Pharmacological Research in Great Britain.

THE second Annual Report of the Pharmacological Laboratories of the Pharmaceutical Society of Great Britain (1927) gives a brief summary of the research work carried out during the year, and indicates the part the laboratory is beginning to play in the physiological standardisation of different drugs for commercial manufacturers. In February of last year the Vitamin-testing Department, under Dr. Katharine H. Coward, was ready to carry out its first tests, and these now occupy an important place in the laboratory's work.

The director, Dr. J. H. Burn, has continued his researches on the metabolism of rats on a fat diet: he has found that in summer the excretion of acetone bodies in the urine of a 100-150 gm. rat reaches a maximum of 50 mgm. in a day, whilst in winter the maximum may not be greater than 5 mgm. The summer acetonuria can be inhibited by injection of pituitary extract or adrenalin, indicating that these hormones control the metabolism of fat as well as that of carbohydrate. On the other hand, daily injections of insulin, after a day or two, increase the winter acetonuria, and this increase is not simply related to the fall in the blood-sugar, since the latter occurs to about the same extent on all days on which the injections are given.

Some work has been carried out on the assay and preparation of extracts of ergot, and also, in conjunction with Mr. A. Bourne, on the clinical value of pituitary and ergot extracts. It was found that during labour a dose of 2 units of pituitary extract was quite sufficient to hasten its conclusion, and also that of the possibly active substances present in extracts of ergot, the specific alkaloid ergotamine or ergotamine produces, after a short latent period, a

prolonged contraction of the uterus *postpartum*, whilst histamine causes an immediate powerful but short-lived contraction, and tyramine is inert.

A paper on the oestrus-producing hormone has been published by Drs. Burn and Coward: it was found that the individual variation between different rats or different mice is as much as 1000 per cent. The authors therefore define the unit as the dose necessary to produce oestrus in 50 per cent. of ovariectomised animals. They have constructed a standard curve relating the percentage of rats in which oestrus occurs to the dose injected from observations on a group of 90 animals. A curious point that emerged from this work was that the mouse unit has exactly the same value as the rat unit, in spite of the difference in body weight between the two species.

In the vitamin department, a stock colony of Wistar rats is in process of being built up, by in-breeding the animals and maintaining them on a constant diet: the most suitable diet, however, has not yet been determined. A sample of irradiated ergosterol is being used as a standard for vitamin D assay: a unit has been defined as the amount of antirachitic activity contained in 0.0001 mgm. of this sample. This definition has been rendered necessary by the fact that certain workers are defining the unit of vitamin D as the least amount which will cure rats of rickets, when they are maintained on a rachitogenic diet: such a unit may vary by 400 to 500 per cent. in different experiments. It is hoped to use a sample of the unsaponifiable matter of cod-liver oil as a standard for vitamin A in the near future. The report also gives the number of samples of the different preparations which have been assayed during the year: approximately 170 were tested.

The Synthesis of Cane Sugar.¹

By Prof. AMÉ PICTET and H. VOGEL.

THE fine researches of Haworth and of Irvine have shown that fructose (levulose) does not possess the same chemical composition when it is in one of its natural combinations (cane sugar, inulin) as when it has been extracted. Hence it must be admitted that it can exist in two isomeric forms, one of which, to which the name of γ -fructose has been given, is unstable and changes spontaneously into the other, called normal fructose, as soon as it is set free. Haworth and his collaborators have made it very probable that the formulæ which should be attributed to these two forms are the following:

It follows from these facts that if it is attempted to realise a synthesis of saccharose by the union of its two constituents, glucose and fructose, it cannot be effected by utilising the second of these sugars in its normal form, the only one available. It would

be necessary to start with one of the artificial derivatives in which it occurs in the γ form. Some of these are known (methyl, ethyl), but none of these would be available for the operation in question, since the substituted groups that they contain are too firmly fixed to the rest of the molecule to permit of their being detached, once the condensation with the glucose had been carried out.

Hence the synthesis of saccharose necessitates the preliminary preparation of a derivative of γ -fructose containing only substituent groups relatively easy to remove. The following observation has furnished us with a substance which fulfils this condition.

We have found that when the tetracetate of normal fructose is prepared by the method of Hudson and Brauns (*Jour. Amer. Chem. Soc.*, **37**, p. 2739; 1915), that is, by treating fructose at a low temperature with acetic anhydride and zinc chloride, on crystallising the product from alcohol, a second compound is formed in small quantity which remains in the mother liquors. On evaporating these in a vacuum a thick syrup is obtained which, on contact with cold water, is slowly converted into a solid vitreous mass. Up to the present, this substance has not been obtained in the crystalline condition, but its analysis, and the fact that it easily reduces alkaline copper solutions, proves that it consists of a second tetracetate. Moreover, its rotatory power, much lower than that of the normal tetracetate, would suggest that it belongs to the γ series.

The formation of a derivative of this nature would be explained by admitting (as already suspected by

¹ Translated from *Comptes rendus* for Mar. 19 of the Paris Academy of Sciences.

Ohle) that when fructose goes into solution, an equilibrium is established between its normal form and the γ form. This would take place in acetic anhydride as in any other solvent and each of these forms would then be acetylated on its own account. Under the conditions of our experiment, the equilibrium would appear to be approximately 97 parts of normal fructose and 3 parts of γ -fructose.

It would have been easy to prove the γ nature of the new acetate by methylating it, and then saponifying the product; the methyl- γ -fructoside prepared by Irvine should thus have been obtained. But there was another method, more simple still, and that was to combine it with glucose tetracetate: it should then, if really derived from γ -fructose, give rise to the octacetate of saccharose.

Glucose tetracetate + γ -fructose tetracetate = saccharose octacetate + water.

This experiment was carried out by dissolving in chloroform equal weights of our tetracetate and that of glucose (prepared according to the method of E. Fischer and Delbrück), and this solution was shaken for 15 hours with phosphorus pentoxide. On evaporation in a vacuum, it left a syrupy residue, which, taken up in warm alcohol, deposited fine crystals on cooling. These presented the principal characters of saccharose octacetate

Melting-point of our crystals	70° C.
" " of saccharose octacetate	70° C.
" " of their mixture	70° C.
Rotatory power in chloroform solution	+ 59°·4
" " of saccharose octacetate	+ 60°·0

It may be noted that the same substance was obtained in two series of experiments, in one of which a fructose prepared by inversion of saccharose was the starting-point, and in the other a fructose extracted from inulin.

The saponification of the synthetical octacetate, carried out by Zemplen's method, finally gave an anhydrous, non-reducing disaccharide, of crystalline structure and very sweet taste. The comparison of its principle properties with those of cane sugar gave the following figures:

Analysis (per cent.)	C 42·3, H 6·6 (calculated for $C_{12}H_{22}O_{11}$: 42·1 and 6·5).
Cryoscopy in water	Molecular weight found: 344 (calculated 342).
Melting-point of our sugar	183° C.
" " of saccharose	184° C.
" " of their mixture	184° C.
Rotatory power in aqueous solution of our sugar (C = 5·07)	+ 66°·3
of saccharose at the same concentration	+ 66°·5
of our sugar after inversion	- 20°·6
of saccharose after inversion	- 20°·7

From the concordance of these figures the identity of these two substances must be regarded as proved.

We still have to clear up certain points concerning the intermediate products of this synthesis, and to give an account in greater detail of the whole of our operations. These results will be published in due course.

The Development of Cyclonic Depressions.

IN the *Monthly Weather Review* for November 1927, two articles by W. J. Humphreys appear, both of which deal with the growth of cyclonic depressions in the United States and Canada.

The first article gives an explanation of the great increase in size and intensity of a depression that so often takes place when it moves north-east across the eastern parts of the United States or of Canada. Since such an increase of intensity with increasing latitude is not a world-wide phenomenon, the idea that it may be due to change with latitude of the deflective force of the earth's rotation is rejected. If, on the other hand, contrast of temperature is regarded as essential for cyclonic development, an obvious explanation is afforded by the fact that the farther north the depression goes, the shorter is the distance through which the incoming supply of polar air has to pass, and the colder that air will be on arrival, while the high temperature of the equatorial air is largely maintained by latent heat set free by condensation of its water vapour, even when the distance travelled from equatorial regions is very great, the result being an increase of temperature contrast between the parts of the depression fed, respectively, by these two supplies of air. Such opportunities for increasing temperature contrast as exist over eastern North America and the western part of the North

Atlantic are available in few if any other parts of the world.

The second article seeks to explain why depressions moving north-eastwards across the United States in winter increase in size and intensity more rapidly by night than by day. Thermal considerations are again made use of: it is pointed out that the cold portions of the depression have as a rule clearer skies than the relatively warm portions, and consequently are far more strongly cooled by radiation at night, an increase of temperature contrast due to this effect being added to the general effect of latitude mentioned above. During the daytime, on the other hand, not only is the polar air with its clearer skies warmed more than the equatorial air, so as to reduce the contrast of temperature, but also, being so warmed, thermal convection will normally set in and obstruct to some extent the simple cyclonic wind-system.

It may be pointed out that the effect dealt with in this second article is not generally regarded as characteristic of depressions crossing the British Isles. This is not surprising, however, when we consider how comparatively small the nocturnal fall of temperature is in polar air that has been charged with water vapour, if not with cloud, during a long passage across the North Atlantic, as generally happens with polar air reaching the British Isles.

Earthquakes in the Crimea in 1927.

PROF. A. V. VOZNESENSKY in *Priroda* (No. 12, 1927) gives the preliminary results of observations on the Crimean earthquakes of last summer. The data on which the account is based are admitted to be somewhat fragmentary and inexact, since the Crimea was considered not to be subject to earthquakes and there was no seismological station there before, though

one is established now in Feodosia. Apart from that, observations on the spot during the earthquakes were not organised properly and have been made without system or knowledge.

The first tremor occurred on June 26, when many buildings were partially destroyed, and afterwards slight tremors were experienced for five months, until