In doses of 0.08 to 0.1 gm. per kgm. body-weight, this compound produces a fall in the blood-sugar of 30 per cent. without any obnoxious symptoms: larger doses cause a primary hyperglycemia, followed by a fall in the blood-sugar and convulsions. The next higher homologue of agmatine, amino-pentylene-guanidine, has a more powerful hypoglycaemic action than the former compound: 0.2 gm. per kgm. body-weight is a convulsive dose, and the symptoms are similar to those produced by insulin, which was not the case with the other compounds investigated. Further, both substances resemble insulin in that the symptoms can be relieved by administering glucose.

Synthalin is closely related to the last two guanidine derivatives, being a diguanidyl derivative of a long chain aliphatic hydrocarbon, but the exact constitution has not yet been published. The toxic effects have been still further dissociated from the hypoglycaemic, doses as low as 0.003 gm. per kgm. body-weight producing a definite decrease in the blood-sugar. In applying these results to cases of human diabetes, Frank found that 20-25 mgm. constituted a suitable dose, and that up to 150 mgm. could be given in the course of four days. Such a dosage resulted in the utilisation of 40-50 gm. of glucose, which would otherwise have been excreted in the urine. If 125 mgm. cause the utilisation of 160 gm. of glucose in four days, 1 mgm. is equivalent to 1.24 gm. glucose, or, roughly, to one unit of insulin. Weight for weight, synthalin is therefore considerably less potent in causing a fall in the blood-sugar than the best samples of insulin.

The use of synthalin has in its favour the facts that it can exert its action after oral administration, and that this action, although slower in onset than that of insulin, is much more prolonged: to its disadvantage is the fact that unpleasant symptoms may be produced by it in many patients. The probable mode of action of the drug throws some light on the origin of these symptoms. Workers at the National Institute for Medical Research in London have found that synthalin only produces a decided fall in the blood-sugar in the normal animal in doses which also exert a definitely toxic action on the liver (*Lancet*, vol. 2, p. 517; 1927). This effect on the liver presumably results in a depression of the new formation of glucose which occurs in that organ, and also explains in part the unpleasant symptoms of nausea, anorexia, etc., frequently encountered in patients taking the drug: these symptoms have been found by Continental observers to be mitigated by the administration of a bile salt derivative, sodium dehydrocholate, to stimulate bile secretion, during the period of action of the synthalin: the toxic effect of the latter on the liver is believed to be counteracted by the simultaneous increase in the activity of the organ.

Apart from its action on the liver, synthalin also accelerates the disappearance of glucose from the circulation in the eviscerated spinal preparation, although the sugar vanishing is not laid down as glycogen in the muscles as is the case with insulin: moreover, large toxic doses of synthalin are necessary to demonstrate this effect. It therefore appears that the two main actions of insulin, depression of new formation of glucose in the liver and accelerated metabolism of sugar present in the blood, are represented in the effect of synthalin, but the fate of the sugar disappearing, which, in the case of insulin action, is partly laid down in the muscles as glycogen and partly burnt to carbon dioxide and water, is not absolutely similar in the two cases.

The clinical usefulness of the compound appears then to depend on how far its insulin-like action can be dissociated from its toxic effects: and this seems to occur to a different degree in different people. In Great Britain, the Medical Research Council has set on foot clinical investigations in a number of different centres, preliminary reports of which have recently been published (*Lancet*, vol. 2, p. 517; 1927): the same journal also contains a paper by E. G. B. Calvert on the treatment of diabetes by the drug (*ibid.*, p. 649). The results of these investigations show conclusively that synthalin is not a complete substitute for insulin. In certain patients, roughly one-third of the cases so far treated, it exerts a definitely toxic effect, the symptoms suggesting intestinal irritation, although a hepatic element may also be present. In a certain number it appears to be without action, but in others it enables the dosage of insulin to be reduced, although very rarely can its use be abandoned altogether. It has more effect in reducing the glycosuria than in reducing the blood-sugar.

The difficulties of estimating the value of synthalin, or that of any similar therapeutic agent, are considerable: thus, in a case in which synthalin has exerted a favourable influence, the patient may remain well, after withdrawal of the drug, on simple dieting alone; or if symptoms of gastro-intestinal irritation supervene, the accompanying loss of appetite, by reducing the food intake, may suffice to reduce the glycosuria and ameliorate some of the symptoms of the disease. Finally, since synthalin has a toxic action on the liver, it is possible that apparently good results may be due to a mild degree of this toxic action, in which case only time can disclose its real value even in the cases which appear to react successfully to it at the present moment.

Synthalin, then, is not a substitute for insulin: its real usefulness lies rather in the encouragement its discovery brings to the further investigation of synthetic compounds having an insulin-like action.

The Control of Plant Diseases.

"Be ye ashamed, oh ye husbandmen; howl, oh ye vinedressers, for the wheat and for the barley; because the harvest of the field is perished. I have smitten you with blasting and mildew."—JOEL i. 11 and AMOS iv. 9.

IN opening the discussion between Sections K and M on the control of plant diseases, at the Leeds meeting of the British Association, Mrs. N. L. Alcock chose the above text, and passing lightly over the superstitions of the past regarding disease, she turned to the problem of control as seen to-day by the pathologist and agriculturalist. From the practical point of view, the first full recognition of the importance of plant diseases came with the epidemic of American gooseberry mildew. In 1905, Prof. Salmon,

of Wye Agricultural College, while Ireland alone of the British Isles was definitely affected by the disease, gave a clear warning of the need of legislative control of both American gooseberry mildew and of potato wart disease. In another direction the warning was spread in 1909 by Prof. Sommerville in his references to the white pine blister rust, *Cronartium ribicola*, which he stated was still unknown in America, though it was to be feared that the day was not far distant when its footing in North America would be secured. To-day the losses in America due to this disease are credibly reckoned as enormous.

Neither the spread of American gooseberry mildew in Britain, however, nor the ravages in American

forests by pine blister rust, served to awaken fully the British people to the need of strict control. The full awakening came with the spread of wart disease, which, though described as a new malady of the potato in England by Prof. Potter and Mr. Massee in 1902, was not recognised as a menace to our food supplies until some years later. Happily, the lesson had been partly learned from the spread and havoc of mildew and blister rust, and legislation was initiated, at first haltingly, in an effort to devise rules for disease control, and later, as experience widened, amendments followed and mildew was lessened generally. The credit for the decline of mildew may be given to legislation, but it must not be forgotten that as in human infectious diseases, so also in plant diseases, there is probably an ebb and flow, not yet fully understood.

At first little was heard of wart disease, though a further warning of the dangers which it created was given by Prof. Salmon, but its spread led in 1907 to the Destructive Insects and Diseases Act, which may be considered the first important step in legislation for the control of plant diseases, and served to bring the subject of control into prominence. The establishment of inspectors to administer the control, and of mycologists and entomologists to recognise and to teach others to recognise plant pests, followed naturally.

In 1909 a further landmark was reached with the discovery that certain varieties of potato were immune to wart disease. With the work on this discovery the names of Mr. Gough and Mr. Snell will always be associated. Little is yet known as to the nature or degree of permanence of this immunity, but so far the latter has generally been maintained. Here geneticists have helped greatly, since there is cause for the belief that immunity may be a Mendelian character which, through breeding, may yield increasing crops of disease-resisting plants. But in this field of research there is still much to do before our crops are immune to disease, mature quickly, are hardy and produce acceptable fruit in abundance, and until the possibilities of success on these lines are assured, effort must be centred largely on the control of existing disease. At the present moment the English Phytopathological Service consists of three sections—official, inspectorate, and advisory respectively—and comprises entomologists, mycologists, an administrative unit forming part of the Horticultural Division of the Ministry of Agriculture, the Ministry's inspectorate—all members of which have received training in pathology—a corps of advisers—consisting of an entomologist and a mycologist in each agricultural province—and research workers on both entomology and mycology, who are stationed at Rothamsted Experimental Station, Long Ashton Fruit Station, Bristol, the Imperial College of Science, London, the Fruit Station at East Malling, the Lee Valley Station, Cheshunt, the London School of Tropical Medicine, and other institutions.

For the full effectiveness of such a service the convinced and willing co-operation of the grower is an essential factor, for not only must the grower play his part in an advisory council, but he must also take his part in the framing and enactment of agricultural legislation. The business value of measures of control must never be forgotten. The knowledge of those who are to administer control must be accurate and wide, and above all practical. Thus, for example, in some parts of Scotland the spraying of gooseberries against American gooseberry mildew with washing soda is cheap and effective; in other parts of Scotland such spraying is harmful and destroys all hope of a crop. The use of weights and

measures familiar to the grower, the need of clear and simple language in the exposition of the facts of the grower's problems, and moderation in policy in the framing of rules and regulations for the guidance of the grower, are vital to the successful co-operation of the administrative body and the producer.

There is to-day great need of a full investigation of common seed-borne diseases; for wheat may bear bunt spores, flax-seed may carry the resting mycelium of *Colletotrichum linicolum*, and both the pycnidia of *Phoma betæ* and the sori of the rust *Uromyces betæ* may be transmitted by the seed of the sugar-beet. At least some seventy common diseases are thus carried. On this aspect of control there is much need for chemical research with the view of the elimination of disease before the seed is sown.

It may be considered fortunate that Great Britain has not yet been faced by a disastrous plant-disease epidemic, but in America the loss by wheat-rust alone is reckoned at not less than 100,000,000 dollars. Nevertheless, the constant and steady toll taken from our food resources is formidable and must amount annually to tens of thousands of pounds. It may, however, be held that the greatest available field for the exercise of control of disease lies in horticulture, for here the margin of profit is relatively broad, labour is adequate, there is no lack of interest on the part of the grower, and much good can be done. Here also is wide scope for the exercise of plant sanitation, for clean cultivation, the destruction of diseased plants, the removal of weeds and moribund tissues, and the destruction of refuse by fire. The incidence of disease may also be lessened by careful selection of site, while much may be gained by closer co-operation between growers and the staffs of our botanic gardens. Both for horticulture and forestry the importance of nurseries calls for fuller recognition, for while in horticulture many diseases may be fought with reasonable hope of success in adult plants, to avoid disease in the nursery is better than to control it in later life. With forestry the matter of nursery control is more urgent, for in many cases there is little hope of disease control other than by the elimination of the cause in the nursery itself.

Dr. W. B. Brierley, who spoke from the point of view of agriculture, dealt at length with the training and supply of workers, the financing and staffing of laboratories, and the field and administrative services for research on disease control, and strongly urged the need for careful gradation from pure to applied research, without which the full integration of investigation could not be realised. In urging the claim for extended research foundations in our universities and for crop stations, he held that by the enlargement of such foundations and stations the work of control could now be best advanced. There is still great need for the popularisation of knowledge regarding the nature and dangers of plant diseases, and he held that by oral instruction to the grower, and by the wider use of clear and concise printed matter, disease control would be materially promoted. In his opinion there was, however, a danger that the training of plant pathologists might remain a function of pure botany rather than become one of agriculture, and this he considered a matter for regret and correction.

Miss E. Welsford, who followed, spoke from her experience of the control of the diseases of the clove in Zanzibar, and urged the need for improvements in the methods of cultivation and plant hygiene for all crops. In her experience the practical sides of healthy plant physiology were of greater importance in the battling of disease than cure; for while the latter would ever be essential, the primary duty of the plant

pathologist must increasingly become the avoidance of disease by assuring healthy growth for crops as a whole.

Some of the difficulties in control were referred to by Sir Daniel Hall, who discussed the breeding of plant varieties immune to disease. In his opinion such breeding must be slow in securing satisfactory results, since the starting-point is immunity to known diseases in a few varieties which may still be prone to, and may be even more prone to, other diseases than they were before immunisation to one. He warned all who must deal with the practice of agriculture that progress in one line of control would not assure immunity for crops as a whole, and that step by step the problem must be probed until a sound knowledge of the effects of environment on immune varieties has been attained. With a widened understanding of the advantages and defects of a known environment for a known crop would come a surer foundation on which all could co-operate in the elimination of disease.

Dr. Malcolm Wilson strengthened the plea of Sir Daniel Hall for the extended study of environment, and while laying emphasis on the need for fuller knowledge of the condition of individual crops at the time of infection, he held that the plant pathologist could best be fitted for the practical work of agriculture relating to the cure of disease by the fullest possible training in both healthy physiology and pathology.

Mr. W. A. Millard discussed the processes of green manuring as preventive of scab on potatoes, and described experiments which threw light on the beneficial effects of such treatment.

Dr. W. G. Smith discussed the differences between the work of the adviser and that of the agricultural inspector, and while admitting that the present system of administration was advanced and enlightened, he urged the need for the fuller study of plant diseases on the spot, for by such study the complications of the problem of disease could often be more fully appreciated and approached than by other means.

Prof. Link spoke of the close parallelism between the problems of disease control in Britain and the United States of America, and stated that the work of control in America was still hampered by the inadequate training of plant pathologists in pure botany. On the other hand, there are other directions in which improvements are indicated, and in particular it must be assured that a closer relation is established between the research worker and the grower. By such a relation the work of both the investigator and the grower would be accelerated.

In conclusion, Mr. Stoughton discussed the methods of propaganda against plant disease, and emphasised the importance of the personal factor for both the investigator and the grower, by which investigation could be stimulated on one hand and knowledge accepted on the other, to the benefit of all concerned and the assurance of unbroken progress.

J. McL. T.

University and Educational Intelligence.

CAMBRIDGE.—Prof. A. Hutchinson, professor of mineralogy, has been elected Master of Pembroke College.

Sir Arthur Shipley, late Master of Christ's College, left £5500 to Christ's College for the endowment of a fellowship, along with various other bequests, including some relics of Darwin. As we announced in our issue of Oct. 29, p. 640, parts of his library are going

to the Molteno Institute of Parasitology, the Balfour Library, and the Cambridge Philosophical Society.

THE Education Committee of the West Riding of Yorkshire announces in its report for 1926–27 a new departure in regard to provision of education for the adolescent: the inauguration at Castleford of a “centre for social and physical training” at an estimated cost of £500. Nine other similar centres are to be established in the course of the years 1927–1930, under the direction of a juvenile organisations committee, representative of all the local organisations engaged in social work amongst the young. Fifty-one scholarships tenable in universities were awarded in 1926–27, the average value being £78 a year. The field of selection of candidates (now 250 annually) has been widened by the grant of ‘continuation’ scholarships covering tuition, travelling, and maintenance expenses of preparation for the Higher School Certificate examination. Eighty per cent. of the pupils above sixteen are scholarship holders. Secondary school entrance scholarships were awarded to 2030 out of 5·5 times that number of candidates. Technical exhibitions numbered 3291.

THE Rockefeller Foundation has issued another, the eighth, series of “Methods and Problems of Medical Education.” Of the 37 articles in this series, 7 deal with British practice and institutions. Sir Lenthal Cheate discusses “English Surgery: Practice, Teaching, and Research,” and Sir Archibald Garrod the “Teaching of Clinical Medicine in England.” The medical and surgical ‘units’ of St. Bartholomew's Hospital are described by Prof. Fraser and Prof. Gask respectively. Details are given of the Electrocardiograph Department, Edinburgh Royal Infirmary, by Dr. W. T. Ritchie, and of the Department of Surgery, University of Edinburgh, by Prof. Wilkie. The new obstetric hospital, University College Hospital, is described by Sir George Blacker and Prof. Browne. The remaining articles mostly deal with special medical departments of institutions in America and Europe, including a useful one on medical postgraduate work in Germany, by Prof. Curt Adam. The volume is profusely illustrated with photographs and plans and contains useful information on staffing and finance.

THE appointments to Ramsay fellowships in chemical science for this session, British, Dominion, and foreign, are practically completed. At the present time ten fellowships are being held in the universities and colleges of Great Britain. The list of awards for the present session is as follows, the institution selected by the fellow for his research being given: *British Fellowships*: Dr. R. F. Hunter, Imperial College of Science and Technology, London; Mr. A. M. Taylor, University of Cambridge; *Glasgow Fellowship*: Mr. James D. Fulton, University of Manchester; *Canadian Fellowship*: Dr. W. H. Barnes, Royal Institution, London; *Danish Fellowship*: Miss Augusta M. Unmack, University of Oxford; *French Fellowship*: M. Robert le Guyon, University College, London; *Italian Fellowship*: Dr. Gastone Guzzoni, Royal School of Mines, London; *Japanese Fellowship*: Dr. Yohei Yamaguchi, University College, London; *Spanish Fellowship*: Senor Fernando Calvet, University of Oxford; *Swedish Fellowship*: Mr. H. Liander, University College, London. The total value of the annual amount of the fellowships that is awarded is approximately £4000, of which about £3000 is provided by grants from Dominion and foreign sources.