not made effective.

Of the fellows appointed by the Council for the academic year 1938–39, Dr. R. R. Bomford and Mr. Ian Mackenzie worked at the Rockefeller Institute, New York ; Dr. Bomford investigated problems of erythropoiesis under Dr. C. P. Rhoads, and Mr. Mackenzie studied the relation of viruses to tumours under Dr. F. P. Rous ; Dr. R. M. Heggie also worked at this centre, on problems of influenza under Dr. W. A. Sawyer and Dr. Bauer, and later at the Rockefeller Institute Hospital, where he engaged in research on pneumonia under Dr. O. T. Avery ; Dr. T. Colver investigated certain aspects of thyroid disease under Dr. J. H. Means at Boston ; Mr. I. G. Williams made a study of supervoltage X-ray therapy at a number of centres in the United States ; and Dr. G. G. E. Smyth worked in Paris under Professor I. Bertrand, mainly on the pathology of the thalamus.

Dorothy Temple Cross Research Fellowships in Tuberculosis

In the special field of tuberculosis, the Council have awarded a tenth series of Dorothy Temple Cross Research Fellowships from the benefaction in that name of which they are the trustees. These fellowships—generously endowed by the late Mrs. Odo Cross—are awarded to suitably qualified British subjects of either sex 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.

The fellowships for the academic year 1939–40 were awarded to the following: Dr. R. R. Henderson, Resident Assistant Physician, St. Thomas's Hospital, London; Mr. A. H. M. Siddons, Chief Assistant, Genito-Urinary Department, St. George's Hospital, London; Dr. J. M. Vaizey, Medical First Assistant and Registrar, London Hospital. Arrangements had been made for these fellows to work at centres abroad, but owing to the war the awards were not made effective.

All the fellows of the ninth annual group worked at centres in the United States during the period 1938–39. Dr. N. C. Oswald and Dr. J. O. Westwater were engaged mainly in pathological studies of tuberculosis, while Dr. J. F. Paterson and Dr. K. M. A. Perry studied chiefly clinical aspects of the disease.

X. PERSONNEL AND REPRESENTATION

Obituary References

During the past year the Council suffered a heavy loss through the death of one of their own number, Professor John Mellanby. He died on 15th July 1939, after a short illness, at the age of sixty-one. He had since 1936 been Waynflete Professor of Physiology in the University of Oxford, having previously for many years held the Chair in the same subject at St. Thomas's Hospital, London. He had made many notable contributions to knowledge over a wide field of physiological research. The Council wish to take this opportunity of expressing their high appreciation of his distinguished services to science and of the assistance he had given to their own work.

The Council have also to regret the recent death of two former members of their body. Mr. Charles John Bond, Hon. Consulting Surgeon to the Leicester Royal Infirmary, was one of the original members of the Council in 1920, and also a member of the predecessor Medical Research Committee ; more recently he had served on the Industrial Health Research Board. Mr. Wilfred Trotter, formerly Professor of Surgery at University College Hospital, London, was a member of the Council from 1929 to 1933, and at the time of his death was continuing to assist them by serving on their Clinical Committee. Both men represented surgery on the Council, and had wide interests in many branches of medical and biological science.

Mr. A. T. Pitts, who also died during the year, had given the Council valuable assistance as an active member of their Dental Committee over a long period.

Membership of the Council

At the end of the period under review the two members of the Council to retire in rotation were Professor H. S. Raper, of the Chair of Physiology in the University of Manchester, and Professor John A. Ryle, of the Chair of Medicine in the University of Cambridge. The Council hope that both of them will continue to give active co-operation in other ways. The new members appointed into these vacancies on the Council are Professor A. J. Clark and Professor T. R. Elliott ; and Professor E. D. Adrian has been appointed into the vacancy caused by the death of Professor John Mellanby.

Scientific Committees

The Council continue to depend greatly on the advice and assistance which they receive from the various special committees dealing with particular parts of their programme. To the many scientific men and women who so freely give their help by serving on these committees, the Council would again express their sincere gratitude. A complete list of the members of the different committees, as at present constituted, is given in the Appendix. Particular mention

may be made, also, of some who have recently retired after long periods of service : Sir Frederick G. Hopkins and Sir Arthur Harden have respectively retired from the Nutrition Committee and the Accessory Food Factors Committee ; Dr. G. Fildes has relinquished his membership of the Radiology Committee.

A new Committee on Research in Preventive Medicine has been appointed by the Council during the year and is likely to play an important part in the future development of their programme in normal times. A Respirators (Poliomyelitis) Committee was also appointed during the year for a temporary purpose, and has already completed its task. Several other committees have recently been appointed to deal with emergency services or problems arising from the war. All these subjects have been discussed in the Introduction.

Of the members of the Industrial Health Research Board, Mr. R. Coppock and Professor J. A. Nixon have retired and have been succeeded by Mr. Harold E. Clay, National Secretary of the Passenger Services Group, Transport and General Workers' Union, and Dr. Donald Hunter, Physician to the London Hospital. Sir Duncan R. Wilson has ceased to represent the Home Office on the Board on retiring from his position as H.M. Chief Inspector of Factories, but has been specially invited by the Council to remain as an additional member of the Board in a personal capacity for a further period : the new official representative is Mr. G. R. A. Buckland, Assistant Under-Secretary of State at the Home Office.

Representatives and Nominees

Sir Edward Mellanby, Secretary of the Council, has with their willing consent accepted an invitation to serve as Chairman of a new Flying Personnel Research Committee set up by the Air Ministry to direct investigations into physiological problems of aviation.

At the Third International Congress of Microbiology, held in New York in September 1939, the Council were represented by Sir John C. G. Ledingham and Dr. Paul Fildes.

BALFOUR OF BURLEIGH,
Chairman of the
Medical Research Council.

E. Mellanby,
Secretary of the Council,
C/o The London School of Hygiene
and Tropical Medicine,
Keppel Street,
London, W.C.1.

19th January, 1940.

APPENDIX

INVESTIGATION COMMITTEES FOR SPECIAL SUBJECTS

Clinical Science

Professor G. E. Gask, C.M.G., D.S.O., F.R.C.S. (*Chairman*).
The Rt. Hon. Viscount Dawson of Penn, G.C.V.O., K.C.B., K.C.M.G., M.D., F.R.C.P.
Professor T. R. Elliott, C.B.E., D.S.O., M.D., F.R.C.P., F.R.S.
Sir Thomas Lewis, C.B.E., M.D., F.R.C.P., F.R.S.
Professor J. A. Ryle, M.D., F.R.C.P.
Professor L. J. Witts, M.D., F.R.C.P.
Sir Edward Mellanby, K.C.B., M.D., D.Sc., F.R.C.P., F.R.S., K.H.P. (*Secretary*).

Therapeutic Trials of New Remedies

Professor T. R. Elliott, C.B.E., D.S.O., M.D., F.R.C.P., F.R.S. (*Chairman*).
T. Carnwath, D.S.O., D.Sc., M.B.
Professor A. J. Clark, M.C., M.D., F.R.C.P., F.R.S.
Sir Henry H. Dale, C.B.E., M.D., F.R.C.P., F.R.S.
W. Allen Daley, M.D., F.R.C.P.
The Rt. Hon. Viscount Dawson of Penn, G.C.V.O., K.C.B., K.C.M.G., M.D., F.R.C.P.
T. Watts Eden, M.D., F.R.C.S.
Professor A. W. M. Ellis, O.B.E., M.D., F.R.C.P.
Professor F. R. Fraser, M.D., F.R.C.P.
Professor J. A. Gunn, M.D., D.Sc., F.R.C.P.
Colonel L. W. Harrison, D.S.O., M.B., F.R.C.P.E.
A. Bradford Hill, D.Sc.
Surgeon Rear-Admiral J. W. McNee, D.S.O., M.D., D.Sc., F.R.C.P.
Professor J. A. Ryle, M.D., F.R.C.P.
Professor L. J. Witts, M.D., F.R.C.P.
F. H. K. Green, M.D., M.R.C.P. (*Secretary*).

Anaesthetics

(*Jointly with the Anaesthetics Section of the Royal Society of Medicine.*)

J. Blomfield, O.B.E., M.D. (*Chairman*).
Sir Henry H. Dale, C.B.E., M.D., F.R.C.P., F.R.S.
C. Langton Hewer, M.B., D.A.
H. King, D.Sc., F.R.S.
Professor R. R. Macintosh, D.M., F.R.C.S.E.
Professor C. A. Pannett, M.D., F.R.C.S.
W. R. Spurrell, M.Sc., M.B., F.R.C.S.
C. F. Hadfield, M.B.E., M.D., D.A. (*Secretary*).

Preventive Medicine

Sir W. Wilson Jameson, M.D., F.R.C.P. (*Chairman*).
J. A. H. Brincker, M.B., D.P.H.
J. Fenton, C.B.E., M.D., M.R.C.P.
J. Ferguson, M.B.
W. M. Frazer, M.Sc., M.D., D.P.H.
E. H. R. Harries, M.D., M.R.C.P., D.P H.
A. Bradford Hill, D.Sc.
W. D. Hood, M.B., D.P.H.
J. R. Hutchinson, M.D.
R. A. McCance, M.D., Ph.D., F.R.C.P.
A. S. M. MacGregor, M.D., D.P.H., K.H.P.
R. H. Parry, M.D., M.R.C.P., D.P.H.
Professor R. M. F. Picken, M.B., D.P.H.
W. M. Scott, B.Sc., M.D.
J. C. Spence, M.C., M.D., F.R.C.P.
Professor W. W. C. Topley, M.D., F.R.C.P., F.R.S.
D. K. M. Chalmers, M.D., D.P.H. (*Secretary*).

Additional members of sub-committees:

Isabella D. Cameron, M.D.
A. A. Moncrieff, M.D., F.R.C.P.
A. W. Forrest, M.D.
Hugh Paul, M.D.
D. M. Livingstone, M.D.
V. D. Allison, M.D.
B. A. Peters, M.D.
Professor Hedley D. Wright, M.D., D.Sc.
Joyce Wright, D.M.
G. Chesney, M.D.
P. Hartley, C.B.E., M.C., D.Sc., F.R.S.
H. P. Newsholme, M.D., F.R.C.P.
H. C. M. Williams, M.R.C.S., D.P.H.
J. A. Charles, M.D., F.R.C.P., D.P.H.

Respirators (Poliomyelitis)

Professor L. J. Witts, M.D., F.R.C.P. (*Chairman*).
Professor G. R. Girdlestone, M.B., F.R.C.S.
R. G. Henderson, M.D., D.P.H.
Phyllis M. T. Kerridge, M.Sc., Ph.D., M.R.C.P.
Professor G. W. Pickering, M.B., F.R.C.P.
C. L. G. Pratt, M.D., M.Sc.
Edgar Schuster, D.Sc.
Andrew Topping, T.D., M.D., D.P.H.
Norman F. Smith, D.M. (*Secretary*).

Human Nutrition

Sir Charles J. Martin, C.M.G., M.B., D.Sc., F.R.S. (*Chairman*).
Harriette Chick, C.B.E., D.Sc.
Professor S. J. Cowell, M.B., F.R.C.P.
Professor J. C. Drummond, D.Sc.
Professor M. Greenwood, D.Sc., F.R.C.P., F.R.S.
Major-General Sir Robert McCarrison, C.I.E., D.Sc., M.D., F.R.C.P., I.M.S.(ret.).
Sir Edward Mellanby, K.C.B., M.D., D.Sc., F.R.C.P., F.R.S., K.H.P.
Sir John Boyd Orr, D.S.O., M.C., D.Sc., M.D., F.R.S.
R. A. McCance, M.D., Ph.D., F.R.C.P. (*Secretary*).

Accessory Food Factors (Vitamins)

(Jointly with the Lister Institute of Preventive Medicine.)

Sir Edward Mellanby, K.C.B., M.D., D.Sc., F.R.C.P., F.R.S., K.H.P. *(Chairman)*.
Katharine H. Coward, D.Sc.
J. M. Hamill, O.B.E., M.D., D.Sc.
E. Margaret Hume, M.A.
T. F. Macrae, D.Sc.
Professor R. A. Peters, M.C., M.D., F.R.S.
O. Rosenheim, D.Sc., F.R.S.
S. S. Zilva, D.Sc.
Miss Harriette Chick, C.B.E., D.Sc. *(Secretary)*.

Iodine Deficiency and Thyroid Disease

(Jointly with the Agricultural Research Council.)

Sir John Boyd Orr, D.S.O., M.C., D.Sc., M.D., F.R.S. *(Chairman)*.
H. H. Green, D.Sc.
Professor C. R. Harington, Ph.D., F.R.S.
Sir Robert Robertson, K.B.E., D.Sc., F.R.S.
A. W. Spence, M.D., F.R.C.P. *(Secretary)*.

Dental Disease

Sir Norman G. Bennett, M.B., L.D.S. *(Chairman)*.
Sir Patrick P. Laidlaw, B.Ch., F.R.C.P., F.R.S.
Lady Mellanby, D.Sc.
Margaret M. Murray, D.Sc.
E. L. Sheridan, L.D.S., F.R.C.S.I.
J. A. Woods, M.D.S.
M. Young, M.D., D.Sc.
Air Vice-Marshal Sir David Munro, K.C.B., C.I.E., M.B. *(Secretary)*.

Mental Disorders

Professor E. D. Adrian, M.D., F.R.C.P., F.R.S. *(Chairman)*.
Sir Hubert Bond, K.B.E., D.Sc., M.D., F.R.C.P.
Professor W. E. le Gros Clark, D.Sc., F.R.C.S., F.R.S.
F. L. Golla, M.B., F.R.C.P.
J. G. Greenfield, M.D., F.R.C.P.
Bernard Hart, M.D., F.R.C.P.
Professor D. K. Henderson, M.D., F.R.C.P.E.
E. O. Lewis, D.Sc., M.R.C.S.
T. A. Ross, M.D., F.R.C.P.
C. P. Symonds, M.D., F.R.C.P.
J. H. Quastel, D.Sc., Ph.D., F.I.C.
Professor L. J. Witts, M.D., F.R.C.P.
Air Vice-Marshal Sir David Munro, K.C.B., C.I.E., M.B. *(Secretary)*.

Tuberculosis

(Jointly with the Agricultural Research Council.)

Sir Joseph A. Arkwright, M.D., F.R.C.P., F.R.S. *(Chairman)*.
Sir Merrik Burrell, Bart., C.B.E.
Professor J. B. Buxton, F.R.C.V.S.
D. A. E. Cabot, M.R.C.V.S.
Professor T. Dalling, M.R.C.V.S.
A. Stanley Griffith, C.B.E., M.D., Ph.D.
P. D'Arcy Hart, M.D., F.R.C.P.
P. Hartley, C.B.E., M.C., D.Sc., F.R.S.
Geoffrey Marshall, O.B.E., M.D., F.R.C.P.
Professor G. S. Wilson, M.D., F.R.C.P.
G. W. Dunkin, M.R.C.V.S. *(Joint Secretary)*.
N. F. Smith, D.M. *(Joint Secretary)*.

Additional members of sub-committees:

W. H. Andrews, D.Sc., M.R.C.V.S.
J. M. Hamill, O.B.E., M.D., D.Sc.
Sir Percy L. J. Kelland, M.R.C.V.S.
Lieut.-Col. P. J. Simpson, D.S.O., F.R.C.V.S.

Radiology

(*Jointly with the British Empire Cancer Campaign.*)

Sir Cuthbert S. Wallace, Bart., K.C.M.G., C.B., F.R.C.S. (*Chairman*).
A. E. Barclay, O.B.E., M.D., D.M.R.E.
A. Burrows, M.D., M.R.C.P., D.M.R.E.
M. Donaldson, M.B., F.R.C.S.
H. T. Flint, D.Sc., Ph.D., M.R.C.S., D.M.R.E.
Professor G. E. Gask, C.M.G., D.S.O., F.R.C.S.
Professor F. L. Hopwood, D.Sc.
Professor B. A. McSwiney, M.B., Sc.D.
J. M. Woodburn Morison, M.D., F.R.C.P.E., D.M.R.E.
J. C. Mottram, M.B.
Professor E. K. Rideal, D.Sc., F.R.S.
F. G. Spear, M.D., D.M.R.E.
G. F. Stebbing, M.B., F.R.C.S.
Professor Sidney Russ, C.B.E., D.Sc. (*Secretary*).

Radium Beam Therapy

(*Jointly with the Department of Scientific and Industrial Research.*)

Professor G. E. Gask, C.M.G., D.S.O., F.R.C.S. (*Chairman*).
E. V. Appleton, D.Sc., F.R.S.
Professor Seymour G. Barling, C.M.G., M.S., F.R.C.S.
Colonel John Beattie, D.Sc., M.D.
Professor A. S. Eve, C.B.E., D.Sc., F.R.S.
Professor F. L. Hopwood, D.Sc.
Geoffrey Pearce, F.R.P.S.
Cecil Rowntree, M.B., F.R.C.S.
Dorothy S. Russell, M.D.
F. G. Spear, M.D., D.M.R.E.
Sir Cuthbert S. Wallace, Bart., K.C.M.G., C.B., F.R.C.S.
F. H. K. Green, M.D., M.R.C.P. (*Joint Secretary*).
L. G. Grimmett, B.Sc. (*Joint Secretary*).

Vision

Sir John H. Parsons, C.B.E., D.Sc., F.R.C.S., F.R.S. (*Chairman*).
Professor F. C. Bartlett, M.A., F.R.S.
Sir W. Stewart Duke-Elder, M.D., D.Sc., F.R.C.S.
Professor H. Hartridge, M.D., Sc.D., M.R.C.P., F.R.S.
Sir William Lister, K.C.M.G., K.C.V.O., M.D., F.R.C.S.
J. W. T. Walsh, D.Sc.
R. J. Lythgoe, M.D. (*Joint Secretary*).
Air Vice-Marshal Sir David Munro, K.C.B., C.I.E., M.B. (*Joint Secretary*).

Additional members of sub-committees:

Wing-Commander P. C. Livingston, O.B.E., F.R.C.S.E., R.A.F.
Surgeon-Commander M. B. MacLeod, M.B., R.N.
L. C. Martin, D.Sc.
Lieut.-Colonel F. R. B. Skrimshire, M.R.C.S., R.A.M.C.

Hearing

Professor T. Graham Brown, M.D., D.Sc., M.R.C.P., F.R.S. (*Chairman*).
Professor F. C. Bartlett, M.A., F.R.S.
F. J. Cleminson, M.Ch., F.R.C.S.
A. W. G. Ewing, Ph.D.
C. S. Hallpike, M.B., M.R.C.P., F.R.C.S.
C. S. Myers, C.B.E., M.D., Sc.D., F.R.S.
J. H. Shaxby, D.Sc.
Major W. S. Tucker, O.B.E., D.Sc.
Phyllis M. T. Kerridge, M.Sc., Ph.D., M.R.C.P. (*Joint Secretary*).
Air Vice-Marshal Sir David Munro, K.C.B., C.I.E., M.B. (*Joint Secretary*).

Hormones

Sir Henry H. Dale, C.B.E., M.D., F.R.C.P., F.R.S. (*Chairman*).
P. M. F. Bishop, B.M.
Professor E. C. Dodds, M.V.O., M.D., D.Sc., F.R.C.P.
Professor C. R. Harington, Ph.D., F.R.S.
Professor V. Korenchevsky.
F. H. A. Marshall, C.B.E., Sc.D., F.R.S.
A. W. Spence, M.D., F.R.C.P.
A. S. Parkes, Sc.D., F.R.S. (*Secretary*).

Bacteriology

Professor W. W. C. Topley, M.D., F.R.C.P., F.R.S. (*Chairman*).
Sir Joseph A. Arkwright, M.D., F.R.C.P., F.R.S.
Professor S. P. Bedson, M.D., D.Sc., F.R.S.
Professor J. Cruickshank, M.D.
Professor T. Dalling, M.R.C.V.S.
Sir Patrick P. Laidlaw, B.Ch., F.R.C.P., F.R.S.
Sir John C. G. Ledingham, C.M.G., D.Sc., F.R.C.P., F.R.S.
Professor H. B. Maitland, M.Sc., M.D.
Professor H. Raistrick, Sc.D., F.R.S.
Professor H. D. Wright, M.D., D.Sc., M.R.C.P.E.
P. Fildes, O.B.E., M.B., F.R.S. (*Secretary*).

Bed-Bug Infestation

Sir John C. G. Ledingham, C.M.G., D.Sc., F.R.C.P., F.R.S. (*Chairman*).
S. A. Ashmore, B.Sc.
Professor P. A. Buxton, M.R.C.S.
Professor G. R. Cameron, M.B., D.Sc.
W. C. Gunn, M.D.
W. H. Howes.
J. Macmillan, D.S.O., M.C., M.B.
G. W. Monier-Williams, O.B.E., M.C., Ph.D., F.I.C.
Professor J. W. Munro, D.Sc.
R. E. Stradling, C.B., M.C., D.Sc., Ph.D., M.Inst.C.E.
P. G. Stock, C.B., C.B.E., M.B., F.R.C.P.
Major A. W. McKenny Hughes, D.I.C., F.R.E.S. (*Secretary*).

Chemotherapy

Sir Henry H. Dale, C.B.E., M.D., F.R.C.P., F.R.S. (*Chairman*).
Professor C. H. Browning, M.D., F.R.S.
Professor J. H. Burn, M.D.
Sir S. Rickard Christophers, C.I.E., O.B.E., F.R.S. (late I.M.S.).
Colonel Leonard Colebrook, M.B.
Lt.-Col. S. P. James, C.S.I., C.M.G., M.D., F.R.S.
Professor D. Keilin, Sc.D., F.R.S.
Sir Gilbert T. Morgan, O.B.E., D.Sc., F.R.S.
Sir Robert Robinson, D.Sc., F.R.S.
Professor Warrington Yorke, M.D., F.R.C.P. F.R.S.
H. King, D.Sc., F.R.S. (*Chemical Secretary*).
C. H. Andrewes, M.D., F.R.C.P., F.R.S. (*General Secretary*).

Statistics

Professor M. Greenwood, D.Sc., F.R.C.P., F.R.S. (*Chairman*).
Professor E. L. Collis, C.B.E., D.M., M.R.C.P.
P. N. Harvey, F.I.A.
A. Bradford Hill, D.Sc.
L. Isserlis, D.Sc.
P. L. McKinlay, M.D.
Sir Arthur S. MacNalty, K.C.B., D.M., F.R.C.P.
Air Vice-Marshal Sir David Munro, K.C.B., C.I.E., M.B.
Professor E. S. Pearson, D.Sc.
P. Stocks, M.D.
M. Young, M.D., D.Sc.
E. Lewis-Faning, B.Sc., Ph.D. (*Secretary*).

School Epidemics

Sir Arthur S. MacNalty, K.C.B., D.M., F.R.C.P. (*Chairman*).
Sir W. Dalrymple-Champneys, Bart, D.M., F.R.C.P.
Surgeon Rear-Admiral S. F. Dudley, O.B.E., M.D., R.N.
G. E. Friend, M.R.C.S.
J. A. Glover, O.B.E., M.D., F.R.C.P.
Professor M. Greenwood, D.Sc., F.R.C.P., F.R.S.
F. Griffith, M.B.
L. R. Lemprière, O.B.E., M.B.
Professor W. W. C. Topley, M.D., F.R.C.P., F.R.S.
Joyce Wilson, M.B. (*Secretary*).

Physical Exercise

Sir Henry H. Dale, C.B.E., M.D., F.R.C.P., F.R.S. (*Chairman*).
Professor E. P. Cathcart, C.B.E., D.Sc., M.D., F.R.S.
The Rt. Hon. Viscount Dawson of Penn, G.C.V.O., K.C.B., K.C.M.G., M.D., F.R.C.P.
Professor A. Hemingway, M.Sc., M.B.
Professor A. V. Hill, O.B.E., Sc.D., F.R.S.
Professor B. A. McSwiney, M.B., Sc.D.
Sir Edward Mellanby, K.C.B., M.D., F.R.C.P., F.R.S., K.H.P.
Professor H. S. Raper, C.B.E., D.Sc., M.B., F.R.C.P., F.R.S.
F. J. C. Herrald, M.B., M.R.C.P.E. (*Secretary*).

Human Genetics

Professor J. B. S. Haldane, M.A., F.R.S. (*Chairman*).
Julia Bell, F.R.C.P.
E. A. Cockayne, M.D., F.R.C.P.
Professor R. A. Fisher, Sc.D., F.R.S.
Professor L. Hogben, D.Sc., F.R.S.
J. A. Fraser Roberts, D.Sc., M.B.
A. Landsborough Thomson, C.B., O.B.E., D.Sc. (*Secretary*).

Tropical Medical Research

Sir John C. G. Ledingham, C.M.G., D.Sc., F.R.C.P., F.R.S. (*Chairman*).
Professor A. J. Clark, M.C., M.D., F.R.C.P., F.R.S.
N. Hamilton Fairley, O.B.E., D.Sc., M.D., F.R.C.P.
Sir W. Wilson Jameson, M.D., F.R.C.P.
Sir Edward Mellanby, K.C.B., M.D., F.R.C.P., F.R.S., K.H.P.
A. J. R. O'Brien, C.M.G., M.C., M.B., M.R.C.P.
Muriel Robertson, D.Sc.
Maj.-Gen. Sir Leonard Rogers, K.C.S.I., C.I.E., M.D., F.R.S., I.M.S. (ret.).
H. H. Scott, C.M.G., M.D., F.R.C.P.
C. Morley Wenyon, C.M.G., C.B.E., M.B., F.R.S.
Professor Warrington Yorke, M.D., F.R.C.P., F.R.S.
A. Landsborough Thomson, C.B., O.B.E., D.Sc. (*Secretary*).

THE INDUSTRIAL HEALTH RESEARCH BOARD
and the Related Scientific Committees

The Board

Professor E. P. Cathcart, C.B.E., D.Sc., M.D., F.R.S. (*Chairman*).
G. R. A. Buckland.
Sir Duncan R. Wilson, C.V.O., C.B.E.
R. E. Lane, M.B., M.R.C.P.
Professor B. A. McSwiney, M.B., Sc.D.
Professor F. C. Bartlett, M.A., F.R.S.
Sibyl G. Horner, M.B.
Sir Henry H. Bashford, M.D., M.R.C.P.
Sir Kenneth Lee, LL.D.
H. E. Clay.
D. Hunter, M.D., F.R.C.P.
Air Vice-Marshal Sir David Munro, K.C.B., C.I.E., M.B. (*Secretary*).

Industrial Pulmonary Disease

C. G. Douglas, C.M.G., M.C., D.M., F.R.S. (*Chairman*).
A. E. Barclay, O.B.E., M.D.
J. C. Bridge, C.B.E., F.R.C.S.E., K.H.P.
S. W. Fisher, M.D.
A. Bradford Hill, D.Sc.
Air Vice-Marshal Sir David Munro, K.C.B., C.I.E., M.B.
D. A. Powell, M.D.
R. L. Rawlinson, B.Ch.
Professor M. J. Stewart, M.B., F.R.C.P.
C. L. Sutherland, M.D.
Professor H. M. Turnbull, D.M., F.R.C.P., F.R.S.
E. L. Middleton, M.D. (*Secretary*).

Toxicity of Industrial Solvents

Sir Joseph Barcroft, C.B.E., F.R.S. (*Chairman*).
J. C. Bridge, C.B.E., F.R.C.S.E., K.H.P.
Professor G. R. Cameron, M.B., D.Sc.
Professor A. J. Clark, M.C., M.D., F.R.C.P., F.R.S.
A. G. Green, M.Sc., F.R.S.
Professor J. A. Gunn, M.D., D.Sc., F.R.C.P.
L. A. Jordan, D.Sc., F.I.C.
H. B. Morgan, M.D.
J. Davidson Pratt, O.B.E., B.Sc.
Air Vice-Marshal Sir David Munro, K.C.B., C.I.E., M.B. (*Secretary*).

Industrial Psychology

Professor Cyril Burt, D.Sc. (*Chairman*).
Professor F. C. Bartlett, M.A., F.R.S.
Charles S. Myers, C.B.E., Sc.D., M.D., F.R.S.
Professor T. H. Pear, M.A.
Sir Charles S. Sherrington, O.M., G.B.E., M.D., Sc.D., F.R.S.
P. E. Vernon, Ph.D.
S. Wyatt, D.Sc.

Heating and Ventilation

(*Jointly with the Building Research Board of the Department of Scientific and Industrial Research.*)

C. G. Douglas, C.M.G., M.C., D.M., F.R.S. (*Chairman*).
A. C. Egerton, F.R.S.
Mrs. M. Fishenden, D.Sc.
Ezer Griffiths, D.Sc., F.R.S.
Professor B. A. McSwiney, M.B., Sc.D.
B. H. C. Matthews, Sc.D.
Air Vice-Marshal Sir David Munro, K.C.B., C.I.E., M.B.

SPECIAL COMMITTEES RELATING TO THE WAR

Emergency Immunological Supplies

Sir John C. G. Ledingham, C.M.G., D.Sc., F.R.C.P., F.R.S. (*Chairman*).
F. Griffith, M.B.
N. W. Hammer, M.R.C.S.
P. Hartley, C.B.E., M.C., D.Sc., F.R.S.
Major-General H. Marrian Perry, C.B., O.B.E., K.H.S.
A. Landsborough Thomson, C.B., O.B.E., D.Sc.
Professor W. W. C. Topley, M.D., F.R.C.P., F.R.S.
F. J. C. Herrald, M.B., M.R.C.P.E. (*Secretary*).

Emergency Public Health Laboratory Service

Professor W. W. C. Topley, M.D., F.R.C.P., F.R.S. (*Chairman*).
T. Carnwath, D.S.O., D.Sc., M.B.
N. W. Hammer, M.R.C.S.
Sir W. Wilson Jameson, M.D., F.R.C.P.
Sir John C. G. Ledingham, C.M.G., D.Sc., F.R.C.P., F.R.S.
Sir Edward Mellanby, K.C.B., M.D., F.R.C.P., F.R.S., K.H.P.
W. M. Scott, B.Sc., M.D.
A. Landsborough Thomson, C.B., O.B.E., D.Sc.
D. K. M. Chalmers, M.D., D.P.H. (*Secretary*).

Emergency Blood Transfusion Depots

Professor G. Payling Wright, D.M., M.R.C.P. (*Chairman*).
H. F. Brewer, M.D.
M. Maizels, M.D., M.R.C.P.
J. O. Oliver, M.B.
Professor W. W. C. Topley, M.D., F.R.C.P., F.R.S.
Janet M. Vaughan, D.M., M.R.C.P.
F. H. K. Green, M.D., M.R.C.P. (*Secretary*).

Additional members of research sub-committee :

A. N. Drury, M.D., F.R.S.
Professor C. R. Harington, Ph.D., F.R.S.
P. Hartley, C.B.E., M.C., D.Sc., F.R.S.
F. J. W. Roughton, Ph.D., F.R.S.

Registration of Pathologists

Professor W. W. C. Topley, M.D., F.R.C.P., F.R.S. (*Chairman*).
Professor S. P. Bedson, D.Sc., M.D., F.R.S.
J. A. H. Brincker, M.B.
S. C. Dyke, D.M., F.R.C.P.
D. Embleton, M.B.
J. G. Greenfield, M.D., F.R.C.P.
F. Griffith, M.B.
Professor G. Hadfield, M.D., F.R.C.P.
Professor J. McIntosh, M.D.
Major-General H. Marrian Perry, C.B., O.B.E., K.H.S.
Professor R. M. F. Picken, B.Sc., M.B.
A. Landsborough Thomson, C.B., O.B.E., D.Sc.
Professor G. Payling Wright, D.M., M.R.C.P.
P. N. Panton, M.B. (*Secretary*).

Traumatic Shock

Professor G. E. Gask, C.M.G., D.S.O., F.R.C.S. (*Chairman*).
G. L. Brown, M.Sc., M.B.
A. N. Drury, M.D., F.R.S.
Professor H. W. Florey, Ph.D., M.B.
J. McMichael, M.D.
Professor G. W. Pickering, M.B., M.R.C.P.
Colonel L. E. H. Whitby, C.V.O., M.C.
Professor W. C. Wilson, M.B., F.R.C.S.E.
Professor F. R. Fraser, M.D., F.R.C.P. (*Joint Secretary*).
Professor B. A. McSwiney, M.B., Sc.D. (*Joint Secretary*).

War-time Therapeutic Requirements

Professor L. J. Witts, M.D., F.R.C.P. (*Chairman*).
Professor A. J. Clark, M.C., M.D., F.R.C.P., F.R.S.
H. Davis, Ph.D., B.Sc.
Professor J. A. Gunn, D.Sc., M.D., F.R.C.P.
P. Hamill, D.Sc., M.D., F.R.C.P.
R. D. Hutchinson.
A. Mortimer.
C. H. Hampshire, M.B. (*Secretary*).

Food Rationing (Special Diets)

(An advisory committee appointed at the request of the Ministry of Food, Ministry of Health, and Department of Health for Scotland.)

Sir Edward Mellanby, K.C.B., M.D., F.R.C.P., F.R.S., K.H.P. (*Chairman*).
Professor L. S. P. Davidson, M.D., F.R.C.P.E.
The Rt. Hon. Viscount Dawson of Penn, P.C., G.C.V.O., K.C.B., K.C.M.G., F.R.C.P.
Professor F. R. Fraser, M.D., F.R.C.P.
R. D. Lawrence, M.D., F.R.C.P.
R. A. McCance, M.D., Ph.D., F.R.C.P.
J. C. Spence, M.C., M.D., F.R.C.P.
Professor H. P. Himsworth, M.D., F.R.C.P. (*Secretary*).

Brain Injuries

Professor E. D. Adrian, M.D., F.R.C.P., F.R.S. (*Chairman*).
Professor F. C. Bartlett, F.R.S.
Professor H. W. B. Cairns, D.M., F.R.C.S.
N. M. Dott, M.B., F.R.C.S.E.
J. G. Greenfield, M.D., F.R.C.P.
Professor G. Jefferson, M.S., F.R.C.S.
A. J. Lewis, M.D., F.R.C.P.
G. Riddoch, M.D., F.R.C.P.
Group-Captain C. P. Symonds, M.D., F.R.C.P.
E. A. Carmichael, M.B., F.R.C.P. (*Secretary*).

INDEX TO SUBJECTS OF RESEARCH

(The investigations mentioned in the text of the Report are there grouped under administrative headings—depending, for instance, on whether the work is done at the National Institute for Medical Research, by members of the Council's staff elsewhere, or by the recipients of grants in hospitals and universities. It thus happens that cognate researches may be described in widely separated sections. The following cross-classification by scientific subjects is accordingly given, reference to the same work being made under more than one title when it is of interest from different points of view. This may perhaps be found to serve a wider purpose than a detailed alphabetical index to items of investigation.)

INDEX TO INSTITUTIONS

(*a*) LOCAL LIST OF RESEARCH CENTRES, ETC.

(*b*) GENERAL LIST OF GOVERNMENT DEPARTMENTS, OFFICIAL AND OTHER BODIES, ETC.

INDEX TO PERSONAL NAMES