Aspects of Carbohydrate Metabolism.

I. Blood and Urine 'Sugar'.

THE form in which carbohydrate circulates in the body is glucose: it is frequently of clinical importance to determine the amount of this substance in the blood, but estimation of blood-sugar may not be synonymous with determination of blood-glucose. Different methods of estimation give somewhat different results, but this is of little importance clinically, provided the same method is always used. It is, however, of some interest to inquire into the causes of these discrepancies and a certain amount of work has been recently devoted to this subject. After fermentation with yeast, blood still gives a residual reduction with oxidising agents, which is obviously not due to glucose: according to I. M. Rabinowitch (*Biochem. Jour.*, vol. 22, p. 753; 1928) the amount of the non-fermentable reducing substances present in normal or diabetic human blood is about 0·025 per cent expressed as glucose. It is very constant in the same individual, is not affected by insulin or by the administration of glucose by mouth, and is the same in venous as in arterial blood: in all these respects it shows a marked contrast with glucose.

F. K. Herbert, M. C. Bourne, and J. Groen have investigated the nature of the non-glucose reducing substances in human blood (*ibid.* vol. 23, p. 339; 1929: vol. 24, pp. 291 and 299; 1930). In the first paper the distribution of reducing substances between plasma and corpuscles was determined by several different blood-sugar methods. By those of MacLean, Hagedorn and Jensen, and Benedict, there appeared to be more sugar in the plasma than in the corpuscles; by those of Folin and Wu and Shaffer and Hartmann (as modified by Somogyi) the distribution was approximately equal; whilst when the Hagedorn-Jensen method was carried out on the Folin-Wu blood filtrate, there appeared to be slightly more in the corpuscles than in the plasma. Blood filtrates prepared by the tungstic acid method from whole blood or corpuscles reduced the Folin-Wu copper reagent in the cold, but not those from plasma; nor was such a reaction given by filtrates prepared by the use of colloidal ferric hydroxide or zinc hydroxide.

It appears, therefore, that the corpuscles contain non-glucose reducing substances which are precipitated by iron and zinc hydroxides but not by tungstic acid: they are not fermentable with yeast. The most important of these is probably glutathione, since uric acid, creatine, creatinine, and ergothioneine are present in too small concentrations to affect the estimation of blood-glucose. In the second paper of the series it was shown that when pure glutathione was estimated in the presence of 0·1 per cent of glucose, it produced a reduction of 56 per cent of that given by a corresponding amount of the latter when the Hagedorn-Jensen method was used, of 39 per cent with the Shaffer-Hartmann method, and of 20 per cent with that of Folin and Wu: it failed to affect Benedict's reagent. It was also shown that a zinc hydroxide filtrate, provided the precipitation had been carried out at a slightly alkaline reaction, contained none, whilst all the glutathione present passed into a tungstic acid filtrate. The third paper applies these results to blood, and a description is given of a new method of precipitating the proteins: the corpuscles are kept intact by using sodium sulphate as diluent instead of water, the precipitation being carried out by means of tungstic acid. The four methods of blood-sugar estimation agreed when compared on zinc hydroxide or the modified tungstic acid filtrates; on the original tungstic acid filtrates higher values (except with Benedict's method) were obtained and the methods disagreed. The discrepancies could all be explained by the known reducing powers of glutathione in the presence of the reagent used. The amount of this substance in the blood is about 0·05 per cent, a higher figure than that given by Rabinowitch.

J. M. Gulland and R. A. Peters (*ibid.* vol. 24, p. 91; 1930) have investigated the nature of the reducing substances in pigeons' blood. The Hagedorn-Jensen method was used: relatively high values for blood-sugar were obtained, but it was found that even after the injection of insulin, or after the blood had been exposed to anaerobic glycolysis, a residual reduction of 0·07 per cent was still observed. Deduction of this figure from the 'blood-sugar' value indicated that the true glucose of the blood was not very much higher than that of mammals. The residual reducing substances were almost confined to the corpuscles: about half of them reduced the ferricyanide in the cold, suggesting the presence of sulphydryl groups. It was found that, by this method, the reducing power—in terms of glucose (100)—of uric acid was 53, of glutathione 17, and of ergothioneine 56; by the ordinary Hagedorn-Jensen method glutathione was found to be equivalent to 45 of glucose (agreeing with Herbert *et al.*). From these estimations, and others carried out on tungstic, trichloroacetic, and zinc filtrates, it was concluded that the non-glucose reducing substances in pigeons' blood are ergothioneine, uric acid, creatinine, creatine, and one or more unidentified compounds, possibly a purine-carbohydrate or a phosphoric ester.

E. N. Allott (*ibid.*, vol. 22, p. 773; 1928) has shown that the rates of utilisation of α, β, and $\alpha\beta$ glucose when injected into the veins of rabbits are the same. O. J. Nielsen (*ibid.*, vol. 22, p. 1490; 1928), by estimates of the blood-sugar at intervals of 1–5 min., has shown that it is not, in man, subject to violent fluctuations, remaining fairly constant or falling or rising steadily according to the conditions at the moment: the observations were carried out after fasting and after the ingestion of food or glucose on both normal and diabetic subjects.

Two other papers on carbohydrates may be referred to briefly here. C. Rimington (*ibid.*, vol. 23, p. 430; 1929) succeeded in isolating a carbohydrate derivative from alcohol-denatured serum proteins, by hydrolysis with baryta, treatment with lead acetate, and precipitation with ammonia: the lead ammonia precipitate was dissolved in weak acid, the lead removed, and the filtrate treated with mercuric chloride solution: after removal of metals the solution was concentrated and the carbohydrate precipitated with methyl alcohol and ether. The yield was 2 per cent. On analysis it was found to contain 4·1 per cent nitrogen, and molecular weight determinations indicated that it was a disaccharide, having the empirical formula $C_{12}H_{23}O_{10}N$; further investigation showed that it was a disaccharide of glucosamine and mannose. Both albumin and globulin yielded the same derivative, and it was also obtained after tryptic digestion of serum protein. It is considered probable that the mannose is attached to the nitrogen atom of the glucosamine. From the amount present the minimum molecular weight of the albumin or globulin must be of the order of 17,000, a figure which agrees with estimations made by other methods. It is possible that this carbohydrate plays some part in the immunological reactions of the plasma proteins.

H. Sobotka and M. Reiner (*ibid.*, vol. 24, p. 394; 1930) have investigated the configuration of certain sugars by means of the differences in their reducing powers for the ferricyanide reagent of Hagedorn and Jensen. Their results lead to the conclusion that in aldo- and keto-hexoses the configuration between the third and fourth carbon atom is the determining factor: in aldopentoses the configurations between these two atoms and the second and third share the influence on the reducing power. The *trans* arrangement of OH is more active than the *cis*.

The question of the nature of the reducing substances in urine, especially in human beings, has always aroused interest. It is generally held that small amounts of glucose are normally excreted; during lactation, lactose may appear, whilst the excretion of a pentose is a rare abnormality. J. Patterson (*ibid.*, vol. 20, p. 651; 1926) considers, however, that the carbohydrate in normal urine is not glucose, since it is not fermented by baker's yeast and forms a phenylosazone of different crystalline form and properties from those of glucosazone, although its analysis suggests that it is a hexosazone. Hydrolysis of urine usually sets free a fermentable reducing sugar. A. Hassan, however, considers that glucose is present in normal urine, although accompanied by another sugar which forms a different osazone (*ibid.*, vol. 22, p. 1332; 1928). Both authors agree that interfering substances must be removed before attempting to form an osazone; Patterson employs the mercuric nitrate reagent and Hassan charcoal. The latter author also found that the number of urines giving typical glucosazone crystals as well as mixed crystals, instead of the latter only, was increased following a meal but not following the administration of glucose alone.

Social Biology.*

DARWIN'S "Descent of Man" was a challenge to the complacent dualism which had permitted utilitarian science and humanistic philosophy to pursue an independent course from the days of the schoolmen to the middle of the nineteenth century. To-day it is evident that the social sciences can no longer progress within the framework of a philosophical tradition brought into being by the conditions of the city State and nurtured from Abelard to Kant in servile association with the requirements of apologetics. Economic science has already severed its moorings to moral philosophy. There is a growing disposition among other branches of social science to do the same. To-day the application of scientific method to the study of human society is philosophically guaranteed by the generally accepted conclusion that millionaires and metaphysicians, statesmen and seventh-day adventists are products of the same secular agencies as have fashioned the rest of the brute creation. The far-reaching implications of the change in outlook which Darwin's doctrine has brought about are becoming more apparent in our time, because biologists are now undertaking the analysis of the characteristics of conscious behaviour in animals and the behaviourist school of psychologists is applying the new methods to man himself.

Man is an animal as the ant is an animal. The biologist as a biologist confines his attention to those characteristics which ants and antiquarians have in common. The sociologist confines his inquiries to certain characteristics which distinguish men and women from ants and all other animals. Their respective fields of investigation overlap in the attempt to define what characteristics of human society are determined by those characteristics which men share with all other animals and what characteristics of human society are referable to characteristics which distinguish man as one species of animal from all other species of animals.

We must be prepared to recognise that issues which made the first claim on the attention of men like Huxley, Galton, and Spencer are no longer topical. The misguided opposition of the Churches compelled biologists of Darwin's generation to concentrate on emphasising the characteristics which we share with other animals. Social biology has now to undertake the task of defining in biologically significant terms the characteristics which distinguish man as one species of animal from all other species of animals. The work of physiologists like Sherrington and Pavlov is opening the way to a biological interpretation of those peculiarities which are most diagnostic of the human species. A well balanced view of the rôle which inheritance and social tradition respectively play in determining differences which distinguish different social groups will only be possible when the biological study of behaviour and the methods of the geneticist can be brought into working harmony.

The great danger lies in undue haste to establish conclusions which may be made the basis of legislation. The genetic basis of occupational and racial stratification in human societies is a problem which calls for discipline, detachment, and restraint. Nothing could make the exercise of these wholesome virtues more difficult than to bring issues which are still problematical to scientific workers before the forum of political controversy. Much research directed to elucidate genetic variations in human communities has been vitiated by a failure to envisage the complexity of the problem. A genuine scientific analysis of genetic variation in human society must be sustained by the recognition that human society is a unique biological phenomenon, inasmuch as the family is a unit for the cumulative communication of old and new environmental stimuli as well as a group delimited by genetic affinity. The pre-eminent need of the moment is investigation rather than propaganda. The first task of the social biologist is not to advocate the sterilisation of the unfit but to undertake the sterilisation of the instruments of research before operating on the body politic.

In our own generation the population problem embraces a variety of issues in which the sociologist and the biologist have a common interest. A clear appreciation of the biological issues necessitates the prosecution of research into the physiology of reproduction, the genetic basis of human behaviour, and the incidence of changes in fertility. The analysis of this intricate problem will not be facilitated by an unduly alarmist attitude. The sceptical inquirer may approach the differential fertility of the social classes which has accompanied the decline in the birth-rate as a conundrum rather than a catastrophe. We have inadequate scientific evidence to justify the belief that extensive genetic differences do distinguish the social classes. If we had such knowledge it would be necessary to ascertain how such differences are transmitted before justifying the belief that a temporary disparity in fertility will necessarily produce

* Substance of an inaugural lecture delivered by Prof. Lancelot Hogben at the London School of Economics and Political Science on Oct. 23.