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THE LISTER INSTITUTE
OF
PREVENTIVE MEDICINE.

Report of the Governing Body,
1925.

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

May 20th, 1925.

The Lister Institute of Preventive Medicine,

CHELSEA BRIDGE ROAD, LONDON, S.W. 1.
ELSTREE, HERTS; MARAZION, CORNWALL.

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* A recognised Teacher of the University of London.

ANNUAL GENERAL MEETING
OF
The Lister Institute of Preventive Medicine,
May 20th, 1925.

REPORT OF THE GOVERNING BODY.

The Governing Body has the honour to present the Institute's 31st Annual Report.

GOVERNING BODY.

At the last Annual Meeting, the Council re-elected Sir Frederick W. Andrewes, Professor W. Bulloch, and Sir James K. Fowler to represent it until December 31st, 1925.

To the universal regret of his colleagues, Sir Frederick Andrewes has found it necessary to resign his seat on the Board on account of other increasing demands upon his time and energy. The vacancy created by Professor Andrewes' resignation will be filled by the Council at its next meeting.

COUNCIL.

At the last Annual Meeting, the retiring members of Council, Professor A. Harden and Dr. H. de R. Morgan, representatives of the members of the Institute, and Professor W. Somerville, the representative of the Royal Agricultural Society, were re-elected. Professor W. Bulloch was elected to the vacancy occasioned by the death of Professor S. G. Shattock.

The three members who retire from the Council by rotation this year, but who are eligible for re-election, are Sir William Leishman, Professor R. T. Hewlett, and Dr. L. C. Parkes; all three are representatives of the members of the Institute.

A further vacancy has occurred owing to the death of Sir Rickman Godlee, who formerly represented the Royal College of Surgeons, England, and latterly the Members of the Institute upon the Council. Sir Rickman was particularly interested in the work of the Institute, and his relationship to Lord Lister gave to his connection with it a more intimate character than that implied by membership of its Council. The Governing Body feel that, by his death, the Institute has lost a valued councillor and a kind friend.

MEMBERS.

The Governing Body regrets to announce the death during the year of Professor E. Klein, a member since the amalgamation of the Institute with the College of State Medicine in 1893, Dr. Horace T. Brown, who was for some time a member of Council, and the Earl Curzon of Kedleston.

STAFF.

Dr. Muriel Robertson is still absent on sick-leave, but it is hoped that she will be able to resume duty later in the year.

Dr. Bedson has been seconded to work under the Foot and Mouth Disease Committee of the Ministry of Agriculture. Part of the investigation of the Committee is being carried out at the Institute, and will be referred to again later in this Report.

Dr. R. G. White, formerly bacteriologist to the Hygienic Institute, Cairo, was made a temporary member of the staff of the bacteriological department in November last, but resigned in April of this year when he was appointed director of the serum laboratories of the Metropolitan Asylums Board.

Dr. R. Robison and Dr. Ida Smedley MacLean have been recognised by the University of London, as teachers of Biochemistry at the Institute.

Dr. Hunter Brown and Dr. Margaret Boas have held the Jenner Memorial and Grocers' Research Studentships respectively during the year.

RESEARCH WORK.

Before proceeding to review the scientific activities of the various departments of the Institute, the Governing Body desires to again record its appreciation of the support rendered by the Medical Research Council to these activities. During the past year, in addition to furnishing the salaries of the staff of the National Collection of Type Cultures, the Council has provided two whole time workers in the Department of Bacteriology, Dr. Woodcock and Mr. Bruce White, one in the Department of Biochemistry, Dr. Zilva, and five in the Department of Experimental Pathology, Professor Korenchevsky, Miss Hume, Miss Soames, Miss Carr, and Miss Henderson Smith. Their work is carried out under the direction of Professors Ledingham, Harden and Martin respectively, and accommodation for them and the expenses of their researches are supplied by the Institute.

Department of Bacteriology.

Vaccinia and Avian Molluscum. Professor Ledingham has continued his study of the vira of *Vaccinia* and *Avian Molluscum*, with particular reference to their alleged epidermotropic affinities, their immunological relationships and their filterability with a view to cultural experiment. His work, dealing with the experimental histology of rabbit *vaccinia* and avian *molluscum* appeared in December, and the conclusion was reached that, so far as the skin is concerned, the primary point of attack of these vira is the vascular system of the dermis and not as commonly supposed, the Malpighian elements of the epidermis. So far it has been impossible to establish any definite immunological relationships between *vaccinia* and *molluscum* by experiment on the domestic fowl, which is susceptible to both vira, and in this respect his experience coincides with that of Loewenthal, whose work has just appeared. Filtration of emulsions containing *vaccinia* virus through Chamberland and Seitz filters has not once resulted in a potent filtrate—a result in striking contrast to the ease with which the foot and mouth virus passes similar filters. Material from cases of the mild small-pox now prevailing in England is also being investigated.

Bacteriophage action. Dr. Arkwright has continued his work on bacterial variation and the bacteriophage phenomenon and has made use of two additional strains of phage. He has extended his observations on the respective sensitiveness or resistance to the same phage of different variants from the same strain of *B. dysenteriae* or *B. coli*. He has confirmed his previous experiments showing that the activity of a certain phage, is closely related to the "roughness" and the salt agglutinability of the culture of bacteria on which it is acting. The character of roughness is acquired gradually, the earlier variants representing intermediate stages, which may superficially have a near resemblance to either the smooth or the rough form, but in reality, these are graded in their characters. Forms of *B. coli* which have remained apparently purely rough and sensitive to phage for many months, may again yield smooth colonies with lessened sensitiveness and, later, further forms manifesting reversion to all the "smooth" characteristics, and apparently possessing complete resistance to phage. Experiments are being made to test the effect of strongly alkaline and acid culture media as stimulants to variation.

Nutrition and the Inflammatory reaction. Continuing his work with Dr. Zilva, Dr. Arkwright has demonstrated the great difference between the inflammatory reaction produced by irritants, according to whether the animal is well or ill nourished. This difference is most obvious in the case of young growing animals; full-grown guinea-pigs, even after a considerable reduction in weight, still, as a rule, give a medium response to small doses of diphtheria toxin while young animals proportionally reduced, react very much less, and there may be no palpable swelling. Preliminary experiments have been made with rats in order to discover the most suitable substance with which to promote an inflammatory response. The reason for using rats is that these animals can much more readily be fed on diets deficient in different directions. Rats are very resistant to many toxins and irritants, but this initial difficulty appears to have been overcome and the attempt is being made to identify the dietary factors on which a large and oedematous inflammatory reaction depends. Dr. Arkwright has also given a good deal of his time to supervising the work on foot and mouth disease which is being carried out at the Institute and referred to later.

Splenectomy and Experimental Purpura. In continuation of his work on experimental purpura, Dr. Bedson has investigated the effect of splenectomy on this condition. He has shown that removal of the spleen in the guinea-pig produces a rapid and enormous increase in the number of platelets in the circulation. The platelets again fall to normal limits in the course of three to four weeks. Splenectomised guinea-pigs were found to be more resistant to the inoculation of antiplatelet serum than normal animals, but this relative immunity disappeared with the return of the platelet count to the original level. From these experiments he concludes that the spleen plays no essential rôle in the production of purpura, and suggests that splenectomy cannot be relied upon to give permanent relief in the treatment of purpura hæmorrhagica. With Miss M. E. Johnston, he has published a further contribution to the subject of the origin of the blood platelet.

Plague Prophylactic. Dr. Schütze has carried out a series of immunity tests in guinea-pigs with various plague prophylactics, in view of the very considerable demands on the Institute for plague vaccine for use abroad. In the light of work by the late Sydney Rowland, this vaccine during and since the war, has been prepared from cultures of *B. pestis* grown on agar flushed with horse serum, and not, as formerly, from old broth cultures (Haffkine's prophylactic). The strain used at this Institute is always one that has recently been passed through the guinea-pig, and with such a strain Dr. Schütze prepared two types of vaccine for the immunisation of guinea-pigs: (1) by the Institute method, using agar flushed with serum, and (2) using plain agar only. Observations were also made with a sample of Haffkine's vaccine kindly supplied by the Parel laboratory, Bombay. After immunisation, the guinea-pigs in each series were inoculated with a dose of *B. pestis*, which killed 100% of control animals. The highest survival percentage (44%) was given by the agar-serum vaccine, Haffkine's prophylactic yielding only a 14% survival rate. A further series of immunisation tests is now being carried out on rats.

Experimental tuberculosis and diet. Dr. Schütze has, in collaboration with Dr. Zilva, investigated the effect of diet on the development of tuberculosis in rats. After intraperitoneal inoculation, tuberculosis of the omentum develops in a large proportion of the rats fed on a basal diet containing sufficient vitamin A (supplied by cod liver oil) for growth purposes. When the diet contains an excess of this factor, tuberculosis of the omentum is found in a much smaller percentage of the inoculated animals. The effect of including chaulmoograte in the dietary of infected rats is also under investigation.

Meningococcus and Gonococcus. Dr. Atkin has been following up the work he published last year, showing that the different types of *meningococci* had characteristic cultural appearances on certain nutritive media, when the colonies were given the opportunity to grow extensively by using a greater depth of medium. The closely allied organism, *gonococcus*, has been examined, and evidence of change from one serological type to another has been obtained. This organism has been found to be very susceptible to alterations in its environment. By keeping a fresh strain from an acute case of gonorrhoeal urethritis on a medium which is too alkaline for its optimum growth to take place, its serological affinity was modified. While it was originally agglutinated by its own homologous serum and by sera made from fresh strains from acute cases, it gradually changed to a variety which was no longer agglutinated by its original homologous serum, but only by a serum prepared from strains which had long been cultivated on the alkaline medium. Simultaneously, a change occurred in its cultural characters. Instead of forming a thin, energetically-growing translucent colony with papillae dotted about its surface, it grew as a dense yellowish colony with a smooth surface free from papillae. The *gonococcus* seems to be subject to similar changes in the human body when it is living in unsuitable sites, e.g., the vagina. If this change in type is fully substantiated, it will throw light on the problem of the origin of bacterial types within the species. Such types have hitherto been regarded, for practical purposes, as immutable.

Corynebacteria. Pathogenicity for rats and mice. Mrs. Barratt has published in detail her work on the biochemical and other characters of virulent and non-virulent diphtheria bacilli from the human throat and of the diphtheroids other than *C. diphtheriae* which may be found in this situation. Comparatively little is known of the pathogenicity of members of the genus *Corynebacterium* for laboratory animals other than the guinea-pig, and Mrs. Barratt has turned her attention to this important subject. The organisms chiefly used have been of animal origin, *C. pseudotuberculosis ovis*, *C. pseudotuberculosis murium*, and a species of *corynebacterium* obtained from the heart-blood of two rats dying in the course of a dietetic experiment. This latter strain resembles *C. pseudotuberculosis murium* morphologically, culturally and biochemically. With these strains it has been found easier to produce acute illness and death of the animals rather than the more chronic lesions met with in natural infections. The acute illness and death produced in the rat by intraperitoneal inoculation of *C. pseud. ovis* and the rat diphtheroid referred to, and in the mouse by both rat and mouse strains, is of considerable interest as it is in marked contrast to the comparative immunity of these animals to *C. diphtheriae* and diphtheroids of human origin, even when the latter possess the same biochemical characters as the animal strains. Intracutaneous inoculation has also revealed important differences between diphtheroids of human and animal sources.

Pasteurisation of milk and B. tuberculosis. Dr. R. G. White, late of the Hygienic Institute, Cairo, has undertaken, on behalf of the department, a study of the effect of pasteurisation on tubercle bacilli that may be contained in milk. The need for some further enquiry into this aspect of pasteurisation has arisen from the fact that, in this country at least, reflections have been cast not only on the capacity of commercial pasteurising plants to destroy tubercle bacilli in milk, but also on the available laboratory data dealing with this subject. There appeared to be still room for an ampler laboratory enquiry in which the official constants of pasteurisation (62.5° C. for 30 min.), were adhered to, while the numbers of tubercle bacilli exposed to the pasteurisation varied over a wide range. Experiments have been conducted with milk artificially infected with a culture of bacilli, with naturally-infected milk from cows with tuberculous udders, and with milk to which material from tuberculous glands from infected guinea-pigs had been added.

Physiological reaction to the intravenous injection of Colloids. Miss D. B. Steabben has, during the second year of her Beit Fellowship, continued her studies on this subject. In the first group of experi-

ments which had special reference to the action of colloidal substances on blood elements and antibody content, it was found that all the colloids employed, both metallic and organic sols, when injected into normal rabbits, caused reactions similar in type but varying with the nature of the colloid used. This reaction—a leucopenia followed by a leucocytosis, a rise of temperature and an increase, followed by a decrease, in the concentration of the red cells, with a return to normal in about 24 hours, suggests that an increased activity of the vascular system and an acceleration of the metabolic rate, form the primary defensive response of the animal organism. The reputed therapeutic value of colloidal injections may perhaps be associated with this stimulation of the normal body processes. This effect was shown in later experiments, in which a higher agglutinin titre was developed when colloid and antigen were injected simultaneously than when antigen was injected alone. An injection of colloidal substance alone did not cause an increase in a stationary agglutinin titre. Further experiments have shown that the blood changes produced by colloidal substances in infected animals are similar to those occurring in normal animals, and work is in progress to determine what effect, if any, such colloidal substances have upon the course of infection.

Food-poisoning micro-organisms and their antigenic constitution. Mr. P. Bruce White, a grantee of the Medical Research Council, has at the request of the Council, been given facilities for research at the Institute. He commenced work in September, 1924. Since that date he has been able to complete his studies on the antigenic constitution of the bacteria of the Salmonella group. These will shortly be published in the form of a supplement to the M.R.C., Special Report Series, No. 91. He is now engaged upon a study of the late lactose-fermenting "dysentery" bacilli, sometimes responsible for outbreaks of food-poisoning.

B. typhosus and B. enteritidis. Dr. A. N. Goyle has continued his work with rough and smooth variants of *B. typhosus* and *B. enteritidis* and has shown that the "R" forms of these bacteria are closely interrelated serologically as regards their "O" or heat-stable antigens. In extension of his former work showing that the "R" forms of these bacteria have lost their "O," or normal heat-stable antigen, but retained the normal "H," or heat-labile antigen, he has demonstrated that the rough forms have in addition acquired a fresh heat-stable antigen, unlike that found in the smooth or normal form. This new heat-stable antigen which is peculiar to the "R" form is serologically identical in the two species *B. typhosus* and *B. enteritidis*. In addition to this relationship some strains appear to have identical heat-stable antigens in the "S" form. The outcome of this work explains the old observation that certain strains of *B. typhosus* and *B. enteritidis* cross-agglutinate and gives a more detailed analysis of the phenomenon, with a suggestion as to how these facts may be explained on a theory of multiple antigens. Dr. Goyle's recent work has been incorporated in a thesis for the degree of Ph.D. in Bacteriology, in the University of London, and will later be published independently, apart from that portion which has already appeared in collaboration with Dr. Arkwright.

Encephalitis and Microsporidia. Dr. H. M. Woodcock has, with the aid of a grant from the Medical Research Council, commenced a study of the peculiar spore-like bodies which have been found in association with spontaneous encephalitic lesions in rabbits, and which have been placed by some authorities in the family of Microsporidia. The occasional occurrence of such lesions in rabbits employed for transmission experiments in connexion with encephalitis lethargica and other neurotropic virus has led to considerable confusion, and careful investigation of the matter is imperative. Already these "microsporidia" have been found in one of three normal rabbits from the Institute stock. For comparison, material has been secured from angler fish suffering from "microsporidiosis" of the central nervous system. A supply of these fish has been arranged.

The living micro-organism as immunising agent. Major McGillivray (late I.M.S.), before his departure in June, 1924, to take up the duties of Bacteriologist to the Board of Health, Western Australia, was able to complete an interesting experiment showing very clearly that in guinea-pigs the most effective prophylactic agent against highly virulent hog cholera bacilli, administered intraperitoneally, is the living organism introduced subcutaneously. The killed organism had no protective power whatever, but a limited form of protection was afforded by an attenuated living member of the allied paratyphoid group. The experimental result is in keeping with previous work carried out at this Institute by Pratt-Johnson, and supports the old Pasteurian view that, in animals at least, the attenuated live virus yields the surest prophylaxis against highly virulent infections.

Immunisation by the cutaneous route. Dr. A. Hunter Brown (Jenner Memorial Research Student), was owing to ill-health unable to bring work on this subject to a conclusion. His experiments were concerned mainly with the production of staphylococcal lesions in the skin of the guinea-pig and the effect thereon of previous immunisation of skin surface. So far as they went, they lent little or no support to the claim that the application to the skin of guinea-pigs, of poultices containing staphylococcal filtrates, produced a general immunity of skin to staphylococci introduced intradermally.

Tuberculin effects in the tuberculous guinea-pig. Dr. S. Andrews (Musgrave Research Student, Queen's Univ., Belfast), has commenced an investigation of so-called tuberculin "shock" as manifested

by tuberculous guinea-pigs following a dose of tuberculin, with special reference to the influence of antituberculous serum thereon.

Streptococcal toxin and Scarlet Fever. Dr. C. Ionescu-Mihaesti (Roumania), Rockefeller Foundation Fellow, has undertaken an investigation of scarlatinal streptococci, and strains from other sources, with a view to studying the question of toxin production and the demonstration of that toxin by other methods than inoculation into human beings—the only method so far available.

Effect of radiations on immunity. Dr. D. Combesco (Roumania), Rockefeller Foundation Fellow, is investigating the "bactericidal" action of whole blood on certain micro-organisms with special reference to the increase of lethal power which has been stated to occur after exposure to radiations. He also proposes to study the factors which, singly or jointly, account for the disappearance of organisms added to whole blood *in vitro* and incubated.

Antigenic constitution of vibrios. Dr. J. G. Balteanu (Roumania), Rockefeller Foundation Fellow, is investigating the antigenic constitution of the cholera vibrio and allied vibrios, pathogenic and non-pathogenic, with a view to elucidating the inter-relationships and phylogeny of closely related species.

The hospitality of the department has also been extended to various workers, including Dr. E. F. Knight and Dr. Mohammed (Cairo).

Department of Biochemistry.

Alcoholic Fermentation. The discovery by Harden and Robison that, in addition to a hexosediphosphate, a hexosemonophosphate is formed by yeast preparations from mineral phosphates and sugar, has rendered it necessary to re-investigate the reaction by quantitative methods, in order to ascertain how far the equation previously proposed by Harden and Young requires modification. This is being done by Professor Harden and Mr. Henley, but the results are not yet ready for publication. Other questions relating to the intimate processes of fermentation by dehydrated yeast preparations, which have an important bearing on the condition in which the enzyme in living yeast and in yeast preparations exists, are being studied by Professor Harden.

Chemical constitution of Hexosemonophosphate and Hexosediphosphate. Experiments on this subject are being made by Professor Harden and Dr. Robison, the plan being to convert these compounds into methylglucosides and then from these to prepare methylated derivatives, eliminate the phosphoric acid groups, and examine the resulting methylated sugars.

Synthesis of fat and carbohydrate by vegetable organisms. Fat is readily formed from carbohydrates in the animal body and by vegetables, but the transformation has never been effected in the laboratory. It still remains a biochemical mystery. Dr. Smedley MacLean has addressed herself to this problem for some years. Latterly, with the assistance of Miss Hoffer, she has been studying the conditions under which fat is formed from carbohydrates in yeast, as it is likely that the chemical mechanism involved is essentially similar in this unicellular plant and in the animal cell. The addition of phosphates to a medium containing only glucose or fructose produces a marked increase in the fat content of yeast incubated in it. In both cases the medium was oxygenated throughout the period of incubation. The addition of alkali phosphates to the fructose solution doubles the fat content of the yeast incubated in it; with a solution of glucose the addition of phosphate produces an increase which may be as big, but is not so regular. These results suggest that the first stage in the change from carbohydrate to fat consists in the formation of a hexosephosphate compound and that a subsequent stage is the oxidation of this substance.

Another side of the same problem is being attacked by Mr. Naganishi (Japan), who is investigating the enzymic production of polysaccharides by yeast preparations, with the special object of ascertaining whether phosphates play a fundamental part in such changes. No definite evidence of the intervention of phosphate has so far been obtained.

The Phosphoric esters which occur in blood and other animal tissues, and the enzymes (phosphoric-esterases) by which they are synthesised and hydrolysed in the body. This has formed the subject of an extended investigation by Dr. Robison along with a number of colleagues. With Dr. M. Martland, he has shown, by examining cartilages and bones of human foetuses and infants, that the enzyme which hydrolyses hexosemonophosphate is not present in any cartilage prior to the appearance of a centre of ossification, but is found wherever active ossification is taking place. The conclusion is drawn that the production of this enzyme forms part of those cellular activities which lead to the formation of bone.

The same enzyme has been previously shown by Dr. Robison to occur in equally high degree in the small intestine and the kidney, where its function cannot be concerned with calcification. In the intestine, it may be required to effect the hydrolysis of phosphoric esters present in foodstuffs, but it is not clear why it should be present in the kidney. The significance of the enzyme in cells of the kidney is being investigated by Dr. Eichholtz and Dr. Robison in Professor Starling's laboratory at University College. Their experiments are not yet completed, but the results, as far as they go, indicate that the phosphoric esters present in the blood are hydrolysed in the kidney, and inorganic phosphates secreted

into the urine. This discovery has disclosed a hitherto unsuspected mechanism for excreting phosphates into the urine without interfering with the concentration of inorganic phosphates in the blood.

Considerable progress has been made towards the identification of the individual esters present in blood. Two different compounds have been isolated, although neither as yet in pure condition. One of these exhibits the general properties of a hexosemonophosphoric ester, and is completely hydrolysed by the bone enzyme. A preliminary note of these results has been published in conjunction with Mr. H. W. Goodwin, who was associated with the earlier stages of the work. The further investigation and purification of these compounds is being actively prosecuted.

Variations in the amounts of these esters in the blood of normal and rachitic animals have been studied by Dr. Robison and Miss K. M. Soames, who have also investigated the effect of injecting phosphoric esters into rats fed on a rickets-producing diet. From these experiments, and from the chemical analyses of the bones of the experimental animals, they conclude that the defective calcification which results from a lack of anti-rachitic vitamin in a diet containing a sufficiency of calcium and phosphates, is not due to any deficiency of inorganic phosphate, or of the specific phosphoric ester in the blood, or of the enzyme in the bone by which this ester is hydrolysed. With the co-operation of Dr. L. Wills, of the Infants' Hospital, Vincent Square, London, the investigation is now being extended to the blood of normal and rachitic children.

In collaboration with Dr. F. S. Hansman and Dr. M. Martland, the phosphoric esterase of blood has been shown to affect the hydrolysis of the second phosphoric ester, which is not attacked by the bone enzyme. Hydrolysis occurs whenever blood is laked, or in whole blood which has been very slightly acidified. On the other hand, when the blood is made alkaline, synthesis of phosphoric ester occurs. The variation in reaction which determines whether synthesis or hydrolysis occurs is small. Dr. Martland has found that *in vitro* at a p_H above 7.35, synthesis predominates, while at a p_H below 7.30, hydrolysis is the more rapid. Similarly, hydrolysis or synthesis appears to result from acidosis or alkalosis in the living body.

Vitamins.—The Antiscorbutic Vitamin. Professor Harden and Dr. Zilva are investigating the source of the antiscorbutic vitamin formed during the germination of seeds.

Dr. Zilva has continued his studies on the chemical properties of the antiscorbutic factor. He has found that this principle can be concentrated, from various sources, by the same reagents as he previously found effective with lemon juice. He has studied in some detail the chemical nature of the ultimate concentrated fraction which he has obtained from lemon juice. Dr. Zilva has also been superintending the preparation of large quantities of lemon juice for the stores of the *Discovery* whaling expedition. The various observations made by him on the stabilisation of the antiscorbutic factor are being put into practice, and the results obtained by the use of this juice will be awaited with interest. With Dr. E. H. Lepper, Dr. Zilva has been studying the blood sugar of guinea-pigs in various stages of scurvy, in order to find out whether Palladin's statement that a hyperglycemia and a hypoglycemia occur in the early and later stages, respectively, of scurvy in guinea-pigs.

Fat soluble Vitamins. Dr. Zilva and Miss Soames along with Professor J. C. Drummond, of University College, Captain J. Golding, and Mr. J. Mackintosh, of the National Institute for Dairy Research, Reading, are investigating the relative antirachitic and growth-promoting properties of butter produced by cows fed on diets supplemented by green fodder, ensilage, and cod liver oil.

Diet and resistance to infection. Dr. Schütze and Dr. Zilva have continued to investigate the influence of the state of nutrition of animals upon their resistance to infection by various strains of tubercle bacilli. The effect of an inadequate and excessive supply of fat soluble vitamins is being more particularly studied. Rats are being used for the experiment. Tuberculosis develops slowly in these animals and large numbers of experiments will have to be performed before conclusions can be drawn. The results, so far obtained, afford some justification for the generalised belief that cod liver oil is useful in the treatment of tuberculosis.

Dr. Zilva has also co-operated with Dr. Arkwright in a study of the effect of the nutritive state of the animal upon the local inflammatory response to bacterial toxins and other irritants. This research is referred to in some detail above in the account given of the scientific activities of the department of bacteriology.

Experiments upon the value of Chaulmoogra Oil in the treatment of tuberculosis. The benefit ascribed to chaulmoogra oil, its soaps or ethyl esters, in the treatment of leprosy, has led to the recommendation of similar compounds as a remedy in tuberculosis. Drs. Schütze and Zilva find that soaps of chaulmoogra oil, although they have a very decided bactericidal action on the tubercle bacillus *in vitro*, do not perceptibly impede the development of the bacillus *in vivo*.

Influence of Fats on digestion. Miss M. Maughan has carried out an investigation on the effect of fats on the rate of tryptic digestion *in vitro*. An adequate method has been worked out and the final experiments are now being made.

The hospitality of the department has also been extended to Mrs. Balfour, Professor H. Katqui, and Professor R. J. Manning.

Department of Experimental Pathology.

The Respective Influences of Temperature and Moisture upon the Survival of the Indian Rat Flea (X. cheopsis). Observations on the above subject were commenced some years ago by Mr. Bacot and Dr. Martin; they have recently been completed and published. The object of the enquiry was to see whether certain climatological features of epidemics of plague in India could be explained by the influence of combinations of temperature on the one hand and drying capacity of the air on the other. In the experiments, temperature was kept constant and saturation deficiency varied and *vice versa*, by surrounding the insects with air in equilibrium with appropriate mixtures of sulphuric acid and water at the desired temperatures.

When the temperature was constant, the survival of the fleas was found to be inversely proportional to the saturation deficiency of the air; when the saturation deficiency was constant their length of life was about halved by each 10°C. rise in temperature.

A range of temperature and saturation deficiency such as occurs in Northern India might, therefore, vary the longevity of wandering fleas 30 to 1. A difference of this magnitude in the time available to a plague-infected flea to find a new host would, it is concluded, determine the maintenance or subsidence of an epidemic.

Influence of Sexual Glands upon Metabolism. Eunuchs and castrated animals are less active and generally tend to the deposition of fat, suggesting that the sexual glands exert a profound influence upon metabolism, in addition to their specific action upon the growth and development of secondary sexual characters. Professor Korenchevsky has completed and published the results of his first series of experiments concerning the influence of castration upon nitrogen and gaseous metabolism. He finds that about 60% of castrated animals increase in weight, but the remaining 40% do not. There is a corresponding decrease in the nitrogen and gaseous metabolism of the former group of castrated animals, whereas, in the latter group of "thin" castrated animals this effect was usually less pronounced or even absent. As an explanation of the different results of castration upon metabolism, Professor Korenchevsky has suggested that the sexual glands influence metabolism, not directly, but indirectly, owing to secondary changes produced by castration in the thyroid, hypophysis, adrenals or pancreas. Further experiments, performed jointly with Miss Carr, have shown that subcutaneous injections of an emulsion of prostate, or of both prostate and testis, increased the nitrogen metabolism of rabbits about 10%, whereas those of kidney or of testis alone, slightly decrease it. These experiments suggest the existence of an inner secretion from the prostate by means of which the nitrogen metabolism is influenced. The increase in nitrogen metabolism following injection of extract of prostate is a new fact discovered by Professor Korenchevsky. Whether it acts directly upon the cells of the body or indirectly influences the activity of some other endocrine gland is being investigated. The failure to increase nitrogen metabolism by injections of testis emulsion was unexpected. Possibly this gland contains principles which influence nitrogen metabolism in contrary directions. Enquiry into this is being pursued by observing the action of extracts of testis obtained by different methods.

Effect of Diet and Management of a Cow upon the Vitamin Content of Her Milk. Dr. Ethel M. Luce (Beit Memorial Fellow) has been awarded a Rockefeller Research Fellowship and is now working in the Department of Pediatrics in Yale University. The investigation on the effect of diet and management of the cow upon the vitamin content of her milk, begun in 1922, was continued until the date of her departure. The same cow was employed throughout the study. It was maintained under carefully controlled conditions at the Serum department, under the supervision of Dr. MacConkey. Previous results had shown conclusively the high growth-promoting and anti-rachitic value of summer, pasture-fed milk, as compared with that produced on dry fodder and under the conditions of stall-feeding. The latter part of the investigation was arranged to study the effect of diet apart from light, and the results obtained indicate that, while the diet of the cow is the principal factor determining both the growth-promoting and anti-rachitic value of her milk, the amount of light impinging upon the cow has a subsidiary effect in determining its anti-rachitic value.

In view of the importance of the subject it was decided to continue the research with a modified technique and to keep the animal for longer periods under the different conditions. It was hoped in this way to obtain more decisive results upon the separate rôle played by light and diet. This is being done by Dr. Harriette Chick with the assistance of Miss H. M. Rosecoe, B.Sc. Dr. MacConkey is giving valuable support to the enquiry by undertaking the management of the cow and supervising the collection of the samples of milk.

The effect upon the anti-rachitic value of the milk of administering cod liver oil directly to milch cows during the winter has also been investigated by Dr. Chick. The work has been carried out with the collaboration of Drs. Wagner and Wimberger (assistants physicians at the University Kinderklinik, Vienna). Professor v. Pirquet supported the investigation by lending the dairy upon his estate for the purpose of the research. The cows were given 100 to 200 cc. of cod liver oil daily for several months. Samples of the milk were charged with CO₂, pasteurised and conveyed to London, and the anti-rachitic value assayed in the department. The same milk was given to children suffering from rickets in Professor

Pirquet's clinic. Contrary to expectation, only an insignificant increase in anti-rachitic value was discovered by animal experiments, and the children suffering from rickets failed to improve in the absence of other specific treatment.

In conjunction with Dr. Zilva, of the Biochemical Department, Miss Soames is studying the relative growth-promoting and anti-rachitic potency of butter from pasture-fed and from stall-fed cows when their diet is supplemented with green food, ensilage and cod liver oil respectively. The enquiry is being carried out on eight cows at the National Institute for Research in Dairying, Reading, with the co-operation of Capt. Golding and Mr. Mackintosh, who are responsible for the management of the animals and the milk analyses.

The Phosphoric Esterase of Ossifying Cartilage. Miss Soames has collaborated with Dr. Robison in a study of the distribution and biological significance of the enzyme discovered by the latter two years ago. Miss Soames has been responsible more particularly for the histology and animal experimentation involved in the research. Arising out of this work, a further investigation has been carried out on the variation in the total and relative amounts of inorganic phosphates and different forms of organic phosphates in the blood of normal and rachitic animals. The investigation is also being extended to the study of the blood of rachitic children before, during, and at the completion of different forms of curative treatment.

Effect of Injection of Glycerophosphates on Calcification. Professor Korenchevsky's experiments on the effects upon the skeleton of rats, of subcutaneous injection of calcium glycerophosphate, sodium glycerophosphate, and sodium diacid phosphate, referred to in the previous report, have been finished. They showed that subcutaneous injections of calcium glycerophosphate and also to a lesser extent, those of sodium glycerophosphate, produced an increase in the calcification of the skeleton of rats kept on a diet deficient in fat soluble factor. Sodium diacid phosphate did not produce the same effect.

The Active Fraction of Cod Liver Oil. It has been shown by Steenbock and Boutwell, and also by Drummond, that the active principle of cod liver oil resides in the non-saponifiable fraction. Professor Drummond, at University College, is endeavouring to effect a further purification of the anti-rachitic vitamin. After removal of the soaps, the bulk of the cholesterol is separated, and the residue fractionated by distillation *in vacuo*. Miss Soames has undertaken the biological assay of the different fractions.

Antirachitic Vitamin in Green Leaves. Miss M. A. Boas (Beit Memorial Fellow), using the method previously published by her for studying the Ca and P metabolism of young growing rats, has been able to demonstrate the capacity of spinach to increase Ca and P retention when these are added to diet deprived of fat soluble vitamins. This property has been denied to green leaves by several American observers, but the methods they employed to ascertain the presence of anti-rachitic vitamins were too severe to detect the not inconsiderable amounts present. This research was submitted by Miss Boas as a Thesis for the Ph. D. degree of the University of London, and the degree granted.

Dr. Harriette Chick is also engaged upon a study of the amount of Vitamin A and antirachitic vitamin in green leaves. She is endeavouring to ascertain to what extent plants are dependent upon sunlight for the manufacture of these two vitamins respectively. The first question has practical importance connected with the feeding of cattle destined to provide food in the form of meat and milk. The second has a wide scientific significance in regard to the origin of fat soluble vitamins in nature.

Fat Soluble Vitamins in Brewers' Yeast. Dr. Luce, in collaboration with Dr. Ida Smedley MacLean has determined the vitamin content of the fat contained in brewers' yeast. Fat from yeast was found to restore growth in rats whose weight had become stationary upon a diet deficient in fat soluble vitamins, and also to induce an improved calcification of their bones. This fat is synthesised by the yeast during its growth and multiplication in the brewers' vat. Whether the fat soluble vitamins are manufactured by the yeast plant in the nearly total absence of light, or derived from the malt used, is not clear.

Action of Fat-soluble Vitamins when Introduced Parenterally. It has been denied that the fat-soluble vitamins of cod liver oil produce their beneficial effect when injected subcutaneously. If this is true, it would localise their action, in the first instance, to the alimentary canal. Accordingly, their availability when introduced under the skin or intraperitoneally has been re-examined by Miss Soames. Absorption of the oil is slow and imperfect in either situation, and presumably but a small fraction of the fat-soluble vitamins introduced, is brought into circulation. The animals on a deficient diet showed, however, increased growth and calcification, but in neither case equal to that produced by cod liver oil when taken by the mouth.

Improvements in Technique for the Biological Assay of Fat-soluble Vitamins. The usual method ignores the reserves of vitamins which may be present in the young animal at the beginning of the observation. It has been shown by work from these laboratories that these reserves vary greatly according to the diet of the mother during pregnancy and lactation, and in recent years the breeding stock has been fed upon a uniformly constituted diet. Nevertheless, the response of the young animals, when placed upon a deficient diet, has been sufficiently irregular to compromise experiments to which much labour had been devoted. The discrepancy is associated with the season and appears to be due to

the fact that the milk and other foodstuffs supplied to the mothers vary as regards vitamin content at different times of the year. Acting on this assumption it has been possible to produce litters which have behaved with greater uniformity.

The evaluation of anti-rachitic properties in foodstuffs presents problems of especial difficulty. The rat, being naturally somewhat insusceptible to rickets, is a less suitable animal for experimental work in this subject than puppies, pigs or monkeys, but possesses great advantages on grounds of convenience. Hitherto, it has been found necessary to reduce abnormally the mineral constituents, in addition to the specific fat soluble vitamin, in the diet of rats in order to induce rickets with certainty. Using this diet, the test for antirachitic properties in foodstuffs given as a supplement, is a very severe one and substances possessing the property in moderate or slight degree, escape detection. Dr. Chick is attempting to discover conditions under which young rats may be rendered susceptible to rickets without being deprived of calcium or phosphorus. This attempt, if successful, will also be a step forward in the study of the mechanism by which fat soluble vitamins influence Ca and P metabolism. The complications introduced by depriving the animals of these elements has hitherto hindered the study of this problem with the use of rats.

Inter-relation of Vitamins and Ultra-violet Radiations. Miss E. H. Hume and Miss H. H. Smith have continued their researches on the influence of ultra-violet radiations upon the growth of, and calcification of, bone in rats maintained on deficient diets. From their earlier observations they were inclined to attribute the beneficial effects from irradiating their immediate environment with ultra-violet light, to ionization of the air. This conclusion has been shown by Miss Hume and others to be unjustified. The mistake arose from neglecting to take into account the sawdust in the glass jars on which the animals were bedded. Irradiated pine sawdust appears to be the active agent in producing the effect they had discovered. How the sawdust operates has been the subject of lengthy investigation and is not yet settled. The experiments have been directed to ascertain whether it is due to an emanation, or a secondary radiation from the sawdust, or whether it is necessary for the animals to eat it.

Dr. Lucas, who joined the department recently as a voluntary worker, is materially assisting the enquiry by studying the secondary radiations emitted by various substances after exposure to ultra-violet light.

Meantime the discovery has been made by Steenbock at the Wisconsin Agricultural Station, that lard and olive oil, which are usually devoid of fat-soluble vitamins, acquire the properties of promoting growth and calcification, after exposure, in a thin layer, to ultra-violet light. Steenbock's observations have been confirmed by Hess and by Miss Hume, and found to apply to other fat and lipoid-containing food stuffs. They constitute an important advance towards the understanding of the origin and ultimately of the nature of the antirachitic vitamin. They also illuminate the mystery that healing of a rickety child may follow either eating cod liver oil or exposure to sunlight.

The discovery of Steenbock permits a rational interpretation of this hitherto mysterious power of light, to complement a qualitative deficiency in food supply. As light of high refrangibility activates, by photodynamic action, some constituent of a crude fat which is otherwise inert, it is not unreasonable to suppose that activation can take place, either before the fat is eaten, or whilst it is circulating in the superficial capillaries of skin which are exposed to sunlight.

The Influence of Drying upon the Nutritive Properties of Egg-White. In the course of some of her metabolism experiments Miss Boas has discovered, incidentally, that whereas fresh egg-white satisfies the protein requirements of young rats, it no longer does so after drying at a temperature of 37°C. Animals fed upon a diet in which dried egg-white provides the exclusive source of nitrogen, suffer, after a few weeks, from a curious and definite train of symptoms and ultimately die, unless some other form of protein is given to them. The first symptom noticed is a diminution in the rate of growth. This is soon followed by cessation of growth and shedding of the hair. Subsequently all epidermal structures are desquamated, the animal becoming completely bald. Before this has occurred the gait of the animal is observed to become spastic and incoordinate. No untoward effects follow feeding with egg-white which has been boiled previously to drying. The nature of the change which renders dried egg-white unsuitable as an exclusive source of nitrogen for the growing animal is being investigated. Dried egg-white is largely used by confectioners and the observations show how dangerous it is to tinker with food without ascertaining by trial what the effect may be.

Coagulation of Blood. Dr. Barratt has continued his work on this subject. The particular aspect which has occupied his attention during the year under review is the nature of the action of the anti-coagulants, hirudin or leech extract and peptone. Dr. Barratt's researches do not readily lend themselves to concise summary and will be embodied in a series of papers which are at present being prepared for publication. The first of these is of an introductory character and deals with the mathematics of the type of curve which would obtain and the limiting values met with, on the supposition that the ratio of free thrombin to total thrombin is determined (1) by hydrolytic dissociation of the complex formed between thrombin and the anti-coagulant, (2) by adsorption. The methods which have been found most useful in the determination of the constants to the curves are also discussed. In the succeeding communications the question whether hirudin and peptone influence coagulation *in vitro* by acting upon

fibrinogen or thrombin, or both, is dealt with, and the results of experiments designed to throw light upon the essential nature of the action of these anti-coagulants are given.

The general result is to show that the action of anti-coagulants is upon thrombin and that fibrinogen does not take part in the inhibiting reaction and that the constant to the curves expressing the ratio of free thrombin to total thrombin under varying conditions is not such as would be obtained if the process were one of adsorption, but is consistent with the interpretation that a chemical union occurs which is subject to a considerable measure of hydrolytic dissociation.

A micro-method for titrating the alkali reserve of the blood serum. Dr. E. H. Lepper and Dr. Martin have improved the method devised by the latter during the war, for use under conditions where the means of carrying out van Slyke's gasometric measurement were not available. The shortcomings of the indicator in the original method have been obviated and it is capable of giving results which agree with the gasometric within a small margin of error. As it only requires 0.25 cc. of serum, it is suitable for work with small animals and does not necessitate venesection in clinical use.

The reaction and alkali reserve of the blood in Scurvy. Using the method referred to above, Dr. Lepper and Dr. Zilva have completed their observations on the alkali reserve of the blood in scurvy. They have at the same time determined the p_H of the blood by the method of Dale and Evans. They find that the blood of guinea-pigs, which were the animals used in their experiments, is normally subject to greater variations in both p_H and alkali reserve than are met with in man. The observations have afforded no indication that increased hydrogen ion concentration or diminished alkali reserve plays an essential part in this disease. Animals on a scorbutic diet develop scurvy notwithstanding that the alkali reserve of their blood be maintained in excess of normal by adding sodium citrate to their diet. They are cured by Zilva's concentrated antiscorbutic. This contains no alkali or alkaline salts of organic acids.

The Salt-error in the indicator method of determining Hydrogen ion concentration. Coloured indicators are now generally employed for estimating the hydrogen ion concentration of biological fluids. The method is a valuable one, but it has been known for some time that the presence of electrolytes exercises a disturbing influence. Dr. Lepper and Dr. Martin have determined the discrepancy between the electrometric and colorimetric estimation of the hydrogen ion concentration for some commonly used indicators over a range of .001 to 1 normal NaCl. This was undertaken because the information was necessary for some experiments they had in view, but it will be of service to other workers.

The specific dynamic action of proteins and carbohydrates. Miss Hindmarsh, B.Sc., was obliged to return to Australia before the completion of her work on this subject. The experiments she was able to do, after she had mastered the technique of metabolism work, show that the increase in metabolism from protein ingestion runs closely parallel to increase in blood urea, but the rise and fall in the latter curve is about one hour later than the former. The increased metabolism from carbohydrate absorption is closely associated in time with increased blood sugar, metabolism and blood sugar rising and falling together.

The Central Nervous Mechanism of Respiration. Dr. T. Lumsden has completed his study of the respiratory centres by investigating chelonian breathing. He found that in the tortoise the mechanism was less complex than in the higher animals and formed an intermediate stage between amphibian and mammalian respiration. The highest (pneumotaxic) regulating centre was absent and breathing consisted of a series of inspiratory pauses (apnoeuses) of very variable duration, sometimes lasting for hours. A similar variety of breathing is found in many reptiles and in aquatic mammals, such as the whale and sea-lion.

Tissue Culture. Dr. Lumsden has found that the experience of previous workers that serum had an inhibitory effect on the growth of tissues *in vitro*, was due to the serum having been allowed to become too alkaline, by losing its CO_2 from exposure to the air. If this is prevented, or if the appropriate amount of CO_2 is replaced by exposing the serum to expired air, both normal tissues and tumour cells can be cultivated in serum alone. It appears to be a matter of indifference whether the serum is from the same species as the cells cultivated or not. The use of serum considerably simplifies the technique of tissue culture and renders the method more readily available for use in studying various morphological and bacteriological problems.

Cancer Research. Dr. Lumsden, using the method of tissue culture in pure serum referred to above, has shown that by repeatedly inoculating the cancer of mice or rats into animals of another species, antibodies more or less specific to the cancer cells can be produced. An antiserum produced in this way has been used as a medium for the cultivation of normal tissues and the homologous cancer cells. In it the normal tissue cells survive and grow for many days, while fragments of the cancer with which the antiserum was produced, placed alongside them in the same culture cell, are rapidly killed. This discovery is being exploited to ascertain whether an antiserum prepared as above will modify the growth of its homologous tumour in the living animal.

Standardisation of Antidysentery Serum. The lack of a reliable method of testing the potency of antidysentery serum in the laboratory has been frequently referred to in these reports. It has been a serious handicap to the therapeutic use of this serum. The problem has occupied Dr. MacConkey for many years and the antidysentery serum issued from the serum department has always been standardised as accurately as knowledge at the time permitted. Dr. MacConkey has made valuable observations upon this subject, and last summer he attended a conference called by the Health Committee of the League of Nations at Geneva, where he placed his experience before his colleagues. At the conference, it was agreed that the potency of antidysentery serum should be measured by its antitoxic content as estimated by titration against the toxin of the "Shiga" bacillus. It was also decided that the subject needed further research, and the directors of the principal serum laboratories in Europe and Japan were asked to co-operate. In order to ensure more uniformity in this work, a provisional form of titration was adopted.

Dr. Dumas (France) notified the Conference that experiments carried out by himself and Dr. Ramon on the flocculation of antidysentery serum by dysentery toxin, indicated that it might be possible to establish a method for the titration of antidysentery serum, without the necessity of experiments with animals, as Ramon had already succeeded in accomplishing in the case of antidiphtheritic serum and diphtheria toxin. Attempts to apply Ramon's method to the standardisation of antidysentery serum have been made in the Institute's serum laboratories, but, up to the present, with indifferent results. The investigation is being pursued, as is also the subject of standardisation of antidysentery serum generally, along lines agreed upon by the Conference.

Active immunisation of horses against Tetanus. As the horse is so very susceptible to tetanus, it is the usual practice in the Institute's laboratories to give new horses a short prophylactic course of inoculation with tetanus toxin—the last dose being about 100,000 minimal lethal doses for a guinea-pig. In the majority of cases, this has proved effectual, but one horse which had been thus immunised in 1921, and which was being used for the production of antimeningococcus serum, developed during 1924, a fatal attack of tetanus. It would thus seem advisable to carry the preliminary prophylactic immunisation further, or else to revaccinate at intervals.

Puerperal infection amongst guinea-pigs. An infection attacking the breeding stock of guinea-pigs occurred during the latter part of the year. The breeding sows alone were infected; the boars and young animals were exempt. Deaths occurred within a week or so of kindling down. Investigation of the disease was undertaken, as it presented some features hitherto unencountered. The disease appears to be a chronic one, but becomes acute *post partum*. A pneumococcus was readily isolated from the heart blood and uterus of fatal cases, and in some instances from pneumonic patches in the lungs. It was also found in the foetus. With the object of producing an active immunity the whole stock of guinea-pigs was treated with a multivalent vaccine prepared from the strains isolated. The results were encouraging.

Scarlet Fever. During the past two years there has been, largely as the outcome of American work, a renewal of interest in the view that streptococci present in the throats of scarlet fever patients may be primarily responsible for the disease. The new evidence would suggest that the symptom-complex of scarlet fever may be the result of a toxæmia attributable to toxin-producing streptococci proliferating in the throat. The facts adduced so far in support of this hypothesis may be here briefly summarised:— (1) *Hæmolytic streptococci* from scarlet fever throats produce a toxin which causes a skin reaction in a susceptible human subject when introduced intradermally. (2) The immunity or susceptibility of man to this toxin would seem to depend on the presence or absence of specific neutralising substances in the blood. Such substances are present in the blood of convalescents and in a proportion of normal individuals varying according to age-group. (3) G. F. Dick and G. H. Dick in America, appear to have succeeded in producing scarlet fever by inoculating scarlatinal streptococci in the throats of human volunteers. (4) The streptococci recovered from scarlet fever cases belong to a homogeneous group. (5) Serum prepared by immunising horses with the toxin of scarlatinal streptococci has had a very favourable effect therapeutically in scarlet fever. Research in the direction of standardising the scarlatinal toxin and the therapeutic serum is hampered by the fact that so far as we know at present, laboratory animals are not susceptible to the toxin introduced intradermally and human volunteers must be requisitioned. Some help, however, is afforded by the fact elicited by Schultz and Charlton in 1918 that the serum of convalescent scarlet fever cases when introduced into the exanthematous area of a fresh case, produces a blanching of the rash.

At Elstree, during the past year, "scarlet-fever toxin" has been prepared from American strains kindly provided by Dr. Dochez and horses have been immunised therewith. The serum of these horses is now being tested therapeutically. That it contains specific neutralising substances is shown by the fact that it causes blanching of the rash in a certain proportion of scarlet fever cases; also, when introduced in small doses prophylactically in contacts incubating the disease, the rash, when it appears, avoids the skin areas under which the serum has been inoculated. The quantity of serum injected in these experiments, was but 2 c.c., an amount evidently insufficient to produce general prophylaxis. The subject is being further investigated as opportunity offers and the Biological Standards Committee of the

Medical Research Council is arranging for tests with a view to establishing some reliable method of standardising the serum and toxin. Material for this purpose is being provided by the serum department.

As in past years, the Governing Body has pleasure in expressing its thanks to the Director of the Hygienic Laboratory, U.S.A. Public Health Service, Washington, for his continued kindness in sending supplies of standard antitoxin.

Department for the Preparation and Study of Anti-variola Vaccine.

Dr. Green has been studying the reaction of animals to re-vaccination. As found by von Pirquet and Prowazek some years ago, an accelerated reaction was observed. This allergic response occurred about twenty-four hours after inoculation and was characterised by marked erythema and slight swelling at the seat of inoculation. The effect was transient. It was observed in all the animals experimented with. The occurrence of an accelerated reaction to vaccination has been recommended for the diagnosis of doubtful cases of small-pox, but in view of the above observations its applicability would appear to be confined to unvaccinated persons.

FOOT AND MOUTH DISEASE RESEARCH.

In August last the Governing Body was asked by a Committee appointed by the Ministry of Agriculture to investigate Foot and Mouth Disease, whether facilities could be afforded at the Institute for carrying out a portion of the researches contemplated by the Committee. The Committee is composed of representatives of the veterinary profession and pathologists. It is presided over by Sir William Leishman, a former member of the Governing Body, and includes amongst its members, Professor Bulloch, a member of the Governing Body, Dr. Martin and Dr. Arkwright of the staff of the Institute.

The Governing Body agreed to place one of its laboratories, together with a suitable isolated and self-contained animal house, at the disposal of the Committee. It also agreed to second Dr. Bedson to work under the Committee. Two other workers, Dr. Maitland, formerly acting Professor of Pathology, University of Toronto, and Mrs. Burbury have been appointed by the Committee to work with Dr. Bedson. The work which is being carried out at the Institute has the advantage of the general supervision of Dr. Arkwright, who had already devoted some time to research into Foot and Mouth disease on behalf of a previous Committee of the Ministry of Agriculture.

NATIONAL COLLECTION OF TYPE CULTURES.

During the past year applications for cultures amounted to over 4,000 and many interesting and valuable types were added to the collection. At the present time over 2,000 different strains are being maintained. A new catalogue is in the press.

Pathogenic Plant Bacteria.—Dr. Brooks, Miss Rhodes and Dr. Nain, made a biochemical and serological investigation of 40 different "species" of pathogenic plant bacteria. Interesting serological and other groupings have been found which indicate that the number of species might, with advantage to systematic nomenclature, be considerably reduced. No definite links with animal pathogens have emerged but some serological connexions are apparent with the fluorescent group of saprophytic bacteria. A communication on this subject has recently appeared.

GENERAL AND FINANCIAL.

In last year's report reference was made to a legacy under the will of Mr. W. H. Clarke, of which the sum of £5,000 had been received. A further £750 was received in 1924 on account of this bequest.

The Jenner Memorial Fund, of the original value of £5,768 0s. 11d., has hitherto been shown in the balance sheet as one of the items of the Capital Fund, while the investments representing the fund have appeared under a separate heading on the credit side. The interest on the fund was for some years applied to support a Jenner Memorial Studentship, but as during, and for some years subsequent to the war, a student was not appointed, a considerable unexpended sum had accumulated. As the Jenner Memorial Fund was given to the Institute to perpetuate the name of Jenner, the Governing Body decided to transfer to the fund the unexpended dividends, which amounted at 31st December, 1924, to

£2,101 9s. 11d., thus increasing the corpus of the fund to £7,869 10s. 10d. The Governing Body has also decided to show this portion of the capital of the Institute as a separate item on the debit side of the balance sheet under the designation "Jenner Memorial Research Studentship Fund." The income and expenditure of the fund is now also shown separately from the other accounts.

During the year, the quinquennial valuation of the Pension Fund for those members of the staff not eligible for membership of the Federated Superannuation System, has been made by the Institute's Actuary. Mr. Elderton reports that provided no alterations in its provisions occur, and its investments continue to produce an equal rate of interest in future as at present, it is unnecessary to augment the fund at present. Recently, however, the Governing Body has had under consideration some improvement of the benefits by the addition of a gratuity, equal to one year's salary, if the beneficiary die after the completion of five years' service and before becoming entitled to a pension, and on actuarial advice it has allocated to the fund a sum of £2,000 to cover this liability, from the credit balance of 1924.

The Accounts and Balance Sheet for the year ended December 31st, 1924, show balances to the credit of the Pension Fund of £21,034 5s. 6d., the Sinking Fund of £13,009 0s. 0d., and of the Capital Fund of £484,293 14s. 0d., the latter figure including the credit balance of £11,232 7s. 7d. from the past year's working.

No necessity of drawing upon the Contingency Fund arose in the period under review and this remains unaltered at £14,228 18s. 1d.

Investments made during the year were: For the General Fund, £5,000 4% Funding Stock, 1960/90, and £3,000 Conversion Loan 4½% Stock; for the Pension Fund, £1,000 Conversion Loan 3½% Stock; for the Jenner Memorial Research Studentship Fund, £2,000 4% Funding Stock, 1960/90, and £426 0s. 4d. Liverpool Corporation 3½% Stock, and for the Sinking Fund, £1,000 Conversion Loan 3½% Stock. £7,350 5% War Stock was converted into £7,570 10s. 0d. Conversion Loan 4½% Stock, 1940/44, for the Sinking Fund.

Receipts from sales of the Institute's products and investigation fees show a net increase of £2,732 2s. 5d., compared with last year, viz., Bacterial Vaccines, &c., increase £6,992 6s. 6d.; Diagnosis Fees, decrease £284 1s. 11d.; Antitoxins and Sera, decrease £2,988 7s. 1d.; and Anti-Variolous Vaccine, decrease £987 15s. 1d.

The total expenditure for the year was £37,453 0s. 0d., against £43,107 7s. 8d. in 1923. Repairs, Alterations and Renewals show a decrease of £3,277 4s. 3d., while practically all other items except Gas, Water and Fuel, Vaccine Laboratory Expenses and Library, show decreases compared with the previous year.

In conclusion, the Governing Body desire to express their appreciation of the cordial co-operation of the Director and all Members of the Staff in carrying out the work of the Institute.

ERNEST H. STARLING.

Acting Chairman of the Governing Body.

BALANCE SHEET

AND

ACCOUNTS.

Dr.

The Lister Institute

BALANCE SHEET

	£	s.	d.	£	s.	d.	£	s.	d.	£	s.	d.
To CREDITORS										1,659	3	9
To PENSION FUND—												
Balance at 31st December, 1923							18,119	5	7			
Add												
Balance of Income and Expenditure Account, 1924							2,914	19	11			
										21,034	5	6
To JENNER MEMORIAL RESEARCH STUDENTSHIP FUND—												
Jenner Memorial Fund (1899)				5,768	0	11						
Add												
Unexpended Dividends, 1911/23				2,083	3	7						
							7,851	4	6			
Balance of Income and Expenditure Account, 1924							18	6	4			
										7,869	10	10
To CONTINGENCY FUND—												
As per Account 31st December, 1923										14,228	18	1
To SINKING FUND to 31st December, 1924										13,000	0	0
To CAPITAL FUND to 31st December, 1924—												
Balance of Income and Expenditure to 31st December, 1923				120,740	6	0						
Less												
Unexpended Dividends of Jenner Memorial Fund, 1911/23, transferred to Jenner Memorial Research Studentship Fund				2,083	3	7						
							118,657	2	5			
Donations, &c., received to date from the following:—												
Dr. Ludwig Mond (1893)				2,000	0	0						
The Berridge Trustees (1893/98)				46,879	10	1						
The Grocers' Company (1894)				10,000	0	0						
Lord Iveagh (1900)				250,000	0	0						
Lord Lister's Bequest (1913) as per Account at 31st December, 1923				18,904	5	8						
William Henry Clarke Bequest (1923/4)				6,750	0	0						
Other Donations (1891-1920)				20,870	8	3						
Add							473,061	6	5			
Balance of Income and Expenditure Account, 1924							11,232	7	7			
										484,293	14	0

ERNEST H. STARLING, *Acting Chairman.*

G. W. ADDISON, *Hon. Treasurer.*

£542,094 12 2

REPORT OF THE AUDITORS

We have audited the above Balance Sheet. We have obtained all the information and explanations we have required. sum of £18,267 9s. 11d. has been paid, being held by the Institute on behalf of the Scientific Staff. In our opinion, such affairs, according to the best of our information and the explanations given to us and as shown by the books of the Institute. London, April 17th, 1925.

By CASH—		£	s.	d.	£	s.	d.
At Bankers: Deposit Account		7,000	0	0			
Current Accounts		5,430	17	4			
In hand		40	2	4	12,470	19	8
By INVESTMENTS (at cost)—							
£5,000 London & North Eastern Railway 3 per cent. Debenture Stock	..	4,570	11	0			
£8,680 London, Midland & Scottish Railway 4 per cent. Preference Stock	..	10,460	8	6			
£5,000 Great Central and Midland Railway Joint Committee 3½ per cent. Guaranteed Stock	..	5,123	19	3			
£2,900 New South Wales 5½ per cent. Stock, 1922-32	..	2,897	16	0			
£1,000 Cape of Good Hope 3½ per cent. Stock	..	1,000	0	0			
£1,505 7s. 3d. New South Wales 4 per cent. Stock, 1942-62	..	1,500	0	0			
£353 London & North Eastern Railway 4 per cent. First Guaranteed Stock	..	499	11	0			
£43,800 5 per cent. War Stock, 1929-1947	..	42,633	14	3			
£21,000 4 per cent. Funding Stock, 1960-1990	..	17,667	0	1			
£20,000 Local Loans 3% Stock	..	9,962	0	7			
£3,000 Conversion Loan 4½ per cent. Stock, 1940/44	..	2,921	11	0	59,236	11	8
By INVESTMENTS, LORD IVEAGH'S DONATION (at cost)—							
£25,006 2s. 6d. New Zealand Government 3 per cent. Inscribed Stock, 1945	..	24,117	17	6			
£25,000 Victorian Government 3 per cent. Inscribed Stock, 1929-1949	..	23,875	0	0			
£25,000 Natal 3 per cent. Inscribed Stock, 1929-1949	..	24,484	7	6			
£25,000 New South Wales Government 3 per cent. Inscribed Stock, 1935..	..	24,937	10	0			
£26,100 South Australian Government 3 per cent. Consolidated Stock, 1916 or after	..	24,860	5	0			
£25,000 Cape of Good Hope 3 per cent. Inscribed Stock, 1933-1943	..	23,850	0	0			
£20,000 Southern Railway Preferred Ordinary Stock	..	32,000	0	0			
£13,750 London & North Eastern Railway 4 per cent. First Preference Stock	..	26,000	0	0			
£15,625 London, Midland & Scottish Railway 4 per cent. Preference Stock, 1923	..	20,375	0	0			
£25,000 East Indian Railway 3 per cent. New Debenture Stock	..	25,500	0	0	250,000	0	0
By INVESTMENTS, JENNER MEMORIAL RESEARCH STUDENTSHIP FUND (at cost)—							
£2,650 Southwark and Vauxhall Water Co. 3 per cent. Debenture Stock "B"	..	2,756	10	0			
£1,596 Southern Railway 5 per cent. Preference Stock	..	2,740	5	0			
£726 11s. 4d. Liverpool Corporation 3 per cent. (1942) Stock	..	556	15	6			
£2,000 4 per cent. Funding Stock, 1960/90	..	1,797	14	0	7,851	4	6
By INVESTMENTS, LORD LISTER'S BEQUEST (at cost)—							
£1,937 Grand Trunk Railway Company of Canada 4 per cent. Guaranteed Stock	..	1,733	12	4			
£300 Grand Trunk Railway Company of Canada Great Western Borrowed Capital 5 per cent. Perpetual Debenture Stock	..	936	0	0			
£1,875 Port of London 4 per cent. B. Stock	..	1,800	0	0			
£3,400 Gas Light and Coke Company Ordinary Stock	..	3,638	0	0			
£300 Ontario and Quebec Railway 5 per cent. Debenture Stock	..	984	0	0			
£681 Madras and Southern Mahratta Railway 4 per cent. Debenture Stock	..	656	19	7			
£500 Canada 4 per cent. Stock, 1940-1960	..	492	11	0			
£700 Western Australia 4 per cent. Stock, 1942-1952	..	698	7	0			
£600 Union of South Africa 4 per cent. Stock, 1943-1963..	..	594	2	0			
£1,200 London & North Eastern Railway 3 per cent. Debenture Stock	..	891	2	9			
£8,467 4 per cent. Funding Stock, 1960-1990	..	6,479	11	0	18,904	5	8
By INVESTMENTS, SINKING FUND (at cost)—							
£7,570 10s. 0d. Conversion Loan 4½ per cent. Stock, 1940/44	..	6,916	12	7			
£5,550 4 per cent. Funding Stock, 1960-1990	..	4,227	17	7			
£2,300 Conversion Loan 3½ per cent. Stock	..	1,783	6	6	12,927	16	8
By INVESTMENTS, PENSION FUND (at cost)—							
£22,000 4 per cent. Funding Stock, 1960-1990	..	17,165	3	5			
£2,000 Conversion Loan 3½ per cent. Stock	..	1,560	4	0			
Balance uninvested	..	2,308	18	1	21,034	5	6
(The above Investments, at the market value, 31st December, 1924 show a depreciation of approximately £76,705.)							
By LOANS ON MORTGAGES					7,500	0	0
By DEBTORS					7,856	5	5
By STOCK OF BACTERIAL VACCINES					40	11	6
By FURNITURE, FITTINGS, SCIENTIFIC APPARATUS AND BOOKS—							
As per account, 31st December, 1920					2,471	17	2
By EXPENDITURE ON INSTITUTE BUILDINGS AT CHELSEA—							
As per account, 31st December, 1910, including purchase of freehold site, £6,000					70,916	3	1
By PURCHASE OF FREEHOLD LAND ADJOINING "THE STUDIOS," CHELSEA, as per account, 31st December, 1912							
.. .. .					169	6	8
By LEASE OF "THE STUDIOS," CHELSEA, as per last account							
.. .. .		1,913	10	9			
Less Amount written off		65	2	0	1,848	8	9
By QUEENSBERRY LODGE FARM, ELSTREE—							
Purchase of freehold land and buildings and Expenditure on new buildings, as per account, 31st December, 1912..					20,455	10	0
Stock of Animals and Forage		325	7	11			
Stock of Anti-Toxins and Bottles		6,588	2	5			
Stable Utensils, Farm Implements and Sheds, as per account, 31st Dec., 1903		138	1	4			
Laboratory Apparatus, as per account, 31st December, 1903		466	1	3			
Furniture, as per account, 31st December, 1903		315	8	0	7,733	0	11
By PURCHASE OF HILL VIEW COTTAGE							
.. .. .					678	5	0
* Nothing has been charged for depreciation of Furniture, &c. since new purchases made during the year to a greater amount than the estimated depreciation (10%) have been written off.							
					£542,094	12	2

TO THE MEMBERS.

The Superannuation Scheme for the Scientific Staff provides for Life Policies and National Savings Certificates for which the Balance Sheet is full and fair, and properly drawn up so as to exhibit a true and correct view of the state of the Institute's

COOPER BROTHERS & CO.,
Chartered Accountants. } Auditors.

Dr. INCOME AND EXPENDITURE ACCOUNTS

INCOME.						£	s.	d.
To Interest and Dividends on General Investments	...	...	...	...	...	18,575	9	3
To Interest and Dividends on Sinking Fund Investments	...	...	...	...	...	455	12	6
To Investigation, Diagnosis and Analysis Fees, &c. ...	...	...	...	...	...	3,641	18	6
To Sales of Sera, Vaccines, &c., and Stock at 31st December, 1924, less Stock at 31st December, 1923	...	...	...	...	...	30,203	4	4
To Rent of Rooms in the Institute, &c. ...	...	...	...	...	...	314	10	0
To Refund of Corporation Profits Tax (1923)	...	...	...	...	...	494	13	0

£48,685 7 7

Dr.

Pension

						£	s.	d.
To Interest and Dividends on Investments	...	...	...	...	...	914	19	11
To Special Contribution from General Funds	...	...	...	...	...	2,000	0	0
						£2,914	19	11

Dr.

Jenner Memorial Research

						£	s.	d.
To Interest and Dividends on Investments	...	...	...	...	...	168	6	4

£168 6 4

Preventive Medicine.

for the year ending 31st December, 1924.

Cr.

EXPENDITURE.							£	s.	d.
By Rent, Rates, Taxes and Insurance	...	...	...	...	...	...	4,356	6	4
By Salaries and Wages of Staff	...	...	...	...	...	...	18,649	11	6
By Premiums on Federated Superannuation Policies	...	...	...	...	...	...	987	10	8
By Stationery, Printing and Postage	...	...	...	...	...	...	356	16	6
By Printing of Collected Papers	...	...	...	...	...	...	240	7	7
By Office Expenses, Law Charges, and Sundries	...	...	...	...	...	...	201	3	8
By Travelling Expenses	...	...	...	...	...	...	17	12	1
By Auditors' Fee	...	...	...	...	...	...	60	0	0
By Gas, Water and Fuel	...	...	...	...	...	...	1,526	18	4
By Electric Light and Power	...	...	...	...	...	...	306	6	6
By Experimental Pathology Laboratory Expenses, including General Apparatus	...	...	...	...	...	...	507	18	10
By Bacteriological Laboratory Expenses, including Apparatus	...	...	...	...	...	...	291	16	10
By Vaccine Laboratory Expenses, including Bottles	...	...	...	...	...	...	513	14	9
By Water and Bio-chemical Laboratory Expenses, including Apparatus	...	...	...	...	...	...	486	5	2
By Serum and Calf Lymph Laboratories Expenses, including Apparatus and Cost of Bottles	...	...	...	...	...	...	1,199	4	11
By Culture Media	...	...	...	...	...	...	151	16	11
By Animals	...	...	...	...	...	...	1,463	13	5
By Animal House Expenses and Forage	...	...	...	...	...	...	1,268	19	11
By Repairs, Renewals and Alterations, including Workshop Expenses	...	...	...	...	...	...	1,190	11	3
By Library Expenses	...	...	...	...	...	...	357	3	2
By General Stores	...	...	...	...	...	...	382	7	7
By Bad Debts	...	...	...	...	...	...	5	6	0
By Special Contribution to Pension Fund	...	...	...	...	...	...	2,000	0	0
By Depreciation of the Lease of "The Studios," Chelsea	...	...	...	...	...	...	65	2	0
By Sinking Fund ($\frac{1}{2}$ % per annum on Cost of Buildings and Interest on Investments)	...	...	...	...	...	...	866	6	1
By Balance, being Excess of Income over Expenditure, transferred to Balance Sheet	...	...	...	...	...	...	11,232	7	7
							<u>£48,685</u>	<u>7</u>	<u>7</u>

Fund.

Cr.

	£	s.	d.
By Balance, being Excess of Income over Expenditure, transferred to Balance Sheet	2,914	19	11
	<u>£2,914</u>	<u>19</u>	<u>11</u>

Studentship Fund.

Cr.

	£	s.	d.
By Salary—Dr. A. Hunter Brown	150	0	0
By Balance, being Excess of Income over Expenditure, transferred to Balance Sheet	18	6	4
	<u>£168</u>	<u>6</u>	<u>4</u>

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THE LISTER INSTITUTE
OF
PREVENTIVE MEDICINE.

Report of the Governing Body,
1926.

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

June 9th, 1926.

The Lister Institute of Preventive Medicine,

CHELSEA BRIDGE ROAD, LONDON, S.W. 1.
ELSTREE, HERTS; MARAZION, CORNWALL.

THE GOVERNING BODY.

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(Medical Research Council.)

Director :

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Curator :

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Assistant Curator :

MABEL RHODES.

* A recognised Teacher of the University of London.

ANNUAL GENERAL MEETING
OF
The Lister Institute of Preventive Medicine,
June 9th, 1926.

REPORT OF THE GOVERNING BODY.

The Governing Body has the honour to present the Institute's 32nd Annual Report.

GOVERNING BODY.

During the temporary absence abroad of Sir David Bruce, Professor Starling acted as Chairman of the Board.

At the last Annual Meeting, the Council re-elected Professor W. Bulloch and Sir James K. Fowler to represent it until December 31st, 1926. Professor A. E. Boycott was elected in place of Sir Frederick Andrewes as the third representative of the Council upon the Governing Body until the same date.

The Governing Body offers to Sir John Rose Bradford, its late Chairman, sincere congratulations upon his recent election to the Presidency of the Royal College of Physicians, London.

COUNCIL.

At the last Annual Meeting, the retiring members of Council, Sir William Leishman, Professor R. T. Hewlett and Dr. L. C. Parkes, all three representatives of the Members of the Institute, were re-elected, and Professor E. H. Starling was elected to the vacancy which occurred owing to the death of Sir Rickman Godlee.

The three members who retire from the Council by rotation this year, but who are eligible for re-election, are Sir John Rose Bradford and Sir William J. Simpson, representatives of the Members of the Institute, and Mr. George K. Morice, one of the representatives of the Worshipful Company of Grocers.

MEMBERS.

The Governing Body regrets to announce the death during the year of Professor A. Cushny, a member of the Institute for many years.

STAFF.

Dr. Martin has been granted three months sick-leave and Dr. Harden has been appointed Deputy Director during his absence.

Dr. Muriel Robertson who has been absent for a considerable period on sick-leave resumed duty during the year.

Dr. MacConkey, who joined the staff of the Bacteriological department in 1901, and in 1906 succeeded the late Dr. George Dean as Bacteriologist in charge of the Serum department, completed his term of office in April, when he retired under the terms of his agreement with the Institute under the Federated Superannuation System. The Governing Body desires to place on record its high appreciation of the services rendered to the Institute by Dr. MacConkey during his occupation of the post of Bacteriologist at the Serum department, and for the very able manner in which he surmounted the difficulties met with in the preparation of antitoxic sera sufficient to meet the needs of the Military and Naval authorities during the late war.

Dr. G. F. Petrie, late assistant in the Serum department, has been appointed to succeed Dr. MacConkey.

Dr. Bedson resigned his position of Assistant Bacteriologist, on appointment as Research Bacteriologist to the Clinical Laboratories, London Hospital.

Mr. G. Cooper, late Secretary and Accountant, whilst still retaining the latter post, has been succeeded by Mr. A. L. White, as Secretary.

Dr. H. M. Woodcock and Mr. W. T. J. Morgan, M.Sc., have been appointed to the Jenner Memorial and Grocers' Company Research Studentships respectively during the year.

Dr. S. S. Zilva has been recognised by the University of London as a teacher of Biochemistry at the Institute.

RESEARCH WORK.

Before proceeding to review the scientific activities of the various departments of the Institute, the Governing Body desires again to record its appreciation of the support rendered by the Medical Research Council to these activities. During the past year, in addition to furnishing the salaries of the staff of the National Collection of Type Cultures, the Council has provided two whole time workers in the Department of Bacteriology, Dr. Woodcock and Mr. Bruce White, one in the Department of Biochemistry, Dr. Zilva, and six in the Department of Experimental Pathology, Professor Korenchevsky, Miss Hume, Miss Soames, Miss Carr, Miss Henderson Smith and Miss Leigh Clare. Their work is carried out under the direction of Professors Ledingham, Harden and Martin respectively. Dr. Lumsden's work on Cancer, referred to later in this report, is carried on under a grant from the British Empire Cancer Campaign. Accommodation for all these workers and the expenses of their researches are provided by the Institute.

Department of Bacteriology.

Variola, Vaccinia and Avian Molluscum. In continuation of his study of these viruses Professor Ledingham has tested the affinity for the rabbit of virus collected from mild small-pox cases now occurring in this country. It is known that small-pox virus can produce characteristic lesions after scarification on the rabbit cornea, but that direct "takes" from man only very rarely succeed on the shaved and scarified skin of the rabbit. On the other hand, the intracutaneous route, which has proved of such value in the practical titration of vaccinia virus, has been but little used for experiments involving the direct passage of small-pox virus to the rabbit, though the occurrence of an inflammatory reaction has been noted after intradermal inoculation. All the samples examined by Dr. Ledingham from small-pox cases gave very definite intracutaneous reactions, which were invariably neutralised by antivaccinal serum. No definitely positive results were obtained when the same material was inoculated cutaneously by scarification. Attempts to raise the virulence by frequent passage of material from abortive sites also failed. While, therefore, small-pox virus is of sufficient virulence for the rabbit to take with uniformity in the dermis, cutaneous takes have not been successful. The explanation for the anomaly has yet to be sought, and its solution may throw valuable light on the irregularities met with in converting small-pox to the vaccinal form—a transformation which involves increased virulence of the original virus for the rabbit and a diminished virulence for man.

Harben Lectures, 1925. In one of the Harben lectures delivered in December, 1925, Dr. Ledingham gave a detailed account of his recent studies of the viruses mentioned above. In the other two lectures he dealt with (1) Some problems of Natural Immunity and Prophylaxis and (2) The Carrier Problem in relation to Enteric Fever and Diphtheria. These lectures, which embodied original data hitherto unpublished, appeared in the *Journal of State Medicine*.

Bacterial Variation, in relation to Antigenic Structure, Virulence and Immunising Capacity.

Dr. Arkwright has continued his observations on the variation of bacteria *in vitro* especially as regards *B. paratyphosus A*. He has obtained a number of variants, four of which differ very obviously in their agglutination reactions and pathogenic properties for guinea-pigs. The most virulent of these was one which showed characteristics such as would formerly have been regarded as evidence of degeneration. The variants also differed in their immunising properties when used as dead vaccines for guinea-pigs. By growing in different samples of rabbit serum *in vitro* he found that the characters of these strains of bacteria were markedly altered, particularly in the direction of spontaneous agglutinability and with a corresponding change in their serum reactions. The sera which effected these changes most definitely were those which contained antibodies for the cultures with which they were inoculated. Some of these sera preserved the original characters of the inoculated organism unaltered. These observations may have an important bearing on pathogenesis in acute infections in animals and man and also in chronic disease and the carrier-state.

Dr. Balteanu (Rockefeller Foundation Fellow) has studied the group of Cholera and Cholera-like vibrios with a view to investigating more completely than has hitherto been attempted, the variants occurring in this group. From several strains of *V. cholerae* he has obtained a form which differs culturally and antigenically from the normal and has some relation to the variant forms known as "H" and "O" and "R" and "S" in the *B. coli-typhosus-enteritidis* group. His studies are now nearly completed.

Miss Brice, M.B. (Melbourne) has compared the subcutaneous and intravenous routes for antigen inoculation with a view to testing certain hypotheses put forward by Felix with reference to differences in the quality and quantity of the antibodies produced.

Plague Prophylactic. Dr. Schütze completed his investigation into the relative potency of three recognised types of plague vaccine (1) Haffkine's prophylactic, (2) an agar-grown heat-killed vaccine and (3) the serum-agar preparation of the Lister Institute. It was shown that of guinea-pigs immunised with Haffkine's prophylactic and heat-killed vaccine, 14 per cent. and 22 per cent. respectively were protected against a lethal dose of *B. pestis* subsequently administered, whereas 44 per cent. of those immunised with the Institute serum-agar vaccine were protected. In rats, on the other hand, all the vaccines afforded protection to some 90 per cent. of the animals.

Serological Position of certain Old Strains of *B. tuberculosis*. Dr. Schütze is now carrying out a series of agglutination and absorption tests with a number of mammalian and avian strains of *B. tuberculosis*. These have been in artificial cultivation for many years, and some of them having lost virulence are regarded as specially useful in the preparation of vaccines for therapeutic and immunising purposes.

Pasteurellosis in Mice. Prophylactic Value of Living and Heat-killed Vaccines. Dr. Mohammed (Cairo) performed some preliminary experiments on this point under Dr. Schütze's direction. It appeared that the living vaccine owed its superiority largely to its power of multiplying in the tissues of the animal and that the heat-killed vaccine if given in sufficient dosage might be equally effective. The question, however, is not settled, and Dr. Schütze is at present continuing the investigation. The value for vaccine purposes of a *Pasteurella*, non-virulent for mice, is also being studied.

Types of *Gonococcus*. Dr. Atkin has completed his work on the significance of *Gonococcus* types. By comparing a considerable number of organisms, freshly isolated from patients, with some old laboratory strains, a close parallel was found to exist between the serological reactions and the cultural appearances on certain special media, as had been found in the case of the *Meningococcus*. Two serological types have been established and examples of all gradations between them have been observed. Apparently an artificial selection takes place when the *Gonococcus* is maintained on culture media, the more viable organisms forming the basis of each subculture. This seems to result in a progression from Type I. to Type II., and some evidence of this change was observed, but the process is evidently a very slow one and would possibly have to be followed for some years in order to observe the complete metamorphosis.

***Pneumococcus* and the Bile-solubility Test.** While examining the behaviour of the *Pneumococcus* on similar lines to the *Gonococcus*, Dr. Atkin has obtained an insight into the rationale of the bile-soluble property of this organism. He has shown in some experiments, which are now almost completed, that bile acts by accelerating the normal autolysis of the *Pneumococcus*. This species autolyses in artificial cultures, different strains exhibiting this property in varying degrees. He has found that bile-solubility and degree of autolysis go hand in hand. Moreover the papillae or daughter colonies, which develop on primary colonies under certain conditions and which contain no autolysin, are quite insoluble in bile. The true significance of the bile-solubility test is important, as it has hitherto been accepted as a feature distinguishing the *Pneumococcus* from the *Streptococcus*, which is not bile-soluble.

Pasteurisation of Milk and Bovine Tuberculosis. The experiments which were undertaken by Dr. R. G. White, with a view to obtaining fresh evidence on what has hitherto been a somewhat disputed question, viz., the effect of pasteurisation of milk on tubercle bacilli that may be present therein, were brought to a conclusion. The results showed clearly that naturally infected milk from cows with tuberculous udders or milk to which cultural tubercle bacilli or emulsions of tuberculous glands were added was rendered incapable of producing tuberculous infection in guinea-pigs after an exposure to a temperature of 62.5°C. for 30 minutes.

Adaptation of Mouse Cancer to Rats. Experiments on this subject which were begun in Strassburg, in 1924, were continued by Dr. Gheorghiu (Roumania) (*Rockefeller Foundation Fellow*) on his arrival here in the late summer of 1925. By employing new-born rats or rats less than 24 hours old, as Gye had done in 1915, he succeeded in propagating a primary mouse cancer in rats through 20 passages over a period of 12 months. During these passages it was noted that the grafts became progressively better adapted to the rat organism, the periods of development to maximal dimensions and of subsequent absorption being very considerably prolonged. It was occasionally possible with material from the later passages to infect rats several days old, but no success was obtained with adult rats. The tumor at the end of the rat passages had lost none of its affinity for mice.

Scarlet Fever and *Streptococci*. Dr. G. H. Eagles (*Beit Memorial Research Fellow*) has been studying haemolytic streptococci recovered from scarlet fever, erysipelas and puerperal septicæmia. All strains from scarlet fever have been found to elaborate toxic filtrates and also a large number of strains from erysipelas and puerperal fever. Laboratory animals have not been found to give satisfactory skin tests and for most of the experiments he has used his own arms. Methods of purification of these toxic filtrates are being studied and neutralisation experiments with immune sera are in progress.

Hydrogen Peroxide and Bacterial Growth. Dr. J. H. Burnet (Melbourne) has been carrying on work commenced in Australia on the part played by hydrogen peroxide in the processes of bacterial growth. He showed there that certain organisms produce diffusible substances in the course of their growth that can destroy peroxide and that also seem to be responsible for allowing growth of bacteria under a number of otherwise unsuitable conditions. At present he is endeavouring to define the conditions under which these entities are produced and to demonstrate their relation to the adoption of aerobic or anaerobic growth by organisms capable of existence in either state. It has been found that cyanide has a specifically inhibitory effect on growth in the presence of oxygen and that this effect can be destroyed by the same entities which destroy peroxide. It is hoped by the use of this reagent to gain some further insight into the differences between the two modes of existence. Several peroxide-producing organisms are also being studied along similar lines.

Encephalitis and Microsporidia. Dr. H. M. Woodcock, as a grantee of the Medical Research Council and Jenner Memorial Research Student, has continued his work on the parasite, *Encephalitozoon cuniculi* of rabbits and mice, which is associated with the condition known as spontaneous encephalitis. His observations go to show that the parasite is of rare occurrence in stock laboratory animals in this country, this conclusion being in agreement with the negative results reported by other workers who have searched for it. He has recently obtained a good infection associated with well-marked lesions in a rabbit which had been inoculated five months previously with a strain of Kling's encephalitic virus kindly sent by this worker. The parasites in this case, as in that of the normal stock rabbit previously found infected at the Institute, are of the "continental" type (i.e., as described by Doerr and Zdansky, Levaditi, and others). For comparison he has been able to study Cameron and Maitland's "Canadian" type from material kindly given by Dr. Maitland, and he finds that the two types of parasite are quite different and do not show transition forms from one to the other. On the other hand, he has carefully studied *Glugea lophii* which infects the central nervous system of the angler fish (*Lophius piscatorius*) and finds, contrary to his first opinion, that there is, in many cases, a very great similarity between the spore elements of the continental type of *Encephalitozoon* and those of this fish parasite.

Physiological Reaction to the Intravenous Injection of Colloids. Miss D. B. Steabben (*Beit Memorial Research Fellow*) has continued her work on the physiological effects of the injection of colloidal substances into normal and experimentally infected animals. In normal animals and those in the early stages of infection all the preparations used cause a reaction typical of that occurring when they are employed therapeutically—a reaction which involves the same general changes in the blood but which can be made to vary from a slight leucocytosis to fatal colloidal shock. The beneficial effect of such injections appears to depend upon the increase of normal function which is provoked by the necessity of eliminating the foreign substance, in order to preserve the constancy of environment essential to the living cell. The stimulation of antibody production which is said to follow the injection of non-specific substances may and does occur, but the effect is not constant and cannot be predicted. The injection of colloids into normal rabbits may temporarily increase phagocytosis and also the bactericidal power of whole blood and serum. Experimentally infected animals gradually lose the power to react as the infection advances. A protein injection into an animal suffering from an acute infection may cause a fatal reaction analogous to shock. If the animal is in the advanced chronic stage of disease the injection of a colloid may cause a marked focal reaction which may aggravate the condition. In the earlier stages such an injection appears to delay temporarily the course of infection.

Corynebacteria. Pathogenicity for Rats and Mice. The experiments on the comparative immunity or susceptibility of laboratory animals to members of the genus *Corynebacterium* have been continued by Mrs. Barratt and the results are being prepared for publication. Further work has confirmed the preliminary experiments in showing that though the rat and mouse are comparatively immune to *C. diphtheriae* and diphtheroids of human origin, an acute illness and death can readily be produced in both these animals with organisms of animal origin, *C. pseudotuberculosis ovis* and *C. pseudotuberculosis murium*. With suitable doses of the latter organism a chronic illness similar to that occurring naturally in mice could be readily induced in these animals and in at least one instance in the rat, but the results with the latter animal were less constant than with the mouse. The guinea-pig, on the other hand, is comparatively immune to *C. pseudo. murium*, but highly susceptible to *C. pseudo. ovis*.

Salmonella Group Studies. Mr. P. Bruce White, grantee of the Medical Research Council, has continued his studies of the variation phenomena and inter-relationships of *Salmonella* forms. A full report on his work of the past two years will shortly appear in the Medical Research Council Special Report Series now in the press. The main results of the investigations during the past year are as follows:—

Classification:—Analysis of further strains of the complex *Suipestifer-Hirschfeld* type and demonstration of the heterogeneity of the German *Paratyphosus B*; identification of the *Breslau* type and several so-called animal *Paratyphoid B* strains, with *B. aertrycke*; determination of the exact relationship of the *Binns* strain (Schütze) with *B. aertrycke*; recognition and confirmation of several new types.

Variation:—Confirmation and extension of his thesis (Special Report Series, No. 91) that "rough" variation (Arkwright) is associated with change in the nature of the heat-stable antigens and of these alone, while in specific phase-non-specific phase variation (Andrewes), the heat-labile substances are alone involved; confirmation of Schütze's observations on the "cosmopolitan" agglutination of "rough" variants and demonstration of the fact that this non-specificity depends solely on the heat-stable antigens peculiar to "roughness." It has also been noted that extraction of rough cultures with alcohol renders them saline-stable without damaging those substances which differentiate them serologically from "smooth" forms.

Serological relationships:—He has made an exhaustive study of some 20 *Salmonella* types and the accumulated data form the basis of a general discussion on *Salmonella* constitution and relationships with the presentation of a definite theory of *Salmonella* phylogeny based on the ontogeny of the individual organism. This, it is hoped, may carry us a step further in our understanding of the evolution and diversity of enteric diseases.

The hospitality of the Department has also been extended to various workers, including Major J. Horne, I.M.S. (ret.).

Department of Biochemistry.

In this department the work in progress last year has been continued and extended.

Alcoholic Fermentation. The reaction which occurs between sugar and phosphate in the course of alcoholic fermentation has been investigated quantitatively by Professor Harden and Lord Henley, with special reference to the quantities of the mono- and di-phosphoric esters produced. A satisfactory method of estimation has now been worked out and it is hoped that definite results will shortly be obtained. The function of phosphate in the enzymic production of polysaccharides from sugars by yeast has been studied by Mr. Naganishi (Japan) who has found no evidence of the intervention of phosphate in this change.

Professor Katagiri (Japan) has been engaged in studying the effect of fatty acids and their salts on alcoholic fermentation by living yeast, in order to find some satisfactory standard with which to compare the action of accelerating and inhibiting agents on fermentation. He has found that the rate of fermentation is greatly diminished by the free acids, formic acid being 5—8 times as effective as acetic, whereas the salts of the acids have very little effect.

Synthesis of Fat and Carbohydrate by Vegetable Organisms. Dr. Smedley MacLean and Miss D. Hoffert have extended their work on this subject by studying the effect of sodium sulphite on the storage of fat and carbohydrate by yeast. The sodium sulphite is used as a fixation agent (Neuberg) to combine with and detect any acetaldehyde which may be formed as an intermediate stage in the process. They have found that sulphite in this way greatly diminishes the yield of fatty acids from simple compounds such as alcohol and acetic acid, but not from the sugars. This result indicates that acetaldehyde is an intermediate stage in the formation of fat from alcohol or acetic acid but not from sugars, a fact which, together with other evidence, lends strong support to the view, first suggested by Emil Fischer, that sugar is built up into fat without being broken down to simpler molecules. Simpler compounds, on the other hand, appear first to pass through the stage of acetaldehyde and are then synthesised to a sugar which is finally converted into fat. Sugars would most probably yield fats containing 18 carbon atoms (3 molecules of sugar forming 1 of fat). The numerous fats containing even numbers of carbon atoms which are found in nature (*e.g.*, in butter) would on this view be degradation products of the 18-carbon atoms fat, formed by successive oxidative removal of 2 carbon atoms (by β -oxidation). This, if confirmed, is a result of fundamental importance in the physiology of carbohydrate and fat.

The ether-soluble substance isolated from yeast may contain as much as from 30 to 40 per cent. of unsaponifiable matter consisting largely of the sterol characteristic of the fungi, ergosterol. The proportion of sterol in the fat is considerably reduced by the addition of sulphite to the sugar solution in which the yeast is incubated; it seems probable, therefore, that there is a direct path from acetaldehyde to sterol without preliminary conversion to sugar.

Chemical constitution of Hexosemonophosphate and Hexosediphosphate. The investigation of this question by Professor Harden and Dr. Robison has been continued on the lines mentioned in last year's report.

Mr. W. T. J. Morgan, the newly appointed Grocers' Research Student, is now working on this problem and has made considerable progress in the preparation of the fully methylated derivatives, from which it is hoped to deduce the position of the phosphoric acid groups in the sugar molecule. The methyl glucosides of both esters have been obtained in the form of salts, and it has been found that the brucine salts are crystalline.

Improved methods for the separation of the mono- and di-esters from the products of fermentation are also being worked out, and will, it is hoped, materially lessen the time and labour hitherto required in order to obtain these esters in sufficiently pure condition.

The Phosphoric Esters which occur in Blood and other Animal Tissues, and the Enzymes (Phosphoric Esterases) by which they are Synthesised and Hydrolysed in the Body. Dr. Robison has continued his work on the isolation of the phosphoric esters occurring in blood. Progress was delayed by the loss of most of the accumulated material which had been stored in the form of the dry lead salts. These proved to be unexpectedly susceptible to attack by certain moulds and were found after the summer vacation completely decomposed. A fresh start was made with large quantities of horse blood obtained by the co-operation of Dr. MacConkey and the various phosphoric esters have been separated by a modified method which is proving satisfactory.

The further purification and investigation of the salts of these esters is now in progress. Although the bulk of these esters occurs in the corpuscles, most workers have found a small but definite amount in the plasma. Recently this has been disputed on the ground that the amounts found lie within the experimental error in the estimation of organic P. The question is of importance, since, if the esters do not pass into the plasma, it is difficult to see how they can be utilised by the bone enzyme in the process of calcification.

Experiments carried out with Dr. Martland have confirmed the presence of these small amounts of phosphoric esters in the plasma and a search is now being made for conditions under which the amounts may increase. The enzymes (phosphoric esterases) which effect synthesis and hydrolysis of these esters in corpuscles and in plasma have also been further investigated.

The experiments carried out with Miss Soames on the distribution of phosphorus compounds in the blood of rachitic and normal infants gave similar results to those previously obtained with rats and did not throw any fresh light on the cause of the deficient calcification.

In collaboration with Miss Soames further experiments have also been made on the calcification of bones *in vitro*, under conditions approximating more closely than before to those obtaining in the animal body. A considerable measure of success has been attained and the experiments so far confirm the previous conclusions as to the rôle played by phosphoric esters and by the bone enzyme in the process of calcification.

The investigation of the significance of the enzyme in the kidney to which reference was made in the last report, has been completed and the results have been published. This work was carried out in Professor Starling's laboratory at University College by Dr. Eichholtz, Dr. Brull and Dr. Robison. The completed results fully bore out the preliminary statement made last year that phosphoric esters introduced into the blood are hydrolysed by the kidney enzyme and the inorganic phosphate thus produced is secreted into the urine. The suggestion was made that this mechanism may be responsible for a considerable part of the normal phosphate excretion.

Hexosephosphates and Transformation of Sugars. In order to gain more information as to the participation of hexosephosphates in transformation of sugars, work has been commenced by Professor Harden in collaboration with Miss Edna C. Smith on the remarkable conversion of starch into cane-sugar which occurs in potatoes when they are stored at 0°C, but no definite results have yet been obtained.

Vitamins. Professor Harden is conducting experiments on the nature of the substance contained in yeast and many vegetable extracts, which has a powerful stimulating effect on the growth of yeast and is considered by many workers to belong to the class of vitamins. Using lemon juice as the source of this material it has so far been found possible to concentrate it very considerably and to separate it from the antiscorbutic vitamin.

The experiments carried out by Professor Harden and Dr. Zilva on the source of the antiscorbutic vitamin in germinated seeds have been continued but have not yet led to definite results.

Dr. Zilva has pursued his chemical investigations of the antiscorbutic factor. Continuing the purification of the active fraction he has studied the relation of the antiscorbutic activity to the reducing substances which are so closely associated even with the purest preparations. In collaboration with Mr. C. G. Daubney he has made a detailed study of the behaviour of the inorganic constituents of lemon juice in the process of fractionation. The presence of minute quantities of the order of 0.1 mg. per litre of certain elements has been established in the purest preparations. A remarkable parallelism was observed to exist between some of these elements and the active principle in the various chemical and physicochemical manipulations, an observation which is receiving further attention. Attempts have also been made, so far without success, to regenerate by various reducing methods the activity a antiscorbutic solutions which have been inactivated through the agency of oxidation.

In order to throw some light on the behaviour of the antiscorbutic factor in the process of digestion, Dr. Zilva has investigated the action of proteolytic enzymes on the vitamin *in vitro*. It was found to be resistant to the action of pepsin and trypsin in the presence and in the absence of protein, when acted upon by these enzymes for a few hours.

Dr. Zilva has also attempted to obtain an antibody by immunising rabbits with antiscorbutic preparations previously treated with protein. This attempt has not proved successful. With Dr. E. H. Lepper he has continued the study of the blood-sugar of guinea-pigs in various stages of scurvy, but the results are so far indeterminate.

At the request of the *Discovery* Committee of the Colonial Office, Dr. Zilva has been superintending the preparation of further large quantities of lemon juice for the whale marking vessel, *William Scoresby*, which is joining the *Discovery* expedition.

The investigation carried on by Dr. Zilva and Miss Soames in collaboration with Captain J. Golding and Mr. J. Mackintosh, of the National Institute for Dairy Research, Reading, and Professor J. C. Drummond, of University College, on the relative antirachitic and growth-promoting properties of butter obtained from cows fed on diets supplemented by green fodder, ensilage and cod-liver oil, has been continued, with the view of supplementing the evidence obtained last year. The results of this work will not be available before October.

The hospitality of the department has also been extended to Dr. Stern, Mrs. Balfour and Miss Maughan.

Department of Experimental Pathology.

Acid-base equilibria of the blood. Dr. Elizabeth H. Lepper and Dr. Martin have been working at some aspects of this problem. For the purpose of their enquiry they have developed a micro-method for the determination of (1) the bicarbonate content of serum; (2) the H^+ concentration of the capillary blood. The former requires but 0.5 c.c., and the latter only a single drop of blood; nevertheless, the methods are sufficiently accurate for most purposes. Venesection is, therefore, unnecessary, and frequent observations can be made—a great advantage in many investigations.

They have also determined the discrepancy of colorimetric observations of pH, depending on the content of the solution in NaCl. They find it is the concentration of the kation which is significant in the case of the sulphonephthalein indicators, and that with blood serum the error is negligible, when the standard solutions with which the colour is compared contain the same concentration of the same kations. Fortunately this happens to be very nearly the case, when Sørensen's M/15 phosphate solutions are used and the range of pH is that encountered in blood.

The change in the pH of the blood with temperature, (1) when the pressure of CO₂ is maintained constant, (2) when the concentration of CO₂ is maintained constant has also been studied. The unexpected result has been obtained that, within the error of the experiments, the effect of temperature upon the pH of the corpuscles and of the plasma is the same. Previous observations, therefore, on the correction to be applied to determinations of the pH of plasma at room temperature to obtain the pH of the plasma at 37°C. hold with sufficient accuracy to arrive at the pH of the corresponding blood circulating in the body.

The Fat-Soluble Vitamins. (Anti-ophthalmic vitamin A and antirachitic vitamin D).

I. Methods of Study and Titration. Much time and attention has been given during the past year to the development of trustworthy methods for the assay of the two fat-soluble vitamins, A and D, recent research having thrown considerable doubt upon those previously employed and upon the results obtained. The researches of Steenbock and his co-workers in the United States, taken in conjunction with those of Hume and Goldblatt and Soames in this country, have made it clear that the antirachitic vitamin D is not less necessary for growth than vitamin A.

Experimental Animals. The provision of a steady supply of young rats with a constant endowment of vitamin reserves is an essential preliminary to satisfactory work in this field but has proved very difficult to attain. In the above department the breeding of rats for nutritional work is now undertaken by Miss Henderson Smith, who has found that although the diet has been maintained constant throughout the year, great variations in the animals' subsequent resistance to deficient diets have occurred at the different seasons. The disturbing factor has been finally tracked to the seasonal variations in the vitamin content of the fresh milk which was an important constituent of the diet of the breeding stock. The requisite degree of constancy in the young animals has been achieved by the expedient of employing the same preparation of dried milk throughout the year. This is now included in the diet of mothers during the last days of pregnancy and in that of mother and young from the time of birth until needed for experiment.

Titration. The biological method previously used for titration of vitamin A in foodstuffs, by observing the degree of growth restored by administering such foodstuffs to young rats which have ceased to grow on artificial diets deprived of both fat-soluble vitamins, is obviously untrustworthy unless excess of vitamin D be provided at the same time. Miss Hume and Miss Henderson Smith are now engaged upon an exhaustive examination of methods for vitamin A titration, in which this reform is embodied.

II. Distribution in Nature. Fresh Green Leaves. Dr. Harriette Chick and Miss Roscoe, with the collaboration of Miss Hume, have completed an exhaustive study of the vitamin content of the fresh leaves of spinach (*Spinacia oleracea*), this material being selected for study as being available at all seasons of the year and acceptable to the experimental animals. Winter spinach, while rich in vitamin A, was found to be devoid of any appreciable action on calcium-deposition as judged by the analysis of the skeleton of the experimental animals. Summer spinach, grown under the maximum conditions of natural illumination contained small but appreciable amounts of vitamin D, while similar material irradiated with ultra-violet light from a mercury vapour arc lamp was found to be potently antirachitic. This discrepancy between the effect of natural and artificial illumination remains unexplained, but is consistent with the result recently published of Hess, Weinstock, and Sherman, showing that natural sunlight is without effect upon pure cholesterol, which acquires anti-rachitic properties if irradiated with ultra-violet light from artificial sources. In the prevention of rickets, the biological action of these two types of illumination has been found to be identical, and it may be that the difference noted in this instance is caused by quantitative differences in the intensity of irradiation with light of a particular wave length. In any case, the result has an important bearing upon the current theories regarding the source of antirachitic vitamin in nature and its existence in fish-liver oils. It is generally supposed that the antirachitic properties of these oils can be traced ultimately to the marine plant life which supplies the food of the smaller marine animals and thus indirectly of the larger fish. This theory can hardly be accepted if marine green algae should prove to be as poor a source of vitamin D as the green leaves of land plants. Miss Leigh Clare, therefore, is re-investigating the vitamin content of the common marine green diatom, *Nitzschia*, known to be a rich source of vitamin A, but of which the antirachitic value has not yet been investigated.

Dr. M. A. Boas has concluded a study of the antirachitic value of the fresh leaves of winter spinach by means of metabolic experiments in which the calcium and phosphorus retention of young rats was directly measured. The rats were maintained on a diet deprived of fat-soluble vitamins. No improvement in the rate of Ca retention was observed as the result of this treatment and the conclusion has been drawn that winter spinach contains amounts of vitamin D which are negligible as compared with its content of vitamin A.

Cow's Milk. From the investigations of Dr. Ethel M. Luce, carried out in this Department (1922-1924) on the influence of diet and management of the cow upon the vitamin content of the milk, it appeared that diet was the principal factor concerned in the vitamin A value of the milk. Her experiments, however, did not yield conclusive results as to the conditions responsible for the antirachitic vitamin D value of the milk. The importance of the subject appeared to warrant expenditure of more time and energy in an attempt to settle this point. Accordingly, Dr. Chick, jointly with Miss Roscoe, has investigated the effect of a complete set of changes in diet and illumination upon the milk yielded by a cow. The results of the new investigations, which are now being prepared for publication, confirm those of Dr. Luce in showing (1) maximal value of both vitamins to be present in the milk when the cow is fed on pasture in summer, (2) that diet is the important factor determining the vitamin A content. This is unaffected by the degree of insolation enjoyed by the cow. With regard to the antirachitic value (vitamin D content) of the milk, however, the influence of diet appears to be almost negligible, the degree of illumination of the cow being the determining factor. It was immaterial whether the animal were fed upon fresh green grass or on the usual winter feed of cereals and roots. The work has been carried out as before with the co-operation of Dr. MacConkey and his staff at Elstree, where the cow has been kept under strictly controlled conditions.

III. Comparison of Biological and Colorimetric Methods of Titrating Vitamin A. The League of Nations Conference on Standardisation of Biological Remedies, meeting in Geneva in September, 1925, under the Chairmanship of Dr. H. H. Dale, undertook to arrange for an impartial comparative test to be made of the existing biological methods for titrating vitamin A and the colorimetric method recently described by Drummond and Rosenheim. Professor Poulsson (Oslo) provided six samples of Norwegian cod-liver oil, and it was arranged that the vitamin A value should be determined colorimetrically by Dr. Rosenheim, and biologically in six independent laboratories, two in the United States and four in this country. Among the latter the Lister Institute was requested to carry out the biological tests. This work, which is already in progress, has been entrusted to Miss K. M. Soames, assisted by Miss Leigh Clare, both working in this Department with grants from the Medical Research Council. In order to obtain a comparison of more general usefulness, the investigation is being extended beyond the requirements of the League's Committee so as to include oils and fats of other origin. Titration of the antirachitic value is also being included.

The unsaponifiable matter of cod liver oil, freed from cholesterol and purified by Professor Drummond by fractional distillation *in vacuo*, has been tested biologically by Miss Soames for the vitamin A and vitamin D content of the different fractions. From the results obtained it would appear that the vitamin A, as demonstrated by colour tests, is more readily destroyed than the vitamin D by steam distillation and subsequent distillation *in vacuo*. Further tests, with improved technique, will be carried out for the exact determination of the vitamin A content of the different fractions.

The Influence of Dehydration upon the Nutritive Properties of Egg-White. Dr. Margaret A. Boas (*Beit Memorial Research Fellow*) has continued the investigation of this problem. She has found that when raw egg-white is dehydrated either by means of evaporation at temperatures below the coagulation point in presence of air or *in vacuo*, or by treatment with alcohol, it suffers some fundamental change. The use of such preparations of egg-white as the sole protein in an otherwise complete diet is invariably followed by the development by the experimental rats of the definite train of symptoms described in last year's report. It is not yet clear whether the change in the egg-white consists in the production of some toxic substance or whether some dietary essential, not present in the rest of the diet, has been destroyed. In support of the latter hypothesis is the discovery that certain substances, such as raw potato, when added in sufficient quantity to the experimental diet, possess the power of rendering it a satisfactory one for growth and well being. It is hoped that a series of more extensive experiments now in progress will throw further light upon this complicated problem.

Biological Action of Light. Miss E. M. Hume and Miss H. Henderson Smith have completed their researches on the influence of pine sawdust irradiated with ultra-violet light upon the growth and calcification of rats fed on a diet deficient in fat-soluble vitamins. The means by which the irradiated sawdust acts upon the rats has been investigated, and it has been definitely proved that the sawdust exercises no action when a transparent quartz plate is interposed between it and the rat, thereby showing that no secondary radiations are given off, capable of influencing growth and calcification in the rat. It is also concluded that, in spite of certain indications to the contrary, there is no real evidence that the irradiated sawdust can exercise any antirachitic action, except when it is actually eaten by the rats.

Dr. N. S. Lucas, working at the same problem, has obtained results in accordance with the observations of Miss Hume. Irradiated wood, sawdust or cholesterol, if placed near, though not in contact, were shown to have acquired the property of fogging a photographic plate, but the effect could not be demonstrated if a quartz plate was interposed with air tight joints. The conclusion drawn is that these materials after irradiation give off some gaseous emanation, probably hydrogen peroxide, capable of reducing silver salts, but that there is no evidence that they emit any radiant energy.

Miss Hume and Miss Henderson Smith, in conjunction with Dr. Lucas, are now engaged in a study of the mechanism by which ultra-violet light acts upon the skin of animals in the prevention of rickets. This work includes an investigation of the permeability of skin for pre-formed vitamin A when applied as irradiated cholesterol. Observations have been carried out upon the growth of rats and the prevention of rickets in rabbits, when irradiated cholesterol is rubbed into the shaved skin, the animals being maintained on the appropriate defective diets. These experiments present considerable technical difficulty, the chief problem being to ensure that none of the irradiated cholesterol reaches the animal's mouth. Some, however, have been successfully carried out with promising results. Those so far obtained appear to indicate that the growth of young rats on a defective diet can be stimulated, and rickets in young rats and rabbits can be prevented by the absorption of irradiated cholesterol through the skin.

Dr. Lucas is also engaged in re-investigating the transparency of human and animal skin for ultra-violet light of various wave lengths. Observations on this subject have not been made for twenty years, and meantime the methods available have improved and better quantitative measurements can be made.

Coagulation of Blood. Dr. Barratt has repeated and extended his observations on the anti-coagulant effect of hirudin. The conclusions already reached have been confirmed and additional data, bearing upon the nature of anti-coagulant action, obtained; the latter have enabled an approximate estimate of the physical constants of the equation representing the interaction of hirudin and thrombin to be made. The technique of experiment has been developed and to some extent simplified.

The curve obtained by plotting the period of coagulation of fibrinogen against the amount of thrombin added to produce clotting has been the subject of further study and numerous experiments have been made with the object of ascertaining the respective modifications of the character of the curve, brought about when extremely high and exceedingly low concentrations of thrombin are employed. The applicability of various hypotheses, in explanation of the experimental results obtained is being tested by appropriate experiments.

Endocrinology. Professor Korenchevsky, in co-operation with the staffs of several London hospitals, has studied the influence of extracts made from the adrenal glands in the treatment of senility and tuberculosis. The results obtained by the use of glycerol emulsions prepared from the adrenals of bulls have shown only a slight improvement in the intelligence and memory of senile patients and no appreciable change in tuberculous patients.

Jointly with Miss M. Carr, Professor Korenchevsky has determined the influence of injecting emulsions prepared from the testes and prostate gland on the N-metabolism of rabbits. Insulin-like substances have been isolated from testes and these, when injected into rabbits, produce the same influence upon the N-metabolism and urinary flow as emulsions made from the whole testis. This similarity suggests that the fall in N-metabolism produced by injections of testis emulsion is in part due to the presence of insulin-like substances in these glands.

Experiments on thyroidectomised rabbits have shown that thyroid hormones appear to counter-balance the depressive influence on the N-metabolism of rabbits produced by injection of insulin or emulsions of testes. Injections of prostate emulsion caused a considerable increase in the N-metabolism of normal rabbits but when injected into thyroidectomised rabbits caused no increase. This suggests that the prostate gland secretion acts indirectly by stimulating the activity of the thyroid gland.

Professor Korenchevsky has also devised useful modifications of the method for the study of N-metabolism in rabbits by means of which more accurate results are obtained.

Cancer Research. Dr. T. Lumsden has continued his investigations on the effects of antisera on mouse carcinoma and rat sarcoma. He has found that when a sarcoma had been implanted in each hind foot of a rat, injection of anti-serum into one of these tumours along with coincident stoppage of the circulation caused retrogression of this growth, and that a week or so later the untreated tumour of the other foot invariably began to be absorbed. When both tumours had disappeared the rat was found to be immune to further implantations of sarcoma in any part of the body. Dr. Lumsden has also shown that when a fragment of the sarcoma, to which the animal is now immune, is cultured *in vitro* in the rat's own serum along side the tissues of such an immunised rat, both normal and malignant tissues grow freely. This appears to indicate that the acquired immunity to the sarcoma is not humoral.

Dr. Lumsden has recently found that an anti-serum obtained from a sheep by inoculating it repeatedly with human breast cancer kills cultured mouse carcinoma cells rapidly, while it is non-toxic to the normal mouse tissue. Tests are now being made to ascertain whether, conversely, an anti-mouse cancer serum will kill human cancer cells.

Miss A. C. Kohn Speyer, who has joined the department as a voluntary worker, has during the last six months been assisting Dr. Lumsden in the technical part of his experiments.

Department for the Study and Preparation of Antitoxic Sera.

Scarlet Fever Antitoxin. The preparation of Scarlet Fever Antitoxin has been continued in view of the publication recently, both in this country and in America, of a number of papers on this subject and supplies have been sent for trial to various Clinicians. It appears that the type of Scarlet Fever occurring in England at the present time is of so mild a character that it is very difficult to be certain of

the effect of the antitoxin upon the course of the disease. First impressions suggest that the administration of Scarlet Fever antitoxin may prove eventually to be the best method of treatment. Further attempts have been made to find some means of testing this serum by the use of laboratory animals, but unfortunately entirely without success, and we are thus still obliged to rely on the human subject.

Puerperal Fever. The high mortality from puerperal sepsis has recently occasioned much concern. Through the kindness of Sir Almroth Wright a number of strains of streptococci which had been isolated from cases of this disease have been obtained and used in the preparation of a serum which is now ready for trial.

Antidysentery Serum Standardisation. Continued study of this question indicates that more consistent results are obtained when a completely soluble toxin, such as the filtrate of a broth culture, is used instead of a dried powder of the bacillary bodies. The opinion of the French investigators that these liquid broth toxins, after a stage of early deterioration, finally become stable seems warranted, judging by the experiments that have been made in the Institute's laboratories.

Following on the agreement arrived at by the Geneva Conference of 1924, referred to last year, a small supply of the proposed Standard Dysentery toxin and Standard Antitoxin was received in the autumn from the State Serum Institute in Copenhagen. The results so far obtained with these standard preparations confirm those obtained in the Copenhagen laboratories. The proposed unit of the Standard antitoxin neutralises 10 lethal doses of the Standard toxin, but it neutralises 25 lethal doses of a liquid toxin which has been used in the department in some of the routine testing. This emphasises the necessity of basing all tests of the potency of an Antidysentery serum upon a standard antitoxin, as is done in the case of Diphtheria antitoxin and Tetanus antitoxin.

Antiplague Serum. Experiments have been carried out on the testing of Antiplague serum by the intravenous method on mice. The results so far are encouraging and point to this method being more reliable and more economical than that in which rats are used.

Active Immunisation of Horses against Tetanus. Further study of this question has shown that a prophylactic course of inoculations of tetanus toxin, totalling some 400,000 minimal lethal doses, cannot be relied on to protect in every case for more than three years, as in some horses thus immunised the antitoxin content of the blood seems to be on the border line of safety after this period. A communication on this subject is in course of publication.

Anatoxin. Recently it has been stated that the use of "anatoxin" (formalised toxin) for the immunisation of horses produced better results than when immunisation was carried out in the usual way. Several horses have been treated with diphtheria anatoxin and the results appear to depend upon the strength of the original toxin. This is in accordance with what was already known, namely, that a high titre toxin, which had changed in large part to "toxoid" while being kept for some time at room temperature, was better for immunisation purposes than fresh toxin of the same titre. Further, the preparation of antiscorpion serum by injection of horses with formalised scorpion venom has yielded excellent results and has greatly facilitated the process of immunisation.

Immunisation of Horses with Sarcoma Cells. In connection with Dr. Lumsden's work at Chelsea, assistance has been given by immunising horses with sarcomatous material with a view to securing sufficient cytolytic serum for experimental research.

As in past years, the Governing Body has pleasure in expressing its thanks to the Director of the Hygienic Laboratory, U.S.A. Public Health Service, Washington, for his continued kindness in sending supplies of standard antitoxin.

Department for the Preparation and Study of Anti-variola Virus.

Dr. Green has continued his experiments on the artificial culture of the vaccine virus. Some work has also been carried out with regard to the raising of the virulence of the virus on animals. Further work on the filterability of the vaccine virus has been begun by Dr. Green in continuation of a series of experiments he made some years ago.

FOOT AND MOUTH DISEASE RESEARCH.

The work for the **Foot and Mouth Disease Research Committee** of the Ministry of Agriculture has continued as during 1924-5, under the supervision of Dr. Arkwright, in the laboratory specially set apart for the purpose. Dr. Bedson, Dr. Maitland and Mrs. Burbury have been occupied with investigations on this disease. Dr. Bedson resigned to take up another post on 1st March, 1926.

A First Progress Report by the Foot and Mouth Research Committee embodying the results obtained at the Lister Institute, with other researches from the Laboratory of the Ministry of Agriculture, was published by H. M. Stationery Office, in 1925, and in December, 1925, a paper by Drs. Arkwright, Bedson

and Maitland, and Mrs Burbury containing an account of the same observations with greater scientific detail was published in the *Journal of Comparative Pathology and Therapeutics*. There has been a considerable advance in our knowledge of the disease as a result of this work especially as regards (1) the very high potency of Foot and Mouth virus derived from guinea-pigs; (2) the technique of testing for the presence and potency of the virus; (3) the means of preserving sterile filtered virus; and (4) the resistance of the virus to adverse chemical and physical conditions, notably as regards exposure to alcohol and chloroform. Very many experiments have been made in the hope of obtaining means for securing the multiplication of the virus *in vitro* but none has proved successful and the claims of certain German workers in this direction have not been confirmed. The infectivity of Foot and Mouth virus for several British rodents as well as for tame laboratory varieties of this class of animal has been investigated and to a certain extent demonstrated but the limits of their susceptibility have been found such as to discourage the view that they are a common source of infection in the field.

NATIONAL COLLECTION OF TYPE CULTURES.

The past year has seen continued progress in the work of the department, over 2,000 strains being maintained. It is to be regretted, however, that owing to illness, the Curator, Dr. R. St. John Brooks, has had to take long leave of absence to recuperate. Since January, 1926, Dr. J. H. Burnet (Melbourne) has been giving part-time service to the department.

Over 4,000 cultures were distributed during the year.

A second edition of the catalogue was issued in the autumn of 1925.

GENERAL AND FINANCIAL.

In previous reports reference has been made to a legacy under the Will of Mr. W. H. Clarke, of which the sum of £6,750 had been received. A further £300 was received in 1925 on account of this bequest and early in 1926 a further £64 5s. 7d. was received as the balance of the bequest, which amounts in all to £7 11s. 7d.

A bequest of scientific apparatus, including three valuable microscopes has been received under the Will of the late Mr. C. J. Wilson, of Shackleford, Godalming.

The Accounts and Balance Sheet for the year ended December 31st, 1925, show balances to the credit of the Pension Fund of £22,040 2s., the Sinking Fund of £14,052 12s. 9d., and the Capital Fund of £498,195 0s. 5d., the latter figure including the credit balance of £14,420 17s. from the year's working.

No necessity of drawing upon the Contingency Fund arose in the period under review, and this remains unaltered at £14,228 18s. 1d.

Various items of apparatus, etc., to the value of £819 10s. 7d. which have appeared in the Balance Sheet without depreciation since 1903 have been written off, and Hill View Cottage, Hayle, purchased for £678 6s. has been sold, owing to the removal of the Anti-Variolous department to Marazion.

Investments made during the year were: For the General Fund, £15,000 Conversion Loan 4½% Stock; for the Sinking Fund, £1,800 Conversion Loan 3½% Stock; and for the Pension Fund, £4,000 Conversion Loan 3½% Stock.

Receipts from the sales of the Institute's products and investigation fees show a net increase of £2,039 11s. 4d. compared with last year, viz., Anti-variolous vaccine increase, £4,623 19s. 10d.; Anti-toxins and Sera increase, £3,144 12s.; Diagnosis Fees increase £574 1s. 11d. and Bacterial Vaccines decrease £6,303 2s. 5d. The sales of the latter products in 1924 were, however, exceptionally high.

The total expenditure for the year was £36,502 15s. 9d. against £37,453 in 1924. Rent, Rates, Taxes, and Insurance and Gas, Water and Fuel show a decrease, and Serum and Calf Lymph Laboratories Expenses and Repairs, Renewals and Alterations an increase compared with last year. No contribution to the Pension Fund has been made this year.

In conclusion, the Governing Body desire to express their appreciation of the devoted co-operation of the Director and all members of the Staff in carrying out the work of the Institute.

ERNEST H. STARLING.

Acting Chairman of the Governing Body.

BALANCE SHEET

AND

ACCOUNTS.

Dr.

The Lister Institute

BALANCE SHEET

	£	s.	d.	£	s.	d.	£	s.	d.	£	s.	d.
To CREDITORS										1,428	10	2
To PENSION FUND—												
Balance at 31st December, 1924							21,034	5	6			
Add												
Balance of Income and Expenditure Account, 1925							1,005	16	6			
										22,040	2	0
To JENNER MEMORIAL RESEARCH STUDENTSHIP FUND—												
As per Account 31st December, 1924							7,869	10	10			
Add												
Balance of Income and Expenditure Account, 1925.. ..							210	8	11			
										8,079	19	9
To CONTINGENCY FUND—												
As per Account 31st December, 1923										14,228	18	1
To SINKING FUND to 31st December, 1925										14,052	12	9
To CAPITAL FUND to 31st December, 1925—												
Balance of Income and Expenditure to 31st December, 1924						129,889	10	0				
Less written off												
Farm Stable Utensils, Implements and Sheds	138	1	4									
,, Laboratory Apparatus	466	1	3									
,, Furniture	215	8	0									
							819	10	7			
						129,069	19	5				
Donations, &c., received to date from the following:—												
Dr. Ludwig Mond (1893)						2,000	0	0				
The Berridge Trustees (1893/98)						46,379	10	1				
The Grocers' Company (1894)						10,000	0	0				
Lord Iveagh (1900)						250,000	0	0				
Lord Lister's Bequest (1913) as per Account at 31st December, 1923						18,904	5	8				
William Henry Clarke Bequest (1923/5)						7,050	0	0				
Other Donations (1891-1920)						20,870	8	8				
Add									483,774	3	5	
Balance of Income and Expenditure Account, 1925									14,420	17	0	
										498,195	0	5

ERNEST H. STARLING, *Acting Chairman.*

G. W. ADDISON, *Hon. Treasurer.*

£558,025 3 2

REPORT OF THE AUDITORS

We have audited the above Balance Sheet. We have obtained all the information and explanations we have required. sum of £19,816 4s. 11d. has been paid, being held by the Institute on behalf of the Scientific Staff. In our opinion, such affairs, according to the best of our information and the explanations given to us and as shown by the books of the Institute. London, March 19th, 1926.

of Preventive Medicine.

31st DECEMBER, 1925.

Cr.

		£	s.	d.	£	s.	d.
By CASH—							
At Bankers:	Deposit Account	8,000	0	0			
	Current Accounts	4,954	5	0			
	In hand	89	0	9	13,043	14	9
By INVESTMENTS (at cost)—							
£5,000	London & North Eastern Railway 3 per cent. Debenture Stock ..	4,570	11	0			
£8,650	London, Midland & Scottish Railway 4 per cent. Preference Stock ..	10,460	8	6			
£5,000	Great Central and Midland Railway Joint Committee 3½ per cent. Guaranteed Stock	5,123	19	3			
£2,900	New South Wales 5½ per cent. Stock, 1922-32	2,897	16	0			
£1,000	Cape of Good Hope 3½ per cent. Stock	1,000	0	0			
£1,505 7s. 3d.	New South Wales 4 per cent. Stock, 1942-62	1,500	0	0			
£353	London & North Eastern Railway 4 per cent. First Guaranteed Stock ..	499	11	0			
£45,500	5 per cent. War Stock, 1920-1947	42,633	14	3			
£21,000	4 per cent. Funding Stock, 1960-1990	17,667	0	1			
£20,000	Local Loans 3% Stock	9,962	0	7			
£18,000	Conversion Loan 4½ per cent. Stock, 1940/44	17,492	11	0	113,807	11	8
By INVESTMENTS, LORD IVEAGH'S DONATION (at cost)—							
£23,006 2s. 6d.	New Zealand Government 3 per cent. Inscribed Stock, 1945 ..	24,117	17	6			
£23,000	Victorian Government 3 per cent. Inscribed Stock, 1929-1949 ..	23,875	0	0			
£25,000	Natal 3 per cent. Inscribed Stock, 1929-1949	24,484	7	6			
£25,000	New South Wales Government 3 per cent. Inscribed Stock, 1935..	24,937	10	0			
£26,100	South Australian Government 3 per cent. Consolidated Stock, 1916 or after ..	24,860	5	0			
£25,000	Cape of Good Hope 3 per cent. Inscribed Stock, 1933-1943 ..	23,850	0	0			
£20,000	Southern Railway Preferred Ordinary Stock	32,000	0	0			
£18,750	London & North Eastern Railway 4 per cent. First Preference Stock ..	26,000	0	0			
£13,625	London, Midland & Scottish Railway 4 per cent. Preference Stock, 1923 ..	20,375	0	0			
£25,000	East Indian Railway 3 per cent. New Debenture Stock	25,500	0	0	250,000	0	0
By INVESTMENTS, JENNER MEMORIAL RESEARCH STUDENTSHIP FUND (at cost)—							
£2,650	Southwark and Vauxhall Water Co. 3 per cent. Debenture Stock "B" ..	2,756	10	0			
£1,396	Southern Railway 5 per cent. Preference Stock	2,740	5	0			
£726 11s. 4d.	Liverpool Corporation 3 per cent. Stock 1942 or after ..	556	15	6			
£2,000	4 per cent. Funding Stock, 1960/90	1,797	14	0			
	Balance uninvested	228	15	3	8,079	19	9
By INVESTMENTS, LORD LISTER'S BEQUEST (at cost)—							
£1,937	Grand Trunk Railway Company of Canada 4 per cent. Guaranteed Stock ..	1,733	12	4			
£800	Grand Trunk Railway Company of Canada Great Western Borrowed Capital 5 per cent. Perpetual Debenture Stock	936	0	0			
£1,875	Port of London 4 per cent. B. Stock	1,800	0	0			
£3,400	Gas Light and Coke Company Ordinary Stock	3,638	0	0			
£800	Ontario and Quebec Railway 5 per cent. Debenture Stock	984	0	0			
£661	Madras and Southern Mahratta Railway 4 per cent. Debenture Stock ..	656	19	7			
£800	Canada 4 per cent. Stock, 1940-1960	492	11	0			
£700	Western Australia 4 per cent. Stock, 1942-1962	698	7	0			
£600	Union of South Africa 4 per cent. Stock, 1943-1963.. .. .	594	2	0			
£1,200	London & North Eastern Railway 3 per cent. Debenture Stock ..	891	2	9			
£8,467	4 per cent. Funding Stock, 1960-1990	6,479	11	0	18,904	5	8
By INVESTMENTS, SINKING FUND (at cost)—							
£7,570 10s. 0d.	Conversion Loan 4½ per cent. Stock, 1940/44	6,916	12	7			
£5,550	4 per cent. Funding Stock, 1960-1990	4,227	17	7			
£4,100	Conversion Loan 3½ per cent. Stock	3,187	19	6	14,282	9	8
By INVESTMENTS, PENSION FUND (at cost)—							
£22,000	4 per cent. Funding Stock, 1960-1990	17,165	8	5			
£6,000	Conversion Loan 3½ per cent. Stock	4,650	10	8			
	Balance uninvested	224	7	11	22,040	2	0
(The above Investments, at the market value, 31st December, 1925 show a depreciation of approximately £20,535.)							
By LOANS ON MORTGAGES					7,000	0	0
By DEBTORS					8,710	0	0
By FURNITURE, FITTINGS, SCIENTIFIC APPARATUS AND BOOKS—							
	As per account, 31st December, 1920				2,471	17	2
By EXPENDITURE ON INSTITUTE BUILDINGS AT CHELSEA—							
	As per account, 31st December, 1910, including purchase of freehold site, £5,000 ..				70,916	3	1
By PURCHASE OF FREEHOLD LAND ADJOINING "THE STUDIOS," CHELSEA, as per account, 31st December, 1912					169	6	8
By LEASE OF "THE STUDIOS," CHELSEA, as per last account		1,848	8	9			
	Less Amount written off	65	2	0	1,783	6	9
By QUEENSBERRY LODGE FARM, ELSTREE—							
	Purchase of freehold land and buildings and Expenditure on new buildings, as per account, 31st December, 1912.. .. .				20,455	10	0
	Stock of Animals and Forage	963	16	1			
	Stock of Anti-Toxins and Bottles	5,996	19	11			
					6,360	16	0

* Nothing has been charged for depreciation of Furniture, &c. since new purchases made during the year to a greater amount than the estimated depreciation (10%) have been written off.

£558,025 3 2

TO THE MEMBERS.

The Superaunuation Scheme for the Scientific Staff provides for Life Policies and National Savings Certificates for which the Balance Sheet is full and fair, and properly drawn up so as to exhibit a true and correct view of the state of the Institute's

COOPER BROTHERS & CO.,

Chartered Accountants. } Auditors.

Dr. INCOME AND EXPENDITURE ACCOUNTS

INCOME.					£	s.	d.
To Interest and Dividends on General Investments	...	...	...	...	14,043	14	9
To Interest and Dividends on Sinking Fund Investments	...	...	...	...	632	19	2
To Investigation, Diagnosis and Analysis Fees, &c. ...	...	...	...	...	4,216	0	5
To Sales of Sera, Vaccines, &c., and Stock at 31st December, 1925, less Stock at 31st December, 1924	...	...	...	...	31,698	18	5
To Rent of Rooms in the Institute, &c.	...	...	...	...	332	0	0

£50,923 12 9

Dr.

Pension

	£	s.	d.
To Interest and Dividends on Investments	1,005	16	6
	£1,005	16	6

Dr.

Jenner Memorial Research

	£	s.	d.
To Interest and Dividends on Investments	252	2	8
	£252	2	8

Preventive Medicine.

for the year ending 31st December, 1925.

Cr.

EXPENDITURE.								£	s.	d.
By Rent, Rates, Taxes and Insurance	...	...	...	...	...	...	...	8,362	9	1
By Salaries and Wages of Staff	...	...	...	...	...	...	...	18,712	0	1
By Premiums on Federated Superannuation Policies	...	...	...	...	...	...	...	968	13	0
By Stationery, Printing and Postage	...	...	...	...	...	...	...	340	4	5
By Printing of Collected Papers	...	...	...	...	...	...	...	278	13	10
By Office Expenses, Law Charges, and Sundries	...	...	...	...	...	...	...	234	16	5
By Travelling Expenses	...	...	...	...	...	...	...	15	12	7
By Auditors' Fee	...	...	...	...	...	...	...	60	0	0
By Gas, Water and Fuel	...	...	...	...	...	...	...	1,298	17	4
By Electric Light and Power	...	...	...	...	...	...	...	361	4	4
By Experimental Pathology Laboratory Expenses, including General Apparatus	...	...	...	...	...	...	...	535	19	2
By Bacteriological Laboratory Expenses, including Apparatus	...	...	...	...	...	...	...	373	13	3
By Vaccine Laboratory Expenses, including Bottles	...	...	...	...	...	...	...	120	2	1
By Water and Bio-chemical Laboratory Expenses, including Apparatus	...	...	...	...	...	...	...	575	16	10
By Serum and Calf Lymph Laboratories Expenses, including Apparatus and Cost of Bottles	...	...	...	...	...	...	...	2,507	16	1
By Culture Media	...	...	...	...	...	...	...	112	12	9
By Animals	...	...	...	...	...	...	...	1,581	8	9
By Animal House Expenses and Forage	...	...	...	...	...	...	...	1,473	2	3
By Repairs, Renewals and Alterations, including Workshop Expenses	...	...	...	...	...	...	...	1,694	19	11
By Library Expenses	...	...	...	...	...	...	...	267	15	4
By General Stores	...	...	...	...	...	...	...	366	19	9
By Bad Debts	...	...	...	...	...	...	...	7	18	9
By Loss on Sale of "Hill View" Cottage, Hayle	...	...	...	...	...	...	...	143	5	0
By Depreciation of the Lease of "The Studios," Chelsea	...	...	...	...	...	...	...	65	2	0
By Sinking Fund ($\frac{1}{2}$ % per annum on Cost of Buildings and Interest on Investments)	...	...	...	...	...	...	...	1,048	12	9
By Balance, being Excess of Income over Expenditure, transferred to Balance Sheet	...	...	...	...	...	...	...	14,420	17	0
								£50,923	12	9

Fund.

Cr.

By Balance, being Excess of Income over Expenditure, transferred to Balance Sheet	£	s.	d.
	1,005	16	6
	£1,005	16	6

Studentship Fund.

Cr.

By Salary—Dr. H. M. Woodcock	£	s.	d.
	41	18	4
By Balance, being Excess of Income over Expenditure, transferred to Balance Sheet	210	8	11
	£252	2	3

SCIENTIFIC PAPERS PUBLISHED FROM THE LABORATORIES OF THE INSTITUTE DURING THE YEAR.



- | | |
|---|--|
| <p>ARKWRIGHT, J. A., BURBURY, MAISIE, BEDSON, S.P., AND MAITLAND, H. B.</p> | <p>OBSERVATIONS ON FOOT-AND-MOUTH DISEASE. I. TRANSMISSION OF FOOT AND MOUTH DISEASE TO RODENTS. II. THE ATTEMPTED CULTIVATION OF THE VIRUS AND ITS REACTION TO VARIOUS AGENTS, CHEMICAL AND PHYSICAL. <i>Journal of Comparative Pathology and Therapeutics</i>, Vol. XXXVIII., 1925.</p> |
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| <p>BALTEANU, J. G. ...</p> | <p>THE RECEPTOR STRUCTURE OF <i>V. cholerae</i>.</p> |
| <p>" " ...</p> | <p>VARIATIONS IN CHOLERA AND CHOLERA-LIKE ORGANISMS. <i>Journal of Pathology and Bacteriology</i>, Vol. XXIX., 1926.</p> |
| <p>BARRATT, J. O. W. ...</p> | <p>HYDROLYTIC DISSOCIATION CURVES. <i>Biochemical Journal</i>, Vol. XIX., 1925.</p> |
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| <p>BEDSON, S. P. </p> | <p>(See ARKWRIGHT, J. A.)</p> |
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| <p>CARR, MARJORIE ...</p> | <p>(See KORENCHEVSKY, V.)</p> |
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THE LISTER INSTITUTE
OF
PREVENTIVE MEDICINE.

Report of the Governing Body,
1927.

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

May 18th, 1927.

The Lister Institute of Preventive Medicine,

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ELSTREE, HERTS; MARAZION, CORNWALL.

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THE STAFF.

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Department for the Preparation and Study of Anti-Variolous Vaccine, Marazion :

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Accountant :

GEORGE COOPER.

Secretary :

A. L. WHITE.

NATIONAL COLLECTION OF TYPE CULTURES.

(*Medical Research Council.*)

Director :

PROFESSOR J. C. G. LEDINGHAM, C.M.G., D.Sc., M.B., F.R.S.

Curator :

R. ST. JOHN BROOKS, M.A., M.D., D.P.H.

Assistant Curator :

MABEL RHODES.

**A recognised Teacher of the University of London.*

ANNUAL GENERAL MEETING
OF
The Lister Institute of Preventive Medicine,
May 18th, 1927.

REPORT OF THE GOVERNING BODY.

The Governing Body has the honour to present the Institute's 33rd Annual Report.

THE LISTER CENTENARY.

The celebration of the 100th anniversary of the birth of Lord Lister took place in April. In response to an invitation from the Royal Society, the Royal College of Physicians, and the Royal College of Surgeons, over one hundred delegates of learned societies of Great Britain and other countries assembled in London to render homage to his memory.

In the absence of Sir David Bruce, the Institute was represented at the ceremony by Sir James K. Fowler who presented the following address from the Governing Body and Staff of the Institute:

"THE GOVERNING BODY and STAFF of the LISTER INSTITUTE OF PREVENTIVE MEDICINE rejoice in the opportunity afforded by the PRESIDENT OF THE ROYAL SOCIETY, THE PRESIDENT OF THE ROYAL COLLEGE OF PHYSICIANS and THE PRESIDENT OF THE ROYAL COLLEGE OF SURGEONS of joining in the Celebration of the Centenary of the birth of one of the greatest discoverers in the realm of Preventive Medicine.

LISTER, alone of his profession, because his mind was prepared by his researches into the nature of inflammation and suppuration, perceived the full significance for Surgery of PASTEUR'S researches upon fermentation and putrefaction. He inferred that the disastrous complications which were wont to follow wounds and surgical operations were, like putrefaction, due to the chemical activities of germs introduced into the wound and by ingenious experiments he proved the accuracy of this assumption.

LISTER'S development of the Antiseptic System of treating wounds relieved mankind from most of the danger and suffering attendant upon surgical operations and permitted the art of Surgery to advance to unimagined achievements. The obliteration of wound infection which followed the successful practice of antiseptics was, moreover, a stimulus to research into the causation of infectious diseases generally, research with which LISTER manifested the greatest sympathy, because he, like PASTEUR, was convinced that infectious diseases would be found to depend upon the invasion of the body by the lower world of microbes.

Firm in his belief, LISTER took a leading part in establishing in this country an Institute for the experimental study of the causation of disease. As a result of his efforts, together with those of a small band of scientific men, the BRITISH INSTITUTE OF PREVENTIVE MEDICINE, which now bears his honoured name, was incorporated in 1891. He was the first Chairman of the Council of the Institute and subsequently its beloved President and during his life he never ceased to take a keen interest in its development."

Members of the Governing Body and Staff also attended the Memorial Service held in Westminster Abbey, on April 6th, when a wreath from the workers at the Institute was laid under the medallion of Lord Lister.

GOVERNING BODY.

At the meeting held last year, the Council re-elected Professor W. Bulloch, Sir James K. Fowler and Professor A. E. Boycott to represent it until December 31st, 1927.

Sir David Bruce has been appointed by the Governing Body as the representative of the Institute upon the Court of Governors of the London School of Hygiene and Tropical Medicine.

As this report was being printed news came of the sudden death of Professor Starling whilst on a short voyage for the benefit of his health. Professor Starling has been a member of the Governing Body for twenty years during which time he has been unsparing in his efforts on behalf of the Institute. On frequent occasions he has acted as Chairman of the Board which brought him into close association with the staff and other scientific workers to whom, as well as to his colleagues on the Governing Body, his death is a great personal loss.

COUNCIL.

At the last Annual Meeting, the retiring members of Council, Sir John Rose Bradford and Sir William J. Simpson, representatives of the Members of the Institute and Mr. George K. Morice, one of the representatives of the Worshipful Company of Grocers, were each re-elected. To the vacancy caused by the death of Sir William Leishman, Dr. Andrew Balfour was elected as a representative of the Members of the Institute.

The three members who retire from the Council by rotation this year, but who are eligible for re-election, are Mr. J. R. Drake, one of the representatives of the Worshipful Company of Grocers, Professor J. M. Purser, the representative of the University of Dublin and the President of the Royal College of Physicians, London.

MEMBERS.

The Governing Body regrets to announce the deaths of Sir William Leishman, Dr. Stephen Paget and Sir Stewart Stockman, who had been members of the Institute for many years.

STAFF.

Dr. E. Atkin resigned his position of Assistant Bacteriologist, in November last, on appointment as Pathologist to the Brompton Hospital.

Dr. J. A. Arkwright, Senior assistant in the Bacteriological department has resigned his position as a salaried member of the staff but will continue to work in the department as heretofore.

Dr. H. B. Maitland, late Assistant Professor of Bacteriology, University of Toronto and recently engaged in research at the Institute under the Foot and Mouth Disease Research Committee of the Ministry of Agriculture has been appointed an assistant in the department of bacteriology.

Dr. H. M. Woodcock and Mr. W. T. J. Morgan, M.Sc., have held the Jenner Memorial and Grocers' Company Research Studentships respectively during the year.

In response to an invitation from the Rockefeller Foundation, Professor Ledingham visited America in April in order to study Dr. Noguchi's method of preparing and standardising his vaccine for yellow fever.

RESEARCH WORK.

Before proceeding to give a brief survey of the researches which are, or have been, in progress during the year in the various departments of the Institute, the Governing Body desires to record its appreciation of the co-operation it has enjoyed with the Medical Research Council, the Department for Scientific and Industrial Research and the British Empire Cancer Campaign. The financial support given by these bodies to skilled investigators in the different departments has greatly increased the scientific activities of the Institute.

In addition to furnishing the salaries of the staff of the National Collection of Type Cultures, an organisation which has proved of great service to bacteriologists and mycologists throughout the Empire, the Medical Research Council has provided the salaries of one worker in the department of bacteriology, Mr. Bruce White, one in the department of biochemistry, Dr. Zilva, five in the department of experimental pathology, Professor Korenchevsky, Miss Hume, Miss Soames, Miss Henderson Smith and Miss Leigh-Clare, and a half time grant to Dr. Woodcock in the department of protozoology.

Dr. Ida Smedley MacLean, who is an honorary assistant in the department of biochemistry, receives a grant from the Department for Scientific and Industrial Research, which body also supplies the salaries of her research assistant, Mr. Daubney, and of a laboratory attendant. The British Empire Cancer Campaign furnishes the salary of Dr. Lumsden and his research assistant, Miss Kohu-Spyer.

Accommodation for all these workers and the expenses of their researches are provided by the Institute.

Department of Bacteriology.

Vaccinia, Variola, and Avian Molluscum. In continuation of his work on the relation of vaccinia virus to the reticulo-endothelial system, Professor Ledingham has published a new series of experiments the results of which show that the dermal reaction to the virus is annulled wholly or partially if Indian ink is simultaneously injected into the cutis with the virus or if the virus is superposed on sites previously infiltrated with Indian Ink. It would appear that the absence of naked-eye response to the virus under these conditions is to be correlated with the increased local defence following the stimulation of the reticulo-endothelial system by the Indian ink. The experimental results support the view previously advanced by him that the virus of vaccinia (or of variola) attacks primarily the reticulo-endothelial elements wherever situated and not epiblastic or epidermal elements as has been alleged. It may be noted also that vaccinia failed to elicit response in the cutis of the rabbit which had previously been the site of an acute inflammatory process caused by injection of erysipelas streptococci. It is of interest in this connexion that failure of vaccinal response has been recently reported on rabbit skin which has been exposed to X-ray and ultra-violet radiation.

Dr. Emerson Megrail (*Western Reserve University, Cleveland, Ohio*) has commenced a series of experiments to test the filterability of *Avian Molluscum* through porcelain and kieselguhr filters and collodion membranes. This virus is generally believed to be capable of passing through Berkefeld filters, though with greatly diminished potency, but it is hoped to secure more reliable data on the matter by accurate titration of the material before and after filtration through the various types of filters employed.

Variation of the Virulence and Antigenic Structure of Bacteria grown *in vitro* and its significance for the preparation of Prophylactic Vaccines.

B. typhosus and *B. paratyphosus*. Dr. Arkwright has continued his study of variations of bacteria. Latterly his observations have been more particularly concerned with *B. typhosus* and *B. paratyphosus* A. and their antigenic constituents. He has studied the properties of the two main kinds of antigen in the Coli-typhoid group of bacteria, namely, the heat-labile and the heat-stable at 100°C. and their relation to the flagellar and somatic antigens of Theobald Smith and the "H" and "O" receptors of Weil and Felix. The heat-labile antigen, which is associated with flagella appears to correspond to the factor responsible for agglutination by acid of *B. typhosus* at the characteristic hydrogen ion concentration for this species *i.e.*, about pH 5; the heat-stable somatic antigen to some extent corresponds to the factor which determines the second optimum for acid agglutination at pH 3 described in his paper on "*The agglutination of watery extracts of B. typhosus*" in 1914. Of the four variants of *B. paratyphosus* A. studied, two which grew as smooth colonies and afforded the heat-stable antigen have been found to be the more virulent and to make a good protective vaccine for guinea-pigs. The two rough variants, which lack this antigen are only very feebly virulent and make relatively inefficient vaccines. The virulence and the value as a vaccine are, therefore, both related to the content of the heat-stable antigen. That this antigen is the constituent which gives efficacy to a vaccine was supported by the finding that the vaccines after heating at 100°C. had, as a rule, unimpaired prophylactic value. The results with *B. typhosus* vaccine were in the same direction but less distinct.

Seven series of experiments on guinea-pigs each inoculated with three or four different vaccines all supported these conclusions. The heat-labile (100°C.) fraction of a culture which is associated with the presence of flagella and motility appears to constitute a relatively unimportant part of the vaccine. The importance of securing a "smooth" virulent culture for making vaccine, has not hitherto been realised, and the conclusion that a temperature of 100°C. is but little harmful is opposed to most previous opinion.

It is intended to extend these observations.

Dr. Dorothy B. Steabben has begun an experimental study of the antibodies corresponding to the heat-stable antigen in the typhoid-paratyphoid group. These antibodies are believed to be differently affected by heat to those produced by the heat-labile antigens. The need for further knowledge on the subject is the greater in view of the important part which the heat-stable antigen is now believed to play in immunity.

B. pseudotuberculosis rodentium. Examination of cultures of *B. pseudotuberculosis rodentium* by Dr. Arkwright with a view to experiments on prophylactic inoculation revealed the fact that cultures of this bacillus are motile when grown at room temperature, but for the most part non-motile when incubated at 37°C. This observation though made first in 1901, in Germany, has been almost entirely ignored by bacteriologists since. This character serves to distinguish the bacillus from *B. pestis* which it has generally been held to resemble in regard to almost every laboratory criterion except virulence for rats.

V. cholerae. Dr. Balteanu (*Rockefeller Foundation Fellow*) has completed his study of *V. cholerae* and established the existence of variants with characteristic antigenic differences corresponding to the "H" and "O" antigens in the coli-typhoid group. These two antigens have been found to be present regularly in the cultures of the normal form, contrary to the opinion of most previous workers.

The Action of Cyanides on Bacteria. Dr. F. M. Burnet (*Beit Memorial Research Fellow*) has completed and published his work on the effect of cyanide and peroxide on bacterial growth. He found that the readily grown pathogenic bacteria could be divided into two clearly defined groups: (A) those whose growth was inhibited by fairly low concentrations of cyanide or peroxide in the medium and (B) those not affected by considerably larger amounts of these agents. Group A comprised the majority of the forms of bacteria studied, while Group B contained the streptococci, some other Gram positive cocci, and probably the pneumococcus. This division was associated with differences in several aspects of the respiratory function of the bacteria and it was concluded that the mechanism of respiration of the organisms in Group B was of an entirely different type from that characteristic of those in Group A and most other aerobic cells and tissues.

The facilitating effect of a heavy local growth of such an organism as the staphylococcus on the growth of isolated organisms of Group A in its vicinity was further analysed. It was concluded that all the phenomena of this type were primarily due to the power of a bacterial colony to maintain a definite level of oxidation-reduction potential in its vicinity and that under such conditions bacteria were better able to withstand various noxious agents than if exposed to an environment of higher *rH*.

Bacteriophage. Since October, Dr. Burnet has been engaged on a study of types of bacteriophage active against *B. enteritidis* (Gaertner) with a view to their use in the treatment of infections in animals by this organism. A large number of phages has been tested and a series of pure types showing specific differences amongst themselves has been isolated. Very characteristic differences between the action of these types on bacteria grown from smooth and rough forms of colony have been found. The suggestion that sensitivity to phage may thus be linked in some way with the nature of the heat-stable agglutinogenic structure has been followed up by an examination of other *Salmonellas*, particularly those having the power of producing O-agglutinins common to *B. enteritidis*. This has led to the conclusion that amongst the *Salmonellas*, at least, the nature of the heat-stable agglutinin is the most important and possibly the only factor determining whether lysis by a given phage will occur. Typical smooth strains of *B. enteritidis*, *B. typhosus* and *B. pullorum*, for instance, are lysed by the same phages and all possess the same O-agglutinogens. With rough variants there is a much more widespread sensitivity, practically all the *Salmonellas* whilst in this state are sensitive to some or all of the phages developed with rough *B. enteritidis*. This corresponds with the serological resemblance in the heat-stable antigens of all rough types of this group. Work on the treatment of mouse infections by a polyvalent mixture of phages active against the infecting organism, has been commenced, but no conclusions have yet been reached.

Scarlet Fever and Streptococci. Dr. G. H. Eagles (*Beit Memorial Research Fellow*) has extended his work on hemolytic streptococci from scarlatina, erysipelas and puerperal fever. Using commercial scarlet fever antitoxin he has found by testing in the human volunteer that all toxic filtrates, regardless of source, are neutralised. Antitoxic sera produced in rabbits by strains from each source tend to show some specificity in their power of neutralisation which would probably disappear from the serum in the later stages of immunization. Immune horse serum produced by inoculation with toxin-producing strains of erysipelas show a considerable degree of neutralizing value for streptococcus filtrates including those from scarlet fever strains.

The possibilities of using intracutaneous tests in goats to avoid the use of human volunteers has been investigated. This has not proved a satisfactory method owing to the high susceptibility of these animals to horse serum. An attempt is, therefore, being made to produce an antitoxic scarlatinal goat serum. When this is ready it is hoped to come to a definite conclusion regarding the goat as a test animal.

The flocculation test of Ramon has been applied to the toxin and antitoxin of scarlet fever. This has been found to be valueless as a means of titration since the test is non-specific and would seem to be in the nature of a bacterial precipitin reaction rather than a toxin-antitoxin effect.

Pasteurella Group of Bacteria. Dr. Schütze has commenced an investigation of the large group of organisms collected under this heading. A satisfactory correlation of the various members has not already been formulated. It is intended, therefore, to ascertain what agglutinogenic relationships exist between the strains which have been isolated from a variety of animals, attention being paid to the more recent methods of antigenic differentiation. Since October, 1926, Dr. J. T. Cornelius, of the Provincial Hygienic Institute of Lucknow, has taken a share in these studies.

The Oxygen Requirements of *B. pestis*. In the course of examining a collection of cultures of *B. pestis* for the presence in them of rough and smooth varieties of these bacilli, Dr. Schütze's attention was drawn to the fact that isolated cells of *B. pestis* did not readily multiply. Satisfactory colonial growth of *B. pestis* was obtained by adding to the culture medium a small amount of sterilised broth culture of *B. pestis* and many other bacteria. The failure of *B. pestis* to propagate when lying isolated on an agar surface is apparently connected with the oxygen tension, for in the depth of an agar shake, growth takes place readily enough. The influence of sterilised broth cultures on the development of surface-colony growth would, therefore, seem to be due to reducing substances present in these broth cultures. As they are rapidly destroyed at temperatures above 70°C. they are probably of an enzymic nature.

Tuberculosis and Diet. The work undertaken by Dr. Schütze in conjunction with Dr. S. S. Zilva on the effect of diet upon the course of tuberculosis in animals, has been brought to a close and

the results have been published in the *Journal of Hygiene*. Guinea-pigs living on a diet restricted in quantity were found to be considerably less resistant to the progress of a tubercular infection than normally fed controls. Experiments on rats produced no evidence of a beneficial effect of sodium chaulmoograte as shown by the course of the development of tubercular tumours in these animals. On the other hand, there was some evidence for assuming that a large excess of cod liver oil, as well as irradiation with ultra-violet light, did inhibit the formation of such tubercular tumours. The leucocytosis often observed under these two forms of treatment does not seem to be the only agent in this inhibition, if it is concerned with it at all.

No evidence was obtained that lack of fat-soluble vitamins renders tubercle infected rats susceptible to tuberculin shock.

Serological Studies of the Salmonella and Dysentery Groups of Bacilli. Mr. Bruce White (grantee of the *Medical Research Council*) has shown [*J. Path. & Bact.* (1927) XXX., 113] that the susceptibility of rough variants of the *Salmonella*, *Coli* and *Dysentery* groups of bacilli to agglutination, in the presence of electrolytes, is immediately due to the hydrophobe properties of the bacterial lipoids. When these substances are removed by organic extractives the salt-sensitiveness of rough variants is lost but returns when the treated organisms are reimpregnated with the extracted substances.

It was further shown that the development of the salt-sensitive character during change to the rough form is not correlated with any actual increase of the salt-sensitive (lipoidal) substances themselves; clearly the ultimate cause of the appearance of this type of spontaneous agglutinability must be the loss of some factor which increases the stability of the suspension in the presence of electrolytes. It is suggested that this factor coincides with the so-called soluble specific substance, the disappearance of which seems to be the cardinal event in variation from the smooth to the rough type of colony. It was also found that the property of certain cultures of agglutinating with *any* serum is due to their alcohol and chloroform-soluble constituents and disappears when these are removed. This method of extraction was also signally successful in stabilising suspensions of such salt-agglutinable organisms as *B. subtilis* and *B. salmonicida*. While, in the case of motile organisms, the labile flagellar antigens are destroyed during this treatment, the stable body substances both in smooth and rough organisms remain unaltered in their antigenic and serological properties.

Other work in progress deals with the classification of intestinal bacilli along new lines.

Dr. D. Kalic (*Rockefeller Foundation Fellow*) has investigated the *typing* of *Dysentery* bacilli. Utilising the V, W, X, Y, Z, Vz and Wx types of Andrewes, the I., II., III., IV., VII., VIII. and X. types of Aoki, and Kruse's Groups A, D, E, H, I, J, it has been found possible, by means of cross-agglutination and cross-absorption tests, to correlate these three systems of classification to a very considerable extent and to confirm the value of the types as natural groups, by observation on a series of unclassified strains.

Trout Furunculosis. Major J. H. Horne, I.M.S., has been investigating the distribution and method of spread of furunculosis in trout, on behalf of the Kennet Valley Fisheries Association.

This disease was not recognised in England till 1911, when Arkwright and Masterman reported its existence, but has since been found in many rivers.

Young fish from trout farms were examined for *B. salmonicida* with a view to detecting the origin of the infection. Diseased and healthy fish, and samples of water from different parts of the rivers were also examined bacteriologically and an attempt made to correlate the disease with sewage pollution. The problem is one of considerable difficulty and the causes of the annual outbreaks and spread have not been discovered.

Department of Biochemistry.

In this department the work in progress last year has been continued and extended.

Alcoholic Fermentation. The reaction which occurs between sugar and phosphate in the course of alcoholic fermentation has been investigated quantitatively by Professor Harden and Lord Hentley, with special reference to the quantities of the mono- and di-phosphoric esters produced. A satisfactory method of estimation has now been worked out and a considerable number of experiments have been made, the results of which have been published.

Professor Harden has also, in collaboration with Miss M. J. Macfarlane, continued his work on fermentation by dried yeast preparations, with the object of ascertaining the cause of the remarkable effect of dilution on this phenomenon.

Professor Katagiri (Japan) has been engaged upon work on the effect of the fatty acids on alcoholic fermentation by living yeast and has extended his experiments to the hydroxy-acids. These, in contrast to the fatty acids, have no specific inhibitory action but behave in a similar manner to inorganic acids such as phosphoric and carbonic acid.

Hexosephosphates and Transformations of Sugars. The work commenced last year by Miss Edna C. Smith on the conversion of starch into cane-sugar, when potatoes are stored at 0°C., has been continued. The production of cane-sugar has been confirmed and quantitatively determined, but no evidence of the participation of hexosephosphate in the change has so far been obtained.

Another aspect of the same general problem is being attacked by Miss M. J. Macfarlane, who has commenced an investigation on the function of phosphates in bacterial fermentations, to ascertain whether the breakdown of the sugars by these organisms is effected in a similar way to that produced by yeast.

Chemical Constitution of Hexosemonophosphate and Hexosediphosphate. The work on this important problem has been continued by Mr. W. T. J. Morgan (*Grocers' Company Research Student*). Mr. Morgan has succeeded in preparing a fully methylated derivative of hexosediphosphate by direct methylation of the free acid in anhydrous methyl alcohol. The yield was, however, poor and the product difficult to purify. It was, therefore, decided to convert the hexosediphosphoric acid first into the methyl hexoside in order to protect the reducing group from oxidation during the subsequent methylation. A large quantity of barium methyl hexosediphosphate was prepared and from this, two isomeric compounds (probably the α and β modifications) have been obtained by fractional crystallisation of the brucine salts. Acid hydrolysis removes both methyl and phosphoric groups but, by the use of Robison's bone enzyme it is hoped that the phosphoric groups alone may be removed, leaving the stable methyl hexoside, which may prove to be identical with one of the methyl fructosides. A method has been devised by Dr. Robison for obtaining the free sugars from the hexosephosphates and preliminary experiments with the methyl derivatives have already given very promising results. The further methylation of these methyl hexosides is in progress.

In collaboration with Mr. H. P. Marks, at the National Institute for Medical Research, Mr. Morgan has also investigated the effect of hexosediphosphate and hexosemonophosphate on animals (rabbits and mice) suffering from hypoglycæmia as a result of the administration of insulin. If either of these phosphoric esters is formed as an intermediate compound in the metabolism of carbohydrates in the animal body, its administration might possibly, although not necessarily, relieve the hypoglycæmic condition. No such alleviation has been observed.

The Phosphoric Esters which occur in the Blood and other Animal Tissues and the Enzymes by which they are Synthesised and Hydrolysed in the Body. Dr. Robison has continued his work on the phosphoric esters occurring in blood and is at present completing the examination and identification of the several compounds isolated by the method referred to in last year's report. These compounds, together, account for nearly all the acid-soluble phosphorus present in the blood. Another compound, which does not contain phosphorus but reduces alkaline copper solutions, has also been isolated and is being examined. The presence of this compound, which occurs in blood in considerable amount, has been the cause of much of the difficulty met with in the purification of the phosphoric esters.

Dr. Marjorie Martland and Dr. Robison have continued their investigation of the causes affecting the concentration of these phosphoric esters in the blood-plasma. With the co-operation of Dr. Lucy Wills, of the Royal Free Hospital, it has been possible to extend this investigation to the plasma of normal and rachitic children but although considerable variations in the amounts of these esters have been observed it is not as yet possible to draw any definite conclusions as to their cause.

In collaboration with Dr. Martland, Dr. Robison has made an extended study of the properties of the bone enzyme (phosphoric-esterase) and the results are now being prepared for publication. The velocity of hydrolysis of phosphoric esters by this enzyme increases rapidly with increasing alkalinity between the values pH 7.0 and 9.5, but above pH 8.5 this is offset by the gradual inactivation of the enzyme. The synthetic power of the enzyme has been demonstrated, using inorganic phosphate and concentrated solutions of glycerol, glycol, mannitol, glucose, etc. The amount of phosphoric ester synthesised has, under certain conditions, corresponded with as much as 30 per cent. of the total phosphorus present.

CALCIFICATION *in vitro*. These experiments originally undertaken in collaboration with Miss Soames and referred to in previous reports have been continued by Dr. Robison. In order to simulate more closely the conditions in the living animal, a different procedure has been adopted. Bones taken from rachitic animals immediately after death and split in half longitudinally or cut in slices, are placed in tubes through which a slow stream of the experimental solution is caused to flow. The whole of the operations are carried out at body temperature under sterile conditions, the immersion being continued for periods up to 72 hours. Deposition of calcium phosphate has in this way been shown to take place in solutions containing as little as 5 mg. Ca and 5 mg. inorganic P per 100 cc. when small amounts of phosphoric esters are also present. Calcification does not take place with these concentrations of calcium and inorganic phosphorus in absence of the phosphoric ester. Further, the amount of the new deposit is roughly proportional to the concentration of the ester, as little as 0.5 mg. organic P per 100 cc. having been found to produce a significant effect.

The effect of serum proteins in the experimental solution is now being studied.

Vitamins. ANTISCORBUTIC VITAMIN. Continuing his chemical investigations of the antiscorbutic factor, Dr. Zilva has devoted his attention to the improvement of the methods for fractionation of this vitamin. He has found that the active principle is precipitated by lead acetate only within a comparatively narrow range of pH, thus offering the opportunity of removing the bulk of impurities by this reagent before precipitating the vitamin at the requisite reaction which lies in the neighbourhood of neutrality. In this way a moderately pure fraction is quickly and conveniently prepared. The study of the reducing capacity of active solutions of this vitamin has been continued and suggestive information has been obtained.

In collaboration with Mr. E. Hoyle, the investigation on the behaviour of the inorganic constituents of lemon and tomato juices in the process of fractionation has been pursued.

Antiscorbutic tests have been carried out on the duplicate sample of stored lemon juice taken out by the "William Scoresby" to the Arctic circle last year. No appreciable loss in activity could be detected after 12 months' storage.

FAT-SOLUBLE VITAMINS.—Systematically collected whale liver received from Dr. Kemp of the "Discovery" Expedition has been tested by Dr. Zilva for its content of vitamins A and D.

The investigation carried out by Dr. Zilva and Miss Soames in collaboration with Capt. J. Golding of the National Institute for Research in Dairying, on the relative antirachitic and vitamin A properties of butter obtained from cows fed on diets supplemented by green fodder or cod liver oil, has been completed. It has been found that by adding cod liver oil to the diet of the cow, the butter requires enhanced vitamin D and vitamin A activity whilst in the case of the cows receiving green fodder there is only an improvement in the vitamin A content. This investigation is being extended further and clinical experiments in this connection are being conducted by Dr. Helen Mackay, of The Queen's Hospital for Children, Hackney.

Diet and Disease. Dr. Zilva has also collaborated with Dr. Schütze in a research on the influence of diet on the incidence of disease, to which reference is made in the report on work in the Bacteriological department.

Synthesis of Fats, Sterols and Lipins by vegetable organisms. Dr. Smedley MacLean and Mr. C. G. Daubney have endeavoured to trace further the influence of phosphates on the formation of fat by yeast and as a preliminary step have investigated the nature of the phospholipins of yeast. Both lecithin and cephalin are present; from the hydrolytic products of these only two fatty acids, oleic and palmitic, could be identified. The proportion of oleic acid from cephalin is greater than that from lecithin. The chief point of interest lies in the fact that in yeast-fat two unsaturated acids, oleic and linolic, are present, either as glycerol or sterol esters, whereas from the lipins of yeast no linolic acid could be isolated. Investigations previously carried out on animal tissues such as the liver and heart, have shown that the proportion of highly unsaturated acid is greater in the lipins than in the other fat of these tissues. In yeast-fat, which is characterised by a large proportion of sterol ester, the fatty acids bound up in the lipins are less unsaturated than those occurring in the other fat stored in the cell. Bloor has found that in plasma the unsaturated acids circulate chiefly in combination with the sterol and the amount of highly unsaturated acid occurring in the blood lipins is relatively small.

In the course of this work it has previously been shown that the total amount of fat stored in yeast is increased by incubation in a solution of sugar, more especially in one containing phosphates. It has now been established that a large increase in the amount of lipin formed also takes place under these conditions and the proportion of lipin in the total fat is only slightly less than that in the original fat. Since no nitrogen is present in the medium in which the yeast is incubated, the nitrogen necessary must be derived from the breaking down of other nitrogenous products originally present in the yeast cell.

The lipins seem to be as readily extracted from the yeast cell as the rest of the fat present. A very large number of alcoholic extractions are necessary to remove the whole of the fatty matter from the yeast but no evidence could be obtained that the proportion of phosphorus was increased in the later extracts.

The hospitality of the department has also been extended to Dr. Stern, Mr. B. Woolf and Miss Snelus.

Department of Experimental Pathology.

The Protein Error of Indicators. Professor Martin and Dr. Elizabeth Lepper have continued to study the aberrations of the colorimetric method of determining pH caused by the presence of various substances. In the course of some experiments connected with the concentration of horse sera containing antitoxin they had occasion to examine the error of the colorimetric determination of the pH of a strong solution of horse-pseudo-globulin when phenol red and neutral red were used as indicators. They found that with both these indicators the error caused in the colorimetric determination of pH by pseudo-globulin was in the opposite direction to that caused by serum-albumin. Serum-albumin diminished the colour of the indicators; pseudo-globulin increased it.

These results explain some of the contradictory results obtained by previous observers when using neutral red to determine the reaction of sera.

The Acid-Base Equilibria of the Blood. The micro-method of Martin and Lepper for determining the pH of capillary blood, referred to in the last report, has been used by Dr. Elizabeth Lepper and Dr. Marjorie Martland for making observations on the alterations produced in the hydrogen ion concentration of the blood during forced breathing. Doubling the rate of respiration reduces the percentage of CO₂ in the alveolar air to about one-half. Samples of blood taken at intervals of two minutes during forced breathing show a gradual rise in the pH which reaches a maximum in about ten minutes. Forced breathing at the rate of 40 per minute increases the pH of the blood 0.2. Short but violent exercise lowers the pH 0.1 or more. These and other experiments on the variation of the alkalinity of the blood under physiological and pathological conditions are in progress.

Coagulation of Blood. Dr. J. O. W. Barratt's observations on the anticoagulant effect of hirudin have been completed. The experimental results obtained indicate that the interaction of hirudin and thrombin corresponds to that of weak acid upon weak base and show that the hypothesis of an absorption of thrombin by hirudin is untenable. The experiments made also show that both hirudin and thrombin are present in true solution in the concentrations employed. Incidentally, the form of the curves corresponding to the various equations of equilibrium, the applicability of which to this work has been the subject of investigation, has been studied and the curves themselves figured; this forms the subject of a separate paper.

The investigation of the anticoagulant effect of peptone has also been concluded and will shortly be ready for publication. The general lines upon which this work has been carried out are similar to those followed in the case of hirudin.

The action of antithrombin has also been the subject of study and the experiments carried out by different authors have been repeated. At present this work is still in an early stage and the interpretation of the results so far obtained is under consideration.

Endocrinology. Removal of the sexual glands in the male animal produces a profound influence upon its subsequent development and when, shortly after castration, the male sexual glands of another animal are successfully grafted, the influence of castration is prevented. Although these observations and experiments prove the existence of hormones in the testicles, no one has, up to the present time, succeeded in isolating them, in spite of numerous attempts. Even repeated injections of fresh emulsions of the testicles have been unable to prevent development of the features typical of castrated animals. This may be due to the absence of storage of the hormones in the testicles, or to destruction of them by all the methods hitherto used for their isolation.

Professor V. Korenchevsky, in co-operation with Miss M. Schultess-Young, has investigated different lipid and protein fractions, isolated from testes and prostate glands, in order to determine whether the specific sexual hormones can be isolated. Up to the present time, by precipitation at different pH, about 16 protein fractions have been separated, none of which was able to restore atrophied sexual tracts and secondary glands to the normal in castrated animals. However, some of the fractions possess the property of increasing the nitrogen metabolism of normal and castrated animals, an influence of sexual hormones suggested by several experimental and clinical observations. This investigation is being continued in order to discover in what degree the isolated fractions having the above property, can be considered as specific sexual hormones for metabolism.

Professor Korenchevsky has also studied the influence of the removal of the thyroid, parathyroid and sexual glands and of thyroid feeding on the regulation of the body temperature. After thyroidectomy, cooling causes a much more pronounced fall, and warming, a much less increase of the body temperature than is observed in normal animals. Thyroidectomised rabbits cannot support a rate of heat loss which normal rabbits are always able to resist. Parathyroidectomy does not change in a marked degree the above mentioned response of normal or thyroidectomised rabbits to cooling or warming. The influence of castration on the response of rabbits to variations in the rate of heat loss was similar to that of thyroidectomy, but was much less marked. The power of adjustment of thyroidectomised rabbits to variation in the temperature of their environment may be restored to a normal degree by thyroid feeding. After excessive thyroid feeding the animal is severely handicapped when exposed to a temperature previously well supported and the body temperature may rise to 43.5°C. Professor Korenchevsky concludes that the thyroid gland plays an important part in the regulation of the body temperature, and therefore, its condition has always to be taken into account in considering the resistance of different individuals to cold or heat and also in the diseases accompanied by fever.

Nutrition. **VITAMIN A AND VITAMIN D. I. BIOLOGICAL ASSAY.** The divergence between the determinations of the vitamin-value of a number of samples of cod liver oils recently made by different laboratories in this country, on behalf of the Health Committee of the League of Nations, demonstrated that the methods at present employed are far from satisfactory. Greater accuracy of estimation being desirable for every kind of investigation with this vitamin, Miss Hume and Miss Henderson Smith have been engaged in a lengthy research with the fundamental object of improving the technique. The rate of growth of young rats on a basal diet devoid of vitamin A has been used as a criterion as heretofore. Great care has been taken to ensure that this diet is adequate in all other respects, including a sufficient supply of Vitamin D. Various methods of supplying Vitamin D have been tried, and the conclusion reached that better quantitative information is afforded if, instead of exhausting the reserves of the animals previous to adding to the diet various amounts of the material under examination, these are supplied from the commencement. Each individual animal receives daily the same amount of the material, and the amount given to different animals of the same litter increases in geometrical proportion. In this way the graphs drawn by plotting weight against time form a fairly uniform series of curves, approximating to that of the normal animal, as the quantity of vitamin A ingested approaches the essential amount.

Previously the usual method of titrating vitamin D in any material has been to assess the effect on rats of a daily supplement when added to a basal rachitic diet devoid of vitamins A and D and also low in phosphorus. This method, however, violates a first principle of vitamin titration which demands that

the basal diet shall be complete in all constituents except the vitamin in question. Miss Soames, with the assistance of Miss Leigh-Clare, has, therefore, been examining a new method in which the basal diet, deprived of fat soluble vitamin D shall be adequate in fat soluble vitamin A and in phosphorus. On this diet the histological picture is that of osteoporosis rather than of rickets, but it is believed that the antirachitic value of the dietary supplement can be measured by comparing the calcium content of the bones with that of animals receiving the basal diet only. For this work the series of cod liver oils mentioned in a later paragraph, provided useful material as these had already been assayed by the older methods. Miss Soames is also investigating a series of materials which may be suitably included in the basal diet to provide an adequate supply of vitamin A. This is not easy, since most convenient sources of vitamin A have been found to contain vitamin D also in small amount.

II. DISTRIBUTION IN NATURE. Since the introduction of a new technique for estimating vitamin A it has become necessary to revise many old determinations.

Yeast-Fat. Dr. Ethel Luce and Dr. Smedley MacLean, using the old technique, ascribed considerable vitamin A value to yeast-fat and found that it also promoted calcification. Miss Hume and Miss Henderson Smith, in conjunction with Dr. MacLean, have re-investigated yeast-fat for vitamins A and D by the newer methods. They have been unable to detect any value for vitamin A and are now engaged upon an investigation of the vitamin D value, both before and after irradiation, of different samples of yeast-fat. This substance is of great interest owing to its high content of ergosterol.

The study of the distribution of vitamin D in nature has also been continued.

Green Leaves. The previous work of Dr. Harriette Chick and Miss Margaret H. Roscoe showed that the green leaves of spinach (*Spinacia oleracea*) while a rich source of vitamin A, contained vitamin D in small amount only, even when grown in spring and summer under maximal natural illumination. Nevertheless, as Hess first showed, similar leaves after short exposure to ultra-violet irradiation from a mercury arc lamp, acquired high anti-rachitic value.

The strikingly different effect of sunlight and the radiations from a mercury arc might be associated with the much greater intensity of the smaller wave-lengths in the latter or the disappearance of vitamin D from green leaves almost as quickly as it is formed. To test the latter hypothesis Miss Roscoe has grown spinach and gathered it in sunshine and fed it immediately to the experimental animals. Under these circumstances, however, spinach was found to possess only a just detectable anti-rachitic value.

It would appear from the recent discoveries of Rosenheim and Webster and Hess and Windaus that the first explanation is the correct one. They found that vitamin D is activated ergosterol. Ergosterol has a specific absorption for radiant energy of a wave-length absent from sunlight but present in the radiations from the mercury arc.

Miss Leigh-Clare has been searching for vitamin D in the marine diatom *Nitzschia*. This minute organism was shown by Coward and Drummond to be rich in either vitamin A or vitamin D, or both. The state of knowledge at that time did not permit of discrimination. *Nitzschia* or some similar marine diatom, were supposed to be the ultimate source whence the cod derives its stores. Miss Leigh-Clare has been unable to detect the presence of vitamin D in *Nitzschia*. The result was the same whether this diatom was grown in the laboratory behind window glass or on the roof of the Institute, protected with a covering of "windolite," a material fairly transparent to ultra-violet light of the refrangibility occurring in sunlight.

Miss Leigh-Clare has also examined the stomach oil of the mutton bird or Australasian Petrel (*Aestrelata lessonae*) for its content of vitamin D and has found it present in a concentration equal to about one-fifth that found in a good cod liver oil. The interest of this investigation lies in the fact that the mutton bird is believed to consume the same food as the Australasian red cod, i.e., a crustacean known as "Whale Feed."

Marine green organisms such as *Nitzschia* can no longer be regarded as the ultimate source from which the cod and other fish obtain the antirachitic vitamin stored in their liver oils.

III. COMPARISON OF BIOLOGICAL AND COLORIMETRIC METHODS OF TITRATING VITAMIN A. (This work was undertaken at the request of the League of Nations Conference on Standardisation of Biological Values at Geneva in 1925.) The examination of the six samples of Norwegian cod liver oil provided by Professor Poulsen (Oslo) and the one sample of Norwegian cod liver oil provided by Dr. H. H. Dale, has been completed by the Lister Institute and the other three laboratories who undertook the investigation. The results of the biological titration by the different laboratories, indicated a large experimental error, but nevertheless showed the vitamin A value of the various oils to differ from one another by as much as one hundred fold. The results of the colorimetric titration of any one oil by the method of Drummond and Rosenheim agreed with the series of values obtained by the biological method in the different laboratories, as nearly as the latter agreed among themselves.

At the Lister Institute, the work was entrusted to Miss Soames assisted by Miss Leigh-Clare. These workers titrated the antirachitic value of the oils in addition to that of vitamin A with the interesting result that among the whole series of oils the former was found to be much more uniform than the latter. This is possibly attributable to the fact that the oils were no longer fresh and vitamin A is much more unstable than vitamin D.

Vitamin B. Dr. Chick and Miss Roscoe have been re-examining some of the previous work on the relation between water-soluble vitamin B (as found necessary for maintenance of growth and body-weight) and the antineuritic vitamin (necessary for prevention of paralysis and polyneuritis). The opinion generally held that these two principles were identical, is largely based upon the similarity of their distribution in nature among various foodstuffs. This conclusion, however, appears to be premature. Recent work of Goldberger and his colleagues has indicated that "water soluble B" must be regarded as a combination of the antineuritic vitamin with a second factor, "probably identical with the principle in diet which prevents pellagra. Various preparations and concentrates of the antineuritic vitamin have been found unable to sustain growth in rats or pigeons when used as the only source of vitamin B. Miss Roscoe has confirmed the work of Goldberger and has found this to be the case with the antineuritic concentrate prepared from yeast by the method of Peters and Kinnerley. Young rats receiving a daily dose of this material are protected from the collapse or paralysis which usually occurs after 3-4 weeks on a diet deprived of "water soluble B," but later (at 5-7 weeks) develop the characteristic skin disease accompanied by severe intestinal affection which Goldberger considered to be the analogue of pellagra. The work is being continued by a study of the distribution of these two principles (a) "antineuritic" and (b) "anti-pellagra" and an attempt to separate them when present together in various rich sources of "vitamin B."

Biological Value of Proteins. A method has been evolved which permits of accurate observations on the nitrogenous metabolism of small animals, e.g., rats, and Dr. Chick and Miss Roscoe are making re-determinations of the relative values of some of the more commonly occurring proteins for maintaining nitrogenous equilibrium in the rat. It is proposed to examine a series of proteins in their natural as well as purified state and to extend the investigation to naturally occurring nitrogenous substances of a non-protein nature.

The Influence of Dehydration on the Nutritive Properties of Egg-White. As stated in the last report, Dr. Margaret A. Boas (Beit Memorial Research Fellow) has found that when raw egg-white is dried at 37°C. either in air or *in vacuo* it undergoes some obscure change.

A diet of carbohydrate and fat containing 10% of boiled egg-white (reckoned on dry weight) and supplemented by all the vitamins so far known, maintains health and growth in a young animal. When, however, the egg-white has been previously dried it is not capable of doing this. After about a month the animal ceases to grow, shows the definite train of symptoms described in a previous report and dies. These ill-effects do not occur if the carbohydrate given is potato-starch or arrow-root but do occur when it consists of corn-flour or wheat-starch. Raw potato, milk, whole yeast and egg-yolk added to the diet in small amount also counteract the symptoms and the animal remains healthy.

The complete interpretation of the results is not yet forthcoming. They suggest the existence of another dietary factor present in egg-white which is necessary for the proper utilisation of egg-albumin and is destroyed by drying but not by boiling. On this hypothesis it is necessary to conclude that it is also present in the tubers from which arrow-root and potato-starch are derived and becomes absorbed on these starches during the process of their preparation. It does not appear to be identical with any of the known vitamins although having a similar distribution to vitamin B in nature.

Biological Action of Light. Hess showed that rickets could be prevented or cured by feeding with the cholesterol esters in the skin (lanolin) after irradiation with ultra-violet light and suggested that a possible source of vitamin D was the absorption of lanolin which had been activated by sunlight.

Miss Hume, Dr. Lucas and Miss Henderson Smith have experimentally tested this suggestion. Young rats and rabbits were placed upon a diet on which they would inevitably suffer from rickets. 0.2 grams of irradiated cholesterol in hardened cotton-seed oil was applied daily to an area of depilated skin equal to about one square inch, every precaution being taken to prevent the animals ingesting any of the material. The treated animals did not develop rickets, the controls did.

Whether, owing to the opacity of the skin to ultra-violet rays, vitamin D is able to be formed only on its surface or whether sufficient of the activating rays penetrate the epidermis to activate any ergosterol which may circulate in the superficial capillaries, is being investigated.

Dr. Lucas has also been determining the transparency of skin from different parts of the body to ultra-violet light of wave lengths varying from those of visible light to the shortest that occur in sunlight. Many experimental difficulties, associated with the great opacity of the material have been encountered. These have been surmounted and absorption coefficients determined with sufficient accuracy. This has been rendered possible by the generosity of Mr. Spedan Lewis who presented the department with one of Hilger's large spectrographs for use with ultra-violet light.

Miss Hume, Dr. Lucas and Miss Henderson Smith have also made some interesting observations on the beneficial action of a short daily exposure to ultra-violet light on the well-being of marmosets. These animals, like most monkeys and other tropical creatures, fare badly in this country. They ordinarily consume a diet adapted to an environment with abundant sunlight throughout the year. They refuse a diet suited to our climate and suffer from vitamin deficiency with consequent ill-health and rickets. They very rarely breed here, although it is recorded that a pair belonging to Lord Derby 100 years ago gave birth to young which survived a few weeks.

The marmosets have been kept in a stuffy room into which no sunlight penetrates that has not passed through plate glass. They have been fed chiefly upon sweetened milk and bananas and exposed for 10 minutes daily to the rays from a mercury arc lamp. They have enjoyed perfect health and are extraordinarily active and have bred twice in the year. The offspring were well developed but each time, one of the twins was born dead, the other flourished.

Cancer Research. Dr. T. Lumsden, with the assistance of Miss A. C. Kohn-Speyer, has been occupied during the past year with the study of immunity to the implanted tumours of guinea-pigs, rats and mice. Some of the results obtained are as follows:—

EXPERIMENTS WITH HETEROLOGOUS TUMOURS.—If mouse cancer (M_{10}) cells are inoculated into a rat, they proliferate for 7 to 10 days and then die out. If, however, fragments of the tumour are removed when at its maximum size, these can be cultured *in vitro* in the rats own serum for 2—3 weeks. The serum is, therefore, innocuous to rat-grown mouse cancer cells but if this same serum is applied to cultures of mouse cancer cells taken from a mouse, all these mouse-grown cancer cells are killed within 5—10 minutes. It is clear that the serum did contain anti-cancer bodies but their existence could not be demonstrated on rat-grown cells. Yet the rat itself destroyed the mouse-cancer cells left in it within 3 days; obviously some other factor had been called into action. This was not a case of atreptic immunity but of active immunity of the ordinary sort, otherwise the cultured cells could not have outlived those left in the rat.

INVESTIGATION OF HOMOLOGOUS TUMOURS.—As reported in 1926, rat sarcoma (J.R.S.) cells can be grown *in vitro* even in the serum of a rat which has been rendered immune to that tumour. In view of the facts referred to above, the serum of a rat immune to sarcoma was applied to cultures of mouse and of human cancer cells. It damaged both of these and, therefore, contained anti-malignant bodies, yet acting alone the serum did not injure any rat normal or tumour cell. In seeking for some adjuvant factor the peritoneal exudate of normal and of immune rats was investigated, since it contains many white blood corpuscles in addition to blood serum. It was found that such an exudate taken from an immune rat is invariably lethal to cultures of rat sarcoma cells, while it causes no damage to normal rat tissues or to cultures of heterologous tumours, *e.g.*, mouse cancer. If this peritoneal exudate is centrifuged it is found that even the supernatant fluid alone is highly toxic to sarcoma cells. If this liquid is heated to 56°C. for one hour it loses its lethal properties and the addition of fresh serum does not reactivate it. But if washed peritoneal leucocytes are added to the heated liquid its toxicity is completely restored. These facts and others reported elsewhere (*Lancet*, Jan. 15th, 1927) indicate that immunity to homologous tumours, *e.g.*, of a rat to Jensen's rat sarcoma, is the result of two factors (1) the presence of anti-malignant bodies in the blood serum and (2) some excretion from the white blood cells when they have extravasated and are subjected to a low oxygen tension. Each of these factors acting alone, is harmless to homologous tumour cells; together they become effective.

Dr. J. S. Stephens (Beit Memorial Research Fellow) is engaged with Dr. Lumsden in an endeavour to devise means to bring about a leucocytosis in the tumour itself so that when an animal is treated by an immune serum, the second factor, discovered by Dr. Lumsden to be necessary for the destruction of the tumour cells, may be supplied in a situation where it can be effective.

Department of Protozoology.

The Parabasal Body of Flagellates. Dr. Muriel Robertson has been occupied with a morphological study of the two organisms *T. raiæ* and *Bodo caudatus*, with special reference to their method of division and to the nature of the parabasal body. The nucleal reaction of Feulgen was used along with other methods and the distribution of the chromatin received especial attention. The parabasal body or kinetonucleus was found to give the reaction for thymonucleic acid by the Feulgen method.

This study was undertaken as a foundation for experimental work with *Bodo caudatus*. It is a free living flagellate showing a nucleus and a parabasal body, its close relation to the other flagellates of a similar morphological type, such as *Herpetomonas*, *Trypanosoma* and *Trypanoplasma*, suggested that it might react in the same way as some species of trypanosome do to the presence of certain dyes. The reaction in question is the suppression of the parabasal body. This was first discovered by Werbitzki in 1910. A suitable dye was found in acriflavine. After treatment with this dye, a proportion of the bodos while otherwise active and normal in appearance were found to have lost the parabasal body. This phenomenon affords a very interesting opportunity for the study in the first place, of the nature, origin and function of the parabasal body and, secondly, for the investigation of the behaviour of a cell structurally altered in response to an external environmental stimulus. In the progeny of these structurally defective bodos the parabasal nucleus is absent.

A study of *Heteromita* is also being made with particular attention to encystation, excystation and division. It is found that the division which can be readily observed in the living creatures is ordinarily carried out with great promptitude and despatch, occupying about 7 to 10 or 12 minutes. If, however, the final separation of the protoplasmic body in two, after the nuclei have divided, is not achieved in this prompt manner, there seems to be no means of carrying it out until a second nuclear division takes place.

If the important moment is missed in the first instance, the protoplasmic junction between the two complete daughters may be reduced to the slenderest thread but the tough viscous outer protoplasm has regained a consistency that does not permit of actual separation. This is the more remarkable as there is always a certain tendency to an amoeboid condition in *Heteromita*. The double individual goes through an active series of metabolic movements for hours and gives a most realistic simulation of conjugation. Its usual fate is to divide into four, each nucleus dividing into two, and as a rule it gets away with the process at this second attempt.

It is clearly impossible in meeting such a double individual to decide if it is a possible conjugation or a delayed division. These double flagellates can be observed to encyst, and cultures were got with 2 per cent. of binucleate cysts. The nuclei do not fuse in these cysts and excystation induced (after the plate had been allowed to dry and remain in this condition for more than a month) by the addition of culture fluid revealed that among the newly excysted individuals were binucleate creatures. It is not demonstrated that conjugation cannot or does not take place, but it is clear that it must be very carefully disentangled from the process just described.

Encephalitis of Rabbits. Dr. H. M. Woodcock (Jenner Memorial Student), after an unfortunate interruption for some months on account of illness, is now continuing his work on this interesting disease. It is characterised histologically by small-celled perivascular infiltration and the occurrence of focal lesions, constituted in part by large epithelioid cells. Clumps of the small bodies, thought by some to be parasites, and called "*Encephalitozoa*," are found either associated with these zones or separate from them. The disease occurs "spontaneously," at times in the form of an epizootic, both in America and on the Continent, but very seldom in this country. Kling, of Stockholm, considers that he has produced the condition by inoculating rabbits with material from cases of human encephalitis. Dr. Woodcock, working with material kindly sent by Professor Kling, has succeeded in obtaining infection in 20% of the animals so far inoculated. In these cases, the "*Encephalitozoon*"-bodies found are identical with those previously found in a stock rabbit. It is of interest to note that when these bodies occur, well-marked lesions are also present, but characteristic lesions may occur without the bodies being found. Both Kling and Woodcock are of opinion that these elements are not Microsporidian parasites and regard them as cell reaction products.

Sarcocystic Disease of the Mouse. Dr. Woodcock is also investigating the pathology of this disease, which produces the remarkable appearance in the muscles known as "Miescher's tubes." Infection is readily obtained by feeding mice with fragments of infected muscle, but so far Dr. Woodcock has been unable to infect mice by subcutaneous or intravenous inoculation, or by keeping them in close contact with infected animals during many months. The development of the disease is slow and the parasites have not been found in the muscles earlier than 7 weeks from the time of infection. Even after 9 weeks, nothing is visible macroscopically. The condition where the entire musculature is completely riddled with the white streaks must indicate an infection of many months, the invasion of the muscles by the parasites spreading and increasing the whole time. From a study of the very early stages, Dr. Woodcock hopes to be able to arrive at a conclusion as to the true nature of the cysts containing the so-called spores which are characteristic of *Sarcocystis*.

Department for the Study and Preparation of Antitoxic Sera.

Standardisation of Antidysentery Serum. Work on this subject has been carried on throughout the past year chiefly with the two-fold object of finding a more suitable test toxin for routine purposes than the dry bacillary toxin, which has been used here and in other laboratories for many years; and of enquiring into the debated question whether or not dysentery (Shiga) toxin, like diphtheria toxin, consists of a mixture of the lethal toxin and of an atoxic derivate, which, however, is capable of binding antitoxin. The constitution of 18 toxins derived from broth cultures of the Shiga bacillus have been investigated both on mice and on rabbits and the following conclusions reached:—(1) The mouse, estimated per gramme of body weight, is 20 times less sensitive to the lethal action of dysentery toxin than the rabbit. (2) The mouse is a more suitable test animal for evaluating antidysentery serum than the rabbit, because irregularities in the tests are fewer. (3) A suitable broth toxin, i.e., one obtained by filtering an old broth culture, is to be preferred to the dry bacillary toxin for use as a test toxin in routine work. (4) Dysentery toxins, like diphtheria toxin, consist of varying proportions of the lethal toxin and of an atoxic constituent which is capable of combining with antitoxin and also of acting as an antigen for the production of antitoxin.

The Relation of "Roughness" and "Smoothness" of Streptococcus cultures to their virulence and haemolytic power. The Department's stock cultures of the Streptococcus, numbering 280, date from 1913 and are derived from the most diverse sources. It was noted that when grown in broth the oldest cultures were almost uniformly "S" in character, whereas the later additions had a proportionately higher number of "R" cultures amongst them. Tests in mice showed that the oldest "S" cultures were much less virulent than the recently acquired "R" cultures. The haemolytic power of the whole series of cultures was then tested and a definite relation was found to exist between the age of the cultures, their "S" or "R" character, and their power to haemolyse red blood cells. The old "S" cultures gave no haemolysis, whereas the recent "R" cultures invariably brought about haemolysis.

Attempts were made by modifications of the culture medium to change the one type into the other, and it was found that the "R" variety could become "S" but that the character of the old "S" cultures remained fixed. The work as a whole suggests that continued subcultivation in ordinary laboratory media over long periods tends to convert the "R" type into the "S" type. The exact significance of the "S" and "R" types, *i.e.*, whether their antigenic relations are analogous to the "R" and "S" forms described by Arkwright cannot yet be stated.

Pneumococcal infection amongst guinea-pigs. Reference to this epidemic was made in the report for 1925. Not only does this disease possess an interest of its own but it is of practical importance from the point of view of obtaining a healthy stock of animals for testing purposes. During the past year an endeavour has been made to diminish the infection by giving the animals a more generous ration of green food. The good effects of this change in diet were soon apparent, both in regard to the general health of the stock, their increased fertility, and the diminished incidence of the infection. Until Christmas the health of the stock remained exceptionally good, but during the early part of the present year a number of litters were born dead and some of the young died soon after birth. The antenatal mortality and the deaths among the very young were found to be due to the pneumococcus, a result with which we were familiar in the earlier experience of this disease. A striking difference has, however, been noted, namely, that whereas formerly the mothers of the infected young often died about a week after parturition with an acute pneumococcal infection it is now exceptional for them to die in this period; they are in fact healthy carriers of the disease, which they transmit to their young. It is suggested that some essential factor is missing in the nutrition of the foetus by the mother's blood, a constituent which is gradually exhausted during the first half of the winter, and that the absence of this substance is less harmful to the parent than to the young. It is natural to think that the missing element is vitamin D and it is proposed, during next winter, to artificially illuminate some of the breeding stock with a suitable control in order to test the validity of this hypothesis.

The endotoxin of the Plague bacillus. Experiments have been continued with the object of discovering a method for regularly obtaining good plague toxins and of testing their strength on susceptible animals. Dean, Rowland, and MacConkey, in this laboratory, found that methods for obtaining broth toxins were most capricious in their results. However, by following out the method, recommended many years ago by Markl, of growing the cultures at room temperature, quite constant results have been obtained. Further, it has been found that intravenous injection into mice is a sensitive method of testing for plague toxin, the ratios for the subcutaneous, intraperitoneal, and intravenous routes being as one, one-fifth, one-tenth. Unfortunately an endeavour to use this route for the testing of antiplague serum failed. Apparently the avidity of the toxin for the mouse tissues, when introduced directly into the circulation, is so great that dissociation of the toxin from its *in vitro* combination with antitoxin takes place so that no protection is evident even with sera of a relatively high antitoxic titre. The subcutaneous method must therefore be resorted to for testing toxin-serum mixtures.

Experimental production of pneumococcal endocarditis. Fifteen months ago a horse that was being actively immunised against a Type 1 strain of pneumococcus which was highly virulent for the mouse and whose serum was strongly protective for mice against this virulent strain, developed a fatal pneumococcal endocarditis with a pneumococcal septicaemia after a series of intravenous injections with living cultures. The strain recovered from the blood almost daily during the fatal illness lasting about one month proved to be non-virulent for mice and gave no evidence of capsule formation. Work carried out with this avirulent strain leaves little doubt that it is a variant derived from the original virulent strain. F. Griffith, Mair and Hedley Wright were able to produce endocarditis in immune rabbits by intravenous injection of living pneumococcal cultures. Mair succeeded almost at will in producing this condition whereas Wright found it decidedly difficult to bring about. The experience here has been similar to that of Wright, in spite of trying to favour the onset of the infection by injecting into the blood-stream toxic fluids which are likely to damage the endocardial lining of the heart and so afford a nidus for the pneumococcus. Only two positive results have been achieved and in these the strain of pneumococcus isolated from the heart-blood *post-mortem* was found not to have suffered any notable decrease in virulence. The factors involved in the genesis of this variety of endocarditis are not wholly understood so that the condition is not experimentally reproducible at will. Knowledge of these factors is likely to throw a good deal of light on the pathogeny of acute and chronic endocarditis in man.

The production of Diphtheria Toxin. Frequent reference has been made in these reports to the difficulty of ensuring a satisfactory yield of diphtheria toxin in cultures grown for the purpose. During last year, beginning from the month of May, a series of high grade toxins has been prepared without a single intermission by the use of Difco Proteose peptone. The M.L.D.'s. ranged from $\frac{1}{100}$ th to $\frac{1}{10}$ th c.c. and the L+ dose from $\frac{1}{10}$ th to $\frac{1}{100}$ th c.c. These results contrast so strongly with those obtained with Berna peptone broth that the correct composition of the medium must be held to be an essential factor in obtaining a good diphtheria toxin. Exactly what are the requisite elements for toxin production in a suitable peptone is still unknown.

As in past years, the Governing Body has pleasure in expressing its thanks to the Director of the Hygienic Laboratory, U.S.A. Public Health Service, Washington, for his continued kindness in sending supplies of standard antitoxins.

Department for the Study and Preparation of Anti-Variolous Vaccine.

Further attempts to cultivate the vaccine virus artificially have been made by Dr. Green.

Continuing his work on the raising of the virulence of vaccine, to which reference was made last year, Dr. Green has tested Calmette's method of using rabbits for this purpose. While apparently not raising the virulence of a deteriorated strain, the method has proved efficacious in preserving the virulence of an exalted strain.

The fluid carried over by a wick from vaccine emulsion contains the virus, as reported by Coplans. It is an ideal material for experiments on filtration but as this observer found, filtrates of the wick through a bacteria proof filter were inert.

Experiments on the selective influence of germicides on vaccine pulp have been made in continuation of a series by Dr. Green, published some years ago in the Local Government Board Medical Officer's Report. The principal new substance used was eucupinotoxin which has been favourably reported on by Kirstein. Possibly owing to intricacies of technique Dr. Green has not, so far, obtained satisfactory results with this substance.

FOOT AND MOUTH DISEASE RESEARCH.

Dr. Maitland and Mrs. Burbury have continued to devote themselves to the work for the Foot and Mouth Research Committee of the Ministry of Agriculture which has been carried on under the supervision of Dr. Arkwright on the same conditions as in 1925-6.

The Second Progress Report of the Committee which was published early in 1927, is in part based on the work done at the Institute. It contains appendices by Dr. Maitland and Mrs. Burbury dealing with their investigations. A further paper by them giving greater detail will appear in the Journal of Comparative Pathology. Results of considerable importance have been obtained in the following directions:—

1. It has been found possible to give a considerable degree of protection to guinea-pigs against inoculated Foot and Mouth disease by a vaccine consisting of Foot and Mouth Virus killed by means of formalin. 2. The influence of a great variety of conditions upon the survival of the virus has been studied. Survival, sometimes for months, has been observed when the virus has been placed on hay and bran and allowed to dry under ordinary atmospheric conditions. 3. In the bodies of dead guinea-pigs the virus has been found to remain active for many days. 4. The rate of destruction by heating to different temperatures has been ascertained. 5. The behaviour of the infection in rats and rabbits has been further studied. The disease, even when established in these animals, was not passed on naturally by contact, so that their significance as possible carriers of the disease seems small. 6. The protective properties of the serum of immune animals and the method of testing its efficacy have been studied.

Mr. J. McCunn has been working under the Committee upon the histology of the lesions caused by Foot and Mouth Virus.

Mrs. Maitland (Banting Research Fund of Canada) has also been engaged in research into the nature of the local immunity to Foot and Mouth disease which is characteristic of the hairy parts of the skin of guinea-pigs.

Dr. A. Ciuca, Professor of Veterinary Pathology, University of Bucharest, has been working in the Foot and Mouth disease laboratory since early in 1927 and is investigating the types of virus of Foot and Mouth disease prevalent in Roumania and comparing them with those of Western Europe.

NATIONAL COLLECTION OF TYPE CULTURES.

The number of cultures distributed to applicants during the past year remained at the previously high level of somewhat over 4,000. The Curator, Dr. St. John Brooks, will, it is hoped, be able to resume work in May after a prolonged absence. Dr. Dorothy Steabben has, since October, 1926, given part time service in the Department in succession to Dr. F. M. Burnet, who is now a Beit Research Fellow.

GENERAL AND FINANCIAL.

A request from the Empire Marketing Board to the Medical Research Council for advice as to the best means of promoting an investigation into methods of preserving Empire fruits, vegetables and dairy products in order to preserve their vitamins, was, in November last, referred to the Accessory Food Factors' Committee, appointed jointly by the Institute and the Medical Research Council. The Committee reported that an investigation such as proposed was advisable and recommended that it be carried out where research in the subject was already being done, rather than by setting up a special organisation for the purpose, and suggested that it be carried out at the Institute, if the Governing Body was agreeable.

The Medical Research Council adopted the Committee's recommendations. They were subsequently approved by the Empire Marketing Board, and the Governing Body has agreed to undertake the work. The investigation will occupy five years and is being carried out in the Biochemical Department under the general supervision of Professor Harden. Dr. S. S. Zilva (grantee of the Medical Research Council) will be in charge of the investigation. Dr. Zilva will require at least two assistants and some extension of the animal house accommodation at present available will be necessary. The cost of the enquiry will be borne by the Empire Marketing Board.

The Accounts and Balance Sheet for the year ended December 31st, 1926, show balances to the credit of the Pension Fund of £23,044 6s., the Sinking Fund of £15,258 15s. 4d. and the Capital Fund of £506,792 6s. 1d., the latter figure including the credit balance of £8,481 10s. 1d. from the year's working.

No necessity for drawing upon the Contingency Fund arose in the period under review, and this remains unaltered at £14,228 18s. 1d.

Investments made during the year were: For the General Fund, £14,000 Conversion Loan 4½% Stock 1940/44 and £3,000 4% Funding Stock 1960/90; for the Sinking Fund £150 Conversion Loan 3½% Stock, £429 10s. Conversion Loan 4½% Stock 1940/44 and £450 4% Funding Stock 1960/90; and for the Pension Fund £1,500 Conversion Loan 3½% Stock.

Receipts from the sales of the Institute's products and investigation fees show a net decrease of £4,131 3s. 9d. compared with the previous year, viz., Anti-variola vaccine decrease £2,156 15s. 9d.; Antitoxins and Sera decrease £1,622 9s. 7d., Bacterial Vaccines decrease £1,160 10s. 8d., Investigation and Diagnosis fees increase £808 12s. 3d.

The total expenditure for the year was £38,086 19s. 5d. against £36,502 15s. 9d., in 1925. Rent, Rates, Taxes and Insurance, Repairs and Renewals (including the installation of electricity at the Serum department) and Library Expenses show an increase and Gas, Water and Fuel, Electric Light and Power, Serum and Calf Laboratories Expenses and Animals a decrease compared with last year.

In conclusion, the Governing Body desire to express their appreciation of the devoted co-operation of the Director and all members of the Staff in carrying out the work of the Institute.

DAVID BRUCE,

Chairman of the Governing Body.

BALANCE SHEET

AND

ACCOUNTS.

Dr.

The Lister Institute

BALANCE SHEET

	£	s.	d.	£	s.	d.	£	s.	d.
To CREDITORS							2,356	13	4
To PENSION FUND—									
Balance at 31st December, 1925				22,040	2	0			
Add Balance of Income and Expenditure Account, 1926				1,004	4	0			
							23,044	6	0
To JENNER MEMORIAL RESEARCH STUDENTSHIP FUND—									
As per Account at 31st December, 1925				8,079	19	9			
Add Balance of Income and Expenditure Account, 1926.. .. .							11	13	10
							8,091	13	7
To CONTINGENCY FUND—									
As per Account 31st December, 1923							14,228	18	1
To SINKING FUND to 31st December, 1926							15,258	15	4
To CAPITAL FUND to 31st December, 1926—									
Balance of Income and Expenditure Account to 31st December, 1925	143,490	16	5						
Donations, &c., received to date from the following:—									
Dr. Ludwig Mond (1893)	2,000	0	0						
The Berridge Trustees (1893/98)	46,379	10	1						
The Grocers' Company (1894)	10,000	0	0						
Lord Iveagh (1900)	250,000	0	0						
Lord Lister's Bequest (1913) as per Account at 31st December, 1923	18,904	5	8						
William Henry Clarke Bequest (1923/6)	7,114	5	7						
Other Donations (1891-1926)	20,421	18	3						
Add				498,310	16	0			
Balance of Income and Expenditure Account, 1926				8,481	10	1			
							506,792	6	1

ERNEST H. STARLING, *Acting Chairman.*

G. W. ADDISON, *Hon. Treasurer.*

£569,772 12 5

REPORT OF THE AUDITORS

We have audited the above Balance Sheet. We have obtained all the information and explanations we have required. sum of £17,173 11s. 11d. has been paid, being held by the Institute on behalf of the Scientific Staff. In our opinion, such affairs, according to the best of our information and the explanations given to us and as shown by the books of the Institute. London, 31st March, 1927.

of Preventive Medicine.

31st DECEMBER, 1926.

Cr.

		£	s.	d.	£	s.	d.
By CASH—							
At Bankers:	Deposit Account	3,000	0	0			
	Current Accounts	7,315	15	6			
	In hand	87	1	2	10,403	16	8
By INVESTMENTS (at cost)—							
£5,000 London & North Eastern Railway 3 per cent. Debenture Stock ..		4,570	11	0			
£8,650 London, Midland & Scottish Railway 4 per cent. Preference Stock ..		10,360	8	6			
£5,000 Great Central and Midland Railway Joint Committee 3½ per cent. Guaranteed Stock ..		5,123	19	3			
£2,900 New South Wales 5½ per cent. Stock, 1922-32		2,897	16	0			
£1,000 Cape of Good Hope 3½ per cent. Stock, 1929-49		1,000	0	0			
£1,505 7s. 3d. New South Wales 4 per cent. Stock, 1942-62		1,500	0	0			
£353 London & North Eastern Railway 4 per cent. First Guaranteed Stock ..		499	11	0			
£45,500 5 per cent. War Stock, 1929-1947		42,633	14	3			
£24,000 4 per cent. Funding Stock, 1960-1990		20,326	1	1			
£20,000 Local Loans 3% Stock		9,962	0	7			
£32,000 Conversion Loan 4½ per cent. Stock, 1940-44		30,955	4	3	129,929	5	11
By INVESTMENTS, LORD IVEAGH'S DONATION (at cost)—							
£25,006 2s. 6d. New Zealand Government 3 per cent. Inscribed Stock, 1945 ..		24,117	17	6			
£23,000 Victorian Government 3 per cent. Inscribed Stock, 1929-1949		23,875	0	0			
£25,000 Natal 3 per cent. Inscribed Stock, 1929-1949		24,484	7	6			
£25,000 New South Wales Government 3 per cent. Inscribed Stock, 1935 ..		24,937	10	0			
£25,100 South Australian Government 3 per cent. Consolidated Stock, 1916 or after ..		24,860	5	0			
£25,000 Cape of Good Hope 3 per cent. Inscribed Stock, 1933-1943		23,850	0	0			
£20,000 Southern Railway Preferred Ordinary Stock		32,000	0	0			
£18,750 London & North Eastern Railway 4 per cent. First Preference Stock ..		25,000	0	0			
£15,525 London, Midland & Scottish Railway 4 per cent. Preference Stock, 1923 ..		20,375	0	0			
£25,000 East Indian Railway 3 per cent. New Debenture Stock		25,500	0	0	250,000	0	0
By INVESTMENTS, LORD LISTER'S BEQUEST (at cost)—							
£1,937 Grand Trunk Railway Company of Canada 4 per cent. Guaranteed Stock ..		1,733	12	4			
£800 Grand Trunk Railway Company of Canada Great Western Borrowed Capital 5 per cent. Perpetual Debenture Stock		936	0	0			
£1,875 Port of London 4 per cent. B. Stock		1,800	0	0			
£3,400 Gas Light and Coke Company Ordinary Stock		3,638	0	0			
£800 Ontario and Quebec Railway 5 per cent. Debenture Stock		984	0	0			
£661 Madras and Southern Mahratta Railway 4 per cent. Debenture Stock ..		656	19	7			
£500 Canada 4 per cent. Stock, 1940-1960		492	11	0			
£700 Western Australia 4 per cent. Stock, 1912-1962		698	7	0			
£600 Union of South Africa 4 per cent. Stock, 1943-1963		594	2	0			
£1,200 London & North Eastern Railway 3 per cent. Debenture Stock		891	2	9			
£8,467 4 per cent. Funding Stock, 1960-1990		6,479	11	0	18,904	5	8
By INVESTMENTS, SINKING FUND (at cost)—							
£8,000 Conversion Loan 4½ per cent. Stock, 1940-44		7,320	13	7			
£6,000 4 per cent. Funding Stock, 1960-1990		4,611	5	5			
£4,250 Conversion Loan 3½ per cent. Stock		3,251	6	9			
Balance uninvested		75	9	7	15,258	15	4
By INVESTMENTS, JENNER MEMORIAL RESEARCH STUDENTSHIP FUND (at cost)—							
£2,651 Southwark and Vauxhall Water Co. 3 per cent. Debenture Stock "B" ..		2,755	10	0			
£1,596 Southern Railway 5 per cent. Preference Stock		2,740	5	0			
£726 11s. 4d. Liverpool Corporation 3 per cent. Stock, 1912, or after		556	15	6			
£2,000 4 per cent. Funding Stock, 1960-90		1,797	14	0			
Balance uninvested		240	9	1	8,091	13	7
By INVESTMENTS, PENSION FUND (at cost)—							
£22,000 4 per cent. Funding Stock, 1960-1990		17,165	3	5			
£7,500 Conversion Loan 3½ per cent. Stock		5,774	14	11			
Balance uninvested		104	7	8	23,044	6	0
(The above investments, at the market value, 31st December, 1926 show a depreciation of approximately £90,700.)							
By LOANS ON MORTGAGES					6,500	0	0
By DEBTORS					7,372	2	1
* By FURNITURE, FITTINGS, SCIENTIFIC APPARATUS AND BOOKS—							
As per account, 31st December, 1920					2,471	17	2
By EXPENDITURE ON INSTITUTE BUILDINGS AT CHELSEA—							
As per account, 31st December, 1910, including purchase of freehold site, £6,000 ..					70,916	3	1
By PURCHASE OF FREEHOLD LAND ADJOINING "THE STUDIOS," CHELSEA, as per account, 31st December, 1912					169	6	8
By LEASE OF "THE STUDIOS," CHELSEA, as per last account		1,783	6	9			
Less Amount written off		65	2	0	1,718	4	9
By QUEENSBERRY LODGE FARM, ELSTREE—							
Purchase of freehold land and buildings and Expenditure on new buildings, as per account, 31st December, 1912					20,455	10	0
Stock of Animals and Forage		158	12	0			
Stock of Anti-Toxins and Bottles		4,378	13	6			
					4,537	5	6

* Nothing has been charged for depreciation of Furniture, &c. since new purchases made during the year to a greater amount than the estimated depreciation (10%) have been written off.

£569,772 12 5

TO THE MEMBERS.

The Superannuation Scheme for the Scientific Staff provides for Life Policies and National Savings Certificates for which the Balance Sheet is full and fair, and properly drawn up so as to exhibit a true and correct view of the state of the Institute's

COOPER BROTHERS & CO.,
Chartered Accountants, } Auditors.

Dr. INCOME AND EXPENDITURE ACCOUNTS

INCOME.						£	s.	d.
To Interest and Dividends on General Investments	...	...	...	...	...	14,625	2	10
To Interest and Dividends on Sinking Fund Investments	...	...	...	...	...	795	9	0
To Investigation, Diagnosis and Analysis Fees, &c. ...	...	...	...	...	...	5,024	12	8
To Sales of Sera. Vaccines, &c.. and Stock at 31st December, 1926, less Stock at 31st December, 1925	...	...	...	...	...	25,898	5	0
To Rent of Rooms in the Institute	...	...	...	...	...	225	0	0

£46,568 9 6

Dr.

Pension

						£	s.	d.
To Interest and Dividends on Investments	...	...	...	...	...	1,090	0	0
						£1,090	0	0

Dr.

Jenner Memorial Research

To Interest and Dividends on Investments	...	...	...	...	...	£	s.	d.
						261	13	10

Preventive Medicine.

for the year ending 31st December, 1926.

Cr.

EXPENDITURE.							£	s.	d.
By Rent, Rates, Taxes and Insurance	...	...	...	...	...	...	3,602	5	10
By Salaries and Wages of Staff	...	...	...	...	...	...	19,644	5	11
By Premiums on Federated Superannuation Policies	...	...	...	...	...	...	860	2	9
By Stationery, Printing and Postage	...	...	...	...	...	...	380	8	5
By Printing of Collected Papers	...	...	...	...	...	...	229	19	1
By Office Expenses, Law Charges, Auditors' Fee and Sundries	...	...	...	...	...	...	274	5	9
By Travelling Expenses	...	...	...	...	...	...	158	2	5
By Gas, Water and Fuel	...	...	...	...	...	...	1,278	10	8
By Electric Light and Power	...	...	...	...	...	...	286	19	3
By Experimental Pathology Laboratory Expenses, including General Apparatus	...	...	...	...	...	...	619	17	9
By Bacteriological Laboratory Expenses, including Apparatus	...	...	...	...	...	...	200	4	11
By Vaccine Laboratory Expenses, including Bottles	...	...	...	...	...	...	153	8	0
By Water and Bio-chemical Laboratory Expenses, including Apparatus	...	...	...	...	...	...	497	9	0
By Serum and Calf Lymph Laboratories Expenses, including Apparatus and Cost of Bottles	...	...	...	...	...	...	2,145	10	10
By Culture Media	...	...	...	...	...	...	117	6	1
By Animals	...	...	...	...	...	...	1,552	9	10
By Animal House Expenses and Forage	...	...	...	...	...	...	1,498	13	7
By Repairs and Renewals, including Workshop Expenses	...	...	...	...	...	...	2,419	3	0
By Library Expenses	...	...	...	...	...	...	470	5	6
By General Stores	...	...	...	...	...	...	390	7	4
By Bad Debts	...	...	...	...	...	...	8	18	11
By Depreciation of the Lease of "The Studios," Chelsea	...	...	...	...	...	...	65	2	0
By Sinking Fund ($\frac{1}{2}\%$ per annum on Cost of Buildings and Interest on Investments)	...	...	...	...	...	...	1,206	2	7
By Balance, being Excess of Income over Expenditure, transferred to Balance Sheet	...	...	...	...	...	...	8,481	10	1
							£46,568	9	6

Fund.

Cr.

	£	s.	d.
By Pensions	85	16	0
By Balance, being Excess of Income over Expenditure, transferred to Balance Sheet	1,004	4	0
	£1,090	0	0

Studentship Fund.

Cr.

	£	s.	d.
By Salary—Dr. H. M. Woodecock	250	0	0
By Balance, being Excess of Income over Expenditure, transferred to Balance Sheet	11	13	10
	£261	13	10

SCIENTIFIC PAPERS PUBLISHED FROM THE LABORATORIES OF THE INSTITUTE DURING THE YEAR.



ARKWRIGHT, J. A....	...	...	THE IMPORTANCE OF MOTILITY OF BACTERIA IN CLASSIFICATION AND DIAGNOSIS, WITH SPECIAL REFERENCE TO <i>B. pseudotuberculosis rodentium</i> . <i>The Lancet</i> , Vol. I., 1927.
"	"	...	A NOTE ON THE DIFFERENT IMMUNISING VALUES OF VACCINE MADE WITH SMOOTH AND ROUGH FORMS OF BACTERIA. <i>Journal of Pathology and Bacteriology</i> , Vol. XXIX., 1926.
"	"	...	THE VALUE OF DIFFERENT KINDS OF ANTIGEN IN PROPHYLACTIC "ENTERIC" VACCINES. <i>Journal of Pathology and Bacteriology</i> , Vol. XXX., 1927.
ATKIN, E. E.	...	...	THE RATIONALE OF THE BILE SOLUBILITY OF PNEUMOCOCCUS. <i>British Journal of Experimental Pathology</i> , Vol. VII., 1926.
BARRATT, J. O. W.	...	...	THE ANTI-COAGULANT ACTION OF HIRUDIN. <i>British Journal of Experimental Pathology</i> , Vol. VII., 1926.
"	"	...	THE ACTION OF HIRUDIN UPON THROMBIN. <i>Journal of Physiology</i> , Vol. LXIII., 1927.
BEDSON, S. P., MAITLAND, H. B. AND BURBURY, YSOBEL M.	...	...	FURTHER OBSERVATIONS ON FOOT-AND-MOUTH DISEASE: I. EXPERIMENTAL STUDIES OF IMMUNITY IN GUINEA-PIGS TO FOOT-AND-MOUTH DISEASE: II. THE SURVIVAL OF THE VIRUS OF FOOT-AND-MOUTH DISEASE WHEN DRIED UPON VARIOUS MATERIALS: III. FOOT-AND-MOUTH DISEASE IN RABBITS AND RATS. <i>Journal of Comparative Pathology and Therapeutics</i> , Vol. XL., 1927.
BURBURY, YSOBEL M.	...	...	(See BEDSON, S. P.)
BURNET, F. M.	...	...	THE ACTION OF CYANIDES ON BACTERIA. <i>Journal of Pathology and Bacteriology</i> , Vol. XXX., 1927.
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CHICK, HARRIETTE AND ROSCOE, MARGARET H.			ON THE COMPOSITE NATURE OF THE "WATER-SOLUBLE B." VITAMIN. <i>Biochemical Journal</i> , Vol. XXI., 1927.

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- DAUBNEY, C. G. AND ZILVA, S. S. ... THE ACTION OF REDUCING AGENTS ON THE ANTISCORRUTIC FACTOR INACTIVATED BY AERATION. *Biochemical Journal*, Vol. XX., 1926.
- " " " " THE ANTISCORRUTIC FRACTION OF LEMON JUICE.—IV. *Biochemical Journal*, Vol. XX., 1926.
- EAGLES, G. H. ... FURTHER STUDIES ON STREPTOCOCCI FROM SCARLATINA, ERYSIPELAS AND PUERPERAL FEVER. *British Journal of Experimental Pathology*, Vol. VII., 1926.
- GOLDING, J., SOAMES, KATHARINE M., AND ZILVA, S. S. THE INFLUENCE OF THE COW'S DIET ON THE FAT-SOLUBLE VITAMINS OF WINTER MILK. *Biochemical Journal*, Vol. XX., 1926.
- GOYLE, A. N. ... A COMPARISON OF THE PATHOGENICITY FOR MICE OF THE NORMAL AND ROUGH FORMS OF *Salmonella Enteritidis* (GÄRTNER). *Journal of Pathology and Bacteriology*, Vol. XXIX., 1926.
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- MACLEAN, I. SMEDLEY ... (See DAUBNEY, C. G.)
- MAITLAND, H. B. ... (See BEDSON, S. P.)
- MANNING, R. J. ... DECOMPOSITION OF HEXOSEPHOSPHATES BY *B. coli communis*, ESCH.
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- MARTIN, C. J. ... (See LEPPER, ELIZABETH H.)
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- NAGANISHI, H. ... THE FORMATION OF POLYSACCHARIDES BY YEAST PREPARATIONS. *Biochemical Journal*, Vol. XX., 1926.

ROBISON, R.	...	...	...	(See MANTLAND, MARJORIE.)
ROSCOE, MARGARET H.	...	...	...	A FURTHER NOTE ON THE ANTIRACHITIC VALUE OF FRESH SPINACH. <i>Biochemical Journal</i> , Vol. XXI., 1927.
"	"	...	...	(See CHICK, H.)
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THE LISTER INSTITUTE
OF
PREVENTIVE MEDICINE

Report of the Governing Body,
1928.

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

May 23rd, 1928.

The Lister Institute of Preventive Medicine,

CHELSEA BRIDGE ROAD, LONDON, S.W. 1.
ELSTREE, HERTS; MARAZION, CORNWALL.

THE GOVERNING BODY.

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*G. F. PETRIE, M.D., Ch.B., *Bacteriologist-in-Charge.*

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(Medical Research Council.)

Director :

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Curator :

R. ST. JOHN BROOKS, M.A., M.D., D.P.H.

Assistant Curator :

MAUREL RHODES.

* A recognised Teacher of the University of London.

ANNUAL GENERAL MEETING
OF
The Lister Institute of Preventive Medicine,
May 23rd, 1928.

REPORT OF THE GOVERNING BODY.

In presenting the 34th Annual Report, the Governing Body has, with the deepest regret, to record the death on October 7th, 1927, of the Earl of Iveagh. By his many wisely directed philanthropic acts Lord Iveagh diminished the sufferings of the sick, improved the health of the poor and assisted the progress of scientific discovery. The endowment of the Institute, in 1898, was the largest of Lord Iveagh's benefactions for the advancement of medicine by research and it enabled the objects for which the Institute was founded to be pursued on a scale which had previously been impossible.

The Institute is also indebted to Lord Iveagh for much wise counsel. For twenty years he took an active part in guiding its destinies and retired from the Governing Body only when, with advancing years, he found it necessary to reduce his responsibilities.

GOVERNING BODY.

When, after the endowment by Lord Iveagh, the Institute was re-constructed in 1899, it was laid down in the Memorandum of Association that three members of the Governing Body were to be appointed by Lord Iveagh during his lifetime and after his death by such one of his sons as he should nominate for this purpose. By the Will of the late Earl of Iveagh, executed on the 17th January, 1920, the Right Honourable Walter Edward Guinness, M.P., was appointed to succeed to all the rights of appointment and removal of representatives on the Governing Body given or reserved to Lord Iveagh by the Memorandum and Articles of Association of the Institute.

On the death of Professor Starling, on May 2nd, 1927, which was recorded with sorrow in the last report, Viscount Knutsford was appointed by Lord Iveagh to succeed Professor Starling as one of his three nominees on the Governing Body.

At the meeting held last year, the Council re-elected Professor W. Bulloch, Sir James K. Fowler and Professor A. B. Boycott, as its representatives on the Governing Body until December 31st, 1928.

COUNCIL.

At the last Annual Meeting, two of the retiring members of Council, Mr. J. R. Drake, one of the representatives of the Worshipful Company of Grocers and the President of the Royal College of Physicians, London, were each re-elected. Vacancies caused by the retirement of Professor Purser, the representative of the University of Dublin, and by the death of Professor Starling, a representative of the members of the Institute, were filled by the appointment of Professor T. G. Moorhead and Mr. Walter Guinness, respectively.

The three members who retire from the Council this year in accordance with the Articles of Association, but who are eligible for re-election, are Lt.-Col. G. W. Addison, Mr. Walter Guinness and Sir Charles Martin, all representatives of the Members of the Institute.

MEMBERS.

The Governing Body regrets to announce the deaths during the year of three members, each of whom was also a representative upon the Council, viz., Professor Adrian Stokes, the representative of the Royal Irish Academy; Sir Dawson Williams, the representative of the British Medical Association; and Mr. George K. Morico, a representative of the Grocers' Company.

STAFF.

The Governing Body announces with much pleasure that the honour of Knighthood has been conferred upon the Director.

Dr. H. B. Maitland resigned his position of Assistant Bacteriologist in September last, on appointment to the Chair of Bacteriology in the University of Manchester.

Dr. W. T. J. Morgan has resigned the Grocers' Company Research Studentship and has been succeeded by Mr. Eric Boyland, B.Sc. (Manch.).

Dr. G. H. Eagles, late Beit Memorial Research Fellow, has been appointed an assistant in the Department of Bacteriology, and Professor V. Korenchevsky, Dr. T. L. Lumsden and Miss Eleanor M. Hume, have been appointed honorary assistants in the Department of Experimental Pathology.

Dr. Douglas McClean and Dr. R. W. Fairbrother have been appointed to two research fellowships in Bacteriology created by the Governing Body during the year.

RESEARCH WORK.

Before proceeding to give a brief survey of the researches which are, or have been, in progress during the year in the various departments of the Institute, the Governing Body desires to record its appreciation of the continued co-operation it has enjoyed with the Medical Research Council, the Department for Scientific and Industrial Research and the British Empire Cancer Campaign. The financial support given by these bodies to skilled investigators in the different departments has greatly increased the scientific activities of the Institute.

In addition to furnishing the salaries of the staff of the National Collection of Type Cultures, an organisation which has proved of great service to bacteriologists and mycologists throughout the Empire, the Medical Research Council has provided the salaries of Professor Korenchevsky, Miss E. M. Hume and Miss Henderson Smith, in the department of Experimental Pathology.

The department of Biochemistry has been entrusted by the Medical Research Council with a lengthy enquiry into the vitamin-content of Empire products and the effect of preservation and storage thereon. Dr. Zilva is in charge of the investigation which is being carried out with the assistance of Mr. Hoyle, Mr. Shipp and Miss K. M. Soames, under the general supervision of Professor Harden. The cost is defrayed by a grant from the Empire Marketing Board.

Dr. Ida Smedley-MacLean, in the department of biochemistry, receives a grant from the Department of Scientific and Industrial Research, which body also supplies the salaries of her research assistant and a laboratory attendant.

The British Empire Cancer Campaign furnishes the salaries of Dr. T. Lumsden, in the department of experimental pathology, and his research assistant, Miss Kohn-Speyer, and of a laboratory attendant.

Accommodation for all these workers and the expenses of their researches, except those on behalf of the Empire Marketing Board, are provided by the Institute.

DEPARTMENT OF BACTERIOLOGY.

Studies on Vaccinia, Variola, and Fowlpox.

Vaccinia and Variola. In the last report mention was made of Professor Ledingham's experiments which showed that the reaction of the skin to vaccine virus could be modified or annulled by local interference with the reticulo-endothelial system. This question is attracting at present a considerable amount of attention in the study of virus diseases and it has an important bearing on the technique of cross-immunity experiments where a skin site previously submitted to the action of one virus is subsequently employed for the testing of response to another virus with which affinity is alleged. Non-specific inflammatory processes, therefore, require consideration in all investigations where skin responses to viruses are concerned. Two further lines of study have been opened up by Professor Ledingham during the past year. He has elaborated a method of propagating vaccine virus in the dermis of the rabbit. The virus is inoculated intradermally. Subsequently the site of the reaction is excised, the material ground up and diluted with phosphate solution and again passed through susceptible animals. The potency of this passed material reaches a high level, as tested by the intradermal method, but this gain of potency seems to be accompanied by diminution of response when placed on the scarified skin. Three years ago Professor Ledingham showed that smallpox material taken direct from man was capable of producing with regularity a very marked response in the dermis of the rabbit. In recent months he has returned to this question, employing material from the prevailing smallpox in England. Only very moderate success has accompanied attempts to pass the smallpox virus from rabbit to rabbit, after the initial marked response of the rabbit to the human, or monkey-passed, material. The passed material from the dermis seems to lose its virulence rather rapidly and the cause of this requires further investigation. As a laboratory test for smallpox the intradermal inoculation of the rabbit with human material may be recommended.

Cultivation of Vaccine Virus *in vitro* in Association with Chick Embryo. The dermal vaccine above referred to can be obtained entirely free from contaminating bacteria and Dr. Eagles and Dr. McClean (*Research Fellow in Bacteriology*) have been able to employ it successfully as seed in their experiments on the cultivation of the virus *in vitro*. Preliminary experiments on this subject were begun in August, 1927, by Dr. Maitland and Dr. Schütze, following the lines of Carrel and Rivers, but the work had to be suspended owing to Dr. Maitland's transference to Manchester. Their results so far as they went did show that growth of vaccine virus took place under these conditions but with a good deal of irregularity. Dr. Eagles and Dr. McClean are now making a more systematic study of the question.

Fowlpox. Dr. Magrail, who returned to America in the autumn of 1927, succeeded in passing fowlpox virus through Chamberlain filters but with a considerable loss of potency. Adult hens only were employed for experiment. Passage of the virus through collodion membranes was not realised. The virus could not be passed to rabbits and these animals when hyperimmunised with fowlpox produced no demonstrable viricidal antibodies. Hyperimmunisation of hens, however, gave some slight evidence of antibody production—a point on which there has been some difference of opinion.

Studies on Bacterial Variation and the Antigenic Structure of Bacteria.

B. typhosus and *B. paratyphosus*. Dr. Arkwright has examined some of the conditions which appear to determine whether cultures grow in smooth or rough forms and has obtained support for the view that serum containing antibodies for the smooth somatic antigen is particularly apt to convert the smooth into the rough form whilst normal sera generally fail to do so. Miss Pitt, B.Sc., is continuing this investigation. Cultural variants are being tested for virulence in the hope of elucidating alterations in pathogenic activity such as may occur in the animal body.

The connexion between the heat-labile antigen and the flagella of *e.g.*, *B. typhosus* can, as Dr. Arkwright has shown, be directly demonstrated under the microscope. When acted on by an antiserum which agglutinates the H antigen, the living motile bacilli immediately cease to move and become grouped in large loose clumps formed of agglutinated flagella, whereas in the presence of an antiserum for the O antigen, the bacilli adhere by their bodies, the flagella remaining unagglutinated and the clumps are carried about by the active movements of the flagella.

Agglutination by Serum and Acids.

Dr. Arkwright has found that the agglutination of *B. typhosus*, etc., by acids in the characteristic zones described by Michaelis is due to the same heat-labile flagellar substance involved in agglutination by an H serum. The identity of the substances acted upon by the two reagents has been further demonstrated by experiments with the *Salmonella* strain "Stanley," which has two phases. In the specific phase the heat-labile antigen is agglutinated only by *B. typhosus* serum whereas, in the group phase, this antigen is agglutinated by certain *Salmonella* sera but not by *B. typhosus* serum. When acids are employed for agglutination it is now found that, in the specific phase, agglutination takes place in the same zone of acidity as in the case of *B. typhosus*, whereas, in the group phase, the zone of acidity is that characteristic of *B. paratyphosus*. Michaelis' contention that the substances agglutinable by serum and by acid are identical, is made still more probable in the light of these experiments.

B. pseudotuberculosis rodentium. Dr. Schütze has undertaken an investigation of eighteen strains of *B. pseudotuberculosis rodentium* and other organisms whose characters suggested a relationship with it. Although isolated from many diverse species of animals, including man, they were all found to agree in their cultural and biochemical properties and all exhibited motility when grown at room temperature, but not at 37°C. Antigenic analysis has shown that all the strains examined possess the same flagellar heat-labile structure while the somatic heat-stable antigen is not homogeneous throughout the group. By recognition of this fact it has been possible to classify the strains into three types, consisting of 12, 5, and 1 member, respectively, the latter single strain being of human origin. An extremely interesting finding is that one of the pseudotuberculosis groups has a serological affinity with certain *Salmonella* strains. This work will appear in a coming *Festschrift*, in honour of the 70th birthday of Professor Lehmann, of Würzburg.

Strains of the Pasteurella Group. Dr. J. T. Cornelius (Lucknow) has continued his enquiry into the serological relationships of the various animal classes of the Pasteurella group. The difficulties associated with agglutination technique as applied to these organisms are very great and, so far, no satisfactory serological classification has been achieved.

B. aertrycke. Dr. H. M. Ibrahim (Cairo) has commenced an investigation of the toxicity possessed by the flagellar and somatic portions of *B. aertrycke* and is including in his examination both rough and smooth variants of this organism.

Cholera Prophylaxis.

Dr. Fairbrother, recently appointed a Research Fellow in Bacteriology, has concluded since his arrival a piece of work carried out in the main in the laboratory of Professor Besredka at the Pasteur Institute, Paris. He has shown that the antigen contained in the supernatant fluid of centrifuged young cultures of *V. cholera* possesses little or no protective value for guinea-pigs injected therewith. It would appear that such fluids contain only flagellar or heat-labile antigen which is incapable of inducing the development of protective antibodies as Arkwright has shown in the case of *B. paratyphosus A*. Only the heat-stable antigen of an organism appears capable of inducing protection against a lethal dose of the microbes.

Aspergillus Species.

Professor Matsumoto (Department of Plant Pathology, University of Formosa) prepared immune sera for a large number of *Aspergillus* strains obtained from the National Collection of Type Cultures, with a view to their serological analysis. Spore emulsions only were used for immunisation. With these sera he has been unable to demonstrate the presence of specific antibodies by agglutination methods but by complement fixation technique he has obtained evidence of specific antibodies in such sera. The results have enabled him to group these strains in some accordance with the differentiation on cultural and morphological grounds by Thom and Church.

Streptococci and Scarlet Fever.

Dr. Eagles has completed his study of rough and smooth forms of streptococci from scarlet fever sources with special reference to variations in virulence. It would appear that while virulence or lack of virulence may be features of individual colonies proceeding from the same culture, these features are not invariably associated with particular types of colony as formerly believed. In some strains the more rough type of colony is the less virulent or the avirulent type, whereas, in others, and notably in the "Aronson" strain, well-known for its high virulence for mice, the non-virulent form which can be recovered from the mass culture by plating, is associated with a smooth type of colony. The investigation of these variations is of fundamental importance for the systematic study of streptococci in relation to disease in man and animals.

Spore-bearing Anaerobes.

Dr. Arthur Felix (Rothschild Hospital, Jerusalem) has for the past six months collaborated with Dr. Muriel Robertson in a research on the heat-labile and heat-stable antigenic constituents of the spore-bearing motile anaerobes, *V. septique* and *B. tetani*. They have shown that in anaerobic species the properties of these two antigens are analogous to those which have been demonstrated in aerobic species—a subject to which Dr. Felix has in recent years devoted considerable attention. Non-motile variants of *B. tetani* were found to behave as typical O forms and in so far as complement fixation tests went, the sera prepared with the boiled cultures or with the pure O culture, were alone capable of binding complement in the presence of the mass culture and it made no difference to the degree of complement fixation, whether H agglutinins were present in the immune serum or not. Research on the antigenic constituents in the filtered toxins is now in progress and the protective value (*in vivo*) of immune serum prepared with O cultures and O antigen is being tested.

Weil-Felix Reaction in Typhus Fever.

This reaction which is obtained with such constancy in Typhus Fever still remains something of an enigma. Dr. Felix favours the view that *B. proteus* is in some way specifically related to the disease and he has been making control investigations of the agglutinating action of non-typhus sera on certain organisms which have been claimed to be agglutinable in high degree only by typhus sera. Some interesting results have been obtained which suggest that certain non-typhus sera are capable of agglutinating such strains in high titre while remaining incapable of action on *B. proteus*.

Analysis of Streptococci from Agricultural and Dairy Sources.

Dr. Hucker (U.S. Agricultural Station, Geneva, N.Y.) received the hospitality of the Institute for the purpose of carrying out an extensive research on the differentiation of streptococci from dairy sources. Serological and biochemical methods were employed.

The Oxygen Requirements of *B. pestis*.

Working with Mr. M. A. Hassanein, of the Veterinary Pathological Laboratory, Cairo, Dr. Schütze has extended his investigation of the oxygen sensitiveness of *B. pestis*, to that of other organisms. The members of the Pasteurella group are the only organisms which have been found to resemble *B. pestis* in this respect, small inocula refusing to grow on agar surfaces, or in broth, unless the oxygen tension is reduced by the addition to the culture media of such substances as blood, or sterilised broth cultures of various organisms, or by reducing oxygen pressure under the air pump. Rough variants do not exhibit this sensitiveness.

Bacteriophage.

Reference was made in the last report to Dr. Burnet's work showing that sensitivity of a culture to the action of bacteriophage was related to the heat-stable antigenic structure of the organism. *Salmonella* strains possessing the same O agglutinogens were lysed by the same phages, whereas, all *Salmonella* forms in the rough state are sensitive to phages developed from rough cultures of *B. enteritidis*. Dr. Burnet has investigated more fully the nature of the residual colonies which develop following lysis by phages acting only on the rough phase. He found that typically smooth and virulent forms may develop on plaques of rough cultures lysed by phages which act only on rough phases. Quantitative experiments suggest strongly that such forms of opposite phase which appear after lysis are really pre-existent in the population submitted to lysis and are not dependent on phage action for their production. A thesis embodying Dr. Burnet's work on bacteriophage gained for him the degree of Ph.D. of the University of London.

B. welchii and Pernicious Anæmia.

Action of the Toxin of *B. welchii* on Red Cells *in vitro*. It has been claimed that *B. welchii* plays some part in the ætiology of pernicious anæmia and that a form of chronic anæmia can be produced in animals by inoculation with cultures of this organism. Dr. Orr and Dr. Campbell (Queen's University, Kingston, Ont.) have carried out a large series of experiments in which emulsions of red cells are exposed to the action of filtered broth cultures of *B. welchii*. These filtrates usually contain a hæmolysin of variable strength. Samples are taken at intervals and measurements of diameters made on projected pictures. In the presence of the toxin of *B. welchii* it was found that the red cells passed through definite changes, microcytes appearing first, followed by macrocytes, and these again by a stage in which the majority of the remaining cells have resumed their normal diameters. This change in size was not met with when other hæmotoxins (e.g., from *V. septique*, *B. tetani*, streptococci and staphylococci, etc.) were used. By using blood which had been reduced by allowing it to stand in an anaerobic jar or by bubbling CO₂ through it, it was found that hæmolysis could be speeded up considerably and also that the change in size proceeded at a more rapid rate than when ordinary oxygenated blood was used. The degree of change was not more marked, but only the rate.

The interpretation of these observations and their possible relation to the blood picture of pernicious anæmia, are under consideration.

Heterophile Antibodies and the Wassermann Reacting Substance.

Dr. McClean is continuing here some work commenced at the Hospital for Sick Children, Great Ormond Street, on the parallel development of heterophile antibody and the Wassermann reacting substance in rabbits. Observations are also being made on any alteration of resistance to infection with *T. pallidum* which may result from heterophile immunisation.

Furunculosis in Trout.

A report by Major J. H. Horne, I.M.S., on his work on this subject, undertaken on behalf of the Kennet Valley Fisheries Association and the Ministry of Fisheries, has been prepared for publication. The following are the most important findings.

No evidence was obtained of the presence of furunculosis in trout farms. Live trout which proved to be carriers of *B. salmonicida* were taken from the Kennet. Of the three carriers out of 18 live trout examined, two were so-called Black fish. *B. salmonicida* was recovered from the blood of these three carriers. When injected intramuscularly into goldfish, the organism was lethal but not when rubbed into a skin wound. In experimental tanks artificially polluted with *B. salmonicida*, gobies became infected in a few weeks and surviving fish when placed with healthy contacts in unpolluted tanks containing fresh running water, were able to pass on the infection.

The research reveals the importance of the "carrier" in the spread of this disease among river fish.

DEPARTMENT OF BIOCHEMISTRY.

The work in this department has been continued on the same general lines as during last year.

British Empire Marketing Board Grant.

The work under this grant, to which reference was made in last year's report, has been commenced and is in active progress. Details of the work so far done will be found under the headings of Vitamins C, A and D.

Alcoholic Fermentation.

The stimulus given to the renewed study of alcoholic fermentation by the discovery that a closely similar series of reactions occurs in the utilisation of carbohydrates in muscle, has led to a more intensive study of the changes which are produced by yeast preparations in mixtures of sugars and phosphate. Professor Harden and Lord Henley have continued their experiments on the relation between the carbonic acid and the mono- and di-phosphoric esters produced in fermentation and have extended them to dried yeast and the extract obtained from it by maceration. In the same connection Mr. E. Boyland (Grocers' Company Research Student) has commenced work on the intermediate stages of fermentation.

Miss Macfarlane (Carnegie Scholar) has continued her work on the dilution effect shown by dried yeast and has also commenced an investigation of the nature of the hexosephosphates produced by fermentation from glycogen under various conditions.

Preliminary work has also been commenced on the concentration of the co-enzyme of alcoholic fermentation.

Phosphoric Esters produced during Alcoholic Fermentation.

During the past two years, Dr. Robison and Dr. W. T. J. Morgan (Beit Memorial Research Fellow) have made an extended study of the phosphoric esters produced during the fermentation of hexoses by yeast juice, dried yeast and zymine. Dr. Robison's previous work on hexosemonophosphoric acid had suggested that this may be an equilibrium mixture of two isomeric monophosphoric esters of glucose and of fructose, a view which received some support from recent experiments by Meyerhof. Some indication of the presence of other phosphoric esters among the fermentation products had also been obtained and further evidence on these and other points was desired. Although the work is still incomplete, results of much interest have already been obtained. The relative quantities of hexosediphosphate and hexosemonophosphate formed during prolonged fermentation experiments were found to vary greatly with the different types of yeast preparations, the best yields of monophosphate being obtained from yeast juice. With dried yeast and zymine more than 80% of the phosphorus was converted into the diphosphate, while the properties of the remaining fraction showed that it did not consist solely of the hexosemonophosphoric ester, previously described. From this fraction a new ester was isolated and was finally obtained in pure condition by means of its crystalline brucine salt. It proved to be the monophosphoric ester of the non-reducing disaccharide, trehalose, which occurs in the resurrection plant of S. America, *Selaginella lepidophylla*, in seaweeds, yeast and other fungi. Hydrolysis by acids converted the ester into a mixture of glucose and glucosemonophosphate, but by the action of the bone enzyme, discovered by Dr. Robison, it was possible to remove the phosphoric acid group without hydrolysing the glucoside linkage, and in this way trehalose was obtained in pure crystalline condition. The occurrence of this ester among the products of fermentation provokes speculation as to the possibility that it may represent an intermediate stage of glycogen metabolism in yeast, and eventually also in muscle.

Chemical Constitution of Hexosediphosphoric Acid.

Reference was made in last year's report to Dr. Morgan's work on the methylation of this compound and to the isolation of the α - and β -barium methylhexosediphosphates. In collaboration with Dr. Robison, Dr. Morgan has investigated the action of the bone phosphatase on these isomeric derivatives. By means of this enzyme the phosphoric acid groups were removed and the corresponding α - and β -methylhexosides obtained. The specific rotations and other properties of these compounds showed that they were not the normal α - and β -methylfructosides but were probably derivatives of the reactive " γ "-fructose. Although the quantities available were very small, the further methylation of these hexosides was successfully accomplished and the tetramethylhexose finally obtained was identified with the known derivative of " γ "-fructose. It was concluded from this work that hexosediphosphoric acid is probably the 1:6-diphosphoric ester of " γ "-fructose. Further work on the oxidation products of the fully methylated hexosediphosphoric acid is being carried out by Dr. Morgan in order to confirm this suggested structure.

The Phosphoric Esters and Phosphatases occurring in the Blood and other Animal Tissues.

Dr. Robison has continued his investigation of the phosphoric esters occurring in the blood.

In collaboration with Dr. Marjorie Martland, the study of the methods of purification and the properties of the bone phosphatase has been extended and from the knowledge so gained it has been possible to apply the enzyme very successfully in the investigation of the chemical constitution of phosphoric esters. By its aid the phosphoric groups may be removed without the simultaneous hydrolysis of other glucosidic linkages as would occur if acid hydrolysis were carried out. The study of the kinetics of this enzyme reaction is being continued with the collaboration of Mr. F. N. Appleyard (Chelsea Polytechnic) who has prepared a number of phosphoric esters having different dissociation constants, in order to determine the pH activity curves of the enzyme for each of these esters.

Calcification in vitro.

These experiments have been continued by Dr. Robison and various difficulties in technique have been overcome. The results referred to in last year's report have been confirmed by repeated experiments and have now been published. Further work is in progress.

Investigation of the Antiscorbutic Factor.

Vitamin C. In the chemical investigations on the antiscorbutic factor in lemon juice, Dr. Zilva has devoted his attention to the study of the process of inactivation of the active principle. It was established earlier in these studies that active substances showed reducing properties and, consequent on the observation that phenolindophenol was reduced by antiscorbutic fractions, the relation of the reducing capacity to the antiscorbutic activity was studied in detail. It transpired that in spite of the close association, the reducing agency and the active principle are not identical, but that the former contributes to the stability of the latter. On destroying the reducing properties of an active solution the antiscorbutic activity deteriorates rapidly. Furthermore, it was found that the reducing agency is not the only stabilising principle associated with antiscorbutic solutions. Thus, when antiscorbutic solutions are autoclaved under strictly anaerobic conditions in an acid or neutral medium, the activity is impaired only to a slight degree, but such solutions, if kept *neutral*, lose both the antiscorbutic activity and the reducing capacity quickly. In fact experimental evidence has been obtained which indicates that by the removal of impurities in the chemical fractionation, the antiscorbutic factor becomes very unstable and consequently a stage may possibly be reached in the purification when the activity will not be detected by the ordinary biological method. The properties of these stabilising agencies have been studied and some of the results will be published shortly.

The investigation on the behaviour of the inorganic constituents of lemon juice and tomato juice in the process of fractionation carried out by Dr. Zilva and Mr. Hoyle, has been brought to a close. Manganese, nickel, cobalt and boron are absent from the purest fractions; on the other hand, traces of iron, phosphorus, sulphur and iodine persist in these fractions. Iodine, however, is definitely not associated with the activity and no connection between the other three elements and the antiscorbutic factor has been established.

Dr. Zilva, in collaboration with Mr. H. L. Shipp, has begun an investigation on the influence of scurvy on the metabolism of the organism. The preliminary part of this enquiry was devoted to the study of the excretion of lactic acid. It was found that the concentration of lactic acid in the urine of adult and young scorbutic guinea-pigs is fairly constant. The decline in weight of the animals in the premortal phase is usually associated with polyuria. This phenomenon is, however, not specific of scurvy since it can be observed in guinea-pigs declining in weight on restricted diets containing a sufficiency of the antiscorbutic factor.

An enquiry on the variation of the antiscorbutic factor in apples has been started by Dr. Zilva and Mr. Hoyle. Apples grown and stored under carefully controlled conditions and apples of known history from the various Dominions are being investigated. The results so far obtained make it clear that the vitamin content of apples is by no means uniform and that it is controlled by various physiological factors.

Vitamins A and D.

The work on the relative antirachitic and vitamin A properties of butter obtained from cows fed on various diets has been continued by Dr. Zilva and Miss Soames, in collaboration with Capt. J. Golding, of the National Institute for Research in Dairying. The observation has been made that the daily addition of 2 oz. of cod-liver oil to a winter ration did not significantly raise the vitamin D of the butter. Higher doses of cod-liver oil did so, but a concomitant depression in the percentage of milk fat was also recorded.

Sterols of Yeast.

Dr. Smedley-MacLean has continued her investigation of the nature of the unsaponifiable matter of yeast fat, now the main source of ergosterol (provitamin D) and has isolated from it a second sterol, to which the name of zymosterol has been given. Like ergosterol, zymosterol is highly unsaturated, containing three ethylenic linkages, and is precipitated by digitonin. The separation of the two sterols is, therefore, not easy. Zymosterol is distinguished from ergosterol by its greater solubility in organic solvents, its dextro-rotation and the absence of selective absorption in the ultra-violet region. The biological properties of the irradiated sterol are being tested in conjunction with Miss Hume and Miss Henderson Smith.

Oxidation of Fatty Acids.

The work previously carried out on the nature of the fatty acids obtained from the lipins and neutral fats in yeast, has led Dr. Smedley-MacLean and Mr. C. G. Daubney to study the oxidation of these substances, with a view to obtaining chemical evidence as to the probable occurrence of desaturation as a preliminary stage in the oxidation of the higher fatty acids occurring in the body. The method of oxidation used was the action of hydrogen peroxide in the presence of iron, which appears to resemble most closely the normal method of oxidation in the body. Under the experimental conditions devised,

stearic acid is very little attacked, palmitic somewhat more readily and oleic rapidly. In all cases the products of the reaction are acetic acid, formic and carbonic acids and formaldehyde. The mechanism of this reaction is at present under investigation.

The hospitality of the department has also been extended to Dr. Janet Brown and Miss Edna Smith.

DEPARTMENT OF EXPERIMENTAL PATHOLOGY.

The Reducing System in Boiled Meat and the Anærobic Cultivation of Bacteria.

Dr. Lepper and Professor Martin have been studying the thermostable reducing system in cooked flesh and other animal tissues, discovered by Hopkins in 1922. Hopkins found that the insoluble residue of cooked muscle after thorough washing had but slight tendency to combine with molecular oxygen in the absence of some hydrogen acceptor such as "oxydised" glutathione. This is confirmed, but it is found that with muscle from which the blood has not been washed out before boiling it, the meat still exerts a powerful reduction potential and continues to take up oxygen for many weeks at no inconsiderable rate. This appears to be due to the presence of hæmachromagen derived from the hæmoglobin in the flesh or the tissue on boiling. The hæmochromagen left in the meat takes the place of glutathione in Hopkins' system; it combines with molecular oxygen and is in turn reduced by the substance, yet unknown, in the insoluble residue of the flesh. It has not been found possible to separate this unknown substance from muscle and all attempts to get it into a soluble form have led to its disappearance.

The reduction system described above is clearly the reason why the addition of boiled meat to media permits the anærobic cultivation of bacteria in open vessels and why damaged muscles form an excellent *nidus* for the propagation of those anærobic bacilli which cause gas gangrene.

Coagulation of the Blood.

Dr. J. O. W. Barratt's investigation of the anticoagulant effect of peptone in citrated plasma shows that this is due to an action exerted upon fibrinogen; no action upon thrombin has been obtained.

The anticoagulant effect of antithrombin present in normal human blood plasma has also been studied. It has been found possible to separate antithrombin from the greater part of the protein present in plasma. In its anticoagulant action, antithrombin presents points of similarity with hirudin. Part of these observations will shortly be ready for publication. Attempts to obtain antithrombin in a greater degree of purity are being continued and the effect of variation of temperature upon the action of antithrombin is being determined.

In connection with this work the estimation of thrombin and antithrombin has been the subject of study which is still in progress.

Endocrinology.

Testicular and Prostatic Hormones. Dr. V. Koronchevsky, in co-operation with Miss M. Schultess-Young, has completed the investigation of the influence of lipid and proteinic fractions, isolated from normal testes and prostate. Several methods have been tested for this purpose. The first difficulty was the unexpected presence of large quantities of insulin-like substances in testicular tissue. These were isolated and tested. Having a depressant action on metabolism and probably on the general inner-secreting function of the testes, it was deemed probable that they masked the influence of the sexual hormones, when the latter were introduced in an impure form in testicular extracts. Therefore, several methods of extraction were tried in order to remove from the testicular tissue these insulin-like substances without the simultaneous removal or alteration of the sexual hormones. The most efficient, but still unsatisfactory method, so far used by Dr. Koronchevsky, seemed to be the extraction of testicular tissue with 80% alcohol, which removes the greater part of the insulin-like substances. None of the fractions isolated was able to prevent the atrophy of sexual tracts and secondary glands.

One of the lipid fractions, isolated from testes and prostate, when injected separately, had no influence on nitrogen metabolism, whilst the prostatic and testicular fractions, when injected simultaneously, increased the nitrogen metabolism of some rabbits as much as 20%.

Of the proteinic extracts of testes and prostate, the more active are those precipitated at pH 4.0 or obtained by a second salting out after the removal of the fractions previously precipitated. When injected simultaneously, they increased the nitrogen metabolism of some rabbits up to 29%.

Insensibility to a second injection of the extracts was noticed in several experiments. It is interesting that the presence of substances stimulating nitrogen metabolism was found both in the lipid and in the water-soluble protein-like fractions of the male sexual glands. The same is true for the ovarian hormone, for Doisy and his co-workers, extracted the ovarian hormone by lipid solvents, whilst Laqueur and his co-workers, and Dickens, Dodds and Brinkworth, by their method, obtained a powerful extract in water. It seems that the male and female hormones are similar in this respect.

Effect of Ovarian Extract on Nitrogen Metabolism. Lipoid ovarian extract, isolated by the Allen and Doisy method, has been found to decrease the nitrogen metabolism of normal and castrated male rabbits by 13% and 24% respectively. In thyroidectomised rabbits the changes of nitrogen metabolism after injection of ovarian extract were insignificant. In most female normal and castrated rats the nitrogen metabolism also decreased by about 11% during the period of injections.

The Effect of Parathyroid Extract on Nitrogen Metabolism. Parathyroid extract freshly prepared for subcutaneous injections, by a commercial firm in America, and very active in increasing the blood-calcium, produces in normal and parathyroidectomised male rabbits a moderate, but persistent decrease in nitrogen metabolism, noticeable even ten days after injection. This effect was theoretically expected, as the removal of the parathyroid glands, according to the previous experiments of Dr. Korenchevsky and his co-workers, produces an increase in nitrogen metabolism. Therefore, it would seem that parathyroid hormones and insulin are similar in their action upon nitrogen metabolism and antagonistic to that of the thyroid gland. This view of the correlation between the inner-secreting tissue of the parathyroid and pancreas is supported by the experiments of L. Winter and W. Smith, who observed a greatly increased fall of sugar content of the blood and the appearance of cramp with smaller doses of insulin, when insulin was injected simultaneously with parathyroid extract.

Pituitary Gland. Feeding with dried anterior or posterior parts of the hypophysis did not affect the nitrogen metabolism in a significant degree.

Injections of glycerin emulsions of the anterior part of the hypophysis decreased the nitrogen metabolism of rabbits and rats by about 20%. These observations coincide with the results obtained by B. Robertson on mice, fed with tethelin, an extract prepared from the anterior lobe of the gland. Robertson found, that tethelin had an influence on the growth and nutrition of the animals, but did not investigate the metabolism in detail.

Experiments on Nutrition.

Vitamin B. Dr. Harriette Chick and Miss Roscoe have continued their study of the two active constituents of water-soluble B vitamin. It has been suggested that these should be called provisionally:—

Vitamin B₁, the antineuritic, more heat-labile, constituent;

Vitamin B₂, the so-called "anti-pellagra," more heat-stable constituent.

When young rats receive a diet complete in all respects, but devoid of vitamin B₁, they survive only 3—4 weeks and die with or without symptoms of paralysis. If, on the other hand, the diet is deficient only in vitamin B₁, life may be prolonged for 2—3 months or longer, but there is no significant increase in weight, and growth is at once restored if vitamin B₁ is given. The occurrence of the skin lesions (dermatitis and loss of fur) which are characteristic of vitamin B₂ deficiency, and considered by Goldberger and his colleagues to be the analogue of human pellagra, was found to be uncertain and when these occurred, the time of onset was found to be very variable. A good deal of time has been devoted to investigating the cause of this irregularity, which now appears to have been due to unrecognised variations in the basal diet caused by incomplete purification of the caseinogen used as the source of protein. Since the caseinogen has been submitted to an elaborate purification (reprecipitation by acid followed by prolonged extraction with acidified water and alcohol) the characteristic skin lesions have been developed consistently on the diet deficient only in vitamin B₁. Vitamin B₂ appears to be very readily adsorbed on caseinogen and other substances of a protein-like nature and to be removed with difficulty. The high nutritional value of casein as a protein may, therefore, be due not only to the nature of its amino-acid constituents, but also to the fact that it may contain vitamin B₂ as a contamination, unless it is highly purified. This circumstance may explain the observation of Goldberger and his colleagues, that whereas milk (full milk, skim milk or butter milk) has great value in diet for the prevention of human pellagra, disappointing results were obtained when large daily rations up to 90 g. of purified casein were tried. It is clear that conclusions regarding the "biological value" of casein and other proteins, will need revision.

Attempts to Isolate vitamin B₂. Both vitamins B₁ and B₂ are present in yeast. It has been found that by the method of Peters and Kinnersley, a concentrated preparation of the antineuritic vitamin B₁ can be prepared, which is devoid of vitamin B₂. Attempts are now being made to isolate the other vitamin and to study it apart from vitamin B₁. Each stage of the Peters-Kinnersley process has been examined in order to track its disappearance. It has been found that the disappearance takes place in stages, the vitamin being carried down in each of the successive precipitation processes (lead acetate, acid mercuric-sulphate, etc.) of which this method consists. Attempts are now being made by Miss Chick to free it from the combination formed with these precipitates.

Distribution of vitamin B₂ in Foodstuffs. The existing knowledge regarding the distribution of what was called vitamin B has been compiled chiefly on the results of experiments upon the prevention and cure of polyneuritis in pigeons and, therefore, has reference only to distribution of vitamin B₁. A suitable method, using rats as test animals, is now available for studying the distribution of vitamin B₂, for by means of the Peters' yeast extract, vitamin B₁ can be included in the basal diet unaccompanied by vitamin B₂. This work has been begun and information is accumulating regarding the distribution of vitamin B₂ in different whole cereals and their constituent parts.

"Refection," the spontaneous occurrence of the capacity to thrive on diets deprived of B vitamins. This curious phenomena which has been studied recently by Fridericia and his colleagues in Copenhagen, and called by them "Refection," was also discovered independently at the Institute. A certain proportion of rats when nourished on diets containing starch and devoid of B vitamins, acquire the ability to develop and grow in weight, notwithstanding this deprivation. At the same time they excrete bulky white faeces which contain a large proportion of undigested starch. Miss Roscoe has made a study of the phenomenon and confirmed the observations of Fridericia, showing (1) Induction of "refection" in rats on diets devoid of B vitamins by feeding with white faeces from spontaneously "refected" rats. (2) Impossibility of inducing refection in rats on diets containing carbohydrate as sugar or dextrin in place of starch. Miss Roscoe has also found that spontaneous "refection" does not occur when the diet devoid of B vitamins has been previously cooked.

The phenomenon of "refection" seems to be of a general rather than specific nature, and when it is established, deficiencies in diet of vitamins B₁ or B₂, or both, are corrected, and the unfavourable diet studied by Miss Boas containing dried egg-white as the source of proteins, is rendered satisfactory. The most reasonable explanation and the one adopted by Fridericia, is that the alimentary tract of the animal becomes infected with some yeast or other organism and thus the materials are produced which are needed to correct these different defective diets.

Influence of dehydration of the nutritive properties of egg-white. Miss M. A. Boas (Beit Memorial Research Fellow) has continued her investigation into the change which occurs in the nutritive properties of egg-white as the result of desiccation at moderate temperatures. As stated previously, young rats, receiving dried egg-white as the sole course of protein in an otherwise complete diet, develop a definite train of symptoms culminating in death.

Certain substances such as raw potato, whole yeast, egg-yolk, milk, commercial caseinogen, etc., were found to possess the power when added to the diet, of rendering it satisfactory. It was, therefore, suggested in last year's report that there was present in egg-white a dietary factor necessary for the proper utilisation of egg-albumen, this factor being destroyed by desiccation but not by heat.

Experiments carried out during the past year, however, do not support this hypothesis and rather tend to indicate the presence of some toxic substance in the dried egg-white. Pure ovalbumen, which would have presumably lost the hypothetical factor during crystallisation, was used with complete success as the sole protein. Furthermore, no change occurred in its nutritive properties when solutions of crystallised ovalbumen were dried.

It has not yet been ascertained which component of the egg-white produces the toxic substance, but it has been shown that the albumen fraction is not implicated.

The nature of the factor which is able to counteract the ill effects of ingestion of the dried egg-white is as yet undetermined. Though not identical with either of the vitamins, B₁ or B₂, it seems to be related to them. Rats fed on the dried egg-white diet have shown a phenomenon very similar, if not the same, as the "refection" observed in rats deprived of B vitamins. Sometimes this occurs spontaneously. It can be induced equally by feeding the bulky brown faeces passed by refected rats receiving the diet containing dried egg-white, or by feeding the bulky white faeces passed by refected rats on diets deprived of B vitamins.

Titration of Vitamin A. Miss Hume and Miss Henderson Smith have been occupied with a laborious research upon the above subject, which was undertaken at the request of the Accessory Food Factors Committee of the Medical Research Council. This Committee is entrusted with the responsibility of recommending conditions for the biological assay of vitamin A in commercial products. Some improvement in the technique is much to be desired, for parallel tests recently undertaken on behalf of the Committee by a number of laboratories, showed that the methods at present employed lack accuracy. Although vitamin D, free from vitamin A, can now be supplied to the animals used for the tests, a further difficulty arises from the varying reserve of vitamin A held by the animals. It has been found that when steps are taken to overcome this difficulty by completely exhausting these reserves of vitamin A, the health of the animals is so much imperilled that irregular happenings follow from infections and other causes. Notwithstanding careful attention to the breeding of the litters and to the diets of the mothers, the trouble has not been entirely obviated.

Titration of Vitamin D. The usual method of estimating the antirachitic value of foodstuffs, i.e., their content of the antirachitic vitamin D, has been to determine the minimum daily dose which will prevent the development of rickets in young rats maintained on one of the well-known rachitogenic diets. These diets, however, are not only deprived of vitamin D, but are usually deficient also in vitamin A and invariably contain calcium and phosphates unfavourable both in amount and proportion. This diet fails to satisfy the requirement that the diet shall be complete in every respect and lacking only in vitamin D. On such a diet histological rickets is not developed in young rats but the lack of the antirachitic vitamin is manifested by failure to grow, development of osteoporosis and by the lowered calcium content of the bones. Miss Soames and Miss Leigh-Clare have attempted to discover such a diet. The problem resolves itself into finding a source of vitamin A unaccompanied by vitamin D. Both vitamins are fat soluble and although the latter is much more sparsely distributed in natural foodstuffs, there are few sources of vitamin A which are free from traces of vitamin D. Wheat embryo, however, when included in the diet to the extent of 20%, or hog millet to the extent of 50%, have been found to provide adequate vitamin A without any appreciable quantity of vitamin D.

Zymosterol as a Possible Source of Vitamin D. It has been found by Dr. Smedley-Maclean that yeast fat contains another unsaturated sterol, besides ergosterol, which she has named zymosterol. It is known that ergosterol is activated by ultra-violet light to produce vitamin D and the question is being investigated by Miss E. M. Hume and Miss H. H. Smith, whether the second sterol is also capable of activation in the same way. It has not been found possible to prepare the zymosterol entirely free of ergosterol but it is possible to determine spectroscopically the approximate degree of impurity. It is certain that the zymosterol, on irradiation, does not produce weight for weight as much vitamin D as does ergosterol, under the same conditions, but it has not yet been possible to decide whether some vitamin D is derived from irradiated zymosterol itself, or whether such activity as the zymosterol appears to possess after irradiation is not really due to the impurity of ergosterol in it. Three different diets have been used for the experimental rats, but none of them has so far yielded an absolutely certain result. A fourth is now being tried which it is hoped will permit of a definite answer.

Biological Action of Light.

The influence of the radiant energy comprising the near ultra-violet region of the spectrum upon bodily processes, is one of the more important physiological discoveries of recent years, and the evidence that ergosterol is photodynamically converted into vitamin D by these rays is the first step towards the comprehension of the way radiant energy may operate.

The extreme opacity to ultra-violet light hitherto attributed to the epidermis has, however, made it difficult to understand how sufficient light energy of the requisite wave length could penetrate as far as the capillaries. That penetration is not essential was clear from the experiments of Dr. Lucas, Miss Hume and Miss Henderson Smith, showing that vitamin D in irradiated cholesterol was absorbed by the unbroken skin.

As mentioned in the last report, Dr. Lucas has been re-investigating the opacity of epidermis to ultra-violet light of different wave lengths. His experiments indicate that previous measurements have exaggerated its opacity, and that a considerable amount of ultra-violet light, even up to wave length 240μ , penetrates the epidermis of the skin of the arm.

The lack of optical homogeneity of the epidermis and the consequent scattering of the pencil of light, a fact not taken into account in previous measurements, has so far prevented him from arriving at a numerical value for the opacity of epidermis. It is not clear how this difficulty is to be overcome but Dr. Lucas is trying to find a means by which it can be circumvented.

The Amount of the Radiant Energy of the Sun Absorbed by the Body. The assessment of the proportion of the total energy absorbed when sunshine falls upon the skin has engaged the attention of Professor Martin for some considerable time. As the amount absorbed cannot be directly measured, it was hoped to arrive at it by determining what was not absorbed, i.e., the amount irregularly reflected. For this purpose, delicate thermopiles were exposed alternately to a bare parallel beam of light and to a surface of skin illuminated by it under a variety of conditions. Some interesting comparative data were obtained, but it was found impossible to use the observations quantitatively and until this could be done the aim of the research could not be attained. The difficulties, experimental and mathematical, have recently been surmounted, the latter owing to the collaboration of Professor Milne, of Manchester, and it is now possible to make the correction for the restricted angles of aperture of the thermopiles.

The Influence of Ultra-violet Light on the well-being of Tropical Monkeys. Under the care of Miss Hume, Miss Henderson Smith and Dr. Lucas, the marmoset colony has been maintained in health for another year, by the use of ultra-violet light. The animals have bred again, one female giving birth to triplets. The original offspring, born in August, 1926, has now become adult and is bigger and heavier than any other member of the colony. He has been provided with a wife and it is hoped that a second generation may appear before long.

A pair of squirrel monkeys (*Chrysothrix sciurea*) are receiving regular irradiation. These creatures have the reputation of being even more difficult to keep in our climate than marmosets, but after nine months they appear to be in excellent health, much better than at the time of arrival.

Cancer Research.

Dr. T. Lumsden, with the assistance of Miss A. C. Kohn-Speyer, has investigated the feasibility of producing a vaccine effective against malignant tumours. Many attempts were made to attenuate tumour cells outside the body so that, when inoculated into an animal, they should fail to produce a new growth, but, instead, protect against a subsequent implantation of virulent untreated cells. These attempts were, as a rule, unsuccessful, although two methods, anaerobic treatment of the tumour cells with antisera, and simple drying at low temperature and pressure, gave results worthy of further investigation.

Much more consistently satisfactory results were obtained by attempting to produce vaccines in the living body by local treatment of tumours already growing therein. Antisera can be produced which kill cancer cells *in vitro* invariably and specifically, but when injected into a growing tumour, these antisera are so rapidly absorbed into the general circulation that they become ineffective.

In collaboration with Dr. J. G. Stephens (Beit Research Fellow) the effect of adrenalin in preventing this rapid absorption was investigated. It was found that by combining the use of antiserum with adrenalin, about 50% of rat sarcomata could be caused to disappear and that the rats so cured were immune to subsequent implantation of sarcoma and also of rat cancer.

In the case of these rapidly fatal implantable tumours, two things appear to be necessary. Firstly, to delay, by treatment, the growth of the tumour, and secondly, to so damage some of its cells as to produce a vaccine in the body adequate to evoke an active immunity which shall complete the cure and prevent regression. Formalin, which has been much used in the production of bacterial vaccines and which fixes cells with but little alteration of their chemical composition, suggested itself as an agent which might be capable of producing both these effects. When this possibility was investigated, it was found that by injecting 1% formalin into growing tumours, over 90% of them disappeared and the animals so cured were highly resistant to subsequent implantation of the tumour concerned. A method of treatment effective against implantable tumours of the rat has, thus, been found. The evident corollary whether such treatment would be applicable to spontaneous tumours of the rat and of man is now being investigated, but on account of the difficulty of obtaining appropriate material, the point may take some time to settle.

Miss Kohn-Speyer has published a paper confirming the observation that the different antibodies produced by an animal inoculated with a heterologous tumour have very different heat-lability. Antibodies which are purely antimalignant are destroyed by 6—7 hours heating at 56°C., while antispecies (rat-mouse group) antibodies resist such heating for 40—60 hours.

These investigations have shown that (1) Antibodies specifically lethal to malignant tumour cells can be produced; (2) It is possible by local treatment of an implanted tumour growing in a rat to produce a vaccine which gives rise to active tumour immunity in the animal treated.

DEPARTMENT OF PROTOZOOLOGY.

The work on *Heteromita*, begun last year by Dr. Muriel Robertson, was concluded, a study having been made of the division and of the peculiar phenomenon of the production of double individuals simulating syngamy. These are really delayed divisions.

Experiments upon *Bodo caudatus* exposed to the influence of acriflavine have been continued. Various experimental methods have been evolved; the work is laborious and proceeds somewhat slowly as the final understanding of the results can only be obtained from the study of the stained preparations taken at intervals from the experimental plate culture. An adequate technique has, however, been found and the data afforded are sufficiently complex to give a satisfactory account of what is taking place both in regard to the behaviour of cultures as a whole and of the individual cells.

The points in behaviour capable of observation and enumeration are (1) resistance or the power of survival and (2) the production of a particular cell modification. The modification is one which is visible in stained preparations and consists in the suppression of the parabasal body or kinetoneucleus. These two features in the behaviour are not necessarily correlated and can be followed separately.

The following results are selected from among the data which have been obtained up to date. Any exposure to acriflavine greatly increases the resistance of bodos against subsequent exposure and increasingly high concentrations can be withstood after acclimatisation by means of repeated exposures. Subculture of some weeks duration upon media free from the drug does not appreciably lower resistance to the drug upon subsequent exposure, but the limits of this have not, as yet, been sufficiently worked out. If a single bodo is isolated from a resistant culture the resultant single cell culture seems to have lost at least some of its acquired insusceptibility. A gradual treatment by means of exposure to low concentrations of acriflavine or a previous treatment with pyronin produces strains whose resistance is high and this can be further increased but they are characterised by a low percentage (4%—8%) of modified bodos and no increase in this is obtained by higher concentrations of the drug.

Initial exposures on the brink of the lethal limits (what might be called "shock exposures") produce strains with a high percentage up to 50%—73% of modified bodos, and this character of producing many modified cells whenever exposed to the drug is an established quality of the strain. The actual drug resistance of the two types of culture appears to be practically the same though the experiments have not tested this point out to complete finality.

The modified bodos are capable of division but a completely and permanently modified strain has not yet been produced. There is no evidence up to the present that the changes produced can be considered to be mutation.

Encephalitis of Rabbits.

Dr. H. M. Woodcock (*Jenner Memorial Research Student*) has continued his work on this subject. Rabbits have been successfully inoculated intracerebrally with an emulsion of an infected kidney of a dying rabbit kindly provided by Dr. Maitland. In a smear of the brain a few encephalitozoa were seen. Macroscopically, the kidney was pathological and yellowish patches were observed on the surface. Microscopically, the encephalitozoa were seen to be scantily distributed in the cells of the tubules, and in considerable numbers in the lumina, the latter being often partially blocked with masses of necrotic cells and disintegrated nuclear material. In the successfully inoculated rabbits, which showed the bodies and the characteristic lesions in the brain, neither *encephalitozoon* nor manifest histological change was observed in the kidney. A rabbit inoculated intraperitoneally with the same material was unaffected. Some rabbits have been inoculated intravenously with a fine emulsion of brain-material, to see whether, by this method, a more generalized infection can be obtained. Mice have also been inoculated intraperitoneally to see if they become infected with this form from the rabbit.

Sarcocystic Disease.

Sarcocystis infection (*S. tenella*) occurs frequently in the musculature of the gullet of sheep. In this animal the parasites occur as definite cysts, oval in shape, and not in the form of long, thin streaks, lying parallel to the course of the muscle-fibres, as in the mouse. The spores of these two forms have been compared by Dr. Woodcock. They appear practically indistinguishable, in size, shape and minute structure, when stained. Contrary to the usual account, no sign of a firm, resistant membrane has been observed in the spores of the sheep-parasite. Attempts to infect mice with the sheep-parasite have so far proved unsuccessful. Such transmission is claimed to have been successfully carried out, but the possibility of an already existing infection with *S. muris* itself was not eliminated. The plan adopted has been to periodically open the body-wall of the mouse and examine the pectoral muscles, in which the Miescher's tubes are always first seen, and then stitch it up again. If nothing is visible after about three months, such a mouse can safely be used for experiments with the sheep-form. All attempts to infect mice intravenously, with its own parasite, have failed.

Dr. Gordon, from the Liverpool School of Tropical Medicine, and Mr. A. B. Standfast, of King's College, Cambridge, spent some weeks in the laboratory during the year, studying methods.

DEPARTMENT FOR THE STUDY AND PREPARATION OF ANTITOXIC SERA.

The Preparation of Plague Toxins and of Anti-Plague Serum.

Attempts are being made by Dr. Petrie to discover a simple method for extracting the toxic nucleoprotein of the plague bacillus, and to stabilise the toxic solution so that it may be used as a test toxin. Up to the present distilled water seems to be the most suitable extracting medium. Glycerine and lactose are being tested as stabilising agents both for the toxic filtrates of broth cultures and for toxic bacillary extracts, but sufficient time has not yet elapsed to form a definite conclusion.

The question has been debated whether a purely antitoxic serum is an adequate therapeutic agent in the treatment of plague or whether the serum should contain, in addition, an antibacterial component, as the experimental work of some of the early observers indicated (Albrecht and Gohn, Markl, and G. Dean). Horses are now being immunised with the object of obtaining sera that are both antitoxic and antibacterial, and it is hoped to arrange for trial of these sera in the treatment of plague patients.

The Use of Formalised Antigens in the Production of Therapeutic Sera.

For nearly a year exclusive use has been made of formalised toxins for the production of antitoxic sera. Such relatively atoxic antigens have the advantage over unmodified toxins that they are less liable to cause severe reactions in the horses, although as a matter of fact, quite considerable reactions are occasionally seen.

When an unmodified tetanus toxin is used the production of antitoxin in the horse, even with the protection afforded by an occasional dose of tetanus serum, is not free from the risk of local or generalised tetanus. The use of a formalised toxin appears to make the immunising procedure a perfectly safe one, and gives excellent results in a comparatively short time.

The results obtained in the production of diphtheria antitoxin have been equally satisfactory. In a group of nine horses, six proved to be suitable, and these gave a maximum unitage varying from 500 to 1,600 antitoxic units per c.cm. Formalised dysentery and plague toxins have also acted as efficient antigens.

The Experimental Production of Pneumococcal Endocarditis.

As stated in last year's report, work on this subject showed that it was very difficult to bring about this condition experimentally by injecting living virulent cultures intravenously into immunised rabbits. Evidence has now been obtained by Dr. Petrie that an infective endocarditis is readily induced in rabbits by intravenous injections of living cultures, if in addition they are subjected to recurring blood losses by means of cardiac puncture. The cultures isolated *post mortem* from animals that died from the infective endocarditis proved to be an avirulent variant of the strain injected. It by no means follows that this avirulent culture was in any way responsible for the production of the cardiac lesions.

The Experimental Production of Arteriosclerosis in Rabbits.

A great deal of work has been done on the experimental production of arteriosclerosis in rabbits, but the pathogenesis of the condition both in man and animals is still obscure. In the course of his work on pneumococcal endocarditis Dr. Petrie observed minute lesions resembling atheromatous patches in the aorta of some of the rabbits. Subsequent observations have indicated that this morbid condition occurs with marked frequency in rabbits that have received recurring injections of pneumococci intravenously, and that have been rendered temporarily anaemic by a dose of an antiserum against the red blood cells of the rabbit. The condition is not reproducible by a series of pneumococcal injections or by the induction of an anaemic state alone; the combination, however, is effective.

The Maintenance of a Healthy Stock of Guinea-Pigs.

A notable regularity is now a feature of the routine tests with guinea-pigs, and is apparently correlated with the absence of infectious diseases in the testing stock. During the past year the health of the breeding stock of guinea-pigs has shown a further improvement, although occasional deaths from pneumococcal infection have occurred. The original infected stock has now been wholly replaced, chiefly with the progeny of animals which have shown a good breeding history. The incidence of infectious diseases amongst the stock animals is greatest in winter and early spring and on the assumption that this is associated with the absence of sunlight, half of the breeding stock is being irradiated with ultra violet light, while the other half is kept under otherwise similar conditions as a control. The experiment will be continued until a definite conclusion upon the value of irradiation has been reached.

The Governing Body has pleasure in expressing its thanks to the Medical Research Council for their kindness in furnishing supplies of standard antitoxins.

DEPARTMENT FOR THE STUDY AND PREPARATION OF ANTI-VARIOLOUS VACCINE.

Dr. Green's chloroform method of destroying the extraneous micro-organisms of vaccine lymph has been applied to lymphs issued since the beginning of July, 1927. It has been ascertained that the extraneous micro-organisms contained in the raw lymph can be almost entirely eliminated in an hour or so, while, by repeated passage of air through the treated emulsion for 24 hours, all traces of chloroform are removed. No difference in virulence of the chloroformed and un-chloroformed portions of the same vaccine has been observed, and the reports received have shown high ease and insertion success results.

Work on the exaltation of the virulence of vaccinia virus has been initiated and attempts to cultivate the virus artificially have been continued.

FOOT AND MOUTH DISEASE RESEARCH.

Investigations on Foot and Mouth disease, for the Research Committee of the Ministry of Agriculture, have been continued at the Institute during the year in the special laboratory and animal house set apart for the purpose. The experimental work has been carried out by Dr. H. B. Maitland (until appointed Professor of Bacteriology at Manchester University), Dr. Mary Maitland (Banting Research Fund of Canada), Dr. T. Hare (until appointed Professor of Pathology at the Royal Veterinary College), Mrs. Y. M. Burbury and Dr. A. Ciuca (Professor of Veterinary Pathology, Bucharest) under the supervision of Dr. J. A. Arkwright, who is a member of the Committee.

The lines of investigation pursued have included an enquiry into the cause of the restriction of the lesions to the feet and mouth; the fate of the virus in the bodies of convalescing animals; the survival of the virus upon various materials, and under a variety of conditions; the susceptibility of wild animals to infection, and a general study of artificially induced immunity to foot and mouth disease. The results of these enquiries are included in the Third Progress Report of the Foot and Mouth Disease Research Committee, which is now in the press and will be published shortly.

NATIONAL COLLECTION OF TYPE CULTURES.

The activities of the Collection in providing cultures for workers in all parts of the world have been maintained at a high level. Many valuable additions to the Collection have been made during the past year and it is hoped that on his return from sick leave in May, the Curator, Dr. St. John Brooks, may be able to make a commencement with the preparation of a new catalogue.

GENERAL AND FINANCIAL.

As mentioned earlier in this report an investigation into methods of preserving Empire fruits, vegetables and dairy products in order to preserve their vitamins has been entrusted to the Institute by the Medical Research Council. Increased accommodation was found necessary for the large number of animals involved in the investigations and has been provided by building a second storey on one of the animal houses at a cost of approximately £2,000. Four new rooms have been added and those existing so improved that a complete unit suitable for research on nutritional problems is now available.

An invitation has recently been received from the International Committee for the Study of Infantile Paralysis, of which Committee, Dr. W. H. Park, City of New York Health Department, is chairman, for the Institute to co-operate with five other scientific institutions in America and Europe in a further investigation concerning poliomyelitis for which funds have been provided by Mr. Milbank, a citizen of New York. The invitation which includes an offer of £2,000 annually for three years towards the cost of the research, has been accepted by the Governing Body and the investigation will be carried out in the bacteriological department, under the supervision of Professor Ledingham.

The Accounts and Balance Sheet for the year ending December 31st, 1927, show balances to the credit of the Pension Fund of £24,122 7s. 0d., the Sinking Fund of £16,408 10s. 7d., and the Capital Fund of £506,792 6s. 1d., the latter figure being unaltered from that of last year, as the balance on the year's working has been utilised to write down the value of certain of the General Fund Investments which show great depreciation.

The Contingency Fund remains unaltered at £14,228 18s. 1d.

Investments made during the year were: For the General Fund, £10,000 Local Loans 3% Stock and £6,000 4% Funding Stock 1960/90; for the Sinking Fund £1,450 Conversion Loan 3½% Stock, and for the Pension Fund £1,500 Conversion Loan 3½% Stock.

Receipts from the sales of the Institute's products and investigation fees show a net increase of £1,443 8s. 1d., compared with the previous year, viz., Antitoxins and Sera increase £1,943 4s. 4d.; Calf Vaccine increase £656 14s. 7d., Bacterial Vaccines decrease £988 1s. 4d., and Investigation and Diagnosis Fees decrease £168 9s. 6d.

The total expenditure for the year was £39,801 11s. 6d., against £38,086 19s. 5d., in 1926. Rent, Rates, Taxes and Insurance, Gas, Water and Fuel, Serum and Calf Lymph Laboratories Expenses and Alterations, Repairs and Renewals show an increase and Travelling Expenses, Animals, Library Expenses and General Stores a decrease compared with last year.

In conclusion, the Governing Body desire to express their appreciation of the devoted co-operation of the Director and all members of the Staff in carrying out the work of the Institute.

JAMES K. FOWLER,

Acting Chairman of the Governing Body.

BALANCE SHEET

AND

ACCOUNTS.

Dr.

The Lister Institute

BALANCE SHEET

						£	s.	d.	£	s.	d.
TO CREDITORS	..	..	..	..	..				1,956	4	5
TO PENSION FUND—											
Balance at 31st December, 1926	..	..	..	..	..	23,044	6	0			
Add Balance of Income and Expenditure Account, 1927	..	..	..	..	..	1,078	1	0			
									24,122	7	0
TO JENNER MEMORIAL RESEARCH STUDENTSHIP FUND—											
As per Account at 31st December, 1926	..	..	..	..	..	8,091	13	7			
Less Balance of Income and Expenditure Account, 1927	..	..	..	..	..	30	16	2			
									8,060	17	5
TO CONTINGENCY FUND—											
As per Account, 31st December, 1923	..	..	..	..	..				14,228	18	1
TO SINKING FUND to 31st December, 1927	..	..	..	..	..				16,408	10	7
TO CAPITAL FUND to 31st December, 1927—											
Balance of Income and Expenditure Account to 31st December, 1926	..	..	..	..	..	151,972	6	6			
Donations, &c., received to date from the following:—											
Dr. Ludwig Mond (1893)	..	..	..	..	..	3,000	0	0			
The Berridge Trustees (1893/98)	..	..	..	..	..	46,379	10	1			
The Grocers' Company (1894)	..	..	..	..	..	10,000	0	0			
Lord Ivesagh (1900)	..	..	..	..	..	250,000	0	0			
Lord Lister's Bequest (1913) as per Account at 31st December, 1923	..	..	..	..	..	18,904	5	8			
William Henry Clarke Bequest (1923/6)	..	..	..	..	..	7,114	5	7			
Other Donations (1891-1926)	..	..	..	..	..	20,421	18	3			
									506,792	6	1

J. K. FOWLER, *Acting Chairman.*G. W. ADDISON, *Hon. Treasurer.*

£571,569 3 7

REPORT OF THE AUDITORS

We have audited the above Balance Sheet. We have obtained all the information and explanations we have required, paid, being held by the Institute on behalf of the Scientific Staff. In our opinion, such Balance Sheet is full and fair, and information and the explanations given to us and as shown by the books of the Institute.

London, April 19th, 1928.

of Preventive Medicine.

31st DECEMBER, 1927.

Cr.

By CASH—							£	s.	d.	£	s.	d.
At Bankers: Deposit Account							4,500	0	0			
Current Accounts							5,208	8	9			
In hand							40	4	8	9,748	13	5
By INVESTMENTS, GENERAL FUND (at cost, less amounts written off)—												
£26,200 London & North Eastern Railway 3 per cent. Debenture Stock ..							5,461	13	9			
£8,650 London, Midland & Scottish Railway 4 per cent. Preference Stock ..							10,160	8	6			
£5,000 Great Central and Midland Railway Joint Committee 3½ per cent. Guaranteed Stock							5,123	19	3			
£2,900 New South Wales 5½ per cent. Stock, 1922-32							2,897	16	0			
£1,000 Cape of Good Hope 3½ per cent. Stock, 1920-40							1,000	0	0			
£1,505 7s. 3d. New South Wales 4 per cent. Stock, 1942-62							1,500	0	0			
£353 London & North Eastern Railway 4 per cent. First Guaranteed Stock ..							499	11	0			
£45,500 5 per cent. War Stock, 1929-1947							42,633	14	3			
£38,487 4 per cent. Funding Stock, 1960-1990							32,029	15	1			
£30,000 Local Loans 3% Stock							16,357	10	7			
£32,000 Conversion Loan ½ per cent. Stock, 1940-44							30,955	4	3			
£25,006 2s. 6d. New Zealand Government 3 per cent. Inscribed Stock, 1945 ..							24,117	17	6			
£25,000 Victorian Government 3 per cent. Inscribed Stock, 1929-1949							23,875	0	0			
£25,000 Natal 3 per cent. Inscribed Stock, 1929-1949							24,484	7	6			
£25,000 New South Wales Government 3 per cent. Inscribed Stock, 1935..							24,937	10	0			
£26,400 South Australian Government 3 per cent. Consolidated Stock, 1916 or after ..							24,860	5	0			
£25,000 Cape of Good Hope 3 per cent. Inscribed Stock, 1933-1943							23,850	0	0			
£20,000 Southern Railway Preferred Ordinary Stock							27,000	0	0			
£18,750 London & North Eastern Railway 4 per cent. First Preference Stock ..							22,648	7	3			
£15,625 London, Midland & Scottish Railway 4 per cent. Preference Stock, 1923 ..							20,375	0	0			
£25,000 East Indian Railway 3 per cent. New Debenture Stock							25,500	0	0			
£1,937 Grand Trunk Railway Company of Canada 4 per cent. Guaranteed Stock ..							1,733	12	4			
£300 Grand Trunk Railway Company of Canada Great Western Borrowed Capital 5 per cent. Perpetual Debenture Stock							936	0	0			
£1,875 Port of London 4 per cent. B. Stock							1,800	0	0			
£3,400 Gas Light and Coke Company Ordinary Stock							3,638	0	0			
£300 Ontario and Quebec Railway 5 per cent. Debenture Stock							984	0	0			
£661 Madras and Southern Mahratta Railway 4 per cent. Debenture Stock ..							656	19	7			
£500 Canada 4 per cent. Stock, 1940-1960							492	11	0			
£700 Western Australia 4 per cent. Stock, 1942-1962							698	7	0			
£600 Union of South Africa 4 per cent. Stock, 1943-1963..							594	2	0	402,101	11	10
By INVESTMENTS, SINKING FUND (at cost)—												
£8,000 Conversion Loan ½ per cent. Stock, 1940-44							7,320	13	7			
£5,000 4 per cent. Funding Stock, 1960-1990							4,611	5	5			
£5,700 Conversion Loan 3½ per cent. Stock							4,349	17	3			
Balance uninvested							126	14	4	16,408	10	7
By INVESTMENTS, JENNER MEMORIAL RESEARCH STUDENTSHIP FUND (at cost)—												
£2,850 Southwark and Vauxhall Water Co. 3 per cent. Debenture Stock "B" ..							2,756	10	0			
£1,598 Southern Railway 5 per cent. Preference Stock							2,740	5	0			
£726 11s. 4d. Liverpool Corporation 3 per cent. Stock, 1942, or after							556	15	6			
£2,000 4 per cent. Funding Stock, 1960-90							1,797	14	0			
Balance uninvested							200	12	11	8,060	17	5
By INVESTMENTS, PENSION FUND (at cost)—												
£22,000 4 per cent. Funding Stock, 1960-1990							17,165	3	5			
£9,000 Conversion Loan 3½ per cent. Stock							6,919	3	11			
Balance uninvested							37	19	8	24,122	7	0
(The above Investments, at the market value, 31st December, 1927 show a depreciation of approximately £74,800.)												
By LOAN ON MORTGAGE										6,000	0	0
By DEBTORS										7,413	15	9
* By FURNITURE, FITTINGS, SCIENTIFIC APPARATUS AND BOOKS—												
As per account, 31st December, 1920										2,471	17	2
By EXPENDITURE ON INSTITUTE BUILDINGS AT CHELSEA—												
As per account, 31st December, 1910, including purchase of freehold site, £8,000 ..										70,916	3	1
By PURCHASE OF FREEHOLD LAND ADJOINING "THE STUDIOS," CHELSEA, as per account, 31st December, 1912										169	6	8
By LEASE OF "THE STUDIOS," CHELSEA, as per last account							1,718	4	0			
Less Amount written off							65	2	0	1,653	2	9
By QUEENSBERRY LODGE FARM, ELSTREE—												
Purchase of freehold land and buildings and Expenditure on new buildings, as per account, 31st December, 1912..										20,455	10	0
Stock of Animals							394	10	0			
Stock of Anti-Toxins							1,712	17	11			
										2,047	7	11
* Nothing has been charged for depreciation of Furniture, &c. since new purchases made during the year to a greater amount than the estimated depreciation (10%) have been written off.												
										£571,569	3	7

* Nothing has been charged for depreciation of Furniture, &c. since new purchases made during the year to a greater amount than the estimated depreciation (10%) have been written off.

TO THE MEMBERS.

The Superannuation Scheme for the Scientific Staff provides for Life Policies for which the sum of £16,256 14s. 9d. has been properly drawn up so as to exhibit a true and correct view of the state of the Institute's affairs, according to the best of our

COOPER BROTHERS & CO.,

Chartered Accountants. } Auditors.

Dr. INCOME AND EXPENDITURE ACCOUNTS

INCOME.								£	s.	d.
To Interest and Dividends on General Investments	...	...	...	...	...	...	...	15,302	0	5
To Interest and Dividends on Sinking Fund Investments	...	...	...	...	...	...	...	739	1	8
To Investigation, Diagnosis and Analysis Fees, &c. ...	...	...	...	...	...	...	...	4,856	3	2
To Sales of Sera, Vaccines, &c., and Stock at 31st December, 1927, less Stock at 31st December, 1926	...	...	...	...	...	...	...	26,582	5	8
To Rent of Rooms in the Institute	...	...	...	...	...	...	...	421	13	4
To Donations	...	...	...	...	...	...	...	252	0	0

£48,153 4 3

Dr.

Pension

								£	s.	d.
To Interest and Dividends on Investments	...	...	...	...	...	...	...	1,156	10	0
								£1,156	10	0

Dr.

Jenner Memorial Research

								£	s.	d.
To Interest and Dividends on Investments	...	...	...	...	...	...	...	261	3	10
To Balance, being Excess of Expenditure over Income, transferred to Balance Sheet								30	16	2
								£292	0	0

Preventive Medicine.

for the year ending 31st December, 1927.

Cr.

EXPENDITURE.							£	s.	d.
By Rent, Rates, Taxes and Insurance	...	...	...	...	...	...	4,081	19	3
By Salaries and Wages of Staff	...	...	...	...	...	...	19,257	1	2
By Premiums on Federated Superannuation Policies	...	...	...	...	...	...	1,178	2	6
By Stationery, Printing and Postage	...	...	...	...	...	...	401	7	4
By Printing of Collected Papers	...	...	...	...	...	...	185	5	2
By Office Expenses, Law Charges, Auditors' Fee and Sundries	...	...	...	...	...	...	333	7	1
By Travelling Expenses	...	...	...	...	...	...	20	16	5
By Gas, Water and Fuel	...	...	...	...	...	...	1,438	2	7
By Electric Light and Power	...	...	...	...	...	...	299	9	10
By Experimental Pathology Laboratory Expenses, including General Apparatus	...	...	...	...	...	...	954	5	0
By Bacteriological Laboratory Expenses, including Apparatus	...	...	...	...	...	...	267	15	11
By Vaccine Laboratory Expenses, including Bottles	...	...	...	...	...	...	86	19	10
By Water and Bio-chemical Laboratory Expenses, including Apparatus	...	...	...	...	...	...	429	17	11
By Serum and Calf Lymph Laboratories Expenses, including Apparatus and Cost of Bottles	...	...	...	...	...	...	3,004	0	8
By Culture Media	...	...	...	...	...	...	184	18	5
By Animals	...	...	...	...	...	...	1,427	15	6
By Animal House Expenses and Forage	...	...	...	...	...	...	1,361	10	0
By Alterations, Repairs and Renewals, including Workshop Expenses	...	...	...	...	...	...	3,025	11	6
By Library Expenses	...	...	...	...	...	...	321	0	1
By General Stores	...	...	...	...	...	...	306	6	1
By Bad Debts	...	...	...	...	...	...	1	2	0
By Depreciation of the Lease of "The Studios," Chelsea	...	...	...	...	...	...	65	2	0
By Sinking Fund ($\frac{1}{4}\%$ per annum on Cost of Buildings and Interest on Investments)	...	...	...	...	...	...	1,149	15	3
By Amount written off General Fund Investments	...	...	...	...	...	...	8,351	12	9
							£48,153	4	3

Fund.

Cr.

	£	s.	d.
By Pensions	78	9	0
By Balance, being Excess of Income over Expenditure, transferred to Balance Sheet	1,078	1	0
	£1,156	10	0

Studentship Fund.

Cr

	£	s.	d.
By Salary—Dr. H. M. Woodcock	250	0	0
By Income Tax	42	0	0
	£292	0	0

SCIENTIFIC PAPERS PUBLISHED FROM THE LABORATORIES OF THE INSTITUTE DURING THE YEAR.



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- ARKWRIGHT, J. A., BURBURY, SYMPOSIUM ON "FOOT AND MOUTH DISEASE." *Annals of Applied*
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- BARRATT, J. O. W.... THE ACTION OF HIRUDIN UPON THROMBIN. *Journal of Physiology*, Vol. LXIV., 1927.
- " " THE ANTICOAGULANT ACTION OF PEPTONE *in vitro*. *Biochemical Journal*, Vol. XXII., 1928.
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- BURBURY, YSOBEL M. (See ARKWRIGHT, J. A.; also MAITLAND, H. B.)
- CHICK, HARRIETTE AND ON THE COMPOSITE NATURE OF THE WATER-SOLUBLE B. VITAMIN.
ROSCOE, MARGARET H. *Biochemical Journal*, Vol. XXI., 1927.
- DAUBNEY, C. G. AND THE CARBOHYDRATE AND FAT METABOLISM OF YEAST. IV. THE
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- " " " " ... NOTE ON THE UNSAPONIFIABLE MATTER OF YEAST-FAT. *Biochemical Journal*, Vol. XXI., 1927.
- EAGLES, G. H. THE APPLICATION OF THE RAMON FLOCCULATION TEST TO THE TOXIN AND ANTITOXIN OF *Streptococcus scarlatinae*. *British Journal of Experimental Pathology*, Vol. VIII., 1927.
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- FELIX, A. AND ROBERTSON, MURIEL SEROLOGICAL STUDIES IN THE GROUP OF THE SPORE-BEARING ANAEROBES.
I. THE QUALITATIVE ANALYSIS OF THE BACTERIAL ANTIGENS OF *B. oedematis maligni* (*Vibrio septique*) AND *B. tetani*. *British Journal of Experimental Pathology*, Vol. IX., 1928.

- GOLDING, J. AND ZILVA, S. S. ... THE INFLUENCE OF THE COW'S DIET ON THE FAT-SOLUBLE VITAMINS OF WINTER MILK. II. *Biochemical Journal*, Vol. XXII., 1928.
- HARDEN, A. AND HENLEY, F. R. ... THE EQUATION OF ALCOHOLIC FERMENTATION. *Biochemical Journal*, Vol. XXI., 1927.
- HENLEY, F. R. ... (See HARDEN, A.)
- HOYLE, E. AND ZILVA, S. S. ... THE ANTISCORBUTIC FRACTION OF LEMON JUICE. VI. *Biochemical Journal*, Vol. XXI., 1927.
- HUME, ELEANOR M... (See LUCAS, N. S.)
- HUME, ELEANOR M., LUCAS N. S., AND SMITH, HANNAH H. ON THE ABSORPTION OF VITAMIN D FROM THE SKIN. *Biochemical Journal*, Vol. XXI. 1927.
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REPORT OF THE ACCESSORY FOOD FACTORS COMMITTEE.

ESTIMATION OF VITAMIN A IN COD LIVER OIL. A COMPARISON BETWEEN THE COLORIMETRIC (ROSENHEIM, DRUMMOND) AND THE BIOLOGICAL METHOD OF DETERMINING VITAMIN A IN COD LIVER OIL. *Lancet*, L., 1928. (*Report to the League of Nations Health Organisation*.)

THE LISTER INSTITUTE
OF
PREVENTIVE MEDICINE

Report of the Governing Body,
1929.

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

June 19th. 1929.

The Lister Institute of Preventive Medicine,

CHELSEA BRIDGE ROAD, LONDON, S.W. 1.
ELSTREE, HERTS; MARAZION, CORNWALL.

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ANNUAL GENERAL MEETING
OF
The Lister Institute of Preventive Medicine,
June 19th, 1929.

REPORT OF THE GOVERNING BODY.

The Governing Body has the honour to present the Institute's 35th Annual Report.

GOVERNING BODY.

In the absence of Sir David Bruce during the Winter, Sir James Fowler acted as Chairman of the Governing Body.

At the meeting held last year, the Council re-elected Professor W. Bulloch, Sir James K. Fowler and Professor A. E. Boycott, as its representatives on the Governing Body until December 31st, 1929.

COUNCIL.

At the last Annual Meeting, the three retiring members of Council, Lt.-Col. G. W. Addison, Mr. Walter Guinness and Sir Charles Martin, each a representative of the Members of the Institute, were re-elected.

Vacancies caused by the deaths of Professor Adrian Stokes, the representative of the Royal Irish Academy, Sir Dawson Williams, the representative of the British Medical Association, and Mr. G. K. Morice, one of the representatives of the Worshipful Company of Grocers, were filled by the appointment of Dr. F. W. Brambell, Professor W. E. Dixon and Colonel Ralph Key Harvey respectively.

The three members who retire from the Council this year in accordance with the Articles of Association, but who are eligible for re-election, are Sir James Fowler, a representative of the Members of the Institute, Sir David Bruce, the representative of the Royal Society and Dr. F. W. Brambell, the representative of the Royal Irish Academy.

STAFF.

Dr. W. T. J. Morgan, Beit Memorial Research Fellow, who has been working in the Biochemical Department of the Institute for the past four years, has been appointed to the Staff of the Serum Department. It is confidently hoped that the accession of a trained chemist to the Staff will relieve Dr. Petrie of some of the routine duties and materially increase the research activities of the department.

Dr. Dorothy Steabben, late Beit Memorial Research Fellow, has been appointed an assistant on the staff of the Bacteriological Department.

Dr. E. Weston Hurst, late Pathologist to the Miller General Hospital, has been temporarily added to the staff of the Department of Bacteriology to take part in the portion of the investigation into Poliomyelitis allotted to the Institute by the International Committee for the study of this disease, the funds for which have been generously provided by Mr. J. Milbank of New York.

Dr. Douglas McClean and Dr. R. W. Fairbrother have been re-appointed to the two research fellowships in Bacteriology created by the Governing Body in 1927.

Dr. H. M. Woodcock resigned the Jenner Memorial Research Studentship and has been succeeded by Dr. A. Felix.

Mr. E. Boyland has been re-appointed Grocers' Company Research Student for a second year.

RESEARCH WORK.

Before proceeding to give a brief survey of the researches which are, or have been, in progress during the year in the various departments of the Institute, the Governing Body desires to record its appreciation of the continued co-operation it has enjoyed with the Medical Research Council, the Department for Scientific and Industrial Research, the British Empire Cancer Campaign and the International Committee for the Study of Infantile Paralysis. The financial support given by these bodies to skilled investigators in the different departments has greatly increased the scientific activities of the Institute.

In addition to furnishing the salaries of the staff of the National Collection of Type Cultures, an organisation which has proved of great service to bacteriologists and mycologists throughout the Empire, the Medical Research Council has provided the salaries of Professor Korenchevsky and Miss E. M. Hume and their assistants, in the department of Experimental Pathology.

The expenses of the investigation bearing on the vitamin content of various Empire products, which is being carried out in the Department of Biochemistry by Dr. Zilva, assisted by Messrs. Hoyle and Humphrey and Mesdames Soames, Crawford, Bracewell and Perry, are defrayed by a grant to the Medical Research Council from the Empire Marketing Board.

Dr. Ida Smedley-MacLean in the department of Biochemistry, continues to receive a grant from the Department of Scientific and Industrial Research, which body also supplies the salaries of her two research assistants.

The British Empire Cancer Campaign furnishes the salaries of Dr. T. Lumsden, in the department of Experimental Pathology, and his research assistant, Miss Kohn-Speyer, and a laboratory attendant.

The salaries of Dr. E. Weston Hurst and his assistants, together with the expenses of the investigation, are borne by the grant from the International Committee for the Study of Infantile Paralysis.

Accommodation for Professor Korenchevsky, Miss Hume, Dr. Lumsden, Dr. Smedley-MacLean, Dr. Hurst and the National Collection of Type Cultures, together with the expenses of the researches of the first three named are provided by the Institute.

DEPARTMENT OF BACTERIOLOGY.

Studies on Vaccinia.

Professor Ledingham has, in collaboration with Dr. McClean (Research Fellow) published experiments demonstrating the possibility of propagating vaccine virus from dermis to dermis of the rabbit by intracutaneous inoculation. In the course of such passage the virus appears to acquire a greatly increased capacity for proliferation in the dermis and a correspondingly diminished capacity for proliferation in the shaved skin. The dermal virus has the merit of being free from contaminating bacteria and it has been employed in the cultural experiments of Dr. Eagles and Dr. McClean referred to below.

In collaboration with Dr. Mary Barratt, Professor Ledingham has also been investigating certain problems concerned with the generalisation of the lesions of vaccinia in the body. It has been reported by other observers that the introduction, intravenously, of vaccine virus of high virulence has, in the rabbit led to the production of generalised lesions in the skin and various viscera. During the past winter similar lesions have been observed among rabbits inoculated with vaccinia at the Institute. All these animals, however, suffered from snuffles and organisms of the *Pasteurella* group were isolated from them. Certain of the stock rabbits at the time also showed symptoms of active pasteurellosis. Dr. Ledingham is, therefore, of opinion that generalised lesions following the intravenous inoculation of highly virulent virus may be due to activation of latent pasteurellosis in the rabbits by vaccinia and not to the unaided action of the virus itself.

Professor Ledingham has also studied the "elementary bodies" in vaccine virus which were first described by Paschen in 1906. These bodies (0.2μ in diameter) may or may not represent the actual virus, but in any case they deserve more attention than has yet been given them, particularly in view of the fact that the virus in vaccine lymph is held back by bacterial filters.

A systematic study of the cultivation of vaccine virus *in vitro* is being carried out by Dr. Eagles and Dr. McClean and certain important points have been established. Using the technique of Carrol and Rivers for the culture of the tissues of chick embryo, vaccine virus has been cultivated successfully through four generations. An increase to five million times the amount of virus in the original inoculum occurred. For the most part, dermal virus obtained under suitable conditions from a rabbit, has been employed as seed virus. Considerable irregularity in multiplication of the virus is observed although the method usually results in excellent tissue proliferation. This, together with the fact that a large increase in virus may be obtained without any obvious tissue growth, makes doubtful the generally accepted view that actively growing cells are necessary to the propagation of the virus. That the virus had not changed its character through cultivation became apparent when lesions before and after cultivation were compared by scarification and intradermal inoculation of the skin of rabbits; moreover, virus propagated *in vitro* is neutralised by antivaccinal serum from an immune rabbit. Unlike calf lymph, it deteriorates rapidly, even when kept in the cold room at a temperature of $0^{\circ}\text{--}2^{\circ}\text{C}$. Attempts to overcome this disadvantage have, so far, been only partially successful, and there is evidence that changes in oxidation-reduction potential are important factors. Various staining methods are being employed to determine what changes can be detected in the living cells when virus is grown in conjunction with them.

Research on Poliomyelitis.

In the last report mention was made of the offer to the Institute by Mr. Milbank, of New York, of £2,000 annually for three years towards the cost of research on poliomyelitis, such research to be carried out in conjunction with five other selected Institutes in Europe and America. Dr. E. Weston Hurst accepted a research appointment under this Fund and with him has been associated Dr. R. W. Fairbrother (Research Fellow). Professor Ledingham, under whose supervision the work is being carried out, has been greatly indebted to Dr. Flexner, of the Rockefeller Institute, for a supply of potent virus. The work so far undertaken may be summarised under the following headings.

Histology of the experimental disease in monkeys. The histology has been re-investigated with the aid of improved methods in neuropathological technique. The previous work on this subject dates from 1909 to 1913, and a divergence of opinion as to the nature of the cellular reaction, both in monkeys and in the human disease, has existed. The majority of authors have also expressed themselves in favour of a primary interstitial inflammation with secondary involvement and destruction of the nerve cells. Since the period mentioned, the use of the newer silver-impregnation methods devised by Del Rio Hortega has resulted in the discovery in the nervous system of new types of cell and among them the microglia which has now been found to play an important rôle in the cellular response to infection with the virus under discussion. The various stages in the evolution of these cells correspond to the "elongated glial cells" and "polyblasts" of the older authors, the origin of which was previously more or less obscure. The application of the oxidase reaction has shown that polymorphonuclear leucocytes, at any rate in the earlier stages of the disease, play a much greater part than has been generally believed. The present studies have also shown clearly that the nerve cell destruction is to be regarded as a primary event and not due to the interstitial changes.

The rôle of "Streptococci" in Poliomyelitis. The part attributed to bacteria, especially various coccal organisms, in the aetiology of experimental poliomyelitis has been investigated. During this investigation cocci have been seldom isolated either from the brain, heart-blood or cerebrospinal fluid of monkeys whatever the stage of the disease. Cocci have also been obtained from the tissues of both healthy monkeys and from those suffering from other diseases. All these cocci from different sources have been examined and from their morphology and the fermentations they produce they appear to be closely related. Similar cocci have also been recovered from the air of the rooms in which the various operations are performed. The results indicate that such organisms are not in any way aetiological connected with the disease but are most probably air-borne contaminants, though it is possible that organisms of a similar type belonging to the nasopharyngeal flora may occasionally gain access to the blood stream in the course of the disease.

The relationship of the so-called "globoid" bodies to the disease is now being examined.

Transmission to rabbits. Attempts have been made to reproduce poliomyelitis in rabbits, but so far without success.

Convalescent serum. Samples of serum from poliomyelitis convalescents, obtained from different sources, have been tested and found to possess neutralising properties. Monkeys intracerebrally inoculated with mixtures of serum and virus have remained well. No immunity was acquired as all succumbed to a later inoculation of virus.

Path of spread of virus in the experimental animal. An investigation of this problem is now well advanced.

Post-vaccinal and other forms of Encephalitis. An arrangement has been made for the examination (histological and experimental) by Drs. Hurst and Fairbrother of any material that may become available from such cases.

Studies on Antigenic constitution, Serological grouping and Immunising properties of Bacteria.

Rough and smooth types. Dr. Arkwright in the course of further investigation of the different kinds of bacterial agglutination has shown that the two types of agglutination by acids which he described in 1914, correspond to the flagellar and somatic agglutination by specific serum and are in all probability due to the same flagellar and somatic substances.

Miss R. M. Pitt has continued her work on the effect of growing *B. typhosus* in normal serum and in serum containing antibodies. She has found that the somatic smooth antibodies have a definite effect in producing changes in the character of the cultures, whereas no such effect is determined by the flagellar antibodies.

Pasteurella Group. Dr. J. T. Cornelius, of the Provincial Hygienic Institute, Lucknow, completed his study of the serological relationships of this group and a Thesis based on his work gained for him the degree of Ph.D. of the University of London. He found it possible by agglutinin-absorption

tests to group 17 out of 26 strains at his disposal. These fell into four groups of 7, 5, 3 and 2 strains respectively, while 9 defied classification. No relation was established between the serological grouping and the animal source, so obviously the old nomenclature segregating the strains in accordance with animal origin is biologically unsatisfactory.

Prophylaxis by "H," "O," and "R" antigens in Salmonella infection. Dr. Schütze in collaboration with Dr. Ibrahim, of Cairo, has made a study of the prophylactic values of the "H," "O," and "R" antigens of *Salmonella aertrycke* in mice. Previous observations on the lack of protective power aroused by the "R" antigen of rough strains and the non-participation of the "H" or flagellar portion of the bacillus in the production of immunity were confirmed.

Heating of bacterial emulsions to 100°C., though it does not destroy the agglutinogenic power of the "O" antigen, appears to reduce considerably its immunogenic value. A comparison of the rough and smooth variants of the same *aertrycke* strain indicated that the rough variant possessed about a quarter of the toxicity of the smooth, and that heating to 100°C. lowered the toxicity of the smooth variant to a quarter of that of the unheated. It appears, therefore, that for making vaccines it can be said that the use of a smooth strain is essential and that sterilisation at a temperature of 100°C. is to be avoided.

Antigenic constitution in spore-bearing Anaerobes. Work on various aspects of this subject, both theoretical and practical, has been continued by Dr. Felix and Dr. Muriel Robertson. The subdivision of *V. septique* and *B. tetani* into serological races has been shown to depend upon the "H" antigen. Apart from serological races each species possesses a uniform soluble toxin and it is now found that the serological types are bound together by the possession of a common "O" antigen. The biological importance of the "O" antigen seems to be further strengthened by this fact.

Heterophile antigen in Anaerobes. The occurrence of heterogenetic antigen in some of these organisms was established in the course of these investigations. The possible interference of heterophile immune bodies in complement-fixation tests with these organisms requires further enquiry.

Passive protection against Anaerobic infections by Anti-bacterial sera.

In order to obtain potent serum for this work horses have been immunised by Dr. Petrie with cultures of *B. tetani* and *V. septique* steamed at 100°C. The sera, which contained no antitoxin, were shown by complement-fixation to contain "O" immune body. Serum made from *V. septique* had a definite protective action when injected 24 to 48 hours before the infecting dose. It prevented the rapid and fatal evolution typical of gas gangrene. Instead, a transitory local necrotic lesion from which the animals recovered, occurred in every case. Purely antitoxic sera were less beneficial, being unable to protect at all in cases where an infecting dose of high virulence was used. The passive protective value of antibacterial serum appears, like the active immunity aroused by "O" antigen, to be dependent on the "O" immune body.

Weil-Felix reaction in Tropical Typhus.

Interesting and at first incomprehensible observations on the serum reactions of cases of tropical typhus were published recently by Fletcher and Lasslar from the Federated Malay States. Dr. Felix and Miss Rhodes have investigated the antigenic relationship between the so-called Kingsbury strain of *B. proteus* X19 and genuine and variant strains of X19. The results obtained suggest that the Kingsbury strain is a variant derived from the *B. proteus* X19 which Dr. Kingsbury originally obtained from the National Collection of Type Cultures. This result is of importance for the serological diagnosis of typhus and has a direct bearing on the theory of the Weil-Felix reaction.

Diet and Resistance.

Pursuing their investigations into the effect of diet on susceptibility to disease, Dr. Schütze and Dr. Silva have been studying the influence of a diet deficient in fat-soluble vitamins on the development of sensitivity to tuberculin in rats infected with tuberculosis. The experiments are still in progress.

Observations on the avirulent strain of the Tubercle bacillus (B.C.G.) advocated for Immunisation by Dr. Calmette.

Facilities have been given to Dr. M. Malkani (Bombay) to pursue his investigation of dissociation of B.C.G. cultures into virulent and avirulent types, a subject of study which he commenced in Dr. Petroff's laboratory in America.

The following have in the course of the year received the hospitality of the Department for longer or shorter periods: Miss I. J. F. Williamson, of the Fishery Board for Scotland, Dr. Gohar (Cairo), and Mr. Hassanein (Cairo).

DEPARTMENT OF BIOCHEMISTRY.

Alcoholic Fermentation.

The function of phosphates in alcoholic fermentation has been further investigated with the object of ascertaining the way in which they facilitate the rupture of the sugar molecule, which seems to occur in a similar manner in the production of lactic acid by muscle and of alcohol and carbon dioxide by yeast.

Professor Harden and Dr. Robison have studied the fermentation by zymine of the two monophosphates which are obtained from the products of the action of yeast-juice on a mixture of sugar and phosphate and by the partial hydrolysis of hexosediphosphate respectively. Both these compounds undergo a reaction with inorganic phosphate in the presence of zymine, which is comparable in rate with that of fructose under the same circumstances, but the volume of CO_2 evolved only corresponds with the fermentation of a small fraction of the amount of substance present. Work on this interesting phenomenon is being continued.

Professor Harden and Lord Henley have found that, in spite of great variations in the amounts of diphosphoric and monophosphoric esters produced in the fermentation of mixtures of sugar and phosphate by yeast preparations, the carbon dioxide produced is always approximately equivalent to the amount of phosphate esterified, slightly more with dried yeast, slightly less with yeast-juice.

Mr. Boyland (Grocers' Company Research Student) has studied the time relations of esterification and evolution of carbon dioxide in fermentation effected by dried yeast and has found that the evolution of gas at first lags behind the esterification but finally overtakes it, the ultimate result being a slight excess of CO_2 . The phosphoric ester found to be present in the early stages is the diphosphate, but as the reaction proceeds, a small amount of monophosphate is also found to be present, most of which appears to be trehalosemonophosphate. This line of investigation is now being applied to other yeast preparations.

Miss M. MacFarlane (Carnegie Scholar) has continued her work on fermentation by dried yeast and the study of various accelerating agents present in yeast preparations.

Phosphoric Esters produced during Alcoholic Fermentation.

Further results of considerable interest have been obtained by Dr. Robison and Dr. W. T. J. Morgan (Beit Memorial Research Fellow) from their study of the phosphoric esters produced during the fermentation of sugars by various yeast preparations. The isolation of a new ester, trehalosemonophosphate, from the products obtained with dried yeast was reported last year. Further work has shown that the production of this ester can be largely controlled by varying the conditions of the fermentation. Trehalosemonophosphate is formed, or accumulates, only when the concentration of inorganic phosphate falls to a low level, as when the fermentation is prolonged, but under these conditions it may amount to more than 70% of the monophosphate fraction. There is evidence that the remainder does not consist solely of the known hexosemonophosphates but contains still another phosphoric ester which may be a derivative of a reducing disaccharide. The interest of such a compound is increased by the possibility of it proving to be an intermediate stage in the synthesis of glycogen, a physiological process of which we have still very little knowledge.

The partial hydrolysis of trehalosemonophosphate has provided a means of obtaining pure glucosemonophosphoric ester, whose properties have been studied for comparison with those of the hexosemonophosphate of fermentation. The latter was thought to be a mixture of two esters of glucose and fructose respectively and Dr. Robison and Dr. E. J. King (Research Associate of the Department of Medical Research, University of Toronto) have succeeded in isolating the chief constituent in the pure state by means of its beautifully crystalline brucine salt, and have identified it as a glucosemonophosphoric ester by the study of its oxidation products. They have also obtained the second constituent in sufficiently pure form to identify it as a fructosemonophosphate.

The constitution of the glucose ester has been further investigated by Dr. Morgan and Dr. King who have prepared the methyl glucosidemonophosphates under different temperature conditions and have obtained products which, from their behaviour towards hydrolysis, were judged to be of the normal and "γ" type respectively. From these results, combined with other evidence, they conclude that the phosphoric acid group is attached to the third carbon atom of the glucose molecule. The glucosemonophosphoric ester obtained by the agency of yeast is of especial interest because the hexosemonophosphoric ester obtained from muscle has been shown by Pryde and Waters (Cardiff) also to be a glucose derivative, and it is of great importance from the point of view of carbohydrate metabolism to ascertain whether these two compounds are identical. The constitution of the two esters is being studied here and at Cardiff and the results are being correlated as work progresses.

Dr. Morgan has also continued his work on the constitution of hexosediphosphoric ester and has brought forward further evidence in favour of the formula previously proposed for this compound by Morgan and Robison. The investigation has, however, been interrupted by Dr. Morgan's appointment to the staff of the Serum Department, Elstree.

For the study of these phosphoric esters it was very important to have a satisfactory method for distinguishing between derivatives of glucose and of fructose. The reducing power towards alkaline solution of iodine has been employed for this purpose, but the methods described by various authors were found unreliable when applied to the estimation of very small amounts. These methods have been critically examined by Dr. Robison and Miss Morna MacLeod, who have determined the conditions necessary for obtaining satisfactory results.

The Bone Phosphatase.

Dr. Marjorie Martland and Dr. Robison have continued the study of the bone phosphatase and of its use as a biochemical reagent. As an example of the latter they have investigated the nature of the sugar obtained by the action of the enzyme on hexosediphosphoric ester and have obtained results which suggest that the biochemical synthesis and hydrolysis of phosphoric esters may play a part in the conversion of one sugar to another, such as occurs in the animal tissues. This suggestion is being followed up.

Dr. Robison has also collaborated with Dr. Honor B. Fell (Director of the Strangeways Research Laboratory, Cambridge) in an investigation of the origin and development of this phosphatase in the cartilage and bone of the embryo chick whilst in the egg, and also when minute portions of the embryo which represent the future limbs are isolated and propagated *in vitro*. Phosphatase they find is not present in the pre-cartilagenous stage of the limb buds of the three day embryo but can be demonstrated in those of five and six day embryos and increases regularly from this age onwards, this increase running parallel with the development of hypertrophic cartilage and of bone. During culture of the limb buds *in vitro* a similar development of phosphatase occurs when the cultures are made from those removed on the sixth day. The primitive cartilage in these, as previously shown by Dr. Fell, gives rise progressively to hypertrophic cartilage and to bone. When, however, cultures are made from three and four day limb buds, the cartilage which is formed remains of the small-celled type and no phosphatase is produced even after many weeks' culture. These results provide very strong evidence of the truth of Dr. Robison's earlier conclusion that the phosphatase is secreted by the hypertrophic cartilage cells and osteoblasts, but not by small-celled cartilage, which never ossifies.

Calcification in vitro.

These experiments have been continued by Dr. Robison and definite progress has been made. With suitable solutions a dense new deposit can be produced in slices of the bones of rachitic rats in periods as short as four hours. Under these conditions the effect of increasing concentrations of phosphoric esters in the solutions is pronounced and it is probable that for these short periods the enzyme activity of the cartilage is at its maximum, very little of the enzyme being lost by diffusion into the surrounding fluid.

The experiments have brought to light some perplexing problems of permeability which are being further investigated.

Oxidation of Fatty Acids.

The attempts to oxidise the higher fatty acids by means of hydrogen peroxide in the presence of iron, made in the department last year by Mr. C. G. Daubney had led to variable results. In some experiments a large proportion of the oleic acid was oxidised to acetic and formic acids, but the conditions necessary to produce constant results could not be determined. Miss Battie and Dr. Smedley-MacLean have since found that if copper be substituted for iron, constant results are obtained. Sodium oleate is readily attacked and the oleic acid can be completely broken down to carbon dioxide, acetic and formic acids with a little succinic acid. Sodium palmitate is similarly attacked though to a less extent, but the stearate is only slightly affected.

The action of the cupric salts in catalysing this reaction appears to be unknown. The catalytic action of copper upon the oxidation of a number of the lower fatty acids, *e.g.*, succinic, tartaric, lactic, pyruvic and malonic, has, therefore, been studied. In all cases oxidation occurred, being especially rapid in the case of tartaric acid. This oxidation of the higher fatty acids by H_2O_2 in the presence of cupric salts appears to resemble the biological oxidation of these acids, in that it proceeds straight through to simple products without the appearance of any intermediate acids containing even numbers of carbon atoms, such as might be expected from the theory of β oxidation. The relative rates of attack upon these intermediate acids is the subject of further investigation.

Nature of Unsaponifiable Matter of Vegetable Fat.

Dr. Smedley-Maclean has produced evidence that a third unsaturated sterol accompanies the zymosterol and ergosterol present in yeast. Zymosterol has probably not yet been obtained in a pure condition. Unlike ergosterol, it is not isomerised by the action of dry HCl in dry chloroform solution, but forms an addition compound containing one atom of chlorine.

The unsaponifiable matter of the fatty substances extracted from spinach leaves was examined and a hydrocarbon hentriacontane isolated. Since this may be prepared in the laboratory by the condensation and reduction of palmitic acid, in the plant it is probably derived from this source. A similar hydrocarbon was isolated from cabbage.

Experimental Researches on the Anti-scorbutic Principle (Vitamin C.).

Dr. Zilva, who is working for the time being on a research entrusted to the Institute by the Medical Research Council on behalf of the British Empire Marketing Board, is continuing the chemical investigation of the antiscorbutic factor in lemon-juice and is devoting further attention to the study of the cause of the spontaneous inactivation of the vitamin. As mentioned in a previous report, the antiscorbutic vitamin is associated in fruits and vegetables with a reducing substance and protected thereby from oxidation.

Efforts have been made to obtain concentrated fractions of the reducing principle free from antiscorbutic activity. Such fractions would greatly help to elucidate the relationship of the reducing principles to the vitamin in the plant. The properties of a third and "thermolabile factor" have been also studied with the special object of ascertaining whether a substance or substances of the nature of an enzyme were concerned in the modification of the stability of antiscorbutic activity of neutral solutions which have been previously heated under anaerobic conditions. These studies of the antiscorbutic principle of lemon-juice were supplemented by similar investigations of the juices of the tomato, cabbage and swede. Although a number of facts have been disclosed by these experiments the work has not yet reached a stage at which definite conclusions can be drawn.

Metabolism of Animals Affected by Scurvy.

Continuing the investigation on the influence of scurvy on the metabolism of the organism, Dr. Zilva and Mr. H. L. Shipp have studied the nitrogen absorption and retention of scorbutic guinea-pigs. It was found that there was no alteration either in the absorption or in the retention of nitrogen during the period preceding the onset of scurvy and during the early stages of the disease. In the premortal phase or when the scurvy was acute, the nitrogen balance was markedly negative, attributable to starvation of the organism. This investigation is being continued in collaboration with Mr. F. G. Humphreys.

The Distribution of Vitamin C. in Empire Fruits.

The enquiry on the variation of the antiscorbutic factor in apples has been continued by Dr. Zilva, Mr. E. Hoyle and Miss M. F. Bracewell. It is found that the variation in activity is more dependent on the variety of the apple than on its origin. Baking the cooking variety in its skin did not destroy the antiscorbutic activity of the apple to any appreciable extent. The mode of storage seems to influence the determination of the antiscorbutic activity of the apple, gas-storage being less favourable than cold-storage.

An investigation of the influence of maturity upon the antiscorbutic activity of citrus fruits has been started. Attention has, so far, been devoted to the orange and the grape fruit. The materials for the investigation have been carefully collected with the help of officials attached to the Empire Marketing Board, in the first case in Palestine and in the second case in British Honduras.

Australian sultanas and raisins prepared by the hot and cold "dip" processes have been assayed for Vitamin C, but very little antiscorbutic activity was found in any of the samples.

A representative sample of a West Indian honey and a freshly made sample of honey prepared under known conditions at Rothamsted Experimental Station have been investigated by Mr. Hoyle for their content of Vitamins A, B, C, and D. The results show that the specimens of honey did not contain significant quantities of any of these Vitamins and it is not proposed to continue work of this kind on honey.

The Influence of various factors on the Vitamin content of Dairy products.

Preliminary experiments for an exhaustive enquiry into the vitamin content of Dominion dairy products and the influence of environment, breed of cow, transit, storage and other factors have been commenced by Dr. Zilva, Miss Soames and Miss Crawford. Samples of butter prepared in New Zealand under carefully controlled conditions in January, 1928, have been tested for Vitamins A and D. The data so far available point to the fact that these butters are rich in both Vitamins. Butters were also prepared at the National Institute for Research in Dairying, Reading, under conditions resembling as nearly as possible those prevailing in Australia and New Zealand and these have been placed in cold storage to be tested at a later date. Parallel experiments on the fat-soluble Vitamins in a commercial brand of margarine and their behaviour on storage have also been made.

Attempts to improve Methods for Vitamin assay.

Dr. Zilva, Miss Soames and Miss Perry have commenced an investigation into the limitations in the accuracy of some of the methods of assay of the Vitamins. Attention is being specially devoted to Hojer's test for Vitamin C, which is based on the observation made by Zilva and Wells, in 1919, that microscopical changes can be observed in the teeth of guinea-pigs in the early stages of scurvy and to the "line test" for Vitamin D. The object of these studies is to ascertain whether less lengthy and costly methods can be introduced in the above investigations without sacrificing accuracy and whether greater accuracy can be obtained by supplementary tests.

DEPARTMENT OF EXPERIMENTAL PATHOLOGY.

The Reducing System in Boiled Meat and the Anaerobic Cultivation of Bacteria.

Dr. Elizabeth Lepper and Professor Martin have completed their investigation of the principles underlying the usefulness of adding cooked muscle or other tissues to culture media in order to cultivate anaerobes. They have found that two chemical mechanisms are involved. One of these is an autoxidation of the unsaturated fatty glycerides in the lipoids of the tissue under the catalytic influence of the haematin and parahaematin present. By this means the oxygen in the medium is soon removed. When this is accomplished, a sulph-hydril grouping fixed to one or other of the coagulated proteins of the tissue comes into action and produces a reduction potential sufficient to favour the propagation of all the anaerobes tried. The thermostable autoxydisable system involved in the former action, turns out to be the same as that discovered by E. Robinson in her study of the oxidation of linseed oil. The catalysis by haematin and its compounds differs from that produced by iron in its capacity to act efficiently in neutral and alkaline as well as in acid solutions.

Coagulation of the Blood.

Dr. J. O. W. Barratt's investigation of the anticoagulant action of antithrombin, contained in blood plasma, indicates that the action of antithrombin is directed to thrombin. The experiments made showed also that antithrombin has no action upon fibrinogen. It was found that in the presence of a large excess of distilled water antithrombin could be heated to 100°C. without being destroyed.

Further investigation has been undertaken with a view to determining the type of the action of antithrombin upon thrombin and, based upon the results obtained, an attempt has been made to devise a method of estimating the amount of antithrombin present in plasma. Closely associated with this is the estimation of thrombin, which has also been the subject of a considerable amount of study. An attempt to determine the values of the constants of the equation employed to represent the interaction of antithrombin and thrombin is in progress.

The influence of temperature upon the action of antithrombin upon thrombin is also being investigated.

Endocrinology.

Dr. V. Koronchovsky in co-operation with Mrs. M. Dennison, has continued the investigation of the inner secretions of the testicle and prostate, and of the effect of injection of the pituitary gland.

Testicular and Prostatic Hormones. So far all efforts to obtain a specifically active extract by various means have been negative although extracts which increase nitrogen metabolism have been obtained. This result is astonishing in view of the ease with which active extracts can be obtained from the ovaries.

Special attention has latterly been directed to the investigation of the nutrition of cryptorchid animals, as compared with castrated or normal animals, and to the study of the influence of injections of extracts prepared from cryptorchid testes. Cryptorchism was produced experimentally in young and adult animals by pushing the descended testes back into the abdomen from the scrotum and occluding the inguinal canal, in order to prevent the redescend of the testes into the scrotum. As a result of this procedure nearly all the generative tissue disappears from the testes and the interstitial tissue or Leydig's cells, which are supposed to possess an inner-secreting function, hypertrophy.

The object of these experiments was to obtain and use glands having as much as possible of this special secreting tissue and devoid of generative tissue.

The operation was performed on rats and rabbits and in a few cases, on guinea-pigs and domestic pigs. The experiments on domestic pigs were performed with the co-operation of Captain J. Golding at the National Institute for Research in Dairying, Reading. Cryptorchid pigs were found to grow larger and fatter than either normal or castrated animals. As compared with controls, their appetite is greater and their growth and nutrition better. The increase in weight is over 10% and may give this work economic importance.

The results of these experiments were corroborated by numerous experiments on rats. Whilst the cryptorchid rats were heavier and their appetite greater as compared with normal controls, castrated animals weighed less and had smaller appetites than the corresponding normal controls. There is a striking difference in these respects, between cryptorchid and castrated rats.

Injections of the extracts prepared from cryptorchid testes did not entirely prevent atrophy of the prostate, seminal vesicles and penis which always occurs in castrated animals. Some of the extracts, however, did delay the atrophy of these organs. Addition of the prostatic extract to that of cryptorchid testes did not have an additional inhibiting action on the atrophy. In most cases the injection of these extracts increased the amount of fat, as measured by the weight of intra-abdominal fat. This agrees with the increased amount of fat in animals made cryptorchid, i.e., in those in which the amount of inner-secreting tissue of the testes had been increased.

The influence of the extracts on nitrogen metabolism was indefinite,

The Pituitary Gland. A study was made of the influence of injections of glycerine extracts, prepared from fresh anterior lobe of the glands of bulls and oxen, on the weight of rats, their predisposition to adiposity as measured by weighing the intra-abdominal fat, and on the weights of some of their endocrine glands, namely, testes, ovaries, prostate, adrenals and thyroid.

The injections were made into animals having (i.) a normal amount of sexual hormones (normal rats), (ii.) an increased amount of sexual hormones (cryptorchid rats), and (iii.) a lack of sexual hormones (castrated rats). Only in normal rats could any growth-promoting influence of the injections be observed, none being detected in castrated or cryptorchid rats. A slight growth-promoting influence on the sexual glands was noted except in the case of the prostate, which was uninfluenced. The uterus was found to be heavier in injected rats as compared with that of uninjected control females.

Of the remaining endocrine glands only the adrenals were influenced by the injections. These glands showed an increase in weight in injected rats.

Histological investigations are not yet completed. No definite difference was found between the influence of extracts from the anterior lobe of the bull and the anterior lobe of the ox.

Experiments in Nutrition.

Water-Soluble B Vitamins. (1) **Antineuritic, anti-beri-beri, more heat-labile vitamin B₁;** (2) **Anti-dermatitis, anti-pellagra, more heat-stable vitamin B₂.** Dr. H. Chick and Miss Roscoe have continued their efforts to isolate vitamin B₂ from yeast and to this end have examined each stage of the Kinnersley-Peters process by which an antineuritic (vitamin B₁) concentrate is prepared, free from vitamin B₂. About one-half to two-thirds of the vitamin B₂ contained in the original yeast was found to be carried down in the precipitate formed when lead acetate is added to an extract of the washed yeast-cells made with boiling dilute acetic acid. From this precipitate a relatively pure preparation of vitamin B₂ can be obtained by decomposition with SH₄, the success of the operation depending on the careful adjustment of the reaction of the solutions in which the precipitation takes place. In some cases a preparation of vitamin B₂ free from vitamin B₁ has been obtained but this result was not constant and seems to depend on the relative amounts of the two vitamins present in the original yeast..

Properties of Vitamins B₁ and B₂. All the preparations and concentrates of vitamins B₁ and B₂ which have been studied, contain nitrogen. Peters has shown that treatment of his antineuritic concentrate with nitrous acid (to decompose any amino groups present) does not impair the vitamin B₁ potency of his preparation. Levene, working at the Rockefeller Institute, has made the announcement that amino-nitrogen is, however, an integral part of vitamin B₂. This result has not been confirmed. After treatment with nitrous acid, Miss Chick has found no diminution in the potency of the vitamin B₂ material prepared from yeast.

She finds that vitamins B₁ and B₂ possess the same capacity to dialyse through membranes and are both stable in presence of dilute acids. Vitamin B₂ is much the more stable to heat, being reduced only by about one-half if heated 5 hours at 120°C., whereas vitamin B₁ is completely destroyed by this treatment. Vitamin B₂ is insoluble in strong alcohol (82% and over), whereas vitamin B₁ is soluble. Vitamin B₂ is more readily absorbed on precipitates and various finely divided materials than vitamin B₁, and the range of reaction over which this occurs (pH 4-pH8) is much greater.

Distribution of Vitamins B₁ and B₂ in Natural Foodstuffs. Dr. Chick and Miss Roscoe have worked out biological methods, based on growth response in rats, for the quantitative assay of vitamins B₁ and B₂ respectively. In estimating the content of these vitamins in foodstuffs, comparison is made of the minimum dose of the food in question necessary to restore normal growth (10-12 g. increase in weight weekly) in young rats which had ceased to put on weight owing to lack of the vitamin concerned. In the estimation of B₁, vitamin B₂ is added to the basal diet as Peters' antineuritic concentrate; in the estimation of B₂, vitamin B₁ is supplied by a daily ration of yeast in which the vitamin B₁ originally present is destroyed by autoclaving at 120°C. for 5 hours. Egg-white has also been found a convenient source of vitamin B₂, unaccompanied by vitamin B₁.

Using the above method, Dr. Aykroyd (Beit Memorial Research Fellow) and Miss Roscoe have made a systematic assay of vitamin B₁ in wheat and maize grains and their constituent parts. These two cereals were chosen because if vitamin B₁ were indeed concerned in the prevention of pellagra, as is suggested by the clinical and experimental researches of Goldberger and his colleagues in the United States, a striking discrepancy in their content of vitamin B₁ might explain the connection between pellagra and the consumption of maize. The results obtained do not lend much support to that interpretation. The germ and bran of wheat proved to be fair sources of vitamin B₁, and whole wheat to be somewhat richer in this respect than whole maize. Comparison of the respective endosperms of these two grains, as represented by white flour and maize grits or polenta, showed little difference, both being poorly endowed with vitamin B₁. The immunity to pellagra of people using wheaten bread would seem, therefore, to be due to other constituents in the diet commonly consumed by such populations.

The cereals, even those parts richest in vitamin B₁, were found to be poor sources of this factor compared with yeast and many foods of animal origin, as, for example, liver, egg-white, milk, meat-muscle, and to a less degree, egg-yolk. The results obtained correspond with the relative values of these foods for the prevention and cure of pellagra observed by Goldberger and his colleagues and thus support their view of its aetiology.

The embryos of cereals, on the other hand, have long been known to be one of the chief sources of the antineuritic vitamin B₁, while milk and meat contain relatively little, and egg-white none of this vitamin. Egg-yolk is somewhat richer in vitamin B₁ than in vitamin B₂, and yeast contains both in abundance.

Excretion of Vitamins B₁ and B₂ in the Faeces. Following her work described in last year's Report on "Refection" (or the capacity under certain conditions to thrive on diets deprived of B vitamins), Miss Roscoe has investigated the result of faeces consumption upon vitamin B deficiency. Rats on a diet devoid of B vitamins, will readily eat their own faeces, especially if these are previously dried, and as a result, will frequently maintain fair health with subnormal growth, showing none of the specific signs of vitamin B₁ or B₂ deficiency for a period of several months from the time of weaning. It has been suggested that these vitamins are synthesised by the activity of bacteria inhabiting the lower part of the alimentary tract, but that, either they can only be absorbed in the stomach or small intestine, or that although the excreta contain large quantities of the necessary organism, repeated re-infection of the upper part of the alimentary canal is needed. Miss Roscoe is continuing her work.

Influence of dehydration on the nutritive properties of Egg-white. Dr. M. A. Boas (Beit Memorial Research Fellow) continued the investigation of the change which occurs in the nutritive properties of egg-white as the result of desiccation. It has already been suggested by her that the symptoms produced in young rats, fed upon a diet in which dried egg-white was the sole source of protein, might be due to a toxic substance in the dried egg-white. This theory has received further support from her recent work. The albumen itself is harmless, for a preparation of the total albumen fraction from the "toxic" dried egg-white was used as the sole protein of the diet, without the production of any of those symptoms which follow the use of the parent substance.

It is not yet clear from which component of the egg-white the toxic substance originates. It has, however, been shown that neither the globulins, nor the albumens, nor the ovomucoid are implicated, so that it would appear to be some non-protein constituent.

Zymosterol as a possible source of Vitamin D. Miss E. M. Hume and Miss H. Henderson Smith, in conjunction with Dr. I. Smedley-Maclean, have completed the biological examination of irradiated zymosterol, the new sterol recently discovered by Dr. Smedley-Maclean in yeast. The results obtained have finally excluded the possibility that zymosterol can act as a parent substance of vitamin D. The specificity of ergosterol, in acting as pro-vitamin D thus remains unchallenged, in spite of the fact that both these sterols from yeast show a high degree of unsaturation.

The possible Synthesis of Ergosterol in the Animal Body. Miss Hume and Miss Smith are also engaged in trying to obtain some evidence as to the possibility of the synthesis of ergosterol in the animal body. For this purpose rats are being fed on a diet devoid of sterols. The diet is complete in all other ways. One of the chief difficulties has lain in the preparation of a supply of vitamin A, which shall be sterol-free. This preliminary has now been satisfactorily accomplished by preparing a petrol-ether extract from spinach, saponifying it and precipitating the sterols in the unsaponifiable fraction with digitonin. The ultimate product is taken up again with liquid paraffin, in which form it can be conveniently fed to rats in drop doses and is found to be a satisfactory source of vitamin A.

Occurrence and Nature of Vitamin A. In the course of the preparation of the supply of sterol-free vitamin A, it became apparent that vegetable extracts as a source of vitamin A would repay a combined chemical and biological investigation. The former is being undertaken by Dr. Smedley-Maclean with the help of Miss D. L. Collison, while Miss Hume and Miss Henderson Smith are carrying out the latter.

The Relation of Vitamin A to Carotene. Coincidentally with the formation of chlorophyll under illumination, carotene appears in the leaves of plants. The unsaponifiable matter and vitamin A value of extracts from green and white cabbage, and the relationship of vitamin A to carotene from various sources are, therefore, being investigated. In extracts from white cabbage, vitamin A is found to be absent or only present in such small traces as might be accounted for by the not quite complete aetiolation of a few of the leaves used, the transition from white to green in the heart of a cabbage being very gradual. From green cabbage an imperfectly purified preparation of carotene has been obtained which shows a beneficial effect on rats suffering from deficiency of vitamin A, in doses as low as 1000 mg., and which is powerfully curative in doses of 100 mg. The mother liquors from the recrystallisation of the carotene were comparatively inactive.

Biological Action of Light.

The Proportion of the total energy of Sunlight absorbed by the Body. Everyone is aware that sunlight warms the body and is either comforting or oppressive according to circumstances. The amount of energy radiated from the sun which reaches the earth is known and the amount absorbed by the atmosphere according to its clarity and to the altitude of the sun can be assessed, but hitherto the actual quantity of this energy which the body may derive from sunlight has only been guessed at.

To fill this blank in knowledge, Professor Martin has been endeavouring to determine what proportion of the total radiant energy of sunlight is absorbed by the skin and various fabrics and converted into heat. This can only be indirectly found by ascertaining the proportion scattered and turned back.

It was reported last year that the difficulties in arriving at a method for measuring the amount of light scattered by, for instance, skin or a piece of paper, had been surmounted. During last summer there were sufficient clear days with steady sunlight to continue the investigation and the absorption through the skin of a number of Europeans with fair and dusky skins was determined and also that of Indians and a negro. The proportion absorbed varied from 65% in the very fair to 87% in the negro.

It is calculated that the total solar energy impinging upon the surface of a man of average size is about 4,000 calories per minute when the air is clear and the altitude of the sun is 45°. If three-quarters of this is absorbed, this supplement to the heat normally formed in the body at rest would increase the rate of heating fourfold. It is, therefore, understandable how well-browned children at an Alpine Sanatorium can run about naked on the snow without becoming cold, although the temperature of the air may be some degrees below freezing point, as long as they are in the sun and there is no wind.

Absorption of Ultra-violet light by the Epidermis. The important effect of ultra-violet light upon calcium metabolism and rickets has rendered it desirable to ascertain to what extent the epidermis is permeable to radiation capable of activating ergosterol and giving rise to vitamin D.

In the last report the endeavours of Dr. N. S. Lucas to arrive at a numerical value for the coefficient of absorption of epidermis for ultra-violet light of different wave-lengths was referred to and it was pointed out that the optical heterogeneity of the tissue had so far frustrated his efforts. A method has since been devised to obtain an approximate estimate of the amount of scattering of the light, which can be applied to the calculation and thereby the real transparency arrived at. Other observations of Dr. Lucas indicate that the transparency to ultra-violet light of keratin, chitin and epidermis, which is smaller than that of other proteins, is due to the high content of cystin and aromatic groupings in the former.

Influence of Ultra-violet Light on the well-being of Tropical Monkeys. Dr. Lucas, Miss Hume and Miss Henderson Smith, have continued their observations on the marmoset colony irradiated with ultra-violet rays.

The English-born male "Evil," now 2½ years old, mated with a Brazilian female, produced twins, which, however, owing to their exceptional size, were born dead at full term. This female subsequently died from empyema. A macroscopic examination showed no abnormality of the bones. The older Brazilian pair, though healthy, seem to have stopped breeding. They appear to be of considerable age.

A second younger Brazilian-born pair has produced female twins, now 9 months old, perfectly developed and almost fully grown. It is hoped that these, when mated with "Evil" will produce a wholly English-bred second generation. The same Brazilian pair, in February, 1929, has also produced male twins, which promise as well as the female twins. It is hoped in the immediate future to compare the breeding capacity of marmosets fed on vitamin D with that of those in which the vitamin has been produced by direct irradiation.

The squirrel monkeys have not continued to thrive. It is now clear that they require more energetic anti-rachitic treatment than do the marmosets; several interesting factors may be involved.

Factors Governing the rate of Loss of Heat from a sweating Body.

Dr. A. J. Canny (Rockefeller Fellow, Sydney University) is engaged upon a research, in collaboration with Sir Charles Martin, into the laws governing the rate of loss of heat from a sweating body at constant temperature as the temperature and humidity of the air and wind velocity are varied.

Cancer Research.

Dr. T. Lumsdon, with the assistance of Miss A. C. Kohn-Speyer, has continued to investigate tumour immunity.

Tissue Culture Experiments. The nature of the substances existing in the serum of any animal which are cytotoxic to the tumour and normal tissue cells of animals of a different species, has been investigated. These substances (*heterolysins*) form a first line of defence against the invasion of any animal's tissues by foreign cells. They are of the nature of heat-labile, non-specific, antibodies and are

present in but small quantity in the serum. In nearly related animals they may prove ineffective, so that mouse cancer cells may escape destruction at their hands and grow in the body of a rat until the rat elaborates, after 7-10 days, its second line of defence, consisting of much more heat-stable, and specific, anti-mouse-cancer bodies. Those, with the assistance of a cytase produced by extravasated white blood corpuscles, invariably succeed in destroying the mouse cancer cells which had begun to proliferate in the rat. Strong confirmation of the existence of specifically anti-malignant-cell bodies was obtained by inoculating rats with chicken tumour cells. The serum of these rats was applied to mixed cultures of mouse cancer and mouse normal tissue cells. The cancer cells were killed after a few minutes, the normal tissue cells were quite uninjured, i.e., the anti-chicken-tumour serum from a rat was thus shown to contain antibodies lethal to tumour cells which were not those used as an antigen. The effective antibodies were, therefore, specifically anti-malignant, and not simply anti-chicken or anti-mouse bodies.

Vaccine Treatment of Implanted and Spontaneous Tumours. Further experience of the vaccinal effect produced by injection of 1% formalin into implanted tumours *in corpore* has accentuated the value of this treatment. It is found that not only rat sarcoma but also rat carcinoma and mouse carcinoma (Twort) can be cured in this way, leaving the animals immune to any subsequent re-inoculation. A considerable degree of cross-immunity is also induced; thus, rats cured of Jensen's rat sarcoma are found to be immune to a rat sarcoma of a different variety (L. S.) and also to rat carcinoma. Spontaneous tumours are less amenable to this form of treatment than implanted tumours, but there is some evidence that similar principles are involved and measures are being sought to make it possible to obtain equally good results in each case.

Preventive Vaccination against Implanted Tumours. After many failures results are now being obtained which promise some success in this direction.

Rat sarcoma cells, attenuated (by treatment with a weak solution of formalin) to a progressively diminishing degree, are inoculated at weekly or fortnightly intervals into rats. After 4-5 injections the rats are given a test inoculation of untreated active tumour cells. In a high and increasing percentage of cases the treated rats are found to have been rendered immune and the implanted tumours fail to grow, while implantations of identical test material into untreated control rats grow as progressive tumours in practically every case.

A strain of mice in which 70% of the females develop, sooner or later (5 to 20 months), spontaneous mammary cancer, has been received from Dr. Burton T. Simpson, of Buffalo, U.S.A. These mice are breeding freely and should supply material sufficient to determine whether results such as are referred to above in the case of implanted tumours, can be achieved in tumours arising spontaneously.

DEPARTMENT OF PROTOZOOLOGY.

An heritable modification in structure imposed upon a non-conjugating Protozoon and its significance for Chemotherapy. Dr. Muriel Robertson's study of the effect of acriflavine upon cultures of *Bodo caudatus* has been continued. The drug has the property of producing a percentage of modified bodos without parabasal bodies but no permanent aparabasal strains have been produced. A technique was devised whereby the resistance, as judged by two different types of survival experiment, could be correlated with the percentage of modified bodos produced when the strain is put to grow in an ascending series of concentrations of acriflavine incorporated in the culture medium. A further method of analysis was afforded by the testing of single cell cultures isolated from various mass cultures.

The proportion of altered bodos in relation to the concentration of acriflavine in which it occurs is found to be the index of the sensitiveness of the strain at that date. The maximum reaction, as gauged by the numbers of modified bodos produced in an untreated strain of average sensitiveness, is about 70 to 75% and this occurs in so low a concentration as one in a million. One in five million gives a count below the maximum and one in fifty million produces only 1 to 4% according to the sensitiveness of the strain.

A strain resistant to any particular concentration shows none or only a very small percentage (less than 5%) of modified bodos in that concentration, but will show modified forms in higher concentrations than the one to which it has been acclimatised.

The untreated strain was unable to evolve at any time upon plates containing $\frac{1}{5000}$ acriflavine, while the strains which had been made resistant would live continuously in $\frac{1}{1500}$ acriflavine plates. No evolution took place in $\frac{1}{1000}$ although the bodos of the resistant strains could survive for some days in this concentration.

A high resistance once acquired is retained through prolonged cultivation upon drug-free media. A gradual loss occurs, partly by a dilution through multiplication of the character impressed and partly by the survival of the variants of less resistance to acriflavine but of perfect viability in other circumstances, and the competition of these within the strain. The loss of resistance is greatly accelerated in single cell cultures isolated from the resistant strains, but up to the present no treated strain has entirely lost the effect of the original exposures to the drug. The longest time elapsing between the creating of a partially resistant strain and its test for a resistance above that of an untreated culture, is one year.

DEPARTMENT FOR THE STUDY AND PREPARATION OF ANTITOXIC SERA.

The Preparation of Anti-Plague Serum.

During the past twenty years, Dean, Rowland and MacConkey, working in this department, prepared plague antitoxin by immunising horses with the endotoxin of the plague bacillus. The efficacy of this antitoxic sera was carefully tested by the Plague Research Commission in India, with the result that no significant difference was evident in the mortality rate of patients to whom the serum was administered and of patients who did not receive this form of treatment. There are, however, reasons for believing that an antiplague serum should possess not only antitoxic but also antibacterial properties. With this consideration in view Dr. Petrie has recently prepared antiplague sera from two horses. The value of these sera in protecting laboratory animals against a living virulent culture is being estimated and if the results prove to be satisfactory it is proposed to apply the method to the treatment of human plague. Sera prepared with the explicit aim of neutralizing plague toxin and at the same time of inhibiting the multiplication of the bacillus in infected tissues have not hitherto been available.

The Preparation of a Serum against *B. welchii*.

Dr. Petrie has been co-operating with Dr. Muriel Robertson and Dr. Felix in the preparation of sera for use in the treatment of anaerobic infections in man, in view of the observations by the last two on the antigenic complexity of these microbes, referred to in the review of the researches of the bacteriological department above.

The Preparation of a Dysentery (Shiga) Toxin Suitable for Use as a Test Toxin.

Numerous attempts have been made in the department to extract the specific toxin from the bodies of the Shiga strain of dysentery bacillus in a relatively pure, concentrated and stable form. The experimental conditions for achieving this result are not yet wholly apparent, and it has not proved possible to obtain a satisfactory yield of toxin at each successive attempt. Nevertheless the results obtained by Dr. Petrie are encouraging, since, for example, a toxin has been prepared which has proved superior as a test toxin to any which he has used hitherto. The dose of this preparation which corresponds to the standard unit of antitoxin is less than $\frac{1}{30}$ th c.cm., and it has remained stable. On one occasion recently, a toxin was obtained which, when administered intravenously to mice, proved fatal in a dose of $\frac{1}{1750}$ c.cm. The experiments are being continued.

The Experimental Production of Pneumococcal Endocarditis.

Evidence has been obtained by Dr. Petrie that an infective endocarditis can be readily induced in immune rabbits by intravenous injections of living cultures of a virulent strain of pneumococcus, provided that in addition, they are subjected to recurring losses of blood by cardiac puncture. An obvious possible explanation for the occurrence of endocarditis after this procedure is that the slight trauma occasioned by puncturing the heart may facilitate an infective focus, which forms the starting point of a vegetative endocarditis. The experimental technique was, therefore, modified by substituting for cardiac puncture repeated withdrawals of blood from the jugular vein. Although in a number of rabbits thus treated, an amount of blood equal to the total blood volume has been removed, signs of cardiac disease have not so far appeared. On the other hand, a rabbit rendered anæmic by a series of sub-lethal intravenous injections of an anti-rabbit-red-cell serum developed a typical mitral endocarditis which ended fatally. This animal was treated in exactly the same way as those just mentioned except that blood-letting was not practised. From the heart-blood of this rabbit an avirulent variant of the original strain of pneumococcus was isolated. The experiments suggest that the injurious action of anti-red-cell serum on the vascular endothelium, as well as upon the red cells, predisposed to the infective process. A fresh series of experiments on similar lines has been begun to test the correctness of the theory, which, if confirmed, may throw light upon the pathogenesis of infective endocarditis in man.

The Maintenance of a Healthy Stock of Guinea-Pigs.

The pneumococcal infection of guinea-pigs to which reference has been made in previous reports still persists among the breeding stock, but to a diminished extent. It was thought that the higher incidence of this infection during the early months of the year might be attributable to the lack of sunlight, and it was decided to make good the deficiency by means of irradiation. One half of the breeding stock, therefore, was regularly irradiated by means of a mercury vapour lamp, the other half serving as a control. The experiment lasted for one year and the conclusion drawn was that no benefit accrued from the light treatment; indeed, as it happened, the control stock appeared to give better results both as regards general health and fertility. The improvement in the stock as a whole is probably ascribable to the regular administration of an adequate diet, especially of suitable green food, and to the selection for breeding purposes of the progeny of animals that have a "clean" breeding history, and that presumably possess a natural resistance to infection with the guinea-pig strain of the pneumococcus. An endeavour is, indeed, being made to breed a pure line of resistant animals.

DEPARTMENT FOR THE STUDY AND PREPARATION OF ANTI-VARIOLOUS VACCINE.

Further work has been done by Dr. Green with the view of raising the virulence of the vaccine virus *in vitro*. Initial experiments have been made in an endeavour to ascertain whether vaccine virus other than a dried preparation can be kept at a high stage of potency at ordinary temperature.

FOOT AND MOUTH DISEASE RESEARCH.

The experimental work for the Research Committee of the Ministry of Agriculture has been continued at the Institute during the year, under the supervision of Dr. J. A. Arkwright, by Mrs. Gibbs (formerly Mrs. Burbury) and Dr. A. Ciuca (Bucharest).

Mrs. Gibbs has made a number of interesting observations on the infection of hedgehogs by inoculation and by contact. As the result of experiments on the effect of inoculating guinea-pigs with mixed Foot and Mouth disease and Vaccinia viruses it was found that both or one of these diseases might develop unaltered. It was easy to detect Foot and Mouth virus when mixed with Vaccinia virus by the generalised vesicles produced by Foot and Mouth virus, but not by Vaccinia. The results of these experiments depended largely on whether the part of the skin inoculated was more susceptible to one or the other virus. The immunity of guinea-pigs which had been treated with killed Foot and Mouth virus, such as is used as a vaccine, and virus respectively, was further examined and it was found that the immunity resulting from a dose of formalised Foot and Mouth virus was one of the same kind as in animals recovered from an attack of the disease, but of less degree.

Experiments on the electric charge carried by the Foot and Mouth virus have been completed.

Professor Ciuca has examined four samples of Foot and Mouth virus from Rumania and found that three of them appeared to be identical with Vallee's virus "O" which is the commonest type in western Europe, but the fourth sample belonged to a slightly divergent type. Professor Ciuca has shown that the three main types of this virus, *i.e.*, types "O," "B," and "C," can be distinguished from one another *in vitro* by a complement fixation technique without animal inoculation.

The Third Progress Report of the Foot and Mouth Research Committee of the Ministry of Agriculture was published in 1928 and included a review of the present knowledge of the virus of this disease by Sir Charles Martin, Chairman of the Committee. The report also contains in an Appendix, an account of the work done at the Lister Institute for the Committee by Dr. H. B. Maitland, Mrs. Y. M. Burbury, Dr. T. Hare, and Mrs. M. Cowan Maitland.

NATIONAL COLLECTION OF TYPE CULTURES.

During the year the National Collection of Type Cultures has shown expansion, both in the number of strains received and in the number of cultures distributed to workers at home and abroad. Over 300 new strains were added to the Collection and over 5,000 cultures were distributed.

The activities of this department are not to be measured simply by the accession of cultures to the Collection and their distribution to workers in the field of microbiology. Though this side of the work has very gratifyingly extended and workers in many lands have acquired the habit of depositing strains in the Collection for permanent reference, many useful investigations are constantly being carried out in connection with the identification of interesting strains on behalf of biologists who do not possess equipment and conveniences for such work.

The Governing Body rejoices to report that the Curator, Dr. St. John Brooks, after a protracted convalescence, is restored to health and resumed his work last year in May.

During part of the year the hospitality of the department was extended to Dr. George O. Cooper, of the Department of Botany, University of Wisconsin, U.S.A., for an investigation into the morphology and taxonomy of the genus *Monilia*.

A new edition of the Catalogue of the Collection is in preparation and will be issued as soon as circumstances permit.

GENERAL AND FINANCIAL.

A self contained laboratory and two bungalows together with about six acres of land at the Serum Department, Ilstree, have been rented to the Cancer Hospital for investigations by members of the staff of the Research Institute of that Hospital. A new road to these laboratories has been made. The bungalows were erected to house two assistants of the Research Institute.

The £6,000 loan on mortgage shown in last year's accounts has been repaid and £20,000 of the Institute's holding of 5% War Stock has been sold. The proceeds of these transactions have been re-invested in 4% Consolidated Stock and are included in the new investments referred to below.

The Accounts and Balance Sheet for the year ending December 31st, 1928, show balances to the credit of the Pension Fund of £25,160 1s. 0d., of the Sinking Fund of £17,618 14s. 2d., and of the Capital Fund of £506,792 6s. 1d., the latter figure being unaltered from that of last year, as the excess of income over expenditure for the year has again been utilised to write down the value of certain of the General Fund Investments which still show a considerable depreciation.

The Contingency Fund remains unaltered at £14,228 18s. 1d.

Investments made during the year were: For the General Fund £43,000 4% Consolidated Stock; for the Sinking Fund £1,500 3½% Conversion Stock, and for the Pension Fund £1,300 3½% Conversion Stock.

The net income from the sale of the Institute's products during the year 1928 was £32,801 9s. 2d. After adjustment of the stock of sera on hand at the beginning and end of the year, income from this source appears in the accounts as £32,906 18s. 7d. Compared with last year there were increases in the receipts from sales of Antitoxins and Sera, Bacterial Vaccines and Vaccine Lymph. Diagnosis and Investigation fees on the other hand show a slight decrease.

The total expenditure for the year was £40,799 3s. 2d., against £39,801 11s. 6d., in 1927. Vaccine Laboratory Expenses, Serum and Calf Vaccine Laboratory Expenses, Office Expenses, Library Expenses and General Stores show an increase, and Rent, Rates, Taxes and Insurance, Gas, Water and Fuel, and Alterations, Repairs and Renewals a decrease compared with last year.

In conclusion, the Governing Body desires to express its appreciation of the devoted co-operation of the Director and all members of the Staff in carrying out the work of the Institute.

JAMES K. FOWLER,

Acting Chairman of the Governing Body.

BALANCE SHEET

AND

ACCOUNTS.

Dr.

The Lister Institute

BALANCE SHEET

						£	s.	d.	£	s.	d.
To CREDITORS									2,141	12	6
To PENSION FUND—											
Balance at 31st December, 1927						21,122	7	0			
Add											
Balance of Income and Expenditure Account, 1928						1,037	14	0			
									25,160	1	0
To JENNER MEMORIAL RESEARCH STUDENTSHIP FUND—											
As per Account at 31st December, 1927						8,060	17	5			
Less											
Balance of Income and Expenditure Account, 1928						9	12	10			
									8,051	4	7
To CONTINGENCY FUND—											
As per Account at 31st December, 1923									11,228	18	1
To SINKING FUND to 31st December, 1928									17,618	14	2
To CAPITAL FUND to 31st December, 1928—											
Balance of Income and Expenditure Account to											
31st December, 1926						151,972	6	6			
Donations, &c., received to date from the following:—											
Dr. Ludwig Mond (1893)						2,000	0	0			
The Berridge Trustees (1893/98)						16,379	10	1			
The Grocers' Company (1894)						10,000	0	0			
Lord Iveagh (1900)						250,000	0	0			
Lord Lister's Bequest (1913) as per Account at											
31st December, 1923						18,904	5	8			
William Henry Clarke Bequest (1923/6)						7,114	5	7			
Other Donations (1891-1926)						20,421	18	3			
									506,792	6	1

J. K. FOWLER, *Acting Chairman.*G. W. ADDISON, *Hon. Treasurer.*

£578,995 16 5

REPORT OF THE AUDITORS

We have audited the above Balance Sheet. We have obtained all the information and explanations we have required, paid, being held by the Institute on their behalf. In our opinion, such Balance Sheet is full and fair, and properly drawn and the explanations given to us and as shown by the books of the Institute.

London, 19th April, 1929.

By CASH—						£	s.	d.	£	s.	d.	
At Bankers: Deposit Account						5,500	0	0				
Current Accounts						5,172	1	11				
In hand						59	3	3	10,731	5	2	
By INVESTMENTS, GENERAL FUND (at cost, less amounts written off)—												
£43,000 4 per cent. Consolidated Stock						37,771	0	9				
£32,000 4½ per cent. Conversion Stock, 1940-44						30,955	4	3				
£38,467 4 per cent. Funding Stock, 1960-1990						32,029	15	1				
£25,500 5 per cent. War Stock, 1929-1947						22,491	1	9				
£30,000 Local Loans 3% Stock						16,357	10	7				
£1,875 Port of London 4 per cent. B. Stock						1,800	0	0				
£500 Dominion of Canada 4 per cent. Registered Stock, 1940-1960						492	11	0				
£1,000 Cape of Good Hope 3½ per cent. Consolidated Stock, 1920-40						1,000	0	0				
£25,000 Cape of Good Hope 3 per cent. Consolidated Stock, 1933-1943						23,850	0	0				
£25,000 Natal 3 per cent. Consolidated Stock, 1929-1949						24,484	7	6				
£25,000 New South Wales 3 per cent. Inscribed Stock, 1935						24,937	10	0				
£1,505 7s. 3d. New South Wales 4 per cent. Stock, 1912-62						1,500	0	0				
£2,900 New South Wales 5½ per cent. Inscribed Stock, 1922-32						2,897	16	0				
£25,006 2s. 6d. New Zealand Government 3 per cent. Inscribed Stock, 1945						24,117	17	6				
£26,100 South Australian Government 3 per cent. Consolidated Stock, 1916 or after						24,860	5	0				
£600 Union of South Africa 4 per cent. Consolidated Stock, 1943-1963						594	2	0				
£25,000 Victorian Government 3 per cent. Consolidated Inscribed Stock, 1929-1949						23,875	0	0				
£700 Western Australia Government 4 per cent. Inscribed Stock, 1942-1962						698	7	0				
£20,000 Southern Railway Preferred Ordinary Stock						24,000	0	0				
£6,200 London & North Eastern Railway 3 per cent. Debenture Stock						5,461	13	9				
£5,000 Great Central and Midland Railway Joint Committee 3½ per cent. Guaranteed Stock						5,123	19	3				
£353 London & North Eastern Railway 4 per cent. First Guaranteed Stock						409	11	0				
£8,650 London, Midland & Scottish Railway 4 per cent. Preference Stock						10,460	8	6				
£13,625 London, Midland & Scottish Railway 4 per cent. Preference Stock, 1923						17,375	0	0				
£18,750 London & North Eastern Railway 4 per cent. First Preference Stock						19,648	7	3				
£25,000 East Indian Railway 3 per cent. New Debenture Stock						20,390	0	0				
£661 Madras and Southern Mahratta Railway 4 per cent. Debenture Stock, 1938						656	19	7				
£800 Grand Trunk Railway Company of Canada Great Western Borrowed Capital 5 per cent. Perpetual Debenture Stock						936	0	0				
£1,937 Grand Trunk Railway Company of Canada 4 per cent. Guaranteed Stock						1,733	0	0				
£800 Ontario and Quebec Railway 5 per cent. Permanent Debenture Stock						984	0	0				
£3,400 Gas Light and Coke Company Ordinary Stock						3,638	0	0				
By INVESTMENTS, SINKING FUND (at cost)—												
£8,000 4½ per cent. Conversion Stock, 1940-44						7,320	13	7	405,619	7	9	
£5,000 4 per cent. Funding Stock, 1960-1990						4,611	5	5				
£7,200 3½ per cent. Conversion Stock						5,535	19	0				
Balance uninvested						150	16	2	17,618	11	2	
By INVESTMENTS, JENNER MEMORIAL RESEARCH STUDENTSHIP FUND (at cost)—												
£2,650 Southwark and Vauxhall Water Co. 3 per cent. Debenture Stock "B"						2,756	10	0				
£1,596 Southern Railway 5 per cent. Preference Stock						2,710	5	0				
£726 11s. 4d. Liverpool Corporation 3 per cent. Stock, 1912, or after						556	15	6				
£2,000 4 per cent. Funding Stock, 1960-90						1,797	14	0				
Balance uninvested						200	0	1	8,061	4	7	
By INVESTMENTS, PENSION FUND (at cost)—												
£22,000 4 per cent. Funding Stock, 1960-1990						17,165	3	5				
£10,300 3½ per cent. Conversion Stock						7,951	4	5				
Balance uninvested						43	13	2	25,160	1	0	
(The above Investments, at the market value, 31st December, 1938 show a depreciation of £58,307.)												
By DEBTORS									8,950	8	9	
* By FURNITURE, FITTINGS, SCIENTIFIC APPARATUS AND BOOKS—												
As per account, 31st December, 1920									2,471	17	2	
By EXPENDITURE ON INSTITUTE BUILDINGS AT CHELSEA—												
As per account, 31st December, 1910, including purchase of freehold site, £6,000									70,916	3	1	
By PURCHASE OF FREEHOLD LAND ADJOINING "THE STUDIOS," CHELSEA, as per account, 31st December, 1912												
By LEASE OF "THE STUDIOS," CHELSEA, as per last account						1,653	2	9	169	6	8	
Less Amount written off						65	2	0	1,588	0	9	
By QUEENSBERRY LODGE FARM, ELSTREE—												
Purchase of freehold land and buildings and Expenditure on new buildings, as per account, 31st December, 1912.. .. .									20,455	10	0	
Stock of Animals						445	10	0				
Stock of Anti-Toxins						1,818	7	4				
									2,263	17	1	
										£573,995	16	5
* Nothing has been charged for depreciation of Furniture, &c. since new purchases made during the year to a greater amount than the estimated depreciation (10%) have been written off.												

* Nothing has been charged for depreciation of Furniture, &c. since new purchases made during the year to a greater amount than the estimated depreciation (10%) have been written off.

TO THE MEMBERS.

The Superannuation Scheme for certain of the Staff provides for Life Policies for which the sum of £18,002 10s. 7d. has been up so as to exhibit a true and correct view of the state of the Institute's affairs, according to the best of our information

COOPER BROTHERS & CO.,
Chartered Accountants, Auditors.

Dr. INCOME AND EXPENDITURE ACCOUNTS

INCOME.								£	s.	d.
To Interest and Dividends on General Fund Investments	...	...	...	...	...	...	...	15,765	16	8
To Interest on Sinking Fund Investments	...	...	...	...	...	...	...	799	10	0
To Investigation, Diagnosis and Analysis Fees, &c. ...	...	...	...	...	...	...	...	4,562	10	8
To Sales of Sera, Vaccines, &c., and Stock at 31st December, 1928, less Stock at 31st December, 1927	...	...	...	...	...	...	...	82,906	18	7
To Rent of Rooms	...	...	...	...	...	...	...	875	0	0

£54,909 15 6

Dr.

Pension

	£	s.	d.
To Interest on Investments	1,195	0	0

£1,195 0 0

Dr.

Jenner Memorial Research

	£	s.	d.
To Interest and Dividends on Investments	261	3	10
To Balance, being Excess of Expenditure over Income, transferred to Balance Sheet	9	12	10

£270 16 8

Preventive Medicine.

for the year ending 31st December, 1928.

Cr.

EXPENDITURE.

	£	s.	d.
By Rent, Rates, Taxes and Insurance	1,789	6	11
By Salaries and Wages of Staff	21,062	6	1
By Premiums on Federated Superannuation Policies	1,162	8	8
By Stationery, Printing and Postage	431	17	10
By Printing of Collected Papers	148	11	2
By Office Expenses, Law Charges, Auditors' Fee and Sundries	401	5	1
By Travelling Expenses	14	16	7
By Gas, Water and Fuel	1,225	1	0
By Electric Light and Power	286	0	4
By Experimental Pathology Laboratory Expenses, including General Apparatus	658	11	3
By Bacteriological Laboratory Expenses, including Apparatus	386	13	10
By Vaccine Laboratory Expenses, including Bottles	337	3	7
By Water and Bio-chemical Laboratory Expenses, including Apparatus	362	8	4
By Serum and Calf Lymph Laboratories Expenses, including Apparatus and Cost of Bottles	4,014	7	2
By Culture Media	118	4	1
By Animals	1,441	18	6
By Animal House Expenses and Forage	2,247	19	2
By Alterations, Repairs and Renewals, including Workshop Expenses	2,731	15	2
By Library Expenses	384	14	11
By General Stores	312	18	11
By Bad Debts	5	0	0
By Depreciation of the Lease of "The Studios," Chelsea	65	2	0
By Sinking Fund ($\frac{1}{2}\%$ per annum on Cost of Buildings and Interest on Investments)	1,210	3	7
By Amount written off General Fund Investments	14,110	12	4
	<u>£54,909</u>	<u>15</u>	<u>6</u>

Fund.

Cr.

	£	s.	d.
By Pensions	157	6	0
By Balance, being Excess of Income over Expenditure, transferred to Balance Sheet	1,037	14	0
	<u>£1,195</u>	<u>0</u>	<u>0</u>

Studentship Fund.

Cr.

	£	s.	d.
By Salaries	270	16	8
	<u>£270</u>	<u>16</u>	<u>8</u>

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THE LISTER INSTITUTE
OF
PREVENTIVE MEDICINE

Report of the Governing Body,
1930.

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

June 18th, 1930.

The Lister Institute of Preventive Medicine,

CHELSEA BRIDGE ROAD, LONDON, S.W.1.
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ANNUAL GENERAL MEETING
OF
The Lister Institute of Preventive Medicine,
June 18th, 1930.

REPORT OF THE GOVERNING BODY.

The Governing Body has the honour to present the Institute's 36th Annual Report.

GOVERNING BODY.

In the absence of Sir David Bruce during the Winter, Sir James K. Fowler again acted as Chairman of the Governing Body.

At the meeting held last year, the Council re-elected Professor W. Bulloch, Sir James K. Fowler and Professor A. E. Boycott, as its representatives on the Governing Body until December 31st, 1930.

Sir David Bruce has been re-appointed as the representative of the Institute upon the Court of Governors of the London School of Hygiene and Tropical Medicine.

COUNCIL.

The Governing Body regret to announce the death, in August last, of Sir E. Ray Lankester, a member of Council as a representative of the Members for many years. He was also a member of the Governing Body as one of the Council's representatives during 1917-1918.

At the last Annual Meeting, the three retiring members of Council, Sir James K. Fowler, a representative of the Members of the Institute, Sir David Bruce, the representative of the Royal Society, and Dr. F. W. Brambell, the representative of the Royal Irish Academy, were each re-elected.

A vacancy created by the retirement of Sir William Somerville, the representative of the Royal Agricultural Society, was filled by the appointment of Lord Mildmay of Flete.

The three members who retire from the Council this year in accordance with the Articles of Association, but who are eligible for re-election, are Professor A. E. Boycott, a representative of the Members of the Institute, The President, representing the Royal College of Veterinary Surgeons, and Professor G. H. F. Nuttall, the representative of the University of Cambridge.

STAFF.

The Members of the Institute will share with its Governing Body the pleasure experienced on the announcement that the Nobel Prize in Chemistry for 1929, had been awarded to Professor Harden for his researches into the chemistry of alcoholic fermentation. These researches have been steadfastly pursued by Professor Harden and his collaborators in the laboratories of the Institute for a period of over 25 years. The secrets revealed by their discoveries have significance far beyond the yeast-cell and have afforded important clues to the chemical dynamics underlying muscular activity.

In addition to the bestowal of this international honour upon the Head of its Biochemical department, the scientific work which has been carried on in its laboratories has received further recognition by the election of Dr. Robison to Fellowship of the Royal Society.

Towards the end of this year, Sir Charles Martin and Professor Harden will complete their term of service as they will have reached the age of 65 years. At the meeting of the Board held to consider the action to be taken in consequence of these retirements, it was resolved:—

That the Governing Body view with great regret the approaching termination of the services of Sir Charles Martin and Professor Harden, who have been on the staff of the Institute for 27 and 33 years respectively.

They desire to record their high appreciation of the administrative ability of Sir Charles Martin which has contributed so much to place the Lister Institute in its present sound financial position; of the valuable additions to scientific knowledge which he has himself made and which have been made by others working under his direction; of the harmony which he has invariably secured amongst the scientific staff and also amongst other workers who have enjoyed the hospitality of the Institute, and of the valuable services he has rendered as a member of scientific commissions and committees engaged in the investigation of problems of preventive medicine.

Also, they desire to place on record their high appreciation of Dr. Harden's long and distinguished service and of the important part he has taken as Head of the Department of Biochemistry, in the scientific development of the Institute. The valuable contributions which he has made to the Science of Chemistry have led to the inclusion of his name in the group of distinguished men to whom the Nobel Prize has been awarded and the researches which have been conducted in his laboratories have enhanced the estimation in which the Institute is held as a centre of scientific work.

The Governing Body has decided that the retirements shall date from December 31st, 1930, and have appointed Professor J. C. G. Ledingham, F.R.S., to succeed Sir Charles Martin, as Director, and Dr. R. Robison, F.R.S., to succeed Professor Harden as Head of the department of Biochemistry.

Professor Ledingham joined the Serum department of the Institute in 1905, and next year accompanied the late Dr. George Dean when he was transferred to Chelsea and became Head of the Bacteriological department. On the appointment of Dr. Dean to the Chair of Pathology, at Aberdeen, in 1908, Dr. Ledingham was chosen to succeed him as Head of the Bacteriological department. Dr. Robison joined the staff of the Biochemical department in 1912 and has been first assistant in the department since 1919.

Dr. T. W. Lumsden, on his appointment as Director of Cancer Research at the London Hospital resigned his honorary assistantship in the department of Experimental Pathology in December last.

Dr. D. McClean and Dr. R. W. Fairbrother have been re-appointed to the two research fellowships in Bacteriology created by the Governing Body in 1927.

Mr. E. Boyland resigned the Grocers' Company Research Studentship on his appointment to a Beit Memorial Research Fellowship and has been succeeded by Dr. R. R. McLaughlin.

Miss M. H. Roscoe resigned her assistantship in the department of Experimental Pathology on her appointment to a Beit Memorial Research Fellowship and has been succeeded by Miss A. M. Copping.

RESEARCH WORK.

Before proceeding to give a brief survey of the researches which are, or have been, in progress during the year in the various departments of the Institute, the Governing Body desires to record its appreciation of the continued co-operation it has enjoyed with the Medical Research Council, the Department for Scientific and Industrial Research, the British Empire Cancer Campaign and the International Committee for the Study of Infantile Paralysis. The financial support given by these bodies to skilled investigators in the different departments has greatly increased the scientific activities of the Institute.

In addition to furnishing the salaries of the staff of the National Collection of Type Cultures, an organisation which has proved of great service to bacteriologists and mycologists throughout the Empire, the Medical Research Council has provided the salaries of Professor Korenchevsky and Miss E. M. Hume and their assistants and also of Mrs. Fixsen in the department of Experimental Pathology.

The expenses of the fundamental vitamin investigation with special bearing on the vitamin content of various Empire products, being carried out in the department of Biochemistry by Dr. Zilva, including the salaries of Dr. Zilva and of his assistants—Messrs. Humphrey and Johnson, and Mesdames Soames, Crawford, Bracewell and Perry—are defrayed by a grant to the Medical Research Council from the Empire Marketing Board.

Dr. Ida Smedley-MacLean, in the department of Biochemistry continues to receive a grant from the Department of Scientific and Industrial Research, which body also supplies the salaries of her two research assistants.

The British Empire Cancer Campaign furnished the salary of Dr. T. Lumsden, in the department of Experimental Pathology until his departure in December, and also that of his research assistant, Miss Kohn-Speyer, and a laboratory attendant.

The salaries of Dr. E. Weston Hurst and his assistants together with the expenses of the investigation are borne by the grant from the International Committee for the Study of Infantile Paralysis.

Accommodation for Professor Korenchevsky, Miss Hume, Dr. Smedley-MacLean, Dr. Hurst, Dr. Lumsden and the National Collection of Type Cultures, together with the expenses of the researches of the first two named are provided by the Institute.

DEPARTMENT OF BACTERIOLOGY.

Studies on the viruses of Vaccinia, Variola, and Fowlpox.

Visceral lesions accompanying experimental vaccinia in rabbits. In the last report mention was made of the occasional occurrence of generalised dermal and visceral lesions in rabbits inoculated intradermally or intravenously with potent strains of vaccinia which had been propagated in rabbit organs (brain and testicle). In view of the fact that these findings in the winter months 1928-29 had been complicated by the presence of *pasteurella* infections in the stock rabbits, Professor Ledingham expressed the view that the virus of vaccinia might not be solely responsible for these lesions, as some workers had stated. Accordingly, with the help of Dr. M. M. Barratt, he carried out a further series of experiments in the summer of 1929. The results showed fairly conclusively that so far as the production of multiple necrotic lesions (in lungs, liver, spleen, adrenals, etc.) was concerned, only the vaccinia virus could be held responsible. No evidence was forthcoming, in this series, of activation of parasitic bacterial infections by the introduction of vaccinia virus. The absence of concomitant bacterial infections gave confidence to the histological study and interpretation of these interesting lesions. The production of generalised lesions by strains propagated through organs and apparently not by strains of cutaneous or dermal origin, raises new problems of adaptation on which work is proceeding in the Department.

Immunisation of the horse with vaccinia virus. In order to secure an abundant supply of antiviral serum for various purposes, Dr. Petrie has successfully immunised a horse with vaccinia virus and potency tests with the concentrated serum are being carried out by Professor Ledingham. Its content of antiviral substance proves to be large. In view of statements to the effect that some cases of postvaccinal encephalitis have benefited by the administration of serum from convalescent vaccinees it is proposed to offer the serum for trial in such cases. Its value in the treatment of smallpox also requires investigation.

Elementary bodies in vaccinia and fowlpox. Further investigation is being made by Professor Ledingham of these minute bodies in vaccine pulp with a view to establishing their aetiological importance. As was shown many years ago, fowlpox virus contains similar bodies and apparently in much greater numbers than in vaccinia. This may possibly explain why the filtration of fowlpox virus through Berkefeld filters has usually succeeded whereas vaccine virus has, as a rule, failed to come through. The small size of these bodies renders their manipulation as test objects difficult, but progress is being made.

Cultivation of vaccinia virus *in vitro*. Dr. Eagles and Dr. McClean have continued their study of this question. After many experiments the technique of Carrel and Rivers has failed to give uniformly satisfactory results owing to irregularity in multiplication for which no adequate reason has yet been found. The technique introduced by Professor and Mrs. Maitland at Manchester, and which in their hands has given excellent results, has also been under investigation. Its simplicity is a great advantage. Unfortunately the expected regularity in proliferation has not so far been realised, but it is probable that some quite small technical factors to which attention is now to be given may explain the discrepancy between the results here and at Manchester.

Conservation of "culture" virus. It is generally agreed that vaccine virus cultivated by the Carrel-Rivers technique deteriorates rapidly at 2°C. In the attempt to explain this deterioration the effect on survival of strict anaerobiosis at -18°C, 2°C, and room temperature is being studied. Some evidence has been obtained that anaerobic conditions at 2°C. are more favourable than aerobic at this temperature. The effect on survival of the medium in which the virus is suspended has also been studied. Plain broth, hormone broth and colloids such as agar and gelatin are found to exercise some protective effect, but the results are not regular. It is of considerable interest that virus cultivated by the Maitlands' technique survives well either at 2°C. or in the frozen state. The two types of "culture" virus therefore present, in the matter of survival, an interesting antithesis which calls for explanation.

The enhancement of the dermal response to virus by addition of extract of testicle. (Duran-Reynals effect.) Dr. McClean, who has been studying the mechanism of this phenomenon, finds that the enhancing substance in the testicular extract passes through a Berkefeld filter but is retained by parchment membrane. It has the peculiar property, not possessed by other organ extracts or substances such as histamine and sodium nucleinate, of diffusing rapidly after intradermal inoculation.

Cowpox and smallpox viruses. Dr. Eagles is studying the properties of a strain of cowpox recovered from a vesicular lesion on the arm of a milker. On rabbits and monkeys it produces, after scarification, lesions which differ somewhat from those following scarification with calf-propagated lymph, in the intensity of the associated dermal inflammation and hæmorrhagic tendency. Monkeys vaccinated with this strain fail to respond to smallpox virus recovered from cases of the mild form now prevailing in England.

It may be recalled that in 1925 Professor Ledingham reported the fact that smallpox virus when inoculated intradermally in rabbits produced a characteristic lesion which is neutralised by antivaccinal serum. McKinnon and Defries of Toronto, and Sobernheim of Berne, have recorded similar findings, but so far it has been impossible to secure propagation of the virus from rabbit to rabbit beyond one or two passages. Dr. Eagles is again attacking this problem of adaptation. If a method of propagation succeeds, it may be the means of securing new strains of vaccinia at will from smallpox cases and investigating their properties.

Experimental production of Trachoma in monkeys.

A number of monkeys (*M. rhesus*) were inoculated eleven months ago with the organism (*B. granulosis*) isolated and studied by the late Dr. Noguchi. The inoculations were made subconjunctivally in the tarsal region. One or two animals have shown considerable post-tarsal granulation and some fine scattered granules on the tarsus, but it cannot be said that definite transmission of the disease has yet succeeded. Mr. S. Mayou, F.R.C.S., has very kindly given us the benefit of his clinical experience in the interpretation of the experimental lesions.

Research on Poliomyelitis.

(*International Committee for the Study of Infantile Paralysis.*)

Path of spread of the poliomyelitis virus in the experimental animal. The research on this problem by Drs. Fairbrother and Hurst has now been brought to a conclusion. The theory of spread formerly most in favour was that the virus entering the body by the naso-pharyngeal mucosa or by the intestinal tract, reached the central nervous system by the perineural lymphatics and was then disseminated by the cerebrospinal fluid. The primary lesion was held to be a meningitis which spread inwards along the vessels of the anterior fissure to affect the anterior horns of the spinal cord. Minute histological examination during the incubation period and the symptomatic stages of infection, combined with search for the virus at the same periods, produced no evidence in support of this theory. On the contrary, all the facts and especially the mode of advance of the lesions and the distribution of the virus after intracerebral inoculation, pointed to the axis-cylinders as the chief routes of transmission of the infective agent. Meningitis was never observed in the early phases of the disease which began as a primary degeneration of the anterior horn cells, accompanied by foci of interstitial inflammation in the interior of the brain and cord. The mode of development of the disease following intranasal inoculation also supported this view. Whatever the route of inoculation, histologically the infection spread from above downwards, while the first symptoms were nearly always referable to the lumbar cord. The virus occurs most abundantly in those regions of the nervous system which show the most marked neuronal changes. In the cerebral cortex, for example, where such lesions as may be present are mainly interstitial without nerve-cell destruction, the occurrence of the virus is inconstant. After direct inoculation into the parieto-occipital cortex, the virus rapidly disappears from the site of injection and can be detected successively in the optic thalamus, brain stem and spinal cord.

Post-vaccinal and other forms of Encephalitis. A number of cases of the former disease and two cases of a similar condition occurring as a complication of smallpox have been studied by Drs. Hurst and Fairbrother. While yielding no new information as to the essential nature of the morbid process, the histological study permits the identification of the encephalitis following smallpox with that arising in the course of vaccination and other exanthemata. Numerous attempts to transmit the encephalitis to monkeys and rabbits by the intracerebral or intramuscular injection of human brain material, combined in some cases with cutaneous vaccination, have been unsuccessful, as have endeavours to demonstrate the vaccinia virus in the nervous tissues by repeated intradermal passage in rabbits.

Experimental vaccinal Encephalitis. With a view to determining the rôle played in post-vaccinal encephalitis by the virus of vaccinia, a study of the encephalitis produced by that organism in the monkey and rabbit has been undertaken by Drs. Hurst and Fairbrother. It was not found possible to excite nervous lesions by intradermal inoculation of ordinary vaccine lymph or neurovaccine of rabbit or monkey origin. On the other hand, intracerebral inoculation of monkey or rabbit neurovaccine was effective in both species of animals. Particular attention was paid to the lesions resulting in the monkey. The reaction is primarily and mainly meningeal with secondary changes in the cortex underlying the areas of most severe meningitis. These lesions differed entirely from those of postvaccinal encephalitis and the characteristic perivascular demyelination of that disease was never reproduced. Virus was present in large amount in the nervous tissues and also in the spleen, which was the seat of marked alterations. Smaller amounts were present in various other organs.

The effect of subcutaneous administration of normal brain emulsions to rabbits. The cases of paralytic accident arising in the course of antirabic treatment have sometimes shown a histological picture closely resembling that in postvaccinal encephalitis. Many observers have ascribed these accidents to the toxic action of the foreign brain material introduced during treatment and have claimed, usually without adequate histological control, to have reproduced the condition in experimental animals,

particularly rabbits. The importance of these observations, if confirmed, in throwing light on the causation of disseminated encephalomyelitis is obvious. Accordingly rabbits were inoculated subcutaneously with guinea-pig, sheep, human or monkey brain, by Dr. Hurst. Profound toxic effects resulting in emaciation and death ensued. During the course of the inoculations a small number of animals developed paralysis for which the most careful examination of the brain, spinal cord and peripheral nerves revealed no cause. Similar paralyzes were noted at Elstree during the course of various experiments and again no anatomical basis was discovered. It was concluded that while paralysis might occur in the rabbit injected with foreign nervous substance, such paralysis could not be brought into relationship with the paralytic accidents in man and that the histological picture seen in man could not be reproduced in rabbits by such means.

Immunisation of the horse with poliomyelitis virus. Of the various sera used therapeutically in poliomyelitis, only human convalescent serum has been found to contain antiviral properties demonstrable by the neutralisation test. The use of this serum is obviously very restricted. Attempts were therefore made to immunise a horse. With the co-operation of Dr. Petrie and Dr. Morgan at Elstree, a horse was immunised by a series of intramuscular injections of increasing doses of a virulent monkey cord filtrate. At the end of the course the serum was shown by Dr. Fairbrother to possess antiviral properties comparable with those possessed by human convalescent serum. Before immunisation, the horse serum did not possess this property. It is hoped that the serum of this horse may be made available for therapeutic trial in man.

Complement-fixation with poliomyelitis virus and the corresponding immune serum. Attempts by Dr. Fairbrother to obtain complement-fixation with poliomyelitis virus as found in cord emulsions and filtrates and convalescent human and monkey sera, were entirely negative. With the serum of the immunised horse complement-fixation occurred but it also occurred with normal monkey cord as antigen. After ether extraction of the virus emulsion, the residue which still contained active virus, gave no fixation with the horse serum. An investigation of the part played by the virus of vaccinia in the complement-fixation reaction is now being conducted, particularly with reference to the case of antigen contained in brain material.

Studies on combined virus activity. Drs. Fairbrother and Hurst have started experiments to determine whether coincident infection with vaccinia has any power to modify the reaction of the central nervous system to poliomyelitis.

Studies on antigenic constitution and immunising properties of bacteria.

Rough and smooth types. Dr. Arkwright has been investigating rough and smooth strains of *B. typhosus* and *B. dysenteriae* with a view to detecting differences in their fermentative action on carbohydrates. Some indications pointing to differences in this direction have been obtained.

Miss R. M. Pitt has demonstrated fully the effect of cultivating *B. typhosus* in normal serum and in serum containing antibodies for the somatic or O part of the bacterial antigen. She has shown that serum containing antibodies to the "smooth" or somatic antigen transforms smooth cultures seeded in it to rough, without apparently affecting the flagellar component of the organism. A serum prepared with *B. enteritidis* which has the same O component as *B. typhosus* possesses a similar property. Miss Pitt has also been testing out methods of turning rough *B. typhosus* into smooth, but so far without success.

***B. subtilis*.** Dr. N. C. Graham (Belfast) during some months' work at the Institute investigated the nature of the so-called S and R variants of *B. subtilis* and showed that they were in no way analogous to the S and R forms studied in the *Coli-typhosus* group. The terms S and R had been applied to certain *Subtilis* variants simply by reason of colonial differences. The so-called R colonies of *B. subtilis* have an uneven surface which is an expression of growth in chains and they should more fitly be called medusa-head varieties. Dr. Graham showed that four kinds of variants could be obtained, viz., (1) motile short bacilli; (2) motile long forms; (3) non-motile short rods and (4) non-motile long forms. The two former had both somatic and flagellar antigen and evoked somatic and flagellar antibodies while the two latter had only somatic antigen. The variants were not characterised by those serological differences which help to separate rough from smooth in other groups.

Prophylactic value of somatic antigen in Salmonella infections. Dr. Schütze, continuing his immunity studies in mice has shown that only the O or somatic content of the bacterial vaccine is capable of conferring protection against *S. aertrycke* and *S. enteritidis* infections. The presence or absence of H or flagellar antigen in the vaccine is without effect on the prophylactic value. An efficient vaccine may be prepared from an alien species so long as the somatic antigen in each is identical. For example a *paratyphoid B.* vaccine will protect against an *aertrycke* infection and *typhoid* vaccine will protect against a *gaertner* infection. Heating the vaccine to 100°C. for a short period, e.g., 14 minutes, does not damage the prophylactic value of the vaccine. Before administering the test dose in these immunisation experiments, Dr. Schütze made estimations of the anti-O titre of the sera of these experimental mice. He finds no precise correlation between such titre and the degree of protection conferred.

Spore-bearing anaerobes. Dr. Felix has made a preliminary investigation of the H and O antigenic constituents in many species of anaerobes, including those involved in gas gangrene. The presence of H antigen was found to coincide with the motility of the organisms as in the aerobic groups. *B. welchii*, for example, which is non-motile, possesses no H antigen. A more detailed study of the O antigens of the serological types of *V. septique* showed that their relationship is much closer than that known to obtain between main and group O antigens in the typhoid-paratyphoid group.

Passive protection against anaerobic infections by antibacterial (anti-O) sera. Work on this subject by Dr. Muriel Robertson and Dr. Felix was continued during the year. The anti-O serum was found to be strictly specific, affording protection only against infection with *V. septique* of the same serological group. The very high degree of specificity in the *in vivo* protective action of this O immune serum came as something of a surprise in view of the considerable overlapping of the O antigen established previously in agglutination and complement-fixation tests between the groups. This O immune serum, which is completely devoid of antitoxin content, was tested for protective action against the living culture as distinct from the spore-calcium suspension employed in the general experiments. Here also it possessed a high protective value, although a local gangrene of considerable severity was set up, while the control animals died within 16 hours of a fulminating gangrene. Work is now in progress with *B. tetani* and *B. welchii*, but up to the present the titre of the O immune serum to *B. tetani* has not been sufficiently high to protect mice against infection with spore-calcium suspensions.

Weil-Felix reactions in Tropical Typhus.

Dr. Felix has tested sera from cases of tautsugamushi disease against various types of *B. proteus* X. He was able to confirm Fletcher's observation that such sera from patients in the Federated Malay States agglutinate the so-called Kingsbury strain in low dilutions, but do not react with the X19 and X2 types of *B. proteus* X. Sera of cases of this disease from Sumatra and Japan react in the same way. The results suggest that further serological varieties of typhus may yet be recognised among the typhus-like diseases in different parts of the world.

Diet and Resistance.

It has recently been asserted that tubercle-infected rats on a —A diet are particularly sensitive to tuberculin on the ground that the lethal dose of tuberculin for such rats is considerably smaller than that for rats on a similar diet but not so infected. Dr. Schütze and Dr. Zilva have been able to show that this phenomenon is a purely non-specific one. Rats infected with *B. tuberculosis* are indeed hypersensitive to the toxic action of tuberculin, but they are equally hypersensitive to other bacterial toxins, e.g., to killed cultures of *B. paratyphosus* A. Moreover, the *post-mortem* picture of animals which succumb to tuberculin in no way resembles that found in animals dying from tuberculin shock in the strict sense of the term.

The avirulent strain of the Tubercle Bacillus (B.C.G.) advocated for immunisation by Dr. Calmette.

This attenuated strain is being employed as a living inoculum for prophylaxis against tuberculosis, Calmette and his school considering that there is complete safety in so doing, as the strain has completely lost its virulence for man and laboratory animals. Dr. Moti Malkani, of Karachi, India, working with a strain obtained from the Pasteur Institute, has come to the conclusion that the virulence of the strain is not completely gone, and that when introduced into the less resistant animals it may be capable of causing widespread and even fatal infection. Some 28 guinea-pigs and 18 rabbits were inoculated by various routes. Of these animals 18 showed extension of infection beyond the site of inoculation to glands and other organs. In one of them the lesions were particularly pronounced and of a caseous nature. Two guinea-pigs died, to all appearances, as the result of infection with B.C.G. This strain, therefore, though much attenuated, cannot be regarded as avirulent for laboratory animals. It will depend on the degree of resistance it meets with in the animal whether it disappears from the system or leads to a process that may terminate fatally.

The oxygen requirements of *B. pestis* and organisms of the *pasteurella* group.

Dr. Schütze, in collaboration with Mr. M. A. Hassanein (Cairo), has demonstrated the impossibility of obtaining on ordinary agar plates discrete single-cell colonies from seedings of *B. pestis* and other species of the genus *Pasteurella*. The phenomenon was found to be due to the oxygen sensitivity of these strains. The addition to the agar of such substances as blood, sodium sulphite, or sterilised broth cultures of various bacteria, permits the development of single-cell colonies. Anaerobic conditions of growth also permit this development. The accessory substances mentioned probably act as reducing agents, while those in the broth cultures appear to be enzymic in nature.

Dr. Henderson (Calcutta) received the hospitality of the Department for a short period during the year.

DEPARTMENT OF BIOCHEMISTRY.

Alcoholic Fermentation.

Work on this subject has again been continued in several directions.

Phosphoric Esters produced during Alcoholic Fermentation. Professor Harden and Lord Henley have studied the different effect of the phosphates of potassium and sodium on fermentation by yeast preparations. It is known that potassium ions play some specific part in the fermentation process and in accordance with this it is found that potassium phosphate produces a more rapid reaction than the sodium salt. At the same time the proportion of the phosphoric esters produced is slightly altered, the potassium salt yielding rather less mono- and more di-phosphate than the sodium salt.

Dr. Robison has continued the investigation of the various phosphoric esters produced during the fermentation of hexoses by yeast juice, dried yeast and zymine. A general account of the work done during the past four years in collaboration with Dr. W. T. J. Morgan has been published. In this paper the great variations in the proportions of the esters produced by the different yeast preparations are again emphasised and the difficulties involved in their quantitative separation and estimation are enumerated and discussed. The barium salt of trehalosemonophosphoric ester, described in previous reports, which was first isolated as an amorphous compound very soluble in water has now been obtained in a second form, beautifully crystalline and very sparingly soluble. The empirical composition of the two forms is identical but their molecular relationship is as yet a matter of conjecture.

The completion of the work on glucosemonophosphoric esters by Dr. Robison and Dr. E. J. King was delayed by the latter's return to Toronto, but the results are now being prepared for publication. Further evidence of the existence of yet another ester has been obtained but the isolation of this elusive compound has not so far been achieved.

The interesting results obtained by Dr. Morgan and Dr. King from the investigation of the methyl glucosidemonophosphates, prepared under different conditions of temperature have been confirmed by Dr. R. McLaughlin who has been appointed Grocers' Company Research Student. This work is being continued.

It was mentioned in the last report that the hydrolysis of the phosphoric esters by means of the bone phosphatase throws an interesting light on the nature of the sugar constituents of these esters. This method of investigation is being further studied by Dr. Robison and Miss M. Macleod. Miss Macleod is also studying various derivatives of hexosephosphoric esters which are likely to be of use in their purification.

Miss Macfarlane (Carnegie Fellow) has been investigating the conditions of hydrolysis of hexosediphosphate by the yeast enzymes. She finds that, contrary to the contention of Raymond, the co-enzyme is not concerned in this reaction. On the other hand, the action of arsenate in accelerating fermentation, which has been generally ascribed to acceleration of the action of the hexosephosphatase, does not occur with washed zymine, which still retains a powerful hexosephosphatase. The conditions of this action are being further investigated.

Fermentation by Yeast preparations. Striking features of all fermentations by yeast preparations are (1) that they proceed much less rapidly than fermentations by living yeast and (2) that they are susceptible to acceleration by the action of phosphate. Experiments on this subject by Professor Harden and Miss Macfarlane have shown that in the preparation of yeast juice by grinding yeast, this change takes place during the operation of grinding; only minor modifications can be effected by grinding the yeast in presence of different materials (*e.g.*, calcium carbonate instead of kieselguhr). A similar, but often less pronounced change occurs when yeast is treated with certain toxic substances (*e.g.*, toluene, ether, etc.), whilst other reagents (*e.g.*, formaldehyde, phenol, pyridine, etc.) not only kill the cell but also destroy completely the fermenting power.

Miss M. B. Patterson (Victoria Soldiers' Orphans Scholar) has commenced work on the action of cyanide on fermentation by yeast preparations.

Pyrophosphates in Yeast. Mr. E. Boyland (Beit Memorial Research Fellow) has made an interesting study of the function of pyrophosphates in alcoholic fermentation. Pyrophosphates have recently been shown to play a prominent part in the chemistry of muscular contraction and hence it was important to ascertain how far these substances are concerned in alcoholic fermentation. The results are reassuring inasmuch as the pyrophosphate of yeast, which is probably present in combined form as a nucleotide, undergoes no change during the process. On the other hand sodium pyrophosphate is readily hydrolysed by yeast preparations, yielding orthophosphate, which then undergoes the normal reaction. The hydrolysis is effected by an enzyme (pyrophosphatase) which appears to be distinct from hexosephosphatase.

Ossification.

Dr. Robison has continued to collaborate with Dr. Honor B. Fell, Director of the Strangeways Research Laboratory, Cambridge, in the investigation of the development of cartilage and bones of the embryo chick, both in the egg and when isolated and cultivated *in vitro*. The work has now been extended to the study of membrane bone, for which purpose the jaw bone has been found most suitable. In the fowl embryo the mandibular skeleton consists of a rod of cartilage (Meckel's cartilage) enclosed by a sheath of membrane bone. The production of phosphatase during normal development of the membrane bone has been demonstrated as in the case of the long bones. On the other hand the Meckel's cartilage does not ossify *in vivo* (except possibly at the articular end) and has been shown to remain devoid of phosphatase. When cultivated during several weeks *in vitro* this cartilage produces neither hypertrophic cells nor phosphatase.

The results obtained in these investigations are of such interest that work on similar lines but with mammalian cartilages has been commenced by Dr. Janet Niven at the Strangeways Research Laboratory. Although the culture technique for mammalian cartilages has not yet been perfected a certain amount of histological development *in vitro* has already been obtained.

Calcification *in vitro*. These experiments have been continued by Dr. Robison, Miss M. Macleod and Miss A. Rosenheim, and the formation of new deposits in slices of the bones of rachitic rats has been investigated under various conditions. It was found that increased and more rapid deposition always occurs in the presence of phosphoric ester, even in very low concentrations.

A modified basal solution has been used, with a salt content more nearly approaching that of the plasma. It has been shown that the higher concentration of sodium bicarbonate (0.2%) beneficially affects calcification, a fact which supports the suggestions that the salt deposited in ossification may be a carbonate-phosphate of the apatite type. Magnesium in concentration of 0.002 M. exerts an inhibitory effect which is, however, largely masked in presence of phosphoric ester. The inhibitory effect of the potassium ion and of sodium chloride seems to be very slight. At a pH less than 7 calcification does not occur in solutions containing only inorganic salts, but if phosphoric ester is present deposition may take place at a pH as low as 6.3.

Evidence has been obtained of the existence of two mechanisms favouring calcification in hypertrophic cartilage, the enzyme mechanism producing supersaturation of the solution by increasing the inorganic phosphorus concentration, and a further mechanism favouring deposition of salts from the supersaturated solution thus formed. This second mechanism is injured or destroyed by treatment with various agents which do not effect the enzyme, as for example 0.01 M. KCN, but, when it no longer functions, deposits to all appearances similar to those in untreated bones can be obtained in solutions containing phosphoric ester. 10% formalin, which inactivates bone phosphatase, destroys both mechanisms. Dehydration of the bone slices *in vacuo* over sulphuric acid, or soaking them in acetone or 90% alcohol completely prevents subsequent calcification in inorganic solution, but calcification still takes place if phosphoric ester be added to the solution, the enzyme mechanism being unimpaired.

Calcification *in gels*. In order to gain information on the nature of the second mechanism, referred to above, Dr. Robison and Miss M. Maclean are studying the deposition of calcium salts in colloid gels, under conditions similar to those used in the experiments with bone slices. Deposits were readily obtained in gelatin and agar gels containing bone phosphatase, in the presence of calcifying solutions containing phosphoric ester. Deposits of very characteristic appearance have now been obtained in some cases in agar gels in the absence of phosphatase and phosphoric ester, employing solutions which produce calcification in slices of rachitic bone and which are definitely supersaturated with respect to calcium or carbonate-phosphate. These deposits are not formed so readily in gels of 10 per cent. commercial gelatin, but experiments are in progress with the turbid gels of highly purified gelatin.

Oxidation of the Fatty Acids.

Dr. Smedley MacLean and Miss Pearce have continued the investigation of the oxidation of fatty acids by hydrogen peroxide in the presence of cupric salts. A quantitative study of the oxidation of oleic and palmitic acids is being carried out under conditions which allow the existence of intermediate products. The nature of the latter depends on the temperature at which the reaction takes place. The separation and identification of these various substances is now in progress.

Study of the unsaponifiable matter of plants.

The oxidation of the zymosterol previously isolated from yeast, results under certain conditions in the formation of peroxides. Dr. Smedley-MacLean has found that terpene alcohols of comparatively simple structure may be obtained from these, and the investigation of their structure promises to throw light on the constitution of the sterols.

With Miss D. L. Collison the nature of the unsaponifiable matter of green leaves is being examined. The occurrence of the hentriacontane previously isolated from spinach leaves having been questioned and conflicting results having been published, it was considered desirable to repeat this work. The

hentriacontane was again obtained and its structure confirmed by an X-ray photograph taken by Dr. Piper. Palmitic, stearic and cerotic acids were found in the leaf and two alcohols whose structure is now under investigation. The sterol of spinach presents some interesting features. It melts at 161°C. and is more highly unsaturated than the sterols commonly found in plants.

Experimental researches on the Anti-Scorbutic Principle (Vitamin C).

Dr. Zilva has continued his investigation of the spontaneous inactivation of the antiscorbutic factor, and more light has now been thrown on the cause of the modification of the stability in neutral solutions of the vitamin produced by autoclaving active solutions. It was at first surmised that this modification was due to the destruction of a "thermolabile stabilising factor." New experimental facts, however, do not support this view, since attempts to fractionate the alleged factor have failed. On the other hand, it has been found that the addition of autoclaved active solutions to untreated neutral juices also brought about an acceleration in the inactivation of the vitamin, which suggests that a substance, or substances, is produced in the process of autoclaving which is responsible for the acceleration. There are indications that the substance thus produced by exposure to air and the product of oxidation, with the help of a thermostable peroxidase, oxidises in its turn the reducing principle present in antiscorbutic solutions, which has been shown by Dr. Zilva to have a protective action on the vitamin. The inactivation of the antiscorbutic factor by these coupled reactions proceeds at a very much speedier rate in neutral than in acid medium. Attempts are being made to identify the substances in these reactions. The available results suggest that the oxidisable substance formed on autoclaving is of a phenolic nature.

Metabolism of Animals affected by Scurvy.

The metabolism of phosphorus and of calcium in scurvy and the influence of the disease in its various stages of development on the phosphorus and calcium content of the blood, have been studied by Dr. Zilva and Mr. F. G. Humphreys. No evidence has been obtained indicating that the production of scurvy is due to the derangement in the metabolism of these elements, although the behaviour of some of the experimental animals in this respect deviates from the normal. This deviation cannot be traced to faulty experimental technique and the cause of it is being investigated.

The Physiological Function of Vitamin C in Fruits.

The investigation instituted by Dr. Zilva to ascertain whether a functional relationship exists between the antiscorbutic factor and any other factor or factors in the apple and in citrus fruits has been extended in several directions. Experiments on the connection between the vitamin and various physiological factors are being carried out in collaboration with Drs. Kidd and West of the Low Temperature Station for Research, Cambridge, whilst the effect of various cultural factors on the antiscorbutic activity of the fruit is being studied in conjunction with members of the staff of the Agricultural and Horticultural Station, Long Ashton. The preliminary results obtained during the first two years of the inquiry have been published by Dr. Zilva, Mr. Hoyle, and Miss Bracewell.

Influence of Various Factors on the Vitamin Content of Dairy Products.

The inquiry into the vitamin content of dairy products as influenced by environment, breed of cow, transit, storage, and other factors has been continued by Dr. Zilva, Miss Crawford and Miss Perry, and a further number of controlled samples of butter has been assayed.

The association of vitamins A and D with various constituents of the milk has been studied in collaboration with Captain John Golding of the National Institute for Research in Dairying, Reading.

Attempts to Improve Methods for Vitamin Assay.

Dr. Zilva, Mrs. Balfour and Miss Perry have continued the investigation into the limitations in the accuracy of some of the methods of assay of vitamin D ("line test") and C (Höjer test). Although a number of very careful experiments have been performed, the investigation has not yet reached a stage when a full critical survey can be published, but the evidence obtained has made it plain that these methods are not entirely satisfactory, and consequently that results obtained by their use are to be accepted with caution.

Promising results are being obtained by a method based on the X-ray assessment of the prophylactic action of vitamin D. This work is being carried out in collaboration with Drs. Bourdillon and Webster of the National Institute for Medical Research.

DEPARTMENT OF EXPERIMENTAL PATHOLOGY.

The Oxidation-Reduction Potential of Culture Media before and after Inoculation with Various Organisms.

Dr. Elizabeth Lepper and Sir Charles Martin have continued their studies upon the oxidation-reduction potential of various anaerobic culture media by electrometric methods. The results confirm their previous conclusions from experiments with Clark's indicators.

They have also followed electrically the changes which occur in the potentials of the media after inoculation with various aerobic and anaerobic organisms.

Electrodes both of gold and of iridium were employed. In tubes sown with microbes in which there was not obvious evolution of gas the E.M.F. at the gold electrode and at the iridium electrode agreed within a few millivolts. During 60 hours the E_h fell steadily from -0.18 , the E_h of the media, to between -0.35 and -0.4 volts in different experiments, coincident with the formation of reducing substances from the disintegration of the proteins of the media.

In tubes sown with gas-forming anaerobes such as *B. welchii* and *B. oedematiens*, the readings of E.M.F. afforded by the gold and iridium electrode were quite different. After one hour a rapid fall of about 0.2 volts coincident with the formation of gas bubbles was always observed with iridium electrodes, but was absent with gold electrodes. Although nascent hydrogen was produced the gold electrode failed to register any significant change in E.M.F.

The iridium electrode affords the truer measure of the reduction potential in the medium for it requires a potential more negative than the hydrogen electrode to set free nascent hydrogen.

Moreover, the strongly electro-negative dyes neutral red and sapronin, if added to the medium, are decolorised by the action of *B. welchii*.

The explanation of the different behaviour of electrodes of gold and iridium when gas is evolved appears to be that as the formation of hydrogen by the microbes is an irreversible process and gold being relatively insensitive to hydrogen, there is no reversible oxidation-reduction system present with a more negative range than parahaematin-haemochromagen with which the gold electrode can come into electro-chemical equilibrium. The iridium electrode behaves otherwise because it becomes charged with hydrogen from the solution and functions as a hydrogen electrode.

The Laws Governing Rate of Heat-Loss from a Sweating Body.

Dr. A. J. Canny (Rockefeller Fellow, Sydney) and Sir Charles Martin have completed their investigations into the laws of cooling of moist bodies. Evaporative, convective and radiant heat losses have each proved to be accessible to experimental determination. A large number of experiments made under varying conditions of atmospheric temperature and humidity and in winds of different velocity have been made. They have shown that a simple, even if lengthy, formula which includes no term that cannot be justified on physical principles, may be used to predict the rate of loss of heat from a given moist body under any environmental conditions. For this prediction only the wet and dry bulb temperature of the atmosphere, the wind speed and the internal temperature of the cooling body need be known. Several constants must be available to allow of a calculation of heat loss but these are easily obtained in a simple system by a few experiments.

In particular it has been shown how the temperature of the evaporating surface itself can be measured. This is a quantity whose value seems so far to have eluded experimenters in this field.

It is hoped that the principles developed will be of general application though the absolute quantities obtained in this investigation are applicable only to the particular system used.

Endocrinology.

Dr. V. Koronchovsky with the assistance of Mrs. Dennison, has continued his investigations into the male sexual hormones and the interaction between the sexual glands, the thyroid, anterior pituitary and adrenal glands.

Testicular and Prostatic Hormones. The influence of cryptorchidism and castration upon the metabolism and fat deposition in animals and upon the development of the male generative organs, thyroid, adrenals and hypophysis has been compared.

The former procedure eliminates the hormonal activity of the seminiferous cells (which almost entirely disappear) but leaves Leydig's interstitial cells in a hypertrophied condition, whilst the latter removes both germinal and interstitial cells.

An analysis of the results obtained in his experiments has led Dr. Koronchovsky to the following conclusions:—

- (a) The seminiferous cells secrete hormones which stimulate metabolism and the development of the thyroid glands.
- (b) Leydig's cells produce hormones which are necessary for the normal growth and development of the adrenals and the anterior part of the hypophysis.

- (c) Hormones stimulating the growth of the generative organs are produced by both the seminiferous and the Leydig cells.
- (d) The development of the generative organs is influenced by the hormones produced by Leydig's cells in co-operation with the anterior portion of the hypophysis and the adrenals, whilst the hormones of the seminiferous cells co-operate with the thyroid gland to produce the same effect.

Obesity develops after cryptorchidism and castration as the result of a decrease (in cryptorchids) or exclusion (in castrates) of the hormones, which are produced by the seminiferous cells and which stimulate metabolism directly and also indirectly by stimulation of thyroid activity.

Hormones of the Anterior Pituitary. Active extracts from the anterior portion of the pituitary gland can be made both by acid and alkaline watery solutions. Dr. Korenchevsky finds, in confirmation of Evans' experiments, that the former stimulate the development of the generative organs and the cortical portion of the adrenals, whereas the latter, he finds, have the opposite effect. At the same time the nitrogen metabolism of animals is reduced below the normal.

The influence of the continuous administration of these alkaline extracts has been observed upon cryptorchid and castrated animals as well as upon normal ones.

The synergy of the three endocrine glands, testes, adrenals and anterior hypophysis, has long been evident from pathology: Dr. Korenchevsky's work is a contribution towards the solution of this complicated problem.

Coagulation of the Blood.

Dr. J. O. W. Barratt has studied further the anticoagulant action of antithrombin present in human blood plasma. The interpretation of experimental work has been placed upon a more satisfactory basis, but all attempts to obtain a reliable method of estimating the amount of antithrombin present in plasma have so far been fruitless.

The equation representing the interaction of thrombin and fibrinogen has been the subject of a re-investigation in considerable detail, and results have been obtained of greater precision than was at one time thought possible.

Further observations upon the period of onset of coagulation have thrown additional light upon the significance of the coagulation period, and have afforded a method for the estimation of the amount of thrombin present in coagulant mixtures.

The anticoagulant action of heparin is also being investigated.

Cancer Research.

Dr. T. Lumsden and Miss A. C. Kohn-Speyer have continued to investigate tumour immunity.

Vaccine Therapy. The possibility of producing a vaccine effective against rat sarcoma by attenuation of the tumour cells *in vitro* has been fully investigated. The sarcomatous tissue was reduced to a very fine state of division by means of the Latapie mincing apparatus. The tumour cells were thereafter mixed with an excess of weak formalin solution (1 in 2,000 of normal saline) and allowed to stand for varying periods before being injected into the normal rats which it was intended to immunise. The best results were obtained when the rats were inoculated weekly over a long period with tumour cells less and less attenuated. Even with the greatest care only two-thirds of the animals were found to be effectively protected against a test inoculation of virulent tumour cells. Many other methods of attenuation, heat, evaporation to dryness, ether, etc., were tried, but with less satisfactory results.

Auto-Vaccine Treatment. It had been shown by experiments previously reported that the most effective means of immunising rats against Jensen's rat sarcoma was to implant tumours in them and then cure them gradually by inoculation of antiserum or of 1% formalin locally into the growth. It was held that the absorption of the dying tumour cells acted like a vaccine and accounted for the immunity of the cured animals, when tested subsequently by implantation of virulent tumour fragments.

Since, however, Jensen's rat sarcoma is a tumour which gives rise to a considerable amount of concomitant immunity, there was room for doubt as to whether it was justifiable to regard the immunity as due to auto-vaccination, or not.

The point has now been settled in favour of the vaccine hypothesis by experiments on mice suffering from an implanted mammary carcinoma (M_{m}) which never regresses naturally and which gives rise to no appreciable degree of concomitant immunity.

It was demonstrated that a large proportion of these tumour-bearing mice could be cured and immunised against subsequent test implantation by repeated inoculation of 1% formalin into the growths. Where implanted tumours are concerned therefore, auto-vaccination treatment is a true cure, viz., it causes the disappearance of the existing tumour and it precludes the possibility of recurrence or of metastasis formation.

The strain of American tumour-bearing mice in which 94% of the female suffer from spontaneous mammary cancer has been successfully propagated. The nine mice originally sent by Dr. Burton Simpson, of Buffalo, U.S.A., have now a progeny of something like 800. Of the original females sent, one died of pneumonia before the tumour-bearing age. The remaining five have all developed mammary cancer. It is hoped that these mice will make it possible to determine whether the auto-vaccination treatment, so effective in the case of implanted tumours, is also applicable to tumours appearing spontaneously.

Experiments in Nutrition.

Water Soluble B vitamins. Work on the isolation of vitamin B₂ is being continued by Dr. Harriette Chick and Miss Copping. Attempts are being made to prepare concentrations of this vitamin from egg-white, in which it occurs unaccompanied by vitamin B₁, and from mammalian liver.

Heat Stability of Vitamin B₂. Dr. Harriette Chick, Miss Roscoe (Beit Memorial Research Fellow) and Miss Copping, have made a quantitative study of the heat stability of vitamin B₂ in yeast and yeast extracts and of its sensitiveness to the presence of alkali. In acid solution (pH 5.0) no loss in potency could be detected after two hours at 90-100°C., while 50% loss occurred after 4-5 hours at 123° (pH 5.0-8.0). When the reaction was alkaline (pH 8-10) the loss in potency was 30% after ten days at room temperature, 50% after two hours at 90-100°C. and 75-100% after four hours at 123°. The same results were obtained whether the criterion for assay of the residual vitamin B₂ after these treatments was (1) the promotion of growth on an experimental diet deficient only in this vitamin, (2) the cure of the specific skin lesions developed on such a diet.

Evidence for the existence of additional components in the Vitamin B complex. This sensitiveness of vitamin B₂ to alkalis at high temperatures is opposed to the conclusions of other workers in this field (Drummond and co-workers; Reader), who consider that vitamin B₂ is stable to the action of alkalis at high temperatures but that yeast contains an additional dietary factor, "vitamin B₃," which is heat and alkali-labile. Evidence that a third, hitherto unrecognised, dietary factor exists in yeast has been accumulated in the course of the above research, but the evidence points to its being heat-stable. For example, the growth of young rats on "synthetic" diets in which the vitamin B₁ is provided by Peters' concentrate and the vitamin B₂ by preparations from egg-white, is inferior to that attained when the latter vitamin is furnished by autoclaved yeast products. Further, the repeated failure experienced, in common with other workers, in attempts to breed young from rats reared to maturity upon diets which contain all the recognised necessary B vitamins and other dietary factors also points to the existence of at least one unknown factor which is indispensable for correct nutrition. Search for this unknown substance is being made among both purified substances and ordinary foodstuffs. Miss Roscoe, Miss Copping and Dr. Chick are engaged in this work.

Distribution of Vitamins B₁ and B₂ in Natural Foodstuffs. Using the methods of assay with young growing rats worked out in this department, Miss Roscoe has extended the work on distribution to green and root vegetables and has found lettuce, cabbage and spinach to be valuable sources of vitamin B₂, and much richer in this vitamin than in vitamin B₁.

Dr. Aykroyd (Beit Memorial Research Fellow), at present assisted by Miss Gaffikin, is continuing on a larger scale the previous work on the cereals (wheat, rice, maize, millet and their constituent parts) with the aim of throwing further light on the epidemiology of pellagra. Foods rich in vitamin B₁, viz., meat, milk, eggs, and green vegetables, coincide with those which have been found most effective in practice for the prevention and cure of this disease. Cereals as a class, however, are poor in this vitamin, but since pellagra occurs almost exclusively among maize eaters and is almost unknown among populations whose staple food is wheat, rice or millet, the vitamin B₁ content of milled maize should be found appreciably lower than that of the other milled cereals, if lack of vitamin B₁ is to be accepted as the primary cause of the disease. For it is unlikely that the association of pellagra with maize could be accidental and due to deficiencies in other constituents of the maize-eaters' diet. Attention is also being paid to the possibility that some toxic factor may be present in maize.

The cereals above mentioned are also being assayed for their content of vitamin B₂ to see if the results are in accord with the vitamin (B₁) theory of the etiology of beriberi.

Clinical Work on Deficiency Disease. Dr. Aykroyd spent the summer of 1929 in Newfoundland and Labrador for the purpose of investigating food deficiency disease among the population. Beriberi was found to be fairly common and to affect chiefly the poorest among the fishermen, who are able to afford little variety in their diet and in winter and spring subsist chiefly on a diet very low in vitamin B₁, consisting mainly of white bread, molasses, and salt meat and fish. The occurrence of beriberi on a milled cereal diet other than rice is additional evidence in favour of the vitamin deficiency origin of the disease. With regard to beriberi, clinical observations in Labrador fit well with experimental evidence.

Some investigations were also made on functional night-blindness, a condition not uncommon in Newfoundland and often thought to be associated with faulty diet. It occurred among those whose diets were obviously deficient in vitamin A and yielded at once to treatment with vitamin A-containing foods.

Dr. Aykroyd is greatly indebted to the International Grenfell Association for help and hospitality received in the course of these researches.

Biological Value of Proteins. Dr. Margaret A. Fixsen, in collaboration with Dr. Chick, is investigating the biological value of proteins and the possible rôle played by vitamins B₁ and B₂ respectively, in determining the minimum intake of nitrogen necessary to secure equilibrium. A satisfactory technique has been evolved using the adult rat as experimental animal.

The experimental results suggest that both vitamins are required for an economical use of nitrogen. The effect is, however, an indirect one, for absence of either causes a loss of appetite. The diminished calorie intake is apparent in about 48 hours, by the utilisation of some of the animal's own protein to supply fuel. The power of the rat for storage of vitamins B₁ and B₂ would appear to be very limited.

Most previous estimations of the biological value of different proteins suffer from the defect that an inadequate supply of B vitamins was supplied during the observations as materials rich in them also contain enough nitrogen to vitiate the experiment. In the method used by Dr. Fixsen the necessary B vitamins are administered as concentrates containing only minimal amounts of nitrogen; it is hoped, therefore, to obtain more trustworthy estimations of the biological values of the proteins contained in the commoner foodstuffs than has hitherto been possible.

The Relation of Carotene to Vitamin A. Miss Hume and Miss Henderson Smith have been carrying out a biological investigation of the relation of carotene to vitamin A, in collaboration with Dr. Smedley-Maclean and Miss D. L. Collison, who are making a chemical investigation of the relationship.

Carotene, prepared from several sources, green cabbage, spinach and carrots, has been found in every case to have approximately the same biological value as a source of vitamin A. The biological value increased with the purification and appeared to be proportional to the intensity of the yellow colouration. The minimum dose of carotene, from any of the sources mentioned, which would maintain life for four weeks in a rat depleted of vitamin A was found to be about .003 mgs.

The exact relation of carotene to vitamin A has been, and, to some extent still is, problematical. It is quite clear that when vitamin A is derived from animal sources, such as liver-oils or butter, carotene cannot be responsible for the whole vitamin A activity, for there is no apparent quantitative relation between the vitamin A value and the depth of yellow colouration. In plants, on the other hand, the relation between depth of yellow colour and biological activity seems to hold good throughout. The fact that vitamin A cannot always be carotene has tended to discount the possibility that it sometimes may be. This fact, coupled with Drummond's pronouncement that highly purified carotene has no vitamin A value, had caused the subject to be dropped, although the association of carotene and vitamin A activity in plant organs is so striking that it could hardly be fortuitous.

The problem was attacked again recently by Euler, to whom it appeared possible that omission of vitamin D from the basal diet of the experimental rats might have accounted for Drummond's failure to find carotene active as a source of vitamin A. Using his own technique, Euler found that carotene had remarkable activity as a source of vitamin A, even when many times recrystallised, and his findings were shortly after corroborated by Moore. In the course of their examination of the unsaponifiable fraction from green leaves, Dr. Smedley-Maclean and Miss Hume were led to the same conclusion. Drummond, however, maintained the standpoint that activity was only manifested when the carotene was impure. He kindly supplied samples of his own carotene, which were tested by Miss Hume and by other workers. All agreed in finding these samples active, and the problem was therefore reduced to one of a difference of technique at some point. Subsequently, the factor causing the discrepancy was identified, and it is now generally accepted that highly purified carotene has the power to function as vitamin A, though it cannot be affirmed with absolute certainty that the activity is not due to the presence, as an impurity, of the colourless substance which represents vitamin A in liver oils. If this is the case, the impurity, it must be supposed, is always present in a definite quantitative ratio, and to defy all ordinary chemical methods of separation. It is claimed that the minimum dose of colourless vitamin A for a rat must be of a very much lower order than the .003 mgs. which is the minimum dose found for carotene, and that it is quite possible for this small dose of carotene to contain a much smaller but sufficient dose of vitamin A as impurity. The problem as it now stands is a difficult one, lending itself only to indirect modes of attack.

Technique of estimating Vitamin A. In the course of the above investigation, Miss Hume and Miss Henderson Smith have made much use of the biological test for vitamin A, and by the introduction of certain modifications have been able to make it yield more satisfactory results than formerly. A very substantial increase in the supply of B vitamins in the basal diet of the experimental animals has made it possible to evoke from them a larger and more consistent growth performance; at the same time, pneumonia, which was formerly a scourge, has practically disappeared.

For the minimum dose of any substance under investigation, it has been found more accurate to ascertain the dose which just maintains life for a set period, rather than the dose which will give a definite growth response. The behaviour of rats in the former respect seems to be somewhat less variable than in the latter. The method has, however, the disadvantage that in animals on marginal doses, infections of the mucous tract, particularly of the bladder and kidney, become disturbingly frequent and tend to mar the final result.

The behaviour of rats during and after the experimental period of testing for vitamin A, suggests that there is still some factor or factors, not included in the diet, which ought to be present for growth and development to be normal when vitamin A is added; the absence of this factor or factors mars any long term dietary experiment and is constantly under investigation, concurrently with the vitamin A tests.

DEPARTMENT OF PROTOZOOLOGY.

The observations on the reactions of *Bodo caudatus* to acriflavine and the study of resistance and adaptation to which they led, have been brought to a conclusion by Dr. Muriel Robertson and though further work on this will be carried out later, the matter is for the present in abeyance.

The Effect of Gamma irradiation on the growth of *Bodo caudatus*.

The knowledge of the cultural conditions of *Bodo caudatus* obtained in the course of her previous work has been used by Dr. Robertson in an attempt to test the effect of exposure to radium upon the growth of cultures under various experimental conditions. This work is in its earliest stages and the first preoccupation is to find a suitable type of experiment and devise a sound method of estimating the changes brought about by the exposure to radium.

In the first place *Bodo* is very resistant to the gamma rays and the actual death of a culture has not so far been achieved by exposure to a combination of radon and radium equal to 175-200 mg. of radium (screened with 0.5 mm. of lead sheeting) at a distance of 1 cm. for five days.

Two types of experiment have been tried. In the first an actively growing culture is divided equally between two hard glass tubes, one of these is exposed to radium the other is not and serves as the control. From these two tubes, plates are made at various intervals under precisely parallel conditions. The growth on the plates is followed by means of sample films made at intervals; the films are stained and the numbers in division and the various phases of division are counted per thousand individuals. In this type of experiment a composite or general radium effect is produced on the cultures as a whole. Thus with an irradiation from 30 mg. of radium, after 60-72 hours, the inoculum of equal volume taken from the two tubes to be placed upon the plates contained very different numbers of bodos. There was a consequent lag in the plates from the radium tube as compared with the control and the growth curve showed differences, but there was no subsequent change in general capacity for multiplication. This type of experiment while giving information in many directions was also open to criticism and left certain factors beyond accurate estimation, such as for instance, the absolute numbers, so that the analysis of the various elements in the radium effect was not sufficiently delicate. It had been devised in the hope of finding a progressive death rate and of obtaining an end point.

A second type of experiment is now being worked out in which the bodos are cultivated upon plates but in such a manner that the plate sequence—of initial lag and active rise of multiplication which drops gradually to a cessation of division with high absolute numbers and a final dying down to low numbers in an almost quiescent state as regards division—is reduced to a minimum and the bodos which are moved daily on to a fresh plate are kept multiplying continuously at an approximately uniform rate.

The plates are so arranged in regard to the quantity of fluid that they can be divided into two exactly equal daughter plates at any transfer, so that excellent controls can be obtained. The absolute numbers can also be estimated by Thoma-Zeiss counts of the inoculum put on to the plate and of the final number taken off at the end of 24 hours. Growth curves, estimated by the actual numbers in division per 1,000 individuals, are obtained from frequent samplings taken upon cover-slips which are fixed and stained and counted at leisure. In addition plates allowed to run through the full sequence cycle can be made at each transfer with an inoculum of known numbers. The first experiment according to this method has been carried out and the data is in process of being worked through.

This work is being carried out in association with Mr. Bernard W. Williams of the Surgical Unit at St. Thomas's Hospital. Dr. Robertson is indebted to the hospital authorities and to the Directors of the Surgical and Medical Units for kind co-operation.

DEPARTMENT FOR THE STUDY AND PREPARATION OF ANTITOXIC SERA.

The titration of anti-pneumococcus serum.

Within recent years much work has been done on this subject, chiefly by American investigators, and particularly by Felton of the Harvard University Medical School, but up to the present no standard method of titration has been agreed upon. The test, as usually carried out, consists in introducing into the peritoneal cavity of mice measured doses of a virulent culture and of the serum. The results are seldom free from irregularities, such as the curious circumstance that the mice receiving the largest and smallest doses of serum may die, while those receiving intermediate doses survive—the so-called zone effect. Recently, the necessity for re-titrating some time-expired serum afforded Dr. Petrie the opportunity

for examining afresh the factors involved in the estimation of the potency of anti-pneumococcus serum, with the result that he has devised a modification of the test which has eliminated the irregularities, so that a closer determination of the titre of antibody-containing solutions appears to be attainable.

Experiments have been carried out by Dr. Petrie with a serum prepared from a virulent pneumococcus Type I. strain, and the protective value of the natural serum and of the various protein fractions has been investigated. The antibody in this serum, when concentrated, was found to be associated chiefly with the pseudo-globulin fraction. Dr. Felton has kindly supplied a sample of his concentrated solution of antibody, and in confirmation of his estimate of potency the solution has been found to possess a very high protective value in mice; one c.cm. is capable of neutralising the effect of 500 million *certain* lethal doses of a virulent Type I. culture. Reports from the United States give a favourable account of the clinical value of Felton's solution in the treatment of lobar pneumonia. A horse is being immunized against two types of the pneumococcus (I. and II.) with the object of producing a serum of similar potency.

The components in antiplague serum which confers protection upon experimental animals against the living virulent culture.

With the co-operation of Dr. B. P. B. Naidu, of the Haffkine Institute, tests have been carried out in Bombay on susceptible (Madras) rats with serum produced in two horses at our laboratories, one of which received serial injections of plague toxin intramuscularly and suspensions of plague bacilli, which had been heated at 60°C. for one hour, intravenously; the other received similar treatment except that the bacillary suspensions had been heated at 100°C. for two hours. The experiments were arranged in two ways—(1) the serum was given 48 hours before the test dose of living virulent culture, and (2) the serum and culture were given simultaneously at different sites. The antitoxic value of the sera was also estimated. The results of the experiments indicate that the serum from the horse which received the steamed bacilli has no protective value against the living culture, although it contains antitoxin. On the other hand, experiments with the serum from the horse which received intravenous doses of bacilli that had been killed at a moderate temperature show clear evidence of protection against the living culture, and, as might be expected, the serum is more effective when administered 48 hours before inoculation with the living culture. A concentrated serum has been prepared from this horse and the various fractions will be tested in the same way. The experiments definitely favour the view that an antibacterial component is an important constituent of an effective plague serum.

The preparation of a test toxin for titrating Anti-dysentery Serum (Shiga).

Dr. Petrie has been occupied with this problem for some time, but the methods adopted have not yet given consistent results, presumably because the conditions for successful extraction of the endotoxin from bacillary suspensions have not been wholly realised. The problem appears to be one of so arranging the experimental conditions that the endotoxin may readily diffuse through the bacterial cell-envelope into the surrounding extraction fluid. Comparative estimates of the toxicity of the whole bacterial suspension and of the filtrate from the suspension give evidence of partial retention of the toxin within the cell. A notable result that has emerged from this work has been the absence of signs, as judged by microscopical appearances, of any marked alteration in the structure of the cell, even after submission to apparently drastic methods of treatment, both chemical and physical, designed to bring about its rupture and the escape of its contents. It seems certain that the bacterial cell has quite remarkable powers of resistance to disintegrative agencies. The work is being continued.

The experimental production of Pneumococcal Endocarditis.

Dr. Petrie's experiments have been continued during the past year, and have now furnished clear evidence that recurring blood losses definitely predispose to the production of valvular lesions in highly immune rabbits which are given repeated intravenous doses of living virulent pneumococci. Confirmatory evidence was sought by administering intravenously sublethal doses of an anti-rabbit-red-cell serum alternately with the doses of living pneumococci. As a sequel, a high proportion of the animals eventually succumbed and were found to have the lesions of infective endocarditis. The pathogenic action of this anti-serum is attributable either to the chronic anaemia it causes or to its toxic action upon the vascular endothelium. There is, too, the possibility that the system of phagocytic cells may be adversely influenced by the serum. Films of the organs of animals which died with endocarditis showed in every case active phagocytosis, and this was particularly apparent in preparations made from the bone-marrow. The repeated injections of living culture within relatively short intervals doubtless acts deleteriously by putting an excessive strain upon the clearing function of the R-E system of cells. The experiments, as a whole, throw some light upon the pathogenesis of infective endocarditis in man, for they indicate the risk of an infective valvular lesion lighting up in consequence of the leakage of bacteria (streptococci or pneumococci) into the blood-stream from a cryptic focus, especially in a patient who is suffering from a secondary anaemia. An acquired immunity to the infective organism does not necessarily interpose a barrier to the lodgment and proliferation of the cocci upon the endocardium.

The maintenance of a healthy stock of Guinea-pigs.

The pneumococcal infection to which reference was made by Dr. Petrie in last year's report still persists among the breeding stock, but not to any serious degree. A statistical analysis of the results of irradiating one-half of the breeding stock by means of a mercury vapour lamp during a period of twelve months has been completed with the kind co-operation of Dr. P. L. McKinlay, lately of the London School of Tropical Medicine and Hygiene. No evidence was obtained that irradiation reduced the incidence of the infection or had any beneficial influence upon the general health and fertility of the breeding stock. Recent researches have suggested that the regular administration of iodine may increase resistance to spontaneous infections in domesticated animals by its influence upon the thyroid gland and the metabolic processes in general. An experiment is now in progress in which one-half of the stock receives an appropriate daily dose of potassium iodide, whereas the other half serves as a control. The results will be reported upon after the experiment has lasted for twelve months.

The observations accumulated during the past three and a half years on the incidence of the pneumococcal infection in the stock of guinea-pigs indicate the importance of the genetical aspect of the problem, and it is proposed to analyse the records from this point of view.

The production of experimental Sera.

An anti-vaccinal serum has been prepared from a horse and the various protein fractions have been separated with the object of ascertaining the locus of the specific antibody. Dr. Ledingham at whose instance the work was done, has carried out titrations with these preparations. A horse has been immunised with the thermostable antigen of *B. tetani*, and another horse with the thermostable antigen of *B. welchii*. Dr. Felix and Miss M. Robertson, on whose behalf these horses were immunised, are at present engaged in the titration of these sera.

The production of a protective sera against the virus of Poliomyelitis.

A horse has been successfully immunised by Dr. Morgan by repeated intramuscular inoculations with a filtrate of a potent poliomyelitis virus. The serum has been tested on monkeys by Dr. Fairbrother and found to possess antiviral properties comparable with convalescent sera. It is of interest to note that during the whole course of the immunisation no definite signs of a reaction in the horse were observed.

The different serum proteins have been separated and purified by the methods in general use for the concentration of diphtheria and tetanus antitoxins. The examination of a limited number of such preparations makes it appear that a considerable part of the antiviral substance is in the euglobulin fraction. The reconcentrated pseudoglobulin and the serum albumen are apparently free from the protective substance.

The specific soluble substance of the dysentery bacillus (Shiga).

Attempts by Dr. Morgan to isolate and purify the specific soluble substance of a smooth strain of the dysentery bacillus (Shiga) have yielded a colourless syrup which is specifically precipitable by the homologous immune serum in dilutions up to about 1:50,000. The material has not yet been freed from non-specific substances, and the quantity that has been prepared is too small to allow of a precise investigation into its nature, so that an exact description of its properties cannot at present be given. Purification and analysis of the crude substance will be carried out when a sufficient stock has accumulated.

Autolysis of *B. dysenteriae* (Shiga).

By measuring the distribution of nitrogen during the autolysis of bacterial suspensions of this bacillus Dr. Morgan has obtained evidence of autolytic changes as the result of its own enzyme action. Thus, in the course of 60 hours autolysis at 36°C. the amino-nitrogen, as measured by van Slyke's nitrous acid method, increases as much as 80% above its original value. There is also a large increase in the nitrogen which is non-precipitable with 5% trichloroacetic acid; this nitrogen is not, however, due to free ammonia. The powerful proteolytic enzyme, to which the autolysis is due, has normally a very limited sphere of action, mostly intracellular, since, when grown in stab cultures, *B. dysenteriae* does not liquefy gelatin. The proteolytic changes cease when the amino-nitrogen has risen from the original value of 9% to 17%; only very occasionally does the value reach 20%. On the acid side of neutrality there is no evidence of proteolysis, an indication that a pepsin-like enzyme does not exist in the bacterial cell. On the alkaline side, at pH 7.0 to 9.0, there is considerable enzymic activity with an optimum pH between 8.0 and 8.5, a range which coincides with the optimum pH for the growth of the organism under normal cultural conditions. Exposure of bacterial suspensions to a temperature of 100°C. for 10 minutes destroys the proteolytic enzyme. The degree of autolysis of the rough and smooth varieties of *B. dysenteriae* (Shiga), as measured by the activities of their proteolytic, lipolytic and sueroclastic enzymes is being investigated.

While attending a Physiological Congress held in Boston, Mass., during the summer, Dr. Morgan had an opportunity of visiting some of the leading American Serum laboratories, where he was shown the methods of serum concentration used in that Country.

The Governing Body has pleasure in expressing its thanks to the Medical Research Council for its kindness in sending supplies of standard antitoxins.

DEPARTMENT FOR THE STUDY AND PREPARATION OF ANTI-VARIOLOUS VACCINE.

The Filtration of the Virus of Vaccinia. The virus of vaccinia has been stated to be filterable through a Berkefeld filter by Negri and others, but most bacteriologists have not been able to accomplish this. Last year, Yacoi and Kasai (Japan) published results indicating that if an emulsion of vaccine lymph was made just alkaline (pH 8) previously to filtration, the virus generally passed Berkefeld V and N and Chamberland L3 filters. Subsequently, these observers obtained even better success by taking advantage of an artifice similar to that successfully employed by Holderer to filter enzymes. The interstices of the filter were coated with protein by the previous filtration of 10 c.c. of a 1 in 4 solution of egg-white. After this treatment the absorption of the virus was much less.

Dr. Green has repeated the experiments of the Japanese investigators, and finds that by closely following their method, vaccine virus can be filtered. The concentration of virus in the filtrate is a good deal diminished but the method should be useful for many researches in which virus material free from bacteria is a desideratum.

Dr. Green has also been engaged in endeavouring to enhance the potency of vaccine virus in lymph destined for export when it has to travel long distances at high atmospheric temperatures.

FOOT AND MOUTH DISEASE RESEARCH.

Part of the work of the Research Committee of the Ministry of Agriculture has been continued at the Institute during the year by Dr. J. T. Edwards, formerly director of the Veterinary Research Institute at Muktesar, India.

Many investigations recently pursued in the laboratories of the Institute have been directed to the discovery of conditions favourable and unfavourable to the survival of the virus of foot and mouth disease outside the bodies of infected animals. Dr. Edwards has been concerned more particularly with the possible part played by the potentiality for oxidation and reduction of the medium which is contaminated by the virus upon its survival. To this end he has studied the oxidation-reduction potential at the seat of the lesion in the skin where the virus is propagating abundantly, and compared this with that of materials such as moist bran and hay, which have been previously found unexpectedly favourable, and with others, such as serum, which are unfavourable to survival. Subsequently the survival of the virus in nutrient media containing substances by means of which the oxidation-reduction potential could be varied at will has been determined.

His experiments indicate that the virus of foot and mouth disease is very sensitive to small changes in the oxidation-reduction potential of the medium and that the optimum E_h for survival is between +0.27 and +0.10, varying somewhat according to the pH of the medium and its composition. Dr. Edwards suggests that the virus does not long survive in or on materials which do not stabilise the reduction potential within a range compatible with the respiratory activity of the virus.

Experiments are also being carried out with hedgehogs to test the efficacy of vaccination with killed virus against natural infection. It is possible to do this with hedgehogs, for they readily contract the disease by contact.

NATIONAL COLLECTION OF TYPE CULTURES.

The expansion of the National Collection of Type Cultures, referred to in the previous report, has continued in the year under review both with regard to the number of cultures distributed to workers in various fields of microbiology at home and abroad, and to the number of fresh types received. Over 5,000 cultures have been distributed and some 350 new strains have been added to the Collection.

Investigations have also been carried out on the identification of many strains deposited for maintenance.

A new edition of the catalogue of the National Collection has been prepared and is now awaiting publication when circumstances permit. The classification of a considerable number of groups has been revised in the light of present knowledge, and while the scheme employed can only be regarded as tentative and subject to modification, it is hoped that it will prove of practical value to investigators. In this connection it may be observed that the difficult subject of bacteriological nomenclature will be dealt with by a Nomenclature Committee to be set up by the International Society of Microbiologists at their First International Congress, in Paris, next July.

In addition to the general catalogue of the Collection, referred to above, the staff have prepared a revised edition of the list of fungi, &c., which appeared in the Transactions of the British Mycological Society some years ago. The list, which will be published in an early number of these Transactions, will comprise micro-organisms of importance in phytopathology, medical or veterinary science, technical and soil bacteriology and types useful for teaching purposes.

GENERAL AND FINANCIAL.

The Accounts and Balance Sheet for the year ending December 31st, 1929, show balances to the credit of the Pension Fund of £26,194 4s., of the Sinking Fund of £18,881 7s. 9d., and of the Capital Fund of £506,792 6s. 1d., the latter figure being unaltered from that of last year, the excess of income over expenditure for the year being again utilised in writing down the value of certain of the General Fund Investments, which still show a depreciation.

The Contingency Fund remains unaltered at £14,228 18s. 1d.

Investments made during the year were:—

For the General Fund: £6,000 4½% Conversion Loan; £4,000 4% Consolidated Stock; £2,533 4% Funding Stock; £1,125 Port of London 4% B. Stock; £1,000 Cape of Good Hope 3½% Consolidated Stock, 1929-1949; £500 4% Canada Stock; £494 12s. 9d. New South Wales 4% Stock, 1942-1962; £8,500 5% Conversion Stock, 1944-1964 (£10% only paid).

For the Sinking Fund: £1,450 4% Funding Stock, 1960-1990.

For the Pension Fund: £1,400 3½% Conversion Stock.

£6 2s. 6d., New Zealand Government 3% Stock, 1945, belonging to the General Fund, was sold.

The net income from the sale of the Institute's products during the year 1929 was £38,326 15s. 5d. After adjustment of the stock of Sera on hand at the beginning and end of the year, income from this source appears in the accounts as £38,418 19s. 5d. Sales of Sera show a slight decrease, while sales of Bacterial Vaccines, Vaccine Lymph, and also Diagnosis and Investigation Fees each show an increase compared with last year.

The total expenditure for the year was £42,612 10s. 4d., against £40,799 3s. 2d. in 1928. Vaccine Laboratory Expenses, Serum and Calf Vaccine Laboratory Expenses, Animals, Animal House Expenses, and Forage show an increase, and Rent, Rates, Taxes and Insurance, Alterations, Repairs and Renewals and Library Expenses a decrease compared with last year.

In conclusion, the Governing Body desires to express its appreciation of the devoted co-operation of the Director and all members of the Staff in carrying out the work of the Institute.

JAMES K. FOWLER,

Acting Chairman of the Governing Body.

BALANCE SHEET

AND

ACCOUNTS.

Dr.

The Lister Institute

BALANCE SHEET

	£	s.	d.	£	s.	d.
To CREDITORS				2,687	4	3
To PENSION FUND—						
As per Account at 31st December, 1928	25,160	1	0			
Add Balance of Income and Expenditure Account, 1929	1,034	3	0			
				26,194	4	0
To JENNER MEMORIAL RESEARCH STUDENTSHIP FUND—						
As per Account at 31st December, 1928				8,051	4	7
To CONTINGENCY FUND—						
As per Account at 31st December, 1923				14,228	18	1
To SINKING FUND to 31st December, 1929				18,881	7	9
To CAPITAL FUND to 31st December, 1929—						
Balance of Income and Expenditure Account to 31st December, 1926	151,972	6	6			
Donations, &c., received to date from the following:—						
Dr. Ludwig Mond (1893)	2,000	0	0			
The Berridge Trustees (1893/98)	46,379	10	1			
The Grocers' Company (1894)	10,000	0	0			
Lord Iveagh (1900)	250,000	0	0			
Lord Lister's Bequest (1913) as per Account at 31st December, 1923	18,904	5	8			
William Henry Clarke Bequest (1923/6)	7,114	5	7			
Other Donations (1891-1926)	20,421	18	3			
				506,792	6	1

J. K. FOWLER, *Acting Chairman.*G. W. ADDISON, *Hon. Treasurer.*

£576,835 4 9

REPORT OF THE AUDITORS

We have audited the above Balance Sheet. We have obtained all the information and explanations we have required, paid, being held by the Institute on their behalf. In our opinion, such Balance Sheet is full and fair, and properly drawn and the explanations given to us and as shown by the books of the Institute.

London, 5th May, 1930.

By CASH—		£	s.	d.	£	s.	d.
At Bankers:	Deposit Account	7,000	0	0			
	Current Accounts	5,037	16	6			
In hand		47	16	3	12,085	12	9
By INVESTMENTS, GENERAL FUND (at cost, less amounts written off)—							
£27,000	4 per cent. Consolidated Stock	41,091	6	9			
£38,000	4½ per cent. Conversion Stock, 1940-44	36,717	9	9			
£8,500	5 per cent. Conversion Stock, 1944-64 (£10 per cent. paid)	850	0	0			
£41,000	4 per cent. Funding Stock, 1960-1990	34,276	8	3			
£25,500	5 per cent. War Stock, 1929-1947	22,491	1	9			
£30,000	Local Loans 3 per cent. Stock	16,357	10	7			
£3,000	Port of London 4 per cent. B. Stock	2,686	17	7			
£1,000	Dominion of Canada 4 per cent. Registered Stock, 1940-1960	928	4	6			
£2,000	Cape of Good Hope 3½ per cent. Consolidated Stock, 1929-49	1,802	12	0			
£25,000	Cape of Good Hope 3 per cent. Consolidated Stock, 1933-1943	23,850	0	0			
£25,000	Natal 3 per cent. Consolidated Stock, 1929-1949	24,484	7	6			
£25,000	New South Wales 3 per cent. Inscribed Stock, 1935	24,937	10	0			
£2,000	New South Wales 4 per cent. Stock, 1942-62	1,882	3	4			
£2,900	New South Wales 5½ per cent. Inscribed Stock, 1922-32	2,897	16	0			
£25,000	New Zealand Government 3 per cent. Inscribed Stock, 1945	24,114	1	2			
£26,100	South Australian Government 3 per cent. Consolidated Stock, 1916 or after	24,860	5	0			
£500	Union of South Africa 4 per cent. Consolidated Stock, 1943-1963	594	2	0			
£25,000	Victorian Government 3 per cent. Consolidated Inscribed Stock, 1929-1949	23,875	0	0			
£700	Western Australia Government 4 per cent. Inscribed Stock, 1942-1962	698	7	0			
£20,000	Southern Railway Preferred Ordinary Stock	18,503	10	8			
£6,200	London & North Eastern Railway 3 per cent. Debenture Stock	3,961	0	0			
£3,000	Great Central and Midland Railway Joint Committee 3½ per cent. Guaranteed Stock	3,623	0	0			
£363	London & North Eastern Railway 4 per cent. First Guaranteed Stock	499	11	0			
£8,650	London, Midland & Scottish Railway 4 per cent. Preference Stock	7,960	0	0			
£15,525	London, Midland & Scottish Railway 4 per cent. Preference Stock, 1923	14,375	0	0			
£18,750	London & North Eastern Railway 4 per cent. First Preference Stock	17,148	0	0			
£25,000	East Indian Railway 3 per cent. New Debenture Stock	17,890	0	0			
£661	Madras & Southern Mahratta Railway 4 per cent. Debenture Stock, 1938	656	19	7			
£800	Grand Trunk Railway Company of Canada Great Western Borrowed Capital 5 per cent. Perpetual Debenture Stock	936	0	0			
£1,937	Grand Trunk Railway Company of Canada 4 per cent. Guaranteed Stock	1,733	0	0			
£800	Ontario and Quebec Railway 5 per cent. Permanent Debenture Stock	984	0	0			
£3,400	Gas Light and Coke Company Ordinary Stock	3,638	0	0			
					401,303	4	5
By INVESTMENTS, SINKING FUND (at cost)—							
£3,000	4½ per cent. Conversion Stock, 1940-44	7,320	13	7			
£7,450	4 per cent. Funding Stock, 1960-1990	5,850	5	3			
£7,200	3½ per cent. Conversion Stock	5,535	19	0			
Balance uninvested		174	9	11	18,881	7	9
By INVESTMENTS, JENNER MEMORIAL RESEARCH STUDENTSHIP FUND (at cost)—							
£2,650	Southwark and Vauxhall Water Co. 3 per cent. Debenture Stock "B"	2,756	10	0			
£1,596	Southern Railway 5 per cent. Preference Stock	2,740	5	0			
£726	11s. 4d. Liverpool Corporation 3 per cent. Stock, 1942, or after	556	15	6			
£2,000	4 per cent. Funding Stock, 1960-1990	1,797	14	0			
Balance uninvested		200	0	1	8,051	4	7
By INVESTMENTS, PENSION FUND (at cost)—							
£22,000	4 per cent. Funding Stock, 1960-1990	17,165	3	5			
£11,700	3½ per cent. Conversion Stock	9,014	2	2			
Balance uninvested		14	18	5	26,194	4	0
(The above Investments, at the market value, 31st December, 1929 show a depreciation of £57,815.)							
By DEBTORS					12,343	7	3
By FURNITURE, FITTINGS, SCIENTIFIC APPARATUS AND BOOKS—							
At cost, less depreciation as per account, 31st December, 1929					2,471	17	2
By EXPENDITURE ON INSTITUTE BUILDINGS AT CHELSEA—							
As per account, 31st December, 1910, including purchase of freehold site, £6,000					70,916	3	1
By PURCHASE OF FREEHOLD LAND ADJOINING THE "STUDIOS," CHELSEA—							
As per account, 31st December, 1912					169	6	8
By LEASE OF THE "STUDIOS," CHELSEA, as per last account		1,588	0	9			
Less Amount written off for the year		65	2	0	1,522	18	9
By QUEENSBERRY LODGE FARM, ELSTREE—							
Purchase of freehold land and buildings and Expenditure on new buildings—							
As per account, 31st December, 1912					20,455	10	0
By STOCK OF ANIMALS		529	17	0			
By STOCK OF ANTITOXINS		1,910	11	4			
					2,440	8	4
* Nothing has been charged for depreciation of Furniture, &c. since new purchases made during the year to a greater amount than the estimated depreciation (10%) have been written off.							
					£576,835	4	9

TO THE MEMBERS.

The Superannuation Scheme for certain of the Staff provides for Life Policies for which the sum of £20,110 15 7 has been up so as to exhibit a true and correct view of the state of the Institute's affairs, according to the best of our information

COOPER BROTHERS & CO.,

Chartered Accountants. } Auditors.

The Lister Institute of

Dr. INCOME AND EXPENDITURE ACCOUNTS

INCOME.								£	s.	d.
To Interest and Dividends on General Fund Investments	...	...	...	...	...	...	...	16,329	15	6
To Interest on Sinking Fund Investments	...	...	...	...	...	...	...	852	0	0
To Investigation, Diagnosis and Analysis Fees. &c. ...	...	...	...	...	...	...	...	4,960	13	6
To Sales of Sera, Vaccines, &c., and Stock at 31st December, 1929. less Stock at 31st December, 1928	...	...	...	...	...	...	...	38,418	19	5
To Rent of Rooms	...	...	...	...	...	...	...	1,050	0	0

£61,811 8 5

Dr.

Pension

	£	s.	d.
To Interest on Investments	1,252	15	0

£1,252 15 0

Dr.

Jenner Memorial Research

	£	s.	d.
To Interest and Dividends on Investments	261	3	10
To Institute Salaries and Wages...	238	16	2

£500 0 0

Preventive Medicine.

for the year ending 31st December, 1929.

Cr.

EXPENDITURE.								£	s.	d.
By Rent, Rates and Insurance	...	...	...	...	...	...	...	1,324	0	9
By Salaries and Wages of Staff	...	...	...	...	...	...	...	22,723	7	8
By Premiums on Federated Superannuation Policies	...	...	...	...	...	...	...	1,403	18	1
By Stationery, Printing and Postage	...	...	...	...	...	...	...	448	6	9
By Printing of Collected Papers	...	...	...	...	...	...	...	193	1	7
By Office Expenses, Law Charges, Auditors' Fee and Sundries	...	...	...	...	...	...	...	348	10	1
By Travelling Expenses	...	...	...	...	...	...	...	54	19	8
By Gas, Water and Fuel	...	...	...	...	...	...	...	1,822	7	2
By Electric Light and Power	...	...	...	...	...	...	...	346	17	9
By Experimental Pathology Laboratory Expenses, including General Apparatus	...	...	...	...	...	...	...	753	0	2
By Bacteriological Laboratory Expenses, including Apparatus	...	...	...	...	...	...	...	338	19	0
By Vaccine Laboratory Expenses, including Bottles	...	...	...	...	...	...	...	1,006	19	4
By Water and Bio-chemical Laboratory Expenses, including Apparatus	...	...	...	...	...	...	...	171	9	8
By Serum and Calf Lymph Laboratories Expenses, including Apparatus and Cost of Bottles	...	...	...	...	...	...	...	3,585	17	0
By Culture Media	...	...	...	...	...	...	...	142	18	3
By Animals	...	...	...	...	...	...	...	1,776	17	4
By Animal House Expenses and Forage	...	...	...	...	...	...	...	2,689	13	11
By Alterations, Repairs and Renewals, including Workshop Expenses	...	...	...	...	...	...	...	1,963	18	11
By Library Expenses	...	...	...	...	...	...	...	373	2	7
By General Stores	...	...	...	...	...	...	...	312	1	1
By Bad Debts	...	...	...	...	...	...	...	4	8	0
By Amount written off Lease of the "Studios," Chelsea	...	...	...	...	...	...	...	65	2	0
By Sinking Fund ($\frac{1}{2}$ % per annum on Cost of Buildings and Interest on Investments)	...	...	...	...	...	...	...	1,262	13	7
By Amount written off General Fund Investments	...	...	...	...	...	...	...	18,998	18	1
								£61,611	8	5

Fund.

Cr.

	£	s.	d.
By Pensions	218	12	0
By Balance, being Excess of Income over Expenditure, transferred to Balance Sheet	1,034	3	0
	£1,252	15	0

Studentship Fund.

Cr.

	£	s.	d.
By Salary	500	0	0
	£500	0	0



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- | | | |
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THE LISTER INSTITUTE
OF
PREVENTIVE MEDICINE

Report of the Governing Body,
1931.

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

June 10th, 1931.

The Lister Institute of Preventive Medicine,

CHELSEA BRIDGE ROAD, LONDON, S.W. 1.
ELSTREE, HERTS; MARAZION, CORNWALL.

THE GOVERNING BODY.

MAJ.-GENL. SIR DAVID BRUCE, K.C.B., D.Sc., LL.D., F.R.S., A.M.S., *Chairman*.
LT.-COL. G. W. ADDISON, R.E., *Hon. Treasurer*.
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PROFESSOR W. BULLOCH, M.D., LL.D., F.R.S.
THE RIGHT HON. WALTER GUINNESS, D.S.O., M.P.
THE VISCOUNT KNUTSFORD.
(vacancy.)

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THE PRESIDENT OF THE ROYAL COLLEGE OF PHYSICIANS	Royal College of Physicians, London.
SIR FREDERICK W. ANDREWES, M.D., F.R.S.	Royal College of Physicians, London.
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SIR JOHN ROSE BRADFORD, BART. K.C.M.G., M.D., F.R.C.P., F.R.S.	" "
PROFESSOR W. BULLOCH, M.D., LL.D., F.R.S.	" "
SIR WALTER M. FLETCHER, K.B.E., M.D., F.R.S.	" "
SIR JAMES KINGSTON FOWLER, K.C.V.O., C.M.G., M.D.	" "
THE RIGHT HON. WALTER GUINNESS, D.S.O., M.P.	" "
PROFESSOR ARTHUR HARDEN, D.Sc., LL.D., F.R.S.	" "
PROFESSOR R. T. HEWLETT, M.D., F.R.C.P.	" "
SIR CHARLES J. MARTIN, C.M.G., M.B., D.Sc., LL.D., F.R.S.	" "
LOUIS C. PARKES, M.D., D.P.H.	" "
SIR WILLIAM J. R. SIMPSON, C.M.G., M.D., F.R.C.P.	" "

THE STAFF.

Director :

PROFESSOR J. C. G. LEDINGHAM, C.M.G., M.B., D.Sc., F.R.S.

Department of Bacteriology, Serology and Experimental Pathology :

- *J. C. G. LEDINGHAM, C.M.G., M.B., D.Sc., F.R.S., *Professor of Bacteriology in the University of London.*
H. L. SCHÜTZE, M.D., B.S.
G. H. EAGLES, M.D., D.P.H.
A. FELIX, D.Sc.
MARY M. BARRATT, M.B., Ch.B.
DOROTHY B. STEABEN, Ph.D.
E. WESTON HURST, M.D., Ch.B., B.Sc.
J. A. ARKWRIGHT, M.D., F.R.C.P., F.R.S. *Honorary.*
V. KORENCHEVSKY, M.D. *Honorary.*
- } *Attached to the Department.*

Division of Protozoology :

MURIEL ROBERTSON, M.A., D.Sc.

Division of Nutrition :

- *HARRIETTE CHICK, D.Sc.
HESTER M. JACKSON, B.Sc. *Temporary.*
E. MARGARET HUME, *Honorary.*
*S. S. ZILVA, D.Sc., Ph.D., F.I.C. *Honorary.*

Department of Biochemistry :

- *R. ROBISON, D.Sc., Ph.D., F.I.C., F.R.S.
J. M. GULLAND, M.A., Ph.D., D.Sc. (*From September 1st.*)
MARJORIE G. MACFARLANE, B.Sc. *Temporary.*
*IDA SMEDLEY-MACLEAN, D.Sc. *Honorary.*
A. HARDEN, D.Sc., F.R.S. *Honorary.*
ADELE H. ROSENHEIM, B.A. *Grocers' Company Research Student.*
- } *Attached to the Department.*

Department for the Preparation and Study of Antitoxic Sera, Elstree :

- *G. F. PETRIE, M.D., Ch.B., *Bacteriologist-in-Charge.*
W. T. J. MORGAN, M.Sc., Ph.D., F.I.C.
D. McCLEAN, M.B., B.S., M.R.C.S.
F. K. FOX, *Secretary to the Department.*

Department for the Preparation and Study of Anti-Variolous Vaccine, Marazion :

ALAN B. GREEN, M.A., M.D., B.Ch., *Bacteriologist-in-Charge.*

Secretary :

A. L. WHITE.

NATIONAL COLLECTION OF TYPE CULTURES. (Medical Research Council.)

Curator :

R. ST. JOHN BROOKS, M.A., M.D., D.P.H.

Assistant Curator :

MABEL RHODES.

* A recognised Teacher of the University of London.

ANNUAL GENERAL MEETING
OF
The Lister Institute of Preventive Medicine,
June 10th, 1931.

REPORT OF THE GOVERNING BODY.

The Governing Body has the honour to present the Institute's 37th Annual Report.

GOVERNING BODY.

The Governing Body report the resignation through illness of Sir James Kingston Fowler, who up to March last had acted as Chairman of the Board, in the absence abroad during the winter months of Sir David Bruce. Sir James Fowler, who joined the Governing Body in 1918, had always taken a keen interest in the Institute's welfare, and had acted as Chairman of the Serum Department Committee and as a member of the Finance Committee. His enforced resignation has been received with great regret by his colleagues.

At the meeting held last year, the Council re-elected Professor W. Bulloch, Sir James K. Fowler and Professor A. E. Boycott, as its representatives on the Governing Body until December 31st, 1931.

COUNCIL.

The Governing Body regret to announce the death, during the year of two members of Council, viz., Dr. H. de Reimer Morgan and Sir Andrew Balfour, both of whom represented the Members of the Institute upon the Council.

The vacancy created by the death of Sir E. Ray Lankester, was filled at the last meeting by the appointment of Dr. J. A. Arkwright, as a representative of the Members of the Institute.

The three members who retire from the Council this year in accordance with the Articles of Association, but who are eligible for re-election, are Professor T. J. Mackie, the representative of the University of Edinburgh; Professor W. E. Dixon, the representative of the British Medical Association, and Sir Thomas Barlow, one of the representatives of the Members of the Institute.

MEMBERS.

The Governing Body also regret to announce the death in April, of Professor Lorrain Smith and in May, of Dr. A. T. MacConkey, both of whom had been members of the Institute since 1907. Dr. MacConkey was a late member of the Staff of the Institute and from 1906 until his retirement in 1926 had charge of the Department for the Preparation and Study of Antitoxic Sera at Elstree.

STAFF.

Sir Charles Martin and Professor A. Harden retired from the service of the Institute on December 31st, 1930.

Professor J. C. G. Ledingham took up the Directorship of the Institute and Dr. R. Robison succeeded Professor Harden as Head of the Biochemical Department on January 1st, 1931.

Dr. J. M. Gulland has been appointed First Assistant in the Biochemical Department and is taking up his duties on September 1st next.

Dr. A. Felix, late Jenner Memorial Research Student, has been appointed to the staff of the Bacteriological Department, and Dr. D. McClean, Research Fellow in Bacteriology, has been appointed a member of the Staff of the Department for the Study and Preparation of Antitoxic Sera, at Elstree.

Mr. George Cooper, after 40 years' service, first as Assistant Secretary, then Secretary, and later as Accountant, retired on pension on March 31st, 1931.

Dr. R. W. Fairbrother, Research Fellow in Bacteriology, resigned his Fellowship in September, 1930, on being appointed Lecturer in Bacteriology in the Victoria University, Manchester.

Miss A. M. Copping resigned her position on December 31st, 1930, having been appointed a Lecturer at the Victoria University, New Zealand.

Dr. R. R. McLaughlin, Grocers' Company Research Studentship, resigned on December 31st, 1930, on his appointment to the Staff of the Department of Chemical Engineering in the University of Toronto, and has been succeeded as Grocers' Company Research Student by Miss Adele H. Rosenheim.

Miss M. G. Macfarlane (Carnegie Research Fellow) and Miss H. M. Jackson, have been appointed temporary members of the Institute's Staff.

Dr. G. P. Wright (University College Hospital) has been appointed to a Research Fellowship in Experimental Pathology.

RESEARCH WORK.

Before proceeding to give a brief survey of the researches which are, or have been, in progress during the year in the various departments of the Institute, the Governing Body desires to record its appreciation of the continued co-operation it has enjoyed with the Medical Research Council, the Department for Scientific and Industrial Research, and the International Committee for the Study of Infantile Paralysis. The financial support given by these bodies to skilled investigators in the different departments has greatly increased the scientific activities of the Institute.

In addition to furnishing the salaries of the Staff of the National Collection of Type Cultures, an organisation which has proved of great service to bacteriologists and mycologists throughout the Empire, the Medical Research Council has provided the salaries of Professor Korenchevsky and Miss E. M. Hume and their respective assistants.

The expenses of the fundamental vitamin investigation with special bearing on the vitamin content of various Empire products, being carried out in the Division of Nutrition by Dr. Zilva, including the salaries of Dr. Zilva and his assistants, are defrayed by a grant to the Medical Research Council from the Empire Marketing Board.

Dr. Ida Smedley-MacLean and two assistants continue to work under a grant from the Department of Scientific and Industrial Research, in the department of Biochemistry.

The salary of Dr. E. Weston Hurst, together with the expenses of his research on Poliomyelitis, are borne by the grant from the International Committee for the study of Infantile Paralysis. Through the generosity of Mr. Jeremiah Milbank, of New York, who has provided the funds for the studies of the Committee, this research is being continued for another year.

Accommodation for Professor Korenchevsky, Miss Hume, Dr. Smedley-MacLean, Dr. Hurst and the National Collection of Type Cultures, together with the expenses of the researches of the first two named, are provided by the Institute.

DEPARTMENT OF BACTERIOLOGY, SEROLOGY AND EXPERIMENTAL PATHOLOGY.

Studies on the viruses of Vaccinia, Variola and Fowlpox.

Elementary Bodies in vaccinia and fowlpox. Professor Ledingham has continued his study of these bodies with a view to securing evidence of a crucial nature that would establish their ætiological importance. He has been particularly concerned with the Borrel bodies in the lesions of fowlpox. The fact that they occur in enormous numbers in the lesions and are readily demonstrated by appropriate staining methods greatly facilitates their study. An important advance which has been made in our knowledge of these bodies is the demonstration that the well-known large Bollinger inclusion bodies seen in the epithelial cells of the fowlpox lesion are found to consist of agglomerations of Borrel bodies (0.25μ diameter) in a lipoprotein matrix. Like Woodruff and Goodpasture, in America, Professor Ledingham has secured a series of illustrative preparations demonstrating this relationship. As the American workers have shown that a single Bollinger body can infect, it is highly probable that the actual infecting agents are the Borrel bodies, of which the Bollinger inclusions are composed. Fowlpox virus is filterable fairly readily through low grade filters such as the Berkefeld "V." Professor Ledingham has been able to demonstrate in potent bacteria-free filtrates of fowlpox an abundance of Borrel bodies, so that filterability does not preclude the possibility that these bodies may be the ætiological agents. Attempts are also being made to determine whether growth of these viruses in artificial culture is accompanied by an increase of elementary bodies and Dr. M. Huseini (Cairo) is cultivating fowlpox virus *in vitro* with this object in view. The virus disease of mice recently discovered by Marchal (Ectromelia) is associated with the presence of inclusion bodies in the epithelial cells, very similar in appearance to those of fowlpox. Professor Ledingham, who received a sample of this new virus from the National Institute for Medical Research, has been able to demonstrate the presence of elementary bodies in material from the mouse lesions.

Immunisation of the horse with vaccinia virus. In collaboration with Dr. W. T. J. Morgan and Dr. G. F. Petrie, Professor Ledingham has been making a study of the distribution of the antiviral bodies in the serum-proteins as a guide to improvement in concentration technique as applied to antiviral sera. He has also tested the efficiency of the serum in preventing lesions of skin and viscera in experimentally infected animals.

Cultivation of vaccinia virus in cell-free fluid. Dr. G. H. Eagles and Dr. D. McClean report excellent progress in their study of this question. Vaccinia virus has been successfully cultivated and carried through a considerable series in subculture, using an entirely cell-free culture medium. This, called for convenience, "kidney extract," consists of the supernatant fluid after centrifugalising a mixture of finely minced fresh rabbit's kidney and Tyrode's solution. The addition of fresh serum to the medium is not essential to growth of virus. Kidney extract passed through a Chamberland L₁ filter promotes the growth of virus as well as does unfiltered extract and is unquestionably free from cell debris.

Apparent irregularity of virus increase in different flasks of an experiment is encountered in cell-free as in other media. There is evidence that this may, in part at least, be accounted for by variation in reaction to vaccinia virus displayed by individual rabbits. This variation is now controlled by giving an injection of vaccine lymph to every test animal employed for titration purposes.

It is possible that other artificial media may promote the growth of vaccinia.

Experiments are also being made with kidney extracts kept under different conditions in order to determine how far their efficiency as culture media may be affected. In view of the results obtained hitherto, it will be of interest to examine whether the process of adaptation of vaccinia virus to cell-free media is of necessity gradual, as seems most likely, or whether, on the other hand, fresh animal strains can accommodate themselves immediately to such media.

Conservation of vaccinia virus grown *in vitro*. Experiments to determine the keeping properties of culture virus have extended over many months. No satisfactory method of preserving virus grown in the chick embryo and plasma medium of Carrel and Rivers has been discovered. Anaerobic storage in the presence of 0.25% agar at $\pm 1^{\circ}\text{C}$. gave better results than any other methods investigated. Virus cultivated in Maitland and Laing's kidney medium may, on the other hand, be satisfactorily preserved in the cold room under anaerobic conditions for long periods. When cell-free kidney extract is used as a culture medium filtration appears to remove some property essential to survival of vaccinia virus since it deteriorates rapidly under anaerobic conditions in the cold room. Unfiltered kidney extract survives considerably better than the filtered extract under the same conditions of storage. As a general rule Maitland and Laing's kidney medium is more favourable for the survival of virus than other culture media. Aerobic storage is unsuited to survival of culture virus.

Filtration of vaccinia virus. (See Report of work in the Department for the Study and Preparation of Anti-Variolous Vaccine, p. 18).

Small-pox. Attempts by Dr. Eagles to propagate the virus of small-pox in rabbits have not been successful. The initial inoculation in rabbits, intradermally, of fresh small-pox material usually results in a characteristic lesion providing the material is fresh and collected in the vesicular or very early pustular stage. This lesion is neutralised by antivaccinial serum. But it has not been possible to propagate the virus from rabbit to rabbit through more than a few passages. Takes have been obtained up to the eighth passage, using both intradermal and scarification methods, but the weak, fleeting, nature of the reactions indicate that true adaptation is lacking. Adaptation similar to that reported by Gins has not been effected.

The influence of testicular extract on dermal permeability and virus response. Dr. McClean has continued the study of the increased tissue permeability produced by this extract, which was first noticed during the investigation of its virus-enhancing properties. He has shown that the extract will produce its effect in skin removed from an animal killed 48 hours previously and in skin which has been dried *in vacuo*. A definite effect on the fibre bundles in the dermis can be demonstrated. Spermatozoa are rich in the active substance, indicating that it resides in the germinal rather than the interstitial tissue. Preliminary experiments with herring ova suggest that this substance may alter the permeability of the cell membrane. No evidence has been obtained that the lowered surface tension of the solution bears any relation to the increased tissue permeability. Repeated attempts, by various methods, to isolate the active substance have been unsuccessful; further work, with this object in view, is in hand.

Experimental Trachoma in Monkeys. Attempts to produce typical lesions in monkeys with the *B. granulosis* of Noguchi have extended over a period of two years. Some post-tarsal granulation and scattered granules on the tarsus have been obtained but these have regressed without the sequelae met with in human cases. Re-inoculation and passage from monkey to monkey have proved unsuccessful.

Path of spread of the Poliomyelitis virus. Last year Drs. R. W. Fairbrother and E. W. Hurst showed that, after intracerebral or intraneural inoculation, the virus of poliomyelitis was transmitted along the axis cylinders and was not disseminated mainly by the cerebrospinal fluid as had previously been held. The importance of this observation, if true, was sufficient to warrant an attempt at confirmation. By combining intrasciatic inoculation of the virus with mild trauma to the nerve, Dr. Hurst found that he could infect monkeys with regularity and demonstrated the accuracy of the above conception in a striking manner. Virus and lesions first appeared in the lumbar cord, the latter first on the side of the inoculated nerve. The next region of the central nervous system to harbour virus was the leg area of the opposite motor cortex. The cervical cord, the leg area of the homolateral motor cortex and the arm areas of the motor cortex were involved only after appreciable intervals. These experiments show clearly the part played by the axis cylinders; the most direct and abundant connections of the lumbar cord are with the opposite motor cortex and comparatively few intersegmental connections are available to carry the infection to the cervical cord, from which the arm areas of the motor cortex are infected.

Postvaccinal and other forms of Encephalitis. Histological study of fatal cases has been continued as opportunity offered. The number of cases is, however, much smaller than during the previous year; two cases of postvaccinal and one case of postvaricellar encephalomyelitis have been available. No further advance towards an understanding of the pathogenesis of this disease has been made.

Development of intranuclear inclusions in Poliomyelitis. Multiple rounded bodies varying in diameter from 1—4 or 5 μ have been demonstrated by Dr. Hurst in the nerve-cell nuclei of a large majority of cases of monkey poliomyelitis and of one human case. They occurred only in cells showing early stages of degeneration and were consequently difficult to find except in the initial stages of the disease. They were difficult to stain electively but could be coloured by Mallory's phloxin-methylene blue method, and less successfully by Giemsa. These structures appeared to be nuclear inclusions of the same order as those in herpetic encephalitis, Borna disease, etc.

Studies on combined virus activity. Exploring a possible avenue of approach to the problem of post-vaccinal encephalitis, Drs. Hurst and Fairbrother made experiments to determine whether infection with one virus (*e.g.*, *vaccinia*) could in any way modify the reaction of the central nervous system to a second and neurotropic virus (*e.g.*, *poliomyelitis*). The vaccine virus was administered intradermally, intravenously or intracerebrally, and the poliomyelitis virus intravenously or intracerebrally. When both viruses were given intravenously the resulting vaccinal reaction had no power to alter the haemato-encephalitic barrier in such a manner as to permit infection of the central nervous system with poliomyelitis. Intradermal vaccination had no influence on intracerebrally inoculated poliomyelitis virus and did not activate or render more virulent a weak strain of the virus. When both viruses were injected intracerebrally, the two diseases evolved quite independently, and if matters were so arranged that their incubations terminated together the characteristic lesions of both existed side by side without any apparent modification of one by the other.

Preparation of Anti-poliomyelitis serum. Dr. Fairbrother, assisted by Dr. Morgan, continued his observations on immunisation of the horse and the production of an anti-viral serum. After experiments on one horse had proved successful, they attempted to immunise two more horses, but without success. A fourth horse, however, produced a serum greatly superior to the first. Dr. Hurst has tested the serum of this horse and found that 0.005 c.c. will completely neutralise an infective emulsion containing roughly 100 M.L.D. of virus. It is hoped to employ this serum in the treatment of the human disease.

Drs. Morgan and Fairbrother on concentrating this serum found that the antibody was attached, for the most part, to the euglobulin fraction.

The antiviral action of the serum of normal individuals. Dr. Fairbrother examined a small number of human sera provided by Dr. Scott Brown. He found that normal individuals who had been in contact with cases of poliomyelitis, without, however, developing the disease, frequently possessed antiviral bodies in their serum.

Investigation of an obscure nervous epidemic in Trinidad. Dr. Hurst received material for this investigation from Dr. Pawan, Port-of-Spain. Between July 1929, and February 1931, the latter observed no fewer than 17 cases with the clinical features of acute ascending myelitis and terminating invariably in death. At first the disease was thought locally to be a severe type of poliomyelitis. Animal experiments with the cord of one of the cases led, however, to the isolation of a virus identical apparently with that of rabies. The clinical and histological pictures in the inoculated animals (monkeys and rabbits) were typical of rabies and cross-immunity exists between the Trinidad virus and rabies virus-*fixe*. Other cases are now under investigation. The interesting feature of the epidemic is that

rabies is unknown in the island. The most searching enquiries have revealed no history of bites, either animal or insect, in the affected cases nor has there been any observed animal mortality except from so-called botulism in cattle; investigation of the brain of one of the animals dying from this disease has, however, resulted in the isolation of the same virus as from the human cases. The matter is to be the subject of further inquiry as cases arise.

Cultivation of the virus of poliomyelitis. Using the latest technique of Drs. Eagles and McClean, Dr. Czarkowska-Gladney (Warsaw) is attempting the culture *in vitro* of the poliomyelitis virus.

Serological Studies: Antigenic constitution and immunising properties of bacteria.

Bacterial Variation. Dr. J. A. Arkwright has continued his observations on bacterial variation especially with regard to changes in fermentation reactions and the existence of some correlation between antigenic change and fermentative properties.

Miss R. M. Pitt has attempted to obtain a transformation of "rough" into "smooth" types of *B. typhosus* by inoculating animals with dead "S" and living "R" cultures simultaneously. So far she has not succeeded in producing this variation which has been claimed to result from a similar technique with other kinds of bacteria. She has also studied a new variant strain of *B. typhosus* which ferments lactose. This is the only variant of this kind which has been recorded since F. W. Twort described his strain in 1907.

The prophylactic value of anti-plague and other vaccines. An assessment of the prophylactic value of anti-plague vaccines variously prepared has been for some considerable time under investigation by Dr. H. Schütze. Using the rat as experimental animal, he began by comparing the protection conferred against infection with a highly virulent strain of *B. pestis* by means of agar- and broth-grown and bacteriophage-lysed vaccines. It has been customary to compare such vaccines as they are supplied by the laboratories concerned in their manufacture, but the variation of the antigenic value of the strains employed in each case must vitiate a comparison on those lines. Three types of vaccine have been tested viz., (1) broth-grown vaccine prepared according to Haffkine's method, (2) the agar-grown vaccine prepared by the special method employed at the Lister Institute, and (3) the ordinary agar-grown, heat-killed vaccine. In all these tests the superiority of the Haffkine prophylactic has been established and the almost complete valuelessness of an ordinary agar-grown, heat-killed vaccine has been demonstrated. In the course of these experiments there have been indications, suggesting that the type of protein supplied to the plague bacillus for its culture, has an important bearing on the antigenic efficacy of the resultant vaccine. Further experiments based on these indications are in progress.

Envelope of *B. pestis*. An old observation by the late Dr. S. Rowland that *B. pestis* develops at higher temperatures of growth a gelatinous envelope, has been confirmed and it has been noted that with the development of this envelope there is a very definite increase in the antigen which participates in the precipitin reaction. This precipitinogen has been shown to possess both a heat-labile and a heat-stable component.

Spore-bearing anaerobes. The passive protective value of the antibacterial (anti-O) serum to *B. welchii* has been tested by Dr. Muriel Robertson and Dr. A. Felix. A horse was immunised by Dr. Petrie with one strain of *B. welchii* steamed at 100°C. The serum, which was devoid of antitoxin but contained a considerable amount of O immune body, as estimated by agglutination and complement fixation, protected mice against infection with the homologous strain. Some difficulty was experienced in demonstrating the protective action as definitely as in previous experiments with *V. septique*, since the virulence of *B. welchii* cannot easily be maintained at a high and constant level as in the case of *V. septique*. From a preliminary investigation it would appear that different strains of *B. welchii* do not share a common O antigen in a degree as high as that met with in *V. septique*. An anti-O serum to *B. welchii* should, therefore, be polyvalent, *i.e.*, it should be made with a mixture of different strains.

Non-specific agglutination of bacteria in the absence of serum. Strains of various species of gram-negative bacteria (*Salmonella*, *B. proteus* X) were found by Dr. Felix to give less stable suspensions in weak salt solutions and even in distilled water than in normal saline. The phenomenon would appear to be due to precipitation by water of some water-insoluble constituent of the bacterial body. The factor concerned seems to be associated with the O antigen since the phenomenon occurs with both the O and H variants of strains which otherwise exhibit the characters of perfect "smoothness." Different strains of the same species vary considerably in this respect and the degree of instability of the suspension fluctuates on subculturing and apparently depends on some differences in the composition of the agar medium. Correlated with the phenomenon is the agglutinability of such suspensions by glycerol highly diluted with normal saline.

Heterologous agglutination (polyagglutinating capacity of serum.) The agglutination of *B. proteus* X by typhus serum is still considered by certain workers as an instance of heterologous agglutination (polyagglutination). Dr. Felix has shown that the increased agglutinating capacity for certain organisms which have received much prominence in typhus literature is not peculiar to typhus serum. Syphilis and leprosy sera acquire a similar "polyagglutinating" capacity for these

organisms which coincides with increase of serum globulins. On *B. proteus* X, however, these sera do not exercise any increased agglutinating action. The results suggest that increased heterologous agglutination of various saprophytic organisms is due to the combined action of an abundance of preformed normal agglutinins and of augmented serum colloids.

An investigation of some unusual members of the Genus *Corynebacterium* allied to *C. diphtheriae* and recovered from the human nasopharynx. Dr. M. M. Barratt has had under investigation for some time four strains of unusual type. One was described by Mair (J. Path. & Bact., 31, 136), while the other three were isolated at the Institute from diphtheria swab material. When tested for virulence by the intracutaneous method it was noted that all four strains produced a pustular reaction which was not prevented by diphtheria antitoxin. The virulence of these strains for guinea-pigs was definite but of low order (2-4 c.c. or more of a 48-hour broth culture) and as a rule the adrenals were found unaffected at autopsy. Passive protection by diphtheria antitoxin was never complete and surviving animals exhibited for long periods abscesses or sloughs at the site of inoculation. Abscess formation in the subcutaneous tests for virulence and pustular reactions in the intracutaneous tests suggested some possible relationship with the organism of Preisz-Nocard (*C. pseudotuberculosis ovis*) and it was found that these four strains, like the Preisz-Nocard organism, but unlike *C. diphtheriae*, were virulent for rats by intraperitoneal injection. Recently potent toxins have been prepared from the strains and also from the Preisz-Nocard type. Apart from the lack of action on the adrenals, the lesions in guinea-pigs produced by the toxins are not unlike those produced by diphtheria toxin. Neutralisation experiments with these toxins and diphtheria antitoxin are now in progress.

Diet and Resistance to Infection. Dr. H. Schütze and Dr. S. S. Zilva have completed their investigation into the increased sensitivity to tuberculin of rats infected with *B. tuberculosis* as compared with those which are uninfected. The animals in both cases were fed on a diet deficient in the fat-soluble vitamin A and D, a diet considered to enhance the difference in question. This increased sensitivity was, indeed, found to exist but is apparently non-specific for it is similarly displayed by the tuberculous rat towards the toxic bodies of a killed *Salmonella* suspension. This increased sensitivity towards heterologous toxin in the tuberculous animal is not in agreement with the findings of other workers who in their experiments employed the tuberculous guinea-pig and could not demonstrate hypersensitivity, but, on the contrary, an increased resistance in the infected animal towards heterologous toxin. This may well be due to the entirely different type of infection which *B. tuberculosis* occasions in these two animal species.

Dr. Schütze and Dr. Zilva have also resumed their series of experiments which deal directly with diet and resistance to disease. Working with the rat as the experimental animal and *S. suispestifer* as the infecting agent, they have established the existence of a very definitely lowered resistance to infection among the animals deprived of vitamin A, as compared with others whose diet had been a complete one. The work is being continued on similar lines with other dietetic deficiencies.

FOOT AND MOUTH DISEASE RESEARCH.

Experimental work for the Foot and Mouth Disease Research Committee of the Ministry of Agriculture has been continued at the Institute under the supervision of Dr. J. A. Arkwright, who has recently been appointed Chairman of the Committee. Dr. J. T. Edwards has continued his work on the best conditions for survival of the virus *in vitro* as regards the oxidation-reduction and acid-base properties of liquid media in which it is suspended. He has found that the optimum alkalinity for survival is not always pH 7.5 as has been generally believed, but that it varies with other properties of the media used. He has also examined the conditions in the skin of the guinea-pig's foot where the virus multiplies rapidly and finds that the pH in this tissue is much less alkaline than in the blood. The various organic media which he has examined for the optimum conditions for survival show that the virus survives best in relatively reducing and acid conditions compared with some other viruses.

Dr. Edwards has also continued the work on foot and mouth disease in hedgehogs and has noted a very severe and fatal form of the disease in this animal which spreads rapidly by contact. He has also made further observations on methods of preparing a vaccine for protecting small animals against foot and mouth disease.

Endocrinology.

Dr. V. Korenchevsky, with the assistance of Mrs. M. E. Dennison, has studied the influence of the internal secretion of the male sexual glands on the chemical composition of animals.

Method used for the chemical investigation of small animals. Since the investigation of the chemical composition of the whole animal is very difficult, a simple method has been worked out, which gives approximate but accurate data. The hind legs, as containing the principal tissues of the body (skin, muscles and skeleton) are used for the analysis of solids, water and nitrogen content. For the approximate estimation of the deposition of fat in the body, a still simpler method is used, viz., the weighing of the retroperineal and testicular fat.

The influence of castration and cryptorchidism. The amount of fat was increased in both castrated and cryptorchid animals. This increase of fat in cryptorchid animals, in the testicles of which only the seminiferous tissue is degenerated, indicates (i.) the presence of hormones in this tissue and (ii.) the stimulating influence of these hormones on fat metabolism. The nitrogen content was decreased in cryptorchid and in castrated animals, while the content of solid matter was increased. These changes can be explained by an increase of fat deposition. These results corroborate those previously obtained by Korenchevsky, Carr and Dennison, which showed that metabolism decreases after castration and can be increased by the injection of testicular extract into the castrated animals.

The histological investigation of the glands of inner secretion in castrated and cryptorchid animals is not yet completed, but the results so far obtained show considerable changes in the thyroid, adrenal and pituitary glands.

Coagulation of the Blood.

Dr J. O. W. Barratt has been engaged in an attempt to determine the nature of the deterioration observed in fibrinogen and thrombin solutions on keeping, the irregular character of which offers a hindrance to the accurate ascertainment of coagulation periods in experimental work.

This investigation is still in progress, as is also the study of the action of heparin, referred to in last year's report.

During the year the hospitality of the Department has been extended to the following: Dr. Kaul (India), Dr. L. Penrose and Mr. R. A. Alexander (S. Africa).

DIVISION OF PROTOZOOLOGY.

The effect of gamma irradiation on the growth of *Bodo caudatus*.

In the past year further biological studies were carried out by Dr. Muriel Robertson with *Bodo caudatus*. A serum against bodo was made by injecting cultures into rabbits intravenously. Titrations were made by placing known numbers of bodos in descending concentrations of the serum. The test of lysis was failure of a sample to grow upon being placed upon a culture plate flooded with 10 c.c. of Peters' medium. The serum was used with the addition of guinea-pig serum as complement but lysis also occurs without the presence of complement. The study of the action of this serum and the behaviour of the serum survivals opens up an interesting field which, it seems, may afford an insight into the behaviour of such parasitic protozoa as Trypanosomes and may also afford material for the study of serum-fastness.

In the early months of 1930 some investigations had been carried out by Miss Robertson in association with Mr. Bernard Williams upon the effect of gamma irradiation on bodo. In the present year through the kindness of Sir Cuthbert Wallace and the authorities of Mount Vernon Hospital, at Northwood, this work has been continued. A satisfactory method has been evolved whereby the growth of the bodos can be maintained at a desired rate and a daily count of the cells can be made. By this method the material is diluted and the total quantity is made up in equal parts of diluted bodo culture and fresh bacterial suspension.

As a result of growth under the influence of radium there is a reduction in the number of generations produced during the growth period. This is not excessive and with low or moderate doses there is an approximation to the normal as time goes on.

The bodos are not killed by the irradiation so far as can be ascertained. The cultures are certainly not brought to extinction and the reduction in numbers is due apparently to a check in multiplication.

Upon exposing the irradiated bodos and the non-irradiated controls to the lysin in titration tubes and subsequently putting samples to grow upon culture plates, certain interesting differences are to be observed. In the first place in material direct from the irradiated plates there is a definite though not extreme reduction of the resistance to the action of the serum. The death point in the titration is reached in a lower concentration than in the normal controls.

The second and much more striking difference between the irradiated and the non-irradiated cultures in their behaviour upon the serum survival plates is that while the non-irradiated may show a slight and variable stickiness or slight and transitory tendency for a proportion of the bodos to agglutinate in small sticky groups, the irradiated bodos are collected into very large clumps containing uncountable numbers of individuals. This is a very great exaggeration of the slight stickiness which can be seen in some non-irradiated cultures so that the appearance of a plate in which the reaction is well developed is most striking and arresting and forms a sharp contrast to the appearance of the plates from the non-irradiated material. The analysis of this phenomenon is now being attempted. The best evidence at present for this being a radium effect upon the bodo itself, is the fact that it is a progressive phenomenon not to be observed in any great degree in material irradiated for a few days only with the lower doses.

The reaction persists after the removal of the radium and was still present in material transferred for seven days (which amounts to 28 generations of bodos) and undergoing the powerful equalisation as between the non-irradiated and the irradiated, of the daily addition of the fresh (non-irradiated) bacterial suspension. The environment is stabilised daily but the effect is produced by degrees and in one series where a high dose of radium (14 mg. per sq. cm.) was used the striking difference between the appearance

of the reaction in the same series of material irradiated for two days and grown free from radium for one day and of material irradiated for five days and grown free for one day, suggests that the change is probably in the bodies themselves. The phenomenon is, however, a complex one and the interpretation is obscure and requires careful analysis.

It is of obvious interest that this change is titratable and seems to have a time and dose relation in regard to the irradiation and also a relation to the concentration of the serum in the titration tube. The effect is specific and suggests some relation to the adhesion phenomenon exhibited by trypanosomes in the immune serum of mice. There is a suggestion also that the immune serum contains two elements, an agglutinin and a lysin; the evidence for this being that the very marked increase in the clumping phenomenon does not correspond with an alteration of the death-point in the titration series.

DIVISION OF NUTRITION.

Water Soluble B Vitamins.

Vitamin B₂. Further attempts to purify the anti-dermatitis vitamin B₂ and to study its preparation have been made by Dr. H. Chick and Miss Copping. Fractionation with alcohol of the concentrate obtained from yeast extract, by precipitation with lead acetate, has been tried but the results have proved disappointing. Contrary to the results obtained by some other workers, this vitamin has been found sensitive to the presence of alcohol in strengths above 50% and the final products are often found to be inactive.

Vitamin B₂ in common with the more recently described constituents of the vitamin B complex does not appear to be a well-defined or stable chemical entity. Its solubility and precipitation limits have proved to be irregular and uncertain and would appear to be greatly influenced by small variations in the conditions under which they are studied.

Additional components in the vitamin B complex. Work has been continued by Dr. Chick and Miss Copping on the heat stable (anti-dermatitis) vitamin B₂ as contained in egg-white, in which it occurs unaccompanied by the antineuritic vitamin B₁. Concentrates of vitamin B₂ prepared from egg-white have proved effective for cure of the dermatitis which develops in young rats on artificial diets lacking vitamin B₂. Satisfactory growth was not, however, maintained, even when the diet contained the antineuritic vitamin B₁ and all other known essential dietary factors. When, on the other hand, in a similar diet, vitamin B₂ is provided in the form of autoclaved yeast or yeast extracts, young rats can be raised to maturity and satisfactory reproduction secured, although the litters have not so far been satisfactorily reared. These observations are interpreted as showing (1) that a third, hitherto unrecognised water-soluble dietary factor (provisionally called Factor Y) in addition to vitamins B₁ and B₂, is necessary for growth and (2) that this factor while present in yeast extracts is absent from, or present in very small quantities in, egg-white.

Further evidence of the existence of Factor Y and of its distribution in natural foodstuffs has been obtained from comparable experiments on the growth of young rats in which vitamin B₁ was provided in the diet as minimal amounts of various natural foods and vitamin B₂ as (1) egg-white and (2) autoclaved yeast extract respectively. These experiments, which were carried out with Miss Roscoe, showed that Factor Y is present in relatively large amount in yeast, green-leaf vegetables, egg-yolk and ox-liver, and absent from or present in relatively small amount in, wheat embryo, meat (ox-liver), etiolated leaves of green vegetables and onion.

Factor Y, as present in watery yeast extracts, was found to survive prolonged (4 hours at 120-125°C.) heating in alkaline solution (pH. 9-10), a property which distinguishes it from vitamins B₁ and B₂ as well as from the heat-labile vitamins B₃ and B₆ recently described respectively by Williams and Waterman and by Reader.

Synthesis and excretion of vitamin B complex in the rat. Following the theory that refection, the state in which rats can dispense with external sources of the vitamin B complex, is due to an infection of the digestive tract, by organisms capable of synthesising these vitamins, an attempt has been made by Miss Roscoe to induce refection by feeding pure cultures of various yeasts. It was without success.

The effect of coprophagy on the growth of rats deprived of vitamin B₁ and B₂ respectively is being investigated. It is thought that the growth observed in coprophagous rats is due to two causes: (1) utilisation of excreted reserves, larger in the case of vitamin B₁ than in that of vitamin B₂, and (2) infection of the gut with organisms capable of synthesising B vitamins, which may occur at any stage in the life of such rats, with the result that normal growth is sustained. The identity of the latter process with refection is suggested but has not been proved.

It has been shown that fat in diet lessens the need for the antineuritic vitamin B₁. The interrelation of fat with vitamin B₂ has been investigated by Miss Roscoe, but no effect has been observed either on growth or on the dermatitis caused by deficiency of this vitamin.

Distribution of Vitamins B₁ and B₂ in Natural Foodstuffs.

Cereals. Dr. W. R. Aykroyd (Beit Memorial Research Fellow) has continued his work on the distribution of vitamins B₁ and B₂ in cereals with the aim of elucidating further the etiology of beriberi and pellagra.

Beriberi. Using the method for assay of the antineuritic vitamin B₁ worked out in this Department, in which the growth of young rats is taken as criterion, the endosperms of wheat, rice, maize, etc., have been found very poor in this vitamin, as compared with the embryo or the whole grain. This result confirms previous work with pigeons and is in accord with the vitamin theory of the etiology of beriberi.

Interesting results have been obtained with parboiled rice, the consumption of which in rice-eating populations has been associated with protection from beriberi. It has been supposed that in the process of parboiling, the vitamin-rich integuments of the grain are rendered more firmly adherent than in the raw grain and, are therefore, less completely removed during the subsequent operations of milling. Parboiled rice, however, even when so milled that no trace of adherent pericarp could be detected microscopically, has been found to contain abundant vitamin B₁, whereas raw rice of similar origin and similarly milled was found to be devoid of it. The explanation, for which some experimental evidence is available, appears to be that in the process of parboiling (soaking in water for about 36 hours and steaming for 10—15 hours with subsequent drying in the sun) the cells of the grain become permeable to the vitamin B₁ contained in the germ and pericarp and that diffusion takes place through the endosperm. Similarly, the washing of parboiled rice was found to cause loss by diffusion into the wash water, a fact which explains the well-known association of beriberi with consumption of "spoilt" or damaged rice, which is washed before use.

Pellagra. Following the work of Goldberger and his colleagues it has been assumed by many, though on insufficient evidence, that the anti-dermatitis vitamin B₂ is identical with the dietary "P-P" factor postulated by these workers as concerned with the prevention and cure of human pellagra. On this theory, as the incidence of pellagra is almost exclusively confined to populations subsisting on maize as staple cereal, it would be reasonable to expect that maize and maize products would be found poorer in vitamin B₂ than other cereals. This, however, is not found to be the case. The vitamin B₂ content of maize has been found greater than that of rice and little, if at all, lower than that of wheat. Consumption of rice, however, has only been exceptionally found associated with the incidence of pellagra.

These facts form an important argument against the theory associating pellagra with a simple deficiency of vitamin B₂ in the diet. The connection between pellagra and maize consumption might conceivably be due to the presence in maize of some pellagra-producing "toxamin," capable of being neutralised by abundant vitamin B₂ in the diet, since the foodstuffs richest in this vitamin are those which have been found in practice to be most valuable for the prevention and cure of this disease. Attempts made by Dr. Aykroyd to extract any such toxic substances from maize have, however, proved unsuccessful.

Vegetables. Miss Roscoe (Beit Memorial Research Fellow), using the method of assay worked out in this Department, has, with the assistance of Miss D. Graetz, found leaf vegetables (watercress, lettuce, spinach, cabbage) to be rich sources of these vitamins, more especially of vitamin B₂, while onions, carrots, turnips, and potatoes are much poorer. When cooking spinach leaves it was found that ready diffusion of the vitamins took place into the cooking water and that about one-half the original content was lost in fifteen minutes' boiling.

Fat-Soluble Vitamins.

Synthesis of Ergosterol (Provitamin D) in the animal body. Miss E. M. Hume, with the assistance of Miss H. Henderson Smith, has studied the problems connected with the origin in the animal body of ergosterol, the parent substance of the antirachitic vitamin D, concerned in calcium metabolism. It seemed possible to attack the question of ergosterol synthesis by comparing the effect on calcification of diets, respectively very rich and very poor, in ergosterol, the ergosterol being converted into vitamin D by direct irradiation of the rats. At the conclusion of the experiments the ash content of the bones was found to be at the same level for ergosterol-rich rats, irradiated or not irradiated and for ergosterol-poor rats, if irradiated. A significant lowering of the bone ash was shown by the ergosterol-poor rats which were not irradiated. That ergosterol is synthesised in the rat body is one possible explanation of this result, but owing to difficulties in technique, it is unfortunately not the only one.

The foregoing experiment furnished a prolonged observation of the behaviour of rats on a fat-free diet, which, according to various observers in America, causes development of a pathological, scaly condition of the tail. A similar condition of the tail occurred among the rats in the above experiment, but as the condition was seen also among rats on a diet containing fat, it was concluded that the scaly tail condition was due rather to some other defect in the diet.

Vitamin Standards and Methods of Estimation. Miss Hume, with the assistance of Miss Pickersgill, assistant to Professor Korenchevsky, and of Miss M. Gaffikin, has been investigating the Standard solution of irradiated ergosterol issued by the National Institute of Medical Research for use in estimation of vitamin D.

Evidence has been obtained of the stability of this preparation when preserved at 0°C. and data have been collected as to the degree of accuracy of the biological tests, e.g., as to the number of experimental animals on any one dose required to override the large variability in response. Consistent figures have been obtained with averages taken from results with ten animals on each dose. With six animals there was considerable coherence, but with three or four the results were wholly inconsistent.

Attempts have been made to construct a curve which should express the relation between dosage of the standard vitamin D preparation and the response in bone calcification. The use of such a standard curve, if reliable, would be to minimise greatly the number of experiments necessary in the assay of unknown substances for vitamin D value. Considerable progress has been made in this work but it is doubtful whether the curve obtained possesses more than a limited application, for it is probable that the shape of the curve will vary with circumstances.

In connection with the International Conference on Vitamin Standards, to be held in London in June, 1931, at the invitation of the Permanent Standards Commission of the League of Nations, the Accessory Food Factors' Committee has been exploring the possibility of adopting suitable materials to act as standards in the quantitative estimation of other vitamins.

The work has been organised by a series of separate sub-Committees appointed to deal respectively with vitamins A, B and C, in addition to vitamin D. The following materials have been selected as provisional standards and specimens have been distributed to vitamin workers in this Institute and in other laboratories in this country and abroad, together with a series of selected foodstuffs whose vitamin content is to be estimated with their use:—

For vitamin A. A specimen of pure, recrystallised carotene prepared by the National Institute of Medical Research is being investigated by Miss Hume and Miss Henderson Smith.

For the antineuritic vitamin B₁. A concentrate adsorbed on kaolin from an extract of rice polishings, prepared at Batavia, Java, by the method of Jansen and Donath, and provided by Dr. Jansen, of Amsterdam. Tests with this material are being carried out by Dr. H. Chick and Miss H. M. Jackson.

For vitamin C. Decitrated fresh lemon juice, which is being investigated by Dr. Zilva and his staff.

Biological Value of Proteins. Work on the biological value of proteins has been continued by Dr. Margaret D. Fixsen, in collaboration with Dr. Chick, by a method involving the measurement of the minimal daily intake required to secure nitrogenous equilibrium. The adult rat is used as experimental animal and B vitamins are administered as purified concentrates containing minimal amounts of nitrogen. Provided an adequate calorie intake from carbohydrate and fat be secured, the exclusion of vitamin B₁ from the diet has not been found to affect the economical use of protein. In absence of vitamin B₁ the appetite falls off so swiftly that no satisfactory tests can be made.

The mean value of several concordant determinations for purified caseinogen gave the value of 45, that is to say, 100 parts of nitrogen as caseinogen are required to repair the loss of 45 parts of nitrogen derived from the body tissues. This value is much lower than those previously obtained which have ranged from 67—75. The reason for the discrepancy may lie in differences of method or of the degree of purity of the caseinogen used, or in the fact that the vitamin preparations previously used have contained appreciable amounts of nitrogen of high nutritive value. Caseinogen has hitherto ranked among the proteins of relatively high biological value. It is, therefore, interesting to note that in the clinical observations of Goldberger and his colleagues, the failure of large daily rations of purified caseinogen to prevent pellagra in groups of asylum inmates was an important argument for abandoning the accepted theory that the disease was caused by an insufficiency in the diet of protein of high biological value. At the same time the success both in the prevention and cure obtained by relatively small rations of dried yeast was one of the facts suggesting the connection between pellagra and some member of the B group of vitamins, a theory afterwards developed by these workers with experimental support.

The work is being extended by Dr. Fixsen and Dr. Chick to other proteins of animal origin and to those of maize and wheat and rice.

Experimental Researches on the Anti-Scorbutic Principle (Vitamin C.)

Several years' experience of the chemical fractionation of vitamin C in lemon juice revealed that Dr. Zilva's method, based on the precipitation of the vitamin with lead acetate at a definite pH after the preliminary removal of impurities, does not always yield fractions of equal activity. This cannot so far be traced to any unknown factor in the technique. On the other hand, results have been obtained which point to the fact that the variable character of the lemon juice, although its antiscorbutic potency is fairly constant, may be responsible for this differential behaviour in the fractionation. It is being followed up by Dr. Zilva not only with the purpose of improving the method but also with the object of throwing some light on the variable conditions under which the vitamin exists in the plant cell. This, it is hoped, may yield indirect information concerning the identity of vitamin C.

As previously reported, the spontaneous inactivation of vitamin C most probably takes place in a chain of reactions in which at least two substances are concerned, one a reducing compound and another showing characteristics of a phenolic compound. Dr. Zilva and Mr. Johnson have been engaged in studying these substances with the object of identifying them.

Metabolism of Animals affected by Scurvy. Dr. Zilva and Mr. Humphreys have started an exploratory enquiry into the biochemical properties of the liver of scorbutic, partially protected and fully protected guinea pigs as well as of rats, which are very little if at all susceptible to scurvy, with a view of ascertaining whether this organ has functional relationship to the antiscorbutic factor.

The Physiological Function of Vitamin C. in Fruits. Citrus fruits and apples were again employed in this investigation by Dr. Zilva and Miss Bracewell. With the former, experiments were repeated in order to confirm the findings of the previous year. The pomological enquiry was carried out in collaboration with Drs. Kidd and West, of the Low Temperature Research Station, Cambridge, with Mr. Wallace, of the Agricultural and Horticultural Research Station, Long Ashton, and with Mr. Crane, of the John Innes' Horticultural Institution, Merton Park. The following main facts were established:— (1) Apples can be frozen at -20°C . and stored at this temperature for four months without losing appreciably in antiscorbutic activity. This observation is being utilised in developing an improved technique for the estimation of vitamin C in plant and animal tissues. (2) Very small apples gathered 2-3 months before ripening (July) are not more active per gram of tissue than fruit of the same environment gathered normally. The vitamin is, therefore, either supplied to the apple as it grows on the tree or is synthesised by it. (3) Vitamin C in the tissue of the apple increases as the skin is approached from the core and is more than six times as great in the peel as in the flesh near the core. (4) There is an indication that a connection exists between the nitrogen content and the vitamin C content of the apple. The bearing of the genetic character of fruits on their vitamin activity has also been studied.

Influence of various factors on the Vitamin Content of Dairy Products. This investigation is being pursued on the lines previously described and attention was mainly paid during the last year to the behaviour of vitamins A and D on storage in carefully controlled material.

Attempts to improve methods of Vitamin Assay. This investigation in which Dr. Zilva, Mrs. Balfour and Miss Perry are collaborating, is still in progress. The work on "Höjer's test" for vitamin C, which is based on histological changes in the teeth of guinea pigs, had to be extended in another direction in order to establish the variation in the "normal" teeth that may be due to various factors in the history of the experimental animal.

The experiments on the X-ray assessment of the prophylactic action of vitamin D which have been in progress for some time in conjunction with Drs. Bourdillon and Webster, of the National Institute for Medical Research, are still proceeding. Radiographic measurements on a great number of animals, the bones of which were previously analysed, have been made and it is hoped that a report on the work will be published shortly.

A method for the estimation of vitamin D based on increase in weight and in growth of bones (as measured radiographically) is also in progress in collaboration with Dr. Bourdillon.

During the year vitamin tests have also been carried out in this Division in connection with the establishment of a vitamin C standard, the dietary of the members of the British Arctic Air Route Expedition to Greenland, and articles of food intended for the dietary of African natives in industry.

The work done by Dr. Schütze and Dr. Zilva on the reaction to infection of rats on different diets is referred to earlier in this Report.

Biological Action of Light. Dr. N. S. Lucas has re-investigated the permeability of human epidermis to radiations between the wave-lengths of $437\mu\mu$ and $240\mu\mu$. The previous measurements by Hasselbalch had shown so high a degree of opacity to the rays effective in the cure and prevention of rickets as to render difficult the interpretation of the proved antirachitic effect of these radiations when falling on the skin.

It has, however, been found that the transparency of human epidermis to these rays has been much underestimated. This error is due to a lack of appreciation of the amount scattered by the un-homogeneous epidermis. The light which is being scattered does not enter the narrow spectrograph slit, whereas, *in vivo*, owing to the large body surface, it is ultimately transmitted, but not necessarily at a point opposite that of entry. Previous observers reckoned this apparent loss by scattering as absorption.

To minimise the effect of scattering, two methods were used:—(1) Two quartz discs ground on each surface were placed in front of the epidermis so that the incident light was scattered and was calculated as such. (2) The epidermis was rendered nearly homogeneous by inactive clearing agents. Epidermis from a blister produced by chloroform vapour was used. Dr. Lucas found that the percentage of incident light transmitted varied with the wave-length from 96% to 26% between the range $437\mu\mu$ — $294\mu\mu$, which range includes the ultraviolet radiations of sunlight almost in their entirety. These figures are respectively 1.5 to 30 times greater than those stated by Hasselbalch.

Qualitatively, the absorption curve of human epidermis shows remarkable agreement with those of casein, serum-albumen, tryptophane and tyrosine.

DEPARTMENT OF BIOCHEMISTRY.

Alcoholic Fermentation.

During the year a definite stage was reached in Dr. Robison's investigations of the phosphoric esters formed during alcoholic fermentation. The attempt to separate and identify the component esters of hexosemonophosphate was begun some years ago in collaboration with Dr. E. J. King and the isolation of a glucosemonophosphoric ester has already been reported, but the properties of this compound showed that it still contained about 10% of some other ester of lower reducing power. The final stage in its purification has now been achieved. Evidence of the homogeneity of this ester was given by its behaviour on hydrolysis with acids, while the examination of the products obtained from it by hydrolysis and by oxidation and dephosphorylation have proved that it is a monophosphoric ester of glucose. Further evidence was obtained that the phosphoric acid group is attached to the terminal carbon atom of glucose and this conclusion has been confirmed by the study of its methylated products, carried out by Drs. Morgan, King and McLaughlin. A second ester also isolated from hexosemonophosphate was shown to be very similar to Neuberg's fructosemonophosphate, while considerable progress has been made towards the separation of the residual fraction, in which at least one unidentified ester is known to be present.

It has been previously mentioned that hydrolysis of fructosediphosphate by bone phosphatase does not yield pure fructose but a mixture of sugars containing glucose and fructose. A similar result was obtained on hydrolysis of the pure glucosemonophosphate by phosphatase. This increased lability of the hexose molecule during enzymic removal of the phosphate group is of much interest and may possibly throw some light on the mechanism by which esterification with phosphate facilitates the reactions occurring in carbohydrate metabolism.

In the course of this work difficulties have been encountered in the micro-estimation of barium and Dr. McLaughlin (Grocers' Company Research Student) has investigated the sources of error in the methods employed and has shown how these may be avoided.

Dr. E. Boyland (Beit Memorial Research Fellow) has made a further study of the lag between esterification and evolution of carbon dioxide which occurs in alcoholic fermentation and has examined the effect of reducing substances upon it. He has also studied the effect of hydrogen acceptors upon the course of the fermentation.

Miss Macfarlane (Carnegie Fellow) has continued her work on the conditions of hydrolysis of hexosediphosphate by yeast enzymes. Using a hexosephosphatase unable to ferment sugar, she has found that the decomposition of hexosediphosphate is accelerated by arsenate only in the presence of coenzyme and with an accompanying production of carbon dioxide, thus confirming Meyerhof's theory that a direct fermentation of hexosediphosphate is possible.

The induction period of zymoin fermentations is increased by arsenate, but without acceleration of the rate of liberation of inorganic phosphate during this period, indicating that the prolongation by arsenate is not due to its specific action on the fermentation of hexosediphosphate.

Miss Macfarlane has also examined the effect of sodium iodoacetate on the various phases of alcoholic fermentation which closely resembles that of sodium fluoride. It inhibits both the esterification and fermentation of glucose and also the acceleration due to arsenate. Its effect on the hydrolytic activity of hexosephosphatase is comparatively small. The fermentation of glycogen is also inhibited but not its esterification.

Experiments have been made by Professor Harden and Miss Macfarlane on the reducing properties of yeast with special reference to the alleged need for a co-reductase. Dried yeast which has been so thoroughly washed that it will not ferment a hexosephosphate without addition of coenzyme does not reduce methylene blue, but can be reactivated by the addition of boiled yeast extract. Such a preparation can also be reactivated by the addition of a lactate, without any other addition. The reduction of methylene blue which then occurs is accompanied by the evolution of a quantity of carbon dioxide approximately equivalent to the methylene blue reduced, and arising presumably from the decomposition of the pyruvic acid formed from the lactate by oxidation. This observation affords no ground for the assumption that a coreductase is required.

Miss Patterson (Victoria Soldiers' Orphans Scholar) has continued her work on the effect of cyanide on alcoholic fermentation particularly with regard to the induction period of zymoin fermentation and has made a study of the changes which occur during this period in the concentration of inorganic and organic phosphate, etc., in the presence and absence of cyanide, acetate and other compounds.

The Oxidation of the Fatty Acids.

Since oleic acid is present in most fats in greater proportion than any other single acid, Dr. Smedley-MacLean and Miss Pearce have continued their investigation of the oxidation of oleic acid by means of hydrogen peroxide, both with and without the addition of a cupric salt. In the absence of the catalyst even when a large excess of the peroxide acts on oleic acid at 95°C., less than 20 per cent. of the carbon originally present in the acid appears as formic, carbonic and acetic acids. Oxidation appears to take

place in the first instance at the double bond and the 18 carbon chain then appears to undergo successive oxidations in the γ position, acids containing respectively 15 and 12 atoms having been isolated as the zinc salts and analysed. There was no evidence of oxidation in the β - position such as was obtained by Dakin in his investigation on the oxidation of the saturated fatty acids under similar conditions.

In the presence of a cupric salt the action of the peroxide is much increased. At 95°C. more than 70 per cent. of the carbon of the original oleic acid appears as compounds containing not more than two carbon atoms, chiefly formic, carbonic and acetic acids. Some succinic acid is also present. At a lower temperature (60°C.) small quantities of keto- and hydroxy-derivatives of stearic acid occur. The main product is an acid, $C_8H_{14}O_4$, which has been identified as 4-keto-7-hydroxy-caprylic acid, while a considerable proportion of succinic acid is also present. About 20 per cent. of the carbon originally present appears as carbonic, formic and acetic acids.

Oxidation of caprylic acid gives a similar mixture of the acid $C_8H_{14}O_4$ and succinic acid.

The evidence from these laboratory experiments on the oxidation of oleic acid lends no support to the view that β - oxidation occurs when this acid is oxidised in the body. Since oleic acid occurs in fats in greater proportion than any other single acid the method of its oxidation in the body is of considerable importance. The presence of a large proportion of succinic acid among the oxidation products under these mild conditions is of great interest since a powerful specific enzyme for the oxidation of succinic acid is widely distributed in the body.

Study of the Fatty Matter in Plants.

The saturated fatty acids of the cabbage leaf have been studied by Dr. Smedley MacLean and Miss Hume and have been shown to consist of a mixture of palmitic and hebenic acids, while in the spinach leaf palmitic and cerotic acids are present. The fat of the green leaf seems to be characterised by the presence of saturated fatty acids higher than stearic. Ceryl alcohol has also been identified in the spinach leaf as a constituent of the unsaponifiable matter.

Ossification.

Calcification *in vitro*. The experimental results outlined in the last report have been confirmed by further work and have now been published. The investigation of the effect of various factors on calcification *in vitro* has been continued by Dr. Robison and Miss A. Rosenheim and it has been shown that the concentrations of calcium and inorganic phosphate necessary for calcification are considerably raised when protein is added to the calcifying solutions in amount equivalent to that present in serum. This result is in accordance with the known effect of protein in reducing the ionisation of calcium. Glucose, in concentrations even lower than those found in plasma, also exerts a definite inhibitory effect on calcification, which suggests that glucose forms a sparingly ionised compound with calcium. Calcification of bones of rachitic animals in the serum of normal animals is also being studied.

Dr. Robison and Miss M. Maclean have carried out a series of experiments on the formation of precipitates in aqueous solutions of the inorganic salts present in plasma. The concentrations of calcium and inorganic phosphate at which precipitation ultimately occurs are similar to those required for calcification of bone slices while the composition of the precipitates closely approximates to that of the bone salts and suggests the presence of a complex salt of the apatite type.

Dr. Robison's collaboration with Dr. Honor B. Fell, Director of the Strangeways Research Laboratory, Cambridge, has been continued. The process of calcification in osteoid tissue has been further studied using as experimental material normal limb bone and jaw rudiments of the embryonic fowl and explants of mandibular mesoderm in which ossification centres have developed during cultivation *in vitro*. These tissues were immersed for 16 hours in the solutions which have been shown to effect the calcification *in vitro* of bones from rachitic rats. In the osteoid tissue of the normal fowl and in that developed *in vitro* calcification when previously present was markedly extended. This increased deposition and the sharp delimitation of the calcified area in the explants after treatment appeared to indicate that the capacity for undergoing calcification is a special property associated with a definite stage in the development of the intercellular substance. It is probable that the phosphatase is secreted by the cells into this matrix but the possibility that the enzyme is confined to, and functions within, the cells and that the products of its activity diffuse into the matrix, cannot be entirely excluded.

It would seem also that during embryonic growth *in vivo* the actual calcification lags somewhat behind the full capacity of the tissue as revealed by subsequent immersion of the latter in artificial calcifying solutions.

Similar conclusions have been arrived at from experiments with bone rudiments of rabbit embryos, carried out by Dr. Robison and Dr. Janet S. F. Niven, of the Strangeways Research Laboratory.

Dr. C. B. Huggins, of Chicago University, has studied the development of phosphatase during heterotopic ossification in transplants of bladder epithelium of the dog to the rectus sheath. Dr. Huggins had previously shown that bone develops in the connective tissue adjacent to such transplants and in the present experiments the simultaneous appearance of high phosphatase activity in the ossifying tissue was clearly demonstrated using the method devised by Dr. Robison for the estimation of phosphatase in minute tissue fragments.

The Animal Phosphatases. Dr. Robison and Miss M. Macleod have carried out further work on the purification of the bone phosphatase and its use as a biochemical agent. Miss M. Maclean has also begun experiments on the kinetics of the reaction catalysed by the enzyme.

Professor Jean Roche and Madame A. Roche have carried out an investigation of the phosphatase present in red corpuscles, in leucocytes and in plasma. The previous findings of Martland, Hansman and Robison have been confirmed and greatly extended. The phosphatase of the corpuscles is quite distinct in its properties from that present in bone, while the phosphatase which is present in very small amount in the plasma is probably identical with the bone enzyme.

DEPARTMENT FOR THE STUDY AND PREPARATION OF ANTITOXIC SERA.

Gas Gangrene Antitoxin (*B. welchii*.)

Within recent years an increasing interest has been taken in the serum therapy of acute peritonitis, intestinal obstruction, and gangrenous appendicitis. The theory has been formed that the characteristic toxæmia in these conditions is caused by absorption of the toxin of *B. welchii*, which proliferates in the stagnant contents of a paralysed loop of small intestine. In order to combat the toxæmia in these cases a specific antitoxic serum has been administered and the reports upon its use have been favourable. This antitoxin has also been recommended for the treatment of certain puerperal infections which are caused by *B. welchii*. The toxin of this organism is of low potency and is not obtained with reasonable constancy as a routine procedure. Nevertheless the experience at Elstree has been a fortunate one, since very few batches have failed to yield a toxin of adequate strength. Horses are being immunised with the toxin but the serum has not yet reached the requisite titre. A method of testing the serum which permits of quite close titration has been prescribed by the Biological Standards Department of the Medical Research Council. The arbitrary unit of antitoxin has been derived, in accordance with a simple ratio, from that which was originally worked out in the National Institute of Health at Washington, and the modified unit has now been adopted by the Control Authorities in both Washington and London.

The work of Dr. M. Robertson and Dr. A. Felix indicates that a gas gangrene serum may be more effective in practice if it contains an anti-bacterial component. With this end in view a horse is being immunised with the thermostable "O" antigen of *B. welchii*, supplies of which are being provided by these workers. The horse has now reached a fairly advanced stage of immunisation, and a recent sample of the serum, when tested by Dr. Felix, was found to have attained a satisfactory titre in respect of "O" immune-bodies. It is hoped that a supply of the serum will shortly be available for clinical trial in the kind of abdominal emergency to which reference has been made.

The Preparation of a Dysentery Toxin (Shiga) for Use as a Test Toxin.

Dr. Petrie has continued his work on the preparation of a potent glycerinated test-toxin which has been rendered as free as possible from non-specific constituents. A number of preparations of this nature have been tested and have proved to be satisfactory, except, that after storage for some months at ordinary low temperatures deterioration has unaccountably taken place. The reduction in toxic power may conceivably be due to the action of the intracellular proteolytic enzyme which has been investigated by Dr. Morgan, for it is known that the rate of action of certain enzymes, although greatly retarded at temperatures a few degrees above 0°C., does not cease entirely. In order to test the possibility of loss by enzyme action arrangements are being made for prolonged storage of glycerinated toxins at temperatures below 0°C. The extraction methods which are now being employed have yielded powerful toxins, and moreover, it has been possible to concentrate and purify them by a simple method which does not entail loss or risk of injury to the toxin molecules. The minimal lethal dose intravenously for mice of a recent "original" toxin preparation was $\frac{1}{3200}$ c.cm., and after concentration the minimal lethal dose proved to be $\frac{1}{1600}$ c.cm.; a good toxic filtrate prepared from a broth culture kills mice in a dose of $\frac{1}{300}$ c.cm.

The Preparation of Toxic Extracts of the Meningococcus for the purpose of Titrating Antimeningococcal Sera.

Dr. Petrie has been engaged upon experiments with meningococcal suspensions and filtrates on the lines carried out by previous workers, and has reached similar conclusions, namely, that the toxin of the meningococcus is essentially an intracellular one and that the lethal effect of living cocci, when introduced into susceptible animals, is referable to the action of the toxin and not to the virulence of the cocci as manifested by their invasive power in the tissues of the host. The low potency of toxins prepared by the usual method constitutes a serious hindrance in experimental work—0.1 c.cm. of a good toxic extract will kill a young guinea-pig—and another difficulty is the retention of the toxin on the walls of the filter which is used for freeing the toxic solution from the cocci. For these reasons it has not been possible up to the present to obtain for titration purposes a test toxin which contains a sufficient number of lethal doses in an amount which, together with appropriate serum doses, is suitable for injection into the test animals. Attempts are being made to overcome these difficulties by utilising the methods of extraction and concentration which Dr. Petrie has found successful for obtaining potent dysentery toxins.

The Titration of Antipneumococcus Serum.

Experiments on the titration of antipneumococcus serum (Type I.) are being continued by Dr. Petrio with the cooperation of Dr. Morgan. The results that have been obtained indicate that it is possible to titrate sera with a fair degree of accuracy. Special attention is being paid to variations in the culture medium which influence the density of the growth, and so cause differences in the test-dose of the culture. The degree of virulence for mice of a regularly "passaged" culture of the pneumococcus probably remains at a maximum level, so that this factor may be regarded as a constant one in titration experiments. It has been found that the introduction peritoneally into a group of mice of even 10^{-10} of a c.c.m., of a culture grown in a favourable medium will produce a fatal infection in some of them. Attempts are being made to estimate the influence of varying susceptibility of the mice to doses of culture which contain from one to thirty virulent pneumococci. The inclusion of a standard serum in titration work will doubtless help to check the variations in the lethal power of the test dose of culture, but it is obviously desirable to be able to control, if possible, variations of this kind.

The Production of an Antistaphylococcus Serum.

A horse has been immunised with staphylococcal filtrates which have been prepared by Dr. Pantou at the London Hospital. As a result of the immunisation the immune bodies in the serum reached a high titre and a concentrated product has been prepared for clinical use. Dr. Pantou has already obtained promising results with the unconcentrated serum in cases of staphylococcal infection.

The Production and Concentration of a Protective Serum against the Virus of Poliomyelitis.

During the past year two additional horses were immunised with the virus of poliomyelitis in the living state and in one horse a potent antiviral serum was obtained. It is noteworthy that of four horses which have been immunised only two have responded and have yielded an antiviral serum. Dr. Morgan has found that the protein which is precipitated from the immune serum at relatively low concentrations of ammonium sulphate is uniformly much more potent in respect of antiviral action per unit weight of protein, than that which is precipitated at higher concentrations of this salt. The protein fractions of the immune serum which are insoluble in saturated sodium chloride solution and in distilled water have also been shown to possess potent antiviral properties. If further experience confirms these conclusions it would appear that for practical purposes a concentrated antiviral preparation can be obtained if the serum protein which is precipitated up to 34 per cent. by volume of saturated ammonium sulphate is collected and, after dialysis, is redissolved in normal saline. In consequence of the elimination of most of the non-specific protein a concentrated preparation of this kind should possess definite advantages, especially where treatment of the disease by the intraspinal route seriously limits the volume of the antibody solution that can be given.

The Specific Soluble Substance of the Dysentery Bacillus (Shiga).

Dr. Morgan has continued his work on the specific soluble substance of a smooth strain of the dysentery bacillus (Shiga) and has succeeded in isolating a specific polysaccharide. The substance gives specific precipitation with the homologous immune serum up to a dilution of 1 in 6,000,000. The intravenous inoculation of the active polysaccharide into a rabbit does not give rise to the production of demonstrable antibodies, and it therefore appears to be non-antigenic. When hydrolysed with acid the specific precipitating property of the substance disappears and about 65 per cent. of reducing sugars are formed. The nature of the hydrolysis products are at present under investigation.

DEPARTMENT FOR THE STUDY AND PREPARATION OF ANTI-VARIOLOUS VACCINE.

Filterability of the Virus of Vaccinia.

In last year's report reference was made to Dr. Green's success in securing potent filtrates of vaccinia virus by following the prescriptions of the Japanese workers Yaai and Kasai. The filters employed were the Berkefeld V and N and by the two methods recommended, viz., (1) adjustment of the pH of the virus suspension to the alkaline side (pH 8), before filtration and (2) passage of the virus suspension through lined V filters, i.e., filters which had just let through a solution of egg-white, it was possible to obtain fairly uniformly potent filtrates when tested intradermally or by scarification on the rabbit and sheep. In view of Dr. Green's success in this direction Dr. Eagles, at Chelsea, undertook filtration experiments on similar lines and also investigated the method of Ward (1929) who used a suspension of virus in hormone broth and claimed that such suspension after thorough trituration with pyrex glass and passage through paper passed readily through V filters.

Dr. Eagles has tested the effect of adjusting the pH of the suspension and has also employed lined and unlined filters (Berkefeld V and N, English Berkefeld and Chamberland L₂). He finds, like Dr. Green, that the Japanese methods certainly yield potent filtrates, but apparently neither of their two requisites (adjustment of pH and use of lined filters) appears to be essential. Control experiments with unadjusted

material or with unlined filters frequently yielded potent filtrates. The method of Ward was also found to favour filtration. Little success was obtained with N filters or with English Berkefeld filters, so that in all probability the virus of vaccinia, though definitely a filterable virus, is capable of passage only through the lower grade filters such as the Berkefeld V. In the past, what success has been achieved in the filtration of vaccinia by certain workers has been achieved as a rule with V filters, but even with these it has frequently been necessary to concentrate the filtrate in order to demonstrate that it contained viable virus at all. Even now, therefore, it is not possible to state with definiteness what the conditions are which must be satisfied if success in filtering vaccinia virus is to be achieved. Probably, however, the use of fresh virus, its thorough trituration, and the employment of V filters, are essential; above all the employment in recent years of the intradermal method has undoubtedly facilitated the demonstration of potent virus in filtrates. On the assumption that the elementary body (Paschen body) may represent the actual virus, it is probable that a condition for successful filtration may be the age and condition of the lesion yielding the test virus in relation to the associated elementary body. If the later lesions are harvested, the elementary bodies which are free in the early period of the lesion, may be in large part removed in the preliminary filtrations through paper, owing to their adhesion to inflammatory cells of the exudate, as observed by Ledingham. The latter has recently passed material from early fowl-pox lesions through Berkefeld V filters and had no difficulty in demonstrating Borrel bodies in the potent filtrate. It is probable, therefore, that success in filtering vaccinia and fowl-pox in no way precludes the idea that the elementary bodies associated with these diseases may be the actual virus bodies. It may be added that Ward and Tang have shown that filtrates of vaccinia, after centrifugalisation, contain the virus in greatest concentration in the bottom layers.

NATIONAL COLLECTION OF TYPE CULTURES.

During the year under review the number of strains of bacteria and fungi distributed to workers in the various fields of microbiological activity has again exceeded 5,000 and some 200 types, including many new species, have been added to the Collection.

The Curator was present at the Paris Congress of the International Society for Microbiology, held last July, and attended the meetings of the Nomenclature Commission of the Society. An International Nomenclature Committee was appointed with Dr. R. S. Breed of the New York Agricultural Experiment Station and Dr. R. St. John-Brooks as Permanent Secretaries.

During the summer of 1930 the hospitality of the department was extended to Dr. John A. Cranston and Miss Blodwen Lloyd, both of the Royal Technical College, Glasgow, in connection with their researches on denitrifying organisms.

A third and greatly enlarged edition of the Catalogue of the National Collection of Type Cultures has been prepared and will shortly be published. (*Medical Research Council, Special Report Series, No. 64, Third Edition, revised.*)

GENERAL AND FINANCIAL.

The Accounts and Balance Sheet for the year ending December 31st, 1930, show balances to the credit of the Pension Fund of £27,311 2s. 0d., of the Contingency Fund of £14,228 18s. 1d., of the Sinking Fund of £20,202 1s. 4d., and of the Capital Fund of £509,262 1s. 6d., the latter figure including £2,469 15s. 5d., Income Tax paid for the years 1922/1928 and recovered during 1930. The excess of income over expenditure for the year, viz., £17,364 2s. 3d., has again been utilised in writing down the value of certain of the General Fund Investments, which still show a depreciation.

New investments and conversions during the year have been:—

For the General Fund: £3,000 4% Consolidated Stock; £7,000 Local Loans 3% Stock; £5,000 4½% Conversion Stock, 1940/44, and the payment completed for £8,500 5% Conversion Stock, 1944/64, applied for in 1929. In addition, £8,500 5% War Stock, 1929/47 has been exchanged for £8,500 5% Conversion Stock, 1944/64.

For the Sinking Fund: £1,600 3½% Conversion Loan.

For the Pension Fund: £1,300 3½% Conversion Stock.

The income from the sale of the Institute's products during the year 1930 was £37,163 10s. 1d. After adjustment of the stock of Sera on hand at the beginning and end of the year, income from this source appears in the accounts as £37,571 11s. 3d. Sales of Bacterial Vaccines show a decrease, while sales of Sera, Vaccine Lymph, and Diagnosis and Investigation Fees each show an increase compared with last year.

The total expenditure for the year was £44,401 10s. 3d., against £42,612 10s. 4d., in 1929. Salaries and Wages, Gas, Water and Fuel, Water and Biochemical Laboratory Expenses, Alterations and Repairs and Library Expenses show an increase and Experimental Pathology Laboratory Expenses, Vaccine Laboratory Expenses and Animal House Expenses and Forage a decrease compared with last year.

In conclusion, the Governing Body desires to express its appreciation of the devoted co-operation of the Director and all members of the Staff in carrying out the work of the Institute.

WILLIAM BULLOCH,

Acting Chairman of the Governing Body.

BALANCE SHEET

AND

ACCOUNTS.

Dr.

The Lister Institute

BALANCE SHEET

							£	s.	d.	£	s.	d.
To CREDITORS	..	..	..	..	..	..				2,222	2	2
To PENSION FUND—												
As per Account at 31st December 1929	..	..	..	..	..	..	26,194	4	0			
Add Balance of Income and Expenditure Account 1930	..	..	..	..	..	..	1,116	18	0			
										27,311	2	0
To JENNER MEMORIAL RESEARCH STUDENTSHIP FUND—												
As per Account at 31st December 1929	..	..	..	..	..	..	8,051	4	7			
Less Balance of Income and Expenditure Account, 1930	..	..	..	..	..	..	155	11	6			
										7,895	13	1
To CONTINGENCY FUND—												
As per Account at 31st December 1923	..	..	..	..	..	..				14,228	18	1
To SINKING FUND to 31st December 1930	..	..	..	..	..	..				20,202	1	4
To CAPITAL FUND to 31st December 1930—												
Balance of Income and Expenditure Account to												
31st December 1926	..	..	..	..	..	151,972	6	6				
Add Income Tax, 1922/1928, recovered in 1930	..	..	..	..	..	2,469	15	5				
										154,442	1	11
Donations, &c., received to date from the following:—												
Dr. Ludwig Mond (1893)	..	..	..	..	..	..	2,000	0	0			
The Berridge Trustees (1893/98)	..	..	..	..	..	..	46,379	10	1			
The Grocers' Company (1894)	..	..	..	..	..	..	10,000	0	0			
Lord Iveagh (1900)	..	..	..	..	..	..	250,000	0	0			
Lord Lister's Bequest (1913) as per Account at												
31st December, 1923	..	..	..	..	..	..	18,904	5	8			
William Henry Clarke Bequest (1923/6)	..	..	..	..	..	..	7,114	5	7			
Other Donations (1891-1926)	..	..	..	..	..	..	20,421	18	3			
										509,262	1	6

WILLIAM BULLOCH, *Acting Chairman.*G. W. ADDISON, *Hon. Treasurer.*

£581,121 18 2

REPORT OF THE AUDITORS

We have audited the above Balance Sheet. We have obtained all the information and explanations we have required, paid, being held by the Institute on their behalf. In our opinion, such Balance Sheet is full and fair, and properly drawn and the explanations given to us and as shown by the books of the Institute.

London, April 23rd, 1931.

of Preventive Medicine.

31st DECEMBER, 1930.

Cr.

By CASH—						£	s.	d.	£	s.	d.
At Bankers: Deposit Account						5,000	0	0			
Current Accounts						8,680	18	4			
In hand						23	8	11	13,704	7	3
By INVESTMENTS, GENERAL FUND (at cost, less amounts written off)—											
£50,000 4 per cent. Consolidated Stock						43,783	4	0			
£43,000 4½ per cent. Conversion Stock, 1940-44						41,702	3	3			
£17,000 5 per cent. Conversion Stock, 1944-64						15,997	0	7			
£41,000 4 per cent. Funding Stock, 1960-1990						34,276	8	3			
£17,000 5 per cent. War Stock, 1929-1947						14,994	1	2			
£37,000 Local Loans 3 per cent. Stock						20,829	1	7			
£3,000 Port of London 4 per cent. B. Stock						2,686	17	7			
£1,000 Dominion of Canada 4 per cent. Registered Stock, 1940-1960						928	4	6			
£2,000 Cape of Good Hope 3½ per cent. Consolidated Stock, 1920-40						1,802	12	0			
£23,000 Cape of Good Hope 3 per cent. Consolidated Stock, 1933-1943						23,850	0	0			
£23,000 Natal 3 per cent. Consolidated Stock, 1929-1949						23,400	0	0			
£23,000 New South Wales 3 per cent. Inscribed Stock, 1935						22,900	0	0			
£2,000 New South Wales 4 per cent. Stock, 1942-62						1,882	3	4			
£2,900 New South Wales 5½ per cent. Inscribed Stock, 1922-32						2,897	16	0			
£28,000 New Zealand Government 3 per cent. Inscribed Stock, 1945						24,114	1	2			
£26,100 South Australian Government 3 per cent. Consolidated Stock, 1916 or after						20,800	0	0			
£600 Union of South Africa 4 per cent. Consolidated Stock, 1943-1963						594	2	0			
£23,000 Victorian Government 3 per cent. Consolidated Inscribed Stock, 1929-1949						20,800	0	0			
£700 Western Australia Government 4 per cent. Inscribed Stock, 1942-1962						698	7	0			
£20,000 Southern Railway Preferred Ordinary Stock						16,501	10	11			
£6,200 London & North Eastern Railway 3 per cent. Debenture Stock						3,961	0	0			
£5,000 Great Central and Midland Railway Joint Committee 3½ per cent. Guaranteed Stock						3,623	0	0			
£353 London & North Eastern Railway 4 per cent. First Guaranteed Stock						499	11	0			
£8,680 London, Midland & Scottish Railway 4 per cent. Preference Stock						7,960	0	0			
£15,625 London, Midland & Scottish Railway 4 per cent. Preference Stock, 1923						12,300	0	0			
£18,750 London & North Eastern Railway 4 per cent. First Preference Stock						15,118	0	0			
£23,000 East Indian Railway 3 per cent. New Debenture Stock						16,890	0	0			
£661 Madras & Southern Mahratta Railway 4 per cent. Debenture Stock, 1938						656	19	7			
£800 Grand Trunk Railway Company of Canada Great Western Borrowed Capital 5 per cent. Perpetual Debenture Stock						936	0	0			
£1,937 Grand Trunk Railway Company of Canada 4 per cent. Guaranteed Stock						1,733	0	0			
£800 Ontario and Quebec Railway 5 per cent. Permanent Debenture Stock						984	0	0			
£3,400 Gas Light and Coke Company Ordinary Stock						3,638	0	0			
									403,737	3	11
By INVESTMENTS, SINKING FUND (at cost)—											
£8,000 4½ per cent. Conversion Stock, 1940-44						7,320	13	7			
£7,450 4 per cent. Funding Stock, 1960-1990						5,850	5	3			
£8,800 3½ per cent. Conversion Stock						6,846	2	0			
Balance uninvested						165	0	6	20,202	1	4
By INVESTMENTS, JENNER MEMORIAL RESEARCH STUDENTSHIP FUND (at cost)—											
£2,650 Southwark and Vauxhall Water Co. 3 per cent. Debenture Stock "B"						2,756	10	0			
£1,596 Southern Railway 5 per cent. Preference Stock						2,740	5	0			
£728 11s. 4d. Liverpool Corporation 3 per cent. Stock, 1942, or after						556	15	6			
£2,000 4 per cent. Funding Stock, 1960-1990						1,797	14	0			
Balance uninvested						44	8	7	7,895	13	1
By INVESTMENTS, PENSION FUND (at cost)—											
£22,000 4 per cent. Funding Stock, 1960-1990						17,165	3	5			
£13,000 3½ per cent. Conversion Stock						10,038	1	5			
Balance uninvested						107	17	2	27,311	2	0
(The above Investments, at the market value 31st December 1930, show a depreciation of £39,427.)											
By DEBTORS									10,090	10	11
By FURNITURE, FITTINGS, SCIENTIFIC APPARATUS AND BOOKS—											
At cost less depreciation as per account 31st December 1920											
By EXPENDITURE ON INSTITUTE BUILDINGS AT CHELSEA—											
As per account 31st December 1910, including purchase of freehold site, £6,000											
By PURCHASE OF FREEHOLD LAND ADJOINING THE "STUDIOS" CHELSEA—											
As per account 31st December 1912											
By LEASE OF THE "STUDIOS" CHELSEA, as per last account						1,522	18	9			
Less Amount written off for the year						65	2	0	1,457	16	9
By QUEENSBERRY LODGE FARM, ELSTREE—											
Purchase of freehold land and buildings and Expenditure on new buildings—											
As per account 31st December 1912											
By STOCK OF ANIMALS						391	13	6			
By STOCK OF ANTITOXINS						2,318	12	6			
									2,710	6	0
* Nothing has been charged for depreciation of Furniture, &c. since new purchases made during the year to a greater amount than the estimated depreciation (10%) have been written off.											
									£581,121	18	2

TO THE MEMBERS.

The Superannuation Scheme for certain of the Staff provides for Life Policies for which the sum of £21,685 13 3 has been up so as to exhibit a true and correct view of the state of the Institute's affairs, according to the best of our information

COOPER BROTHERS & CO.,
Chartered Accountants, } Auditors.

Dr. INCOME AND EXPENDITURE ACCOUNTS

INCOME.								£	s.	d.
To Interest and Dividends on General Fund Investments	...	...	...	...	...	...	...	17,150	9	8
To Interest on Sinking Fund Investments	...	...	...	...	...	...	...	910	0	0
To Investigation, Diagnosis and Analysis Fees, &c. ...	...	...	...	...	...	...	...	5,083	11	7
To Sales of Sera, Vaccines, &c., and Stock at 31st December 1930, less Stock at 31st December 1929	...	...	...	...	...	...	...	37,571	11	3
To Rent of Rooms	...	...	...	...	...	...	...	1,050	0	0

£61,765 12 6

Dr.

Pension

								£	s.	d.
To Interest on Investments	...	...	...	...	...	...	...	1,303	10	0

£1,303 10 0

Dr.

Jenner Memorial Research

								£	s.	d.
To Interest and Dividends on Investments	...	...	...	...	...	...	...	261	1	10
To Balance, being Excess of Expenditure over Income, transferred to Balance Sheet	...	...	...	...	...	...	...	155	11	6

£416 13 4

Preventive Medicine.

for the year ending 31st December, 1930.

Cr.

EXPENDITURE.								£	s.	d.
By Rent, Rates, Taxes and Insurance	...	...	...	...	...	...	...	1,454	5	2
By Salaries and Wages of Staff	...	...	...	...	...	...	...	24,935	12	5
By Premiums on Federated Superannuation Policies	...	...	...	...	...	...	...	1,126	3	10
By Stationery, Printing and Postage	...	...	...	...	...	...	...	454	2	7
By Printing of Collected Papers	...	...	...	...	...	...	...	194	6	5
By Office Expenses, Auditors' Fee and Sundries	...	...	...	...	...	...	...	811	10	2
By Travelling Expenses	...	...	...	...	...	...	...	31	5	9
By Gas, Water and Fuel	...	...	...	...	...	...	...	1,438	18	3
By Electric Light and Power	...	...	...	...	...	...	...	854	12	0
By Experimental Pathology Laboratory Expenses, including General Apparatus	...	...	...	...	...	...	...	622	6	11
By Bacteriological Laboratory Expenses, including Apparatus	...	...	...	...	...	...	...	354	4	6
By Vaccine Laboratory Expenses, including Bottles	...	...	...	...	...	...	...	164	10	3
By Water and Bio-chemical Laboratory Expenses, including Apparatus	...	...	...	...	...	...	...	409	5	8
By Serum and Calf Lymph Laboratories Expenses, including Apparatus and Cost of Bottles	...	...	...	...	...	...	...	3,697	12	2
By Culture Media	...	...	...	...	...	...	...	110	14	10
By Animals	...	...	...	...	...	...	...	1,836	7	0
By Animal House Expenses and Forage	...	...	...	...	...	...	...	2,526	8	9
By Alterations, Repairs and Renewals, including Workshop Expenses	...	...	...	...	...	...	...	2,214	16	6
By Library Expenses	...	...	...	...	...	...	...	487	12	11
By General Stores	...	...	...	...	...	...	...	342	3	11
By Bad Debts	...	...	...	...	...	...	...	3	14	8
By Amount written off Lease of the "Studios," Chelsea	...	...	...	...	...	...	...	65	2	0
By Sinking Fund ($\frac{1}{2}$ % per annum on Cost of Buildings and Interest on Investments)	...	...	...	...	...	...	...	1,320	13	7
By Amount written off General Fund Investments	...	...	...	...	...	...	...	17,864	2	3
								£61,765	12	6

Fund.

Cr.

	£	s.	d.
By Pensions	188	12	0
By Balance, being Excess of Income over Expenditure, transferred to Balance Sheet	1,116	18	0
	£1,303	10	0

Studentship Fund.

Cr.

	£	s.	d.
By Salary	416	13	4
	£416	13	4

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- BOYLAND, E. PHOSPHORIC ESTERS IN ALCOHOLIC FERMENTATION. III. THE LAG
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- CHICK, HARRIETTE, COPPING, ALICE M., AND ROSCOE, MARGARET H. ... EGG-WHITE AS A SOURCE OF THE ANTIDERMATITIS VITAMIN B₂. *The*
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- CHICK, HARRIETTE AND COPPING, ALICE M. ... THE ALCOHOL-SOLUBILITY OF THE ANTI-DERMATITIS, MORE HEAT-
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- " " " " ... THE COMPOSITE NATURE OF THE WATER-SOLUBLE VITAMIN B₁.
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The following articles have been contributed by members of the Staff and other workers of the Institute to the Medical Research Council's new *System of Bacteriology*.

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" "	...	TRENCH FEVER...	...	(Vol. 7.)
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THE LISTER INSTITUTE
OF
PREVENTIVE MEDICINE

Report of the Governing Body,
1932.

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

May 25th, 1932.

The Lister Institute of Preventive Medicine,

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

ELSTREE, HERTS; MARAZION, CORNWALL.

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Assistant Curator :

MABEL RHODES.

*Recognised Teacher of the University of London.

ANNUAL GENERAL MEETING
OF
The Lister Institute of Preventive Medicine,
May 25th, 1932.

REPORT OF THE GOVERNING BODY.

The Governing Body has the honour to present the Institute's 38th Annual Report.

GOVERNING BODY.

The Governing Body announces with great regret the deaths during the year of its Chairman, Major-General Sir David Bruce and of Viscount Knutsford.

Sir David Bruce, whose reputation as a Scientist was world-wide, joined the Board in 1903 as the representative of the Royal Society and from 1916 until his death on November 27th, 1931, had been Chairman.

Viscount Knutsford who died on July 29th, 1931, joined the Board in 1927 on the invitation of the late Viscount Iveagh as one of his representatives.

At a meeting of the Governing Body held on February 24th, 1932, Professor William Bulloch, was unanimously elected Chairman of the Governing Body.

At the Annual Meeting, in June last year, the Council re-elected Professor W. Bulloch and Professor A. E. Boycott, and elected Professor A. Harden, in succession to Sir James Fowler, resigned, as its representatives on the Governing Body until December 31st, 1932.

On January 18th, 1932, Dr. J. A. Arkwright was appointed by the Royal Society as its representative on the Governing Body in succession to Sir David Bruce.

The Governing Body reports with pleasure the conferment in January of a peerage upon Lt.-Col. Walter Guinness, who has taken the title of Lord Moyne of Bury St. Edmunds.

COUNCIL.

The Governing Body regrets to announce the death, during the year, of three members of Council, viz., Professor W. E. Dixon, Sir William Simpson and Sir Frederick Andrewes, the latter of whom was from 1916 to 1925 also a member of the Governing Body.

At the last Annual Meeting the three retiring members of Council, Professor T. J. Mackie, the representative of the University of Edinburgh, Professor W. E. Dixon, the representative of the British Medical Association, and Sir Thomas Barlow, one of the representatives of the Members of the Institute, were each re-elected.

The vacancies created last year by the deaths of Dr. H. de R. Morgan and Sir Andrew Balfour were filled at the last meeting by the appointment of Professor J. C. G. Ledingham and Viscount Knutsford, respectively.

The members who retire from the Council this year in accordance with the Articles of Association, but who are eligible for re-election, are the President of the Royal College of Surgeons, Professor W. W. C. Topley, the representative of the Victoria University of Manchester, and Professor W. Bulloch, one of the representatives of the Members.

MEMBERS.

The Governing Body regrets also to announce the deaths of Dr. Fallon Whittick, Professor Sir William R. Smith, and Sir William Watson Cheyne, members of the Institute for many years.

STAFF.

During the year the Senate of the University of London conferred Emeritus Professorships upon both Sir Charles Martin and Dr. Harden. The Senate have also conferred the title of Professor of Biochemistry upon Dr. Robison and that of Reader in Biochemistry upon Dr. Gulland.

The Governing Body has pleasure in reporting the conferment of the honour of Commander of the British Empire upon Dr. Harriette Chick in recognition of her researches on nutritional problems at the Institute.

Dr. Robison having received an invitation to deliver the Harter Lectures, in New York, during April, 1931, the Governing Body was pleased to allow him leave of absence for this purpose.

Miss A. H. Rosenheim has held the Grocers' Company Research Studentship during the year and Dr. T. F. Macrae was appointed to an Institute Research Studentship in Biochemistry on October 1st.

Dr. C. Russell Amies (late of the Institute for Medical Research, Kuala Lumpur) was appointed on January 1st to an Institute Fellowship in Bacteriology.

On June 1st, Mr. S. A. White succeeded Mr. Geo. Cooper as Accountant and Miss Ellen Knight was, in February last, appointed Librarian to the Institute.

DONATION.

The Governing Body gratefully acknowledges a gift of One Hundred Guineas annually from Mr. and Mrs. W. A. Macleod, of Harrow-on-the-Hill, during their life and the provision by Will of a further sum of £5,000 to endow a scholarship at the Institute bearing the name of their daughter Morna, who was for three years a voluntary research worker in the Department of Biochemistry, and whose early decease in December, 1931, is deeply deplored.

RESEARCH WORK.

Before proceeding to give a brief survey of the researches which are, or have been, in progress during the year in the various departments of the Institute, the Governing Body desires further to record its appreciation of the continued co-operation it has enjoyed with the Medical Research Council, the Department for Scientific and Industrial Research and the International Committee for the Study of Infantile Paralysis. The financial support given by these bodies to skilled investigators in the different departments has greatly increased the scientific activities of the Institute.

The Medical Research Council has furnished the salaries of the Staff of the National Collection of Type Cultures, an organisation which continues to be of great service to bacteriologists and mycologists throughout the Empire, and also those of Professor Korenchevsky and Miss E. M. Hume and their respective assistants.

The expenses of the fundamental vitamin investigation with special bearing on the vitamin content of various Empire products, being carried out in the Division of Nutrition by Dr. Zilva, including the salaries of Dr. Zilva and his assistants, are defrayed by a grant to the Medical Research Council from the Empire Marketing Board.

Dr. Ida Smedley-MacLean and two assistants have continued to work during the year under a grant from the Department of Scientific and Industrial Research, in the department of Biochemistry.

The salary of Dr. E. Weston Hurst, together with the expenses of his research on poliomyelitis, has been borne by the grant from the International Committee for the study of Infantile Paralysis. The period for which this grant was fixed came to an end on March 31st.

Accommodation for Professor Korenchevsky, Miss Hume, Dr. Smedley-MacLean, Dr. Hurst and the National Collection of Type Cultures, together with the expenses of the researches of the first three named, are provided by the Institute.

Studies on the Viruses of Vaccinia, Variola and Fowlpox.

Elementary Bodies in Vaccinia and Fowlpox. Continuing his studies of these bodies Professor Ledingham has succeeded in securing by a special method of extraction from the raw material of the lesions pure suspensions of the Paschen and Borrel bodies, which lend themselves readily to serological experiment. He has found that experimental animals (rabbits and fowls), after inoculation with the respective viruses of vaccinia and fowlpox develop specific agglutinins for these bodies. So far as vaccinia is concerned it has been possible to demonstrate, in response to a dose of virus, the appearance of agglutinins for Paschen bodies in the blood serum about the fourth or fifth day, a rapid rise thereafter to a fairly high maximal titre, followed by a gradual fall. In all respects the agglutinin response follows precisely the course ordinarily observed after the inoculation of a dose of bacterial or other protein. After inoculation of fowls with fowlpox virus, agglutinin development for Borrel bodies is tardy and so far the highest titres attained have been found during convalescence. It has been noted in previous work with fowlpox that virus-neutralising antibodies appear in the serum only in small amount, if at all. The slow development of agglutinins for the Borrel bodies is, therefore, not unexpected and the problem is being further investigated.

Dr. C. R. Amies (Research Fellow in Bacteriology) has been extending this new field of work and has been engaged in tracing out the development of agglutinins for Paschen bodies in the serum of man and monkey, after inoculation with vaccinia virus. There is now an opportunity for investigating by serological means, the relationship to each other of the viruses of vaccinia, cowpox, variola and alastrim and Dr. Amies, having now secured the necessary virus material, will be occupied with this important problem.

Immunisation of the horse with Vaccinia virus. The results of work on this subject in which Professor Ledingham, Dr. W. T. J. Morgan and Dr. G. F. Petrie collaborated, have appeared in the course of the year. The antiviral body in the serum of the immunised horse was found to be associated with the ouglobulin as well as with the pseudoglobulin fractions of the serum, but none was present in the albumin. The serum, when administered simultaneously with the virus, was shown to be highly effective in controlling experimental infections of rabbits with strains of virus of cutaneous and testicular origin.

Cultivation of Vaccinia virus in Cell-free fluid. In continuation of previous work by Dr. G. H. Eagles and Dr. D. McClean a new series of experiments to determine the possibility of propagating vaccinia virus in serial subculture in a cell-free medium has been carried out by Dr. Eagles with the assistance of Dr. A. H. H. El Kordi (Cairo). Certain changes in the preparation of the cell-free medium were made with a view to obtaining a medium as rich in tissue substances as possible, while at the same time retaining its cell-free character. Minced rabbit kidney was ground without sand in a mortar until a creamy consistency was reached. It was then treated with 9% saline for 1 hour, brought back to normal saline strength with distilled water and spun for 1 hour. The supernatant was again spun for 1 hour and removed from the deposit. In some experiments slow freezing and rapid thawing of the saline-treated kidney material was employed to facilitate the breaking up of the cells and rendering them incapable of survival. The kidney extract was mixed in suitable proportion with fresh rabbit serum, Tyrode's solution and virus, distributed in Carrel flasks and tested after incubation intradermally on rabbits for growth of virus. With this medium a neuro-testicular strain of virus has been propagated through ten subcultures and an increase of 10^{20} obtained over the original inoculum.

It is desired to stress the difficulties encountered during the first two or three subcultures. Great persistence is required to establish primary growth of the virus in the cell-free medium described.

Samples of culture virus from the third and eighth subcultures and from unincubated controls and the virus-free medium have been examined by Dr. Ledingham for elementary bodies. The presence of these in great numbers in both the third and eighth subcultures and their absence in the control materials is significant.

Centrifugalisation of Vaccinia virus Filtrates. This work was undertaken by Dr. Eagles and Professor Ledingham in order to secure further evidence in support of the claim that the Paschen body is the actual etiological agent in vaccinia. It is essentially an elaboration of earlier experiments of Ward and Tang, who found that centrifugalisation of Berkefeld "V" filtrates for long periods at varying speeds resulted in a concentration of the virus in the lower layer of the filtrates. The ease with which potent filtrates, water-clear, and free from tissue debris (as shown by Green and Eagles in former experiments) could be obtained made this investigation possible. A new type of high speed centrifuge, made by Baskerville and Lindsay, Manchester, capable of speeds up to 14,000 revolutions per minute with a 10 c.cm. load was used. Using 4 c.cm. quantities of virus filtrate it has been found possible to render the supernatant fluid inactive when spun for three periods of 1 hour each, the supernatant fluid being completely removed from the faint deposit at the end of each hour, the speed of centrifugalisation being 12-14,000 revolutions per minute. The deposits were taken up in a small quantity of saline (3 standard

drops) and tested along with the supernatants intradermally in rabbits. The deposits, which must be scraped from the glass and suspended in the saline before titration, have alone been shown to contain the virus, the final supernatant being inactive.

By twice washing the deposit after centrifugalisation in saline it has been shown that the deposit retains its infectivity practically unchanged, while the saline washings contain only negligible traces of virus.

The materials submitted to potency test have all been examined for the presence of Paschen bodies and it has been shown that the washed deposits which are alone potent consist almost entirely of Paschen bodies.

The Viruses of Pleuropneumonia and Agalactia. Professor Ledingham, with the assistance of Miss R. M. Pitt and Miss M. Rhodes, has been investigating the peculiar morphology of these organisms in serum broth and in serum agar cultures, with a view to obtaining further knowledge of the systematic position of these very closely allied filterable "viruses." The work is promising and from results which have already emerged it would seem more appropriate to regard these cultures not as filterable viruses in the usual sense but rather as filterable bacteria (or possibly fungi). The nature of that phase or portion of the organismal cycle which succeeds in passing candle filters is being investigated by various methods. The serological affinities of the two organisms are also under investigation.

Research on Poliomyelitis and Cognate Problems.

(International Committee for the Study of Infantile Paralysis).

With the expiry of the grant under the auspices of the Milbank Fund, the work of this department has been brought to a conclusion. Much of the last year has been spent in assembling results for publication, though some new investigations have been undertaken. During the past year Mmo. J. Czarkowska-Gladney (Warsaw) has been attached to the department as a voluntary worker.

Path of spread of the Poliomyelitis virus. Following upon the investigations of Dr. R. W. Fairbrother and Dr. E. W. Hurst on the path of spread of poliomyelitis after intracerebral, intranasal and intraneural inoculation, Dr. Hurst studied the mode of infection following intrathecal inoculation of the virus. The earliest lesions were frequently in the floor of the fourth ventricle, and the influence of axonic transmission in their subsequent spread was again evident. It appeared that penetration of the nervous tissues took place through the ependyma of the fourth ventricle, though an attempt to demonstrate the impermeability of a purely meningeal surface failed. No evidence at present available speaks against an axonic entry of the virus in human cases, or necessitates the participation of the cerebrospinal fluid in its spread through the nervous system.

The Outbreak of Myelitis in Trinidad. As the result of Dr. Hurst's work this disease can now be definitely ascribed to the virus of rabies. Both human cases and the brains of animals suffering from the so-called botulism have yielded a rabic virus giving cross-immunity with the virus fixe (Paris strain). The histology of the spontaneous disease in man and cattle has been studied, as has that of the experimental condition in monkeys and rabbits. The vector of the disease is not finally established, though the clinical histories of recent cases strongly incriminate the vampire-bat.

Postvaccinal Encephalitis and Encephalitis following Smallpox. Only a few cases of the former condition, and none of the latter have occurred during the past year. No further advance in the knowledge of their causation has been made. Dr. Hurst has assisted Dr. J. P. Marsden (L.C.C. Smallpox Hospitals) to collect records for publication of eight cases of post-variolar encephalomyelitis, three of which, as mentioned in previous reports, proved fatal.

The Virus of "Louping-ill." The attempts made by Dr. Czarkowska-Gladney to cultivate the virus of poliomyelitis in living tissue were hampered by the expense of animals (monkeys) necessary for testing the potency of cultures.

At this point, opportunity offered of working with the newly-discovered virus of "louping-ill," a disease of sheep endemic in certain parts of Scotland and transmissible to mice. It was thought that by making similar culture attempts with this virus the expense of the investigation would be greatly diminished, and the chances of determining the indications for successful culture of neurotropic viruses in general greatly enhanced. Unfortunately Mme. Czarkowska-Gladney had to abandon the experiments in an incomplete state although, in the meantime, various preliminary observations on the properties of the virus had been carried out.

Drs. Czarkowska-Gladney and Hurst studied the survival, infectivity and powers of diffusion of the virus under different conditions which might obtain during the growth or storage of cultures.

Dr. Hurst determined the histological features of the experimental disease in the mouse and the monkey. While in the former the virus evokes a diffuse encephalomyelitis, in the monkey its action is characterised by the striking predominance of cerebellar lesions, affording a complete analogy to the remarkable affinity of the virus of poliomyelitis for the motor cells of the spinal cord. Acidophilic structures, apparently of the nature of cytoplasmic inclusions, were present in the nerve-cells of infected mice, but no such bodies were detected in those of the monkey.

Serological Studies: Antigenic constitution and immunising properties of bacteria.

The Prophylactic value of Anti-plague vaccine. Dr. H. Schütze has continued his investigation of the antigens contained in *B. pestis* and their bearing on the problem of acquired immunity to plague in the white rat. The plague bacillus has been shown to contain two antigenic components, one which develops at higher temperatures, e.g., 37°C. and appears to be contained in the gelatinous envelope which, as Rowland showed, encircles the plague bacillus only when grown at this temperature, and another which is contained in the soma of the bacillus. The envelope antigen is of a more labile nature and is rapidly haptenised and then destroyed at 100°C. The somatic antigen withstands this temperature for a considerably longer time.

Experiments on rats have shown that a vaccine, if it is to exhibit high potency, should contain this envelope substance in adequate amount. This necessitates growth of the cultures at 37°C. and not at 26°C. as is usually done because of the more plentiful growth at this lower temperature. By adopting this method of growth at 37°C., it has been possible to prepare a vaccine which will protect 50—100% more of the inoculated animals than would a similar vaccine grown at 26°C.

The Antigenic analysis of *B. pestis* and its relationship to *B. pseudotuberculosis rodentium*. The antigens of *B. pestis* have been shown by Dr. Schütze to consist of a labile envelope substance, comparable in many respects with the flagellar antigen of a mobile *Salmonella* bacterium and of a more stable somatic portion which, however, is not species specific but is identical with one portion of the somatic antigen of *B. pseudotuberculosis rodentium*. It is suggested that this antigen is rough somatic and that *B. pestis* lacks a smooth somatic constituent, being in effect a rough organism. It is on the basis of the agglutination and precipitation reactions of *B. pestis* and *B. pseudotuberculosis rodentium* that this theory has been established.

Antidysentery vaccines. It is well-known that formolisation will detoxicate a Shiga dysentery vaccine. Miss D. Steabben and Dr. Schütze have begun an investigation upon the prophylactic value of such detoxicated vaccines. They have found that the temperature at which the vaccine cultures are grown has an important bearing on their antigenic value, though the reason for this is still obscure.

A serological investigation of *V. cholerae* and allied vibrios. Dr. M. A. Gohar (Cairo) has carried out a serological classification of *V. cholerae* and cholera-like vibrios. Working with a number of recently isolated as well as old laboratory strains, he has demonstrated, by means of agglutination and absorption tests, the complete serological homogeneity of a large group of typical non-haemolytic strains; these are to be regarded as true *V. cholerae*; a small number of serologically abnormal but otherwise typical strains has also been encountered. Haemolytic, but culturally typical strains of the El Tor type have certain H and O antigen factors in common with the true cholera vibrio, but are never identical with it in those respects. Cross-agglutination, particularly of the H variety, is also found between *V. cholerae* and quite atypical water vibrios. The only certain diagnosis of *V. cholerae* is that given by the absorption test. The clinical significance of the serologically diverse, haemolytic or non-haemolytic strains which are otherwise typical can be decided only by a close correlation of laboratory and hospital observations.

Spore-bearing anaerobes. *B. welchii*. The antigenic analysis of numerous strains of *B. welchii* has clearly indicated wide diversity of the bacterial (O) antigen of members of this species. Mixed O antigens of strains of *B. welchii* from different sources, including several strains isolated from cases of intestinal and puerperal infections, have been supplied by Dr. A. Felix to Dr. G. F. Petrie for the continued immunisation of a horse which originally had received a monovalent antigen. As in the case of the anti-O serum to *V. septique*, previously described by Dr. M. Robertson and Dr. A. Felix, very large quantities of these mixed antigens had to be injected before satisfactory titres of O antibodies could be attained.

In order to obtain a concentrated preparation of this polyvalent anti-O serum various protein fractions have been prepared by Dr. W. T. J. Morgan and their antibody content has been estimated by means of agglutination tests. Practically the whole of the O antibody is found by Dr. Felix to be contained in the euglobulin fraction. The concentrated euglobulin preparation is now available for animal experiments.

Oral immunisation with O and H antigens. Recent investigations have shown that the serum of man immunised against T.A.B. by Besredka's oral method contains a considerable amount of O agglutinins while H agglutinins are absent. It seemed possible that the phenomenon might be due to the acidity of human gastric juice which, tested by *in vitro* methods, was found to be sufficiently high to destroy the labile H antigen. This hypothesis was tested by Dr. Felix in experiments with rabbits and guinea-pigs. In both these species the acidity of the gastric juice was found to be of the same order as that in man. Vaccines of *B. typhosus*, *B. paratyphosus* A and B, and *B. proteus* X, containing both the O and H antigens, were administered by the oral and subcutaneous routes and the amounts of corresponding antibodies were estimated. No significant difference in the ratio between H and O agglutinins produced by the two different routes could be established. The absence in the serum of man, immunised by Besredka's method, of H agglutinins for T.A.B. is most probably due to the destruction of H antigen during the process of preparation of the vaccine.

Factors involved in agglutination of bacteria by normal serum. The problem of specificity or non-specificity of natural antibodies has become the object of recent researches. An investigation has been commenced by Dr. Felix with the view of studying the complex nature of normal bacterial agglutination.

Relationship between *B. proteus* X and Typhus virus. The hypothesis of the transformation of typhus virus (Rickettsia) into *B. proteus* X, put forward by Weil and Felix in 1921 and supported by subsequent work by certain authors, has recently come into the fore-ground as a result of researches on typhus and typhus-like diseases in different parts of the world. Dr. Felix has undertaken an investigation with a view to conferring upon *B. proteus* X strains some of the properties characteristic of typhus virus. *In vitro* and *in vivo* methods have been employed. The former again showed the almost unlimited capacity of *B. proteus* to vary with regard to morphology and colonial characters. Infection experiments with guinea-pigs, however, had to be abandoned temporarily owing to latent infections with *B. aertrycke* and *B. enteritidis* Gaertner of the two stocks of guinea-pigs available. The so-called Kingsbury strain of *B. proteus* X, which is receiving increasing prominence in the study of certain serological varieties of typhus, is considered as a variant derived from *B. proteus* X₁₃. The two strains differ with regard to fermentation reactions and indole production, in addition to diversity of their O antigens. Dr. A. H. H. El Kordi (Cairo) has commenced an investigation with the view of obtaining similar variants by means of methods generally employed in the study of bacterial variation.

Antigenic structure and immunising properties of *B. chauvæi*. Mr. D. W. Henderson (Carnegie Research Fellow) has made an investigation of the H and O antigenic constituents in a number of strains of *B. chauvæi*. Ovine and bovine strains isolated in this country and in various parts of the world have so far been found uniform in O antigenic composition. This result was rather unexpected in view of the diversity of antigenic constituents previously established in other species of anaerobes, particularly in *V. septique* and *B. welchii*.

Mr. Henderson has also made a study of the prophylactic value of the O antigen of *B. chauvæi*. Active immunisation of guinea-pigs by subcutaneous or intravenous injections of bacterial suspensions, killed by heating to 100°C, conferred a very high degree of protection against infection with the homologous organism and CaCl₂ as activator. These results indicate that the O antigen is the predominant, if not the sole, immunising factor in the customary methods of prophylactic vaccination against *B. chauvæi*, where suspensions of the living, attenuated organism or products of its autolysis (so-called aggressins) are employed.

Preliminary tests for cross-immunity between strains of *B. chauvæi* of bovine and ovine origin gave results in perfect agreement with those obtained in *in vitro* tests, viz., an equally high degree of protection against infection with homologous and heterologous strains.

Unusual members of the Genus *Corynebacterium* recovered from the human nasopharynx. Attention was drawn to work on this subject by Dr. M. M. Barratt in the last report. During the past year Dr. Petrie and his colleagues at Elstree have greatly extended this work with results of very great interest (see Report of Serum Department later). The data obtained will shortly be prepared for publication.

FOOT AND MOUTH DISEASE RESEARCH.

The work under the Foot and Mouth Disease Research Committee of the Ministry of Agriculture has again been carried on under the supervision of Dr. J. A. Arkwright by Dr. J. T. Edwards. He has sought for improved methods of making a dead prophylactic vaccine and has found that a small dose of vaccine gives as much protection as the same amount of living virus, provided that this is so small as not to cause an actual attack of the disease. Observations have been continued on the exact conditions favourable to survival of the virus in liquids outside the animal body especially in urine. Attempts to concentrate the virus by centrifuging at high speed have not shown that any virus is deposited after 1½ hours at 12,000 to 13,000 r.p.m.

Dr. Edwards has not been able to obtain concentrations of virus in the blood and urine of guinea-pigs by the methods of adsorption reported from the Island of Riems. He has pursued the subject of the infection of hedgehogs and white rats and has been able to pass the disease from one rat to another by inoculation for eight passages. He is also examining the relation of the very variable susceptibility of rats to their nutrition and diet and is making observations on the persistence of infectiousness of these animals after an attack and the existence of carriers with little or no signs of the disease.

Endocrinology

Dr. V. Koronchevsky in collaboration with Mrs. M. H. Donnison, Professor Myra M. Sampson (Smith College, Northampton, Mass., U.S.A.), Miss D. Graetz and Miss R. Shalit has continued his study of the sexual glands particularly under conditions of vitamin A-deficiency.

Methods used for studying the metabolism of rats. Metabolism experiments on small animals such as rats are handicapped by some serious difficulties, namely, variability of the metabolism due to changes in the temperature of the environment, excitability of the rats by sounds and movements made in their environment, scattering of the food and consequent mixing of it with the urine and faeces, the difficulty of accurately separating and collecting the excreta of the different periods and the irregular food consumption. A suitable technique has been designed to overcome these difficulties. The metabolism experiments are performed in a special isolated room in the centre of the building and kept at a regulated constant temperature. The room is entered only at special hours during the day. The rats are trained to consume their food completely during the period of the day when they are not in the gaseous metabolism cage, which has been specially designed for this work. Sufficiently long periods are taken in order to separate more accurately the urine and faeces belonging to the different periods of the experiment.

Methods used for assay of testicular hormone preparations. The present tests used for the assay of testicular hormone preparations, although possessing several advantages, yet have many disadvantages. A method of assay has been designed which aims at giving accurate data showing the influence in all the changes produced in the animal by castration and recording them. The prostate seminal vesicles, penis and thyroids (all of which atrophy after castration) as well as the adrenals and hypophysis (which hypertrophy after castration) are accurately weighed and also the fat, as nearly all castrated rats become obese. A special method of preparing the organs for accurate weighing has been used, by which it is possible to utilise the organs afterwards for histological investigation if necessary. If all the testicular hormones are present in the preparation assayed, after injection of the preparation the organs and glands mentioned above should return to or towards normal. Although giving the most accurate and complete results such an assay requires a comparatively considerable time for its performance. As a quick, simple and sensitive test, however, Professor Korenchevsky has found that an increase in the weight by at least 40% of the prostate plus seminal vesicles of injected control rats, as compared with that of uninjected control rats, can be relied upon. The method gives accurate results in view of the fact that in castrated rats the percentage deviation of weight of the above organs from their average weight is not very great, provided rats are used which come from the same stock and litter and are similarly fed.

The influence of cryptorchidism on the gaseous and nitrogenous metabolism of rats. The chief difference between the testes of cryptorchid and normal animals is the atrophy or complete disappearance of the seminiferous cells in the cryptorchid testes. The gaseous metabolism was found to increase during the period of most active and abundant resorption of the seminiferous cells from the cryptorchid testes. This corroborates the view put forward by Dr. Korenchevsky and his co-workers as the result of previous experiments, that the seminiferous cells, like the interstitial cells, have the function of inner secretion and that they secrete a hormone which stimulates gaseous metabolism. A continuous deposition of nitrogen in the body of cryptorchid rats was observed. These data are thus in agreement with the chemical investigation of cryptorchid animals, in the body of which increased amounts of fat and probably of nitrogen were noted.

The influence of freshness of the testes and of drying the testicular tissue on the yield of testicular hormone. The freshness of bull's testes plays an important part in the yield of hormone since the hormone is only extracted in much smaller amount from testes kept at room temperature for about 20 hours. After boiling the testicular tissue in water acidified with acetic acid up to $pH 4.6$ to 4.8 it is possible to dry it at 37° without appreciably decreasing the yield of hormone. This indicates that besides oxidation the autolytic ferments present in the testicular tissues are probably the most destructive agents of the testicular hormone in testes removed from the organism and kept at room temperature.

On the basis of results obtained, a simplification of the method of extraction of the hormone is suggested, involving direct benzene extraction from testicular tissue which has been first boiled and then dried at 37° .

Changes in the endocrine organs of male rats kept on vitamin A-deficient diet. It is known that animals suffering from vitamin A deficiency are sterile. There is a difference of opinion between previous workers with regard to the changes obtained in the testes and very little is known of the influence of vitamin A deficiency on the other endocrine organs. The present experiments were performed in such a way that the control animals received the same amount of food as that eaten by the animals kept on vitamin-deficient diet. This was done in order to exclude the sometimes considerable changes produced by the variation in quantity of food consumed by deficient rats.

Dr. Korenchevsky's investigation of all the endocrine organs is not yet complete, except in the case of the testes. In the testes the seminiferous tissues gradually degenerate, the greatest changes being obtained in rats kept for the longest period on vitamin A deficient diet without appreciable loss of body weight, but having well developed xerophthalmia. The first sign of degeneration is the disappearance of spermatozoa. In the next stage degenerative changes in the nuclei of the seminiferous cells are seen, of which the bead-like appearance of the nuclei is very typical. These changes are followed by general degeneration of the seminiferous cells with the formation of giant cells. In the last stages all the seminiferous cells disappear leaving very atrophied tubules containing only Sertoli cells. The interstitial tissue seems to be unaffected. The external appearance of the testes at that stage is that of small, oedematous, hyperæmic glands. The prostate and seminal vesicles are atrophied. In contrast with atrophy of the testes the thyroids increase in size and weight. Although the histological investigation of all the thyroid glands is not yet completed, it is possible to suggest that these changes are due to an increased number of cells, and not to an increase in size of the cells.

Experiments on the metabolism of nitrogen and fat in rats kept on vitamin A-deficient diet and the changes produced by such a diet in castrated rats are being undertaken.

Coagulation of the Blood.

Dr. J. O. W. Barratt has completed his study of the conditions under which deterioration of fibrinogen and thrombin occurs on keeping. The degree of deterioration has been measured and it has been shown that bacteria and fungi play no part in the deterioration observed. The results have been embodied in a paper.

The investigation of the action of heparin in retarding coagulation has been concluded and an attempt is being made to determine the nature of the anti-coagulative action of Chicago blue.

DIVISION OF PROTOZOOLOGY.

Dr. Muriel Robertson's work during the last year has consisted in the main in a continuation of the study of the effect of gamma ray irradiation upon the protozoon *Bodo caudatus*.

The growth in the presence of radium is reduced and the circumstances attending this have been approached (1) by observing the behaviour of a parallel series of continuous cultures in plates, one of which is exposed daily to the radium and the other grown under identical conditions in the absence of the radium; (2) by the study of the progressive increase of the numbers on twin plates, one of which is irradiated and the other not, during one growth cycle of $21\frac{1}{2}$ hours and by interpolation of the figures from a series of like plates arrested at various fractions of this time. A third approach has been made by the measurement of the length of the bodos in preparations made at the end of the $21\frac{1}{2}$ hour period at the time when the count of the cells is made. This has revealed that the irradiated material shows quite definitely a greater number of large bodos than the controls. The implications of this are being studied.

In addition, irradiated strains and normal strains exhibit certain striking differences in their behaviour to a serum-lysin made by injecting the bodos into the blood of a rabbit. The changed behaviour persists for many generations after the removal from the radium. It is, however, apparently lost after upwards of 200 generations. But the loss is effected by the number of generations elapsing since irradiation, rather than by the passage of time if the bodos have been reproducing more slowly. This phenomenon of altered behaviour has now been repeated in so considerable a number of tests that its gross relation to irradiation seems established. The analysis is, however, not complete and is still being studied.

Some further work has also been done on the acriflavine-fast cultures which are now of some years standing.

The energies of the department were also directed for a period of a few weeks to producing mass growths of protozoa for use in a joint research with Dr. and Mrs. Joseph Needham.

To the Radium Committee of the Medical Research Council the Institute is greatly indebted for the loan of 400 mg. of radium used in this research.

DIVISION OF NUTRITION.
Vitamin Standards and Methods of Estimation.

The workers on vitamins in this Institute, in common with those in other laboratories in England and abroad, have devoted much time during the past year to the study of the various biological methods in use for estimation of the different vitamins. This has included a thorough investigation of a series of vitamin concentrates selected by the Accessory Food Factors' Committee as worthy of study with a view to their adoption as standards of reference in the biological estimation of vitamins A, D, B₁ and C respectively. The work was undertaken in connection with the International Conference on Vitamin Standards and Units, held in London in June, 1931, at the invitation of the Permanent Standards Commission of the League of Nations. For this Conference, held under the Chairmanship of Dr. E. Mellanby, Dr. H. Chick and Dr. W. R. Aykroyd acted as Secretaries. The results obtained with the selected materials were presented to the Conference in a series of Reports and the suggested standards were unanimously adopted as provisional International Standards of reference, and International Units for the respective Vitamins were defined in terms of these materials. In January, 1932, these standards and units were formally adopted by the Conference on Vitamin Standards of the U. S. Pharmacopoeia Revision Committee, so that international uniformity may be considered to be achieved.

The special investigations carried out in the Institute in connection with these vitamin standards may be summarised as follows:

Vitamin A. Standard adopted: a preparation of pure recrystallised carotene. Tests were made by Miss Hume and Miss Henderson Smith, using the method whereby the minimum amount of material which will maintain a group of depleted rats for 35 days is ascertained. Such minimum doses were found for the standard specimen of carotene and for special samples of cod liver oil, butter and dried cabbage, issued by the Accessory Food Factors' Committee for comparison with the standard. The results were in very tolerable agreement with those of the workers in other laboratories, who had tested the same materials by somewhat different methods. It was considered that the results were sufficiently satisfactory to make the use of carotene as a standard appear feasible.

Further tests on the stability of the standard specimen of carotene after storage for a year are now in progress.

Vitamin D. Standard adopted: a standard solution of irradiated ergosterol prepared and issued by the National Institute for Medical Research. Miss Hume, with the assistance of Miss Galikin, utilising results obtained in their previous investigation of this product and others obtained from new experiments specially designed for the purpose, have succeeded in obtaining standard curves relating dosage to the response in bone calcification of the experimental animals. The curves, which suggest results of great theoretical importance, are being further studied and it is hoped that by their use the accurate estimation of vitamin D in unknown substances may be greatly facilitated. Miss Hume's further work has confirmed the previous conclusions as to the stability of the standard preparation when preserved at 0°C., and its suitability for adoption as an international standard.

Dr. S. S. Zilva and Miss Hume have collaborated with Dr. R. Bourdillon and Miss H. M. Bruce of the National Institute for Medical Research in a comparative study of the methods of vitamin D estimation, employing as respective criteria, chemical analyses of bones and X-ray evidence of rickets.

Antineuritic vitamin B₁. Standard adopted: A vitamin B₁ concentrate obtained by absorption on acid clay from an extract of rice polishings prepared at Batavia, Java, and provided by Professor B. C. P. Jansen of Amsterdam. This material has been investigated by Dr. H. Chick and Miss H. M. Jackson, using the growth method with rats and has been found to be highly potent (minimum daily rat dose about 10 mg.) and convenient to administer. In experiments made to test its stability, no significant deterioration has been detected after 10-12 months, whether stored at 0° or 37°C.

The material has been found to be contaminated with only an insignificant admixture of vitamin B₂. As it is available in large quantities it might, therefore, provide a more convenient source of vitamin B₁, for inclusion in basal diets designed for the study of vitamin B₂, than the vitamin B₁ concentrates at present in use, many of which can only be obtained from yeast or other materials after elaborate and time-robbing processes of purification.

Estimation of vitamin B₁. Dr. Chick, Miss Jackson and Miss M. H. Roscoe (Beit Memorial Research Fellow) have collaborated in an investigation of a "curative" method of estimating vitamin B₁ in which the criterion adopted is the cure of paralysis or convulsions developed in rats on a diet deficient in this vitamin. The method has been found to yield fairly accurate results if comparison is made of the minimal amounts of various materials given as a single dose needed for cure. Attempts to make comparisons between materials or doses causing relief of symptoms for different periods, did not give trustworthy results. The curative method, though more specific, has not been found so exact as that of assay by growth. Cures by subcutaneous injection were as effective as those in which the doses were given by the mouth.

Vitamin C. The standard of reference adopted was decitrated fresh lemon juice prepared according to the method devised by Dr. S. S. Zilva. This material, when used immediately after preparation, has been found to be of uniform potency.

Further researches on the vitamin B complex.

Heat-stable, anti-dermatitis vitamin B₂. The factors influencing the incidence of the so-called "vitamin B₂ deficiency dermatitis" of rats, are still under investigation by Miss M. H. Roscoe. At the same time it is hoped to throw light on the question of the identity, which is now disputed, of the growth-promoting and the dermatitis-preventing properties exhibited by this vitamin.

An unsuccessful attempt has been made to obtain symptoms of vitamin B₁ and vitamin B₂ deficiency in rabbits.

Vitamin B₁. Miss Roscoe has made an attempt, so far unsuccessful, to confirm the work of Reader in obtaining symptoms of vitamin B₁ deficiency in rats.

Distribution of vitamins B₁ and B₂ in natural foodstuffs. Miss Roscoe, with the assistance of Miss D. Graetz, has extended this investigation which has already included meat and milk products, cereals and vegetables, to some of the common fruits. Oranges were found to be a good source of vitamin B₁, tomatoes less good and bananas and apples relatively poor. The vitamin B₂ content was in every case less than the vitamin B₁ content, all the fruits examined being poor sources of this vitamin.

Synthesis of the vitamin B complex in the rat. Further work by Miss Roscoe with coprophagous rats on diets containing soluble starch has led to the conclusion that the beneficial effects of coprophagy in delaying symptoms of deficiency of the B vitamins cannot be attributed alone to a more economic utilisation of the reserve vitamin stores possessed by the experimental animals. A synthesis of these vitamins appears to take place in coprophagous animals. The quantity of either vitamin B₁ or B₂ made available, as shown by the growth of rats, was found to be increased under certain circumstances, as for example, when yeast extracts, not containing these vitamins, were added to the diet. It is suggested that the synthesis is carried out by bacteria in the alimentary canal.

The effects of coprophagy in rats receiving diets containing soluble starch are different from those observed when the diets contain insoluble starch; in the latter case the rats may develop the condition known as "refection." In both cases bacterial synthesis of the B vitamins has been postulated to explain the delay or prevention of the symptoms characteristic of the deficiency of these vitamins; but the processes are, in many ways different in the two cases, and no connection between them, such as a common infection of the alimentary canal, has been established.

Blood chemistry in vitamin B₁ deficiency. In rats suffering from uncomplicated deficiency of the antineuritic B vitamin death occurs very shortly after the onset of the convulsive muscular spasms characteristic of this condition. It has been found that while all the symptoms are swiftly cleared up by the administration of the missing vitamin, the condition of muscular spasm, which appears to be the immediate cause of death, can be postponed and temporarily relieved by the injection of parathyroid extract, suggesting that the muscular convulsions might be caused by a disturbance of the concentration of blood calcium. Analysis of the blood of rats in this condition has, however, failed to show any departure from the normal concentration of calcium. This work was initiated by Dr. Chick and Miss Jackson, with the collaboration of Dr. E. W. Hurst and Dr. A. E. Carmichael (National Institute for Medical Research) and is being continued by Miss MacOwan (Kilgour Research Fellow of the Rowett Institute, Aberdeen). Dr. Hurst has examined the histology of the central nervous system and peripheral nerves of rats suffering from acute or chronic Vitamin B₁ deficiency, but has failed to find any abnormalities.

Vitamins A and D.

Physical properties of carotene as indication of its vitamin A value. In conjunction with Dr. Smedley-MacLean, Miss Hume and Miss Henderson Smith have sought to ascertain whether the biological value of carotene, as a source of Vitamin A, can be reliably inferred from the intensity of its yellow colour. It would appear that this is so but the point has proved to be a difficult one to establish accurately, owing to the instability of the already deteriorated and partly faded specimens of carotene which it is necessary to use for the purpose.

Vitamin A in insects. The fat was extracted from mealworms (*Tenebrio molitor*) by Dr. Lucas. When tested for vitamin A with rats, by Miss Hume and Miss Henderson Smith, the content was found to be extremely small; a daily dose of about 0.3g. failed to protect a rat. The result is surprising in view of the fact that these mealworms were reported to have been reared upon carrots.

Origin and distribution in nature of the antirachitic vitamin D. The origin of the vitamin D contained in fish liver oils, e.g., cod liver oil, presents many interesting and unsolved problems. In the past much research in this Department has been devoted to the examination of the food sources from which the cod might derive this vitamin since the habitat of this and other fish possessing liver oils rich in vitamin D renders it unlikely that the vitamin could be derived from ultraviolet solar radiation. The green marine diatom *Nitzschia*, though rich in vitamin A was found by Miss Leigh Clare to be devoid of vitamin D and during the past year Miss Hume and Miss Gaffikin, working in collaboration with Dr. Atkins of the Marine Biological Station, Plymouth, have examined supplies of copepods which are

believed to form a large portion of the food of the cod fish during the spring and summer months. Only minimal amounts of vitamin D have, however, been detected in preliminary experiments with this material.

After fish liver and body oils, the chief sources of vitamin D are found in the yolk of birds' eggs and in the fat of mammalian milk. Previous work in this department has shown that only very small amounts of vitamin D are contained in fresh green food, even in summer. If sunlight be the only source from which these animals derive their supply the question of storage, probably in the liver, becomes important and has seemed worthy of special investigation. A survey is therefore being made by Miss Gaffikin and Miss MacOwan of the vitamin D content of fowls', pigs' and sheeps' livers, using the special methods of estimation developed by Miss Hume and Miss Gaffikin.

Biological Value of Proteins.

Dr. Margaret Fixsen and Miss H. M. Jackson, with the collaboration of Dr. H. Chick, have extended the work on the biological value of proteins to the proteins of wheat, maize and whole milk in addition to caseinogen and lactalbumin. The previous method has been followed, the adult male rat being used as experimental animal, and the biological value of the various proteins estimated by a balance sheet method, in which the minimum amount required for nitrogenous equilibrium is determined. A special feature of the method used has been the provision of an adequate supply of the B vitamins in the form of concentrates containing minimal amounts of nitrogen.

The proteins of maize endosperm have been found slightly superior in biological value to those of white flour (wheat endosperm), the figures being 69 and 58 respectively when these materials were fed at a 7 per cent. level in the diet. For the proteins of the whole grains the results obtained for wheat and maize have proved to be of the same order (value=about 70 at a 7 per cent. level). These results are unexpected and do not confirm those obtained by some previous workers, who have found the biological value of maize proteins to be much inferior to that of wheat proteins and among the lowest found for the proteins of natural foodstuffs. As 50 per cent. of the protein contained in maize consists of zein, an imperfect protein lacking two important amino acids, tryptophan and lysine, it must be concluded that these deficiencies are supplemented by the other proteins present in the grain. The theory that the connection between maize consumption and pellagra can be wholly explained by the low biological value of the proteins of this cereal is not supported by this work.

Many previous workers on protein metabolism have found that the utilisation of protein becomes less economical as the proportion in the diet is increased, the biological value thus appearing to decrease. Experiments in the present investigation have shown that this is not universally true, caseinogen, for example, maintaining a constant value when supplied in the diet over a large range of different percentages. This discrepancy between different proteins indicates several problems of theoretical importance in protein metabolism and is being further investigated.

The study of caseinogen is of special importance owing to its general use as sole protein in many experimental diets employed in vitamin research. A comparison of caseinogen, as precipitated from milk, with the same product after prolonged heating and purification by washing with acidified water and extraction with dilute alcohol to remove vitamins A and B, has shown a marked deterioration in biological value (from about 70 to about 50) to be associated with this treatment.

The Dietary Factors required for Lactation.

For some years past researches have been carried out on the growth and reproduction of rats on simplified "synthetic" diets. Series of diets have been employed, which contain all the recognised elements essential for nutrition, presented in a simplified and purified form. Satisfactory growth, development and reproduction have been achieved to the extent of successful mating and pregnancy, followed by the birth of litters showing normal numbers and weight. Successful lactation has, however, rarely been obtained without further addition of certain natural foodstuffs to the diet of the females. This result is in agreement with the experience of many other investigators. Experiments are now being made to discover the nature of the food elements required for satisfactory lactation which are missing in the experimental "complete" diets. The work, which by its nature is of slow progress, is being carried out by Miss Hume and Miss Henderson Smith in collaboration with Dr. Chick and Miss Jackson.

Dr. Vincenzo Lippicorella, Lecturer in Medical Pathology in the University of Florence, working as a guest in the Department, investigated the effect on blood elements of extreme variations in diet in the balance of protein, fat and carbohydrate.

Experimental Researches on the Antiscorbutic Principle (Vitamin C.)

It has been previously shown by Dr. Zilva that the best results were obtained in the active "fraction" of lemon juice when an optimum amount of lead acetate was employed. After careful experiments in which the various fractions were balanced for antiscorbutic activity as compared with the original juice, it has been found that if an excess of lead acetate is added in the process of fractionation, some vitamin C disappears from the general medium, since it cannot be recovered in any of the other fractions of the process.

It has been reported previously by Dr. Zilva that after autoclaving decitrated lemon juice, the inactivation of vitamin C in it proceeds very rapidly. Previous researches have shown that the formation of a phenolic substance in the process of autoclaving was most probably responsible for this increased inactivating influence. In view of the importance of ascertaining the details of the process of inactivation of vitamin C, Dr. Zilva and Mr. S. W. Johnson have made a detailed study of the subject and have now definitely established that on autoclaving, a substance closely resembling catechol is formed from the invert sugar of the juice which helps the inactivation after autoclaving.

These conclusions have been arrived at by a comparison of the properties of the ether extracts of autoclaved juice and sugar solutions with various catechol compounds and also from an investigation of a "pseudo-peroxidase" reaction which becomes manifest after autoclaving the decitrated lemon juice. Whether a similar process takes place in the inactivation of the juice under natural conditions is a subject still to be investigated.

A recent claim by Rygh, Rygh and Laland (*Z. Physiol. Chem.* 1932, 204, 105) that they have isolated and synthesised vitamin C aroused considerable interest. Dr. Zilva working in collaboration with Dr. S. Smith and Mr. Grant, of Messrs. Burroughs, Wellcome & Co., has attempted to repeat their work but the results so far obtained furnish no evidence whatsoever in support of the claim of the above authors.

Stability of vitamin C concentrate. Dr. Zilva has also been experimenting on the stabilisation of vitamin C in concentrates and natural products by means of low temperatures. The limitation of the accuracy of the clinical (growth) method of the estimation of vitamin C has also received attention.

Very convincing evidence has been obtained concerning the activity and stability of the antiscorbutic concentrate prepared by Dr. Zilva for the members of the British Arctic Air Route Expedition, to Greenland, led by Mr. H. G. Watkins. This antiscorbutic preparation as well as the general rationing scheme proved very satisfactory. These results will form the subject of a future communication. The case of one member of the expedition, Mr. Augustine Courtauld, is of particular interest. On October 26th, 1930, he set out from the base to the central station situated on the Greenland ice-cap 8,000 ft. high, in latitude 67° 3' North and longitude 41° 49' West. Apart from a little strawberry jam, marmalade and a handful of raisins, prunes and dates, and two-thirds of a frozen ptarmigan, all consumed before December 6th, Courtauld existed until May 5th, 1931, on a dietetically well balanced but vitamin C-free sledge ration. For an antiscorbutic he took one dessert spoonful of the concentrate daily. From March 22nd to May 5th, he was snowed up in his tent and during the last fortnight was without light or heat. He watched carefully for symptoms of scurvy, but apart from general discomfort, he felt normal in every way. His teeth and gums remained in good condition and until the end of the period he could comfortably bite hard, uncooked food. When relieved he was able to ski about one mile unaided from the ice-cap station to the relieving party's camp.

The distribution of vitamin C in fruits. A number of varieties of triploid apples collected from various parts of the world have been carefully tested for vitamin C in order to ascertain whether the previous suggestive observation of the high vitamin C content of triploid apples is general. This investigation is not yet finished, but its general trend indicates an association between high chromosome number and high vitamin C activity in apples. Studies on the vitamin C content of the fruit by grafting stock have shown little or no association between the two.

Further experiments on apples have been carried out in connection with: (1) A possible relationship between the nitrogen content and the C content of the apple, and (2) The relative vitamin C content of very small and large apples of the same variety.

Quantitative experiments on the Indian mango disclosed that the pulp and the skin of the "Alphonso" variety are the most potent sources of vitamin C so far recorded. The "Cawasji Patel" variety is slightly less active in vitamin C. The "Shendrya" variety contains much less vitamin C than the previous two varieties. The pulp of all three varieties contains vitamin A in quantities similar to that possessed by butter, the "Alphonso" variety being somewhat better than the other two in this respect.

The influence of various factors (Preparation, Storage, and Transit) on the vitamin content of dairy products. The first stage, covering a period of four years, of the investigation of the influence of various factors on the vitamin-content of dairy products is now finished and is being prepared for publication.

In connection with the estimation of vitamin C by means of the histological appearance of teeth of guinea-pigs, Dr. Zilva and Miss E. O. V. Perry have been studying the effect of the preliminary dietetic history on the teeth.

Exploratory experiments have been carried out on the antiscorbutic content of rabbit faeces, as estimated on guinea-pigs, in order to ascertain whether a condition of refection exists in the rabbit in connection with scurvy.

The effect of the intestinal flora of guinea-pigs in relation to the onset of scurvy in these animals has also been studied.

Permeability of Epidermis to ultra violet radiations.

Dr. N. S. Lucas has extended his work on human epidermis to the skin of fishes and birds.

DEPARTMENT OF BIOCHEMISTRY.

Alcoholic Fermentation.

Professor R. Robison, continuing his work on the phosphoric esters of alcoholic fermentation, has isolated one of the remaining, unknown esters to which reference was made in last year's report. Although the examination of this compound is not yet completed there is reason to believe that it may prove to be a monophosphoric ester of mannose. If this surmise is correct it will have been shown that in the fermentation of glucose or fructose by non-living yeast preparations the three monophosphates of the allied hexoses, glucose, fructose and mannose are all formed in addition to fructosediphosphate and, under certain conditions, trehalosephosphate.

The conditions governing the relative proportions in which these various esters are produced have also been further studied in collaboration with Dr. M. G. Macfarlane and Dr. C. M. Jephcott (Research Associate of the Department of Physiology, Toronto University). In fermentations with dried yeast it has been found that the ratio of monophosphates to diphosphate varies with the nature of the sugar fermented, being greater with mannose than with glucose or fructose, while the character of the monophosphate fraction also differs. Significant differences were further observed as a result of partially washing the yeast, thus reducing the amount of co-enzyme. The proportion of monophosphates formed from glucose and fructose was greatly increased while that from mannose was unaffected. Further enquiries into the nature of the esters produced under these diverse conditions are being carried out in the hope of throwing light on the mechanism by which esterification of sugars with phosphoric acid assists in their break-down and utilisation within the organism.

This problem was being attacked from a different angle by Professor Robison and Miss M. Macleod who were investigating the hydrolysis of the hexosephosphates by animal phosphatases. At the time of Miss Macleod's death, evidence had been obtained that the monophosphoric ester formed by partial hydrolysis of fructosediphosphate with bone phosphatase is not identical with Neuberg's ester produced by acid hydrolysis or with any of the known monophosphates of fermentation. This work is being continued.

Professor Harden has commenced an investigation on the function of hexokinase in alcoholic fermentation.

Meyerhof found that his solution of the lactic acid-forming enzyme of muscle readily produced lactic acid from glycogen but was almost completely lacking in the power to produce it from glucose and other sugars. He succeeded in obtaining from yeast a substance which he termed hexokinase, which conferred on the muscle enzyme this missing power. It seems probable that the hexokinase has also some function in alcoholic fermentation, but nothing is as yet known about it.

Ossification.

The investigation of calcification in cartilage and bone has been continued by Professor Robison and Miss A. H. Rosenheim (Grocers' Company Research Student) who have obtained further evidence of the duality of the calcifying mechanism. The phosphatase secreted by the hypertrophic cartilage cells and osteoblasts serves to increase the concentration of inorganic phosphate and to produce a condition of supersaturation in the tissue fluids while a second factor favours or determines the precipitation of the bone salt from this supersaturated solution. Experiments have been directed towards discovering the nature of this second factor which appears to be very susceptible to injury by conditions which have little effect on the enzyme. The evidence is gradually accumulating that this factor varies in power according to the state and previous history of the animal and such variation might well prove to be of significance as a contributory cause of the deficient calcification in rickets and other bone diseases.

Professor Robison's collaboration with Dr. Honor B. Fell (Director of the Strangeways' Research Laboratory, Cambridge) has been continued and has again been directed towards the investigation of calcification in avian cartilages and bones. The hypertrophic cartilage in the developing long bones of the embryo chick exhibits certain pronounced differences as regards calcification from the hypertrophic cartilage in the long bones of the rat or rabbit. These differences appear to persist whether the avian bones develop normally in the egg or are isolated and cultivated *in vitro* and it is considered that their further investigation, which is in progress, should give information of value for the general problem of calcification.

Dr. Fell has previously shown that whereas periosteum removed from early embryonic limb bones is able to form bone *in vitro*, that derived from late embryos and young chicks may grow profusely but rarely ossifies, probably owing to damage inflicted on the osteoblastic layer during stripping. Undamaged (endosteal) osteoblasts derived from the Haversian spaces of such late embryonic and early post embryonic bones readily form bone *in vitro*. Dr. Fell and Professor Robison have employed cultures obtained from such material to study the development of the calcifying mechanism in osteoid tissue. They found that the cultures of endosteal bone possessed a high phosphatase activity and that their calcification could be effected or, if already begun, could be greatly increased by immersing the explants for periods of 18 hours in the calcifying solutions employed for the experiments with bones of rachitic rats. On the other hand the non-ossifying cultures of periosteum derived from late embryos possessed no phosphatase activity whatever and could not be calcified by immersion in any of the experimental solutions.

Dr. J. S. F. Niven and Professor Robison have continued their investigation of calcification in early embryonic rabbit bones, begun while Dr. Niven was working at the Strangeways' Research Laboratory. In 18-19 day embryos the hypertrophic cartilage of the long bones was usually found to show little or no calcification but possessed significant phosphatase activity and could be fully calcified by immersion for short periods in suitable calcifying solutions. The activity of the second or "inorganic" mechanism appeared to be definitely greater in such embryonic cartilage than in the hypertrophic cartilage of rachitic rats. This mechanism was injured but not entirely destroyed by immersing the bones in acetone or desiccating them over sulphuric acid.

A comparative study of the phosphatase activity of tissues of various animals at different ages has been begun by Professor Robison, Miss L. M. B. Patterson and Dr. M. G. Macfarlane, using a micro-technique suitable for the very small quantities of material which are available in certain cases. The high activity of ossifying cartilage, the almost complete inactivity of typical non-ossifying cartilage of the rib and the relatively low activity of such tissues as liver, spleen, pancreas and muscle has again emerged from these tests.

In addition to kidney and intestinal mucosa certain other tissues which do not normally calcify have been found to exhibit in certain animals a fairly high phosphatase activity. The significance of this is not yet apparent, but it is very interesting to note that some of these tissues, *e.g.*, the aorta and the kidney, are frequent sites of calcification in pathological conditions such as hypervitaminosis.

Purification of animal phosphatases. The purification of the animal phosphatases and the comparative study of their properties have been the subjects of further work by Professor Robison and Miss M. N. Maclean. Pressure dialysis has been employed to free the bone phosphatase from traces of calcium, magnesium and inorganic phosphate, and the p_H -activity curves have been determined for this purified enzyme with different phosphoric esters and in presence of small amounts of added magnesium, by which the rate of hydrolysis is greatly increased. Unfortunately the stability of this phosphatase becomes lessened as its purification progresses. Similar methods have been used with considerable success in order to free the phosphatase of red blood corpuscles from haemoglobin and from the esters and inorganic salts which are present in relatively high concentration in the corpuscles. This phosphatase is of a different type from that present in bones and a more detailed knowledge of its properties is very desirable.

Posterior lobe of the pituitary gland. Dr. J. M. Gulland and Dr. W. H. Newton (Department of Physiology, University College, London) have completed the preliminary examination of the possibilities of purifying the oxytocic principle by adsorption on norite charcoal from aqueous solutions at different hydrogen ion concentrations. Adsorption is complete at $p_H 2$ and at $p_H 11$, and the active substance may be eluted by glacial acetic acid. The potency of the preparation having the highest activity/weight ratio (adsorbed at $p_H 11$) was 225 international units per mgm., the powdered posterior lobe used as starting material having been assayed at 1.5 units per mgm. A good, but not maximal, contraction of the isolated virgin guinea-pig uterus was given by this preparation at a dilution of 1 in 550 millions. Dr. Gulland's further work on this subject will be based partly on the results already obtained.

Purine Derivatives.

The constitution of the nucleic acids. Although the general character of the structures of the nucleosides is known, the details of their constitution as yet remain uncertain. Dr. Gulland and Dr. T. F. Macrae (Research Student) are investigating the position occupied by the carbohydrate groups in the molecules of the nitrogenous components. Several unexpected difficulties have been encountered in this work, and these have necessitated the trial and subsequent abandonment of a number of methods of attack. The investigation is still in progress.

Palladous chloride as a reagent for purine derivatives and other nitrogenous compounds. In the course of their work on the nucleic acids, Dr. Gulland and Dr. Macrae observed that palladous chloride forms very sparingly soluble, crystalline compounds with many purines and nucleosides. Some closely related compounds did not, however, yield sparingly soluble precipitates, and ultimately the differences observed have been related to the acidity of the solutions employed. The palladous chloride compounds have the formula R_2PdCl_2 . Their sparing solubility enables their formation to be used for the isolation and estimation of purine derivatives, and the crystalline forms of the compounds are in many cases characteristic, and act as an additional means of differentiating between purine derivatives. Palladous chloride oxidises certain compounds, *e.g.*, uric acid, cinchonine, piperidine, cinnamic acids, and polyphenols, and the nature of the products of the oxidations have been elucidated in many cases.

Action of enzymes on guanylic acid and xanthosine. Dr. Gulland and Dr. Macrae have observed that guanylic acid may be converted quantitatively into guanosine by enzymic hydrolysis of the phosphoric ester group with bone phosphatase at $p_H 8.5$ and 37° . They have also attempted to oxidise xanthosine by the xanthine dehydrase of milk in the hope of obtaining the uric acid riboside which Benedict isolated in small amount from blood some years ago. No oxidation occurred at $p_H 8$ or $p_H 6$ and 37° , using methylene blue as hydrogen acceptor. The source of this uric acid riboside in the body remains obscure.

Spermicidal Action of Quinones and Aromatic Aldehydes.

Dr. Gulland has published the preliminary investigation of the lethal action of certain phenols, quinones and quinols on guinea-pig spermatozoa. The quinones, and to a lesser degree the quinols, exhibit high spermicidal activity, and it is probable that this is due to a large extent to the chemical union of the quinone molecule with electron-donating groups in the cell structure. A list of quinones in order of their spermicidal activity is also an arrangement of the same compounds in order of their chemical sensitivity to anionoid reagents.

Dr. Gulland and Mr. T. H. Mead are investigating the spermicidal properties of aromatic aldehydes, and so far have obtained results which are best attributed to chemical inter-action between aldehyde and groups in the cell. Efforts are being made to ascertain not only the nature of this chemical combination, but also the position in the spermatozoon of the groups which take part.

The Oxidation of Fatty Acids.

Dr. Smedley-MacLean and Miss Pearce have continued the investigation of the oxidation of oleic acid by means of hydrogen peroxide, in order to elucidate further the nature of the intermediate products when no copper catalyst is used. The conversion of the 9 : 10-ethylenic group into two carbonyl radicals was confirmed, while the 18-carbon chain becomes successively shortened. Subsequently a mixture of keto-derivatives of caprylic acid is formed, in one of which the carbonyl group is in the α -position. Since caprylic acid derivatives are known to be readily attacked in the body, the formation of these, as described above, from oleic acid suggests that the chain of eight carbon atoms is an intermediate stage in fat metabolism. The α -keto derivatives of octoic, nonoic and decaic acids were synthesised for the purposes of comparison with the oleic acid oxidation products.

Dr. Smedley-MacLean and Miss Ponsford examined the effect of cupric salts on the oxidation with hydrogen peroxide of the dibasic fatty acids, succinic, glutaric and adipic. The oxidation is greatly influenced by the addition of cupric salts, a considerable proportion of carbonic, formic and acetic acids being formed. Evidence was obtained of the presence of a small quantity of levulinic acid, formed in the oxidation of adipic acid.

Dr. Smedley-MacLean and Miss Ponsford in co-operation with Miss Hume have studied the formation of liver glycogen from succinic, acetic and malic acids. Rats were starved for twenty-four hours and then fed for three days on a carbohydrate-deficient diet, to which was added the ammonium salt of one of the above acids, or in some cases an equivalent amount of sugar. A definite increase in glycogen was detected in the livers of the rats which had received succinic or malic acids in their diet, comparable with the increase which occurred when sugar was given. The livers of the rats receiving acetate showed no such increase. On the whole, the amount of fat present in the liver was less in the rats which had high liver glycogen.

DEPARTMENT FOR THE STUDY AND PREPARATION OF ANTITOXIC SERA.

Studies on the Pneumococcus and on the Production and Titration of Anti-Pneumococcus Sera.

During the past year a potent anti-pneumococcus serum (Type I) has been produced in horses and has yielded a concentrated preparation of high value. Work on the production of a Type II. serum is in progress.

Dr. Petrie and Dr. Morgan have made observations on the lethal power for mice of a virulent strain of Type I pneumococcus, and have analysed the factors which cause variations in the test cultures and which influence the chance of infection in the test animals. They have endeavoured to measure the natural resistance of mice to the culture and have found that a small proportion—from 5 to 10 per cent.—possess an innate resistance to the intraperitoneal administration of small doses of pneumococci. Their observations indicate that an average lethal dose—that is, one which gives an even chance of life or death in a group of mice—can be ascertained by the use of a reasonable number of animals, and that it is possible to specify the lethal power of any strain of Type I pneumococcus by noting the percentage mortality, the mean death-time and the distribution of the deaths in appropriate time-intervals, in a group of mice which receive a definite dose of the culture containing, on the average, one diplococcus.

Dr. Petrie and Dr. Morgan have also carried out experiments of the curative action of anti-pneumococcus serum (Type I) in mice. They have found that a single dose of a natural or concentrated serum, when it is given intravenously, is able to cure the infection, even when a bacteriæmia is present, at an interval after the infecting dose of culture which represents one-quarter of the mean death-time of the control mice. As might be expected, the curative effect is related to the time of administration of the serum, so that, for example, a dose of serum which is adequate to exert a curative effect when given 12 hours after the infecting dose must be increased 100 times in order to be effective when the serum is given three hours later. This result has an obvious application to the treatment of acute lobar pneumonia in man by means of a specific serum.

The Toxin-Antitoxin relations of certain members of the diphtheroid group of bacilli.

Dr. Petrie and Dr. McClean have undertaken a study of the toxin-antitoxin relations of certain diphtheroid strains isolated by Dr. M. M. Barratt from the human naso-pharynx and also of the bacillus of Preisz-Nocard (*C. pseudotuberculosis ovis*) which has long been known to be capable of producing a toxin neutralizable to some extent by diphtheria antitoxin. The peculiar strain of diphtheria bacillus described some years ago by Mair has been met with by Dr. Barratt in the course of her work, and has likewise been examined. The experiments that have been carried out indicate that the Preisz-Nocard bacillus is very closely related to the diphtheria bacillus, for its toxin is readily neutralizable by diphtheria antitoxin. A specific antitoxin for the Preisz-Nocard toxin does not, however, seem to be easy to produce. Thus, a horse which received serial doses of a relatively weak Preisz-Nocard toxin developed paralysis of the hindquarters which resembled true diphtheria paralysis. This experience is in agreement with other evidence which has been obtained at Elstree and makes it uncertain whether the toxin formed by the Preisz-Nocard bacillus is antigenic in the strict sense of the term.

The bacillus first described by Mair produces a toxin that is neutralizable by diphtheria antitoxin, but the experimental evidence obtained by Dr. Petrie and Dr. McClean gives reason for doubting whether this organism is a true diphtheria bacillus.

Three diphtheroid strains which were isolated by Dr. Barratt from throat-swabs have been found to fall into a quite different group, since the toxin formed by them possesses none of the characters of diphtheria toxin and is not neutralized by diphtheria antitoxin. Inoculation of the toxin produced by these strains into the skin of the rabbit causes characteristic lesions, whereas this procedure is without effect in the guinea-pig. A horse has been immunised with the toxin of one of the strains, and has furnished an antitoxin which is capable of preventing the development of the skin lesions.

The work as a whole indicates: (1) that diphtheroid strains exist whose kinship to the true diphtheria bacillus is so close as to suggest the possibility that they are variants of it, and (2) that toxigenic diphtheroids are occasionally found in the upper respiratory tract of man which bear no relationship to the diphtheria bacillus.

Experimental work upon the Meningococcus and upon the production of Anti-meningococcus Serum.

The prevalence of cerebro-spinal fever in this country has provided an opportunity for reviewing the problems connected with the production of effective sera for the treatment of the disease. At the present time there are no satisfactory methods by means of which the virulence and antigenic quality of different types and strains of the meningococcus may be compared, nor is there any acceptable laboratory test for estimating the therapeutic efficacy of the specific sera. Dr. Morgan and Dr. McClean are investigating the antigenic potency of freshly isolated strains, kindly supplied by Dr. W. M. Scott of the Ministry of Health laboratories, and are attempting to follow changes that may occur in this respect when the organisms are subjected to varying conditions of cultural maintenance. Thus, for example, a comparison is being made between freshly isolated strains and strains that have been grown for many years in artificial culture media.

Dr. Petrie and Dr. McClean are engaged upon an inquiry into the characters of the so-called endotoxin of the meningococcus. The work is directed towards obtaining the toxin with a reasonable degree of certainty by extraction methods, in order that experiments may be carried out on the nature of the toxin and its relation to antimeningococcus serum. The relatively feeble toxicity of meningococcal suspensions and extracts, the heat-stability of the toxin, and the difficulty of obtaining potent filtrates of toxic suspensions have been noted, and the observations in general are in agreement with those of Gordon and other investigators. The resistance of the toxin to physical and chemical agents that are known to modify or destroy diphtheria and tetanus toxin points to some fundamental difference in molecular structure.

A specific precipitin reaction associated with bacterial growth on Agar Plates.

Dr. Petrie has made a number of observations upon a specific precipitin reaction which is demonstrable when varieties of "smooth" bacteria are grown on agar to which the corresponding specific serum has been added. After growth has proceeded for a day or two a halo appears round the colonies, apparently due to a specific precipitate that is formed by the interaction of the bacterial polysaccharide and the antibody. The reaction has been obtained with the pneumococcus (Type I.), *B. dysenteriae* (Shiga), and Type I. and Type III. meningococcus. The halo may assume the form of concentric rings, which are reminiscent of the Liesegang rings. The corresponding "rough" cultures do not appear to give the characteristic reaction. This technique may prove to be useful in differentiating cultures whose smooth or rough character is not readily perceptible on ordinary culture media.

An Investigation of the polysaccharides of *B. dysenteriae* (Shiga.)

Dr. Morgan has continued his work on the polysaccharide substances of *B. dysenteriae* (Shiga) and has made use of certain refinements in the technique of isolation and purification. Fractional precipitation of the crude polysaccharide preparations with acetic acid has yielded the specific polysaccharide free from accompanying non-specific polysaccharides. The purified specific substance $[\alpha]_{5461} + 107^\circ$ contains 1.6 per cent. nitrogen and gives precipitation with the homologous immune serum up to a dilution of 1 in 12,000,000. A benzoyl derivative $[\alpha]_{5461} + 80^\circ$ (in acetone) and an acetyl derivative $[\alpha]_{5461} + 84^\circ$ (in acetone) of the specific polysaccharide have been prepared. Hydrolysis of these derivatives with potassium hydroxide yields the specific substance unchanged in its chemical and immunological properties. Prolonged treatment of the specific polysaccharide with nitrous acid fails to liberate the nitrogen and does not destroy the specific immunological properties of the substance. The intravenous inoculation of as little as 0.02 mgm. of the purified specific substance produces a typical and fatal anaphylactic shock in guinea-pigs that have been passively sensitized with the homologous antibacterial serum. A nitrogen-free non-specific polysaccharide $[\alpha]_{5461} - 47^\circ$ has also been isolated from Shiga's bacillus. The absence of this polysaccharide from the uninoculated culture medium makes it appear probable that this substance is a true somatic constituent of the bacillus or is a product of its metabolism. The nature of the acid hydrolysis products will be investigated as soon as a sufficient amount of the purified polysaccharides has accumulated. A mould which has not yet been identified has been found to be capable of rapidly destroying the activity of the specific polysaccharide. Dr. Morgan is attempting to isolate from this mould the enzyme which causes hydrolysis of the specific substance.

The concentration of Anti-Plague Serum.

Dr. Morgan is co-operating with Dr. B. D. P. Naidu (Bombay) in devising a method for the concentration of the antibodies that are present in the serum of buffaloes, bulls and sheep which were hyperimmunised by Dr. Naidu in Bombay with living virulent plague cultures.

The distribution of the "O" Antibodies for *B. welchii* in an immune horse serum.

During the past year a horse has been immunised with the thermostable "O" antigen of *B. welchii*. With a view to the preparation of a concentrated antibacterial serum for therapeutic use in infections with *B. welchii* in man, Dr. Morgan, in collaboration with Dr. Felix, has investigated the distribution of the antibodies in the various proteins of the serum of this horse.

The action of testicular extract on Cell permeability.

Dr. McClean and Dr. Morgan have continued the study of the diffusible substance which Dr. McClean has shown to be present in extracts of mammalian testicle and in the spermatozoa. They have obtained a sample of purified extract which is active in high dilution, and which is protein-free and heat-stable. Pressure of other work has obliged them to postpone the analysis, but they hope to prepare a further supply of the purified material and to proceed with its chemical examination.

Early last year Dr. McClean carried out preliminary experiments with herring ova which indicated that the permeability of the cell membrane is increased by the action of this substance. Alterations of permeability in the ovum are known to occur at fertilisation, and it was therefore felt that the observations should be extended. Through the kindness of the University of London, Dr. McClean was able to enjoy the hospitality of the Marine Biological Laboratory, Plymouth, last August and to co-operate with Mr. J. A. Hobson, of the Department of Zoology, Edinburgh, who was engaged there upon problems of fertilisation. The supply of suitable marine material proved unfortunately to be scanty owing to the lateness of the season and the unfavourable weather. However, some observations were made on the effect of testicular extract upon the fertilisation time, the swelling and the cleavage rate of ova of *Thalassema neptuni*, *Psammechinus miliaris*, and *Holothuria*. The permeability of *Psammechinus* ova to neutral red at varying hydrogen ion concentrations was also investigated. No definite or constant effect of the extract from mammalian tissue or from the sperms of marine animals could be demonstrated on any of the ova tested; but in view of the inadequate experimental conditions, further work at a more favourable season with the aid of an improved technique may be worth undertaking.

Pneumococcal infection in Guinea-Pigs.

Sporadic pneumococcal infections in the breeding-stock of guinea-pigs at Elstree have been noted during the past few years. Professor Neufeld is familiar with this disease in Berlin and has ascertained that all the strains isolated by him belong to a single type. Dr. F. Griffith (Ministry of Health Laboratory) has found that these strains agglutinate with the anti-pneumococcus serum Type XIX., as classified by the co-workers of Dr. Park in New York, which strain is occasionally met with also in the

pneumonias of children. Dr. Griffith kindly examined a few strains that had been isolated from the Elstree stock of guinea-pigs, with the result that they also proved to be Type XIX. A specific agglutinating serum has been prepared by Dr. Petrie, and up to the present every strain of pneumococcus isolated from the stock has conformed to this type. The identity of the Elstree and Berlin strains suggests that the infection, wherever it may be found, is essentially a homogeneous one, and raises the problem of the relationship of the human and animal strains. An investigation of the degree of susceptibility of the guinea-pig to the various types of pneumococcus of human origin may provide the key to its solution.

DEPARTMENT FOR THE STUDY AND PREPARATION OF ANTI-VARIOLOUS VACCINE.

Reference was made in last year's report to Dr. A. B. Green's experiments in connection with the filtration of vaccinia virus and the extension of these in certain directions by Dr. G. Eagles, at Chelsea. In view of the entire freedom of these filtrates from ordinary lymph-contaminants, it is desirable to secure information regarding their stability under various conditions of storage. The matter is of considerable theoretical, if not at the moment, practical interest and Dr. Green is giving it his attention as time permits.

NATIONAL COLLECTION OF TYPE CULTURES.

During the year the number of cultures of bacteria and fungi distributed to workers at home and abroad again exceeded 5,000 and over 200 new types have been deposited for maintenance in the collection.

The health of the Curator, Dr. R. St. John Brooks, happily now restored, unfortunately broke down in June, 1931, and necessitated his wintering abroad. The brunt of the work of maintaining the collection has consequently fallen on Miss M. Rhodes with the assistance of Mrs. R. Barnes.

The Third Edition of the Catalogue of the Collection appeared in June of last year.

GENERAL AND FINANCIAL.

The Accounts and Balance Sheet for the year ending December 31st, 1931, show balances to the credit of the Pension Fund of £27,311 2s. 0d.; of the Contingency Fund of £14,228 18s. 1d.; of the Sinking Fund of £21,578 14s. 11d., and of the Capital Fund of £509,262 1s. 6d. The balance of income over expenditure of the Pension Fund, viz., £966 9s. 0d., has this year been transferred to the General Fund, for the part payment of premiums on the Federated Superannuation System policies of the staff. The excess of income over expenditure of the General Account, viz., £18,091 5s. 6d., has again been utilised in writing down the value of certain investments, which still show a depreciation.

New investments during the year have been :—

For the General Fund: £13,000 4% Consolidated Stock and £1,000 5% War Stock, 1929-47.

For the Sinking Fund: £1,600 4½% Conversion Stock, 1940-44.

The income from the sale of the Institute's products during the year 1931 was £34,695 0s. 6d. After adjustment of the stock of Sera on hand at the beginning and end of the year, income from this source appears in the accounts as £35,186 8s. 3d. Sales of Bacterial Vaccines, Vaccine Lymph, and Diagnosis and Investigation Fees show an anticipated decrease, while sales of Sera show an increase compared with last year.

The total expenditure for the year was £41,205 14s. 2d. against £44,401 10s. 3d. in 1931. Serum and Vaccine Lymph Departments' Expenses, Water and Biochemical Laboratory Expenses, Alterations and Repairs and Library Expenses show an increase, and Salaries and Wages, Gas, Water and Fuel, Bacteriological Laboratory Expenses, Animals and Animal House Expenses and Forage a decrease, compared with last year.

In conclusion, the Governing Body desires to express its appreciation of the devoted co-operation of the Director and all members of the Staff in carrying out the work of the Institute.

WILLIAM BULLOCH,

Chairman of the Governing Body.

BALANCE SHEET

AND

ACCOUNTS.

Dr.

The Lister Institute

BALANCE SHEET

	£	s.	d.	£	s.	d.
To CREDITORS				2,578	10	7
To PENSION FUND—						
As per Account at 31st December, 1930.. .. .				27,311	2	0
To JENNER MEMORIAL RESEARCH STUDENTSHIP FUND—						
As per Account at 31st December 1930	7,895	13	1			
Add Amount transferred from Income and Expenditure Account, 1931 ..	261	1	10			
				8,156	14	11
To CONTINGENCY FUND—						
As per Account at 31st December 1923				14,228	18	1
To SINKING FUND to 31st December 1931				21,578	14	11
To CAPITAL FUND to 31st December 1931—						
Balance of Income and Expenditure Account to 31st December 1930	154,442	1	11			
Donations, &c., received to date from the following:—						
Dr. Ludwig Mond (1893)	2,000	0	0			
The Berridge Trustees (1893/98)	46,379	10	1			
The Grocers' Company (1894)	10,000	0	0			
Lord Iveagh (1900)	250,000	0	0			
Lord Lister's Bequest (1913) as per Account at 31st December, 1923	18,904	5	8			
William Henry Clarke Bequest (1923 6)	7,114	5	7			
Other Donations (1891-1926)	20,421	18	3			
				509,262	1	6

WILLIAM BULLOCH, *Chairman.*G. W. ADDISON, *Hon. Treasurer.*

£583,116 2 0

REPORT OF THE AUDITORS

We have audited the above Balance Sheet. We have obtained all the information and explanations we have required. being held by the Institute on their behalf. In our opinion, such Balance Sheet is full and fair, and properly drawn and the explanations given to us and as shown by the books of the Institute.

London, 28th April, 1932.

of Preventive Medicine.

31st DECEMBER, 1931.

Cr.

By CASH—						£	s.	d.	£	s.	d.
At Bankers:	Deposit Account	..	..	..	..	4,000	0	0			
	Current Accounts	..	..	..	..	13,275	17	6			
In hand	..	..	..	..	..	50	6	10	17,326	4	4
By INVESTMENTS, GENERAL FUND (at cost, less amounts written off)—											
£63,000	4 per cent. Consolidated Stock	..	..	..	..	55,474	2	0			
£43,000	4½ per cent. Conversion Stock, 1940-44	..	..	..	..	41,702	3	8			
£17,000	5 per cent. Conversion Stock, 1944-64	..	..	..	..	15,997	0	7			
£41,000	4 per cent. Funding Stock, 1960-1990	..	..	..	..	34,276	8	3			
£21,000	5 per cent. War Stock, 1929-1947	..	..	..	..	18,959	7	2			
£37,000	Local Loans 3 per cent. Stock	..	..	..	..	20,829	1	7			
£3,000	Port of London 4 per cent. B. Stock	..	..	..	..	2,686	17	7			
£1,000	Dominion of Canada 4 per cent. Registered Stock, 1940-1960	..	..	..	..	928	4	6			
£2,000	Cape of Good Hope 3½ per cent. Consolidated Stock, 1929-49	..	..	..	..	1,802	12	0			
£23,000	Cape of Good Hope 3 per cent. Consolidated Stock, 1933-1943	..	..	..	..	23,850	0	0			
£25,000	Natal 3 per cent. Consolidated Stock, 1929-1949	..	..	..	..	21,400	0	0			
£25,000	New South Wales 3 per cent. Inscribed Stock, 1935	..	..	..	..	22,900	0	0			
£2,000	New South Wales 4 per cent. Inscribed Stock, 1943-62	..	..	..	..	1,882	3	4			
£2,900	New South Wales 5½ per cent. Inscribed Stock, 1922-3	..	..	..	..	2,897	16	0			
£25,000	New Zealand Government 3 per cent. Inscribed Stock, 1945	..	..	..	..	22,114	0	0			
£26,100	South Australian Government 3 per cent. Consolidated Stock, 1916 or after	..	..	..	..	16,800	0	0			
£600	Union of South Africa 4 per cent. Consolidated Stock, 1943-1963	..	..	..	..	594	2	0			
£25,000	Victorian Government 3 per cent. Consolidated Inscribed Stock, 1929-1949	..	..	..	..	19,800	0	0			
£700	Western Australia Government 4 per cent. Inscribed Stock, 1942-1962	..	..	..	..	698	7	0			
£20,000	Southern Railway Preferred Ordinary Stock	..	..	..	..	13,500	0	0			
£6,200	London & North Eastern Railway 3 per cent. Debenture Stock	..	..	..	..	3,961	0	0			
£5,000	Great Central and Midland Railway Joint Committee 3½ per cent. Guaranteed Stock	..	..	..	..	3,623	0	0			
£353	London & North Eastern Railway 4 per cent. First Guaranteed Stock	..	..	..	..	499	11	0			
£8,680	London, Midland & Scottish Railway 4 per cent. Preference Stock	..	..	..	..	7,960	0	0			
£15,625	London, Midland & Scottish Railway 4 per cent. Preference Stock, 1923	..	..	..	..	11,300	0	0			
£18,750	London & North Eastern Railway 4 per cent. First Preference Stock	..	..	..	..	13,028	6	7			
£25,000	East Indian Railway 3 per cent. New Debenture Stock	..	..	..	..	13,890	0	0			
£661	Madras & Southern Mahratta Railway 4 per cent. Debenture Stock, 1936	..	..	..	..	656	19	7			
£300	Grand Trunk Railway Company of Canada Great Western Borrowed Capital 5 per cent. Perpetual Debenture Stock	..	..	..	..	936	0	0			
£1,937	Grand Trunk Railway Company of Canada 4 per cent. Guaranteed Stock	..	..	..	..	1,733	0	0			
£300	Ontario and Quebec Railway 5 per cent. Permanent Debenture Stock	..	..	..	..	984	0	0			
£2,400	Gas Light and Coke Company Ordinary Stock	..	..	..	..	3,638	0	0			
									401,302	2	5
By INVESTMENTS, SINKING FUND (at cost)—											
£9,600	4½ per cent. Conversion Stock, 1940-44	..	..	..	..	8,806	16	7			
£7,430	4 per cent. Funding Stock, 1960-1990	..	..	..	..	5,850	5	3			
£8,800	3½ per cent. Conversion Stock	..	..	..	..	6,846	2	0			
	Balance uninvested	..	..	..	..	75	11	1			
									21,578	14	11
By INVESTMENTS, JENNER MEMORIAL RESEARCH STUDENTSHIP FUND (at cost)—											
£2,650	Southwark and Vauxhall Water Co. 3 per cent. Debenture Stock "B"	..	..	..	..	2,756	10	0			
£1,596	Southern Railway 5 per cent. Preference Stock	..	..	..	..	2,740	5	0			
£726	11s. 4d. Liverpool Corporation 3 per cent. Stock, 1942, or after	..	..	..	..	556	15	6			
£2,000	4 per cent. Funding Stock, 1960-1990	..	..	..	..	1,797	14	0			
	Balance uninvested	..	..	..	..	305	10	5			
									8,156	14	11
By INVESTMENTS, PENSION FUND (at cost)—											
£22,000	4 per cent. Funding Stock, 1960-1990	..	..	..	..	17,165	3	5			
£13,000	3½ per cent. Conversion Stock	..	..	..	..	10,038	1	5			
	Balance uninvested	..	..	..	..	107	17	2			
									27,311	2	0
(The above Investments, at the market value 31st December 1931, show a depreciation of £63,836.)											
									8,711	14	6
By DEBTORS											
By FURNITURE, FITTINGS, SCIENTIFIC APPARATUS AND BOOKS—											
At cost less depreciation as per account 31st December 1920									2,471	17	2
By EXPENDITURE ON INSTITUTE BUILDINGS AT CHELSEA—											
As per account 31st December 1910, including purchase of freehold site, £6,000									70,916	3	1
By PURCHASE OF FREEHOLD LAND ADJOINING THE "STUDIOS" CHELSEA—											
As per account 31st December 1912									169	6	8
By LEASE OF THE "STUDIOS" CHELSEA, as per last account						1,457	16	9			
Less Amount written off for the year						65	2	0			
									1,392	14	9
By QUEENSBERRY LODGE FARM, ELSTREE—											
Purchase of freehold land and buildings and Expenditure on new buildings—											
As per account 31st December 1912									20,455	10	0
By STOCK OF ANIMALS						513	17	0			
By STOCK OF ANTITOXINS						2,810	0	8			
									3,323	17	3
* Nothing has been charged for depreciation of Furniture, &c. since new purchases made during the year to a greater amount than the estimated depreciation (10%) have been written off.									£583,116	2	0

TO THE MEMBERS.

The Superannuation Scheme for certain of the Staff provides for the Life Policies for the time being in existence up so as to exhibit a true and correct view of the state of the Institute's affairs, according to the best of our information

COOPER BROTHERS & CO.,
Chartered Accountants. Auditors.

Dr. INCOME AND EXPENDITURE ACCOUNTS

INCOME.								£	s.	d.
To Interest and Dividends on General Fund Investments	...	...	...	...	...	...	...	17,827	5	0
To Interest on Sinking Fund Investments	...	...	...	...	...	...	...	966	0	0
To Investigation, Diagnosis and Analysis Fees, &c. ...	...	...	...	...	...	...	...	3,520	5	2
To Sales of Sera, Vaccines, &c., and Stock at 31st December 1931, less Stock at 31st December 1930	...	...	...	...	...	...	...	35,186	8	3
To Rent of Rooms	...	...	...	...	...	...	...	830	12	3
To Pension Fund—excess of Income over Expenditure transferred	...	...	...	...	...	...	...	966	9	0

£59,296 19 8

Dr.

Pension

	£	s.	d.
To Interest on Investments	1,335	0	0

£1,335 0 0

Dr.

Jenner Memorial Research

	£	s.	d.
To Interest and Dividends on Investments	261	1	10

£261 1 10

Preventive Medicine.

for the year ending 31st December, 1931.

Cr.

EXPENDITURE.							£	s.	d.
By Rent, Rates, Taxes and Insurance	...	...	...	...	...	...	1,396	10	3
By Salaries and Wages of Staff	...	...	...	...	...	...	22,365	1	1
By Premiums on Federated Superannuation Policies	...	...	...	...	...	...	1,324	0	11
By Stationery, Printing and Postage	...	...	...	...	...	...	443	16	4
By Printing of Collected Papers	...	...	...	...	...	...	201	14	2
By Office Expenses, Auditors' Fee and Sundries	...	...	...	...	...	...	325	4	5
By Travelling Expenses	...	...	...	...	...	...	28	19	8
By Gas, Water and Fuel	...	...	...	...	...	...	1,331	0	10
By Electric Light and Power	...	...	...	...	...	...	362	9	11
By Nutrition, Protozoological and Experimental Pathology Expenses, including Apparatus	...	...	...	...	...	...	616	11	4
By Bacteriological Laboratory Expenses, including Apparatus	...	...	...	...	...	...	274	7	6
By Vaccine Laboratory Expenses, including Bottles	...	...	...	...	...	...	78	14	7
By Water and Bio-chemical Laboratory Expenses, including Apparatus	...	...	...	...	...	...	474	7	1
By Serum and Vaccine Lymph Laboratories Expenses, including Apparatus and Bottles	...	...	...	...	...	...	4,406	11	0
By Culture Media	...	...	...	...	...	...	88	15	0
By Animals	...	...	...	...	...	...	1,213	17	9
By Animal House Expenses and Forage	...	...	...	...	...	...	1,846	18	4
By Alterations, Repairs and Renewals, including Workshop Expenses	...	...	...	...	...	...	2,359	3	6
By Library Expenses	...	...	...	...	...	...	442	3	9
By General Stores	...	...	...	...	...	...	181	1	2
By Bad Debts	...	...	...	...	...	...	2	10	0
By Amount written off Lease of the "Studios," Chelsea	...	...	...	...	...	...	65	2	0
By Sinking Fund ($\frac{1}{2}$ % per annum on Cost of Buildings and Interest on Investments)	...	...	...	...	...	...	1,376	13	7
By Amount written off General Fund Investments	...	...	...	...	...	...	18,091	5	6
							£56,296	19	8

Fund.

Cr.

	£	s.	d.
By Pensions	368	11	0
By Balance, transferred to General Income and Expenditure Account	966	9	0
	£1,335	0	0

Studentship Fund.

Cr.

	£	s.	d.
By Income, transferred to Balance Sheet	261	1	10
	£261	1	10

SCIENTIFIC PAPERS PUBLISHED FROM THE LABORATORIES OF THE INSTITUTE DURING THE YEAR.



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- " " *VARIATION OF BACTERIA. Extrait du 1^{er} Congres International de Microbiologie, Paris, 1930.*
- AYKROYD, W. *THE EFFECT OF PARBOILING AND MILLING ON THE ANTINEURITIC VITAMIN (B₁) AND PHOSPHATE CONTENT OF RICE. Journal of Hygiene, Vol. XXXII., 1932.*
- BALDWIN, E. *(See NERDHAM, DOROTHY.)*
- BRACEWELL, MARY F. AND *VITAMIN C IN THE ORANGE AND THE GRAPE FRUIT. The Biochemical Journal, Vol. XXV., 1931.*
ZILVA, S. S.
- BROOKS, R. ST. JOHN *THE ANEROBIC ACTINOMYCES. System of Bacteriology, Vol. 8, 1932.*
- CRANE, M. B. AND ZILVA, S. S. ... *THE ANTISCORBUTIC VITAMIN OF APPLES, IV. Journal of Pomology and Horticultural Science, Vol. IX., 1931.*
- CZARKOWSKA-GLADNEY, J. *SOME DATA CONCERNING THE INFECTIVITY, SURVIVAL AND POWERS OF*
AND HURST, E. W. ... *DIFFUSION OF THE VIRUS OF "LOUPING-ILL." British Journal of Experimental Pathology, Vol. XII., 1931.*
- DENNISON, MARJORIE *(See KORENCHESKY, V.)*
- EAGLES, G. H. AND *VACCINIA AND THE PASCHEN BODY: INFECTION EXPERIMENTS WITH*
LEDINGHAM, J. C. G. ... *CENTRIFUGALISED VIRUS FILTRATES. The Lancet, Vol. I., 1932.*
- EDWARDS, J. T. *SUSCEPTIBILITY OF DIFFERENT SPECIES OF ANIMAL (TO FOOT-AND-MOUTH DISEASE): FURTHER EXPERIMENTS WITH HEDGEHOGS.*
- " " *THE RESPIRATORY EXCHANGE OF THE FOOT-AND-MOUTH VIRUS: ITS SIGNIFICANCE IN DETERMINING THE CONDITIONS REQUIRED FOR THE SURVIVAL AND GROWTH OF THE VIRUS. Further Progress Report of the Foot-and-Mouth Disease Research Committee. The Ministry of Agriculture and Fisheries, London, 1931.*
- FAIRBROTHER, R. W. AND *OBSERVATIONS ON THE PRODUCTION OF ANTIPOLIOMYELITIS SERUM IN*
MORGAN, W. T. J. ... *HORSES AND THE DISTRIBUTION OF THE ANTIBODY AMONG THE SERUM FRACTIONS. The Lancet, Vol. II., 1931.*
- FIXSEN, MARGARET A. BOAS... ... *THE EFFECT OF DESICCATION UPON THE NUTRITIVE PROPERTIES OF EGG-WHITE. II. The Biochemical Journal, Vol. XXV., 1931.*

- GULLAND, J. M. ... THE SPERMICIDAL ACTIVITY OF QUINONES AND QUINOLS. *The Biochemical Journal*, Vol. XXVI., 1932.
- GRAETZ, DORIS M. ... (See KORENCHEVSKY, V.)
- HARDEN, A. ... ALCOHOLIC FERMENTATION. THE EARLY STAGES OF FERMENTATION IN THE YEAST CELL. *Ergebnisse der Enzymforschung*. I. Leipzig, 1932.
- HUGGINS, C. B. ... THE PHOSPHATASE ACTIVITY OF TRANSPLANTS OF THE EPITHELIUM OF THE URINARY BLADDER TO THE ABDOMINAL WALL PRODUCING HETEROTOPIC OSSIFICATION. *The Biochemical Journal*, Vol. XXV, 1931.
- HURST, E. W. ... THE EFFECTS OF THE INJECTION OF NORMAL BRAIN EMULSION INTO RABBITS, WITH SPECIAL REFERENCE TO THE AETIOLOGY OF THE PARALYTIC ACCIDENTS OF ANTIRABIC TREATMENT. *The Journal of Hygiene*, Vol. XXXII., 1932.
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- " " ... (See CZARKOWSKA-GLADNEY, J.)
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THE LISTER INSTITUTE
OF
PREVENTIVE MEDICINE

Report of the Governing Body,
1933.

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

May 24th, 1933.

The Lister Institute of Preventive Medicine,

CHELSEA BRIDGE ROAD, LONDON, S.W. 1.
ELSTREE, HERTS; MARAZION, CORNWALL.

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(Medical Research Council.)

Curator:

R. ST. JOHN BROOKS, M.A., M.D., D.P.H.

Assistant Curator:

MABEL RHODES.

**Recognised Teacher of the University of London.*

ANNUAL GENERAL MEETING

OF

The Lister Institute of Preventive Medicine,

May 24th, 1933.

REPORT OF THE GOVERNING BODY.

The Governing Body has the honour to present the Institute's 39th Annual Report.

GOVERNING BODY.

On June 13th, the Hon. Sir William Henry Goschen was appointed by Lord Moyne as one of his representatives on the Governing Body in succession to the late Lord Knutsford.

At the meeting held last year, the Council re-elected Professor W. Bulloch, Professor A. E. Boycott and Professor A. Harden as its representatives on the Governing Body until December 31st, 1933.

COUNCIL.

At the Annual General Meeting last year the three members of Council retiring by rotation were The President of the Royal College of Surgeons, Professor W. W. C. Topley and Professor W. Bulloch. The President of the Royal College of Surgeons and Professor Bulloch were each re-appointed and Professor H. B. Maitland succeeded Professor Topley as the representative of the Victoria University of Manchester.

Vacancies created by the deaths of Sir David Bruce, Professor W. E. Dixon, Lord Knutsford and Sir William Simpson were filled by the appointment of Dr. J. A. Arkwright, as representative of the Royal Society, Sir Humphry D. Rolleston, as representative of the British Medical Association and of Professor W. W. C. Topley and Dr. Harriette Chick as representatives of the Members of the Institute, respectively.

The members of Council, who, in accordance with the Articles of Association, retire this year by rotation, but who are eligible for re-election, are Sir Walter M. Fletcher, one of the representatives of the Members of the Institute, Professor Georges Dreyer, the representative of the University of Oxford and Dr. John Fawcett the representative of the University of London.

MEMBERS.

The Governing Body regrets to announce the death, during the year, of Dr. F. J. Allan (late Medical Officer of Health, Westminster) a member of the Institute since 1894.

STAFF.

Dr. E. Weston Hurst, whose investigations on behalf of the International Committee for the Study of Infantile Paralysis were completed during the year, was on October 1st appointed to the staff with the title of Reader in Experimental Pathology in the University of London, and on the same date Dr. Ida Smedley-MacLean, a recognised teacher of the University of London, was appointed to the staff of the Department of Biochemistry.

Leave of absence was granted to Dr. E. Weston Hurst to enable him to study for some time at the Rockefeller Institute, Department of Animal Pathology, by invitation of the Rockefeller Institute, and to Dr. Harriette Chick to proceed to the United States of America and Australia with a view to visiting centres of nutrition study.

Miss A. H. Rosenheim, Grocers' Company Research Student, Dr. T. F. Macrae, Research Student in Biochemistry and Dr. C. Russell Amies, Research Fellow in Bacteriology, have continued to hold their respective appointments during the year. Dr. L. A. Elson was appointed Jenner Memorial Research Student in May last, and Dr. M. H. Finkelstein (late Lecturer in Bacteriology, Edinburgh University) to a second Research Fellowship in Bacteriology in March, 1933.

The Morna Macleod Research Studentship, the endowment of which is due to the generosity of Mr. and Mrs. W. A. Macleod has been held by Mr. R. O. Jones since October 1st.

RESEARCH WORK.

Before surveying the scientific work carried out during the year in the various departments, the Governing Body desires to record its appreciation of the continued co-operation it has enjoyed with the Medical Research Council and the Department for Scientific and Industrial Research. Salaries of the staff of the National Collection of Type Cultures, of Miss Hume and her assistants, of Professor Korenchevsky and his assistants and of Dr. Fixsen are furnished by the Medical Research Council, which body, also, since April of this year has made itself responsible for the salaries of Dr. Zilva and his assistants, owing to the lapse of the special subsidy to the Medical Research Council provided by the Empire Marketing Board for the purpose of Dr. Zilva's investigations.

Accommodation for Miss Hume, Professor Korenchevsky, Dr. Zilva and the National Collection of Type Cultures together with expenses of the researches of the first three named are provided by the Institute.

The Grant provided by the Department for Scientific and Industrial Research for the work of Dr. Smedley-MacLean and her assistants has been reduced during the past year and will terminate finally in September, 1933.

DEPARTMENT OF BACTERIOLOGY, SEROLOGY AND EXPERIMENTAL PATHOLOGY.

Studies on Viruses.

Vaccinia and Variola. That the elementary bodies demonstrable in the lesions of vaccinia represent the actual virus agents, would now appear to be fairly completely established.

Professor Ledingham has carried out a further series of titrations of the agglutinins for elementary bodies in the sera of vaccinated rabbits observed over prolonged periods and has noted the immediate response in agglutinin-development to fresh doses of virus given at lengthy intervals. This line of work has been extended in several directions by Dr. C. R. Amies (Research Fellow in Bacteriology).

Dr. Amies has found that while pure suspensions of the elementary bodies of vaccinia are readily agglutinated by antivaccinial serum from man, monkey, or rabbit, the serum of patients convalescent from variola has failed to give any uniform agglutination reaction with such suspensions. A suspension of variola elementary bodies was, therefore, prepared from the skin pulp of *M. rhesus* monkeys inoculated with human variola virus. For this purpose two strains of virus were used, a highly virulent strain obtained from Calcutta, and a relatively avirulent strain from a typical case of the mild small pox (alastrim) which occurs at the present time in England. Elementary body suspensions obtained from both of these strains were agglutinated by sera from patients convalescent from either the English or the Indian smallpox. Antivaccinial serum obtained from rabbits either fails to agglutinate these variola elementary body suspensions, or agglutinates them to a lower titre than that given by a vaccinial suspension. A strain of cowpox obtained from a case of "milker's dermatitis" has also been studied by similar methods. A suspension of cowpox elementary bodies is agglutinated by the homologous antiserum and also by antivaccinial serum. Human antivariola serum uniformly failed to agglutinate this suspension, but a hyperimmune antivariola serum, prepared by giving repeated injections of the virus to a monkey, agglutinated the cowpox suspension to a fairly high titre. This same antiserum also agglutinated a vaccinia suspension to approximately the same titre. Variola virus can be readily changed into a strain indistinguishable from vaccinia serologically. Human variola virus was inoculated cutaneously into a monkey. The monkey skin pulp, removed on the fifth day, was injected intratesticularly into a rabbit, when a reaction similar to that given by a neurotesticular strain of vaccinia was produced. After three transfers through rabbit testis this virus was found to produce a severe reaction when rubbed into the skin, and its virulence is being easily maintained by passage. An elementary body suspension prepared from this strain was readily agglutinated by known antivaccinial and anti-cowpox sera, but failed to show a reaction with human antivariola serum. It would appear, therefore, that variola and vaccinia are antigenically very closely related, the differences noted being largely quantitative rather than qualitative.

Varicella. Many years ago Aragao and Paschen reported the finding of elementary bodies in human varicella fluid. This observation has been fully confirmed by Dr. Amies. These bodies are a little smaller than those of vaccinia-variola, otherwise they resemble the latter in appearance and staining characteristics. They are found in enormous numbers in the clear fluid taken from early vesicles, but rapidly disappear when the contents of the vesicles become pustular.

By employing a somewhat similar technique to that used in the vaccinia agglutination reaction it has been possible to procure pure suspensions of these bodies in formol-saline and to demonstrate that such suspensions are agglutinated specifically by convalescent chicken-pox serum. Of 30 sera so far examined, 27 have given a positive agglutination reaction. Agglutinins have been demonstrated in the blood as early as the fifth day following the appearance of the eruption, and reach a maximal titre at about the tenth day. They can still be found two months later.

Attempts to infect rabbits intratesticularly with human varicella virus have so far yielded unsatisfactory results. These attempts are being continued, however, since it is highly desirable to have a laboratory strain of the virus.

This new finding, based on serological evidence, makes it highly probable that the elementary bodies found in chickenpox represent the actual aetiological agents.

The Public Health Department of the London County Council has very kindly given Dr. Amies facilities for securing variolar and varicellar material from their Fever hospitals.

Cultivation of Vaccinia Virus in Cell-Free Media. Reports of successful experiments in this direction by Dr. G. H. Eagles and collaborators have been published, and the work is being actively continued. The fundamental problem of obtaining a medium unquestionably free from cell debris while at the same time retaining its nutrient value is of great importance. While filtration of the medium through candle filters would tend to solve the difficulty it has been found that by its use the fine particles, derived probably from cells or nuclei, are entirely removed. In view of the great hesitation of vaccine virus to propagate itself in a cell-free medium, it seemed advisable to retain in the medium all possible cell material short of actual whole cells. In a new series of sub-cultures fresh rabbit kidney was treated as in previous experiments with 9 per cent. saline and ground in a mortar to a creamy consistency. After restoring normal saline strength the material was spun for 30 minutes at about 10,000 revolutions per minute. The supernatant, removed with great care from the cell deposit, and mixed with fresh rabbit serum and Tyrode's solution, constituted the culture medium.

Stained smears of this supernatant fluid showed enormous quantities of granular material but no definite cell structures. With this material a fresh strain of neuro-testicular virus was propagated through seven sub-cultures with an increase of 30° over the original inoculum. In a short series of sub-cultures in which the extract was spun for a second period of 30 minutes at a speed of about 12,000 revolutions per minute multiplication of virus was obtained but with greater irregularity. Examination of the second supernatant and the final deposit showed that most of the granular material had been removed by the second period of centrifugalisation.

Some preliminary attempts to cultivate the virus in filtered kidney extract have so far been unsuccessful.

It is hoped to investigate the possibility of obtaining pure cultures of washed elementary bodies from filtrates of vaccine lymph. For this purpose cell-free medium should be most useful. It is interesting to speculate on the nature of reproduction of the elementary bodies in vaccinia and other viruses and some experiments are being carried out to ascertain whether these bodies are capable of reproduction on the surface of specially prepared solid media.

Louping-ill: cultivation *in vitro*. Mr. D. W. Henderson (Beit Memorial Research Fellow) has commenced a study of the properties of "louping-ill" virus grown under *in vitro* conditions.

Using a mouse strain of brain virus and a medium consisting of whole mouse embryo tissue, sheep plasma and Tyrode solution, the virus has been passed through seven serial subcultures. The tissue, with adsorbed virus, is grown in Carrel "D" flasks, incubated at 37°C. It is estimated that over seven subcultures the virus increase over the original inoculum has been 3.8×10^4 .

The presence of virus in all material has been tested by the intracerebral inoculation of mice and the subsequent appearance of the clinical syndrome after an incubation period ranging from 4-10 days.

In each subculture, with a single exception, the virus has shown a regular increase and, so far as it has been possible to test the virus content of various flasks from any one subculture, misses have been few.

In preliminary experiments on the optimum incubation period at 37°C. for virus increase the relatively short period of 48 hours may frequently yield a satisfactory result.

Experiments on the simplification of media for *in vitro* cultivation are now in progress.

Histological examination of the central nervous system of mice which have succumbed to the "culture" virus reveals the characteristic lesions.

The Viruses (so-called) of Pleuropneumonia and Agalactia. Professor Ledingham with the assistance of Miss R. M. Pitt has continued his investigation, by aid of a special impression technique, of the growth cycle on solid media of the filterable but readily cultivable organisms responsible for these diseases. The successive stages in the growth of the highly polymorphic organism of pleuropneumonia have been ascertained with considerable definiteness and it may shortly be possible to attack the problem of its systematic position.

Serological Studies: Antigenic constitution and immunising properties of bacteria.

The Prophylactic Value of Anti-Plague Vaccine. Dr. H. Schütze is continuing his studies upon the antigen concerned in the immunity conferred by anti-plague vaccine. After establishing the importance of the heat-labile envelope antigen which develops most abundantly at higher temperatures such as 37°C., he is investigating methods for the best production of this antigen, and, in particular, whether the vaccine should be grown in a fluid medium in the same way as Haffkine's prophylactic or on a solid medium, as most vaccines are. It may be expected that the latter type, lacking the products of

prolonged growth, will also lack the toxicity which is such an undesirable feature of the broth-grown Haffkine vaccine. Also, in view of the fragility of the envelope antigen which has been seen to be most readily haptenised and destroyed in an alkaline environment, it will be of importance to ascertain the influence of pH not only upon the development of this antigen but also upon its stability when produced.

Dr. Schütze is also proceeding with his studies on the antigenic relationship existing between *B. pestis* and *B. pseudotuberculosis rodentium*.

Anti-dysentery vaccines. The investigations of Miss D. Steabben and Dr. Schütze upon the immunological value of anti-dysentery vaccine prepared from bacteria grown at temperatures higher than 37°C. are proceeding. Such vaccines appear to afford greater protection than those grown at the usual body temperature, but their detoxication by formalin is not easily accomplished, the reason for which is not at the moment clear.

Spore-bearing Anaerobes. *C. chauvoei*. Mr. Henderson has completed his study of the antigenic structure and immunising properties of *C. chauvoei* of bovine and ovine origin. The findings are embodied in three papers.

All strains tested from various parts of the world were found to possess the same O antigen. The H antigen was found to be uniform among all strains except the English ovine. These latter shared an overlapping H component with the other strains but also possessed a specific H antigen.

The prophylactic value of the O antigen, steamed for two hours at 100°C. was such that guinea-pigs thus immunised withstood 100-1,000 certain killing doses of an infecting suspension activated with CaCl₂. Complete cross protection was demonstrated against all strains tested. With an extension of these experiments to field trial, such sterile, reliable, and innocuous vaccines may lead to improved technique in prophylaxis.

Anti-O sera from two goats immunised respectively with one ovine and one bovine strain, were used for passive protection experiments with mice. One serum protected 60% of mice against 10 certain infecting doses of homologous and heterologous strains while the other serum was less satisfactory, giving only 25% protection. The O agglutinin titre of the two sera reflected their relative value in passive protection and suggested that the O antigen functioning in agglutination was responsible for the production of the protecting immune body.

C. oedematis maligni. The role of the bacillary body in the formalised whole-culture vaccines of the spore-bearing anaerobes is not yet clearly established, although passive protection against infection with *C. oedematis maligni* was demonstrated by Robertson and Felix in 1930 by means of an O immune serum devoid of antitoxin content. Mr. Henderson is conducting experiments on active immunisation against *C. oedematis maligni* using bacillary suspension (O antigen) freed from toxin and rendered sterile by steaming for two hours at 100°C. The results so far show that guinea-pigs can be protected against at least 500 certain infecting doses of an activated suspension. Cross immunity tests are now under consideration.

C. tetani. Mr. Henderson has commenced a study of anti-bacterial mechanisms in *C. tetani* prophylaxis. A polyvalent O antigen prepared from seven strains of *C. tetani* is being supplied to Dr. G. F. Petrie, who has kindly undertaken the immunisation of horses at Elstree for the preparation of a polyvalent anti-O serum. From three horses under preliminary treatment for five months, the one showing the highest content of O antibody, as estimated by agglutination tests, has been selected for continued immunisation. Dr. Petrie is now fractionating the immune serum from this horse for use in the preliminary animal experiments.

Studies on the Typhus Group of Diseases.

Work on various aspects of this subject has been continued by Dr. A. Felix.

Serological Varieties of Typhus.

(a) **Sao Paulo Endemic Typhus.** This is one of the recently studied forms of typhus of particular malignity. Sera from cases of this disease have been tested by Dr. Felix against types of *B. proteus* X. Contrary to the statements of the Brazilian authors these sera were found to differ from those from cases of all the varieties of typhus hitherto tested; they contained group agglutinins for type XK in addition to high titre agglutinins for type X₁₉. The virus of endemic typhus of Sao Paulo is thus shown to represent a serological variety of virus which possesses a main antigen of type X₁₉ and a group antigen of type XK.

(b) **Fièvre boutonneuse of the Mediterranean.** The relationship of this disease to classical typhus has for some years been a matter of controversy, based on the negative results of cross-immunity tests and on the irregular agglutination reactions obtained with *B. proteus* X strains. Felix and Rhodes in 1931 first interpreted these facts as indicating that the virus of "fièvre boutonneuse" is another serological variety of virus which possesses only group antigens in common with the classical typhus virus. Subsequently Durand in 1932 published results of agglutination tests with the serum from cases

of "fièvre boutonneuse" from Tunis which were in complete agreement with this conclusion. Dr. Felix has examined a series of these patients' sera and obtained analogous results. Accordingly, the agglutination of types X_{10} and X_2 in "fièvre boutonneuse" is of the order of group agglutination, whereas the type of the main antigen of this virus is still unknown. Failure to obtain cross-immunity between this virus and that of classical typhus is thus shown to coincide with dissimilarity in the agglutinogenic properties of the two viruses.

Types of *B. proteus* corresponding to local varieties of Typhus. A strain of *B. proteus* has been isolated by Dr. Carvalho Lima of Sao Paulo from the faeces of a healthy child living in the area where Sao Paulo endemic typhus has occurred in recent years. The culture has been diagnosed by Dr. Lima as *B. proteus* X_{10} and has been sent to Dr. Felix for re-examination. The cultural and biochemical properties of this strain were found to be identical with those of X_{10} and the two strains were also indistinguishable by cross-agglutination tests. The Brazilian strain, however, produced in the majority of inoculated rabbits significant group agglutinins for OXK, whereas none of the genuine X_{10} strains isolated in various localities in Eastern Europe and Asia Minor contains any group antigen of the type OXK. The Brazilian strain also possesses a specific H factor in addition to the H antigenic complex which it shares with other X strains. The Lima strain, therefore, represents the type of *B. proteus* which clearly reflects the agglutinogenic properties of the virus of Sao Paulo endemic typhus.

Another *proteus* strain corresponding to a local variety of typhus has been sent to Dr. Felix by Dr. Martin, Federated Malay States. This strain had been isolated from the pus of a case of empyema in a native of the country where tropical typhus of the type KK is endemic. Martin's finding with regard to the O antigen of this strain was confirmed; it is identical with that of strain KK (Kingsbury). On the other hand, the H antigens of the two strains were found to be entirely different.

These results indicate that serological types of *B. proteus* may yet be isolated, which correspond to the still unknown main agglutinogens of the viruses of "fièvre boutonneuse," the tick-bite fever of South Africa and other varieties of typhus. The importance of such *proteus* types is quite obvious, since the present means for diagnosing these diseases by the demonstration of low titre group agglutinins are very unsatisfactory.

Relationship between *B. proteus* X and Typhus Virus.—Attempts have been made to confer upon *B. proteus* X strains some of the properties of typhus virus. Cultures of OX_{10} and OXK, grown in different ways, were injected by various routes into male rats and guinea-pigs. Testicular washings and suspensions of the brain and other organs of these animals were used for serial transmission. The animals were kept on a diet deficient in vitamin A, since such treatment has been shown by Zinsser and Castaneda to enhance the multiplication of *Rickettsia* in animals infected with typhus virus. Neither regular fever curves nor testicular reactions could be produced in rats and guinea-pigs. Testicular washings and suspensions of organs from these passage animals were also injected into rabbits. Significant curves of agglutinin formation for OX_{10} or OXK could, however, not be demonstrated.

Following the work of Mooser, Castaneda and Zinsser on the rôle of the rat louse (*Polypylax spinulosus*) as one of the vectors transmitting typhus virus from rat to rat, experiments were conducted with the view of establishing in rats a "passage virus" through the bite of rat lice which had had an opportunity of sucking the blood of rats injected with cultures of OX_{10} and OXK. These attempts were equally unsuccessful as those already described, although bacteraemia lasting for 24 hours was demonstrated in some of the rats injected with the *proteus* cultures.

Miss Pitt collaborated in the examination of a number of dissected lice and excreta of lice collected at various intervals from *proteus*-infected rats. No indisputable evidence of the presence of *Rickettsia*-like bodies has as yet been obtained.

The Rat as Experimental Animal in the Study of the Typhus Group of Viruses.—The importance of the rat as a reservoir of the virus of endemic typhus has been established beyond any doubt through recent work of American authors. Wild and tame rats at present play an increasingly important rôle in typhus research in various parts of the world. In the course of his experiments Dr. Felix has found that the association between the rat and *B. proteus* is much closer than has been hitherto recognised. Tame rats, when kept on a diet deficient in vitamin A, developed abscesses in various organs from which *B. proteus* could be isolated in pure culture. Suspensions of organs from apparently normal rats, though sterile, occasionally stimulated formation of *proteus* H agglutinins when injected into rabbits. Although no strain of the three types X_{10} , X_2 and XK has been encountered among these *proteus* cultures, yet O agglutinins of significant titres for one or the other of the three types have been found in the serum of normal, tame rats of London stock. These facts constitute a very serious source of error in experimental work with typhus viruses in the rat.

Typhus murinus.—Following the isolation by American workers of typhus virus from wild rats and rat fleas collected in endemic areas, similar observations, though less authenticated, have been reported from Paris and other localities where human cases of the disease are not known to occur. Dr. Felix has examined a number of London sewer rats, so far with negative results only. Incidentally *S. enteritidis* (Gaertner) was isolated from some of these animals. Suspensions of the organs from Gaertner-infected sewer rats, when injected simultaneously into guinea-pigs and young tame rats produced fatal Gaertner infections in the guinea-pigs, while the rats did not react even with rise in temperature.

FOOT AND MOUTH DISEASE RESEARCH.

Dr. J. T. Edwards has continued his work for the Foot and Mouth Disease Research Committee of the Ministry of Agriculture and Fisheries under the supervision of Dr. J. A. Arkwright. He has pursued his search for evidence of persistence of the virus in the urine or blood of guinea-pigs which have recovered from an attack of the disease, but has been unable to demonstrate the existence of carriers.

He has extended his observations on the susceptibility of wild species of rodents. Continuing his work with tame rats, he has found that their susceptibility is very much influenced by diet and varies according to the age and sex and is more uniform amongst members of a single litter than amongst less closely related animals. Tame rats kept on special diets show very different degrees of susceptibility to the disease, and a relative poverty of diet, especially if sufficient to hinder growth, may prevent the appearance of overt signs of the disease. Some of the rats which have been inoculated without any resulting visible lesions may, nevertheless, have acquired immunity. A similar effect has not been observed in guinea-pigs, which very seldom become immune after inoculation with living virus unless definite vesicles have appeared. The most susceptible were growing young rats about three months old, whereas old rats, when inoculated, often apparently escaped infection. Very young rats were usually not visibly affected, but sometimes were found to have become immune.

Endocrinology.

Dr. V. Korenchevsky, in collaboration with Mrs. M. H. Dennison, Professor Myra M. Sampson (Smith College, Northampton, Mass., U.S.A.) and Miss Alice Kohn-Speyer, studied the action and assay of testicular hormone and the mechanism of the action of vitamin A deficiency on various organs and functions.

On Animals for Assay. In the present experiments, results similar to those previously recorded were obtained with a standardised stock of rats prepared for assay in the same way. The comparison of two different stocks of normal untreated animals, one from the Lister Institute, the other from one of the special breeding nurseries, gave considerable differences in body-weight, in weight of prostate plus seminal vesicles and in weight of spleen. It would seem desirable, therefore, that, for International biological standardisation, a definition of standardised stocks should be worked out, as well as the conditions of preparation of the animals, in order that results as nearly comparable as possible should be obtained.

It may be possible to overcome some of the difficulties associated with the assay of testicular hormone by comb growth test, or of oestrin test on rats and mice, if in addition to the use of standardised stocks of animals, kept under standardised conditions, all data which might influence the results were also taken into consideration; e.g., in the assay of testicular hormone, the age at which castration is performed, the interval between castration and test, as well as the weight and age of the animals at the beginning of the test.

The Rat unit of Testicular hormone and the changes produced in castrated rats by the injection of Testicular hormone for a short period. In the previous report, a method of assay of testicular hormone was described in which castrated rats were used as the experimental animals, and the changes in the weight of the prostate with seminal vesicles were suggested as the basis for the estimation of a rat unit of the hormone. Recent experiments have shown that it is possible to use for the assay not only rats belonging to one litter, as was previously suggested, but also rats belonging to different litters, but in the latter case the rats must belong to the same group, in relation to sexual maturity at date of castration and to the time elapsing between castration and commencement of test. In such rats, on the average, the variations in the weights of body fat, sexual, endocrine and other organs are small, so that any changes produced by the testicular hormone are definitely shown.

From the results obtained both the method used and the rat unit suggested seem to be satisfactory for the assay. The rat unit is defined as the minimum daily dose which, when injected twice a day in half-doses during seven consecutive days into at least three litters of rats castrated before the 30th day after birth, will produce, on the average, an increase of 40% in the weight of the prostate with seminal vesicles as compared with the average weight of these organs in the uninjected litter mates.

A comparison made between the rat unit, as defined above, and the capon unit, as assayed in Schering's laboratories, showed these two units to be nearly equal. On the average, a correlation of direct proportion was found between an increase of dose from 1 to 7.5 RU, and the degree of average increase in the weight of the prostate with seminal vesicles and, less sensitively, of the penis.

The changes produced by Testicular hormone injected for a longer period. In order to show more clearly the changes mentioned above, normal and castrated rats were injected with the testicular hormone for a period of three weeks.

Normal young injected rats, as compared with the controls, showed depression of the development of the testes in most cases with small doses and in all cases with large doses. The prostate with seminal vesicles and penis were, in most cases, slightly decreased in weight with small doses, whilst with large doses an increase in weight was obtained together with an acceleration in the rate of involution of the thymus and a slight increase in the weight of the kidney.

No large or constant changes were found in the weights of the other organs or in the body weight. The appetite of the injected normal animals was nearly the same or sometimes less than that of the controls.

In castrated injected rats, as compared with the controls, the following changes indicating a return of the organs towards a normal condition were observed; a large increase in the weight of the prostate with seminal vesicles and of the penis; a slight increase in the weight of the thyroid, an increased speed of involution of the thymus and a return towards normality in the weight of the adrenals. The injections increased the weight of the liver and of the kidneys, stimulated appetite and produced a larger gain in body weight.

As in the short period experiments a correlation of direct proportion was apparent between the increase of dose from 2.5 CU to 5.0 CU and the degree of average increase in weight of prostate with seminal vesicles. With regard to the penis, the approximate direct proportion between the dose injected and the change obtained was found to be no longer valid when the injections were prolonged from one to three weeks, the increase in the penis being much less than that expected. This is explained by the fact that the penis consists of muscular, vascular and connective tissues, the reaction of which to growth stimuli is slower than that of the glandular tissue of the prostate with seminal vesicles. Another important difference is that in castrated rats the degree of atrophy of the penis is much less than that of the prostate with seminal vesicles, the weight of the former being three to four times and of the latter at least 20 times less than that in normal rats.

The checking of growth which would be theoretically expected with the approach to the normal size of the organ would, therefore, be reached much sooner in the case of the penis than in the case of the prostate with seminal vesicles. The penis of castrated animals is, therefore, similar in this respect to the comb in capons, not only in its structure but also in its response to the injections of testicular hormone.

It was also noticed in these experiments that the effect of the testicular hormone injections was proportional to the number of days of injection.

The experiments have thus demonstrated a manifold and powerful influence of testicular hormone on several organs and functions.

The anabolic properties of the hormone, which are essential for the building of tissues and the growth of the organs and of the animal, were made evident by the increase in weight of body, sexual organs, thyroid, liver and kidneys of the injected castrated rats.

The catabolic or desintegrating properties of the hormone were demonstrated by the acceleration of the involution of the thymus and by the decrease in weight of the adrenals.

The Thyroid gland and Iodine deficiency. In experiments with a synthetic diet, from which cod liver oil was absent and iodine not added, the thyroid glands of the rats were enlarged. The addition to such a diet of an iodide in an amount equivalent to that present in cod liver oil prevents enlargement of the thyroid. Deficiency of iodine is, therefore, followed by hypertrophy of the thyroid gland ("iodine deficiency goitre").

The Mechanism of the Influence of Vitamin A and its "Anabolic" Function.

The factors responsible for the pathological condition leading to the failure of normal growth and changes in the sexual and other organs in animals kept on a vitamin A deficient diet are not definitely known. Experiments have, therefore, been performed by Dr. Korenchevsky and his co-workers to determine whether these changes are produced by any of the following factors:—

- (a) the direct influence of vitamin A deficiency or
- (b) the accompanying reduction in appetite or
- (c) a pathological condition of metabolism and of absorption of food from the alimentary canal in the deficient rats.

Paired feeding experiments were performed, in which the control rats received the same amount of food as was consumed by the deficient rats.

The absorption of food from the alimentary canal was found to be normal during the greater part of the deficiency, being decreased only during the short period preceding the death of the animal. The condition of the mechanism of absorption was not responsible, therefore, for the pathological changes in the deficient animals.

It was found that both the special direct influence of vitamin A deficiency and of the decreased appetite were the chief factors concerned in the changes produced by the deficiency in growth of the rats, in fat deposition and in the changes in some of the organs.

The disturbance in the nitrogenous metabolism, which is increased during the whole period of the deficiency, was due to the direct influence of the vitamin A deficiency.

About two-fifths of the loss of body weight would seem to be due to the loss of appetite, while three-fifths would seem to be caused by some other direct influence of the vitamin A deficiency. These proportions were found to be reversed in the case of the decreased fat deposition in the body.

At the same time it was found that one unit of the vitamin A-deficient diet produced a much smaller increase in body weight than was produced by the same unit of a complete diet. This fact explains the chief direct influence of vitamin A deficiency namely, that vitamin A plays an important part in the constructive "anabolic" process of the metabolism of the organism. Vitamin A seems, therefore, to have in addition to an "appetite-producing" principle an "anabolic principle," both of which are essential for the building of the tissues, for increase in body weight and for growth of the animal.

The direct influence of the vitamin A deficiency and not the accompanying loss of appetite is the chief cause of the decrease in size of the seminiferous epithelium of the testes, previously described. These changes are similar to those which occur in the cryptorchid testes and in the testes of animals kept on a vitamin E-deficient diet.

Oedema of the testes was also noted in most of the vitamin A-deficient rats, sometimes starting at the beginning of the deficiency.

An abundant supply of vitamin E did not prevent the degeneration of the testes.

The small restriction of the ration of the control animals in the experiments on vitamin A deficiency did not produce any degenerative changes in the testes, but was even followed by a slight enlargement of these glands. This supports the view that such a selective protection of the testes has been developed by the living organism in order to prevent the extinction of the species in time of scarcity of food.

While the decreased food intake produced no noticeable effect on the penis, the weight of the prostate with seminal vesicles was slightly decreased; but in vitamin A-deficient animals, in spite of the decreased food intake, there was in most cases a slight increase in the weight of these organs. A reduction in the weight of the thymus was observed in most of the rats on the deficient diet and seemed to be due to the direct influence of vitamin A deficiency.

Vitamin A deficiency in castrated animals. In castrated animals kept on a vitamin A-deficient diet, the influence of the lack of the "anabolic" principle on growth and body weight was as pronounced as in animals from which the testes had not been removed.

The adrenals and the hypophysis of castrated rats fed with a vitamin A-deficient diet undergo the same hypertrophy and the thymus the same retardation of involution as was observed in castrated animals on a normal diet.

Coagulation of the Blood.

Dr. J. O. W. Barratt has been chiefly engaged upon an investigation of methods of estimation of fibrinogen and thrombin. A study of the variations in content of fibrinogen in normal human blood plasma and of the relation between the amounts of fibrinogen and thrombin reacting in the formation of fibrin has enabled suitable concentrations of these substances to be selected as standards, with the aid of which it has been found possible to express the titre of solutions of fibrinogen and thrombin in terms of units. The data upon which these methods of estimation are based are being further extended.

DIVISION OF PROTOZOOLOGY.

Dr. Muriel Robertson has conducted further studies along various lines with the protozoon *Bodo caudatus*.

Effects of anti-bodo serum. The agglutination and lysis of the flagellates by a serum prepared by injecting the organism into the blood of rabbits has received further study and it was found that agglutination, just as with bacteria, was dependent on the presence of salts. Lysis was found, in sera of sufficiently high titre to admit of the dilution of the serum salts, to occur independently of agglutination. It was also shown that an antigen of boiled bodos could produce a serum which agglutinated and lysed the bodos though the titre was lower than that produced by the formalised unheated antigen.

Growth problems. It has been found possible to obtain very steady growth of *Bodo caudatus* in counted cultures transferred daily in various fluids with the addition of a known concentration of separately grown bacteria as food supply. These cultures afford a good opportunity for the study of lag in the early hours of the growth and of encystation in the later hours between the 22nd and 30th hours. It has been found that the addition of the filtrate from a 21 to 30 hour culture very greatly reduces the lag but, so far, this has not been found to alter the behaviour of the culture in regard to encystation.

Exposure to Gamma rays. The work on the effect of the exposure of the *Bodo* culture to gamma ray irradiation has been continued with the radium lent by the Radium Committee of the Medical Research Council. The relative growth in the presence of the radium as compared with the normal control was studied and the results of certain aspects of this were concluded and published.

Certain changes were noted as arising in strains irradiated continuously for long periods such as 5-30 days. These changes were found to persist for long periods after removal from the radium. Single bodos isolated from these modified cultures produced strains which retained the altered characters. It has, however, not been found possible to repeat the production of this heritable change by irradiation in cultures in all media. This matter is being investigated.

The hospitality of the Division was extended to Mr. Norman Laurie for some weeks in the summer of 1932.

DIVISION OF NUTRITION.

Vitamin Standards: Evaluation of Successive Samples.

Further work has been carried on in connection with the International Conference on Vitamin Standards and Units, held in London in June, 1931. Certain of the decisions then taken were regarded as provisional, and it was intended that the Conference should meet again, probably in 1933, for further discussion. It seems improbable now that the Conference can meet again so soon, although some important information has been collected in the interval.

Vitamin A: examination of two samples of carotene; importance of the solvent.

At the 1931 Conference, a certain sample of pure re-crystallised carotene was adopted provisionally as the International Standard for vitamin A. It was resolved to issue a further supply, the biological activity of which should be compared, by workers in different laboratories, with that of the original specimen, issued in 1931, the latter being also re-examined for its stability.

Miss Hume and Miss Henderson Smith, in conjunction with Dr. Smedley-MacLean, have examined this material. Colorimetric tests indicate that the 1931 specimen, although nearly two years older than the later one, is still slightly superior to it, and there can be little doubt that the older one must have suffered some deterioration. The biological results are more or less in conformity with the colorimetric ones, but it was found that the nature of the solvent used is of predominant importance in estimating the biological value of carotene; more extensive investigations on this point were therefore instituted and are reviewed under another heading.

Antineuritic Vitamin B₁: test of a new sample of the standard.

The standard adopted by the Conference was a concentrate, obtained by adsorption on acid clay, from an extract of rice polishings, prepared at Batavia, Java, in 1930, and provided by Professor B. C. P. Jansen, of Amsterdam.

The world demand for the original batch of standard material was so great that it was rapidly in danger of becoming exhausted; a fresh supply had therefore to be tested against the old one, before it could be issued.

The new sample (1932) has been tested in this Department by Mr. T. F. G. Prunty, using the growth method with rats and has been found equal in value for vitamin B₁ with the old sample (1930). The results from four other laboratories are also available for comparison and it is gratifying to find that all five are unanimous in their reports on this point.

Researches on the Vitamin B Complex.

Factor Y. Further studies on the Y factor of the vitamin B complex have been carried out by Dr. H. Chick, Miss A. M. Copping and Miss H. M. Jackson, using Jansen's "activated earth" as a pure source of vitamins B₁ and B₂, and an egg-white concentrate as source of vitamin B₆. Apart from growth-limitation in absence of the factor, no syndrome of factor Y deficiency can be defined, but animals which have remained under experiment for eight months or longer have shown skin lesions which are not typical of vitamin B₂ deficiency.

The Y factor seems to be present in concentrates prepared from brewer's yeast, and growth to maturity and reproduction have been studied on positive control animals, receiving the same synthetic basal diet as was used in the experiment on factor Y deficiency, but in which the vitamin B complex was supplied as an unheated extract of brewer's yeast.

The active fraction in Anaemia. The Department was able to furnish Dr. Lucy Wills, of the Royal Free Hospital, London, with a series of tested fractions of the vitamin B complex, on a scale suitable for therapeutic trials with human cases.

Dr. Wills had already found that Marmite was effective in curing tropical macrocytic anaemia and pernicious anaemia of pregnancy, amongst Indians in Bombay. Strauss and Castle subsequently found that Marmite, administered together with normal gastric juice, was effective in true Addison's anaemia, and they tentatively made the suggestion that the active fraction in Marmite might be vitamin B₁₂. It was, therefore, of peculiar interest to investigate with well authenticated preparations the relation of the active fraction to the vitamin B complex.

Dr. Wills has just returned from India, where she has been able to make the clinical tests, and her results, put briefly, seem to exclude any known fraction of the vitamin B complex as the active factor.

Vitamin B₁₂: its growth-promoting and anti-dermatitis functions. The identity of the growth-promoting and of the dermatitis-preventing factors contained in the heat-stable fraction of the vitamin B complex has been questioned, chiefly because of the irregularity in the appearance of symptoms, on vitamin B₁₂ deficient diets, which are quite consistent in their failure to allow growth. So far no seasonal variation in incidence of symptoms has been detected, nor has any diet been found which specially predisposes to dermatitis.

Whatever may be the factors influencing the development of dermatitis, the factor effecting its cure is closely related to that promoting growth. These two last properties have been shown to run parallel in a number of materials and to be equally affected by heat.

The effect of changes in the pH on the heat stability of vitamin B₁₂ have been further investigated.

Vitamin B₁ in relation to protein metabolism. In other laboratories it has been shown that the growth of rats is retarded when the proportion of protein in the diet is high, unless additional quantities of the heat-stable fraction of yeast extract (? vitamin B₁), are given as supplement. This has been taken as evidence of the existence of a definite relationship between the requirements of protein and of vitamin B₁ in the diet.

Miss M. H. Roscoe and Mr. Prunty have repeated this work and find that the effect is due to the lowered consumption of the high-protein diet, so little being eaten that the total intake of yeast extract is insufficient for growth, when this latter is incorporated as a percentage in the diet, instead of being given separately as a measured supplement. Since crude yeast extracts contain more vitamin B₁ than vitamin B₂, the deficiency is primarily one of the latter vitamin.

Cystine requirements of the rat. Miss Roscoe and Mr. Prunty are investigating the cystine requirements of rats. Mr. Prunty has worked out a modification of Sullivan's method for cystine estimation, which has yielded quantitative results with the foodstuffs employed. Some of the synthetic diets in use, especially those employed in studies of the B vitamins, were found to be poor in this amino-acid.

Biological Value of Proteins.

Dr. Margaret Fixsen and Miss Jackson, working in collaboration with Dr. Chick, have continued their study, by the balance sheet method, of the biological values of certain proteins of animal and vegetable (cereal) origin.

Whole milk proteins proved the most valuable of those studied, being given a value of 86, when fed at a level of 7 per cent. in the diet; caseinogen was next with a value of 76, when fed at a 6 per cent. level. Whole wheat, whole yellow maize, wheat germ, maize endosperm and lactalbumin were of equal value (65-70 at 6 or 7 per cent. levels) and were superior to wheat endosperm. The proteins of lowest value were heated caseinogen and a preparation made from the organs and muscles of rats. The figures indicate that caseinogen is superior to lactalbumin for maintenance, that these two proteins have a supplementary action towards one another and that the proteins of the embryo of wheat are more valuable than those of its endosperm.

It was stated in the previous report that caseinogen suffers a marked decline in biological value during the process of heating, washing with acidified water and extraction with alcohol, which is used in order to purify it from vitamins A, B and D. It now appears, as was anticipated from the results of other workers, that the prolonged heating is the portion of this process which is responsible for the deterioration in biological value.

Maize and Pellagra. It was emphasised in the previous report that the equality in biological value demonstrated for wheat and maize lent no support to the theory that pellagra is the result of an amino-acid deficiency. On the basis of the values obtained, no satisfactory explanation of the association of pellagra with the consumption of maize rather than of wheat can be furnished. The balance sheet method, however, supplies information only as to the relative values of proteins in maintaining nitrogenous equilibrium during short periods. It is conceivable that proteins whose value for this function is equal may yet show considerable disparity when their power of securing growth over long periods is compared.

Dr. Fixsen, Miss Jackson and Mr. J. C. D. Hutchinson have been studying the growth of young rats receiving for 10 weeks diets containing 10 per cent. of protein either from whole wheat or from whole yellow maize. They have found that the rates of growth secured with both these proteins are identical, provided that the total intake of protein is the same. Maize is, however, definitely less appetising than wheat and for this reason the growth curves, as well as the growth secured per gram of protein ingested (which increases progressively with increasing intake), of rats consuming a maize diet, is often inferior to that of litter mates receiving a wheat diet. This observation probably accounts for the fact that other workers have reported maize to be of inferior value to wheat in securing growth. It was further found that the maize diet could, by cooking, be rendered as palatable as the wheat diet, and the apparent inferiority of the maize for growth then quite disappeared.

No difference in digestibility could be found between wheat and maize, cooked or raw.

Vitamins A and D.

Biological value of Carotene as a source of Vitamin A; its value in different solvents. In their study of the carotene used as International Standard for vitamin A, Miss E. M. Hume and Miss Henderson Smith have found that for accurate biological evaluation the choice of the solvent in which the carotene is administered to the rat is of great importance since the stability of the carotene and the capacity of the animal to make the maximum use of the carotene presented to it both vary with the solvent.

The stability may be followed by observing the permanency or fading of the yellow colour of the carotene in the given solvent, and this point has received attention from Dr. Smedley-MacLean. The disappearance of colour from the solution was taken as evidence of oxidation, the colour being determined

by comparison with a standard solution of potassium dichromate. The solvents examined were paraffin ("Internol"), ethyl laurate, hardened cotton seed, arachis, olive and coconut oils. The effect on the colour of the solutions differs widely, that in hardened cotton seed oil being deep orange compared with a pale yellow in Internol or ethyl laurate of the same concentration. After four months at 0°C. the colour of solutions in ethyl laurate and "Internol" showed a slight falling off; in arachis and olive oils no certain effect could be detected; in one specimen of hardened cotton seed oil, the effect was slight, while in another specimen which had been in the laboratory for some years, the carotene was decolorised in a week. The solution in coconut oil was unchanged.

Kept at the laboratory temperature, the colour of the solution in ethyl laurate rapidly changed and at 37°C. was completely removed in a few days; in coconut oil, after a fortnight at 37°C., the diminution in colour was only just perceptible. From the evidence of colour alone, coconut oil seems the most desirable solvent of those tested for the administration of carotene in vitamin A experiments.

When tested on the rat, coconut oil easily stands out as the best solvent, the minimum protective dose of carotene, when dissolved in it, being much smaller than when ethyl laurate or liquid paraffin is used. Indeed the minimum protective dose of carotene for the rat is now found to be considerably smaller than had been previously supposed, being 1.0γ or less. The actual minimum dose has not yet been reached, doses of less than 1.0γ daily having not so far been tested.

Origin and distribution in nature of the Antirachitic Vitamin D. The problem of the origin of vitamin D in the ocean has received further study, using a fresh supply of Copepod material, specially collected by Dr. Atkins of the Marine Biological Station at Plymouth. Miss Gaffikin, working with Miss Hume, had made a preliminary examination of such material for vitamin D by testing it when dried and impregnated with an inactive fat, and also by testing an extract of the dry material, and the dry material after extraction. The extract and extracted material gave an entirely negative result, but the material dried and impregnated with fat, gave definite though weak signs of antirachitic activity. Miss A. M. Copping has continued the investigation but, in view of the foregoing result, no further attempt to test extracts has been made.

Using the line-test, the dried material has been examined and has given evidence of being a fairly good source of vitamin D, and it is hoped that it will be possible to attach a quantitative value to it before long.

Miss Copping has also been engaged in testing plant material for vitamin D. Such material, owing to the fact that its content of the vitamin is frequently very low, presents special difficulties for study. During the months of July, August and September, the vitamin D content of lettuce, fresh picked in the garden and bought in the market, was investigated, using the line-test. Variation was found in the vitamin D content of the green outer leaves and the etiolated heart of the lettuce.

The effects of irradiation of such material, with an artificial source of ultra-violet light, and of keeping after irradiation, were also studied, but material could not be obtained for long enough to complete the work, which will be continued in the summer of 1933.

Experiments have also been made on the formation of vitamin D in sprouting wheat, germinated in the dark, which seem to show that the etiolated shoots and rootlets have a constant weak antirachitic potency, but that after exposure to light and development of green pigmentation, the antirachitic potency can no longer be detected.

Causes of the variation in sensitivity to Rickets of different stocks of Young rats.

Miss Hume and Miss Henderson Smith have commenced a study of this problem by comparing the ash content of the bones of different litters of young rats, before and after a period on a rachitogenic diet. They are also comparing the ash content of the bones of young rats, receiving graded doses of vitamin D and a rachitogenic diet, with and without addition of phosphate.

Dietary Requirements for Reproduction and Lactation.

Work on this subject has been continued by Miss Hume and Miss Henderson Smith, but is necessarily very slow. A synthetic diet has been found on which growth and fertility of rats are normal but on which the birth and rearing of young does not take place normally. When wheat germ is added to this diet, the error appears to be corrected, and four or five normal litters in succession are born and reared, if the females are mated early enough. The next generation also appears able to breed normally.

That the wheat germ does not exercise its beneficial action through supplying vitamin E, is shown by the fact that the diet already contains this factor in the form of hardened cotton seed oil; the reproductive failure moreover does not resemble that in vitamin E deficiency, for males remain fertile throughout and females do not suffer resorption gestations, but bring their young to term. The difficulty appears to be rather one of bringing the young to birth alive, the mother herself not infrequently dying, or if parturition is successful, the young fail to suckle. Whether there is an actual failure to secrete milk is difficult to determine.

Permeability of Epidermis to Ultra-violet Radiations.

Dr. N. S. Lucas has continued his research on the permeability of epidermis to ultra-violet radiations. Using epidermis from a newly born rat, he has found that sufficient radiant energy of the required wavelengths passes through the epidermis to effect the partial conversion of ergosterol in solution into vitamin D. The occurrence of the change was demonstrated physically by absorption spectrograms of the two solutions. It was confirmed biologically by feeding experiments of the curative type, in which young rats on a rachitogenic diet received measured doses of the irradiation product. The degree of cure was estimated by means of the X-ray technique.

Spectrographic Examination of the Oxytocic Hormone.

Dr. Lucas has made observations on Dr. Gulland's preparations of the oxytocic hormone of the pituitary gland of various physiological strengths and varying chemical purity. These observations showed that spectrographic examination in the ultra-violet region may throw some light on the nature of the active substance.

DR. ZILVA AND COLLABORATORS.

EXPERIMENTAL RESEARCHES ON THE ANTISCORBUTIC PRINCIPLE. (VITAMIN C.)

The Chemical Nature of Vitamin C.

The chemical work carried out in connection with vitamin C was mainly devoted to a study of the problem of its identity with hexuronic acid (ascorbic acid). As was mentioned in previous reports, early attempts by Dr. Zilva to isolate vitamin C from lemon juice have shown that active fractions possessed strong reducing properties. This observation taken in conjunction with that made by him on the inactivation of the vitamin by exposure to oxygen, led him to investigate whether the reducing capacity was due to the vitamin itself or to other substances associated with it. By the introduction of the indophenol titration technique he was enabled to follow titrimetrically the relationship between the reducing capacity and the antiscorbatic potency. Although some parallelism between the two functions was found to exist in natural products this was not found to be the case in a great number of chemical fractions from lemon juice. Furthermore antiscorbatically active solutions, when oxidised with the indophenol indicator, retained much of their biological activity. From this Dr. Zilva concluded that vitamin C and the reducing substance were not identical. Recently Prof. Tillmans and his collaborators repeated Dr. Zilva's work and confirmed his main results. They nevertheless consider that the parallelism between the reducing capacity and antiscorbatic activity is near enough to assume that the two are due to the same substance and suggest that it is hexuronic acid, a compound isolated by Prof. Szent-Györgyi some years ago from the adrenal gland and from fruits and vegetables. Prof. Szent-Györgyi has recently also adopted this view on finding that crystalline hexuronic acid is very active, an observation later confirmed by other workers including Dr. Zilva. In order to ascertain whether the identity theory is correct a number of researches are being pursued in this connection.

Dr. Zilva once more found a marked disparity between the reducing capacity and antiscorbatic activity in active fractions obtained from lemon juice. Attempts to trace this disparity to technical errors have so far failed. In collaboration with Dr. Hirst, of the University of Birmingham, further efforts are being made to correlate the antiscorbatic activity, the indophenol reducing capacity and the absorption in the ultraviolet region of the spectrum (hexuronic acid absorbs at 260μ to 265μ) of various active substances.

Tests on a number of specimens of hexuronic acid (some of which were kindly prepared by Messrs. Burroughs Wellcome & Co.) of different degrees of purity and from different sources have shown a variation in activity which falls within the limits of the experimental error of the prophylactic method. More tests are now in progress, in which larger numbers of animals are employed, in order to establish whether this variation is due to an actual difference in activity.

Prof. Tillmans contends that the activity of antiscorbatic solutions oxidised with indophenol observed by Dr. Zilva is due to the formation of a reversibly oxidised form of vitamin C. Dr. S. W. Johnson in order to test this hypothesis has been attempting to regenerate the reducing properties of decitrated lemon juice, oxidised with indophenol, iodine or hydrogen peroxide, by treatment with hydrogen sulphide. This was partially successful, but it was not found possible to establish whether the antiscorbatic activity was proportionately increased at the same time in the treated solution as required by Tillmans' theory, since treatment with hydrogen sulphide interferes with the quantitative estimation of vitamin C by the biological method. Dr. Hirst and Dr. Zilva's work on reversibly oxidised derivatives of hexuronic acid which is now in progress may throw further light on the point.

Dr. Zilva and Dr. Johnson are also engaged in studying the development of the indophenol reducing capacity and the antiscorbatic activity of germinating seeds.

Observations which may have a bearing on the relationship of vitamin C to hexuronic acid have been made by Dr. Zilva. He found that when the suprarenal glands from guinea pigs, which subsisted on a mixed diet with a liberal supply of cabbage, were immersed in silver nitrate, the glands, as Prof. Szent-Györgyi found in the case of the ox, stained black. This is probably due, at least in part, to the presence of hexuronic acid. If, on the other hand, the suprarenal glands from guinea pigs which have been maintained for months on a scorbutic diet but which received about six times the protective dose daily in the form of decitrated lemon juice, were treated in this way, they did not stain. This observation is being extended in collaboration with Dr. Gough, of the Pathological Department, School of Medicine, Cardiff.

The Physiological Function of Vitamin C in Fruits.

Polyploidy and Vitamin C. Experiments carried out in collaboration with Mr. M. B. Crane, of the John Innes Horticultural Institution, Merton, on a number of triploid and diploid apples revealed that all the most active varieties fell within the first category although there were also amongst these triploid apples with low activity. The results, while suggesting that some connection may exist between chromosome numbers and antiscorbutic activity in the apple, do not incontrovertibly prove it.

The effect of Freezing upon Vitamin C of Apples. Experiments carried out in conjunction with the Low Temperature Research Station, Cambridge, have previously shown that when Bramley's Seedling apples were frozen at -20°C . and the disrupted tissues tested immediately, no appreciable loss of vitamin C could be recorded. Further experiments have revealed that very little loss of the vitamin took place even when this tissue was stored for about 14 months at -20°C . Utilising this technique an attempt was made to explore the effects of depth of freezing and duration of storage in a frozen condition upon the loss of vitamin C. Bramley's Seedling apples were therefore stored at -5°C ., -10°C ., -15°C . and -20°C . for about seven months. At the end of this period the apples of the batches stored at the various temperatures were disrupted at -20°C . and tested for their antiscorbutic activity. It was found that in the case of the apples stored at -5°C . the loss in vitamin C was very great, in the case of those stored at -10°C . the loss was less but even in this batch it amounted to almost 50 per cent. In the apples stored at -15°C . there was a very slight loss that was only just appreciable, whilst those stored at -20°C . showed no loss at all.

Relation of Nitrogen to Vitamin C content of Apples. An investigation pursued in collaboration with Dr. T. Wallace, of the Long Ashton Horticultural and Agricultural Experimental Station for several years on the correlation of the nitrogen content with the antiscorbutic potency of the apple has definitely established that the latter is inversely related to the former, although there was no strict proportionality between them. In one variety, namely King Edward VII., the vitamin C content was considerably raised by lowering the nitrogen content of the fruit both by cultural methods and by bark-ringing the trees. Acidity, sucrose and ash constituents on the other hand had no bearing on the vitamin activity of the apples.

Vitamin C content of Mangoes. Miss M. E. F. Crawford and Miss E. O. V. Perry have extended the investigation previously carried out on the vitamin content of mangoes.

DEPARTMENT OF BIOCHEMISTRY.

Alcoholic Fermentation.

The nature of the individual phosphoric esters, formed during alcoholic fermentation and their rôle in the breaking down of the carbohydrates have again been subjects of continued study by Professor R. Robison and his collaborators.

Last year the isolation of a third hexosemonophosphate was reported. This ester has now been definitely identified as mannosemonophosphate, while evidence has been obtained that the phosphoric acid group is in the same position (6) as in glucose- and fructose-monophosphates. In the published account of this work Professor Robison has suggested a scheme to explain the apparently simultaneous formation of these three monophosphoric esters together with γ -fructosediphosphate during the fermentation of glucose or of fructose by yeast preparation.

Since the isolation of the individual esters from the complex hexosemonophosphate of fermentation is very laborious, it is fortunate that a more convenient source of the mannose ester has now been found. In collaboration with Dr. C. M. Jephcott (Research Associate of the Department of Physiology, Toronto University) an examination was made of the relative proportions in which these various esters are produced from mannose, glucose and fructose, when fermented by dried yeast, under different conditions. When fermentation was carried out at 25°C . mannose yielded a higher proportion of monophosphoric esters than glucose or fructose; at 38°C ., the difference became much more pronounced, mannose yielding a very high proportion of monophosphate, which no longer showed the properties of the usual mixed "hexosemonophosphate" but consisted to a very large extent of the mannose ester. From this product pure mannosemonophosphate was prepared by way of its crystalline phenylhydrazone; and, finally, the barium

salt of the ester was also obtained in crystalline form. With this material the further investigation of the compound has been carried out.

The formation of such a large proportion of the mannose ester during the fermentation of this sugar must affect the present views concerning the mechanism of the fermentation process, in particular as regards the conversion of the three hexoses into one common form as a necessary preliminary to their breakdown. The problem is being studied from this aspect in collaboration with Mr. V. N. Patwardhan (Indian Institute of Science, Bangalore). In the first instance the conditions favouring the exclusive formation of the mannose ester during fermentation of mannose with dried yeast were more closely investigated. At 43°C. the yield of mannosephosphate reached 90% of the total esterified phosphorus, while the ratio of the extra carbon dioxide produced to the phosphate esterified fell considerably below unity. It would seem, therefore, that at such abnormal temperatures direct esterification of the mannose must occur and, indeed, must form the predominant reaction; but that this direct esterification does not facilitate the carbohydrate break-down in the same way as does the normal process in which a mixture of fructose, glucose and mannose esters, possibly arising from one intermediate compound, is formed. Mr. Patwardhan has also carried out a number of experiments on the direct phosphorylation of mannose in pyridine solution and has obtained a mixture of esters, which are now under investigation.

Dr. Marjorie G. Macfarlane has continued her investigation of the effect of washing the yeast, thus reducing the amount of co-enzyme. The results are, as yet, difficult to assess owing to the other changes which must necessarily accompany the removal of co-enzyme by such means.

The investigation of the hydrolysis of fructosediphosphate by bone phosphatase which was being carried out in collaboration with Miss M. Macleod, has been continued by Professor Robison and the results have been published. The product of the partial enzymic hydrolysis of fructosediphosphate was shown to consist of a mixture of glucose- and fructose-monophosphates, the chief constituent being a fructose ester, hitherto unknown. After a considerable degree of purification had been effected the properties of the new ester were studied and indicated that its probable constitution is that of fructose-1-phosphate, derived from fructose-1-6-diphosphate by removal of the phosphate group in position 6. The ester is much more rapidly hydrolysed by acids than any of the other known monophosphates; and this accounts for the fact that fructose-6-phosphate (Neuberg ester) is alone obtained from the diphosphate by partial acid hydrolysis. It would appear that bone phosphatase, however, removes the phosphate group in position 6 at least as rapidly as that in position 1 and that, during hydrolysis of the latter group, intramolecular change involving the conversion of fructose into glucose occurs. Several interesting problems suggested by these results are now being investigated in collaboration with Dr. Béla Tankó (University of Debrecen, Hungary).

Professor Robison and Dr. Macfarlane have also continued their attempts to isolate the still unknown esters which are present in the fermentation products. In the course of the experiments a new and simpler method has been evolved, by which fructose-diphosphate can be obtained in a high degree of purity, as indicated by the rate of hydrolysis of the ester in hydrochloric acid. The residual fractions from this purification contained other esters of similar solubility but of lower reducing power. The investigation of these esters is being continued.

Continuing the investigation referred to in the last Report Professor Harden has found that the preparations containing hexokinase increase the rate of fermentation of glucose, fructose and mannose in presence of phosphate, but has not so far found any definite proof that this effect is due to the more rapid conversion of the sugars into a fermentable form. The possibility that a specific hexokinase is produced when a yeast acquires the power to ferment galactose is being tested.

Ossification.

In further experiments on the mechanism of calcification Professor Robison and Dr. Adèle H. Rosenheim (Grocers' Company Research Student) have shown that deposits of barium, strontium and magnesium phosphates can be obtained *in vitro* in hypertrophic cartilage by the agency of the bone phosphatase. In absence of phosphoric esters, however, such deposits were very rarely found even when the cartilage was immersed in highly supersaturated solutions of the respective salts. This behaviour is in marked contrast to that of such cartilage towards supersaturated inorganic solutions of calcium phosphate, and suggests that the second calcifying mechanism is to some extent specific for the bone salt, calcium carbonato-phosphate. Attempts to differentiate the two calcifying mechanisms by heating the bone slices to various temperatures or subjecting them to other adverse conditions have also been carried out. The second mechanism can be largely destroyed without injuring the phosphatase, but the opposite effect has not, so far, been achieved. Calcification *in vitro* has been brought about with the aid of a number of different phosphoric esters, which thus form effective substrates for the bone enzyme.

It has been further shown that calcification *in vitro* of the kidney, lung and aorta of normal and rachitic rats can be obtained by agency of the tissue phosphatases. No calcification of these tissues has, so far, been effected in highly supersaturated inorganic solutions even during prolonged immersion at 37°C. It would seem that these tissues do not possess the second mechanism responsible for calcification in such inorganic solutions. Rabbit aorta, which is recognised as prone to calcification *in vivo*, differs from that of the rat in being devoid of phosphatase. It was, therefore, interesting to find that rabbit aorta could be calcified by prolonged immersion in supersaturated inorganic solutions. The presence of phosphoric ester, as was expected, had, in this case, no beneficial effect on the calcification.

The comparative study of the phosphatase activity of animal tissues, to which reference was made in the last report, has been continued by Professor Robison and Dr. Macfarlane. Tissues of mice, rats, guinea-pigs, rabbits, kittens, dogs and of the human foetus, have been examined by the micro-technique previously used. In general, the different tissues were found to possess similar relative activities in all these animals, but certain striking exceptions were observed; thus, the aorta of the rat possesses a very considerable phosphatase activity while in other animals this tissue is almost inactive. Further investigations are in progress concerning the type of phosphatase present in certain tissues, in the hope of throwing light on their function.

Professor Robison's collaboration with Dr. Honor B. Fell of the Strangeway's Research Laboratory, Cambridge, has been continued on the lines described in last year's report. Their investigations, which are not yet completed, have been concerned particularly with the development of the two calcifying mechanisms in embryonic avian cartilage and osteoid tissue. With Dr. W. Landauer of the Storrs Agricultural Experimental Station, Connecticut, they have further studied the phosphatase development and calcification in the bones of the creeper fowl.

The Oxytocic Hormone of the Posterior Lobe of the Pituitary Gland.

The investigation of the constitution of the oxytocic hormone belongs to a type of problem which is now encountered more frequently than formerly. The hormone has not been isolated, and its isolation offers immense difficulties, both practical on account of its chemical properties, and financial, in view of the minute amount present in the posterior lobe and the great expense of posterior lobe powder. The only method of identifying and assaying the hormone lies in its physiological effect of causing contraction of plain muscle. The investigation of the constitution of such a substance can therefore be pursued along two lines, both of which are rigidly conditioned as follows. Neither the reagents used nor the products of their interaction with glandular material must have sufficient effect on the isolated guinea-pig uterus to invalidate the assay. The choice of methods, therefore, falls firstly on selected organic and physico-chemical processes carefully designed to test for the presence of particular chemical groups, and secondly on a study of the behaviour of the hormone when treated with enzyme preparations of known purity or content. On the basis of the evidence accumulated by these means, synthetic chemistry may build up compounds which satisfy the experimental facts. The physiological examination of such substances will then show which will repay modifications of structure and in what direction further experiments with the hormone are required.

Dr. J. M. Gulland has shown that nitrous acid has a dual action on the hormone. Using a large excess of the reagent, the oxytocic activity falls with great rapidity to one-third of its initial value, and thereafter decreases slowly and steadily. The nature of these changes in the molecule is being explored by further research, since nitrous acid is of too wide an application as a reagent to permit a decision to be made from its action alone. The speculation that it reacts with basic groups in the molecule is attractive.

Dr. Gulland also finds that semicarbazide and hydroxylamine at M/50 concentration are without effect on the hormone. Both substances react with the carbonyl group, and their failure to attack the hormone may be taken as evidence of the absence of an aldehydic or ketonic group. The practical difficulties which have been mentioned are illustrated by the fact that hydroxylamine at a dilution of 1 in 500,000 in the bath may cause a diminution in the response of the uterus to a dose of pituitary extract or of histamine; this diminution corresponds approximately to a reduction of the dose by 15%. Semicarbazide on the other hand appears to have a stimulating effect on the muscle.

During the past decade or more it has been stated by various investigators that the oxytocic hormone is destroyed by the proteolytic enzymes, trypsin, erepsin and papain. From the nature of the preparations of animal enzymes and the dates of these investigations it is clear that the preparations were complex mixtures of enzymes, possibly not even all proteolytic in character. Further, the methods used to obtain preparations of the vegetable enzyme papain, were not such as might be expected to effect enzymic purification. The yeast proteolytic enzymes of the Willstätter school are more easily obtained in greater purity than are the animal proteolytic enzymes, and in addition they are more specific, and might therefore yield more detailed information as to the nature of the hormone. The literature contains descriptions of the isolation of a dipeptidase, an aminopolypeptidase and a proteinase from Munich brewer's yeast, but in view of the variable characters of different yeast strains, it was not to be hoped that this information would apply directly to English brewer's yeast. Using English yeast, and in part Dutch baker's yeast, Dr. T. F. Macrae (Research Student in Biochemistry) has determined the conditions for separating these three enzymes and preparing them in maximal yield. In general, he has found that the English yeasts behave qualitatively like the German yeasts but that the enzymes are liberated more rapidly from the English varieties and that the separations are less easily effected.

Dr. Gulland and Dr. Macrae have found that the oxytocic hormone is rapidly destroyed by preparations of dipeptidase and proteinase, and is slowly destroyed by aminopolypeptidase preparations from English brewer's yeast. Preparations of dipeptidase and aminopolypeptidase, which Dr. Grassmann of Munich kindly supplied, behaved similarly to those obtained from the English yeast. None of these enzymes is responsible for the inactivation, which is caused by a fourth enzyme present in these preparations. This enzyme has been characterised by the determination of its pH-optimum and pH-activity curve.

Papain preparations destroy the hormone rapidly and the pH-optimum and pH-activity curve are the same as those of the yeast enzyme. It is probable that the destruction by papain preparations is due to this enzyme. The shape of the pH-activity curve closely resembles that of Grassmann's prolinepeptidase, which hydrolyses peptides containing proline, of which the imino-group is free and the carboxyl utilised in the peptide chain. The enzyme present in the yeast preparations and in papain which destroys the hormone is not this prolinepeptidase. Experiments are in progress to determine the nature of the substrates on which the hormone-destroying enzyme can act, since their identification should indicate the presence of a similar structure or grouping in the hormone molecule.

In beginning an investigation of the effects of animal proteolytic enzymes on the hormone, Dr. Gulland and Dr. Macrae have found that trypsin preparations cause an extremely rapid inactivation. They have succeeded in showing that this effect is due to an enzyme which is not identical with the enzyme which hydrolyses gelatin, and which has different characteristics from the enzyme present in yeast proteolytic and papain preparations. The substrates characteristic of this enzyme are being sought, and other animal proteolytic enzymes will be studied. It should be mentioned that as a result of these experiments there is no evidence that the oxytocic hormone is peptide in character, except that up to the present the enzymes which destroy it have been associated with proteolytic ones. The investigation is being extended to other types of enzymes.

During the year Dr. Gulland continued attempts to purify the hormone, using as starting material the preparations obtained by charcoal adsorption as described in last year's report. Unfortunately further progress in the purification had to be postponed until a further supply of posterior pituitary powder becomes available.

The Constitution of the Nucleic Acids.

The investigation of the positions occupied by the carbohydrate groups of the purine nucleosides has been continued. Dr. Gulland and Dr. Macrae conclude that the balance of evidence favours the 7-position of the purine molecule, although their results are not decisive.

The Action of Chemical Substances on Cells.

It is well recognised that wide divergences are frequently found in the pharmacological properties of chemical substances which differ even so little as in the position of a single group in the molecule. This phenomenon is much in evidence in chemotherapeutics, but the attempts which have been made to explain the divergences are relatively few. In view of the ease with which their sensitivity to reagents may be assayed, spermatozoa are peculiarly suitable for this type of investigation, and those of the guinea-pig have been used.

Dr. Gulland and Mr. T. H. Mead have almost completed their examination of the action of phenolic aldehydes and their ethers on the spermatozoa. Their work arises from the isolation of the products of condensation of barium glycine with the more spermicidal, but not with the less active, aldehydes. The non-isolation of the products in the latter case could not be accepted as evidence that they were not formed, and a physical method of examining the equilibrium between aldehydes and amino-acids was sought. Polarimetric examination of solutions of *D*-phenylalanine and of 2 : 3-, 2 : 5-, and 3 : 4-dimethoxybenzaldehydes under a variety of conditions showed that at any given hydrogen ion concentration the more spermicidal aldehydes (2 : 3 and 2 : 5) condense more rapidly and more completely with the undissociated amino-group of the amino-acid. Since the amino-group of an α -amino-acid is not comparable with the free amino-groups of proteins, the examination has been extended to a study of the interaction of the same aldehydes with gelatin, the condensation being followed by the preparation of titration curves of the protein alone and in presence of the aldehydes. In presence of the aldehydes a shift of the curve occurs in the direction of greater acidity, indicating their condensation with the basic (amino) groups of the gelatin. This shift is greater in the case of the more spermicidal aldehydes, showing that condensation with these is more complete. A comparison of the pH range over which the shift of the titration curve extends suggests that here also the undissociated amino-groups are attacked. It may be possible to demonstrate the union of the aldehydes with other basic centres in the gelatin.

The Search for New Amino-Acids.

Experiments initiated by Dr. Gulland at Oxford in the direction indicated by the title were pursued by him during the year, and the results obtained warranted work on a large scale. Dr. Gulland and Mr. C. J. O. R. Morris are continuing and extending the investigation.

Oxidation Experiments bearing on the Metabolism of Fat.

The inability of the starving or diabetic organisms to burn fatty acids without producing large quantities of acetone bodies remains an unsolved problem. It is possible, however, that the acetone bodies may be abnormal products of oxidation and that succinic acid or some other substance may be the normal end-product of the metabolism of the fatty acids when carbohydrate is also present.

Dr. Smedley-MacLean and her collaborators have, therefore, studied the effect of catalytic agents on the oxidation of the fatty acids by means of hydrogen peroxide *in vitro*.

It is known that at 90°C. palmitic acid is only slowly oxidised by hydrogen peroxide, evidence of the formation of β , γ and δ acids having previously been obtained. The products of oxidation were keto- and not hydroxy- derivatives. The addition of hydrogen peroxide and a cupric salt to a neutral solution of a palmitate results in rapid action, almost the whole of the palmitic acid being converted to soluble form within half-an-hour. No evidence was obtained of β oxidation, such as occurs in absence of the catalyst. Acting with a large excess of hydrogen peroxide for four hours, 90 per cent. of the original acid was completely broken down, being converted to CO_2 (52 per cent.), acetic (30 per cent.) and succinic (8 per cent.) acids. A study of the intermediate products at different stages of the reaction shows that hydroxylation occurs and that a lactonic acid $\text{C}_{15}\text{H}_{24}\text{O}_4$ is formed at an early stage of the reaction—succinic acid does not appear till later. The large proportion of acetic and succinic acids formed is suggestive in view of the theories which have been advanced as to the mode of oxidation of fatty acids *in vivo*.

Working with the lower fatty acids Mr. R. O. Jones (Morna Macleod Research Student) has found that whereas in one hour at 60°C. hydrogen peroxide alone oxidises only 10 per cent. of formic acid and is almost without action on acetic and propionic acids, the addition of a cupric salt converts to CO_2 practically the whole of the formic, 35 per cent. acetic, 21 per cent. propionic and 8 per cent. butyric, the effect diminishing as the length of the carbon chain increases. At 90°C. with increasing quantities of the peroxide the proportion of butyric acid completely converted to CO_2 rose from 8 per cent. to 70 per cent., the proportion of formic acid also increasing.

The occurrence of both β and γ oxidation is shown by the appearance of acetone and succinic acid, the proportions of which reach a maximum when six atomic proportions of active oxygen are used and diminish as this proportion is increased. The amount of succinic acid found was considerably greater than that of acetone.

The ω -phenyl derivatives of the fatty acids have been used in many animal feeding experiments, since a large proportion of the phenyl acid is excreted in the urine. Their reaction with hydrogen peroxide was, therefore, studied. This reagent is practically without action on benzoic acid, but in the presence of a copper salt the phenyl nucleus is rapidly attacked; within one hour 60 per cent. of the carbon appearing as CO_2 . Gallic acid was identified as an intermediate product. Under similar conditions phenyl-acetic and phenyl-propionic acids are rapidly oxidised, nearly 80 per cent. of the former appearing as CO_2 .

Miss A. P. Ponsford has continued her investigation of the dibasic acids and has shown that suberic, adipic and glutaric acids all yield succinic acid on oxidation with hydrogen peroxide in the presence of a cupric salt. Levulinic acid yields the same product and since levulinic acid is itself formed from adipic acid, oxidation of the α carbon atom must occur in both glutaric and adipic acids. The constitution of various intermediate products is now the subject of investigation.

Stability of Carotene in Solution.

In view of the possibility of using carotene as a standard for vitamin A, the influence of solvents on its stability is of great importance, since the carotene has to be administered in some solvent which is readily absorbed. This question has been investigated by Dr. Smedley-MacLean in collaboration with Miss E. M. Hume, and is referred to under Vitamins A and D earlier in this Report.

DEPARTMENT FOR THE STUDY AND PREPARATION OF THERAPEUTIC SERA.

Studies on the Pneumococcus and on the Titration of Anti-pneumococcus Sera, Type I.

Dr. Petrie and Dr. Morgan have continued their experiments on the lethal action of Type I. pneumococcus and on the titration of anti-pneumococcus serum (Type I.) in mice. Their inquiries have been greatly assisted by the recent introduction of the British Standard Serum (Type I.). This has been prepared in the National Institute for Medical Research under the direction of Dr. Hartley, and it has provided a stable standard of reference, which is independent of fluctuations in the lethal power of the test culture. A provisional unit of protective value has been assigned to the British Standard Serum as the result of comparative tests with a standard liquid serum which was supplied by Dr. L. D. Felton, of Harvard University. Work on the relative potency of these standard reagents has been carried out in the Serum Department at the instance of the Biological Standards Department of the National Institute, and in co-operation with its staff and with the staff of the Wellcome Physiological Research Laboratories.

The general results that have been obtained by Dr. Petrie and Dr. Morgan are briefly as follows:

- (1) the lethal power of a virulent test culture can be maintained within reasonably narrow limits, and
- (2) the method which they have employed during the past three years permits of the titration of sera within limits of accuracy that must be regarded as very satisfactory in view of the inevitable variability of a biological test which involves the use of a living culture.

The titration may be effected either by means of a prophylactic method or by the curative method to which reference was made in last year's Report, the former method having the advantage of practical convenience.

The optimal precipitation method of Dr. Wilson Smith, in which the type-specific polysaccharide serves as the test reagent, has been adopted for the titration of samples of horse serum taken during the course of immunisation, and has proved to be useful.

A horse has been immunised with a "rough" Type I. pneumococcus. The serum when tested in mice, was found to possess a slight but definite protective action against the virulent Type I. strain. A test was carried out to ascertain whether the serum was able to exert an adjuvant effect when administered simultaneously with the type-specific serum, but no evidence was forthcoming of any such reinforcing action. This observation is of interest, since it indicates that the protective action of the type-specific serum in the mouse is directed almost exclusively against the capsular and not against the somatic component of the pneumococcus.

Experimental work upon the Meningococcus and upon the production of Anti-meningococcus Serum.

Dr. Elson (Jenner Memorial Research Student) and Dr. Morgan are engaged in the study of the chemical nature of the substances that are responsible for serological specificity in the meningococcal group. They have isolated from Type I. meningococcus a polysaccharide substance $[\alpha]_D -15^\circ$, which gives specific precipitation with the homologous precipitating serum at a dilution of 1:1,000,000. This material does not precipitate when mixed with a Type III. precipitating serum that has been absorbed with Type I. meningococci. The difficulty of preparing a type-specific precipitating serum for the specific soluble substance of Type II. meningococcus has caused them to suspend work on the subject until a supply of type-specific precipitating sera is available.

In an attempt to gain some knowledge of variations in the virulence and antigenic quality of strains of the meningococcus Dr. Morgan and Dr. McClean have estimated the concentration of specific soluble substance in a number of cultures. Freshly isolated strains, which were kindly supplied by Dr. W. M. Scott, of the Ministry of Health Laboratory, have been examined, together with strains that had been maintained by laboratory culture over a prolonged period. The influence, too, of repeated subculture upon the yield of the specific substance has been considered. Their work has failed to reveal any relation between the yield of specific substance and the period of laboratory maintenance, or the extent of subcultivation.

Dr. McClean has carried out serial subcultures of a strain of meningococcus in a medium containing a "pure" homologous immune serum of high agglutinating titre with the idea of inducing a conversion of the original strain to one with the characters of a "rough" variant. The concentration of the immune serum in the medium was varied and repeated subcultures were made. An examination of the organism by serological and cultural methods after a course of this treatment revealed no significant change in its characters.

Dr. Petrie and Dr. McClean have continued their inquiry into the characters of the endotoxin of the meningococcus. Further attempts to increase the potency of the toxin by extraction and concentration methods have not been successful, and thus the relatively feeble toxicity of the preparations employed has hampered experimental work upon the nature of the toxic substance. However, observations have been made which indicate that the endotoxin possesses a number of characters which distinguish it from the ordinary bacterial toxins. Thus, it is not destroyed by boiling for half-an-hour in N/40 caustic soda or by submitting it to the action of formalin during a period of two months at 40°C .; moreover, it is not readily oxidizable, for hydrogen peroxide has no action upon it; and it resists the action of trypsin and diastase. Dialysis experiments have shown that the endotoxin does not pass through a cellophane membrane. A limited number of animal experiments were carried out to determine whether anti-meningococcus serum was able to exert any protective action against the endotoxin, but the results gave no evidence of any neutralizing effect.

The preparation of "convalescent" human serum for the treatment of Poliomyelitis.

The Institute is co-operating with the Medical Research Council and the Public Health Department of the London County Council in the preparation and issue of a serum for the treatment of poliomyelitis. The serum is obtained from healthy donors who present definite evidence of having suffered from the disease. Before being issued each batch of the serum is tested in monkeys to ensure that it contains the specific antiviral substance. The serum is intended for use only in the preparalytic stage of the disease, since the available evidence does not support its use in the post-febrile stage, when paralysis has already become established.

A stable preparation of a Dysentery Toxin (Shiga) for use as a test toxin.

Two years ago Dr. Petrie prepared a concentrated glycerinated test-toxin which had been rendered as free as possible from non-specific constituents. Formerly he had encountered the difficulty with similar preparations that after storage for some months at 32° — 40°F . deterioration had unaccountably taken place. The glycerinated test-toxin now in use has proved to be stable after two years' storage,

mostly within this range of temperature. Tests have been carried out to ascertain the limits of accuracy of the titration of antidysentery serum, when this preparation is used as the test-toxin. In a series of five consecutive tests a dose of serum was chosen which was known to give a mortality-rate of approximately 50 per cent., and doses of the serum differing from the central dose by ± 5 per cent. were included. When the results are summed up the mortality-rates for the three groups of mice, inoculated with the serum-toxin mixtures, are such as to indicate that differences of dosage of this order can be distinguished; there were eighty mice in each group. A refinement of titration of this degree has apparently not hitherto been attainable, and may be due to the relative purity of the reagents, not only of the toxin but of the serum preparation. The latter is a glycerinated pseudo-globulin solution and serves as a laboratory standard. The combination of the toxin and antitoxin molecules in serum-toxin mixtures is doubtless retarded by the presence of excessive amounts of non-reacting substances in one or both of the test solutions.

The Toxin-antitoxin relations of certain aberrant members of the genus *Corynebacterium*.

Dr. Petrie and Dr. McClean have almost completed their work on the toxin-antitoxin relations of certain diphtheroid strains, which were isolated by Dr. M. M. Barratt from the human nasopharynx. They have included within the scope of their inquiry the bacillus of Preisz-Nocard (*C. pseudotuberculosis ovis*) and the aberrant strain of diphtheria bacillus described some years ago by Mair. Antitoxic sera have been prepared by immunising horses with toxic filtrates derived from each strain, and, in addition, the corresponding antibacterial sera have been obtained from horses after a course of intravenous injections of killed and living cultures. Cross neutralisation tests, which are performed intracutaneously in the rabbit, have led to the conclusion that the aberrant strains isolated by Dr. Barratt, together with Mair's strain and the Preisz-Nocard bacillus, form an inter-related group which has affinities with the true diphtheria bacillus. The strain which was discovered by Mair seems to constitute an important link between the true diphtheria bacillus on the one hand and Dr. Barratt's strains and the Preisz-Nocard bacillus on the other hand. Thus, Mair's strain is able to produce the typical diphtheria toxin and, in addition, it forms a lethal toxin which is not neutralizable by diphtheria antitoxin. The atypical toxic component has affinities with a similar toxin produced by Dr. Barratt's strains and by the Preisz-Nocard bacillus. A number of workers have made the observation that diphtheria antitoxin is able to neutralize to some extent the pathogenic action of the Preisz-Nocard bacillus. The work of Dr. Petrie and Dr. McClean offers an explanation, for they have found that horse sera, and particularly concentrated sera normally contain significant amounts of Preisz-Nocard antitoxin; a result which is not surprising in view of the fact that the Preisz-Nocard bacillus is a natural infecting agent of the horse.

An Investigation of the Polysaccharides of *B. dysenteriae* (Shiga).

Dr. Morgan has continued his investigation of the specific polysaccharide of *B. dysenteriae* (Shiga), with the object of elucidating the nature of the carbohydrate groupings that are associated with specificity in bacterial antigens. During the past year a sufficient amount of the purified polysaccharide has accumulated to permit an examination of the nature of the acid hydrolysis products. A preliminary hydrolysis experiment has resulted in the isolation of galactose and an acetyl-N-aminohexose. In collaboration with Dr. Thaysen, of the Royal Naval Cordite Factory, Dr. Morgan has isolated a micro-organism from humus which, after repeated transfers in a medium containing the polysaccharide as the sole source of carbon, rapidly destroys the specific immunological properties of the polysaccharide. Dr. Thaysen is at present engaged upon the identification of this bacterium.

The estimation of small amounts of specific bacterial Polysaccharide by the induction of Anaphylaxis.

During the year Dr. Morgan has elaborated a method of estimating small amounts of a specific bacterial polysaccharide, which depends upon the induction of a typical and fatal anaphylactic shock in guinea-pigs that have been passively sensitized with the homologous antibacterial serum from the rabbit. A minimal amount of the specific substance, for example, 0.015 mgm., can be detected by the method; the accuracy of the determination is not influenced by the presence of a large excess of non-specific polysaccharide substances.

A Colorimetric Method of Estimating Glucosamine.

Dr. Morgan and Dr. Elson are investigating a micro-colorimetric method for the estimation of glucosamine, which is based on its conversion into the acetyl, propionyl or benzoyl derivative and on the condensation of the resulting derivative with p-dimethylaminobenzaldehyde. The conditions under which a strict proportionality exists between the glucosamine concentration and the intensity of the resulting colour have been determined. The method is applicable to chondrosamine and will probably hold for any 2-aminohexose. Acetylglucosamine semicarbazone and the methyl hexoside of N-acetylglucosamine fail to give coloured condensation products with p-dimethylaminobenzaldehyde.

The Action of Testicular Extract on Tissue Permeability.

Dr. Morgan and Dr. McClean have carried out further experiments with the diffusing substance which is present in extracts of the mammalian testis and in spermatozoa. They have elaborated a method for its concentration, which is based on the precipitation of the active substance as a basic lead salt and its subsequent fractionation with ammonium sulphate and ethyl alcohol. Preparations have been obtained which increase dermal diffusion at a dilution of 1 : 200,000; the minimal diffusing dose contains 0.000001 mgm., of total solid matter. These solutions, when adjusted to pH 4.5, can be heated at 100°C. for 15 minutes without suffering appreciable loss of activity.

Dr. McClean and Dr. Morgan have published an account of the influence of the purified testicular extract upon the rate of absorption of diphtheria antitoxin in the guinea-pig and the rabbit. The addition of the extract to doses of antitoxin administered by the subcutaneous route approximately doubles the concentration of antitoxin in the blood at two and at six hours after each injection; at 24 hours there is still a definite, though less marked, increase. A significant difference was not detectable when, in similar experiments, the antitoxin was administered intramuscularly. Moreover, the injection of large doses of extract intravenously failed to enhance the rate of absorption of antitoxin when this was introduced by the subcutaneous route. The striking difference that is apparent between the activity of the extract in the dermis and the subcutaneous tissue on the one hand, and in the muscular tissue on the other hand involves the problem of its precise mode of action on tissue permeability; this has yet to be determined.

The Immunisation of Horses with the thermostable O Antigen of *C. welchii*, *C. oedematis maligni* and *C. tetani*.

Horses have been successfully immunised with the O antigen of *C. welchii* and *C. oedematis maligni* on behalf of Dr. Felix and with the O antigen of *C. tetani* on behalf of Dr. Henderson.

Dr. Lumsden of the Cancer Department of the London Hospital, has during the past year, been given facilities for his work on the production of an anti-cancer serum.

DEPARTMENT FOR THE STUDY AND PREPARATION OF ANTI-VARIOLOUS VACCINE.

During the year attempts were made by Dr. Green to ascertain whether bacteria-free filtrates of vaccine lymph remained virulent for any length of time. When tested by the intradermal method in rabbits, some degree of virulence could be demonstrated after two months or more, but little or no evidence of potency could be shown after two or three weeks when the method of introduction was by scarification.

NATIONAL COLLECTION OF TYPE CULTURES.

During the year under review the number of strains of bacteria and fungi distributed to workers at home and abroad in the various fields of microbiology has again exceeded 5,000 and some 200 types, including a considerable number of new species, have been added to the collection. Among the strains of micro-organisms acquired during the year, special mention may be made of a valuable collection of yeasts and other micro-organisms of importance in the fermentation industries kindly donated by the executrix of the late Mr. A. Chaston Chapman, F.R.S.

The International Nomenclature Committee of the International Society for Microbiology of which the Curator of the National Collection of Type Cultures, Dr. R. St. John-Brooks, is one of the permanent secretaries, is proceeding with a programme of preliminary work, which has for its object the conservation of *Bacillus* as a bacterial generic name, and the fixing of type species and of type or standard cultures. It has also appointed a sub-committee to advise upon the classification of the *Salmonella* group of organisms. In both these fields of work considerable progress has already been made.

During part of the year the hospitality of the department was extended to Dr. L. F. Hirst, City Microbiologist, Colombo, Ceylon, in connection with his work on the aetiology of sprue in relation to *Monilia* species and other organisms.

GENERAL AND FINANCIAL.

The Accounts and Balance Sheet for the year ending December 31st, 1932, show balances to the credit of the Pension Fund of £27,311 2s. 0d., of the Contingency Fund of £18,000 0s. 0d., of the Sinking Fund of £22,991 8s. 6d., and of the Capital Fund of £515,853 6s. 0d. The balance of income over expenditure of the Pension Fund, viz., £907 16s. 0d., has again this year been transferred to the General Account, towards the payment of premiums on the Federated Superannuation System policies of the staff. Of the excess of income over expenditure of the General Account, viz., £10,362 6s. 5d., £3,771 1s. 11d., has been utilised in increasing the Contingency Fund and the balance, £6,591 4s. 6d., added to the Capital Fund.

New investments and conversions during the year have been:—

For the General Fund: £4,000 5% War Stock 1929/47; £6,000 4% Funding Stock 1960/1990; £7,000 4% Consolidated Stock; the Conversion of £25,000 5% War Stock into £25,000 3½% War Stock, and £2,900 New South Wales 5¼% Stock into £2,900 Commonwealth of Australia 3½% Stock 1936/37.

For the Sinking Fund: £1,400 3½% Conversion Stock.

The income from the sale of the Institute's products during the year 1932 was £31,150 8s. 0d. After adjustment of the stock of Sera on hand at the beginning and end of the year, income from this source appears in the accounts as £31,222 8s. 3d. Sales of Sera, Vaccine Lymph, and Diagnosis and Investigation Fees show a decrease and Bacterial Vaccines show a slight increase compared with the previous year.

The total expenditure for the year was £43,258 9s. 10d., against £41,205 14s. 2d., in 1931. Salaries and Wages, Gas, Water and Fuel, Electric Light and Power and Animal House Expenses and Forage accounted for most of the increase in expenditure as compared with last year.

In conclusion, the Governing Body desires to express its appreciation of the devoted co-operation of the Director and all members of the Staff in carrying out the work of the Institute.

WILLIAM BULLOCH,

Chairman of the Governing Body.

BALANCE SHEET

AND

ACCOUNTS.

Dr.

The Lister Institute

BALANCE SHEET

			£	s.	d.	£	s.	d.
To CREDITORS						2,138	3	1
To PENSION FUND—								
As per Account at 31st December, 1930..						27,311	2	0
To JENNER MEMORIAL RESEARCH STUDENTSHIP FUND—								
As per Account at 31st December 1931 ..			8,156	14	11			
Add Amount transferred from Income and Expenditure Account, 1932			101	16	10			
						8,258	11	9
To CONTINGENCY FUND—								
As per Account at 31st December 1923 ..			14,228	18	1			
Add Amount transferred from Income and Expenditure Account, 1932			3,771	1	11			
						18,000	0	0
To SINKING FUND to 31st December 1932 ..						22,991	8	6
To CAPITAL FUND to 31st December 1932—								
Donations, &c., received to date from the following:—								
Dr. Ludwig Mond (1893)			2,000	0	0			
The Berridge Trustees (1893/98)			46,379	10	1			
The Grocers' Company (1894)			10,000	0	0			
Lord Iveagh (1900)			250,000	0	0			
Lord Lister's Bequest (1913) as per Account at 31st December, 1923			18,904	5	8			
✓ William Henry Clarke Bequest (1923/6)			7,114	5	7			
Other Donations (1891-1926)			20,421	18	3			
Income and Expenditure Account:—								
As per Account at 31st December, 1930..		154,442	1	11				
Add Balance for the year ending 31st December, 1932		6,501	4	6				
						161,033	6	5
						515,853	6	0

WILLIAM BULLOCH, *Chairman.*

G. W. ADDISON, *Hon. Treasurer.*

£594,552 11 4

REPORT OF THE AUDITORS

We have audited the above Balance Sheet. We have obtained all the information and explanations we have required, being held by the Institute on their behalf. In our opinion, such Balance Sheet is full and fair, and properly drawn and the explanations given to us and as shown by the books of the Institute.
London, 13th April, 1933.

By CASH—							£	s.	d.	£	s.	d.
At Bankers:	Deposit Account	..	..	..	..	..	4,000	0	0			
	Current Accounts	..	..	..	..	..	7,465	16	5			
In hand	..	..	..	..	..	..	48	10	3	11,514	6	8
By INVESTMENTS, GENERAL FUND (at cost, less amounts written off)—												
£70,000	4 per cent. Consolidated Stock	..	..	..	..	..	62,740	19	0			
£43,000	4½ per cent. Conversion Stock, 1940-44	..	..	..	..	..	41,702	3	3			
£17,000	5 per cent. Conversion Stock, 1944-64	..	..	..	..	..	15,997	0	7			
£47,000	4 per cent. Funding Stock, 1960-1990	..	..	..	..	..	39,970	13	3			
£25,000	3½ per cent. War Stock	..	..	..	..	..	24,674	13	2			
£37,000	Local Loans 3 per cent. Stock	..	..	..	..	..	20,829	1	7			
£3,000	Port of London 4 per cent. B. Stock	..	..	..	..	..	2,686	17	7			
£1,000	Dominion of Canada 4 per cent. Registered Stock, 1940-1960	..	..	..	..	..	928	4	6			
£2,000	Cape of Good Hope 3½ per cent. Consolidated Stock, 1929-49	..	..	..	..	..	1,802	12	0			
£25,000	Cape of Good Hope 3 per cent. Consolidated Stock, 1933-1943	..	..	..	..	..	23,850	0	0			
£25,000	Natal 3 per cent. Consolidated Stock, 1929-1949	..	..	..	..	..	21,400	0	0			
£25,000	New South Wales 3 per cent. Inscribed Stock, 1935	..	..	..	..	..	22,900	0	0			
£2,000	New South Wales 4 per cent. Inscribed Stock, 1942-62	..	..	..	..	..	1,882	3	4			
£25,000	New Zealand Government 3 per cent. Inscribed Stock, 1945	..	..	..	..	..	22,114	0	0			
£26,100	South Australian Government 3 per cent. Consolidated Stock, 1916 or after	..	..	..	..	..	16,800	0	0			
£2,900	Commonwealth of Australia 3½ per cent. Registered Stock, 1936-37	..	..	..	..	..	2,825	6	0			
£600	Union of South Africa 4 per cent. Consolidated Stock, 1943-1963	..	..	..	..	..	594	2	0			
£25,000	Victorian Government 3 per cent. Consolidated Inscribed Stock, 1929-1949	..	..	..	..	..	19,800	0	0			
£700	Western Australia Government 4 per cent. Inscribed Stock, 1942-1962	..	..	..	..	..	698	7	0			
£20,000	Southern Railway Preferred Ordinary Stock	..	..	..	..	..	13,500	0	0			
£6,200	London & North Eastern Railway 3 per cent. Debenture Stock	..	..	..	..	..	3,961	0	0			
£5,000	Great Central and Midland Railway Joint Committee 3½ per cent. Guaranteed Stock	..	..	..	..	..	3,623	0	0			
£353	London & North Eastern Railway 4 per cent. First Guaranteed Stock	..	..	..	..	..	499	11	0			
£8,650	London, Midland & Scottish Railway 4 per cent. Preference Stock	..	..	..	..	..	7,960	0	0			
£15,825	London, Midland & Scottish Railway 4 per cent. Preference Stock, 1923	..	..	..	..	..	11,300	0	0			
£18,750	London & North Eastern Railway 4 per cent. First Preference Stock	..	..	..	..	..	13,028	6	7			
£25,000	East Indian Railway 3 per cent. New Debenture Stock	..	..	..	..	..	13,890	0	0			
£661	Madras & Southern Mahratta Railway 4 per cent. Debenture Stock, 1938	..	..	..	..	..	656	19	7			
£800	Grand Trunk Railway Company of Canada Great Western Borrowed Capital 5 per cent. Perpetual Debenture Stock	..	..	..	..	..	996	0	0			
£1,937	Grand Trunk Railway Company of Canada 4 per cent. Guaranteed Stock	..	..	..	..	..	1,733	0	0			
£800	Ontario and Quebec Railway 5 per cent. Permanent Debenture Stock	..	..	..	..	..	984	0	0			
£3,400	Gas Light and Coke Company Ordinary Stock	..	..	..	..	..	3,638	0	0			
										417,906	0	6
By INVESTMENTS, SINKING FUND (at cost)—												
£9,600	4½ per cent. Conversion Stock, 1940-44	..	..	..	..	..	8,806	16	7			
£7,450	4 per cent. Funding Stock, 1960-1990	..	..	..	..	..	5,850	5	3			
£10,200	3½ per cent. Conversion Stock	..	..	..	..	..	8,289	5	0			
	Balance uninvested	..	..	..	..	..	95	1	8	22,991	8	6
By INVESTMENTS, JENNER MEMORIAL RESEARCH STUDENTSHIP FUND (at cost)—												
£2,650	Southwark and Vauxhall Water Co. 3 per cent. Debenture Stock "B"	..	..	..	..	..	2,756	10	0			
£1,598	Southern Railway 5 per cent. Preference Stock	..	..	..	..	..	2,740	5	0			
£728 11s. 4d.	Liverpool Corporation 3 per cent. Stock, 1942, or after	..	..	..	..	..	556	15	6			
£2,000	4 per cent. Funding Stock, 1960-1990	..	..	..	..	..	1,797	14	0			
	Balance uninvested	..	..	..	..	..	407	7	8	8,258	11	9
By INVESTMENTS, PENSION FUND (at cost)—												
£22,000	4 per cent. Funding Stock, 1960-1990	..	..	..	..	..	17,165	3	5			
£13,000	3½ per cent. Conversion Stock	..	..	..	..	..	10,038	1	5			
	Balance uninvested	..	..	..	..	..	107	17	2	27,311	2	0
(The book value of the above Investments is, in the aggregate, less than their market value at 31st December 1932.)												
By DEBTORS										7,960	11	10
By FURNITURE, FITTINGS, SCIENTIFIC APPARATUS AND BOOKS—												
At cost less depreciation as per account 31st December 1930										2,471	17	2
By EXPENDITURE ON INSTITUTE BUILDINGS AT CHELSEA—												
As per account 31st December 1910, including purchase of freehold site, £5,000										70,916	3	1
By PURCHASE OF FREEHOLD LAND ADJOINING THE "STUDIOS" CHELSEA—												
As per account 31st December 1912										169	6	8
By LEASE OF THE "STUDIOS" CHELSEA, as per last account							1,392	14	9			
Less Amount written off for the year							65	2	0	1,327	12	9
By QUEENSBERRY LODGE FARM, ELSTREE—												
Purchase of freehold land and buildings and Expenditure on new buildings—												
As per account 31st December 1912										20,455	10	0
By STOCK OF ANIMALS							288	0	0			
By STOCK OF ANTITOXINS							2,982	0	6			
										3,270	0	6
* Nothing has been charged for depreciation of Furniture, &c. since new purchases made during the year to a greater amount than the estimated depreciation (10%) have been written off.										£594,552	11	4

TO THE MEMBERS.

The Superannuation Scheme for certain of the Staff provides for the Life Policies for the time being in existence up so as to exhibit a true and correct view of the state of the Institute's affairs, according to the best of our information

COOPER BROTHERS & CO.,

Chartered Accountants. } Auditors.

Dr. INCOME AND EXPENDITURE ACCOUNTS

INCOME.								£	s.	d.
To Interest and Dividends on General Fund Investments	...	...	...	...	...	...	...	17,560	17	4
To Interest on Sinking Fund Investments	...	...	...	...	...	...	...	1,002	0	0
To Investigation, Diagnosis and Analysis Fees, &c.	...	...	...	...	...	...	...	2,175	14	8
To Sales of Sera, Vaccines, &c., and Stock at 31st December 1932, less Stock at 1st January, 1932	...	...	...	...	...	...	...	31,222	8	3
To Rent of Rooms	...	...	...	...	...	...	...	752	0	0
To Pension Fund—excess of Income over Expenditure transferred	...	...	...	...	...	...	...	907	16	0

£53,620 16 3

Dr.

Pension

	£	s.	d.
To Interest on Investments	1,385	0	0

£1,385 0 0

Dr.

Jenner Memorial Research

	£	s.	d.
To Interest and Dividends on Investments	261	1	10

£261 1 10

Dr.

Morna Macleod Research

	£	s.	d.
To Cash received from W. A. Macleod, Esq.	315	0	0

£315 0 0

Preventive Medicine.

for the year ending 31st December, 1932.

Cr.

EXPENDITURE.

	£	s.	d.
By Rent, Rates, Taxes and Insurance	1,351	6	1
By Salaries and Wages of Staff	24,986	17	0
By Premiums on Federated Superannuation Policies	1,393	15	0
By Stationery, Printing and Postage	388	12	8
By Printing of Collected Papers	223	12	11
By Office Expenses, Auditors' Fee and Sundries	312	15	3
By Travelling Expenses	47	14	1
By Gas, Water and Fuel	1,450	14	7
By Electric Light and Power	400	2	8
By Nutrition, Protozoological and Experimental Pathology Expenses, including Apparatus	603	4	3
By Bacteriological Laboratory Expenses, including Apparatus	262	2	3
By Vaccine Laboratory Expenses, including Bottles	70	10	5
By Water and Bio-chemical Laboratory Expenses, including Apparatus	588	8	1
By Serum and Vaccine Lymph Laboratories Expenses, including Apparatus and Bottles	3,940	18	9
By Culture Media	134	15	9
By Animals	1,283	13	9
By Animal House Expenses and Forage	2,024	6	10
By Alterations, Repairs and Renewals, including Workshop Expenses	1,653	5	2
By Library Expenses	482	5	2
By General Stores	281	14	0
By Amount written off Lease of the "Studios," Chelsea	65	2	0
By Sinking Fund (½% per annum on Cost of Buildings and Interest on Investments) ...	1,412	13	7
By Amount transferred to Contingency Fund	3,771	1	11
By Balance, transferred to Capital Fund	6,591	4	6
	10,362	6	5
	£53,620	16	3

Fund.

Cr.

	£	s.	d.
By Pensions	427	4	0
By Balance, transferred to General Income and Expenditure Account	907	16	0
	£1,335	0	0

Studentship Fund.

Cr.

	£	s.	d.
By Salary and Expenses	159	5	0
By Balance, transferred to Balance Sheet	101	16	10
	£261	1	10

Studentship Account.

Cr.

	£	s.	d.
By Salary, Mr. R. O. Jones	26	5	0
By Cash in hand	288	15	0
	£315	0	0

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- | | | | | |
|---|-----|-----|-----|--|
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| BARRATT, J. O. W.... | ... | ... | ... | DETERIORATION OF FIBRINOGEN AND THROMBIN. <i>Journal of Physiology</i> , Vol. LXXV., 1932. |
| CHICK, HARRIETTE | ... | ... | ... | THE RELATION OF ULTRA-VIOLET LIGHT TO NUTRITION. (Oliver-Sharpey Lectures.) <i>Lancet</i> , Vol. II., 1932. |
| CHICK, HARRIETTE AND JACKSON, HESTER M. | | | | NOTE ON THE INTERNATIONAL STANDARD FOR THE ANTINEURITIC VITAMIN B ₁ . <i>Biochemical Journal</i> , Vol. XXVI., 1932. |
| CRANE, M. B. AND ZILVA, S. S | ... | ... | ... | THE ANTISCORBUTIC POTENCY OF APPLES. V. <i>Biochemical Journal</i> , Vol. XXVI., 1932. |
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| EAGLES, G. H. AND KORDI, A. H. H. | | | | THE CULTIVATION OF VACCINIA VIRUS: A NEW SERIES OF SUBCULTURES IN CELL-FREE MEDIUM. <i>Proceedings of the Royal Society, B.</i> , Vol. 111, 1932. |
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THE LISTER INSTITUTE
OF
PREVENTIVE MEDICINE

Report of the Governing Body,
1934.

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

May 30th, 1934.

The Lister Institute of Preventive Medicine,

CHELSEA BRIDGE ROAD, LONDON, S.W. 1.
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ANNUAL GENERAL MEETING
OF
The Lister Institute of Preventive Medicine,
May 30th, 1934.

REPORT OF THE GOVERNING BODY.

The Governing Body has the honour to present the Institute's 40th Annual Report.

GOVERNING BODY.

No change in the personnel of the Governing Body occurred during the year.

At the meeting held last year, the Council re-elected Professor W. Bulloch, Professor A. E. Boycott, and Professor A. Harden as its representatives on the Governing Body until December 31st, 1934.

COUNCIL.

At the Annual General Meeting last year the three members of Council retiring by rotation were Sir Walter M. Fletcher, Professor Georges Dreyer and Dr. John Fawcett. All three members were re-appointed as the respective representatives of the Members of the Institute, the University of Oxford and the University of London.

The members of Council who, in accordance with the Articles of Association, retire this year by rotation, but who are eligible for re-election, are Lord Mildmay of Flete, the representative of the Royal Agricultural Society, Professor A. Harden and Professor J. C. G. Ledingham, two representatives of the Members of the Institute.

MEMBERS.

The Governing Body regrets to announce the death during the year of Sir Walter M. Fletcher, who had always shown a keen interest in the work of the Institute and was one of the appointed representatives of the Members upon the Council.

STAFF.

Dr. E. Weston Hurst resumed his appointment in April last on his return from America, where he had enjoyed the hospitality of the Rockefeller Institute, Princeton, for some eighteen months.

During the year Dr. C. Russell Amies and Dr. M. H. Finkelstein have held the Institute's two Research Fellowships in Bacteriology, the latter resigning on April 30th to take up the appointment of Special Serologist to the South African Government. Dr. L. A. Elson has continued to hold the Jenner Memorial Research Studentship and Mr. R. O. Jones the Morna Macleod Research Studentship, the endowment of which is due to the generosity of Mr. and Mrs. W. A. Macleod.

Miss A. H. Rosenheim resigned her Grocers' Company Research Studentship in September and was succeeded by Mr. V. N. Patwardhan, B.Sc., and on the resignation of Dr. T. F. Macrae, Research Student in Biochemistry in July, Mr. S. S. Randall, B.Sc., was appointed to the vacancy. Miss H. M. Jackson, temporary assistant in the Division of Nutrition, resigned in September.

RESEARCH WORK.

Before surveying the scientific work carried out during the year in the various departments, the Governing Body desires again to record its appreciation of the continued co-operation it has enjoyed with the Medical Research Council. Salaries of the Staff of the National Collection of Type Cultures, of Miss Hume and her assistant, of Dr. Zilva and his assistants and up to March, 1934, of Professor Korenchevsky and his assistant have been furnished by the Council, while the Institute has provided accommodation for each of these workers and also the necessary materials for the researches of the last three named. Since April 1st, the salary of Professor Korenchevsky has been an equal charge on the Medical Research Council and the Institute.

The hospitality of the Institute's laboratories has been extended to two foreign guests displaced from scientific posts in Germany, viz., Professor Ph. Ellinger, formerly Professor of Pharmacology of the Düsseldorf Academy of Medicine, and Miss E. Klieneberger, Privatdozentin in the Bacteriological Department of Frankfurt University.

DEPARTMENT OF BACTERIOLOGY, SEROLOGY AND EXPERIMENTAL PATHOLOGY.

Studies on Viruses.

Vaccinia. Cultivation on artificial media. Continuing his studies on the cultivation of vaccinia virus on cell-free fluid media, Dr. G. H. Eagles has completed a series of passages in which the washed elementary bodies obtained from deposits of Berkefeld V. filtrates of dermal virus centrifuged at high speed, were used for the initial seeding. "Kidney extract," prepared by grinding, salting and high speed centrifugation, constituted the culture medium. Seven generations of subculture have been carried through without apparent loss of potency, the final subculture representing a multiplication of 20 times the original potency of the seeding as judged by animal titrations.

As in previous series, considerable irregularity was experienced among individual flasks set up at the same time. The few workers in other countries who have attempted the cultivation of vaccinia in cell-free media have not succeeded in securing definite evidence of growth, and in the attempt to reconcile such conflicting results, Dr. Eagles is now, in conjunction with Dr. A. B. Sabin (Fellow, National Research Council, U.S.A.), undertaking a fresh series of experiments and certain possible sources of error are being investigated.

Attempt to cultivate the virus on solid media. Dr. Eagles has used as medium a cell-free extract either of chicken embryo or of adult rabbit kidney stiffened by the addition of hen plasma and a small amount of agar. Washed elementary bodies from centrifuged filtrates formed the inoculum. No visible growth appeared on the inoculated areas though active virus could be obtained by surface washing up to seven days after inoculation.

The use of elementary body suspensions for vaccination against smallpox. These suspensions, derived from filtrates of dermal virus by high-speed centrifugation, possess high activity and can be prepared with ease and economy. As they represent the virus in the purest form and are bacteriologically sterile, an investigation is being made of their activity under various conditions of storage.

Dr. C. R. Amies (Research Fellow in Bacteriology), has found that such suspensions, in a medium of simple broth, retain their activity for considerable periods when kept at room temperature and, indeed, for several weeks, at 37°, the survival periods comparing very favourably with those obtained with crude pulp in saline or glycerol saline. At 0°C. the loss of activity is, as might be expected, small.

Attempted cultivation of vaccinia in symbiosis with yeasts, etc. An important claim has recently been made by Russian workers that vaccinia virus can be readily cultivated *in vitro* in symbiosis with yeasts. They believe that the virus is strongly adsorbed to these micro-organisms and that proliferation takes place, most probably within the cell substance of the yeast or other symbiont. Dr. Amies has conducted a long series of experiments in the effort to confirm these findings but has obtained no evidence whatever either of any strong adsorption of vaccinia virus (in the form of elementary bodies) by bacteria and yeast cells, or of proliferation of the virus under the conditions described. It is suggested that some, at least, of the experimental lesions which are claimed to have been produced in animals by inoculation of such cultures may have been due not to the virus but to the associated micro-organisms.

Complement-fixation with the elementary bodies of vaccinia. Dr. M. H. Finkelstein (Research Fellow in Bacteriology), using a modification of the complement-fixation technique introduced by Mackie and Finkelstein in 1928, has shown that no fixation takes place with hyperimmune sera and material from vaccinia if the elementary bodies are absent. This has been demonstrated by the absence of fixing activity with Seitz filtrates of vaccinia and with the supernatant fluids after high speed centrifugation of Berkefeld V filtrates. The deposits from the latter were active when resuspended in saline.

Varicella and Herpes Zoster. The belief that chickenpox and herpes zoster are in some way related has been entertained for many years on clinical and epidemiological grounds. Recently Paschen reported that elementary bodies similar in size and staining reactions to those of vaccinia and varicella are present in the vesicle fluid of early skin lesions of zoster. Dr. Amies, following up his previous work on varicella, has fully confirmed the finding of elementary bodies in herpes zoster and has obtained pure suspensions of them by high-speed centrifugation of the vesicle fluid. Such suspensions are agglutinated by the serum of the convalescent zoster patient and there is, therefore, a strong inference that these elementary bodies represent the virus of zoster. He has further demonstrated that such convalescent zoster serum agglutinates the elementary bodies of varicella to approximately the same titre and in a few cases varicella convalescent serum has been found to agglutinate both varicella and zoster elementary bodies. These results, if confirmed by larger experience, will lend further support to the belief that these two viruses are closely related, if not identical.

All attempts to infect the usual laboratory animals with varicella virus have so far failed.

Fowl-pox and Pigeon-pox. Dr. Finkelstein has been making an immunological study of the relationship of fowl-pox to pigeon-pox. Hyperimmune sera have been prepared by infecting fowls with fowl-pox and pigeon-pox over lengthy periods. Macroscopic agglutination tests carried out at 55°C. have shown that fowl-pox sera agglutinate pigeon-pox elementary body suspensions to a rather lower titre than the homologous suspensions. On the other hand, pigeon-pox hyperimmune sera have not so far been found to agglutinate fowl-pox elementary bodies.

Pigeon-pox virus is being maintained both by pigeon passage and fowl passage and any effect that the host may have on the response of the elementary bodies to hyperimmune sera in agglutination and agglutinin-absorption tests will be investigated.

Louping-ill virus: cultivation *in vitro*. Mr. D. W. Henderson (Beit Memorial Research Fellow) has conducted another series of experiments on the properties of louping-ill virus grown *in vitro*. The virus has been passed through a series of 12 sub-cultures in a medium consisting of whole mouse-embryo pulp, sheep serum and Tyrode solution and it is estimated that the increase in virus over the series was of the order of 10^{16} .

Modifications of the technique of cultivation have been attempted with varying success. It has now been ascertained that the volume of embryonic tissue employed in the medium may be reduced at least eight times without seriously affecting virus survival. The sheep plasma used in earlier experiments can readily be replaced by sheep serum and it has been found that appreciable amounts of "free" virus can be found in this liquid base. If a portion of the contents of any culture flask are carefully removed and centrifuged to clear it of all cells it can be shown that this cell-free material contains as much virus as that portion which is ground and contains the full complement of cells. Work on the properties of this "free" virus and the relation of living cells to its continued survival are to be continued.

Virus recovered from Acute Ascending Myelitis in Man, associated with Focal Necroses in Viscera ("B" Virus). Dr. Sabin, before his arrival here in January, 1934, had recovered from a fatal case of acute ascending myelitis in New York a virus readily communicable to rabbits in which an ascending paralysis leading to fatal issue regularly followed an intradermal injection after an interval of some days. These animals, like the original human case, presented necrotic foci in certain viscera similar to those associated with highly virulent vaccinia and herpes infections. The further investigation of this virus from the point of view of possible relationship to the herpetic group of viruses is being actively pursued by Dr. Sabin. The virus in the form of rabbit brain or cord is exceedingly active. Even a 1 in 5,000 dilution of a 10 per cent. highly centrifuged brain and cord emulsion still produces paralysis and death after intradermal inoculation though the skin lesion may be minimal or imperceptible. So far, therefore, it has not been possible to secure convalescent rabbit sera for cross-immunity experiments but attempts are being made to immunise with formalinised material.

Rhesus monkeys, on the other hand, can be immunised with the "B" Virus by intracutaneous and intraperitoneal inoculation. Rabbits are also being immunised with the Perdrau E.L. herpetic virus and with Bedson's dermatropic herpes strain so that material will soon be available for cross-neutralisation tests. The "B" Virus was not found to be infective for *M. rhesus* in the tests made in New York, but Dr. Sabin has succeeded here in infecting one rhesus monkey with rabbit virus by intracerebral and intraperitoneal inoculation, the animal showing marked paresis on the second day and succumbing on the third. Brain and cord from this monkey, when inoculated intracutaneously in the rabbit, produced a typical large haemorrhagic skin lesion, ascending paralysis and death.

Mice would also appear to be susceptible to the "B" Virus from tests made by Dr. Sabin with the assistance of Dr. Finkelstein. The majority of mice inoculated intracerebrally and intraperitoneally developed paresis and generalised tremors about the 8th or 12th day after inoculation.

The "B" Virus is filterable through Berkefeld V and N candles and high-speed centrifugalisation of the filtrate has yielded a highly potent sediment and a supernatant entirely free of virus. This observation will facilitate the investigation of the "B" Virus from the standpoint of the elementary bodies it doubtless contains.

The Viruses (so-called) of Pleuropneumonia and Agalactia. The investigation by Professor Ledingham of the growth phases on solid and liquid media of the causative organisms of pleuropneumonia and agalactia, as revealed by an impression technique, was brought to a temporary conclusion in the autumn and published as an illustrated study. The tentative suggestion was made from the evidence adduced that these very similar polymorphic organisms might be enrolled in the family *Actinomycetaceae*, but the question of genus was reserved for further consideration and research. This further study has been taken up in recent months by Dr. Emmy Klieneberger, formerly of Frankfurt University, who has in the past devoted much attention to bacterial morphology. By a modification of Kuhn's technique for the investigation of the structure of bacterial colonies without mechanical disturbance, she has secured an excellent series of stained preparations of pleuropneumonia and agalactia colonies from their earliest stages. Her findings agree closely with those derived from the impression technique used by Professor Ledingham and her study is being published.

Serological Studies : Antigenic Constitution, Virulence and Immunising Properties of Bacteria.

The Antigens of the Plague Bacillus. Dr. H. Schütze's studies of the development, stability and antigenic importance of the heat-labile envelopes of *B. pestis* have been continued. He has been able to demonstrate that while a temperature of 37°C. is necessary for the full development of the envelope, partial development is still possible at a lower temperature such as 26°C., provided the parent culture has been grown at 37°C. The parent culture must, however, be a quite recent one unless storage has taken place in the cold room. The degree to which envelope substance develops in an agar culture at 26°C. is also affected by the mode of inoculation, whether, e.g., the inoculum is solid bacterial growth or a fluid suspension thereof.

The factors concerned with these phenomena are still obscure. That the antigen contained in the envelope of *B. pestis* is sensitive to alkali has been shown by the damage sustained by a vaccine of normal alkaline reaction when it is sterilised by heat in that condition. If the vaccine is neutralised before sterilisation, the envelope substance retains a greater antigenic power, producing in rabbits antibody titres on the average 50 per cent. greater than those of the unneutralised controls.

Anti-dysentery vaccines. Miss D. Steabben has completed her study of the antigenic condition of *B. dysenteriae*, Shiga, when incubated at 45°C. with special reference to its use as a prophylactic agent. Vaccines composed of such organisms had already shown themselves superior in prophylactic value to those prepared in the usual way at 37°C. It has now emerged that a 45°C. vaccine contains, count for count, 50 per cent. more bacterial substance than a 37°C. vaccine and also 4 to 5 times more toxin. More acid is also produced, which makes detoxication by formalin difficult unless neutralisation is first effected. When the toxin content of the two vaccines is equalised, their prophylactic value becomes equal. This lack of any qualitative, as opposed to quantitative, difference is confirmed by the exhibition of complete homogeneity in precipitin, agglutination and absorption tests.

The Pasteurella Group. Difficulties with the agglutination tests in the case of organisms of the Pasteurella group have suggested the precipitin test as an alternative method for classification of strains. Dr. H. S. Yusef (Cairo) has explored the possibilities of this serological reaction and by the use of acid extracts has been able to demonstrate, not only cross-precipitation, i.e., relationship within the group, but also, by the absorption test, differences. On these lines he is now proceeding to establish what antigenic groupings there may be.

Serological Relationships among Intestinal Bacteria. Dr. M. Neustat (Moscow) took the opportunity of a short sojourn at the Institute, as a Rockefeller Student, to examine a series of intestinal organisms for any possible antigenic relationship with members of the Salmonella Group.

What appears to be a quite sporadic and rare relationship in the "O" antigen was discovered in some 4 strains out of a total of 80 examined. The four organisms were *B. neapolitanus*, *B. morgani*, *B. dysenteriae* (Flexner X), and an unclassified coliform, and they disclosed an affinity with the Salmonella Groups A, A, D and B respectively. In no instance was there complete identity of "O" antigen, but in two cases the relationship was very close.

Spore-bearing Anaerobes. *C. oedematis maligni*. Experiments by Mr. Henderson with the "O" antigen of this organism have been extended. Immunisation of guinea-pigs with the antigen (which consists of washed bacillary bodies steamed for two hours at 100°C.) has shown that protection can be afforded against 500—5,000 certain infecting doses of an activated spore-suspension. The course of immunisation, however, has to be carried further than that previously described for *C. chauvoei* prophylaxis.

Cross immunisation experiments with "O" antigen have been conducted, using strains previously differentiated by Miss M. Robertson on the basis of their "H" antigen relationship. It has been shown that certain strains afford a minimal degree of cross protection. A study of the "O" antigen relationship of such strains by agglutination and complement fixation methods has indicated that while a group antigen may be present, there exist among strains of this species, sharply differentiated "O" antigens and the *in vitro* records reflect the results of animal experiments. These results stand in sharp contrast to the complete identity of the "O" antigen previously held to exist among all strains of *C. chauvoei*.

The antibacterial mechanism of protection against infection with the spore-bearing anaerobes is of considerable interest and experiments now in progress are designed to throw light on this subject. Guinea-pigs actively immunised with "O" antigen have been subsequently tested by the intradermal injection of an activated spore suspension and the resulting dermal lesions have given interesting clinical pictures. Specimens thus obtained are being examined histologically, together with specimens from non-vaccinated controls.

C. tetani. Work commenced last year on the antibacterial mechanisms associated with *C. tetani* prophylaxis has been continued. For the production of a polyvalent anti-O horse serum, Dr. G. F. Petrie has kindly continued the immunisation of horses with "O" antigen prepared by Mr. Henderson. The sera now obtained show satisfactory titres as estimated in "O" agglutinins and complement fixation. Passive

protection tests in mice with these sera, however, have, so far, yielded negative results. It is believed that the failure to demonstrate protective antibody *in vivo* may be due to the mode of action of the tetanus toxin and to its unusual potency, together with the lack of invasive power of the tetanus bacillus. Active immunisation experiments with guinea-pigs (using tetanus "O" antigen) and their subsequent test with activated tetanus spore suspensions have been unsuccessful.

Experiments on the efficacy of high titre antitoxic sera in protection against *C. tetani* spore infection have shown that such sera only delay the onset of the disease which later ends fatally. A successful issue may, however, be obtained by repeated intravenous inoculation of antitoxin until the local lesion produced by the activator is no longer effective in maintaining conditions suitable for the reproduction of the organism and the associated toxin production. The survival of spores in such recovered animals is being investigated.

Studies on Virulence and its Relation to "O" Antigen. Dr. A. Felix, in collaboration with Miss R. M. Pitt, has studied the relationship between virulence and susceptibility to the action of the "O" antibody. In previous work, by Felix and Olitzki in 1926, it has been shown that strains of *B. typhosus* and *B. paratyphosus A*, which are highly sensitive to "O" agglutinins, are also highly susceptible to the bactericidal action of serum. In experiments with mice it has now been found that highly agglutinable strains of *B. typhosus* are of low virulence, while inagglutinable strains are highly virulent. Both types of strain were carefully tested by all the known methods for detecting "roughness," and were found to be perfectly smooth. There was also no difference in their content of "H" antigen.

The inagglutinability of these strains is strictly a property of the living organisms. When killed by heat or by treatment with various chemicals, the suspensions are agglutinated by "O" agglutinins to titre limit. In this respect it makes no difference whatsoever whether the "H" antigen is destroyed by the treatment used for killing the organisms, or whether it is left intact. The resistance to "O" agglutinins is also suppressed by growing the cultures for 24 hours on agar containing phenol in a dilution of 1 in 900; simultaneously the virulence of the cultures is reduced to that of strains of the avirulent, agglutinable type.

The nature of the factor underlying the phenomenon is yet entirely obscure. The virulent strains do not possess any demonstrable capsule; when killed, their toxicity for mice is not greater than that of avirulent strains; filtrates from broth cultures and extracts from agar cultures of the virulent strains do not increase the virulence of avirulent strains, nor do they produce any inhibitory effect on "O" agglutination; when suspensions of killed organisms are used in agglutinin absorption tests, no antigenic difference is demonstrable between the two types.

The results do not contradict the view that rough forms are non-virulent, but they do indicate that the mere presence of smooth "O" antigen does not completely define virulence. Some obscure property is required to render this antigen resistant to "O" antibody.

Captain S. S. Bhatnagar (Indian Medical Service, Karachi) has commenced an investigation of the rôle played in phagocytosis by "O" and "H" antibodies. The results so far obtained with *B. typhosus* and with serum from normal rabbits indicate a definite correlation between phagocytosis and the titre of the natural "O" agglutinin.

Serological Varieties of Typhus.

(a) **Rocky Mountain Spotted Fever.** Recent work in the United States of America and in Brazil has shown that the viruses of Rocky Mountain spotted fever and of the tick-borne endemic typhus of Sao Paulo are immunologically identical. Dr. Felix has tested sera from cases of Rocky Mountain spotted fever against the known types of *Proteus X* and found them to react in the same way as previously shown in the case of the Brazilian variety. These results were subsequently confirmed in America and lend further support to the thesis postulated by Dr. Felix that cross-immunity between different varieties of typhus virus is reflected by identity of the serum reactions to *Proteus X*.

(b) **Fièvre boutonneuse of the Mediterranean.** It has been stated by Greek authors that sera from cases of this tick-borne variety of typhus, which is endemic in Greece, fail to react with *Proteus X*. Dr. Felix has tested a series of patients' sera from Athens and the reactions obtained were identical with those previously described in cases from Tunis, i.e. positive either with X_{10} or X_2 or with both these types, and negative with type XK.

Resistance to Infection and Genetic Constitution.

Through the kindness of Dr. L. T. Webster, of the Rockefeller Institute, and Professor J. B. S. Haldane, of University College, selected and pure line races of mice have been obtained and the breeding of them has been successful enough to permit of the testing of groups of these races for resistance to a variety of infective agents, including *S. typhi murium*, *S. enteritidis*, *M. pneumoniae*, and the virus of louping-ill. Dr. Schütze and Dr. Finkelstein, who are conducting these experiments, have already been able to demonstrate very striking differences in the susceptibility of these strains of mice to the test infections selected, and it is hoped in this way to acquire some insight into various processes of immunity.

Studies on Corynebacteria.

C. ovis (Preisz-Nocard). Dr. H. R. Carne, D.V.Sc. (Sydney), who has made extensive investigations on Caseous Lymphadenitis of sheep, a very important disease in Australia from the economic point of view, has, since his arrival in January, been studying certain questions concerned with the toxigenic and pyogenic activities of the causative organism *C. ovis*. The experimental production of immunity towards the pyogenic manifestations of the organisms will constitute his main problem.

C. ulcerans. This name has been given by Dr. Ruth Gilbert of Albany, N.Y., to certain aberrant members of the genus which she recovered from human throats and which are closely related to those studied by Dr. M. M. Barratt at the Institute. These aberrant members appear to possess affinities both with *C. diphtheriae* and with *C. ovis* (Preisz-Nocard). In the course of diphtheria diagnosis during the past year, Dr. Barratt has recovered three additional strains of this group while four others from various sources have been examined. None of the strains isolated in this country would appear to have been associated with serious illness, but in at least two of the American cases Dr. Gilbert is of opinion that they caused a fatal illness which did not respond to diphtheria antitoxin.

Endocrinology.

Dr. V. Korenchevsky, in collaboration with Mrs. M. H. Dennison, Dr. S. Levy Simpson and Miss A. Kohn-Speyer, continued the investigations on the endocrine organs in males, chiefly the sexual glands and those related to them.

Biological Assay of Testicular Hormone. In previous reports a method of assay of testicular hormone on castrated rats was described. More recent experiments have shown that the physiological variations from the average of the weights of the organs investigated were also small in normal rats. Therefore, by comparing the mean of the average changes in the litters of rats and following exactly the technique and precautions previously given, the method described could be applied to normal rats for the study of physiological or pathological conditions or for the assay of substances which influence the weight of one or more organs. Injections of testicular hormone dissolved in oil gave satisfactory results in assay, although at the end of the experiment unabsorbed oil was found in the areas of the more recent injections. This indicates that the hormone, and probably also other substances dissolved in oil, are absorbed from oily solutions during the whole period of injection at some constant rate of absorption.

Variations in the weight of organs of normal rats in relation to age. The organs of normal rats in so far as weight of organ and age of animal are contrasted, may be classified in one or other of the following four groups:—

Group I.—*The actual weight of the organ increases with age, whilst the weight per unit of body weight decreases.* To this group belong the adrenal, thyroid, hypophysis, kidney, heart and spleen. There are some irregularities due to a decrease in the rate of change, e.g., in thyroid and spleen, but on the whole it may be said that, for the organs mentioned, the actual weight is smallest and the weight per unit of body weight largest in the young animal. This relation may indicate a specially active function of these organs in youth.

Group II.—*The actual weight of the organ increases up to the date of sexual maturity, the greatest weight per unit of body weight occurring in the period immediately preceding maturity, after which the organ gradually atrophies.* To this group belongs the thymus, in which the period of most active function—the nature of which is still unknown—coincides with the period preceding sexual maturity.

Group III.—*The actual weight increases with age, while the weight per unit of body weight increases only up to the period of sexual maturity, after which it slowly decreases.* To this group belong the testis and liver. This may indicate an increase in the function of these organs during the development of sexual maturity.

Group IV.—*Both the actual weight and the weight per unit of body weight increase with age.* To this group belong the prostate, seminal vesicles, and, with some irregularities, penis and depot fat. This indicates that the functional capacity of the secondary sex organs is great during the whole period of adult life, while the function of the sex glands is at its maximum during the period of development of sexual maturity, as mentioned above. An increase in the deposition of fat with increasing age probably indicates that metabolism is at a maximum in youth, and that some lowering of metabolism occurs after adult age is reached.

The Effects of Castration. Experiments performed on a large number of male rats have shown that the effect of castration is noticeable not only in the sexual organs, but also in several other organs. Castration produces the following changes: striking atrophy of the secondary sexual organs (prostate, seminal vesicles, penis and preputial glands), slight atrophy of the thyroid and, after about 70 days following

castration, of the liver and kidneys; the involution of the thymus is delayed and the adrenals and hypophysis are hypertrophied. In addition, an increase in fat deposition is shown by most animals, together with a slight decrease in both body weight and in gain in body weight. It is possible that the slight decrease in weight of the heart, which was observed, is also specific. Thus the inner secretion of the sexual glands controls to a greater or lesser degree the normal function of several organs. This also explains the influence of testicular endocrine secretion on general metabolism, which reflects variations in the functioning of organs and tissues. The specificity of the changes produced by castration is supported by the results of injections of testicular hormone into castrated male rats, the injection causing a return towards the normal of these changes, as has been shown by previous experiments.

Effects of Injections of Testicular hormone on Adult Normal and Adult Cryptorchid Rats.

The effect of three weeks' injection of testicular hormone into normal adult rats was small, differing in this respect from the quite definite effect on some of the organs of young rats. Only very large doses slightly reduced the weight of the testes and had a depressing effect on the interstitial cells of Leydig in the testes. Retrogression of the thymus was slightly accelerated. A similar slight effect was noticed on the testes and thymus of cryptorchid rats and in addition the weight of the prostate with seminal vesicles was slightly decreased.

Simultaneous administration of Testicular hormone with some other hormones. After castration, changes are always present in the thyroid and hypophysis, indicating a correlation in the function of these glands with that of the testes. The gonad-stimulating hormone, extracted from pregnancy urine, and desiccated thyroid were, therefore, administered simultaneously with testicular hormone to castrated rats. With the doses given there was no alteration in the specific effects produced by the testicular and thyroid hormones on the organs of castrated rats.

The Adrenal Cortex and Sex. There is a considerable amount of clinical evidence indicating a close relationship between the adrenal glands, the sexual organs and the secondary sexual characteristics.

Experiments were, therefore, performed to elucidate the effect on the sexual, endocrine and other organs, of adrenalectomy in male rats and of injections of extracts of the cortex of the adrenals into normal and castrated rats.

At the present time only these latter experiments are finished. These show no influence of a potent cortical extract on either the weight or histological structure of the organs mentioned above, in either normal or castrated rats. The potency of the extract used was well demonstrated by the prevention of all the symptoms of suprarenal deficiency in the injected rats, namely, loss of weight, diarrhoea, catarrhal condition of the eyes, loss of muscular strength and appetite and general exhaustion leading to death.

Sterility in Males on diets deficient in Vitamin A or Vitamin E. In the previous report experiments on male rats were described in which changes of a varying degree were produced in the testes by deficiency of vitamin A. The first changes are always noticeable in the spermatozoa, while the final changes affect all the seminiferous tissue except the Sertoli and Leydig's cells. These atrophic changes were classified in four stages, which usually appeared in succession.

In recent experiments deficiency in vitamin E was found to produce changes exactly similar to those produced by vitamin A. Since, as a result of these deficiencies, the spermatozoa are affected first, the sterility of such males must be explained by the degeneration of the spermatozoa. The results obtained are in agreement with those of most of the workers investigating this problem.

Coagulation of the Blood.

Dr. J. O. W. Barratt has concluded and published his investigation of methods of estimation of fibrinogen and thrombin.

The nature of the action of heparin and Chicago-blue in delaying or preventing coagulation of fibrinogen by thrombin has been further studied, and additional data have been obtained indicating that the anti-coagulative influence of these substances is exerted upon thrombin and that the action is chemical in nature.

DIVISION OF PROTOZOOLOGY.

During the year Dr. Muriel Robertson's work has been concerned with the study of various aspects of the effect of gamma ray irradiation on the growth of *Bodo caudatus*.

The Action of Anti-Bodo Serum on Irradiated Bodos. It was noted in the last report that the properties of a serum made by immunisation of the rabbit with *Bodo caudatus* were under investigation. This has now been completed and is in course of publication. The sensitiveness of irradiated bodos to such sera is now being tested on the basis of the results obtained with normal cultivated bodos.

A direct test has been devised to show the relative sensitiveness of irradiated and unirradiated strains. For these experiments the flagellates are cultivated in counted series of daily subcultures under exactly controlled conditions. This work is still in progress but the results obtained up to the present show a slightly greater sensitiveness on the part of the irradiated bodos. This greater effect amounts to a distinction in the killing titre of the following order; the normal culture—to cite an individual result—was killed in serum concentration of 1/900, but survived in 1/1200, while the irradiated one was killed in 1/1200 and survived in 1/1600. The importance of these results lies actually not so much in this slight but consistent distinction, as in the fact that they demonstrate that the bodos do not undergo a mutation under the influence of radium emanation into varieties which are resistant to a serum made with the normal strain.

The Effect of Exposure to Gamma Rays on Growth. Certain aspects of the general problem have been chosen as being particularly suitable for investigation with material of this type. For example, the question as to whether the check in the growth described in the earlier reports is exercised uniformly through the whole period between one division of the cell and the next, has received attention, and it appears that in very short exposures, such as two hours, made during the active period of growth of the cultures, the normal and the irradiated increase in numbers almost equally. Thereafter, however, in the irradiated, the multiplication seems to be very nearly arrested so that the discrepancy between the two cultures increases steadily from about the 3rd to the 6th or 7th hour of exposure. After 7 to 8 hours on the radium plaque, the irradiated cells come into division and there is a rather abrupt reduction in the discrepancy. The irradiated growth does not overtake the normal in the conditions of culture obtaining here, but this acceleration following upon the initial check, is of importance and is being further investigated.

Another aspect receiving attention and for which this material is convenient, relates to the question as to whether there is any evidence of a primary stimulation of growth in the presence of the radium as distinct from a compensatory acceleration which follows upon the immediate check. This is being studied along with the acceleration observed upon removing a culture from the radium plaque. Up to the present there is no evidence of direct stimulation, but all the possibilities have not yet been explored. The acceleration upon removal from the plaque is striking, but in the conditions so far studied, it would appear to be compensatory in nature.

Cordial thanks are due to the Medical Research Council for the continued loan of the radium, which renders the carrying out of Miss Robertson's work possible.

Mr. Norman Lawrie (Beit Memorial Research Fellow), spent the month of December working in the Division on the respiration and metabolism of the cultures being used for some of these experiments.

DIVISION OF NUTRITION.

Vitamin Standards.

The Health Section of the League of Nations has announced that the second meeting of the International Conference on Vitamin Standards and Units will be held in London in June, 1934, under the Chairmanship of Dr. E. Mellanby, with Dr. Harriette Chick and Dr. W. R. Ackroyd acting as secretaries, as at the 1931 meeting. The purpose of this Conference will be to report on the working of the provisional standards and units laid down at the last Conference in 1931, to discuss any changes or improvements which may be advisable and to consider matters on which further investigation is to be recommended.

During the last three years, workers on vitamin problems in this Institute have devoted much time and attention to points connected with the Standards adopted at the 1931 Conference, and particularly to those points concerning which further investigation was recommended. The work has been done in connection with various Sub-Committees set up for the purpose by the Accessory Food Factors (Vitamins) Committee of the Medical Research Council and the Lister Institute. The subjects investigated have included the following:

Vitamin A: pure crystalline carotene as standard; influence on stability of temperature and of solvent used; the relative value of various methods of vitamin A estimation (Miss E. M. Hume and co-workers).

Vitamin B₁ (antineuritic): stability at different temperatures of the standard absorption product on acid fullers' earth from rice polishings (Dr. H. Chick, Miss H. M. Jackson and Mr. G. Prunty).

Vitamin C: suitability of pure ascorbic acid as standard in place of the fresh lemon juice previously recommended (Dr. S. S. Zilva and co-workers).

Biological value of Carotene as source of Vitamin A; its value in different solvents. Miss Hume and Miss H. Henderson Smith, in co-operation with Dr. I. Smedley-MacLean, have previously found that of a number of solvents tested, a specimen of coconut oil was the most satisfactory for use with crystalline carotene; several samples of this oil from different sources have now been compared in biological and colorimetric tests. Some small difference between these has been detected and it cannot, therefore, be

assumed that the same sample of carotene dissolved in different samples of coconut oil will always have the same biological value. Addition of hydroquinone to the coconut oil solution does not appear to confer any benefit as a stabiliser.

Recent researches, particularly those of Kuhn and his colleagues at Heidelberg, have established the existence of many isomeric forms of carotene and of certain derivatives, all of which possess biological activity, the essential common factor being apparently the presence of an intact β -ionone ring with four conjugated double bonds attached. β -Carotene differs from the other active carotenes in having two such rings and in showing at least twice their biological activity. The original sample of carotene used as International Standard, though probably consisting chiefly of β -carotene must also contain an admixture of the α -form and it seemed desirable to make a comparison between the International Standard material and a sample of pure β -carotene (furnished by Professor Karrer of Zurich). This comparison is not yet completed, but it is evident that, dissolved in the same sample of coconut oil, the pure β -carotene has a deeper yellow colour and is biologically active in a somewhat smaller dose than the sample used as International Standard. The activity of the latter is probably about 75 per cent. of the former. It is necessary to establish this value more accurately and also to ascertain the exact quantitative relation between the biological activity of pure β -carotene and the purest sample of vitamin A obtainable.

Effect of Vitamin A deficiency on the Eye. Dr. K. Tansley Lythgoe (Medical Research Council Grantee), has been investigating the effect of vitamin A deficiency on the development of the retina and of visual purple in young rats. Mrs. Lythgoe's previous work had shown a delay in regeneration of visual purple to be one effect of vitamin A deficiency and the probable cause of the night blindness, characteristic of this dietary effect. The present work, which is still incomplete, indicates that defects in the structure of the retina and definite retardation of the first appearance of visual purple occur in suckling rats when the mother is suffering from a partial vitamin A deficiency. Evidence has also been obtained that administration of cod liver oil to young animals which have been deprived of vitamin A, restores the staining properties of the retina, but cannot repair any structural damage which may have occurred.

Work on the Vitamin B Complex.

The recent work of Kuhn, György and Wagner-Jauregg in Heidelberg on the separation of crystalline, water-soluble pigments from yeast, egg-white and milk, allied to the lyochrome oxidation ferment of Warburg, has indicated the possible identity or close relationship of these substances with vitamin B₂. Experiments have, therefore, been instituted to examine this hypothesis for which, as yet, there appears to be inadequate biological proof. Some preliminary tests have been carried out with material prepared by Mr. Prunty in this Institute and the investigation is being carried on with the help of Professor P. Ellinger of Düsseldorf. Professor Ellinger's more recent work, before coming to this country, was devoted to this class of compounds and the opportunity of his collaboration at the present time is especially fortunate.

Vitamin D. Origin and Distribution in Nature.

Miss A. M. Copping has continued her work on the origin of vitamin D in the ocean. Further investigation of copepod material, received with the help of Dr. Atkins of the Marine Biological Station at Plymouth, has shown this organism to possess a relatively high vitamin D content. Quantitative work, in which due allowance has been made for the effect of the phosphorus content of the material in mitigating the rachitogenic effect of the low phosphorus and high calcium diets used for the biological tests, has shown that the dried material contained much more than 0.25 International units vitamin D per gramme. The result would seem to afford a partial, if not complete, explanation of the rich depôts of vitamin D in the liver of the cod fish, which is stated to feed largely on copepods at certain seasons of the year.

The examination of plant material for vitamin D has also been continued. In many instances, however, the results have been irregular and difficult to interpret, due apparently to lack of uniformity of the vitamin D reserves of the experimental animals, which becomes a serious source of error when the amounts of vitamin in the test materials are small. Evidence has, however, been obtained that the vitamin D, which is abundantly formed when fresh green leaves are exposed to a powerful ultra violet irradiation, tends to disappear when the material is kept, the rate of disappearance depending on the temperature.

No evidence was obtained of the presence of vitamin D in germinated wheat, contrary to statements of some workers that cereals develop vitamin D as well as vitamin C in the process of germination.

Biological Value of Proteins.

Further work has been done by Dr. Chick and Mr. J. C. D. Hutchinson (Medical Research Council Grantee, and later Research Fellow of the Agricultural Research Council) on the balance sheet method of studying the nutritive value of proteins. In this method comparison is made of the relative values of

proteins to maintain nitrogenous equilibrium in the adult rat. The special points of the study have been :— the time required for “ wash out ” of residual nitrogen, when changing from high to low protein diets and *vice versa* ; the influence of the level (proportion of total calories) at which the protein is present in the diet, the effect of heat and other agencies on the nutritive value of the protein. Most of the work has been done on caseinogen, which has a special interest, owing to its almost universal use as source of protein in the “ synthetic ” basal diets used in vitamin research.

Maize and Wheat Proteins. Etiology of Pellagra. The work on the relative value of wheat and maize proteins for supporting the growth of young rats has been completed by Mr. Hutchinson, working with Dr. Chick. In the diets used, wheat and maize proteins respectively formed the sole source of nitrogen, and when comparison was made only between experiments which correspond exactly as regards the amount of protein and calorie-intake, the value for growth of wheat protein was found to be slightly superior to that of maize protein. The difference, however, was small, and is considered to be of doubtful significance. The results of these experiments of 2-3 months' duration are, therefore, in general accord with those already published, showing the similarity in value of these two classes of protein for maintenance of nitrogenous equilibrium of adult rats in short period experiments.

This work provides another argument against the theory which would explain the association of endemic pellagra with the use of diets containing maize products as the staple cereal (as at present in Egypt, Roumania, Yugoslavia and the Southern States of North America) by an amino-acid deficiency in such diets.

Association of Pellagra with supposed Toxic Substances in Maize. Work has also been carried out by Dr. Chick, Mr. Prunty and Miss Copping to examine the theory held by some authorities, that the occurrence of pellagra on diets composed largely of maize may be explained by a toxic substance contained in this cereal. Rats and mice have been reared on diets in which 90 per cent. of the calories was derived from maize products, without occurrence of any toxic symptom, nor were any deleterious effects noticed when the animals consuming these diets were exposed to ultra violet or visible light from artificial sources.

The “ toxic ” acid substance separated from maize and other cereals by Stockman and his colleagues has been prepared from maize by Mr. Prunty and tested on animals. Only rarely, however, were the paralytic symptoms described by Stockman observed, although large doses (0.5 to 2 mg. per g. body weight), were given subcutaneously and intravenously to mice and frogs.

The association of pellagra in the United States and Roumania with alcoholism following the consumption of whisky distilled from maize or maize sugar, suggested that a toxic substance conducive to the disease might be contained in these products. Samples of maize sugar and maize whisky have been obtained and are being examined.

Biological Value of Fats.

The work of G. O. and M. M. Burr has established that on diets devoid of fat, rats develop a syndrome, characterised in the early stages by depressed growth and a scaly condition of the skin, and eventually, after many months, terminating fatally with pathological changes in the kidney. This condition is not prevented by all fats but only by certain highly saturated fatty acids. Miss Hume and Miss Henderson Smith, in conjunction with Dr. Smedley-MacLean, have satisfactorily reproduced the earlier phases of this syndrome and have confirmed the fact that a protective action is exercised by linseed oil and methyl linoleate. Certain other fatty derivatives are also being tested and an effort is being made to differentiate between the dermatitis due to this particular deficiency and that marked by a characteristic scaliness of tail, which is of obscure dietary origin and tends to occur sporadically in nutritional experiments.

Researches on the Antiscorbutic Principle (Vitamin C).

Vitamin C and Ascorbic Acid. Mention was made in the previous report of some experiments which were instituted with the object of ascertaining whether vitamin C was identical with ascorbic acid. The leading experiments in this inquiry were concerned with the quantitative assessment of the antiscorbutic activity by Drs. Zilva and Hirst, of a number of specimens of ascorbic acid from various natural sources and of different degrees of purity, of reversibly oxidised derivatives of ascorbic acid, and of ascorbic acid obtained by regeneration from these reversibly oxidised derivatives. The disparity in the antiscorbutic activity of the different specimens of ascorbic acid fell within the limits of the experimental error of the biological method of testing. This observation would not in itself have constituted sufficient proof that the two substances were identical. More convincing evidence was, however, obtained in an experiment in which a specimen of ascorbic acid, obtained by reduction of an oxidised derivative of the acid and which was of comparatively low activity, showed the same potency as ascorbic

acid which was not previously oxidised. These observations, taken in conjunction with those claimed by other workers, that synthetic l-ascorbic acid is active, supply rather convincing proof that this compound possesses antiscorbutic activity *per se*. It would, therefore, follow that the observation made by Dr. Zilva some years ago that when vitamin C is oxidised with indophenol, it retains much of its biological activity, is explained on the ground that a highly active, reversibly oxidised, form of the vitamin is produced and not that a substance other than the vitamin is destroyed, as he then supposed. On the other hand, on repeating many of his experiments, Dr. Zilva again found that the indophenol-reducing capacity cannot be taken as a true index of vitamin C.

A number of analogues of the ascorbic acid series prepared in the Chemistry Department of Birmingham University, are being studied in order to ascertain whether there exists a relationship between chemical structure and biological activity.

The Reversibly Oxidised Form of l-Ascorbic Acid. So far, the presence of the reversibly oxidised form of l-ascorbic acid can be established by determining the indophenol-reducing capacity of a substance before and after reduction with hydrogen sulphide and co-ordinating these data with its biological activity. This method is very troublesome and often even unworkable. In view of the potential importance of this oxidised product in biological and pathological work, it was desirable to elaborate a more suitable method for its detection. Attempts were, therefore, made by Dr. Zilva and Mr. A. E. Kellie to explore the possibilities of (a) the formation of coloured metallic salts of its oxime with nickel, iron, copper, cobalt, etc. (b) the formation of a highly coloured phenylhydrazine derivative using phenylhydrazine, p-nitrophenylhydrazine, p-sulphoniophenylhydrazine and 2:4 dinitrophenylhydrazine, (c) differentiating between the reduced and oxidised forms by determining the phenylhydrazine used up in osazone formation, and (d) reduction with standardised titanous chloride. These attempts have so far met with little success.

The Vitamin C Standard. At the request of the Accessory Food Factors (Vitamins) Committee, the potency of ascorbic acid has been evaluated. The results obtained show that the activity of 1 mg. of ascorbic acid is equivalent to 20-30 international units (2-3 cc. of lemon juice).

The Physiological Function of Vitamin C.

Reversible Enzymic oxidation of vitamin C. It was observed by Dr. Zilva some years ago that freshly expressed apple juice, although not reducing indophenol, was antiscorbutically potent. This was considered by him at the time to be due to the destruction of a reducing substance closely related to but not identical with the vitamin. Recent work on vitamin C suggested, however, a more plausible explanation, namely, that the active principle, whilst retaining its activity, was reversibly oxidised by an enzyme present in the apple. This hypothesis, when submitted to experimental test, has proved to be correct. The enzyme in question acts under aerobic conditions only, is thermolabile and is not very sensitive to cyanide. It is not identical with the peroxidase of the apple, nor is it coupled with the latter in an oxidation system. It seems to resemble an enzyme present in cabbage and described by Professor Szent-Györgyi some years ago before the antiscorbutic properties of hexuronic acid (ascorbic acid) were discovered.

Vitamin C in germinated peas. As is well known, seeds acquire antiscorbutic activity on germination. Dr. S. W. Johnson has carried out an investigation with the purpose of establishing whether a quantitative relationship exists between the indophenol-reducing capacity and antiscorbutic activity of extracts of peas in the early stages of germination and whether any of the active principle formed on germination is present in the reversibly oxidised form. He found that only a half of the antiscorbutic activity of the germinated peas could be obtained by the various methods of extraction he employed (aqueous, phosphate and cyanide-phosphate extracts). Furthermore, these extracts were less active antiscorbutically than would have been expected if their indophenol-reducing capacity had been entirely due to ascorbic acid. Even extracts from inactive ungerminated peas were able to reduce indophenol. No evidence could be obtained of the formation of the active oxidised form of the vitamin in the early stages of germination.

Polyploidy and Vitamin C. It was reported last year that experiments on apples indicated a connection between the somatic chromosome number and antiscorbutic activity. Conclusive evidence could not, however, be obtained from these experiments, since, although all of the most active apples were found to be triploid fruits, there were certain of these which showed a low vitamin C content. On the other hand, the activity of some diploid varieties was of a similar order to that of the moderately active triploids. As the parentage of the apples and the origin of the triploid forms were unknown, no strict comparison could be made. The investigation of corresponding triploids and diploids is associated with great difficulties in the case of the apple. Dr. Zilva, in collaboration with Dr. F. W. Sansome of the John Innes Institute, Merton, has, therefore, continued this study utilising the tomato, a fruit in which polyploidy can be induced with ease.

The normal tomato plant is a diploid with 24 somatic chromosomes, but on decapitation, adventitious shoots arise which are tetraploids with 48 somatic chromosomes. Truly comparable diploids and tetraploids obtained in this way with contrasting characters such as tallness and dwarfness, red-fleshed fruit and not red fleshed (yellow) fruit, were examined for their antiscorbutic potency. In every case the tetraploids were found to be about twice as active as the diploids. The genes investigated were found at the same time to have no bearing on the vitamin C content of the fruit. This work is being extended, and it is also hoped to investigate polyploid tumours in this connection.

Vitamin C and the physiological changes in the apple. The experiments carried out in conjunction with the Low Temperature Research Station, Cambridge, last year on the effects of depth of freezing and duration of storage of the intact apple in a frozen condition upon its vitamin content have been repeated and extended. These experiments again yielded the result that there is a considerable loss of potency when the fruit is kept at -10°C . and even at -15°C . for three months without being previously disrupted.

Researches are in progress on the effect of the presence of oxygen and of nitrogen on the deterioration of vitamin C of the apple during senescence. The function of the reversibly oxidised form of the vitamin in this fruit is also being investigated.

Vitamin C in canned apples. Work on the effect of various methods of canning on the fate of vitamin C in the apple has been continued in collaboration with Mr. T. N. Morris of the Low Temperature Research Station, Cambridge.

Vitamin content of Mangoes. Miss M. E. F. Crawford and Miss E. O. V. Perry were able to confirm the previous findings, namely, that the "Alphonso" variety was a highly potent, the "Cawasji Patel" a moderate, and the "Shendrya" a poor source of vitamin C. All these varieties were also found to be fairly good sources of vitamin A, but they contained no appreciable quantities of vitamin D. Environmental conditions have no influence on the high vitamin C content of the "Alphonso" variety.

Vitamin C in Animal and Human Organs. The investigation initiated by Dr. Zilva on the silver nitrate staining capacity of the suprarenal gland was extended in collaboration with Dr. Gough of the Pathological Department, School of Medicine, Cardiff. It was mentioned in last year's report that guinea-pigs receiving about six times the minimum protective daily dose of decitrated lemon juice for months were, when chloroformed, found to be fully protected from scurvy although their suprarenal glands failed to stain with silver nitrate (this reagent is reduced by the ascorbic acid in the gland). Dr. Gough made a detailed histological examination of such glands and has so far been unable to detect in them pathological changes. He has also examined a great number of suprarenal glands from human autopsies and many of these failed to stain with silver nitrate although the patients showed no symptoms of scurvy previous to death. By applying the silver nitrate reaction to other glands, Dr. Gough found that the anterior lobe of the pituitary stained very intensely. In consequence Dr. Zilva tested out quantitatively this tissue from the ox by the biological method and found it to be the most active antiscorbutic substance on record.

Work is also in progress on the following problems: the character of vitamin C in blood and in urine; the respiration of animal tissues in the presence and in the absence of ascorbic acid; and the distribution of the vitamin C oxidising enzyme described above in animal tissues.

DEPARTMENT OF BIOCHEMISTRY.

The work of Professor R. Robison and his collaborators has again been concerned with phosphate metabolism and the part played by phosphoric esters in physiological processes.

Alcoholic Fermentation.

Further knowledge has been gained of the reactions involving phosphoric acid which occur during the breakdown of sugars by the enzyme-complex of yeast.

In collaboration with Dr. M. G. Macfarlane, considerable progress has been made towards the isolation of the fourth component of fermentation hexosemonophosphate. Sufficient has been learned of the properties of this new ester to differentiate it from the remaining components, the monophosphates of glucose, fructose and mannose, but its exact nature is still a matter of speculation. From the residual fractions obtained in the purification of fructosediphosphate, monophosphoglyceric acid has been isolated as a crystalline acid barium salt. This compound had previously been obtained by Nilsson and occupies a central position in the scheme of carbohydrate breakdown put forward by Meyerhof during the past year.

The study of mannosemonophosphate has been continued in collaboration with Mr. V. N. Patwardhan (Grocers' Company Research Student) who has prepared various derivatives of this ester and has obtained confirmatory evidence of its constitution. Quantitative data derived from experiments on the fermentation of mannose by dried yeast at relatively high temperatures may necessitate some revision of previous conclusions regarding the ratio of carbon dioxide evolved to the phosphate esterified.

Dr. Belá Tankó (Debrecen University, Hungary) has collaborated in the further investigation of the hydrolysis of fructosediphosphate by bone phosphatase. The new fructosemonophosphoric ester previously reported has now been isolated in pure condition and additional evidence has been obtained that it possesses the constitution of fructose-1-phosphate. It has been found that the formation of glucose phosphate or glucose, which was previously noted as occurring during the enzymic hydrolysis of fructose-diphosphate, is due to a phosphohexokinase present in the crude bone phosphatase, but gradually removed or inactivated during further purification. The investigation of this kinase is being continued in collaboration with Dr. J. J. Rae (University of Toronto, 1851 Exhibition Research Scholar).

The fermentation of galactose by yeast trained on media containing this sugar is being studied in collaboration with Dr. G. A. Grant (Royal Society of Canada Research Fellow).

Professor A. Harden, with whom Mr. C. Taxner (Department of Agriculture, Budapest) is now working, has continued the work on the relation of hexokinase to the fermentation of galactose, but has not yet obtained any definite results.

Phosphoric Esters and Phosphatases of Animal Tissues.

The investigation of the phosphoric esters occurring in mammalian blood has been actively continued by Professor Robison and Dr. Macfarlane.

Diphosphoglycerate, first isolated by Greenwald, has been obtained in some quantity and is being more closely studied in collaboration with Dr. Rae. Other esters, not yet in pure condition, are being examined, and particular interest is attached to one of these which has certain properties in common with the fourth component of yeast hexosemonophosphate.

Experiments on the purification of the phosphatases of blood and of bone have been carried out by Dr. R. R. McLaughlin (Toronto University) and by Dr. Rae.

Calcification.

The mechanism of calcification in animal tissues has been further studied by Professor Robison and Dr. A. H. Rosenheim (formerly Grocers' Company Research Student) and the results of the past three years' work have been discussed in a series of papers.

It has been shown that the second calcifying mechanism of hypertrophic cartilage is strongly inhibited by iodoacetate and by fluoride in very low concentrations. This suggests that the second mechanism, like the phosphatase, is enzymic in nature and that the two calcifying mechanisms may together form a complex enzyme system analogous to those of muscle and yeast.

In experiments with other tissues calcification was repeatedly obtained in aortae of both rats and rabbits by prolonged immersion in highly supersaturated inorganic solutions. The deposits of calcium salts bore some resemblance to those described as occurring in these tissues in experimental hyper-*vitaminosis D*.

Professor Robison has also continued his collaboration with Dr. Honor B. Fell of the Strangeways Research Laboratory and with Dr. W. Landauer of the Storrs Agricultural Experimental Station, Connecticut.

The Chemical Nature of Antibodies.

Dr. Rosenheim (with a grant from the Medical Research Council) has been engaged in an attempt to repeat and extend the experiments of workers whose claim to have separated typhoid agglutinin from serum proteins by adsorption on kaolin and specific elution has aroused much interest. Various adsorbents and eluents have been used under different experimental conditions, but the results so far obtained have provided no evidence that the "H" agglutinins are of a non-protein nature.

The Oxytocic Hormone of the Posterior Lobe of the Pituitary Gland.

The study of the chemical nature of the hormone has been actively pursued by Dr. J. M. Gulland and his collaborators.

Dr. Gulland has confirmed the dual nature of the interaction with nitrous acid, to which reference was made in last year's report. He has also shown that there is a third, concurrent inactivation in which the hormone is attacked by nitric acid produced by aerial oxidation of the nitrous acid during the experiments. The natural outcome of this observation is an investigation of the effects of other oxidising agents; this is in progress.

Dr. Gulland and Dr. T. F. Macrae (formerly Research Student in Biochemistry) began experiments to identify the inactivating enzymes present in yeast and in trypsin preparations. They defined the criteria by which may be established the identity of a known enzyme which is suspected of inactivating the hormone. As a result of these researches it is apparent that the hormone is not proteinoid as has been held hitherto by other investigators, but that, if it is peptide in character, its molecular weight is relatively small.

Studies of the interaction of the hormone with chemical reagents and with enzymes are being extended in several directions by Dr. Gulland and Mr. S. S. Randall (Research Student in Biochemistry).

Dr. Gulland and Dr. N. S. Lucas have continued their examination of the ultra-violet absorption of preparations of the oxytocic hormone and concomitant substances.

The Constitution of the Nucleic Acids.

The organic chemical investigation of the purine nucleosides has been continued by Dr. Gulland and since December, 1933, by Miss E. M. W. Lavington.

An examination of the ultra-violet absorption of xanthine and its methylated derivatives and of xanthosine, in which Dr. Gulland and Dr. E. R. Holiday (London Hospital Medical School) have collaborated, has yielded valuable evidence as to the constitution of guanosine, xanthosine and guanylic acid. This method of investigating the constitution of nucleosides is being extended to other members of the group.

The Action of Chemical Substances on Cells.

Dr. Gulland and Mr. T. H. Mead have completed their studies of the reactions of spermatozoa towards phenolic aldehydes and, more especially, their ethers. The experiments with three aromatic aldehydes described in the last report have been extended to include those with other aromatic aldehydes, and it has been shown that in general the physiological activity of these substances may be correlated with the varied powers which they exhibit of condensing with the undissociated basic groups of proteins and amino-acids. Nevertheless, such condensations are probably not the sole factors in determining the strengths of the physiological activities of these substances, and other properties must be invoked to explain minor deviations from this generalisation.

Studies in the Amino-Acid Group.

Dr. Gulland and Mr. C. J. O. R. Morris are still engaged in their researches in this field.

Oxidation Experiments bearing on the Metabolism of Fat.

Dr. Smedley-MacLean and collaborators have further investigated the behaviour of the fatty acids in the laboratory under mild conditions of oxidation, such as might afford some analogy with the method of oxidation used in the body. By the action of hydrogen peroxide on palmitic acid in the presence of a cupric salt it has been found possible to obtain *unsaturated* hydroxy-acids as intermediate products of oxidation, a finding which may help to throw light on the desaturation of fatty acids that is known to occur very readily in the body.

In the absence of the cupric salt, hydrogen peroxide attacks palmitic acid slowly even at 90° and produces a mixture of β -, γ - and δ -keto acids. On the addition of a few drops of copper sulphate solution, vigorous action takes place, several points of the long carbon chain being simultaneously attacked and volatile acids of low molecular weight broken off. Intermediate products containing 13, 10, and 6 or 7 carbon atoms were formed. These consisted of unsaturated acids containing hydroxyl groups. Succinic acid was the only dibasic acid isolated.

In collaboration with Miss A. P. Ponsford, the study of the action of the same method of oxidation on the dibasic acids was continued. Here both keto-and hydroxy-derivatives were isolated as intermediates.

The views generally accepted with regard to the oxidation of the fatty acids in the organism have been largely based on feeding experiments on dogs, carried out with ω -phenyl derivatives of the fatty acids. These are broken down in the body to a considerable extent and eliminated coupled with glycine as hippuric or phenylacetic acid.

In collaboration with Mr. R. O. Jones (Morna Macleod Research Student) a comparison has, therefore, been made of the oxidation of benzoic and phenylacetic acids, both when free and when coupled with glycine. The coupled product was much less readily attacked than the free acid. Since there is no evidence that the nonphenylated acid undergoes any such coupling in the body these experiments emphasise the great caution that should be attached to any deductions as to the behaviour of the fatty acids themselves which are based on the behaviour of the ω -phenyl derivatives in the body.

In collaboration with Miss R. McAnally, a study of the carbohydrate and fat metabolism of a strain of *Saccharomyces Froberg* which ferments galactose, has been carried out. When incubated in solutions of glucose, galactose, fructose, sucrose and maltose respectively, fat was formed from the carbohydrate, the proportion of fat being definitely highest when the yeast was incubated in glucose solution and definitely lowest in maltose solution. The amount of fat formed was not appreciably increased when phosphate was added to the medium—a result differing from that obtained in previous experiments carried out with brewer's yeast. Nor does *Saccharomyces Froberg*, when incubated in maltose solution, show the great increase in storage carbohydrate observed with brewer's yeast under similar conditions.

DEPARTMENT FOR THE STUDY AND PREPARATION OF THERAPEUTIC SERA.

Studies on the Pneumococcus and the Production of Anti-Pneumococcus Serum, Type I.

Further experience has shown that it is possible to obtain a concentrated globulin solution which will not give rise to the so-called "thermal reaction" when it is administered by the intravenous route to patients. The need for giving the serum intravenously in pneumonia to ensure the immediate distribution of the specific antibody throughout the infected tissues makes it important to be able to recognise and eliminate the varying factors that provoke reactions of this kind. The causes of serum "accidents" are not yet fully understood, but an endeavour is being made in the Serum Department to produce with regularity reaction-free preparations for intravenous use, and this applies not only to antipneumococcus serum but also to all therapeutic sera which are administered intravenously in a clinical emergency, or as a routine procedure.

A batch of anti-pneumococcus serum (Type 1) which had been kept under proper conditions of storage for nearly a year was re-titrated, with the result that there was no evidence of any significant loss of potency.

The pathogeny of the toxæmia in pneumonia is still obscure, since it has not been possible to find experimental evidence for the presence of a specific toxin in culture-filtrates of any of the types of pneumococcus. This material, however, contains a toxic substance which, when injected into mice, gives rise to a readily recognisable form of purpura. Recent work has thrown light on the nature of the purpurogenic toxin, and it seems to be closely related to the type-specific and species-specific polysaccharides. With the object of defining the part played by this toxin in experimental pneumococcal bacteraemia of mice, Dr. Petrie and Dr. Morgan propose to obtain, by selective breeding, genetically pure lines which are respectively susceptible and resistant to the purpura-producing toxin, and to compare the survival rates when equivalent doses of a virulent test-culture are given to them.

Experimental Production of Purpura in Mice.

While examining a number of pneumococcal culture-filtrates for the purpura-producing agent, Dr. Petrie found that with the dose administered purpuric reactions did not appear, but that a sublethal dose of an anti-mouse-blood serum, when given intravenously at or about the same time, combined to cause purpura in a proportion of the mice, although the injection of this dose of serum alone was inoperative. The explanation of the summation effect seems to be clear. The pneumococcal filtrate contributes to the result by reducing the platelets in the blood-stream and, as Bedson has shown, the anti-mouse-blood serum in addition to causing haemolysis of the red cells, exerts an injurious action on the capillary endothelium. These experiments provide an interesting confirmation of the views held by Ledingham and Bedson on the mechanism of the production of purpura.

Occurrence of a Natural Haemagglutinin for the Mouse in Samples of Horse Serum.

The intravenous administration to mice of a concentrated anti-pneumococcus serum derived from a single horse was observed by Dr. Petrie to be lethal, and the post mortem signs proved to be those of a typical haemolytic jaundice with haemoglobinuria. Enquiry showed that toxic sera of this nature had already been described by Okell and Steed, who found that, fortunately, the sera of only a small percentage of horses possess this property. Such sera have, doubtless, been overlooked in the past, and have been included in batches for issue, and it is improbable that they can exert any harmful influence in man. The active principle in the serum is apparently a normal immune-body (anti-mouse), because a fresh horse, whose serum was innocuous to mice, was immunised intravenously with mouse blood and readily responded by producing a serum with identical effects; the lethal dose for a mouse was about 0.25 cubic centimetre. An attempt to obtain a similar immune-serum in the horse by the ingestion of mouse tissues failed.

Production of Gas-Gangrene Antitoxin (*B. welchii*).

Mention was made in a previous report that within recent years an increasing interest has been taken in the serum treatment of acute peritonitis, intestinal obstruction and gangrenous appendicitis. The theory that has been formed attributes the characteristic toxæmia in these conditions to the action of the toxin of *B. welchii* and this view is supported by encouraging results that have followed the use of a specific antitoxin in this country. There are technical difficulties which complicate the methods of production of the serum. A fresh attempt has been made to simplify the preparation of the toxin and the antitoxin, and the results have been so consistently satisfactory that the methods can now be regarded as purely routine.

Production of Gas-Gangrene Antitoxin (*Vibrio septique*).

The preparation of the specific toxin and antitoxin from *V. septique*, another member of the group of anaerobes associated with gas gangrene, has been begun, and, it is believed, will offer no special difficulty, in view of the experience gained with *B. welchii*, and also because high-titre toxins and sera are known to be obtainable with a fair degree of certainty. The work will be facilitated by the use of the provisional standard serum which has been prepared and supplied through the kindness of Dr. P. Hartley of the Biological Standards Department of the Medical Research Council. The staff at Elstree has collaborated with workers elsewhere in carrying out comparative tests on reagents supplied by Dr. Hartley with a view to the adoption of an International Unit of antitoxin.

Production of Staphylococcus Antitoxin.

Recent work by Panton and his colleagues at the London Hospital, to which the Department at Elstree contributed, and by Dolman in Toronto, has indicated the sphere of usefulness of a specific antitoxin in acute and sub-acute staphylococcal infections and of a toxoid preparation for the treatment of the chronic type of infection. The Biological Standards Department of the Medical Research Council has recently issued a provisional standard serum by means of which it is possible to titrate staphylococcus antitoxin in terms of a standard unit as easily as diphtheria or tetanus antitoxin. Precise methods of titration will have the effect of increasing the potency of sera that are issued for clinical use, and this in turn will enhance the efficacy of the treatment. The Department is co-operating with the Wellcome Physiological Research Laboratories in supplying the specific remedies for clinical tests that are being organised by the Therapeutic Trials Committee of the Medical Research Council.

Preparation of "Convalescent" Human Serum for the Treatment of Poliomyelitis.

Co-operation with the Medical Research Council and the Public Health Department of the London County Council in the preparation and issue of a serum for the treatment of poliomyelitis is being continued. The serum, when it has passed the necessary tests, is sent to the Western Fever Hospital, London, where early cases of the disease are admitted, and whence it is distributed for use in the treatment of patients who are in the pre-paralytic stage of the disease.

Immunisation of the Horse with Poliomyelitis Virus. A new supply of serum from immunised horses has been obtained and found to possess very high virus-neutralising value in tests on monkeys. It is available for prophylactic use in contacts.

Immunisation of Horses with the Thermostable "O" Antigen of *C. tetani*.

Intensive immunisation of horses with this antigen is being continued in connection with Mr. Henderson's study of the prophylaxis of experimental tetanus infections. The resulting samples of immune-sera have been fractionated and are being tested by him.

Observations on the Accuracy of Titration of Anti-Dysentery Serum.

With the aid of the concentrated glycerinated test-toxin referred to in last year's report, Dr. Petrie has carried out further tests to determine the degree of closeness of titration of anti-dysentery serum. He has ascertained that it is possible by the use of this test-toxin to distinguish differences of ± 5 per cent. of one unit of the standard anti-dysentery serum, when the mortality-rates in the groups of test animals fall upon the sensitive portion of the neutralisation curve. The differences are apparent when the groups consist of 30 mice for each dose of serum.

Biochemical Investigations into the Specific Substances of the Meningococcus.

Dr. Elson (Jenner Memorial Research Student) and Dr. Morgan have continued their study of the type-specific and the species-specific substances of the meningococcus group. The difficulty of producing a Type II precipitating serum in the rabbit, which was mentioned in last year's report, has not yet been satisfactorily overcome. A further delay in determining the serological properties of the various carbohydrate fractions which have been isolated from cultures of Type I meningococcus occurred when it became clear that false precipitin reactions were being given by the homologous antibacterial horse sera. Dr. Morgan has found that all specimens of antimeningococcal horse sera examined by him, which had been produced by the intravenous inoculation of massive doses of agar-grown cultures of meningococci, contained a high titre of anti-agar precipitins. These sera reacted with traces of agar which were present in the various fractions that had been isolated from agar-grown meningococci and as a consequence gave false precipitin reactions. Several routine anti-meningococcal horse sera examined during the course of this investigation gave a distinct precipitate when mixed with a 1 : 500,000 dilution of agar but sera obtained from horses

which had been immunised with broth cultures failed to produce precipitates when mixed with a suitable dilution of agar. These observations agree with those of Sordelli and Mayer, who found that agar, when it is adsorbed on bacteria, is rendered antigenic and produces agar antibodies in animals that are immunised with these organisms.

Dr. Petrie is continuing the inquiry into the preparation and characters of the endotoxin of the meningococcus.

The decomposition of specific bacterial polysaccharides by a species of Myxobacterium.

Dr. Morgan has continued his investigation of the decomposition of the specific polysaccharide of *B. dysenteriae* (Shiga) by the action of a species of myxobacterium. The myxococcus grows poorly in a synthetic mineral medium containing the specific polysaccharide as the only source of carbon, but the addition of a small amount of an aqueous extract of rabbit faeces or the presence of culture-filtrates of certain other micro-organisms has been found to increase both the rate and the density of growth.

Dr. Morgan has also investigated the action of this micro-organism on the specific precipitating substances of other bacterial species. He has found that the specific polysaccharides of *B. dysenteriae* (Flexner Y.), *Pneumococcus* (Type II), *Tubercle bacillus* (Human), *S. suispestifer* (Hog cholera bacillus), *B. paratyphosus* B. (Newport) and *Br. abortus* are attacked and their power to form a specific precipitate when mixed with the homologous immune-serum is destroyed. The specific polysaccharides of *Pneumococcus* (Type I), *B. enteritidis* (Gaertner), *B. proteus* (O.X. 19 and H. X. 19) are not decomposed. Experiments are in progress with the object of isolating an active enzyme preparation from cultures of the myxococcus.

Colorimetric methods for the estimation of glucosamine and N-acetylglucosamine.

Dr. Morgan and Dr. Elson have elaborated a method for the estimation of glucosamine which differs in principle from that described in last year's report. By heating glucosamine in alkaline solution with acetylacetone it can be converted into the pyrrole derivative, 2-methyl-3-acetyl-5-tetrahydroxy-n-butyl-pyrrole, which, on subsequent treatment with p-dimethyl-aminobenzaldehyde in alcoholic solution gives rise to a stable red-coloured solution. Within the range, 0.75-3.0 mgm. of the hexosamine, the method gives a good degree of proportionality between the hexosamine content and the colour intensity. The method can also be used for the determination of chondrosamine.

Dr. Morgan and Dr. Elson have modified an existing method for the estimation of N-acetylglucosamine. They have found that N-acetylglucosamine on treatment with hot 0.01 N sodium carbonate solution passed over with loss of water into the disubstituted oxazole derivative, 2-methyl-4- $\alpha\beta\gamma\delta$ -tetrahydroxy-n-butylloxazole, and further investigation showed that this reaction was of general application to all N-acetyl- or N-arylglucosamines. With the modified technique, Dr. Morgan and Dr. Elson have been able to estimate amounts of N-acetylglucosamine or N-acetylchondrosamine as small as 0.10 mgm. Dr. Morgan has used the method for the estimation of the N-acetylhexosamine units which are present in the specific polysaccharide of *B. dysenteriae* (Shiga) and which are liberated by acid or enzymic hydrolysis.

Testicular Extract and Tissue Permeability.

Dr. Morgan and Dr. McClean have continued their investigations into the nature of the dermal diffusing substance in aqueous extracts of the mammalian testis. They have found that sterile, highly purified preparations are unstable in aqueous solution, even when these are kept at 0°C. in sealed neutral-glass ampoules at pH 4.5-conditions which were formerly considered to be optimal for the preservation of the diffusing principle. Attempts to render the active substance stable are being continued. The minimal diffusing dose of the most active preparation contains 0.0000002 mgm. of total solid matter and preparations containing 1×10^6 minimal diffusing doses of the active substance per 1 cc. have frequently been obtained. Freshly prepared, highly active preparations have been found to be strongly dextrorotatory (approximately $[\alpha] +100^\circ$) but this optical activity diminished together with that of the dermal diffusing activity, when the preparations were stored at 0°C. for a few weeks.

Action of Enzymes on the Extract. Dr. Morgan and Dr. McClean have also investigated the action of certain enzyme preparations on purified specimens of the diffusing substance. They have found that dipeptidase at pH 7.5 and aminopolypeptidase at pH 7.0 are without action on the activity of the diffusing principle. Yeast proteinase, however, rapidly abolishes the diffusing activity when allowed to act at pH 7.5, but is without action at pH 5.0. Commercial preparations of trypsin at pH 8.0 destroy the active substance. Experiments with pepsin preparations are complicated by the fact that at acidities greater than those represented by pH 4.0 the active substance itself rapidly becomes inert.

Action of Testicular Extract on Absorption of Antitoxin and on the Response to Active Immunisation. Dr. McClean and Dr. Morgan, with the collaboration of Dr. G. Favilli (University of Florence), completed their investigations on the influence of purified testicular extract on the absorption of antitoxin.

Testicular extract, which increases the permeability of the dermis, doubles the rate of absorption of diphtheria antitoxin, as shown by titration at 2 and 6 hours, when it is mixed with the antitoxin and injected subcutaneously. It has no influence on the rate of absorption following intramuscular injection, nor does it cause any lowering of the antigenic response to diphtheria toxoid when given in association therewith by the subcutaneous route.

Action of Extract on Fragility of Red Cells and on Dispersion of Indian Ink in Dermis. Dr. Favilli and Dr. McClean have studied the influence of testicular extracts upon the fragility of red blood cells and upon the dispersion of indian ink particles in the dermis. Their observations show that the substance in the crude extracts which increases the fragility of red cells is not the same as that which increases dermal permeability, since purified extracts of high diffusing activity have no action upon red cells.

Further, the intracutaneous inoculation of indian ink with crude extracts of testis proved to be a satisfactory method for the determination of their diffusing activity in the dermis, but the method is not satisfactory when purified extracts are used. The intracutaneous injection of purified extracts with a standard dose of diphtheria toxin as originally used by Dr. McClean and the measurement of the resulting enhancement of the toxin lesions, is the more reliable method of titration.

Testicular Extract and Local Immunity Phenomena.

Favilli and his co-workers in Italy have suggested that local immunity, at least so far as it is manifested in the skin, might be explained by a lowered permeability of the tissues. They have reported that ordinary broth, the "antivirus" of Besredka and substances which are known to decrease cell permeability, such as urethane and calcium gluconate inhibit the diffusion of crude testicular extracts in the dermis. They have shown that staphylococcal "antivirus," calcium gluconate, and urethane inhibit the lesions of vaccinia virus in the dermis and they have suggested that the reaction of the dermis to infective agents and the extension of the resulting lesions may be influenced by the relative permeability of the tissues or by any substance which can alter this permeability.

Dr. McClean and Dr. Favilli are collaborating in further experiments on the nature of this local immunity and some interesting results have been obtained. The evidence at present available suggests that the reticulo-endothelial response to the injection of broth, bacterial filtrates, urethane or calcium gluconate may play an important part in controlling the effect of diffusion of testicular extract on the spread of infective lesions.

Dr. T. Lumsden, of the Cancer Department of the London Hospital, has again, during the past year, been given facilities for his work on the production of an anti-cancer serum, by immunisation of sheep.

The hospitality of the Department has been extended to Dr. Denny-Brown of the National Hospital Queen Square, and assistance has been afforded to him by providing him with a supply of animals in which an experimental diphtheritic paralysis had been induced. This work is part of a research into the problems of acute infective polyneuritis in man which he is undertaking on behalf of the Medical Research Council.

DEPARTMENT FOR THE STUDY AND PREPARATION OF ANTI-VARIOLOUS VACCINE.

During the year Dr. A. B. Green has been giving some attention to the egg-method of lymph-production, particularly with a view to ascertaining the viability of such lymph during storage.

NATIONAL COLLECTION OF TYPE CULTURES.

During the year under review the number of cultures of bacteria and fungi distributed to workers at home and abroad again exceeded 5,000, and some 200 new types were deposited for maintenance in the collection.

A new and revised list of the fungi maintained in the National Collection of Type Cultures is being prepared for publication in the *Transactions of the British Mycological Society*. The list will comprise micro-organisms of importance in phytopathology, medical or veterinary science, technical and soil bacteriology and types useful for teaching purposes.

With reference to the work of the Nomenclature Committee of the International Society for Microbiology, of which the Curator of the Collection, Dr. R. St. John-Brooks, is one of the permanent secretaries, the Report on the proposals, submitted by Dr. R. E. Buchanan and Dr. H. J. Conn, relative

to the conservation of *Bacillus* as a bacterial generic name, the fixing of the type species and of the type or standard culture and the Report of the sub-committee on the classification of the *Salmonella* group of bacteria, referred to last year, are now ready for publication.

During part of the year the hospitality of the department was extended to Miss Dagny Erikson, who has given valuable assistance to the staff by critically examining the various species of the genera *Aspergillus* and *Penicillium* conserved in the collection.

GENERAL AND FINANCIAL.

The Accounts and Balance Sheet for the year ending December 31st, 1933, show balances to the credit of the Pension Fund of £27,311 2s. 0d., of the Contingency Fund of £20,000 0s. 0d., of the Sinking Fund of £24,489 2s. 1d., and of the Capital Fund of £520,615 19s. 10d. The balance of income over expenditure of the Pension Fund, viz., £913 19s. 0d., has again been transferred to the General Account towards the payment of premiums on the Federated Superannuation System policies of the staff. Of the excess of income over expenditure of the General Account, viz., £6,762 13s. 10d., £2,000 0s. 0d. has been utilised in increasing the Contingency Fund and the balance, £4,762 13s. 10d., added to the Capital Fund.

New investments during the year have been :—

For the General Fund : £11,000 3½ per cent. War Stock.

For the Sinking Fund : £1,500 3½ per cent. Conversion Stock.

The income from the sale of the Institute's products during the year 1933 was £25,062 17s. 6d. After adjustment of the stock of Sera on hand at the beginning and end of the year, income from this source appears in the accounts as £26,274 11s. 0d. Sales of Sera, Vaccines, &c., show a decrease and Investigation Diagnosis and Analysis Fees a slight increase compared with the previous year.

The total expenditure for the year was £40,995 6s. 7d., against £43,258 9s. 10d. in 1932. Serum and Vaccine Lymph Laboratories Expenses and Alterations, Repairs and Renewals accounted for most of the decrease compared with 1932.

In conclusion, the Governing Body desires to express its appreciation of the devoted co-operation of the Director and all members of the Staff in carrying out the work of the Institute.

WILLIAM BULLOCH,

Chairman of the Governing Body.

BALANCE SHEET

AND

ACCOUNTS.

Dr.

The Lister Institute

BALANCE SHEET

	£	s.	d.	£	s.	d.
TO CREDITORS				2,461	3	5
TO PENSION FUND—						
As per Account at 31st December, 1930..				27,311	2	0
TO JENNER MEMORIAL RESEARCH STUDENTSHIP FUND—						
As per Account at 31st December 1932 ..	8,258	11	9			
Add Amount transferred from Income and Expenditure Account, 1933		11	1 10			
				8,269	13	7
TO CONTINGENCY FUND—						
As per Account at 31st December 1932 ..	18,000	0	0			
Add Amount transferred from Income and Expenditure Account, 1933	2,000	0	0			
				20,000	0	0
TO SINKING FUND to 31st December 1933				24,489	2	1
TO CAPITAL FUND to 31st December 1933—						
Donations, &c., received to date from the following:—						
Dr. Ludwig Mond (1893)	2,000	0	0			
The Berridge Trustees (1893/98)	46,379	10	1			
The Grocers' Company (1894)	10,000	0	0			
Lord Iveagh (1900)	250,000	0	0			
Lord Lister's Bequest (1913) as per Account at 31st December, 1923	18,904	5	8			
William Henry Clarke Bequest (1923/6)	7,114	5	7			
Other Donations (1891-1926)	20,421	18	3			
Income and Expenditure Account:—						
As per Account at 31st December, 1932..	161,093	6	5			
Add Balance for the year ending 31st December, 1933	4,762	13	10			
				165,796	0	3
				520,615	19	10

WILLIAM BULLOCH, *Chairman.*

G. W. ADDISON, *Hon. Treasurer.*

£603,147 0 11

REPORT OF THE AUDITORS

We have audited the above Balance Sheet. We have obtained all the information and explanations we have required, being held by the Institute on their behalf. In our opinion, such Balance Sheet is full and fair, and properly drawn and the explanations given to us and as shown by the books of the Institute.
London, 26th April, 1934.

of Preventive Medicine.

31st DECEMBER, 1933.

Cr.

By CASH—	£	s.	d.	£	s.	d.
At Bankers on Current Accounts..	6,939	17	0			
In hand	73	17	8	7,013	14	8

By INVESTMENTS, GENERAL FUND (at cost, less amounts written off)—	£	s.	d.	£	s.	d.
£70,000 4 per cent. Consolidated Stock, 1957 or after	62,740	19	0			
£43,000 4½ per cent. Conversion Stock, 1940-44	41,702	3	3			
£17,000 5 per cent. Conversion Stock, 1944-64	15,937	0	7			
£47,000 4 per cent. Funding Stock, 1960-1990	39,970	13	3			
£36,000 3½ per cent. War Stock, 1962 or after	33,625	2	11			
£37,000 Local Loans 3 per cent. Stock	20,829	1	7			
£3,000 Port of London 4 per cent. B. Stock	2,686	17	7			
£1,000 Dominion of Canada 4 per cent. Registered Stock, 1940-1960	928	1	6			
£2,000 Cape of Good Hope 3½ per cent. Consolidated Stock, 1929-49	1,802	12	0			
£25,000 Cape of Good Hope 3 per cent. Consolidated Stock, 1933-1943	23,850	0	0			
£25,000 Natal 3 per cent. Consolidated Stock, 1929-1949	21,400	0	0			
£25,000 New South Wales 3 per cent. Inscribed Stock, 1935	22,900	0	0			
£2,000 New South Wales 4 per cent. Inscribed Stock, 1942-62	1,882	3	4			
£25,000 New Zealand Government 3 per cent. Inscribed Stock, 1945	22,114	0	0			
£26,100 South Australian Government 3 per cent. Consolidated Stock, 1916 or after	16,800	0	0			
£2,900 Commonwealth of Australia 3½ per cent. Registered Stock, 1936-37	2,825	6	0			
£600 Union of South Africa 4 per cent. Consolidated Stock, 1948-1963	594	2	0			
£23,000 Victorian Government 3 per cent. Consolidated Inscribed Stock, 1929-1949	19,800	0	0			
£700 Western Australia Government 4 per cent. Inscribed Stock, 1942-1962	698	7	0			
£20,000 Southern Railway Preferred Ordinary Stock	13,500	0	0			
£6,200 London & North Eastern Railway 3 per cent. Debenture Stock	3,961	0	0			
£5,000 Great Central and Midland Railway Joint Committee 3½ per cent. Guaranteed Stock	3,623	0	0			
£353 London & North Eastern Railway 4 per cent. First Guaranteed Stock	499	11	0			
£8,650 London, Midland & Scottish Railway 4 per cent. Preference Stock	7,960	0	0			
£15,625 London, Midland & Scottish Railway 4 per cent. Preference Stock, 1923	11,300	0	0			
£18,750 London & North Eastern Railway 4 per cent. First Preference Stock	13,028	6	7			
£25,000 East Indian Railway 3 per cent. New Debenture Stock	13,890	0	0			
£661 Madras & Southern Mahratta Railway 4 per cent. Debenture Stock, 1938	656	19	7			
£800 Grand Trunk Railway Company of Canada Great Western Borrowed Capital 5 per cent. Perpetual Debenture Stock	936	0	0			
£1,937 Grand Trunk Railway Company of Canada 4 per cent. Guaranteed Stock	1,733	0	0			
£800 Ontario and Quebec Railway 5 per cent. Permanent Debenture Stock	984	0	0			
£3,400 Gas Light and Coke Company Ordinary Stock	3,638	0	0	428,656	10	2

By INVESTMENTS, SINKING FUND (at cost)—	£	s.	d.	£	s.	d.
£9,600 4½ per cent. Conversion Stock, 1940-44	8,806	16	7			
£7,450 4 per cent. Funding Stock, 1960-1990	5,850	5	3			
£11,700 3½ per cent. Conversion Stock, 1961 or after	9,752	11	6			
Balance uninvested	79	8	9	24,489	2	1
By INVESTMENTS, JENNER MEMORIAL RESEARCH STUDENTSHIP FUND (at cost)—	£	s.	d.	£	s.	d.
£2,650 Southwark and Vauxhall Water Co. 3 per cent. Debenture Stock "B"	2,756	10	0			
£1,596 Southern Railway 5 per cent. Preference Stock	2,740	5	0			
£728 11s. 4d. Liverpool Corporation 3 per cent. Stock, 1942, or after	556	15	6			
£2,000 4 per cent. Funding Stock, 1960-1990	1,797	14	0			
Balance uninvested	418	9	1	8,269	13	7
By INVESTMENTS, PENSION FUND (at cost)—	£	s.	d.	£	s.	d.
£22,000 4 per cent. Funding Stock, 1960-1990	17,165	3	5			
£13,000 3½ per cent. Conversion Stock, 1961 or after	10,038	1	5			
Balance uninvested	107	17	2	27,311	2	0

(The book value of the above Investments is, in the aggregate, less than their market value at 31st December 1933.)

By DEBTORS	£	s.	d.	£	s.	d.
By FURNITURE, FITTINGS, SCIENTIFIC APPARATUS AND BOOKS—				7,449	16	9
At cost less depreciation as per account 31st December 1930				2,471	17	2
By EXPENDITURE ON INSTITUTE BUILDINGS AT CHELSEA—	£	s.	d.	£	s.	d.
As per account 31st December 1910, including purchase of freehold site, £6,000				70,916	3	1
By PURCHASE OF FREEHOLD LAND ADJOINING THE "STUDIOS" CHELSEA—	£	s.	d.	£	s.	d.
As per account 31st December 1912				169	6	8
By LEASE OF THE "STUDIOS" CHELSEA, as per last account	£	s.	d.	£	s.	d.
Less Amount written off for the year	1,327	12	9			
	65	2	0	1,262	10	9
By QUEENSBERRY LODGE FARM, ELSTREE—	£	s.	d.	£	s.	d.
Purchase of freehold land and buildings and Expenditure on new buildings—						
As per account 31st December 1912				20,455	10	0
By STOCK OF ANIMALS	£	s.	d.	£	s.	d.
	288	0	0			
By STOCK OF ANTITOXINS	£	s.	d.	£	s.	d.
	4,193	14	0	4,481	14	0

* Nothing has been charged for depreciation of Furniture, &c. since new purchases made during the year to a greater amount than the estimated depreciation (10%) have been written off.

£603,147 0 11

TO THE MEMBERS.

The Superannuation Scheme for certain of the Staff provides for the Life Policies for the time being in existence up so as to exhibit a true and correct view of the state of the Institute's affairs, according to the best of our information

COOPER BROTHERS & CO.,

Chartered Accountants. Auditors.

The Lister Institute of

Dr. INCOME AND EXPENDITURE ACCOUNTS

INCOME.								£	s.	d.
To Interest and Dividends on General Fund Investments	...	...	...	...	...	...	...	16,859	10	4
To Interest on Sinking Fund Investments	...	...	...	...	...	...	...	1,087	0	0
To Investigation, Diagnosis and Analysis Fees, &c.	...	...	...	...	...	...	...	2,391	10	1
To Sales of Sera, Vaccines, &c., and Stock at 31st December 1933, less Stock at 1st January, 1933	...	...	...	...	...	...	...	26,274	11	0
To Rent of Rooms	...	...	...	...	...	...	...	231	10	0
To Pension Fund—excess of Income over Expenditure transferred	...	...	...	...	...	...	...	913	19	0

£47,758 0 5

Dr.

Pension

	£	s.	d.
To Interest on Investments	1,335	0	0

£1,335 0 0

Dr.

Jenner Memorial Research

	£	s.	d.
To Interest and Dividends on Investments	261	1	10

£261 1 10

Dr.

Morna Macleod Research

	£	s.	d.
To Balance from last Account	288	15	0

£288 15 0

Preventive Medicine.

for the year ending 31st December, 1933.

Cr.

EXPENDITURE.

	£	s.	d.
By Rent, Rates, Taxes and Insurance	1,338	16	7
By Salaries and Wages of Staff	25,076	1	11
By Premiums on Federated Superannuation Policies	1,400	8	9
By Stationery, Printing and Postage	378	1	4
By Printing of Collected Papers	166	16	0
By Office Expenses, Auditors' Fee and Sundries	297	13	1
By Travelling Expenses	14	7	8
By Gas, Water and Fuel	1,397	19	6
By Electric Light and Power	340	13	1
By Nutrition, Protozoological and Experimental Pathology Expenses, including Apparatus	621	11	11
By Bacteriological Laboratory Expenses, including Apparatus	253	5	10
By Vaccine Laboratory Expenses, including Bottles	54	13	8
By Water and Bio-chemical Laboratory Expenses, including Apparatus	566	6	0
By Serum and Vaccine Lymph Laboratories Expenses, including Apparatus and Bottles	2,942	3	2
By Culture Media	89	12	1
By Animals	1,145	11	6
By Animal House Expenses and Forage	1,986	4	6
By Alterations, Repairs and Renewals, including Workshop Expenses	718	15	6
By Library Expenses	460	8	8
By General Stores	183	6	1
By Amount written off Lease of the "Studios," Chelsea	65	2	0
By Sinking Fund (4% per annum on Cost of Buildings and Interest on Investments)	1,497	13	7
By Amount transferred to Contingency Fund	2,000	0	0
By Balance, transferred to Capital Fund	4,762	13	10
	6,762	13	10
	£47,758	0	5

Fund.

Cr.

	£	s.	d.
By Pensions	421	1	0
By Balance, transferred to General Income and Expenditure Account	913	19	0
	£1,335	0	0

Studentship Fund.

Cr.

	£	s.	d.
By Salary of Student	250	0	0
By Balance, transferred to Balance Sheet	11	1	10
	£261	1	10

Studentship Account.

Cr.

	£	s.	d.
By Salary of Student	105	0	0
By Cash in hand	183	15	0
	£288	15	0

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