

Editorial.

THE REPORT OF THE MEDICAL RESEARCH COUNCIL FOR THE YEAR 1935-1936.

THE Council heard with great pleasure of the award of the Nobel Prize in Medicine for 1936 jointly to Sir Henry Dale, Director of the National Institute for Medical Research, and to Professor Otto Loewi of the University of Graz, in recognition of their work on the nature of the chemical mechanism involved in the transmission of nerve impulses.

In 1914 Sir Henry Dale found acetylcholine in some samples of ergot and its extraordinary potency in stimulating the parasympathetic nerve-endings and its rapid destruction in hydrolysis suggested that it might have physiological importance. Between the years 1921 and 1926 Professor Loewi showed that the vagus probably acted on the heart by first liberating acetylcholine at the nerve-endings. In 1929 Dr. H. W. Dudley found that acetylcholine was a normal constituent of an animal organ. Later, Sir Henry Dale and his colleagues, Dr. Gaddum, Dr. Feldberg and Dr. G. L. Brown showed that acetylcholine is not only the chemical transmitter of vagus impulses to the heart muscle but that the same mechanism is responsible for all parasympathetic nerve activities and also for sweat secretion. In the past year they have established beyond doubt that acetylcholine is the medium through which motor nerve impulses activate voluntary muscle. It seems probable that the transmission of most efferent impulses throughout the peripheral nervous system is dependent at some stage or other on this chemical action.

For some years the Council have advocated research on the clinical aspects of medicine and have assisted in the establishment of senior clinical posts on a whole-time basis. Clinical research in medicine and surgery has been handicapped by the fact that careers in these subjects have been too closely dependent on success in private practice. The Council, therefore, consider that Lord Nuffield's munificent gift of £2,000,000 to the University of Oxford for research and post-graduate teaching in medical science has been an event of outstanding importance and warmly welcome the new proposals.

At Cambridge a department of clinical research has been established under the direction of Dr. T. A. Ryle.

The Council themselves have offered six post-graduate studentships for medical graduates who have held house appointments and are strongly inclined to a career in clinical science or experimental pathology. They have also offered four research fellowships for candidates of similar qualifications who have already had some experience in the use of research methods, and it is expected that in the future post-graduate students will thereafter pass into this senior category. Those who do well while holding these fellow-

ships may be considered for posts in the Council's service and should find themselves well qualified for academic appointments which are becoming available in increasing numbers.

Investigations on influenza have continued during the past year and substantial progress has been made. The critical experiment of transmission of the disease from an infected ferret to a human being has now been made accidentally in the person of Dr. Stuart Harris. Virus originally obtained from a human case, but since passed through 196 ferrets, was used to infect a small batch of ferrets. One of these, when heavily infected, sneezed violently at close range while it was being examined by Dr. Stuart Harris. After forty-five hours he had a typical sharp attack of influenza. Washings from his nasopharynx up to the fourth day were directly infective not only for ferrets but also for mice. Fortunately a specimen of Dr. Stuart Harris's blood-serum, taken before the attack, was available for examination; this was found to contain no demonstrable antibody for the virus of human influenza. There were indications of such antibody quite early in his attack, but on the eighth day, when the symptoms had subsided, it was strongly developed, and still more strongly on the sixteenth and thirty-first day, after which it underwent a slow decline. This experience provided the important link completing the chain of evidence for the identity of the virus, maintained for over two years in ferrets, as the cause of human influenza; it also provided evidence of the connexion between the virus-neutralizing antibody in the blood and resistance to infection.

The possibility of immunizing man against influenza is more hopeful. Dr. Andrewes and Dr. Smith have produced from the virus a vaccine of sufficient potency and purity to be tested as to its immunizing value for the human subject. By successive passages through mice a virus of such potency has been obtained that the filtrate from the lungs of infected mice is able in a dilution of 1:10,000,000 to infect a mouse. It has been found that this virus can be made completely non-infective without appreciable loss of antigenic value by treatment with very weak formaldehyde. It may be noted that the virus in the living state is apparently innocuous when given by hypodermic injection and that it is being used in this way for immunization trials in the United States. By Dr. Elford's method of selective ultra-filtration it has been possible to free the virus from a number of extraneous substances in solution. This purified vaccine causes in the mouse not only the appearance of antibodies in the blood, but also confers a substantial resistance to infection by the respiratory passages. It remains uncertain whether the amount of antibody circulating in the blood as the result of vaccination in the human subject will confer a significant degree of resistance to naturally acquired infection, and if its immediate effect is to produce a definite resistance. It will be necessary to know the duration of the protective action before an assessment can be made of the practical value of the method.

The popular interest in nutrition continues to grow and the Council consider the most significant action which emphasizes the new importance attached to nutrition is the recent announcement that His Majesty's Government is determined to regard the improvement of physical fitness as a fundamental point of policy. At first this policy was largely interpreted by the public from the angle of physical exercise, but discussions in Parliament and in the press have shown that proper nutrition is considered of even greater importance. It is realized that an improperly fed animal cannot profit to any great extent by opportunities of physical exercise. The foundations of good physical development and health are laid down in infancy and childhood and are largely dependent on good feeding.

In a section on "What People in this Country Eat," the Council draw attention to the most recent report by Professor Cathcart and Mrs. Murray which deals with the actual food eaten in St. Andrews, Cardiff, and Reading, in the course of everyday housekeeping. The results of studies of the type of food eaten by a number of Glasgow families, and also by some women students, have been added to those obtained in the other localities. In Current Literature of the June number we have given a précis of the main points in the report. We noted the constancy of the percentage intake of protein and of the calories eaten by people living far apart, and that this is obtained independently of the kind of foodstuff eaten and seems to represent the result of some kind of instinct.

Professor Cathcart and Mrs. Murray calculated that the actual percentage of calories of food lost by the housewife as refuse and waste in St. Andrews was only 2.6 per cent, but whether the same holds throughout the country is doubtful. Ten per cent is the figure usually given.

Few of the diets examined when considered from the standpoint of energy, protein, fat, percentage of first class protein and mineral salts, could be regarded as really poor. As regards the protective foods many of the diets left much to be desired. It was not entirely a question of the money available as it was noticed that some of the poorest people made a better selection of foods than others with larger incomes.

Professor Cathcart and Mrs. Murray lay great stress on the necessity of educating the average housewife on the relative nutritive value of different foodstuffs by personal contact and by demonstrations in which the cooking utensils are those which the housewives have at command at home.

For many years discussions of food have centred round the calorie value of the diet and the figure of 3,000 calories per man assumed the position of an absolute standard. More recently the figure has been raised to 3,400 calories and diets below this value have been regarded with suspicion. Professor Cathcart and Mrs. Murray, however, found that the daily diet of 109 women students, average age 21, contained only 2,035 calories per person and the general physique and health of these women was reported to be very good. The League of Nations Technical Commission on

Nutrition decided that a daily allowance of 2,400 calories is adequate for the needs of an adult, male or female, living in a temperate climate and not engaged in manual work. The figure 2,400 is *net*; the Commission gave no figure for waste.

The Council consider that probably the limiting factor in a large section of the community is food-purchasing power. In any steps to improve the physical fitness of the community both aspects of the problem, the educational and the economic, must therefore be dealt with. Above all, it must be remembered that the feeding problem is of the greatest concern to the young and adolescent.

The chemical composition of British foods, particularly cooked foods, and the losses they undergo during cooking, have been investigated under the direction of Dr. R. A. McCance at King's College Hospital. Before the inception of this work there were very few analyses of cooked foods and throughout particular attention has been paid to the fact that chemical analysis of a food may be misleading as a guide to its nutritional value. This is particularly the case with the carbohydrate, with calcium and phosphorus contained in plants, and with the iron in all foods. Methods have accordingly been devised to distinguish between the fractions of these constituents which are available for nutrition and those which are not.

The investigators have compared the old data with the new, and in the course of the work it has been found that many of the accepted theories about cooking are not supported by experimental evidence. It has been shown that it makes no difference to the losses whether meat is plunged into boiling water at the start or placed in cold water and slowly brought to the boil. Although vegetables lose nutrients rapidly when they are cooked in cold water, they may be soaked and washed in cold water in the raw state without loss.

The authors of the report have applied their own figures to a study of the individual food intakes of men and women of the middle class and have discovered that the iron intake of women is much lower than that of men. The iron requirements of women, particularly during the child-bearing age, are clearly so much greater than those of men that the authors were led to investigate the matter further and have found that many of the so-called normal women of the middle-class are suffering from a mild degree of anæmia.

The Council refer to the three reports on the influence of diet on the development of the teeth by Mrs. Mellanby which they have published. In order to test the conclusions arrived at as the result of Mrs. Mellanby's studies, the Committee of the Council had to be content with a trial over a restricted period on children living in institutions where the diet could be regulated to a more or less standard pattern and to superimpose the factors it was desired to test on different groups of children under observation. The results convincingly supported Mrs. Mellanby's findings on the beneficial effect of vitamin D in inhibiting the initiation and spread of

caries in the teeth. The Council state that according to our present knowledge the most promising method of improving the dreadful situation presented by the dental condition of this country is to increase the intake of those foods which benefit dental structure and resistance, and reduce those which either actively or passively result in the development of defective teeth. This means practically increasing the consumption of milk and other dairy and market-gardening products, and reducing the consumption of bread and other cereals, especially in the earlier years of life.

In their last Annual Report the Council drew attention to the problem of sepsis in childbirth, and particularly to the report by Dr. Dora Colebrook. They now state that any drug that will have a beneficial action on the infection due to hæmolytic streptococci, which until recently killed annually 1,200 women in the full vigour of life, must have great importance. Two papers by Dr. Leonard Colebrook and his colleagues at Queen Charlotte's Hospital, London, suggests that "red prontosil" and "soluble prontosil" have such an effect. The Council consider that more clinical and laboratory tests are necessary before an accurate appraisalment of the situation can be made. An additional reason for delaying judgment is that present experiments promise even better results with the colourless substance para-amido benzene sulphonamide, with which clinical tests are now being made at Queen Charlotte's Hospital.

Before the introduction of the prontosil compounds, from 1931 to 1935, 495 cases of puerperal sepsis entered Queen Charlotte's Hospital; of these 112 died, giving a fatality rate of 22·7 per cent. In part of the year 1936, 64 cases of puerperal sepsis have been treated with "red prontosil" and "prontosil soluble" in the same hospital; of these only 3 have died, giving a fatality rate of 4·7 per cent. Apart from the reduction of mortality, Dr. Colebrook noticed a sudden reduction in the severity of the peritonitis associated with puerperal sepsis in the cases treated with prontosil, also in no case has a patient developed palpable pelvic or abdomino-pelvic mass or abscess after the beginning of treatment, although this used to be the commonest complication of puerperal infections caused by hæmolytic streptococci.

During the year the Council have issued two reports dealing with the subject of deafness. The accurate study of deafness is stated to be a product of the great advances in sound reproduction and recording associated with telephone engineering and broadcasting.

The success obtained in amplifying sound alone has not solved the problem of defective hearing, as might have been hoped. It appears that individual deaf persons vary in the extent to which they are deaf to different pitches of the auditory range. The object of any hearing aid is, therefore, to modify the sound so as to bring it within the range of hearing which the individual retains.

According to Manchester workers the results of testing deaf persons for a series of pure tones by means of the audiometer provided a reliable index of the intelligibility of speech to the deaf listener. Special attention was given by these workers to the type of amplifying apparatus which gave the best results in deafness, and also to the relative merits of teaching groups of children by a class amplifier or by an individual aid for each child. It was decided that the class amplifier has definite advantages over individual aids.

As a result of an experiment with forty-eight deaf children in London Dr. Kerridge has estimated that of the partially deaf, i.e. those who can hear a conversational voice from two to twenty feet away, 97 per cent would benefit greatly by hearing-aids: whereas among deaf children who cannot hear the conversational voice as far as two feet away, 51 per cent would derive considerable aid from sound-magnification instruments.

Certain workers in the cotton industry especially those known as strippers and grinders are particularly susceptible to a disabling chest trouble due to the inhalation of cotton dust. Clinical examination of these workers reveals the presence of bronchitis and emphysema. The death-rate from bronchitis among male cotton strippers between the ages of 20 and 60 is five and a half times greater than that for all occupied and retired males and ten times greater than such dusty occupations as cement workers and lime burners.

Dr. I. C. Bramwell and Dr. R. Ellis examined for the Council many cotton operatives suffering from cardio-respiratory symptoms believed to be due to the inhalation of cotton dust. The results suggested that some form of sensitization played an important part. Subsequently Professor H. B. Maitland and Dr. A. Browne discovered the unsuspected presence of histamine in the cotton dust. Professor Karl Prausnitz, a distinguished investigator in industrial medicine, was appointed by the Council to follow this clue. The work was done in Professor Maitland's department in the University of Manchester with the co-operation of the employers organizations and trade unions concerned. Prausnitz found the most dangerous particles of cotton dust were those under two microns in diameter which in spite of better systems of ventilation still gained access to the workers' lungs. The fatty fraction of the particles was found to be harmless, but the protein fraction contains some toxic factor which is probably responsible for the respiratory trouble. The workers affected by the disease are hypersensitive to the protein of the cotton dust. Although hypersensitivity is an important factor in the disease Professor Prausnitz did not find that de-sensitization held any promise for improving the condition. The crux of the problem is the exclusion of the minute particles of dust, and since present methods of ventilation do not exclude these particles the solution of the problem depends either on the adoption by the workers of suitable respirators or on the application of some new means for collecting the smaller particles before they enter the general air in the room.