GLYCOSURIA IN PREGNANCY

By Malcolm H. V. Cameron, M.B.

IN 1910 I encountered my first case of glycosuria in pregnancy. My patient consulted me in her fifth month of gestation, and in the routine examination of her urine, I found a reducing sugar in small amount. I made inquiry among my senior colleagues in the hospitals and was assured that a transient lactosuria was a very ordinary concomitant of pregnancy. The literature I then studied confirmed their opinion and I ceased to worry, especially as I found no sign of sugar after the sixth month. The confinement was tedious and choloroform was used to the extent of nearly two ounces. Recovery was uneventful and the patient went to the country to recuperate. She developed an insatiable appetite within a week after this and three weeks later died in diabetic coma despite vigorous treatment. Since this case occurred I have had four hundred and sixty-eight obstetrical cases and have found glycosuria in four. I have permission also to mention two in the practice of Dr. Victoria Reid and two in that of Dr. D'Arcy Frawley. A brief recital of these cases will illustrate the few suggestions as to causation and management of the condition which will be presented in this paper.

Mrs. D., aged twenty-five, primipara, first consulted me in the fourth month of her gestation, May, 1916. In June I found definite glycosuria. Dr. H. M. Tovell determined her carbohydrate tolerance and managed her diet. She was kept sugar-free after July 15th. She was delivered under hyoscine and morphine in the Burnside Hospital, October 24th, 1916. The baby was small, ill-nourished, and only breathed once. Many observations have been made in the interim and her urine has been sugar-free until October, 1918, when she reported herself as three months pregnant. Glycosuria was noted in the fourth month and was immediately brought under control by limiting the diet according to the tables presented by Dr. Tovell in 1916. A trace of sugar was found in

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the last specimen examined, the patient being in the seventh month. She is again noted as case five in this series.

Mrs. S. W., aged twenty-eight years, primipara, brought her first specimen in April, 1918, her fifth month, and glycosuria was discovered on examination. She was at once starved for twenty-four hours and her carbohydrate intake gradually increased according to Joslyn till her tolerance was reached as determined by Dr. Olive Cameron. The diet required constant supervision because of a persistent polyuria until her confinement, August 26th, 1918, when she was delivered of a well-developed male child under morphine and hyoscine with a small quantity of ether in the second stage of labour. No return of the glycosuria has been noted.

Mrs. W. A., aged twenty-five, showed no sign of glycosuria during her first pregnancy, which terminated happily on December 28th, 1916, nor was there any observed until the last month of her second pregnancy. She had a quick and easy delivery conducted, during my absence, by Dr. W. W. Lailey. Specimens of urine examined since then have not shown any trace of sugar until two weeks ago, seven weeks after confinement.

Dr. Reid's cases included a multipara who in four pregnancies showed glycosuria. Each succeeding gestation presented greater difficulty in securing a sugar-free urine, but no diabetes has developed since the birth of her last child. The second case in this series is still under treatment in her last month. She is being restricted practically to vegetables of five per cent. carbohydrate as a diet, but so far has shown no diacetic acid or acetone. There is an associated incompetence of kidney in this case.

Dr. Frawley told me of a case in which a patient, to whom he had been called in consultation, died in diabetic coma ten days after delivery, although the attending physician had satisfied himself that there was no glycosuria at least in the late months of the pregnancy. His latest case was delivered two weeks ago. This patient shewed a true glycosuria of two per cent., or slightly less, for two months before delivery, although she was in apparently excellent health. Examination since delivery has shewn a gradual disappearance of the sugar.

In eight of these cases glucose was, beyond any question, the sugar found. Dr. Reid's first case may have been lactose. My first case must have been glucose, although no differentiating tests were made. In all of the others the fullest examinations of a qualitative nature were done. In two of the cases a condition of true diabetes existed. My first case was evidently diabetic or almost

so before her confinement. For years I have been blaming myself because of having given the chloroform which might have induced the acidosis which precipitated the onset of acute diabetes from which she died. This idea was sustained by another case which came under my notice in which a lad of seventeen, known to be diabetic and under strict diet, was passing urine containing one half of one per cent. sugar. He sustained a Colles' fracture and the nearest practitioner was called, who administered chloroform before reducing the fracture. Two days later the urine was examined and found to contain two per cent. sugar. The diabetes progressed rapidly and the boy died about two months later. I am assured that the labour in the one case and the trauma in the other had probably much more to do with the onset of the diabetes than had the chloroform. At the same time it would appear to be most unwise to use chloroform during confinement in these cases.

In Dr. Frawley's first case it is more than likely that a diabetes of pancreatic origin existed before pregnancy began, but that the fœtal pancreas served for both maternal and fœtal organisms until delivery occurred, when the strain of labour made a demand upon the metabolism of the mother that it was unable to meet in the absence of the temporarily engrafted pancreas of her child. This may also have been the explanation of my first case. Such cases as these without the tragic ending may justify French, in Latham and Crile's work, in saying that some cases of diabetes improve under pregnancy. The other cases require explanation. It is too easy to say that lactose is excreted when the lacteal glands begin to undergo hyperplasia in the months immediately preceding lactation and will be found in the urine. Undoubtedly lactose may appear in the urine and may mean nothing more than the normal stimulation of mammary glands as they are being prepared for their function after the birth of the child. It is also true that glucose may be found in the urine from the same source. An inverting enzyme may break up the lactose into galactose and glucose and the latter be excreted if it cannot be stored in the muscles or the liver. In either of these instances the sugar may be depended upon to disappear from the urine after lactation begins. This simple explanation may be sufficient in many cases but in very many more it is quite inadequate. The excretion of sugar in any form or degree is a matter of derangement in metabolism that is much more complex than can be so briefly indicated, and when the further derangement of pregnancy is added, the complexity is vastly increased.

It is not within the scope of this discussion to attempt to unravel the relations and inter-relations of organ and function in the processes of metabolism, normal or abnormal. I merely beg to offer one or two clinical observations which bear upon the subject.

Dysfunction of the pituitary gland may result in acromegaly and this has frequently associated with it a condition of glycosuria. Dysfunction of the thyroid gland may result in Graves' Disease and this has frequently associated with it a condition of glycosuria. In either case an imbalance in metabolic process occurs, and the cause of such imbalance must be ascertained, if these alterations in function in the glands mentioned or in other glands of the endocrine system are to be explained.

Pregnancy, as we know, does demand a hyperplasia of the thyroid gland, and, as we know almost as well, of the hypophysis also. The generation of the auto-catalyser, by which growth is maintained or accelerated, belongs to the anterior lobe of the pituitary body, as the experiments and conclusions of Brailsford Robertson have placed beyond peradventure. The provision of this catalyser demands a hyperplasia which may run beyond the necessities of the case or which may involve the posterior lobe of the pituitary body, in which case acromegaly may, presumably, develop. This is illustrated by a case in my practice in which a young woman of prepossessing appearance showed, in the last month of her first pregnancy, changes which were strongly suggestive of acromegaly. The skin became coarse, the lips thick, the voice altered and the face acquired a heavy look quite different from her normal appearance. She speedily regained her beauty after her confinement. In her case there was no glycosuria for a reason to be given later. Should this involvement of the posterior lobe affect chiefly or entirely the pars nervosa a condition of polyuria and polydypsia may arise. Of this I have one illustration. A patient now under the care of Dr. Frawley is secreting twelve to fourteen pints of urine daily which has a specific gravity of 1002, but shows no pathological content. This must be of pituitary origin as, were it due to schlerosis of kidney tissue, there would be hyaline casts and other evidences of kidney disease.

The bearing of all this upon the subject is made evident by a careful reading of Cushing's experiments upon the pituitary gland. The condition of pregnancy calls forth a hyperplasia of the hypophysis in order to produce the auto-catalyser of Robertson. This is expended upon the growth of the fœtus or, in the case of the young patient, upon the growth of the mother as well. This hyperplasia,

as it affects the posterior lobe, results in a condition of hyperglycæmia with decreased carbohydrate tolerance, and this, added to the normal hyperalimentation of pregnancy, may result in glycosuria. Should the hyperplasia affect the pars nervosa chiefly, a polyuria, without glycosuria or diabetes insipidus, will follow. Thus it appears that the relation between diabetes insipidus and glycosuria depends upon the very narrow margin of chance, that in a general hyperplasia of the pituitary body in its posterior lobe the pars nervosa acquires a stimulation greater than does its epithelial envelope. Again, should the epithelial portion of the posterior lobe fail to take part in the general hyperplasia or should its secretion be hindered in its entry into the cerebro-spinal fluid, a condition simulating hibernation results. The patient displays a syndrome of adiposity, mental sluggishness, increased carbohydrate tolerance and a definite hypoglycæmia. Should the hyperplasia affect chiefly the anterior lobe, the hyperglycæmia mentioned will not occur and thus, although acromegaly may develop to an extent, glycosuria will not be its accompaniment, although acromegaly usually is associated with glycosuria as the whole gland is affected consistently. This explains the case I have instanced.

The practical conclusions to be deduced from the consideration of this group of cases are important. In four hundred and sixty-eight cases of pregnancy, five cases of glycosuria have been found. In four of these the sugar was definitely identified as glucose by either the fermentation or osazone tests. In the other the patient died of diabetes. The inference is obvious. The finding of a reducing sugar in urine from a pregnant patient is a serious matter. Lactosuria may be a trivial affair, but before a patient whose urine reduces copper hydroxide in a test solution is dismissed as being in no serious condition, the fullest tests should be performed to ascertain if lactosuria be the real condition or not. In my cases lactose was completely excluded. Where glycosuria exists, true diabetes may be about to manifest itself or may be already in existence. The causes of glycosuria other than diabetes have been indicated. Such of these causes as are consequent upon pregnancy and which cease to operate once pregnancy is ended, merely require careful management until they disappear. A regulation of diet more or less strict will keep the symptom in abeyance. A careful selection of anæsthetic and any means possible to lessen the shock of delivery will perhaps prevent the onset of such changes in the endocrine gland system, already strained beyond the normal, as are indicated by the glycosuria and which might result in diabetes. The diag-

nosis of true diabetes in these cases is of supreme importance. Should the glycosuria be controllable by diet regulation, the frequent examination of the urine may be sufficient to protect the patient during gestation. This will not, however, decide whether or not her diabetes is under control because of fœtal hormones. nor will it differentiate a glycosuria due to hyperalimentation or secretion of inverted lactose. The only means of arriving at definite conclusions is by estimation of sugar in the blood. The method is simple provided one has a proper colorimeter. Any one who can make a hæmoglobin estimation with a Sahli apparatus may make a sugar estimation with the proper equipment. In all cases in which sugar occurs early in pregnancy or persists after delivery, a test should be made in order to determine whether or not a hyperglycæmia be present. It can do no harm if carried out in any case of glycosuria and may be the means of averting tragedies such as two of these cases have presented. The ingestion tests for carbohydrate tolerance would arrive at approximately the same conclusions but they are difficult of execution and may be most disagreeable to patients already in a state in which nausea is an ever-haunting spectre.

An alarming increase in the cancer death rate is noted by Dr. Francis Carter Wood, director of the Crocker Special Research Fund of Columbia University and of the pathological department of St. Luke's Hospital. The increase in England and Wales has been enormous and Dr. Wood believes that the same phenomenon will be observed in the United States during the next year or two. For a great many years cancer has been slowly increasing in England, though physicians are at a loss to account for the increase.

In the United States in 1914 the death rate was 79·4 per 100,000. In 1900 it was 63 per 100,000. But this does not compare with Switzerland, where it was 126·7 per 100,000. Under Dr. Wood and Professor William H. Woglom, a course in cancer research will be given at the Columbia Summer School in the Crocker laboratories. The work will consist of lectures and laboratory exercises. The classification of human and animal tumours will be first considered. The method of transplantation of tumours in animals will be shown. The simpler procedures for fixing, sectioning, and staining tissues for diagnosis will be demonstrated.