

colleges of Great Britain and Northern Ireland and of those technical colleges recognized by the Institute. As most universities are now revising their regulations, the information given in the report should be treated with some caution. It is always wise for the intending student to make early and direct application to the university institution or college concerned and to obtain the most up-to-date information. It would have been a good thing if some such indication had been added to the report.

## POSTERIOR PITUITARY GLAND SYMPOSIUM AT CAMBRIDGE

A VERY informative session took place in the Physiological Laboratory, Cambridge, on June 20, when the Society for Endocrinology held a symposium on the posterior pituitary gland. This meeting was unique in the sense that so many of the speakers had made substantial contributions to our knowledge concerning this gland, and that so much more overall information is available for the posterior pituitary than any other endocrine gland.

The control of the secretion of the antidiuretic hormone was discussed from two different points of view. Dr. P. A. Jewell and Prof. E. B. Verney gave an account of their recent work dealing with the localization of the osmoreceptors. Intracarotid injection of hypertonic sodium chloride solution inhibits water diuresis by causing release of the antidiuretic hormone. However, the exact site of the receptor elements (osmoreceptors) stimulated by this hypertonic solution is not known for certain. Anatomical investigation of the vascular bed of the internal carotid artery showed that this vessel supplies the pituitary gland, the anterior hypothalamus including the greater part of the supraoptic and paraventricular nuclei, as well as other parts of the prosencephalon. Proof was given that the osmoreceptors do not lie in the pars nervosa of the pituitary. The findings in an animal in which an internal carotid artery had been tied intradurally suggest that the receptors lie in the prosencephalon. Dr. Mary Pickford emphasized that the supraoptic nerve cells, that give rise to the majority of nerve fibres which supply the posterior pituitary, can be activated by different types of stimuli, some arriving by nervous pathways, some being directly chemical, and some being physical or physico-chemical. She described the release of antidiuretic hormone from the posterior pituitary gland following injection of acetylcholine, nicotine, morphine and ferritin. Acetylcholine is rendered temporarily ineffective in this respect after application of diisopropylfluorophosphate to the supraoptic nuclei. Intracarotid injection of adrenaline given prior to an antidiuretic dose of acetylcholine regularly annuls the action of the latter. It is of much interest that morphine is still effective in inhibiting a high rate of urine flow if applied directly to the supraoptic nerve cells, whether or not the cholinesterase of the cells of the supraoptic nuclei have been inactivated by diisopropylfluorophosphate.

Prof. H. B. van Dyke, of the Department of Pharmacology, College of Physicians and Surgeons, Columbia University, then dealt with the subject of posterior pituitary extracts. Ten years ago van Dyke, Chow, Greep and Rothen<sup>1</sup> extracted a protein from the pars nervosa of the pituitary with the biological

activities of both (antidiuretic - pressor and oxytocic) principles in about the same ratio as they are found in the gland. Its molecular weight was found to be about thirty thousand, and its biological activity was found to be low (1 unit = 61  $\mu\text{gm}$ ). Although considerable evidence has been obtained that oxytocic and antidiuretic activities are present in constant ratios and that the protein is homogeneous, the possibility of adsorption of highly active principles on to an inert protein molecule has not been excluded. The highly purified principles recently isolated by du Vigneaud and his co-workers were discussed by Prof. van Dyke<sup>2-5</sup>. These principles have been isolated in a highly active form, 1 unit of the oxytocic principle being contained in 1.25  $\mu\text{gm}$ . and 1 unit of the antidiuretic - vasopressor principle in 1.6  $\mu\text{gm}$ . The amino-acid content of these two principles has been investigated, and it has been found that tyrosine, cystine, aspartic acid, glutamic acid, glycine and proline are common to both, whereas arginine and phenylalanine characterize the oxytocic principle and leucine and isoleucine characterize the antidiuretic - vasopressor principle. Using these principles, various workers have established that neither the contraction of the isolated rat uterus nor the ejection of milk by the lactating mammary gland is a specific test for the oxytocic principle, whereas the depressor response of the fowl's blood pressure appears to meet this requirement provided that contamination by antidiuretic - vasopressor principle is not excessive. The extremely sensitive antidiuretic test in the dog was found to be specific for the antidiuretic - vasopressor principle. It is not yet possible to decide from the published investigations whether the neurohypophysis secretes a large molecule containing both oxytocic and antidiuretic - vasopressor principles, or smaller molecules of highly active principles. The separate secretion of the latter has more teleological attraction.

In the next contribution, Prof. H. Heller dealt with the fate of the posterior pituitary (antidiuretic) hormone when secreted into the blood. Previous work had shown that antidiuretic extracts are rapidly inactivated by defibrinated blood, serum and liver homogenate. When injected intravenously the antidiuretic activity of posterior pituitary extracts disappears rapidly from the circulating blood, and antidiuretic activity appears in the urine. Recent unpublished experiments of Ginsburg and Heller have shown that the liver and kidney both play a part in the 'clearance' of the antidiuretic principle: it would seem that, in addition to excreting it, the kidney also removes it by another, as yet unknown, process. The question of the renal excretion of the antidiuretic principle, both of endogenous and of exogenous origin, was discussed in further detail.

B. A. Cross described the evidence underlying the present concept of a milk ejection reflex<sup>6-8</sup>. It can now be taken as established that the act of suckling stimulates a nervous reflex excitation of the posterior pituitary gland, and the secretion from this gland causes contraction of some element of the mammary gland and thus a positive ejection of milk from the mother to the young. Recent work using du Vigneaud's highly active oxytocic and antidiuretic extracts indicates that the posterior pituitary principle underlying milk ejection is the oxytocic principle and not a mixture of the two, as had been previously suggested. Mr. Cross also discussed unpublished work in which it was found that previous administration of adrenaline, or electrical stimulation of the posterior region of the hypothalamus with

resultant sympathetic excitation, will inhibit the milk ejection reflex. Since the same procedures inhibit the milk ejection effect of posterior pituitary extract, it is likely that the effect of adrenaline is, at least in part, on the mammary gland itself. Dr. A. G. Lewis dealt with recent work on the secretion of the anti-diuretic hormone in normal man. It is satisfying to know that many of the laboratory findings are being confirmed on the human. After eighteen hours of dehydration a normal subject had posterior pituitary hormone in the circulation with an anti-diuretic activity equal to (approximately) 20 mU. of 'Pitressin'. It seems unlikely that the 5 mU./ml. of anti-diuretic substance which have been detected by rat assay of human serum have any physiological action. Direct assay in the human subject has shown that human serum contains less than 0.1 mU./ml. after twelve hours of dehydration. Emotional stimuli, the intravenous infusion of acetylcholine, or of hypertonic saline, nicotine, morphine, anaesthesia and surgical operations and syncope may all produce large releases of the anti-diuretic hormone in man.

The final speaker at the symposium, Dr. J. E. Cates, described the results of an investigation, in collaboration with Dr. O. Garrod, on fifteen patients with diabetes insipidus. 'Pitressin' tests separate the rare 'Pitressin'-resistant cases. Water deprivation gives results which vary in degree. Hickey and Hare's test with hypertonic saline may be nullified by an osmotic diuresis. Nicotine intravenously causes little or no antidiuresis when given in doses large enough to cause antidiuresis in normal subjects; larger doses usually cause some antidiuresis. The effect of nicotine in clinical diabetes insipidus supports the belief that nicotine stimulates the secretion of the anti-diuretic hormone. The response to large doses suggests that the lesion to the supraoptico-hypophysial system is often not complete.

<sup>1</sup> van Dyke, H. B., Chow, B. F., Greep, R. O., and Rothen, A., *J. Pharmacol.*, **74**, 190 (1942).

<sup>2</sup> Livermore, A. H., and du Vigneaud, V., *J. Biol. Chem.*, **180**, 365 (1949).

<sup>3</sup> Pierce, J. G., and du Vigneaud, V., *J. Biol. Chem.*, **182**, 359 (1950).

<sup>4</sup> Pierce, J. G., and du Vigneaud, V., *J. Biol. Chem.*, **186**, 77 (1950).

<sup>5</sup> Turner, R. A., Pierce, J. G., and du Vigneaud, V., *J. Biol. Chem.*, **191**, 21 (1951).

<sup>6</sup> Cross, B. A., and Harris, G. W., *Nature*, **166**, 994 (1950).

<sup>7</sup> Cross, B. A., and Harris, G. W., *J. Endocrinol.*, **8**, 148 (1952).

<sup>8</sup> Andersson, B., *Acta Physiol. Scand.*, **23**, 1 (1951).

## LONG ASHTON RESEARCH STATION REPORT FOR 1950

THE plant pathologist and the engineer tend to run their separate ways, sparing a modicum of liaison for each other, but rarely understanding the subject of plant pathological engineering as a whole. The annual report of the Agricultural and Horticultural Research Station, Long Ashton, Bristol\*, is perhaps most noteworthy for a determined attempt to consider the problems of the plant pathologist and engineer together. H. G. H. Kearns and N. G. Morgan publish an abridged specification of an experimental 'air-flow' small-volume drift sprayer and duster. This is designed to investigate the most efficient method of conveying very small drops of concentrated control

\* University of Bristol. Annual Report of the Agricultural and Horticultural Research Station (the National Fruit and Cider Institute), Long Ashton, Bristol, 1950. Pp. 217+13 plates. (Bristol: The University, 1951.)

materials to their disease targets, thus dispensing with large volumes of liquid, obtaining better penetration of the spray or dust cloud into foliage, and withal bringing great economy of the fungicide or insecticide. This material is fed into the blast from a fan delivering a large volume of air at low pressure.

New conceptions must not, however, be allowed to overshadow the solid worth of papers on more usual subjects. Nutritional studies include investigations on zinc and copper deficiencies of crop plants (E. J. Hewitt and E. W. Jones), work on iron metabolism in plants by the same authors contributing separate papers, and research on molybdenum and nitrate status in relation to yield and ascorbic acid levels in cauliflower (S. C. Agarwala; W. Plant). The wealth of detail and of interaction in all these results is summarized in the introduction to the report by the director of the Station, Prof. T. Wallace (pp. 13-15). L. C. Luckwill and D. Woodcock have a preliminary report on the nature of the hormone which occurs in the endosperm of the developing apple seed. It is, *inter alia*, acidic, heat stable, soluble in ether and water, is destroyed by hydrolysis with strong acid or alkali, and cannot be identical with indolyl-acetic acid. A further report on pruning systems and tree shape on yield and quality of apples is given by R. M. Jarrett. Any pruning reduces yield; but normal winter pruning improves quality. Allington and Cox's Orange Pippins cropped better as modified leader trees; but Worcester Pearmain gave more produce as an open-centre tree. Continuing their studies of the nutrition of the black currant, C. Bould and E. Catlow find that yield varied as leaf nitrogen status, which decreased according to the following order of manurial treatments: nitrogen plus phosphorus > sewage sludge > nitrochalk plus compost > straw sludge compost > farmyard manure > no manure. D. J. D. Nicholas and W. A. Forster consider the effects of copper, zinc, lead, cobalt, nickel and manganese in excess on tomatoes and other crop plants. This is an important study, for excesses of 'micro' elements figure in advisory work in addition to deficiencies of these elements.

Long-term work on spray materials superior to lime-sulphur for the control of apple scab has been continued by R. J. W. Byrde and R. W. Marsh. They found that glyoxalidine 341-C at 1 quart per 100 gallons equalled the standard lime-sulphur treatments on Cox's Pippin, and was less phytotoxic. The new spray was also less damaging to foliage of Lane's Prince Albert and Stirling Castle than lime sulphur. A phthalimide preparation (SR-406) promises good fungicidal performance and freedom from phytotoxicity.

F. W. Beech and S. W. Challinor discuss changes in the pectin and nitrogen contents of apple juices as a first part of a larger study of maceration and defecation in cider making. Fermentation of ciders can also be controlled by centrifuging; L. F. Burroughs and S. W. Challinor consider the mechanism of this action in some detail. B. T. P. Barker continues his investigation of cider yeast floras with a paper on that of Kingston Black ciders. Margaret E. Kieser and A. Pollard discuss the effect of fruit storage on the processing of apple juice, and, with C. F. Timberlake, the effect of manurial treatment on the composition of black currants. Other shorter papers are included in the report, which is edited by R. W. Marsh, and numerous half-tone and line illustrations help to maintain its usual high standard of production.