# THE EXCRETION OF DEXTROSE IN THE STOMACH AND THE SMALL INTESTINE.*

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## INTRODUCTION.

The question of the elimination of dextrose from the blood into the gastro-intestinal canal has become a subject of experimental investigation and developed in connection with the recent studies on the production of glycosuria by the intravenous injection of solutions of sodium chlorid. The following is a brief review of these studies, some of the results of which gave rise to the investigations which are to be reported in this paper.

About four decades ago, Bock and Hoffmann[1] observed that intravascular injections of sodium chlorid are followed by glycosuria, an observation soon confirmed by Külz.[2] Recently the subject was taken up again by two American investigators, M. H. Fischer[3] and O. H. Brown.[4] While these authors carried out their work at about the same time, but independently of one another and in different laboratories (Fischer working in Loeb's laboratory at the University of California, and Brown in the Physiological Laboratory of the University of Chicago), both were nevertheless stimulated to their investigations by the studies and conclusions of J. Loeb; namely, that sodium salts increase and calcium salts decrease the irritability of nerve and muscle. Fischer found that when relatively large quantities of an M/6 solution of sodium chlorid are injected rapidly into the veins of rabbits the first effect is a greatly increased diuresis, which is followed later by the appearance in the urine of dextrose that may persist for many hours. The appearance of glycosuria, however, can be prevented by the addition of calcium chlorid. An intra-arterial injection of sodium chlorid in the direction of the medulla oblongata causes also, according to Fischer, the appearance of glycosuria which cannot be suppressed by the addition of calcium chlorid. Fischer assumes that the diuresis is produced in

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[1] Bock and Hoffmann, *Arch. f. Anat. u. Physiol.*, 1871, 550.

[2] Külz, *Beiträge zur. Anat. u. Physiol.*, von Eckard, 1872, vi, 117.

[3] M. H. Fischer, University of California Publications, Physiology, 1902–1903, i, 77 and 87; *Arch. f. d. ges. Physiol.*, 1905, cvi, 80; *ibid.*, 1905, cix, 1.

[4] O. H. Brown, *Am. Jour. Physiol.*, 1904, x, 378.

both instances by a stimulation of the kidney cells by sodium chlorid, while the glycosuria is caused by a stimulation of the "diabetic centre" in the medulla.

Underhill and Closson,[5] however, arrived at other conclusions. They analyzed the blood for its content of dextrose during the period of glycosuria produced by the intravascular injection of sodium chlorid and found the result to differ with the mode of injection. After intra-arterial injection of the sodium chlorid a hyperglycemia is produced, and after intravenous injections, a hypoglycemia. In the latter case, an injection of calcium salts causes a return of the dextrose to normal, or even an increase above normal, in the blood. Underhill and Closson assume that the glycosuria after intravenous injection of sodium chlorid presents a condition of "renal diabetes," or one in which the sodium chlorid causes an increase in permeability of the kidney epithelia for sugar with a consequent hypoglycemia; whereas the calcium salts tend to diminish the permeability. On the other hand, that which is caused by the intra-arterial injection of sodium chlorid in the direction of the medulla is brought about by asphyxia, because it interferes, according to these authors, with the activity of the respiratory centre.

McGuigan and Brooks[6] believe that the sugar in the blood is not free, but exists in combination with a protein molecule, and they assume that sodium chlorid and other salts, which cause experimental glycosuria, accomplish it by freeing the dextrose from its combination with the protein molecule; calcium salts, on the other hand, preventing such a liberation of the dextrose. In some of their experiments, solutions of calcium chlorid, when injected into the blood, did not prevent the occurrence of glycosuria, due to subsequent dextrose infusion. The authors see in this effect a proof that calcium does not decrease the permeability of the kidney epithelia to sugar, as was assumed by Underhill and Closson. Underhill and the present writer,[7] however, showed later that the glycosuria in the experiments of McGuigan and Brooks was produced by the action of the strong solutions of the calcium salt upon the respiratory centre, thereby causing respiratory insufficiency and asphyxia. Furthermore, the assumption of Underhill and Closson of the diminution by calcium of the permeability of kidney epithelia had no reference to epithelia of normal kidneys but only to epithelia, the permeability of which had been previously increased by the action of sodium chlorid.

J. B. MacCallum,[8] who also worked in Loeb's laboratory, studied the influence of the intravenous injection of solutions of sodium chlorid upon the elimination of fluid and sugar into the stomach and intestine of rabbits. He found, under these conditions, an increase of secretion of fluid into the stomach and small intestine and that both viscera contained sugar. The quantities of the eliminated fluid and of sugar in the stomach and intestine were increased if the kidneys were removed previous to the infusion of the salt solution. MacCallum speaks of "intestinal polyuria" and "intestinal diabetes," and compares

[5] Underhill and Closson, *Am. Jour. Physiol.*, 1906, xv, 321.

[6] McGuigan and Brooks, *Am. Jour. Physiol.*, 1907, xviii, 256.

[7] Underhill and Kleiner, *Jour. Biol. Chem.*, 1908, iv, 395.

[8] J. B. MacCallum, University of California Publications, Physiology, 1904, i, 125.

the effects upon the stomach and intestine with the effects which the intravenous injections of sodium chlorid exert upon the kidneys. "It seems," he says, "that the infusion of M/6 NaCl solution causes sugar to appear in the blood. On reaching a certain concentration, it is secreted by the kidneys. If the kidneys are cut off from the circulation, the sugar is excreted by the intestine." He looks upon the intestine as a supplementary excretory organ. MacCallum seems to have made altogether only four experiments, and only in one were the kidneys not removed.

While discussing the results and views of MacCallum, Fischer and Moore[9] point out first that the quantity and the concentration of the sodium chlorid solution employed by him were not sufficient to bring on any glycosuria. Then they show by experiment that hyperglycemia alone, produced by the diabetic puncture, injection of morphin, or intravenous injections of dextrose or cane sugar, does not cause an elimination of sugar in the intestine or stomach. However, hyperglycemia having been caused by these injections, an intravenous injection of sodium chlorid, even in quantities and concentrations which alone are insufficient to produce glycosuria, will cause an excretion of dextrose into the small intestine and possibly into the stomach also. Fischer and Moore explain the mechanism of the process on the assumption that sodium chlorid increases the permeability of the intestinal epithelia and thus permits the escape of dextrose from the blood, when it is present there in excess. The findings of MacCallum are explained by Fischer and Moore by the fact that in his experiments the rabbits received 5 c.c. of a 1 per cent. morphin solution, a dose sufficient to produce hyperglycemia, after which the sodium chlorid injection rendered the intestine permeable to this excess of sugar. Fischer and Moore state that the small intestine and stomach of normal rabbits are usually free from dextrose. We may add that they still speak of "hyperglycemia" caused by intravenous injections of sodium chlorid, although there is no evidence in their paper that they reëxamined this point experimentally. As far as we can see, the statement of Underhill and Closson, that when sodium chlorid has been injected intravenously the glycosuria is accompanied by a hypoglycemia, has not yet been controverted by any experimental investigation.

As regards the question of elimination of dextrose into the stomach and intestine,—the question which concerns us particularly in this investigation,—we find in the first place that Fischer and Moore believe that no such elimination takes place under normal conditions. MacCallum's findings seem to agree with this view. Furthermore, MacCallum believes that an elimination of dextrose in the stomach and intestine takes place whenever hyperglycemia exists, and the "intestinal diabetes" after an intravenous injection of sodium chlorid is simply one instance of this general rule. Fischer and Moore, on the other hand, believe that hyperglycemia alone does not lead to an excretion of dextrose in the alimentary

[9] Fischer and Moore, *Am. Jour. Physiol.*, 1907, xix, 314.

canal. According to them, this occurs only when, in addition to the hyperglycemia, the intestinal epithelia are rendered more permeable, which is the case when sodium chlorid is injected intravenously. Finally, there is the statement of MacCallum, that after removal of the kidneys a greater excretion of dextrose in the intestinal canal takes place, a phenomenon to be interpreted, according to him, as brought about by vicarious activity of the intestine.

On the basis of the foregoing considerations, I carried out several series of experiments to obtain answers to the following questions:

(1) Do the stomach and the small intestine of rabbits normally contain dextrose, or a reducing substance, in a demonstrable amount? (2) Will an intravenous injection of dextrose, sufficient to produce glycosuria, cause an elimination or an increase of the elimination of dextrose into the stomach and intestine? (3) Will, in the latter case, a double nephrectomy cause an increase of excretion of dextrose in the gut, and will this increase be, in comparison with the elimination through the kidneys, sufficiently large to constitute an instance of vicarious activity?

## EXPERIMENTAL RESULTS.

### METHODS.

The experiments were performed on rabbits which, in almost all cases, had been fed for several days previously on hay and cabbage; that is, on a diet poor in easily convertible carbohydrates. The analysis for dextrose in the alimentary canal was confined to the contents of the stomach and the small intestine. The contents of the latter were obtained by tying cannulas in the upper part of the duodenum and at the lower end of the ileum; by means of a pressure bottle, the entire small intestine was irrigated *in situ* with about a liter of 0.9 per cent. sodium chlorid. This was done immediately after death. The procedure in all cases was as follows: the animal was etherized, the abdomen opened, the end of the small intestine ligated and then the trachea clamped. Immediately after the last sign of life had passed away, the cannulas were inserted and the irrigation started. The ligation of the intestine was done

to prevent the removal of its contents into the cecum by the violent peristalsis which sweeps over the intestines during the period of asphyxia. Urine was collected by means of a cannula tied into the neck of the bladder. Solutions of dextrose were administered intravenously from a burette connected to a cannula, tied in the left external jugular vein. The kidneys were exposed through the lumbar region and were eliminated by ligating their blood-vessels. All operative procedures were carried out under ether anesthesia, except in a few instances in which a cannula was inserted into a jugular vein under local cocaine anesthesia.

For the determination of dextrose (or rather reducing substances) in the small intestine, the following procedures were employed. The irrigated fluid was acidified with acetic acid, filtered, and concentrated. The concentrated fluid was then either filtered and analyzed or was treated with phosphotungstic acid, filtered, neutralized, and then analyzed. The analysis was made usually by the Pavy-Vernon[10] method. However, in four experiments in which the fluid was treated according to the first mentioned procedure, some analyses were also made by the Allihn method. The following short table shows that the results obtained by the two methods do not differ greatly.

| Number of Experiment. | Pavy-Vernon. | Allihn. |
|---|---|---|
| 55. | 0.16 gm. | 0.15 gm. |
| 56. | 0.17 gm. | 0.14 gm. |
| 66. | 0.07 gm. | 0.04 gm. |
| 70. | 0.24 gm. | 0.24 gm.<br>0.23 gm. |

The stomach contents were macerated with water, strained through cotton gauze and centrifugalized. In some cases, the fluid was merely boiled and then analyzed; however, better results were obtained by treating it with phosphotungstic acid, filtering and neutralizing before subjecting it to the analysis. The determination of the reducing substances was made by the Pavy-Vernon method; determinations by the Allihn method were here unsatisfactory.

[10] Vernon, *Jour. Physiol.*, 1902, xxviii, 156.

No claim is made and can be made for extreme accuracy of the results, on account of the presence of interfering substances in both the intestinal and gastric contents. Whenever the qualitative test was doubtful it is indicated in the tables by an interrogation mark.

The urines were always analyzed by the Pavy-Vernon method.

## THE PRESENCE OF DEXTROSE IN THE STOMACH AND SMALL INTESTINE OF NORMAL RABBITS.

In the four experiments of MacCallum's on the small intestine, it is mentioned in the protocols that the fluid obtained before the infusion of sodium chlorid was started contained no sugar. Regarding the stomach, MacCallum says categorically that in normal rabbits it contains no sugar, although his experience apparently included only one or two experiments.

Fischer and Moore studied the subject in seven rabbits. Sugar was absent from the small intestine in every case. Regarding the stomach they state that it contains sugar in proportion to the character of the food. When the rabbits were fed on cabbage or the tops of carrots there was very little or no sugar; when they were fed with the pulp of carrots sugar was present.

Our experiments were performed on rabbits fed with cabbage and hay. In a series of six normal animals, the contents of the small intestine and of the stomach were analyzed for dextrose. No protocol of an experiment will be given. The following table (table I) presents the results.

TABLE I.

*Normal Rabbits. No Dextrose Injected.*

| Number of experiment. | Weight in kilos. | Dextrose in small intestine in gm. | Dextrose in stomach in gm. |
|---|---|---|---|
| 63 | 1.29 | 0.02(?) | 0.07–0.12(?) |
| 64 | 1.25 | 0.10 | 0.12 |
| 65 | 1.57 | 0.04 | 0.07–0.14 |
| 66 | 1.38 | 0.07 | 0.10 |
| 67 | 1.97 | 0.04–0.07(?) | 0.15–0.18 |
| 69 | 1.67 | 0.03(?) | 0.04 |
| Average | | 0.04 | 0.09 |

As the table shows, our results with the small intestine differ from those of MacCallum and of Fischer and Moore. We found a measurable, though variable, quantity of dextrose present in most of the experiments. Fischer and Moore state expressly that "no reduction is obtained in the intestinal wash water even after pro-

longed boiling with a Fehling's solution." With regard to the stomach contents, our findings are in better agreement with those of Fischer and Moore, although with such a diet as was used in our experiments Fischer and Moore state that there is little or no sugar present. We wish to call attention to the fact that in our experiments the amount of dextrose in the contents of the stomach was in every case definitely larger than in the small intestine.

In three experiments the contents of the stomach and of the small intestine of nephrectomized rabbits, which otherwise received no treatment, were examined for the presence of dextrose. Table II shows the result.

TABLE II.

*Nephrectomized Rabbits—No Dextrose Injected. Operated on the Preceding Day.*

| Number of experiment. | Weight in kilos. | Dextrose in small intestine in gm. | Dextrose in stomach in gm. |
|---|---|---|---|
| 83 | 1.61 | 0.02(?) | 0.04(?) |
| 85 | 1.23 | 0.02(?) | 0.06 |
| 86 | 1.54 | 0.02(?) | 0.03(?) |

The result may seem somewhat surprising. There was perhaps no good reason to expect a greater content of dextrose in the stomach and intestine in nephrectomized rabbits, since normally the kidneys do not excrete sugar. But why should there be definitely less? However, all three animals were operated on the previous day, and we may assume that because they had taken no food or drink the blood of the rabbits contained less fluid as well as less dextrose; hence the diminished dextrose content of the excretion of the intestines.

### THE ELIMINATION OF DEXTROSE INTO THE STOMACH AND SMALL INTESTINE AFTER AN INTRAVENOUS INFUSION OF DEXTROSE.

As stated above, MacCallum assumed that any hyperglycemia leads to an elimination of dextrose into the stomach and small intestine. Fischer and Moore, however, insist that the mere increase of sugar in the blood does not cause an excretion of sugar into the gastro-intestinal canal. In their experiments with morphin and diabetic puncture, which led to glycosuria, no sugar appeared in the

stomach and intestine. Neither was there any sugar found in an experiment in which dextrose was injected intravenously leading to glycosuria. In this experiment, 124.8 cubic centimeters of a one fourth molecular solution of dextrose (4.5 per cent.), *i. e.*, 5.6 grams, were injected intravenously in the course of one hour. The sugar eliminated in the urine amounted to 0.62 gram, that is, only about 11 per cent. of the injected dextrose. The volume of the urine amounted to only twenty-five cubic centimeters and the percentage of the dextrose in it was 2.48 per cent. Fischer and Moore do not state the exact weight of the animal.

In view of the fact that Fischer and Moore made only one experiment of this kind and with a quantity of dextrose which did not lead to a strong glycosuria, we studied this question in a larger series of animals. In our experiments, the warm solution of dextrose was run, as stated, from a burette into one of the external jugular veins. At the end of the infusion, the animal was permitted to live fifteen minutes before being killed and the contents of the viscera were collected in the manner described above. During the experiment, the animal was kept warm by means of an electric thermal pad. The urine was collected throughout the experiment from a cannula in the bladder.

*Normal Rabbits.*—The experiments were carried out in two series of six rabbits each. In the first series, four grams of dextrose per kilo. of body weight were administered. In order that the same volume of fluid per kilo. should be used in both this and the next series, the concentration of the dextrose solution in this series was made 11.4 per cent. The following is an abbreviated protocol of an experiment.

*Experiment 60.*—Female rabbit, 1,470 grams.

Animal placed on an electric thermal pad. Under ether anesthesia, cannulas were introduced into the left jugular vein and into the neck of the bladder.

2:05 P. M. Operation finished.

2:22 P. M. Intravenous infusion of warm 11.4 per cent. dextrose solution started.

2:34 P. M. Urine starts to flow after 18 c.c. of solution have run in.

2:52 P. M. Dextrose infusion finished. Total solution injected, 51.5 c.c. = 5.87 gm. dextrose.

3:07 P. M. Etherized. Abdomen opened and ileum tied near cecum; trachea

(and esophagus) clamped. Soon after death, cannulas were introduced in the upper part of the duodenum and the end of ileum, and the small intestine was irrigated with 900 c.c. 0.9 per cent. sodium chlorid; stomach contents extracted with water. These fluids and the urine were now analyzed as described above. In the urine (39 c.c.) was found 1.62 gm.; in the contents of small intestine, 0.07 gm.; and in that of the stomach, 0.06 gm. of dextrose (or reducing substance); respectively: 27.6 per cent., 1.2 per cent. and 1.0 per cent. of the amount introduced.

The following table (table III) contains the results in detail of these six rabbits.

TABLE III.

*Normal Rabbits. Four Grams of Dextrose per Kilo. of Body Weight Injected Intravenously.*

| Number of experiment. | Weight of animal in kilos. | Duration of dextrose injection in minutes. | Dextrose in urine. | | | Volume of urine in c.c. | Dextrose in small intestine. | | Dextrose in stomach. | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | In grams. | Percentage of amount injected. | As dextrose solution. Percent. | | In grams. | Percentage of amount injected. | In grams. | Percentage of amount injected. |
| 59 | 2.66 | 41 | 4.08 | 38.3 | 4.0 | 102 | 0.15 | 1.4 | 0.23 | 2.2 |
| 60 | 1.47 | 30 | 1.62 | 27.6 | 4.2 | 39 | 0.07 | 1.2 | 0.06 | 1.0 |
| 61 | 0.95 | 20 | 0.63 | 16.2 | 3.3 | 19 | 0.07 | 1.8 | 0.01? | 0.3? |
| 62 | 0.80 | 17 | 0.50 | 15.6 | 4.6 | 10.8 | 0.06 | 1.9 | 0.00 | 0.0 |
| 74 | 1.69 | 23 | 1.52 | 22.6 | 4.8 | 32 | 0.20 | 3.0 | 0.06 | 0.9 |
| 75 | 1.47 | 33 | 1.55 | 26.4 | 7.4 | 21 | 0.11 | 1.9 | 0.13 | 2.2 |
| Average | | | 1.65 | 24.5 | 4.4 | 37 | 0.11 | 1.9 | 0.08 | 1.1 |

As Fischer and Moore state, in regard to the weight of their animal (experiment 5), that it was "medium sized," only an approximate comparison with any of our experiments can be made. The rabbit of our experiment 60, which may be considered medium sized, received about the same quantity of dextrose as Fischer and Moore's rabbit. We may therefore compare the results of these two experiments. Fischer and Moore injected 5.6 grams (as 4.5 per cent.) in one hour and obtained twenty-five cubic centimeters of urine containing 2.5 per cent. dextrose, *i. e.*, 11 per cent. of the amount injected. We gave 5.9 grams (as 11.4 per cent.) in a half hour and obtained thirty-nine cubic centimeters of urine containing 4.2 per cent. dextrose, equivalent to 27.6 per cent. of the quantity injected. It is probable that this striking difference was due to the greater concentration of our solution, as well as to the greater rapidity with which this solution was injected. The average amount of

the dextrose eliminated into the small intestine in this series of experiments was slightly larger than that of the first series of normal rabbits in which no dextrose was injected. There is no perceptible difference in the amount of dextrose in the contents of the stomach of both series.

In another series of six rabbits, seven grams of dextrose per kilo. body weight were injected intravenously, in 20 per cent. concentration. The following protocol will serve as an illustration.

*Experiment 56.*—Gray and black female rabbit, 2,180 grams.
Etherized and operated as in experiment 60.
2:15 P. M. Operation finished.
2:27 P. M. Infusion of 20 per cent. dextrose into the jugular vein begun.
2:29 P. M. Urine starts to flow after 7 c.c. of solution have been injected.
3:04 P. M. Dextrose infusion finished. Total solution injected 76.5 c.c. = 15.3 gm. dextrose.
3:21 P. M. Etherized and proceeded as in experiment 60.
The urine (131 c.c.) contained 6.55 gm. of dextrose; the small intestine, 0.17 gm.; and the stomach, 0.27 gm.; equivalent respectively to 42.8 per cent., 1.1 per cent. and 1.8 per cent. of the amount of dextrose injected.

The details of the results of this series of experiments are presented in table IV.

TABLE IV.

*Normal Rabbits. Seven Grams of Dextrose per Kilo. of Body Weight Injected Intravenously.*

| Number of experiment. | Weight of animal in kilos. | Duration of dextrose injection in minutes. | Dextrose in urine. | | | Volume of urine in c.c. | Dextrose in small intestine. | | Dextrose in stomach. | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | In grams. | Percentage of amount injected. | As dextrose solution, Percent. | | In grams. | Percentage of amount injected. | In grams. | Percentage of amount injected. |
| 52 | 1.84 | 32 | 7.45 | 57.3 | 5.4 | 138 | 0.14 | 1.1 | 0.04(?) | 0.3(?) |
| 55 | 1.53 | 28 | 3.53 | 33.0 | 3.8 | 93 | 0.16 | 1.5 | 0.04 | 0.4 |
| 56 | 2.18 | 37 | 6.55 | 42.8 | 5.0 | 131 | 0.17 | 1.1 | 0.27 | 1.8 |
| 72 | 1.38 | 26 | 3.04 | 31.3 | 4.4 | 69 | 0.09 | 0.9 | 0.07 | 0.7 |
| 73 | 1.69 | 35 | 5.68 | 47.7 | 4.5 | 125 | 0.06 | 0.5 | 0.04 | 0.3 |
| 105 | 1.72 | 43 | 4.00 | 33.3 | 4.6 | 87 | 0.26 | 2.2 | 0.18 | 1.5 |
| Average | | | 5.04 | 40.9 | 4.7 | 107 | 0.15 | 1.2 | 0.10 | 0.8 |

The percentage of dextrose eliminated in the urine is, in this series, definitely larger than in the last, in which only four grams of dextrose per kilo. of body weight were given. The elimination of dextrose into the small intestine is definitely larger than that of the

animals in either of the previous series of experiments, although even these quantities seem to be very small when compared with those eliminated through the kidneys. The elimination into the stomach is, in this series, also slightly increased above that of the other series. However, the increase in the elimination into the stomach and intestine is proportionately far below the increase in the quantity of the injected dextrose. The percentages of elimination into the stomach and intestine are therefore smaller in the series with seven than in the series with four grams per kilo. of body weight.

### INTRAVENOUS INJECTION OF DEXTROSE INTO NEPHRECTOMIZED RABBITS.

In a final series of experiments on six rabbits double nephrectomy was performed and dextrose subsequently injected intravenously in a dosage of seven grams per kilo. of body weight. In two cases, the sugar was injected soon after the nephrectomy; in the remaining experiments the infusion was made on the next day. The following protocol is an example.

*Experiment 80.*—Light brown female rabbit, 1,740 grams.

January 31, P. M. Under ether anesthesia, both kidneys ligatured.

February 1. Under local cocaine anesthesia a cannula was introduced into the jugular vein. Animal placed on electric pad.

1:52 P. M. Intravenous injection of warm 20 per cent. dextrose solution. Animal hyperesthetic.

2:47 P. M. Dextrose injection ended. Total infusion 61 c.c. = 12.2 grams dextrose.

3:02 P. M. Etherized, etc., as described in previous experiments. The small intestine contained reducing substances amounting to 0.27 gram, equal to 2.2 per cent. of the amount of dextrose injected; the stomach contained 0.16 gram or 1.3 per cent. of the total dextrose injected.

Table V shows the details of this last series of experiments.

The amount of dextrose in the stomach and intestine is on the average slightly greater in the nephrectomized animals than in the normal animals which received also seven grams per kilo. of body weight in 20 per cent. concentration. The increase, however, is obviously insignificant, considering especially that the nephrectomized rabbits retain the 40 per cent. and more of the injected dex-

TABLE V.

*Nephrectomized Rabbits. Seven Grams of Dextrose per Kilo of Body Weight Injected Intravenously.*

| Number of experiment. | Weight of animal in kilos. | Duration of dextrose injection in minutes. | Dextrose in small intestine. | | Dextrose in stomach. | | Remarks. |
|---|---|---|---|---|---|---|---|
| | | | In grams. | Percentage of amount injected. | In grams. | Percentage of amount injected. | |
| 70 | 1.61 | 47 | 0.24 | 2.1 | 0.24 | 2.1 | Operated on preceding day |
| 78 | 1.65 | 47 | 0.09 | 0.8 | 0.13 | 1.1 | Operated on preceding day |
| 79 | 1.83 | 37 | 0.27 | 2.1 | 0.09 | 0.7 | Operated on preceding day |
| 80 | 1.74 | 55 | 0.27 | 2.2 | 0.16 | 1.3 | Operated on preceding day |
| 81 | 1.43 | 37 | 0.27 | 2.7 | 0.09 | 0.9 | Operated on same day |
| 82 | 1.33 | 35 | 0.30 | 3.2 | 0.16 | 1.7 | Operated on same day |
| Average | | | 0.24 | 2.2 | 0.15 | 1.3 | |

trose which was eliminated through the intact kidneys of the normal rabbits.

## DISCUSSION.

In a series of normal rabbits in which no dextrose was injected, the small intestine of some contained definitely measurable quantities of dextrose. Neither MacCallum nor Fischer and Moore found any traces of sugar in the small intestine. The latter writers say: "That traces of sugar could be found with more delicate analytical methods is not disputed." But a quantity of 0.1 gram (experiment 64) is surely more than such a trace and is even more than the quantity found by Fischer and Moore in one of their two experiments in which an intravenous injection of dextrose and sodium chlorid was given. We are sure that in our experiments the presence of dextrose was not due to an admixture of blood; this was carefully avoided. Besides, 0.1 gram is probably all the sugar which the entire blood of this animal contained. Neither is it probable that the sugar was simply a remnant of the food; the animals were kept on a diet poorer in readily convertible carbohydrates than the animals of Fischer and Moore. It is also not very probable that the presence of dextrose in our cases was due to an acute hyperglycemia produced by the strangulation of the animal. We are, nevertheless, prepared to state only the fact that in some of our experiments the small intestine of normal animals contained immediately after death measurable quantities of a reducing substance,

preferring not yet to draw the definite conclusion, that in living animals dextrose is eliminated normally into the intestine.

What we said of the intestine applies also to the stomach; here the amounts of dextrose were even larger than those found in the intestine. Our actual findings do not differ materially from those of Fischer and Moore, although they found dextrose in the stomach only when the animals were fed on a diet rich in easily convertible carbohydrates (carrot pulp). MacCallum's opposite statement was based on too few experiments.

The experiments with the intravenous injections of dextrose seem to settle definitely the fact that a certain degree of hyperglycemia will undoubtedly cause an excretion, or, perhaps better, an increase of excretion of dextrose into the intestine and the stomach. In the series of experiments in which seven grams of dextrose per kilo. of body weight were injected in a 20 per cent. solution, the quantities of dextrose in the small intestine were unmistakably larger than those present in the small intestine of the rabbits which received only four grams of dextrose per kilo. of body weight, injected in a concentration of 11.4 per cent. The duration of the injection did not differ materially in either series of experiments. It is therefore evident that the intravenous injection of a larger quantity of dextrose in about the same unit of time causes undoubtedly a greater hyperglycemia for a certain length of time. It is interesting to note that in the series of experiments with seven grams of dextrose per kilo. of body weight, the volume of urine and the amount of sugar eliminated in it were considerably greater than in the series of experiments with only four grams per kilo. of body weight. Evidently the injection of a greater quantity of dextrose in the same unit of time causes also a greater polyuria and glycosuria. In our experiments, the greater elimination of dextrose in the intestine and the stomach was due to the injection of dextrose alone; and since no additional injection of sodium chlorid was made, we need not discuss the possibility of the production of a greater permeability of the intestinal epithelia being a factor in the elimination of dextrose in the gastro-intestinal canal. Fischer and Moore report only one experiment with dextrose. In this experiment, the amount of dextrose injected in a unit of time was much smaller than in our experi-

ments. The failure of these authors to obtain an elimination of dextrose into the gastro-intestinal canal when a hyperglycemia was present was probably due to the fact that the hyperglycemia in these cases was too small to produce such an elimination of dextrose into the alimentary canal. Blumenthal[11] has shown that relatively large quantities of dextrose can be injected intravenously before a glycosuria appears. When we consider how much more readily sugar is eliminated through the kidneys than into the intestine, we may well assume that still larger quantities of dextrose have to be injected intravenously before an elimination into the intestine takes place. The fact that a certain degree of hyperglycemia is sufficient to cause a glycosuria is not yet evidence that the same degree is also sufficient to cause an excretion into the intestine. The very fact that the quantity of dextrose in the urine in Fischer and Moore's experiment amounted only to about 11 per cent. of the injected dextrose, while the dextrose in the urine in our successful experiments was three or four times that percentage, shows that in their experiment the hyperglycemia must have been of a low degree.

While we thus agree in general with MacCallum that the elimination of dextrose into the intestine is dependent upon a hyperglycemia, we can not agree with his view that this elimination constitutes an "intestinal diabetes," and still less can we look upon the slight increase in the excretion of sugar into the alimentary canal as a "vicarious action"; that is, that in the absence of the kidneys, the intestine is capable of assuming the excretory activities of those eliminating organs. Without entering here upon the large question of vicarious activity of organs, we must insist that this assumption is especially inapplicable in the case under discussion. The average percentage of elimination into the intestine of the injected dextrose amounts, for the six normal rabbits which received seven grams per kilo. of body weight, to 1.2 per cent. (table IV). For the nephrectomized rabbits receiving the same quantities of dextrose, the average percentage amounts to 2.2 per cent (table V); that is, the elimination into the intestine of nephrectomized rabbits was increased by 1 per cent. The elimination of the injected dextrose through the kidneys in the rabbits with intact kidneys amounts to 40.9 per cent.

[11] Blumenthal, *Beitr. z. chem. Physiol. u. Pathol.*, 1905, vi, 329.

A theory which assumes that an increase of elimination into the intestine of nephrectomized rabbits of 1 per cent. means a functional compensation for the loss of elimination of 40.9 per cent. is so unsatisfactory that it seems to require no special discussion. We must remember, at the same time, that this increase of 1 per cent. is contributed by the rather large area of the mucous membrane of the entire small intestine. The plausible interpretation of the increase after nephrectomy is that in animals which have received considerable quantities of dextrose intravenously, in consequence of the absence of the specifically eliminating organs, some increase in the elimination of the constituents of lymph and blood occurs in all glands and over the surfaces of all the mucous membranes. The eliminated quantities, however, are usually too small to be readily recognized, except when they are collected from such a large surface as the mucous membrane of the entire small intestine.

## SUMMARY.

The contents of the stomach and small intestine of normal rabbits, kept on a diet poor in easily convertible carbohydrates, when removed immediately after killing the animal (by clamping the trachea), usually contain a very small but measurable amount of dextrose (reducing substances). A preceding nephrectomy does not increase the amounts of the dextrose in these viscera.

An intravenous injection of dextrose, if given in a sufficient quantity in a unit of time, causes a definite excretion, or increase of excretion, into the small intestine and the stomach. The amount of excretion, however, is incomparably smaller than the amount eliminated through the kidneys.

A preceding double nephrectomy increases the gastro-intestinal elimination of the intravenously injected dextrose. The increase, however, is far too small to be considered in the light of a functional compensation for the loss of the considerable elimination through the kidneys.

In conclusion, I desire to express my thanks to Dr. S. J. Meltzer for constant and invaluable aid and advice during this investigation.