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The excretion of sugars by the kidney.

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In studying the excretion of any substance by the kidney there are at first glance three separate things to be considered.

First, the passage from the blood into the kidney cell; second, the transit through the cell substance; and third, the passage from the cell into the lumen of the glomerulus or tubule. It is obvious that if the transfer through either cell boundary is impossible that none of the substance can be excreted, and it is also obvious that if anything prevents the passage through the cell substance itself that the kidney will appear impermeable.

In considering the passage of glucose through the body of the cell there are two well-known facts to be borne in mind that so far as we know have not received sufficient attention in this connection. The first is that the kidney uses a relatively large amount of oxygen and the second is that glucose is one of the main sources of energy for the body in general. It is therefore very probable that the kidney normally oxidizes a certain amount of glucose. Hence, even if both cell boundaries are permeable for glucose not all the sugar that gets into the cell will reach the lumen of the tubule. Normally only the minutest trace of sugar is present in the urine, whereas if the blood sugar rises beyond a certain level some will appear. Although it is true that in certain cases of diabetes there may be only a very slight hyperglycemia yet it is in the main true that glycosuria is dependent on a more or less pronounced rise in the percentage of sugar in the blood. Many hypotheses have been advanced to account for this so-called threshold phenomenon and I hope you will pardon me for dismissing them with the statement that none of them are generally accepted. It has seemed to us that the true explanation lies along the lines indicated above. The sugar normally gains entrance into the kidney cells in proportion to its concentration

in the blood. During its passage through the cell some of it is oxidized and if not too much has gotten in all will be oxidized and none appear in the urine.

In testing out this hypothesis we have referred to published figures for the concentration of various substances in the blood and urine and have also made some experiments of our own. We have found that very roughly speaking a dog of 10 k. body weight with a blood sugar content of .1 per cent. should excrete about .7 g. sugar per hour if the kidney were completely permeable and secreting freely. During marked diuresis Barcroft and Brodie[1] found that about 660 c.c. of oxygen would be required by the dog's kidneys for the same period. 0.7 g. of sugar requires 520 c.c. of oxygen for complete oxidation to CO_2 and water. The correspondence is fairly close.

We have also used published figures for the blood flow through the kidneys and have estimated that the sugar content of the renal vein should be about 80–90 per cent. of the sugar content of the renal artery if the kidney is completely permeable. We obtained simultaneous samples of the blood from the femoral artery and renal vein and found in five experiments a difference of 10–15 per cent., in three experiments no difference and in two a slightly higher content in the renal vein than in the artery. We drew 10 c.c. samples and analyzed the oxalated plasma by Shaffer's method. In only one of our experiments was any glucose found in the urine and then only a trace. We are engaged at present in trying to improve the analytical methods and will not go into further details.

We have tested a number of sugars and the indications are at present that only the sugars that are oxidized by the body will show this so-called threshold phenomenon. We believe we are justified in making the following statement: If the kidney is permeable for a sugar when and only when its concentration in the blood rises beyond a certain level, that sugar is oxidized by the kidney.[2]

[1] Barcroft and Brodie, *Journal Physiol.*, 33, 52 (1905–06).

[2] We even venture to suggest on purely theoretical grounds the following: If the kidney is permeable for any substance when and only when its concentration in the blood rises beyond a certain level, that substance is metabolized by the kidney.