SAPRAEMIC GLYCOSURIA.*

BY

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A NEW truth needs much tenacity of life, for few men like to be disturbed in the opinions that they have been at the pains to form; and I am now venturing to expound once again a true doctrine which, though it was well established twenty-two years ago, has not yet been properly diffused through the medical profession, but has had a narrow escape from oblivion. An illness of my own is the reason why this exposition falls to my lot.

In July, 1909, when I was working in a Berkshire sanatorium, I was suffering so much from a hard carbuncle, four inches in length by three in breadth, almost mesially situated where the occiput joins the neck, that I determined to consult Mr. X., of Harley Street. While waiting for my cab I tested my urine, so as to save the surgeon some trouble. I found that Fehling's solution precipitated copper, indicating that I had glycosuria; and a brother practitioner, concluding that I had diabetes as the foundation for my carbuncle, made to his friends a confident prognosis of my imminent death. My own view was that, in any case, Mr. X. would operate, and that, even if he did not, no harm would be done by consulting him.

As I had no thirst nor hunger, nor emaciation nor polyuria, I doubted whether I had diabetes, and I let my thoughts stray among the exceptional glycosurias of the textbooks. Still, I went to Harley Street thinking that, on the whole, the balance of probability was in favour of diabetes, that I should not live long, and that perhaps, like my grandfather, I ought to be contented with the fifty-one years of life that were already mine. After a swift examination, Mr. X. said: "Don't be surprised or afraid if you get glycosuria with this great carbuncle; you will probably have it." I replied: "Pray do not trouble to prophesy; I have it already." Then Mr. X. uttered, with the utmost confidence, these unexpected words: "And you will lose it." He told me that a fellow-resident of his at St. Thomas's Hospital, now Sir Cuthbert Wallace, had proved that the glycosuria of carbuncle and gangrene was commonly not the cause of those diseases, but that the sapraemia from the carbuncular or gangrenous focus was the cause of the glycosuria, just as phloridzin or other poisons caused glycosuria; and that Mr. Wallace had even gone one step farther, and had found that, while glycosuria would appear in the normal person after eating half a pound of glucose, yet in a person whose carbuncle was not quite sufficiently poisonous to produce glycosuria unassisted, glycosuria would appear on his eating (according to the degree of poisoning) one, two, four or six ounces of glucose. Thus, he jokingly added, there was no excuse for our failing to understand the boast of men who said that they had cured diabetes by amputating a leg! The patient would have been suffering from sapraemic glycosuria generated by a gangrenous focus on the leg, and amputation would have cured the glycosuria by removing its cause. So I endured the cruciform incision, and in three weeks my enemy had sloughed away, and I was free alike from carbuncle and glycosuria.

Six months afterwards I consulted a distinguished physician and told him the facts. He smiled incredulously and at once asked for a specimen of my urine, and he was amazed at finding no sugar. In order to see how normal I was as regards my saturation point for glucose a year after my illness, I found that four hours after I had eaten half a pound of glucose my urine contained $1\frac{1}{2}$ grains of glucose to the ounce, according to both methods, Roberts's and Pavy's; in six hours I found no glucose. (Some days afterwards I tried to eat a pound of glucose, but vomited after 13 ounces.) So I must be considered normal as regards my saturation point, which, as regards alimentary glycosuria, is registrable at eight ounces of glucose. Never since have I had glycosuria, alimentary or sapraemic, nor tried to get it.

History of the Doctrine.

Thirty years ago it was held that "diabetes offers an almost positive bar to any kind of operation" (Treves's

Operative Surgery, i, p. 18, 1891). The present writer, while a student, frequently saw patients suffering from gangrene left to die unhelped by operation because glucose had been found in their urine, and it was through investigation of cases of gangrene complicated by glycosuria that truer views were first reached.

In the *Medico-Chirurgical Transactions*, vol. 75, 1892, is a paper by Mr. W. G. Spencer on amputation in diabetes mellitus. After recording the cases on which he bases his conclusions, Mr. Spencer says:

"Such stress has been laid upon the danger from inflammatory complications in diabetes mellitus that many writers condemn operative procedure without qualification, or at least omit to state the indications for it. Yet there is enough evidence, I believe, to show that by the timely adoption of major amputations life may be prolonged and the amount of sugar excreted reduced to a minimum (the italics are mine) in cases where the attempt to effect this by medicinal treatment, in the presence of a severe inflammatory lesion, has quite failed."

Here we have the definite statement that glycosuria may be reduced to a minimum by the removal of a septic focus. How very near he came to the complete discovery of the true doctrine! Again he says: "To put the conclusions in another form. Diabetic gangrene should be operated upon by following the rules already established for other forms of gangrene." Here we have a direct contradiction of Sir Frederick Treves's statement of the previous year, that "diabetic gangrene of a limb is scarcely within the scope of surgical measures; an amputation in such a condition is almost invariably fatal." Sir Frederick Treves, in view of the articles of Mr. Spencer and Mr. Rickman Godlee, rewrote in subsequent editions his own views in the light of theirs.

In the next volume of the *Medico-Chirurgical Transactions*, vol. 76, 1893, Mr. Rickman Godlee (now Sir Rickman Godlee) wrote an article entitled "On Amputation for Diabetic Gangrene." He writes to much the same effect as Mr. Spencer, and definitely denies the doctrine of 1891:

"In truth the introduction of the antiseptic principle has rendered operations upon diabetics very much less formidable than they used to be when most of the present textbooks on surgery were written. The weakened tissues may be, and often are, able to withstand the mere mechanical injury of an operation, although they cannot endure this as well as the irritation produced by putrefaction. At the same time it must not be forgotten that no amount of antiseptics can do away with the danger of coma or heart failure following an operation, though their wise employment may immensely diminish the chance of sloughing of the flaps."

Here Sir Rickman definitely singles out the successful use of antiseptics as the chief cause of the newly discovered comparative safety of operations on so-called diabetics. The next year, in the *St. Thomas's Hospital Reports*, New Series, vol. 22, 1894, there appeared an article by Sir Cuthbert Wallace on "A Case of Gangrene of Foot with Sugar in the Urine successfully treated by Amputation."

"The amount of sugar," he says, "rose for the first three days after operation—560, 1,360 and 1,460 grains being the respective amounts in twenty-four hours. From this time the quantity fell, except for an occasional rise, continuously until the fifteenth day, when the amount was only 190 grains. Then for three days there was only a trace, when, on the nineteenth day the amount rose to 234 grains, to fall next day to 60 grains. On the succeeding day there was a trace, after which the sugar ceased entirely."

Again: "It happens occasionally that after amputation the sugar disappears or is greatly diminished, and this seems to suggest that it is possible that the gangrene may cause the presence of sugar, possibly through the absorption of septic products." (Italics mine.)

We have often noticed the remark of the textbooks and teachers of to-day that "transient glycosuria may be associated with a carbuncle," which shows that we ought now to be ready for the true theory to fit the observed fact. Formerly the glycosuria used to be considered to be the predisposing cause of the gangrene or the carbuncle associated with it. Here, for the first time, we have the suggestion strongly conveyed that, on the contrary, the sapraemic condition may be the cause of the glycosuria.

In the *Lancet* of December 23rd, 1899, Sir Cuthbert Wallace published another paper on "Gangrene Complicated by Glycosuria." Here we find the whole theory of transient glycosuria elaborated, and based on the observation of typically septic cases of gangrene, carcinoma of rectum, ulcer of rectum, erysipelas, lymphangitis, and carbuncle.

* A paper read at the Medical Institute, Birmingham, before the British Medical Association, on December 16th, 1919. Revised, January 18th, 1921.

The Saturation Point.

There is in normal human blood glucose to the amount of about 1 per 1,000. In diabetes the blood may contain from three to six times as much. The portal vein may in normal life contain 4 per 1,000. This glucose, $C_6H_{12}O_6$, on reaching the liver is arrested there, and stored in the form of glycogen, $C_6H_{10}O_5$, till it is served out to the blood again gradually, in another form, for the needs of bodily heat and work, etc. Normally the liver is not surcharged with glycogen, nor the blood with sugar. That is to say, in Sir Cuthbert Wallace's language, that the saturation point is normally not reached. But when, either because of the liver's insufficiency as a storehouse of glycogen, or because too much glucose is poured into the blood stream, the blood is surcharged with glucose, the saturation point is said to have been reached and passed. Then the blood excretes its surplus glucose into the urine, and glycosuria occurs.

Now the saturation point is by no means constant, and if for any reason it falls, it may happen that even the normal amount of glucose in the body may, through the refusal of the liver to secrete it as glycogen, accumulate excessively in the blood, and the excess may be excreted by the kidneys in the urine. In other words, there may be hyperglycaemia, and consequent glycosuria, merely because of a temporary failure on the part of the liver to secrete from the blood the due amount of glycogen; the saturation point is lowered for the body and hyperglycaemia necessarily follows.

Now one of the most important causes of the lowering of the saturation point is sapraemic poisoning, and in this fact lies the true explanation of the transient glycosuria that is associated with carbuncle or gangrene. As an instance of this, Sir Cuthbert Wallace mentions his Case No. 5:

"A woman, aged 65 years, was admitted into the hospital with a carbuncle of the back of seven weeks' duration. The urine contained 300 grains of sugar in the twenty-four hours. The slough was excised, and the sugar disappeared from the urine in nine days, and was still absent six weeks later." There was no symptom of diabetes in this case except the glycosuria, and the diet was unrestricted.

Again, suppose that the saturation point remains steady. Even so the normal man can pass it if he introduce enough glucose into his blood stream. I myself passed it by eating half a pound of glucose at 6 o'clock one morning.

"It has been shown," says Sir Cuthbert Wallace, "that all persons possess a saturation point; that is to say, that sugar will appear in the urine if a certain quantity of carbohydrate is taken at a meal. A healthy man can dispose of 300 grams (say 9½ oz.) of glucose at a meal and yet none will appear in the urine. This is not so with a patient suffering from septic absorption, as in such a case 50 grams (say 1½ oz.) of glucose will often pass into the urine." Of his Case No. 8, a man of 31, admitted on May 25th, 1898, with diffuse cellulocutaneous erysipelas of the arm, Sir Cuthbert writes: "The urine was acid, with a specific gravity of 1020, and contained no albumin nor sugar. On the 31st 100 grams (say 3½ oz.) of glucose were given, and the urine passed in the next twelve hours was collected and found to have a specific gravity of 1020, and to contain sugar. Fermentation with yeast reduced the specific gravity to 1016 (that is to say, the urine contained four grains of sugar to the ounce). On June 23rd the wounds were healing well, and the temperature was normal. The patient was now given 100, 200 and 300 grams (say 3½ oz., 6 oz. and 9 oz.) of glucose on succeeding days, but no glycosuria resulted." In Case No. 10, Sir Cuthbert Wallace writes as follows: "A man, aged 54 years, was admitted into the hospital for a carbuncle on the neck of the size of a saucer, which he had had for six weeks. Fifty grams (say 1½ oz.) of glucose were given on two successive mornings, and on the second occasion sugar was found in the urine, which on admission had been described as '1016, acid, no albumin, no sugar.' Fermentation reduced the specific gravity by four points (that is, the urine contained 4 grains of sugar in 1 oz.). The carbuncle was scraped, and ten days later another 50 grams of glucose were given, and again sugar appeared in the urine. Fifty grams on the two successive days produced no sugar, nor did 75 grams on the next day. A week later the patient was tested up to 150 grams (4½ oz.), but the urine continued normal."

Dr. R. T. Williamson (whose great learning and industry all of us whom he taught at the Manchester Royal Infirmary have reason to remember) quotes Von Noorden as saying that in a healthy person glycosuria will be caused by a single dose taken on an empty stomach of from 180 to 250 grams of glucose (6 to 8 oz.).

Quoting Naunyn, he says that if distinct glycosuria occurs when a man takes 100 grams (3½ oz.) of glucose two hours after a standard breakfast of ½ litre of coffee and milk and 80 to 100 grams of bread, then the saturation point is distinctly lowered. "Von Noorden found that in four out of fifteen obese persons

temporary alimentary glycosuria was produced by 100 grams (3½ oz.) of glucose; of these four individuals two became diabetic several years later." "In traumatic neurosis or neurasthenia there is often a diminished power of sugar destruction; also Ebstein and Asher have shown that traumatic neurasthenia is sometimes followed by diabetes mellitus." (Williamson's article on Glycosuria in the *Encyclopaedia Medica*.)

Recent Cases.

I have sometimes had under my care women from whom I thought proper to wean their babies, once on account of enterica, at other times on account of some septic condition in the mother. After the weaning the mother's sugar would reduce Fehling's solution for several days, the sugar of the milk being absorbed from the breasts into the blood, which, in its turn being surcharged, excreted the superfluous sugar through the kidneys, so that it was found in the urine.

In my own practice, as well as in my own person, I have found reason to be thankful for the new doctrine:

At the South Manchester Poor Law Hospital in 1916 one of my patients was a middle-aged man with a wooden leg. On his first admission, four years before, his bed-card was marked "Diabetic Gangrene," and a surgeon had boldly amputated the leg for gangrene, despite his diagnosis of diabetes, as Sir Rickman Godlee would have done. I found the man quite well, and he had no glycosuria, so I had the pleasure of telling him that, according to a great discovery recently made and proved, he had never had diabetes, but only a peculiar and temporary blood poisoning from his bad leg; that I had myself suffered blood poisoning in the same way, only from carbuncle of the neck instead of gangrene of the leg; and that, as regards diabetes, both of us were as sound as anyone in Manchester. So he went on his way rejoicing, and I wrote "Sapraemic Glycosuria" on his old bed ticket.

At an epileptic colony the medical officer found Fehling's test for sugar positive in the urine of a young man suffering from a small but angry boil. He asked me, as a puzzle, whether sugar was present or only one of the rare reducing agents described in the textbooks. I diagnosed sapraemic glycosuria, and proved the presence of sugar by the fermentation test. The glycosuria vanished almost as soon as the boil.

A corporal in another war hospital brought me a patient who had been passed in Class A1. I found a large suppurating carbuncle on his neck, and a little glycosuria; no hunger, thirst, emaciation or polyuria. I made the diagnosis of sapraemic glycosuria secondary to carbuncle, and the prognosis of early recovery from both carbuncle and glycosuria. I convinced one of my colleagues, but was gently assured by others that time would falsify my optimistic prognosis. I soon removed the sloughs, and the glycosuria quickly vanished. Query: If the private had by chance gone to one of my sceptical brethren instead of coming to me, would he have been discharged from the army as a diabetic?

Conclusions.

A. To give our textbooks and teachers their due, we must admit that they used to teach us that there was such a thing as "transient glycosuria." The word "transient," however, was of the lowest practical and scientific value, for on the one hand we could never know that the glycosuria was transient until it was gone, and on the other hand the cause of the glycosuria was left undesignated. But the words "sapraemic glycosuria" have high value: in diagnosis, for the cause is named; in prognosis, because an early, happy result—life instead of death—is soundly predicted; and in treatment, because common diet may be used and the modern starvation and starch-free diet (a great nuisance) is forbidden.

B. I believe that carbuncle or gangrene secondary to diabetes is not very common, but I readily see why so debilitating a disease as diabetes can be, like other forms of debility, a real predisposing cause for carbuncle or gangrene.

(1) In sapraemic glycosuria the sugar is relatively small in quantity. The largest quantity recorded in this paper as having been passed in twenty-four hours is 1,400 grains (or 3½ oz.). In diabetes the patient commonly passes from half a pound to three-quarters, say, 4,000 to 6,000 grains daily.

(2) Consequently, in sapraemic glycosuria we find an absence of the great diabetic symptoms—namely, no hunger, no thirst, no emaciation, no polyuria.

(3) In the case of sapraemic glycosuria associated with gangrene there will probably be found enough arterial degeneration in the patient to account for the gangrene without it being necessary to fly to the hypothesis of diabetes.

C. As the sapraemic products of gangrene, carbuncle, erysipelas, etc., differ considerably from each other, it is

* I have recorded here nothing that happened before 1891, but I suspect sapraemic glycosuria in the case recorded by Tribé in 1861. "M. Delpech," he says, referring to a great French surgeon of a hundred years ago, "found sugar in a case of carbuncle of lip and chin, which went on to complete recovery."

probable that one supraemia will differ much from another in its power of lowering the saturation point for sugar. At present gangrene and carbuncle are the most striking and misleading agents in the causation of supraemic glycosuria, but further investigation will doubtless reveal a long series of such agents differing from each other very much in the power of causing supraemic glycosuria.

SELF-INFLICTED INJURIES IN CIVILIAN PRACTICE.

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I.—MR. RENDLE SHORT.

A CASE like the following might so easily get a surgeon into undeserved trouble that it seems desirable to put it on record.

A young woman, giving her age as 18, was admitted into one of my wards at the Bristol Royal Infirmary in November, 1915, with a three weeks' history of appendicular colic. I removed the appendix. There were two small ulcers in its mucosa. She healed well and went back to her home in the country. On January 27th, 1916, she paid us a visit complaining of pain in the scar, but nothing abnormal could be found.

In December, 1918, she was readmitted, with the history from her doctor that she had been in the workhouse infirmary for many weeks discharging pus and fragments of a gauze swab from the scar of the appendix operation. He and his partner had opened up the wound under an anaesthetic, but could not find any gauze, nor did the track go through the muscles of the abdominal wall. As it still did not heal, and fresh bits of gauze came out, they sent her up to me.

Naturally I was very perturbed. It is an absolute rule with us never to put a swab in the abdomen without a tape and artery forceps on it, to count all swabs before and after operation, and almost never to use gauze packing; but to err is human. The patient's age was now given as 24. For the first few days after arrival her temperature was high, about 103°. At first the pulse was also quick, but after a while the slow pulse, normal general appearance, and very irregular high temperature led us to give her the thermometer again, just after it had registered over 101°, and we found that in the mouth it was normal. After that she was deprived of her hot-water bottle when her temperature was taken, and it became normal.

Meanwhile the abdominal sinus discharged freely. I opened it up on January 16th, 1919, and found no gauze. The tracks were extensive amongst the abdominal muscles, but did not go through them to reach the peritoneum. I cleaned it all up very carefully, and drained the wound after partially closing it. It did not heal. Some weeks afterwards a piece of selvedge-edged gauze came out, such as we never use for swabs. This relieved my mind greatly. She was sent home still with a small sinus and returned to the workhouse infirmary. Mentally she behaved and conversed quite normally.

In September, 1919, several more pieces of gauze came out, which were sent me by post. Then she became very ill, and there was a discharge from two openings, one on the abdomen and the other below Poupart's ligament, smelling like faeces. I readmitted her. She now gave her age as 19. On September 22nd I operated, beginning by exploring the abdomen in the middle line. The abdominal cavity was quite normal. The caecum was not adherent to the anterior abdominal wall, and there was no mass in the right iliac fossa. I closed the abdomen again and slit up the sinuses. There was a foul track connecting them, about six inches long, running deep in the subcutaneous fat but not penetrating the muscles. In the deepest part of the sinus was a piece of wool as large as a haricot bean, with a faecal odour. I thoroughly excised the whole track and sewed up the whole incision in clean tissues. Over the dressing we then put on yards and yards of adhesive plaster, completely encircling the thigh and lower abdomen. The operation was performed in the presence of eight or ten most interested spectators, whose names were recorded in the notes as witnesses.

It was, of course, impossible for the patient to get at the wound, strapped up as it was with continuous adhesive plaster, and it had healed up, though rather insecurely on account of deep sepsis, in about a fortnight. One or two small abscesses formed, discharged, and healed up before we could regard the scar as safe. When she went home, soundly healed at last, I roundly accused her of pushing in the gauze and wool herself. She denied it indignantly.

In January, 1920, so her doctor informed us, the scar started discharging again through a fresh sinus, and presently all her urine was passed through this sinus. She became very ill, and nearly died. In June, 1920, she was readmitted to my ward.

She looked thin and ill. There was a large sinus in the lower end of the old appendix incision, through which the whole of her urine escaped. A skiagram was taken, which showed an elongate foreign body lying in the bladder. On June 17th I performed suprapubic cystotomy, and removed a broken piece of a bone knitting needle, four inches long, encrusted with phosphates, which was loose in the cavity of the bladder. When pressed a few weeks after to account for the presence of the needle in the bladder she at first said that her doctor at the workhouse infirmary had lost it in probing the wound, but finally she admitted that she had pushed it into the bladder herself from the abdomen.

When I returned from a holiday at the end of August, though the sinus in the appendix region had healed, the suprapubic opening was still as large as one's finger, and I felt sure that the patient was tampering with it. A catheter had been tied into the bladder through the urethra without hastening healing; on one occasion the catheter was found blocked with wool. Then the end of the catheter disappeared. On August 31st I operated for the fourth time, removed about an inch of the end of the catheter from the bladder, sutured up the suprapubic wound, and secured it with an anchored dressing. To give it a better chance to heal I dilated the urethra sufficiently to give her incontinence for a week or two. By this means the wound eventually healed up, and she was sent out well.

I have recently heard from her doctor (November, 1920) that the suprapubic wound is open again. She makes no secret this time that she did it herself.

It was quite clear to us, from the time of the operation in January, 1919, that these sinuses were the result of self-inflicted injuries, and that the gauze had been pushed in by herself, for the following reasons, quite apart from the routine precautions taken at the original operation in 1915:

1. The original wound healed well, and stayed healed for years.
2. Not one swab, but several small pieces, came out.
3. The sinus did not penetrate the abdominal muscles, so that any swab must have been left, not in the abdomen, but in the abdominal wall, which is scarcely credible.
4. She had already been detected "faking" her temperature.

When later, in spite of two negative explorations of the sinus—one at home and one by me—a piece of selvedge-edged gauze, a lump of wool, and enough separate fragments of gauze to constitute four or five swabs, were found in the track, of course the nature of the case became obvious, and was confirmed by the facts that healing did not take place when she could get at it, but union by first intention took place when she was thoroughly strapped up. Nevertheless, there was a stage when an action at law for negligence in leaving a swab behind would have been all too likely to succeed, and the putting of this case on record may be a protection to some surgeon unjustly accused in the future. Legal proceedings were never threatened against me.

The motive and the state of the patient's mentality are hard to fathom. That she should be an inmate of a hospital and a workhouse infirmary for over two years, and inflict such injuries upon herself as to push a thick bone needle from the right iliac fossa into the bladder, simply to escape work or to excite sympathy (of which she got very little in Bristol), seems hard to believe, yet the only evidence to be found of unsoundness of mind is furnished by these actions. Her behaviour and conversation were otherwise normal.

Perhaps, in view of the incredible nature of the case, it may be as well to state that the facts can be vouched for by a whole succession of my house-surgeons and dressers, and the patient and "finds" have been shown to various surgical meetings. I owe a considerable debt to the acumen of my ward sister, Sister Julia Gross, in clearing up the nature of the case.

One somewhat similar example of a self-inflicted injury has come under my care. Some years ago, when our dermatologist was away at the war, I was asked by the acting out-patient physician, Dr. W. A. Smith, to see a girl, aged about 14, because she got a peculiar rash on her face every Wednesday afternoon at about 1 o'clock. The distribution was that of lupus erythematosus, but the characters were those of irritant dermatitis. Of course the extraordinary time-relation made it quite certain that it was an artefact, though we inquired if there was anything special about her diet on Wednesdays; there was not. I suggested having her up on Wednesday morning