

Editorial.

REPORT OF THE MEDICAL RESEARCH COUNCIL FOR THE YEAR 1928-29.

IN the introduction to the Report the Council pay a tribute to Lord Balfour, who was appointed chairman of the Medical Research Council in 1924, and held this post until July, 1929, when failing health rendered him unable to continue active work in London. Soon after he became chairman of the Research Council, Lord Balfour re-entered the Government as Lord President of the Privy Council, and was entrusted with the duty of setting up the new machinery of the Committee of Civil Research. This new machinery brought great benefits to the Medical Research Council by bringing it into more effective relation with research work of other kinds and in other places, and aiding the passage of completed research work as such to its application in practical affairs.

The late Lord Justice Ronan made a bequest to the Council which enabled the new extension of the National Institute at Hampstead to be completed in 1929.

The National Institute is the centre of research work done in various branches of medical science by workers in the whole-time service of the Council. It also maintains and distributes the national standards for certain remedies, the activity of which can be measured only by biological methods, and so plays a part analogous to that of the National Physical Laboratory in the physical and engineering fields.

The creation of new standards and the preparation and verification of the national standards were in progress at the National Institute before there was a legislative demand for them, or opportunity for their official application.

When, therefore, the Therapeutic Substances Bill was enacted in 1925 the standard materials required for the effective use of its machinery were ready for issue.

The following national biological standards required by the law are maintained at the Institute: diphtheria antitoxin, tetanus antitoxin, anti-dysentery serum (Shiga), tuberculin, insulin, pituitary posterior lobe, arsenobenzene, novarsenobenzene and sulpharsenobenzene. All these are based on international standards, of which those for tuberculin and insulin were prepared at the Institute. The international standards now held there for maintenance and general distribution are those of insulin, sulpharsenobenzene, digitalis, and strophanthin.

In reviewing the work of the past five years the Council state that no part of the work promoted by them has greater biological interest or more practical importance for the cure and prevention of disease than the study of the filter-passing viruses. Whether these are organized as minute ultra-microscopic bodies is still an open question, but they are presumably

too small to have an organization similar to that of cells which hitherto have been regarded as primary units of living matter.

An artificial fluid in which these viruses by themselves can multiply has not yet been prepared. It seems to be a characteristic of a virus that it can multiply only in the presence of living cells which it can infect.

Attempts have been made to produce immunity against the virus by treating it with chemical substances until it is incapable of reproducing the disease when injected into a susceptible animal. Twenty years ago Fermi, in Italy, employed rabies virus treated with carbolic acid to immunize against that disease, and apparently succeeded. At the Council's farm laboratories Dr. Laidlaw and Mr. Dunkin have used for the protection against distemper a virus made harmless by formalin. At the National Institute Dr. Todd has also shown that two or three inoculations of the virus of fowl plague which has been treated with carbolic acid and glycerine until it is no longer capable of giving the disease to a fowl, makes the bird so resistant to the disease that the injection of 300,000 times an otherwise fatal dose of infective virus has no harmful effect.

In the case of foot-and-mouth disease it has been found that immunity can be produced by a treated virus, but as the disease itself gives no lasting immunity this has no great value. But it might be used for checking a wave of invasion, had the disease been due to one virus only. Unfortunately, there appear to be three types of virus, and the effects of one do not protect against the others.

With regard to measles, it seems that the monkey is the only animal susceptible to the virus, and the disease cannot be passed from monkey to monkey. Influenza cannot be transmitted to animals, and human experiments on a large scale are not justifiable. In view of all these difficulties the Council are concentrating on every available method for the study of the actual nature of the virus particles in the hope that such knowledge may bring some gain in the control of virus disease.

In many diseases caused by bacteria the toxin of the invading microbe can be neutralized by the anti-toxin in the blood entering into some chemical combination with it.

Dr. Todd has shown that the virus of fowl plague can be rendered harmless by the addition of the right amount of immune body fluid. But the combination is so unstable that the addition of water renders the mixture again virulent.

Dr. Andrewes has also shown that from a non-infective mixture of virus and immune substance the virus can be obtained in a virulent form by simple filtration.

The distribution of the virus in the blood has been investigated and before the war the Council state that it was shown that the virus of typhus and rinderpest does not float freely like a bacterial invasion in the fluids of the blood but is wholly contained within the bodies of the white blood corpuscles. It was shown, however, first by Kusama and subsequently by

Bacot and Ségal that the virus of typhus is contained in the blood platelets and not in the leucocytes. Last year Dr. Todd found the virus of fowl plague was contained in the white blood corpuscles and Dr. Laidlaw and Mr. Dunkin found the same relation in canine distemper. This year Dr. Wilson Smith has shown it to be true also for vaccinia; on the other hand, at the Lister Institute it has been found that the virus of foot-and-mouth disease is almost wholly, and for all periods, found free in the body fluids, and this has been confirmed by Mr. Galloway in the National Institute.

Although no fluid has yet been discovered in which the invading virus will multiply outside the human body, Dr. Andrewes has found a method of studying virus infection outside the body by infecting with virus small fragments of animal tissue which are kept surviving in suitable fluid media. Evidence of infection is seen by the presence of the so-called "inclusion bodies," which are found microscopically in the tissue cells and are exactly similar to the corresponding appearances which accompany infection of the living body by the same virus. Dr. Andrewes has shown that the virus known as Virus III, of rabbits, will multiply indefinitely in artificial cultures of this kind and will form "inclusion bodies" within the nuclei of the cells.

Five years ago as part of a research on virus diseases the Council arranged with Dr. Gye to take up the study of the Rous sarcoma in fowls. From time to time reports on his work appeared and last year the Council reported that Dr. Gye had been unable to obtain with regularity the results which had led him to a definite view of the mode in which a virus conveyed from a pre-existing malignant growth interacted with another factor in the invaded cell to produce a new tumour. In the past year Dr. Gye has endeavoured to find the cause of the discrepancies in his results but without success, and he has now turned to other aspects of the problem.

Dr. Todd has made some interesting observations on the "individuality" of animal cells which are of special interest in relation to skin grafting and the transplantation of other tissues in operative surgery. It is not known whether all cells of the body or only some of them are stamped with "individual" as well as with "specific" qualities. Auto-transplants in surgery succeed, while hetero-transplants, as when the skin is taken from another person, generally fail.

As regards clinical research and experimental medicine the Council point out that the larger part of their annual income is expended in grants to approved workers in nearly all the Universities and other centres of research throughout the country. Most of the work in the present report has been done in laboratories of physiology, biochemistry, bacteriology and pathology, while only a very small part has been done by men engaged in clinical work and studying disease as it actually occurs in human beings. The Council ask: Is there a science of experimental medicine of which the material for study is the human body? Or is the scientific work of

the physician and surgeon limited to the application in his art of scientific results worked out elsewhere in the laboratory?

The work of a physician is quite different from that of a man engaged in the task of advancing knowledge. The main duty of a physician is to diagnose his case by studying the individual and then to apply appropriate treatment. In the work he makes use of the results of scientific research. The research worker in clinical medicine or surgery does not concentrate on the complex of the individual, but studies the disease process, ignoring individuality completely. Fifteen years ago the Council came to the conclusion that scientific work in clinical medicine could not make progress under the conditions obtaining in modern teaching hospitals. To perform research work the man must be freed from the cares of private practice, and having no teaching or clinical responsibilities, he can then concentrate on some particular clinical work. Embued with these ideas the Council in 1916 started the first hospital "unit" under the Sir Thomas Lewis at University College Hospital and they consider that there can be no doubt as to the value of the results of his work in the scientific study of the heart and blood vascular system. With these results in front of them the Council say now that there is undoubtedly a science of experimental medicine.

As a consequence of a memorandum presented by the Council to the Board of Education, the Government, in 1919, made financial provision for setting up University clinics on the "unit" system in certain selected hospitals in London. After ten years of work the Council consider that the time has come to determine in what degree the University units have contributed to progress in research as well as to progress in education. There is no doubt that in teaching they have done valuable work, but this has crippled their energies for research work. The units have not produced men able and willing to devote themselves to clinical research. The main cause of this is the absence of a stable position with reasonable remuneration. The Council state that there can never be a successful recruitment of young men of ability for clinical research until there are at least a few stable positions in sight, which at middle-age will provide reasonable remuneration and adequate power of educating a family.

The Council declare their intention to encourage still further the scientific and direct study of disease in man. They wish to recruit young men of ability and are prepared to help these recruits to the utmost of their power in a preliminary period of training and will increase the number of workers in the clinical field upon their permanent staff as soon as they are able to select candidates whose work has made the Council confident of their success in a career of research.

Having dealt with the main points in the Introduction to the Report we must make a brief reference to some important results which have been obtained in the departments of the National Institute for Medical Research. In the department of pharmacology and biochemistry very interesting

studies have been made with acetylcholine mentioned in last year's Report as having been obtained from the spleens of large animals like the horse and the ox. The localized flushings and heat which accompany localized pain seem to be due to the liberation of this substance in very minute quantities near the end points of the nerves. This, taken in conjunction with the wide distribution of histamine in the body, points to a wide conception of the chemical machinery concerned in the adjustment of the circulation to the local physiological needs of the body.

Dr. King and Dr. Gough have discovered a new group of aromatic amides containing arsenic which have pronounced curative action in trypanosomiasis analogous to that of sleeping sickness.

In the department of applied physiology and hygiene Dr. Hill and Dr. Campbell have studied the effects on animals of prolonged exposure to high tensions of oxygen. The harmful effects of this exposure have been found to be associated with a poisonously high tension of carbon dioxide in the tissues. This appears to be due to constriction of the blood-vessels and to saturation of the blood with oxygen with a reduction in its power of carrying carbon dioxide. Animals can withstand prolonged exposure to high atmospheric pressures if the proportion of oxygen be suitably reduced. A pressure of ten atmospheres is well tolerated for a long period provided that the oxygen is reduced to 2 per cent in the mixture breathed, and that carbon dioxide is effectively removed. The long-continued excess of dissolved nitrogen in the blood and tissues appears to be harmless.

On the other hand the breathing of pure oxygen for a short period has been shown to accelerate the removal of the dissolved nitrogen after exposure to high pressure. Dr. Hill in a series of tests conducted for the Admiralty at Loch Long has shown that by this means the regulation times for decompression could be shortened by two-thirds and in one case by three-quarters. A record depth of 308 ft. was attained by two divers who had not previously been deeper than 120 ft.

Some sixty pages of the Report are devoted to a brief description of the researches now being carried out in clinical and other units. Statements of the nature of the researches and the names of the workers are given, but for actual details the papers by the various authors, a list of which is given at end of each Report, must be consulted. It would serve no useful purpose merely to give a list of the researches.

It is interesting to note that Professor H. B. Dixon and Dr. W. F. Higgins, working at Manchester for the Committee on Anæsthetics, have examined many cylinders of nitrous oxide made by different firms and purchased in the open market. Carbon monoxide was present in all the samples tested in amounts varying from 5 to 40 parts per million. Tests of nitrate used in the manufacture showed that it was of high purity, but that small fragments of wood from the barrels in which it was supplied became mixed with the charge and so adulterated the product. Gas made from ammonium nitrate carefully sieved from these fragments showed a great reduction in carbon monoxide.