satisfactory plastic operations upon the ureter for vesical grafting. They may be classified as follows:

1. Invaginating the fistulous aperture itself into the bladder after first incising the vesico-vaginal septum.
2. Grafting the ureter to the bladder through the vagina.
3. Grafting the ureter into the bladder by an extraperitoneal route through an incision in the abdominal wall.
4. Grafting the ureter into the bladder by a transperitoneal or intraperitoneal operation.

Since Simon, in 1869, first practised nephrectomy as the remedy for urethral fistula, the operation has frequently been performed for this cause up to the present time. Tuffier, in a recently published communication, refers to twenty-four cases which he had collected. But with our present knowledge of the surgery of the ureter, nephrectomy for fistula has become in most instances, I do not say in all, an unjustifiable procedure. It ought to be reserved for quite exceptional cases, as, for instance, where the state of the kidney itself is prejudicial to health, or when the surgeon, having tried and failed, has given up the attempt to cure a troublesome and loathsome fistula by plastic operation.

Nephrectomy as a primary operation for surgical injuries of the ureter is quite unjustifiable; and as a secondary operation for these injuries it comes under the criticism just made upon it for the treatment of fistula.

As a remedy for movable kidney, nephrectomy has come and gone, never, it is hoped, to return.

In cases of limited suppuration, of circumscribed tuberculous disease, of innocent growths, and in certain injuries of the kidney, partial excisions are now being performed in place of nephrectomy.

In many instances of calculous pyonephrosis irrigation of the renal calyces and infundibulum, followed by suture of the kidney, has taken the place of nephrectomy.

In hydronephrosis a few laudable attempts have been made, and in a good proportion of them with success, to remove the cause of the obstruction, and thus by means of a plastic operation to spare the kidney.

In fact, the tendency of the surgery of to-day is to save as much of the kidney tissue as possibly, consistently with the safety and well-being of the patient.

In this very imperfect survey of the origin and progress of renal surgery, I hope I have succeeded in showing that whilst its origin was nephrectomy, its progress, especially during the last ten years, has been in the direction of rendering nephrectomy more and more an operation to be avoided.

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"ON PRODUCTION OF SUGAR IN THE LIVER, AND ITS UTILISATION IN THE TISSUES": A REPLY.

By F. W. PAVY, M.D., F.R.S.,
Consulting Physician to Guy's Hospital.

IN an article contained in the *BRITISH MEDICAL JOURNAL* of February 26th, Dr. Paton has returned to the discussion on the glycogenic theory upon precisely the same lines as in his previous criticisms of my work, which have been fully dealt with by me. May I ask you to accord me space for a reply?

I accede to what is said about the importance of the question of the treatment of diabetes, but I fear that the busy practitioner who may have read the article will nowhere have found in it the proffered help. If I mistake not, indeed, instead of being able to form an "intelligent judgment," his mind will have been left in a mystified state, and yet the object of the article is assistance boldly professed to be ren-

dered by a physiologist upon a matter bearing upon treatment. On the contrary, I, in my position as a practitioner, have to say that no intelligent judgment to render service in treatment can be framed upon the basis of the glycogenic theory. Can anyone say that he knows anything about diabetes looked at through the glycogenic theory? All that acceptance of the doctrine has done is to lead to serious error in treatment by suggesting to the minds of some that in a system already set wrong by the unnatural presence of sugar within it, matters should be made worse by the administration of carbohydrate, upon the plea that sugar is wanted by the tissues.

To the physiologist, the question of whether the glycogenic theory is right or wrong is not of the same paramount importance that it is to the physician. Whatever may be the view held by the physiologist, in his department Nature goes on working in her own way without being influenced. In the physician's department, on the other hand, an erroneous working is at the foundation of what has to be dealt with, and the essence of the physician's calling is to set the working right. How can this be done upon rational principles without a correct physiological knowledge? In our endeavours to set things right, physiology becomes tested in a manner the opportunity for which is not otherwise afforded, and, viewed in relation to what is learnt from diabetes and its treatment, the glycogenic theory stands in a completely irreconcilable position. If Dr. Paton contends otherwise, let him state his case and deal with the phenomena presented, and show that the glycogenic theory can in reality stand in presence of them. I have stated mine, and have shown that it is not only reconcilable with physiological and medical knowledge, but that it gives us a perfectly intelligible working basis, and a reliable guide in treatment. In the position Dr. Paton has taken, it is due to the medical profession that he should point out the light that the glycogenic theory throws upon the treatment of diabetes.

I cannot think that any useful purpose would be served, even if permission were granted for the occupation of the space required, by following Dr. Paton again in detail as I have done before through the further references upon which his article is based. I have gone through them fully, and the expenditure of time in doing so has prevented my replying earlier to the article.

Dr. Paton relies upon the scattered record that is to be found of the multifarious casual work that is performed. What he has brought forward in this third set of references is of a comparable nature to that examined in my *Epicriticism*¹ and *Rejoinder*.² As I have before stated, there is, perhaps, no subject in physiology in which the experimentalist is beset with so much danger of fallacy as that bearing on the relations of sugar in the animal system, and much, indeed very much, of the work performed and published fails to stand the test of even quite superficial examination. I will touch upon what seem to be the most important points in the article before me, at the same time stating that I am ready to meet any other point should it be considered necessary to do so.

Reference is made to numerous and diverse conditions leading to the conversion of glycogen into sugar in the liver and to the production of saccharine urine. The list given might be added to. The result is admittedly an abnormal one, and, I should have thought, is more in consonance with standing as the issue of an abnormal process than as the issue of an exaggeration of a normal function. It is also just what occurs, even to the production of saccharine urine, if the circulation is maintained by artificial respiration in the dead animal. Dr. Paton appears to think differently; but, if he regards diabetes as due to an exaggerated glycogenic function, the onus rests upon him, as I have said, of reconciling the teachings of diabetes with the glycogenic theory.

In view of the position in which things stand, I am surprised at the question of zymine action being brought forward in the article. Dr. Paton has himself carried the discussion of this subject to the *Journal of Physiology*, where it lies for him to meet the experimental work standing in opposition to him. It may be remembered that in his paper in the *Philosophical Transactions on Hepatic Glycogenesis* (1894), he contended that the *post-mortem* production of sugar in the liver is due to a continuance of a vital process instead of to ferment

action, as has been hitherto generally supposed. The two experiments which stood as the pivot of his paper consisted in pounding the liver immediately after death with sand to destroy the structural integrity, and thence the vitality of the cells, which had the effect, it was alleged, of preventing the active production of sugar otherwise observed to take place. I repeated the experiments and conducted others, spending much time in order that the matter might be settled. The results were given in my *Epicriticism*, and they entirely controverted the allegation that had been made. Shortly after their publication, Dr. Paton promised that they should receive consideration, and in September last an article appeared in the *Journal of Physiology*, entitled *A Further Study on Hepatic Glycogenesis*. In this article three new experiments are supplied in place of the two published in the *Philosophical Transactions*, with the results in each standing in diametrically the opposite direction. Quoting Dr. Paton's words concerning them, they run: "In these experiments the results do not correspond to those previously recorded by me. They show no diminution in the amylolysis in the liver pounded with sand, and confirm Dr. Pavy's statement that destruction of the structural integrity of the cells does not diminish the rate of amylolysis." Dr. Paton was not content with simply making this admission, but he attempted to show by experimental work that the error was attributable to contamination of the sand which he had used with iron from the sand bath whence it was taken; and, further, he introduced experimental work in opposition to mine bearing on zymoin action in alcohol-coagulated liver.

As I demonstrated at the Physiological Society, this later work of Dr. Paton appears to be as much in error as his former. My communication to the Society has been put into the form of an article for the *Journal of Physiology*, and is contained in the number that has just been issued. I mention these particulars to show my grounds for not touching upon the subject here.

A special significance seems to be given to the work of Moise³ bearing on the amount of sugar in hepatic venous as compared with arterial blood by the introduction of the table supplied by the author. I will therefore take it and look into its worth. Assuming that everything was free from vitiating circumstances as regards the collection of the blood by catheterism from the hepatic vein and by a cannula in the crural artery, the analytical table looked at in detail shows not only great want of consistency, but many points of want of harmony with what is contended for. There is a striking disparity in the amount of sugar found in the blood in the different experiments. In two of the instances notably less sugar was discovered in the hepatic than in the arterial blood. In several the excess in the hepatic blood was very slight, whilst in a few it stood out so markedly as to be highly suggestive of error. The first experiment is not included in the table on account of the catheter not having passed further than the inferior cava in the neighbourhood of the heart. Two sets of specimens of blood were collected, one a little time after the other, and in both the figures for the arterial blood are higher, and in one considerably higher, than those for the inferior cava blood. This is contrary to what it should be. In giving the average result from the figures in the table a footnote, which Dr. Paton has omitted to quote, is appended containing words acknowledging that the difference between the arterial and venous blood stands very close to the limit of experimental error. In one analysis of duplicate specimens the comment has to be made that a difference occurs amounting to almost double that representing the average difference found between arterial and venous bloods. Altogether it may be safely said that no reliable conclusion can be drawn from the work.

Further on a consideration is given of Fritz Voit's recent observations⁴ on the injection of different carbohydrates into the subcutaneous tissue of the human being. The subject of intravenous and subcutaneous injection of sugar into animals is one upon which I have conducted an extensive amount of work. From what was recorded in my *Physiology of the Carbohydrates* (pp. 188 *et seq.* and p. 238), the suggestion arose that one kind of sugar was eliminated by the kidney more freely than another. For instance, after the injection of a given proportion of lævulose to body weight the urine contained a larger quantity of sugar than after the injection of a

similar proportion of sugar from honey, which consists of a mixture of lævulose and dextrose. During the last two years, as time has allowed I have prosecuted experiments upon the question, and have given attention to both the blood and the urine. The carbohydrates I have experimented with as yet are dextrose (pure), lævulose (Schering's), maltose, lactose, and glycogen. Up to the present time I have a collection of close upon fifty experiments bearing upon the point, none of which have yet been published, but my design has been, and still is, to put them into a form for communication to the Physiological Society, and subsequent publication when brought to a sufficiently mature state for the purpose.

Dr. Paton has quoted Voit's tabulated results referring to dextrose, lævulose, and galactose. Voit gives the quantities injected and the results of the examination of the urine, but nothing about body weight is mentioned, which is unfortunate, as it deprives the experiments of the precision which, for the sake of comparison with the work of others, it is desirable they should possess. I will examine the results belonging to dextrose, this being the principle upon which special stress appears to be laid. Only three experiments are given. In one, 11.243 g. were injected, and the subject was a man 37 years old. I wonder a more delicate mode of testing was not employed than by Trommer's and the bismuth methods, but by these tests no sugar was discovered. Assuming the weight of the man to have been 65 kilos., or a little over 10 st., the relation of sugar to body weight, is only 0.17 g. per kilo. It is only in accordance with general experimental experience that with this small proportion no effect should be perceptible. In another, 60 g. of dextrose were dissolved in 600 c. cm. of water, and half injected at 10 A.M. and half six hours later. With the same assumed body weight, this would give 0.45 g. per kilo. each time. The result is described as a trace, which again, under the circumstances, is what might be expected. In the remaining experiment the quantity injected was 100 g. in 1,000 c. cm. of water, giving to the previously assumed body weight a relation of 1.5 g. per kilo. Saccharine urine was passed for seven and a quarter hours, but the quantity of sugar—estimated by the gravimetric copper process, which is an objectionable one to have employed on account of the solvent influence of generated ammonia—amounted to 2.639 g.

Reference is also made to Leube,⁵ who is said to have found no production of saccharine urine in dogs (in reality only a single experiment upon a small dog of about 6 kilos. is given) where 25 g. of dextrose were injected subcutaneously. The ratio here is a little over 4 g. per kilo. Voit, on the contrary, found with 1.5 g. (assumed) per kilo. the production of saccharine urine. Dr. Paton does not appear to have noticed this discrepancy.

We are referred also to Biedl and R. Kraus,⁶ and on consulting the reference I find amongst the matter given the following experiments on the intravenous injection of dextrose into a couple of dogs mentioned. Into a dog of 5 kilos. weight 2 g. were injected; this gives a ratio of 0.4 g. per kilo. Urine collected from the catheterised ureters contained 68 per 1,000 of sugar. In the second experiment 5 g. were injected. In one hour, we are told, 35 c. cm. of urine were obtained containing 52 per 1,000 of sugar, and giving a recovery of 1.81 g. of sugar out of the 5 g. employed. Other experiments recorded in the paper tell in the same direction. These results, it must be remembered, are after intravenous injection; but, allowing for this, they may be regarded as standing at variance with those of Voit, and, read by the light that has been thrown upon them, Voit's experiments lose much of the force appearing at first sight to belong to them.

I do not propose entering here into my own work. I see in the month of April, 1897, I was conducting experiments with dextrose. Voit's paper was published in the early part of September, and it came to my knowledge about a couple of months afterwards. It will receive consideration when my own work is dealt with. Thus much I may say in anticipation of the full details to be given hereafter that more or less notable differences are revealed in the extent to which different carbohydrates are eliminated by the kidney after subcutaneous and intravenous injection. After both, even with the employment of small quantities of dextrose, the urine gives unmistakable evidence of influence being exerted.

To rightly see the position, more delicate testing than that resorted to by Voit requires to be adopted. The examination of the blood shows that even two hours after the injection it has not recovered its normal condition. There is a further point that the experiments show in a decided manner, and that will therefore have to be considered by physiologists, namely, that notwithstanding that dextrose has been used, what is found in the urine, and, after the lapse of a little time, likewise in the blood, is a product of much lower cupric oxide reducing power. Baisch's¹ results obtained from normal urine stand in accord.

Towards the conclusion of his article Dr. Paton says: "The evidence may therefore be considered as establishing (1) that glucose is formed in the liver; (2) that glucose is used in the tissues, and is not all excreted by the kidneys." That glucose is susceptible of being formed in the liver is a truism with which everyone is familiar. Under a great variety of abnormal conditions abundant evidence is forthcoming showing that sugar escapes from the liver, and its escape is made manifest by its influence upon the blood and the urine. As regards the second proposition, whilst I contend that the entrance of sugar into the circulation is revealed by its influence upon the urine—that the urine, in fact, stands as an indicator of the state of the blood in relation to sugar—it has not been in my mind that all the sugar that may happen to reach the blood is eliminated by the kidney. At page 236 of my *Physiology of the Carbohydrates*, I say, in connection with the consideration of the subcutaneous injection of glucose: "I have referred to the protoplasmic transmutation of sugar into glycogen in the liver. But the transmutative power by no means exclusively belongs to the liver; indeed, I am disposed to think it exists as a general property of the protoplasmic matter of the body."

What we have broadly to deal with is the application of our food supply of carbohydrate matter within the animal system. Under the glycogenic doctrine, everything is centred in the liver. The liver takes the carbohydrate, stores it as glycogen, and then gives it out to pass as sugar into the circulation, to be conveyed to the tissues for oxidation, and thence heat, or some other form of force-production. Such was the doctrine propounded for the disposal of carbohydrate matter within the animal system; and, further, to meet the want of the tissues, if the tangibly evident supply was not afforded by the food, the liver was alleged to form it out of other material, it not being then realised that with animal food we get a certain amount of supply of carbohydrate matter, sufficient, it appears to me, to account for the glycogen found under the circumstances in the organ. What is the alimentary form of diabetes but this passage of the carbohydrate matter of our food into the general circulation as sugar, and do we not, by cutting down the supply of it, protect the system from the sugar invasion, and thereby bring the urine to a natural state?

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NOTE ON THE ETIOLOGY OF TYPHUS FEVER.

By E. J. McWEENEY, M.A., M.D.,

Professor of Pathology Catholic University Medical School, Dublin.

Of late years opportunities for bacteriological examination of cases of exanthematic typhus have become increasingly rare. Existing observations on this subject appear to be mostly due to foreign observers. Thus Hlava¹ described a diplobacillus, and subsequently fungi, a vibrio which he calls *V. proteus ruber*, and several other organisms as occurring in the blood of patients examined during life. Lewaschew² found cocci which he names micrococcus exanthematicus in the spleen pulp. Calmette³ found what he looked upon as a fungus belonging to the ascomycetes or ustilaginæ. Dubieff and Bruhl⁴ found a diplococcus exanthematicus, which they cultivated and looked upon as the cause of the disease. These researches have failed to obtain confirmation at the hands of other observers. I think it desirable, considering the obscurity of the subject, to publish the following account of an unsuccessful attempt lately made by me to

isolate micro-organisms from the blood of a typical case of spotted typhus.

The patient was a young woman, aged 22, who was admitted into the Hardwicke Fever Hospital, Dublin, under the care of my friend Dr. J. B. Coleman, suffering from a typical attack of typhus fever. Course, temperature, and exanthem were in all respects characteristic. Tested by the Gruber-Widal method, the blood serum gave a negative reaction. The skin of the forearm, having been thoroughly disinfected, the sterilised needle of a sterile antitoxin syringe was introduced into one of the large cutaneous veins, and about 20 c.cm. of blood readily obtained. The blood was at once distributed amongst a number of tubes of glycerine agar and faintly alkaline peptone broth. In some of the agar tubes the blood was allowed to flow over the oblique surface of the medium and settle at the bottom. Others of the agar tubes had been previously melted, and cooled to 40° C. These, after addition of the blood, were poured out on sterile Petri dishes. All were put away at 37° C. to incubate. On the following and subsequent days they were carefully examined, but no signs of growth appeared on any of them. In the broth tubes the coagulated blood formed an opaque flocculent mass, partly floating in the surrounding liquid, which was perfectly clear and bright. That the media were capable of supporting bacterial life was proved by subsequently inoculating some of the tubes and plates with *staphylococcus aureus* and *B. typhosus*, both of which grew luxuriantly. At the time of the examination—the eighth day of the fever—the patient's temperature was 103°, and her skin abundantly covered with the characteristic "mulberry rash." Crisis ensued on the fourteenth day, and recovery followed.

This negative result, obtained under very favourable circumstances—for example, the amount of hæmoglobin introduced into the media must have rendered them very favourable to the growth of strictly obligate parasites—leads me to the conclusion that micro-organisms capable of growing on our nutrient media are at any rate not always present in the blood of typhus fever; and confirms the reports of Szwajcer and Bujwid,⁵ Weinschal,⁶ Thoinot and Calmette,⁷ and Curtis and Combemale,⁸ who found the blood of considerable series of typhus cases absolutely sterile. It would seem probable that our present methods of investigation are not capable of solving the question as to the nature of the *materies morbi* in this disease.

I desire, in conclusion, to express my best thanks to Dr. Coleman for his courtesy in allowing me to examine this case, and for his assistance in obtaining the blood.

[Since writing the above note I have had an opportunity of examining another case, that of a young woman under the care of Dr. Murphy at my own hospital, the Mater Misericordiae, suffering from typical spotted typhus. The blood was aseptically obtained in a Gruber-Widal collecting pipette and inseminated on broth, agar, and obliquely solidified human blood serum. All the media are still (after forty-eight hours at 37° C.) quite free from growth of any kind. In this case also, the serum gave an absolutely negative result by the Gruber-Widal method.]

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MEMORANDA:

MEDICAL, SURGICAL, OBSTETRICAL, THERAPEUTICAL, PATHOLOGICAL, Etc.

TWO CASES OF LARYNGEAL SPASM FATAL IN THE FIRST ATTACK OCCURRING IN THE SAME FAMILY.

THE following cases may be of some general interest from the rarity of a fatal termination to this affection, and also from the strange coincidence of two members of a family being carried off within a couple of days of one another with precisely the same symptoms, both having been perfectly well right up to a few minutes of their death.

One afternoon, in obedience to an urgent call, I went to see a child, living close by, who was said to be suffocating, if not already dead. I arrived at the house within two or three minutes of the receipt of the message, but found the child quite dead, death evidently having occurred only a few minutes before.

The child was a boy, 19 months old, and was one of twins, the other twin having died within a month of its birth. According to the mother's account the child was perfectly well, and had been so for months. Just before his death he