Dr. Griffith being transferred to me for operation, and it is with their kind permission that I am able to publish the cases. I would also wish to thank Mr. Bruce Clarke for his valuable assistance in all the operations.

THE PHYSIOLOGY OF THE CARBOHYDRATES.

A REJOINDER TO DR. PATON'S FURTHER CRITICISM.

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(Concluded from page 650.)

It is impossible not to be struck by the direct manner in which the effects of the experimental injection of sugar into the subcutaneous tissue are revealed by the urine. In these experiments (transcribed in *Epicriticism*, p. 120), owing to the fact that absorption has to take place, the entry of sugar into the circulation can only be gradual. On the supposition that sugar slowly entering the circulation can be conveyed to the systemic capillaries for destruction without accompanying elimination by the urine this slow absorption would favour the escape of the urine from being influenced.

In a foot-note to his reply (p. 727) Dr. Paton writes: "The presence of sugar in the blood in undiminished amount during starvation is a fact strongly opposed to Dr. Pavy's views." I do not concede that authority exists for the use of the words "in undiminished amount," and would ask whether there are any grounds for saying that the sugar of the blood does not, during starvation, participate in the shrinkage of material generally which occurs throughout the system? But with this reservation I admit the statement to be a statement of fact, but so far from being opposed to my views it lends support to them. Irrespective of food, there is always present in the blood a certain limited amount of sugar, just as in all the various tissues of the body. In the one case, as in the other, this certain amount of sugar may, I consider, be looked upon as standing in the position of a constitutional ingredient, and it is not necessary to look to the liver for its source. Operations involving building up and breaking down are everywhere being carried on in the body, and the power of self-maintenance in the presence of constant change is associated with these operations. If, however, a source for the sugar of the blood is to be looked for outside the blood itself, why may we not look upon it as derived from other structures, especially the muscles, instead of from the liver in particular? At the moment of death the position of the liver as regards sugar does not, as was formerly supposed owing to changes due to *post-mortem* effects, differ from that in other parts of the body. Indeed, the statement appears justifiable that there is ordinarily a higher percentage of sugar in muscle than in liver, while the bulk of the former in the body is considerably greater than that of the latter.

Corresponding with the amount of sugar naturally existing in the blood there is a certain amount of sugar encountered in the urine, but this amount is too small to have any significance when viewed in relation to the question of the physiological application of carbohydrate matter within the system.

Since sugar that is permitted to enter the general circulation shows itself in the urine, we are, by arguing backwards, forced to the conclusion that the amount of sugar in normal urine being so small sugar cannot reach the general circulation under normal conditions in quantity sufficient to be compatible with the theory that what is present has anything to do with a functional transit of the carbohydrate matter of our food to the tissues for destruction. Looking at all the facts before us, I do not consider it possible to conclude otherwise than that a close harmony exists between the state of the urine and that of the blood. Can it be thought that sugar is constantly reaching the blood for transit to the tissues without rendering itself apparent by its effect upon the urine? No insignificant amount, as I have elsewhere shown, would have to be transmitted through the circulation if our carbohydrate matter were thus conveyed to the tissues. The teachings of diabetes show in an unequivocal manner that ingress for transit cannot take place without sugar appearing in proportionate amount in the urine. To keep

sugar out of the urine it must be kept out of the blood. In health the carbohydrate matter of the food produces no effect upon the blood of the general circulation, and consequently none upon the urine. The blood of the portal system contains an amount of sugar which fluctuates in accordance with the amount of carbohydrate ingested; the blood of the general circulation does not. In fact, so far as I am aware, no one contends that it does; if it did the amount of sugar in the urine under normal conditions would fluctuate as happens in diabetes.

It is then the power—call it assimilative or what you will—possessed by the healthy individual of disposing of carbohydrate matter before it has an opportunity of entering the general circulation, which, by keeping the blood free from sugar derived from the food, prevents the urine from being influenced by the ingested carbohydrates. Now this power in the healthy subject is not without its limits, and a point may be reached at which the ingestion of carbohydrate in a soluble form such as sugar, especially if taken during fasting when absorption is rapid, is attended by the appearance of sugar in the urine. In diabetes there is either a loss or a greater or less diminution of this power, with the result that carbohydrate matter which can be ingested by a healthy person without producing any effect upon the urine leads to an escape of sugar in a degree proportionate to that in which the power is diminished.

In a particular case, for instance, it may happen that the assimilative power is only a little below what is normal, and here a considerable amount of carbohydrate food may be taken without being followed by saccharine urine; but if the amount exceed the limit at which the power stands, sugar is eliminated in proportion to the extent to which the point is exceeded, although such food would not in the healthy person give any evidence of effect upon the urine. And so it runs in different cases, until even what is considered the diabetic dietary, which, however, is not a dietary totally free from carbohydrate matter, but one containing a greatly diminished amount, is accompanied with a more or less notable elimination of sugar.

It is, in fact, made abundantly clear that we have to do in diabetes with the loss, in varying degree in different cases, of the power of assimilating or disposing of carbohydrate matter in such a way as to prevent its reaching a position—the general circulation—in the form of sugar, whence, as common observation shows, it runs off as waste material in the urine. Everything depends, as regards the state of the urine, upon whether the assimilative power existing is taxed beyond its capacity or not. Up to a certain point, carbohydrate matter can be taken without any effect upon the urine being produced, whilst beyond the particular point sugar is discoverable.

No wonder these cases formerly proved perplexing to practitioner and patient. One day sugar was found and another day not. Variation in food affords the explanation, and a very little will suffice to determine the character of result encountered. It is indeed surprising the exactness observable from day to day, week to week, and even, it may be, for lengthened periods. As long as the patient is confining himself within a certain limit as regards carbohydrate matter taken, his urine presents a normal condition. Directly he exceeds the limit sugar is found, and found in proportion to the extent to which he has done so. We have a parallel condition to that of health, but with the difference that the power of assimilation—the power of preventing carbohydrate from reaching the general circulation as sugar, and thence the urine—exists in diminished amount.

All the facts before us in relation to food conspire to show that for the urine to be kept free from sugar, sugar must be kept out of the general circulation, and that it is the difference in the amount of power existing for the accomplishment of this that constitutes the difference between health and diabetes, and likewise the various degrees of the latter. When carbohydrate food is taken beyond the capacity of assimilating or properly disposing of it, that which is in excess of the capacity straightway passes or filters, as it were, through the system into the urine. Of necessity it must have been permitted to reach the general circulation for the purpose. Two or three hours quite suffice for determining the effect. With the greatest precision and con-

fidence a decision can be arrived at regarding the nature of the food taken, and the patient, to his astonishment, can be told of any dietetic deviation that has taken place. From the examination of specimens of urine passed at different periods of the twenty-four hours the meal can be named at which the error has occurred, and as small an amount of starchy matter as that contained in a thin water biscuit may be sufficient to disclose an effect upon the urine.

As I have said, and as I strenuously maintain, the phenomena alleged to occur under the glycogenic doctrine simply mean diabetes. To escape from diabetes, our carbohydrate, instead of being transmitted under the form of sugar through the circulation to the systemic capillaries for assumed destruction in a way that no one knows anything about, must be assimilated or dealt with in such a manner as to be prevented from reaching the general circulation as sugar. Assimilative action constitutes the key to the situation, and health and diabetes depend upon whether the assimilative power under consideration is possessed to the proper extent or not.

Under the physiological views that I have set forth regarding the application of the carbohydrates, not only is there complete harmony between the facts of health and diabetes—looked at in their entirety—but also between the operations of animal and plant life. To quote from the preface of my work on the *Physiology of the Carbohydrates; their Application as Food and Relation to Diabetes*, 1894, I say:

“The new departure brings the operations of animal and plant life into harmony with each other. The simplest of organisms—a yeast cell, for example—may, indeed, be made use of to illustrate the occurrences taking place in our own bodies. Moreover, the teachings of experience in connection with diabetes, which may be pronounced to be absolutely irreconcilable with the prevailing physiological views, not only agree with, but in the strongest manner support, the doctrine that is in this volume set forth.”

Looked at from the point of view to which we are here brought, nothing can be simpler than the relations of health and diabetes. The issue attendant upon the ingestion of carbohydrate food depends on the amount of assimilative power existing, diabetes being the result of an impairment, in varying degree, of this power. With the light thus afforded we are in a position to judge the lines which treatment should follow, and a rational method is opened out. The fault is in the assimilative power. If it could suddenly be restored to its natural state diabetes would no longer exist, for carbohydrate food could then be taken to the ordinary extent, assimilated, and applied to the needs of the system, instead of being permitted to reach the general circulation, and to run off as waste material with the urine.

The object of treatment thus becomes well defined. The quantity of carbohydrate food to meet what is wanted for establishing a properly balanced state must be brought within the assimilative capacity and the improvement of the existing assimilative capacity is the desideratum. Experience shows that while sugar is being voided, and thus, as an antecedent, permitted to reach the general circulation, and thereby produce a deviation throughout from the natural state, the decline of assimilative power advances. The steady progress from bad to worse, constituting a feature of the history of a case before the recognition of the complaint and subjection to treatment, testifies to the occurrence of what I have referred to. Witness, on the other hand, the immediate alteration that sets in when by treatment the amount of carbohydrate is brought within the assimilative power. Whilst the wrong state is existing, induced by the transmission of sugar, derivable from the malapplication of the carbohydrates of the food through the system, the growth of the pathological condition at the foundation of the wrong chemistry by which the disease is made manifest is evidently favoured, and the assimilative power not only becomes less and less, but eventually the point is attained at which we have no longer a simple alimentary defect to deal with, but a state associated with elimination of sugar derived from tissue breaking down, as well as defective assimilation of food. Under these circumstances dieting is no longer capable of effecting a removal of the sugar from the urine, but still, in a direct manner, influences the quantity eliminated.

It may be said without hesitation that in proportion as

sugar is permitted to reach the general circulation so is harm done. The unnatural state of the blood thereby induced leads to an unnatural performance of all the functions of life. The symptoms and progress of the disease are related to the degree of deviation of the blood from the natural state permitted to exist, and this is revealed by the amount of sugar escaping with the urine. The exclusion from the diet of the carbohydrate principles which, through not being assimilated, give sugar to the blood is in a certain class of case followed more or less speedily, according to the extent to which the wrong state associated with the condition has previously advanced, by a disappearance of sugar from the urine. The circumstances now become favourable to restoration of the defective assimilative power. As the treatment is pursued it may be found that in the course of time a certain amount of starchy food can be taken without influencing the urine, and eventually the amount which can thus be taken may prove to have reached a considerable quantity. From the facts before us it is deducible that carbohydrate matter which before failed to be assimilated and was thus permitted to reach the general circulation as sugar becomes now assimilated and prevented from doing so; and as a remarkable associated phenomenon it is found that as the assimilative power becomes restored so starchy food must be given to obviate loss of weight. For a certain time the weight may increase and then be maintained, when—it may be suddenly and sharply—loss of weight sets in. Assuming that the urine has been kept and is at the time free from sugar, I am able to affirm that this is a sure indication of a return of assimilative power, and that the time has arrived for making a trial of food containing starch in gradually increasing quantities, with good grounds for expecting that, up to a certain quantity, it will be tolerated without leading to the passage of sugar by the urine.

If, as I claim it is permissible to conclude, sugar cannot reach the general circulation without revealing itself to a corresponding degree in the urine, the state of the urine may be taken to afford an indication of what is going on as regards the entry of sugar into the blood. As I have already stated, Dr. Paton has himself narrowed the point at issue by saying: “The great and central question at issue in Dr. Pavy’s work is this: Is there during life a constant production of glucose in the liver? It is upon this point that his theory must stand or fall.” The production of glucose in the liver implies as a sequence its passage into the blood; and, through the state of the urine in health, evidence is afforded that the passage of sugar into the blood, alleged under the glycogenic doctrine to be taking place, cannot in reality occur. On the other hand, it is just what happens in diabetes. In order that the carbohydrate matter of our food may not run off as waste material in the urine, it must be prevented from reaching the blood in the form of free sugar. In health this prevention occurs; in diabetes, on the contrary, the preventive action is not exercised, or is exercised only to a more or less diminished extent.

In view of the facts that stand clearly before us, and after narrowing the ground of discussion, as Dr. Paton himself has done, the remark with which he follows on¹ loses force:

“I have already indicated in my article where the reader may procure some account of the work bearing on this subject, and I would only say that the question must be considered as a whole, and that the indirect evidence of the work of Külz, E. Voit, Demant, Böhm and Hofmann, and of Cavazzani, must be kept in view, as well as the more direct observations of Bernard, Lehmann, Seegen, and the other investigators mentioned in my article.”

There are certain cardinal points belonging to the subject, and to these I gave attention in my book, discussing and submitting to a close scrutiny the work of others upon them, and pointing out the fallacious nature of the grounds upon which the glycogenic doctrine was built up. My position in this matter is not one newly taken up. It has been before the scientific world for thirty-five years, and my contention that the ordinary *post-mortem* examination does not afford a representation of the condition existing at the moment of death is now generally accepted. Arguing from the state existing during life and met with at the moment of death, I contended that the ground was cut from under the glycogenic

¹ *Edin. Med. Journ.*, February, 1896, p. 726.

doctrine, and I have been all along sustained by the teachings of diabetes. Regardless of time, labour, or any other consideration than a conscientious desire to serve the interests of science and of the medical art, I have given the work of a lifetime to this subject. Notwithstanding the fact that the title of my book was *The Physiology of the Carbohydrates*, I am now charged, as I have already said in an earlier part of this "Rejoinder,"² with having by the omission of the consideration of the mass of contradictory material which is to be found recorded in literature on various points lying, in reality, outside the "great and central question at issue," with "dealing hardly fairly with the general medical reader," and am told that had I "published it as a contribution to the subject addressed to physiologists already familiar with both sides of the question such omissions might have been pardoned." What the material that has been adduced by Dr. Paton to overthrow my work is worth I have shown in my *Epicriticism*, and the successive portions of this "Rejoinder." The grounds upon which he based his attacks have been shown to be completely unsound, while the validity of my position has not been in the slightest degree shaken.

I have had to defend myself against a method of criticism for which, I apprehend, it would not be easy to find a parallel in scientific literature. I consider that I have had strong ground for complaint against the manner as well as the matter of my critic. As to manner, without being backed by experimental work of his own in this connection, except in the one particular concerning fat formation, he has thought fit to adopt towards me an authoritative and dogmatic tone which his experience on the subject can hardly be said to justify. As to matter, the multitude of missiles with which he assails me are gathered together from any available source, without an attempt on his part to discriminate their real soundness and worth. It appears to have been assumed that what was wanting in substantiality of material might be made up for by boldness of tone, and that a dialectic advantage might be gained by bold assertions too often founded on distorted versions of the arguments and facts of which he had made himself the self-appointed critic. For it must be said, and others will have recognised this with as much surprise and regret as myself, that during the course of this examination of Dr. Paton's criticisms his want of faithfulness in dealing with the matter at hand has been rendered apparent. I have felt called upon to say this in the interests of science and in justice to myself, for my critic's facile pen and tactical skill have given to his criticisms a fictitious appearance of force and soundness which I have now shown does not of right belong to them. Even when he says, in the much-quoted foot-note to his paper in the *Philosophical Transactions*, "The theory of Pavy, repeated in nearly every textbook, that the liver is a sugar-destroying and not a sugar-forming organ," he uses the expression "sugar-destroying" unfaithfully for "sugar-assimilating," and thereby gives an unjust colour to the matter. In the long run, however, truth and justice must prevail, and I for my part await with well-grounded confidence the judgment which the future will pronounce.

MEMORANDA:

MEDICAL, SURGICAL, OBSTETRICAL, THERAPEUTICAL, PATHOLOGICAL, ETC.

THE USE OF PERMANGANATE OF POTASSIUM IN OPIUM POISONING.

ON March 18th I was called to see a man who, about half an hour before, whilst in drink, had taken laudanum. I gave him hypodermically gr. $\frac{1}{16}$ of hydrochlorate of apomorphine, and repeated the dose in ten minutes, but without procuring emesis. By this time the patient was profoundly narcotised; the pupils were contracted, and the conjunctival reflex lost; the face was livid, and covered with a cold sweat. The stomach was thoroughly washed out, and gr. 20 of potassium permanganate dissolved in a quantity of warm water left in it. The patient had now ceased breathing, and there was no pulse to be found at the wrist; gr. $\frac{1}{32}$ of strychnine sulphate

was given hypodermically, and coffee and a further gr. 10 of the permanganate by the rectum. This was repeated in half an hour's time, artificial respiration having been performed meanwhile, and maintained for an hour and a quarter. The pulse improved, and respiration continued automatically for about three-quarters of an hour; it then became slower, the expirations becoming markedly prolonged. I was obliged again to resort to artificial respiration, and as the pulse again failed at the wrist gr. $\frac{1}{16}$ of strychnine and also gr. 5 of the permanganate were injected hypodermically. After about a quarter of an hour the respirations again continued automatically.

In about five hours after taking the poison the conjunctival reflex returned, and the patient was so far recovered as to be able to be removed to the infirmary, where he could be conveniently watched. He could now be completely aroused by stimulation with the battery.

The patient was a slightly-built man, aged 27 years, and had taken 3vj of the tinctura opii, equivalent to nearly 25 grains of solid opium. This amount was verified by the two chemists from whom he obtained the drug. I attribute his recovery to the use of permanganate of potassium.

Newport (Mon.).

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UTERINE GESTATION COMPLICATED BY HÆMATOMA IN THE LEFT BROAD LIGAMENT.

M. J., aged 36 years, a healthy woman, had been married nine years without conception. The catamenia had always been regular and normal, the last being in March, 1895, followed at the end of April by only a slight appearance. She felt nothing unusual until June, when she was subjected to sudden strain in an effort to avoid falling from a plank. This was soon followed by pain and tenderness in the lower abdomen, and some faintness and nausea, which necessitated her going to bed on her return home in the evening.

When seen by me the next morning the pulse was small and quick, 120, temperature 101°. Abdominal pain was still present with much tenderness. The facial aspect was somewhat altered, the features appearing pinched. A well-defined, smooth, elastic swelling occupied the lower abdomen, having an arched superior border reaching nearly to the umbilicus, simulating five and a-half months' gestation. The mucous membrane of the vagina was congested, the cervix soft, uterus enlarged and displaced to the right by a tense swelling occupying the left pelvis. In the absence of any previous local trouble, the diagnosis strongly pointed either to a ruptured ectopic gestation into the broad ligament, or uterine gestation with simple hæmatoma. The examination, conducted with care, was not carried far in view of the danger of rupture into the peritoneal cavity. Absolute rest was the chief remedial measure observed for some time.

As there was not, nor had been, any hæmorrhagic discharge from the uterus, I was in favour of uterine gestation with hæmatoma in the left broad ligament; this happily proved the case, as though for a time the abdominal swelling diminished from the shrinkage and hardening of the exudation, which did not suppurate, yet the uterus gradually became larger, slowly regaining the normal position coincident with the absorption of the exudation. Uterine *souffle* became distinct at the end of July, and the foetal heart-sounds were first heard in the beginning of August, the patient being delivered at full time after a natural labour in the middle of December; the exudation having become entirely absorbed under local and general treatment, in which ichthyol and iodide of potassium formed the chief therapeutic measures.

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CEREBRAL APOPLEXY IN A LAD 16 YEARS OF AGE. The following case is, from its rarity, I think, worthy of record. C. W., aged 16 years of age, a carpenter's apprentice, who had always enjoyed good health, was taken suddenly ill whilst at his work at midday on November 29th, 1895, complaining of severe pains in his head. He walked with assistance into the house, becoming almost immediately convulsed, throwing his limbs about, foaming at the mouth, and presenting other symptoms of a severe epileptic attack. The bowels acted involuntarily. When seen by me at 5 P.M. the

² BRITISH MEDICAL JOURNAL, February 22nd, 1896, p. 454.