Physiology. — "*The conduct of the kidneys towards some isomeric sugars (Glucose, Fructose, Galactose, Mannose and Saccharose, Maltose, Lactose).*" By Prof. H. J. HAMBURGER and Dr. R. BRINKMAN.

(Communicated in the meeting of September 28, 1918).

It has been proved by former researches [1]), that the glomerulus epithelium of the kidney of the frog is able to hold back glucose if the solution which is passed through the vascular system has a suitable composition. If one passes through the arteria renalis of the frog the following Ringer's solution: NaCl 0,7 %, KCl 0,01 %, $CaCl_2$ 0,0075 %, $NaHCO_3$ 0,02 %, in which 0,1 % glucose has been dissolved, then an artificial urine is excreted containing 0,07 % glucose; 0,03 % glucose has thus been retained by the glomerulus epithelium. If however the Ringer's solution contains 0,285 %, i.e. a quantity that corresponds to the titrational alkalicity of the serum of the frog, then much more sugar than 0,03 % is held back and not seldom the urine is free from sugar.

This phenomenon proves that the glomerus membrane, which is permeable to salts, is under physiological conditions impermeable to the also crystalline glucose.

In order to come to an explanation of this remarkable and useful contrast it seemed interesting to investigate how the glomerulus membrane would behave towards laevulose, galactose and mannose, all isomeric to glucose, and also towards the mutually isomeric saccharose, lactose and mannose.

Let us begin with the four first-named.

As is well known, the structural formula of the monosaccharides ($C_6H_{12}O_6$) can be represented in the following way:

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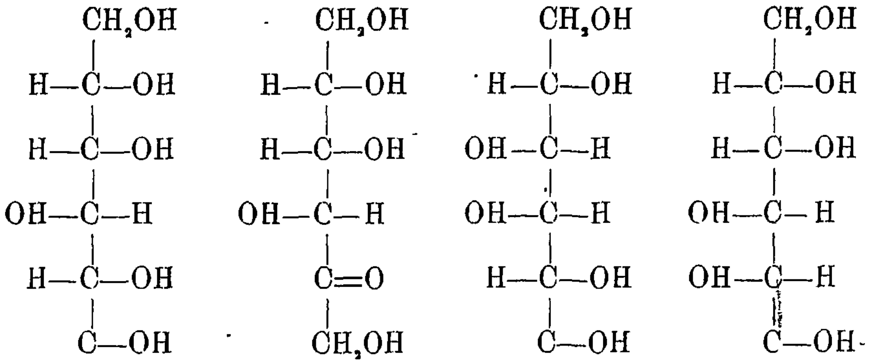
[1]) HAMBURGER and BRINKMAN: Proceedings of the Royal Acad. of Sciences Section of Jan. 27, and Sept. 29, 1917. Also: Biochem. Zeitschr. **88**, 97, 1918.



d-Glucose — Fructose (laevulose) — d-Galactose — d-Mannose

The experiments were made in exactly the same way as was described in the articles cited above. The perfusion liquid was of the following composition: NaCl 0,5 %, $NaHCO_3$ 0,285 %, KCl 0,01 %, $CaCl_2$ 0,2 %. This solution was prepared by mixing

50 ccm. NaCl 10 %,
50 ccm. $NaHCO_3$ 5,7 %,
10 ccm. KCl 1 % and
40 ccm. $CaCl_2$ 5 %

and adding boiled distilled water up to 1 Liter. Certain quantities of the sugars [1]) were dissolved in this solution, but still the reductive capability was estimated before each experiment. This was done in view of the possible errors in weighing or unknown differences in the amount of water contained in the sugars. BANG's method (1916) was used for estimating the reductive capability of the perfusion liquid as well as that of the urine excreted. The reductive power of the various sugars was *expressed in the percentage of glucose contained.*

As is well know the final titration is an estimation of Iodine with the aid of amylum; the amount of glucose contained is then computed from the quantity of Iodine necessary, by means of the formula $(a-0{,}12):4$, in which "a" is the number of *c.c.* solution of Iodine used.

A. Laevulose (Fructose).

Experiment 1 (July 11, 1918)

The perfusion liquid contains 0,1 % laevulose.

The reduction, expressed in glucose, amounts to 0,21 %.

0,1 ccm. urine from the right kidney needs 0,87 ccm. Iodine solution, which corresponds to $\frac{0{,}87-0{,}12}{4} = 0{,}0875\%$ glucose.

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1) We are indebted to Jhr. W. ALBERDA VAN EKENSTEIN, Director of the laboratory of the ministry of Finance and by Prof. H. J. BACKER, for several of the sugars.

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0,1 ccm. urine from the left kidney needs 0,88 ccm. Iodine solution which corresponds to $\frac{0,88-0,12}{4} = 0,19\%$ glucose.

Retained by the right kidney $0,21-0,1875 = \mathbf{0,0225\%}$.
Retained by the left kidney $0,21-0,19 = \mathbf{0,02\%}$.

These quantities are so small that one may say that practically all the laevulose is allowed to pass by the glomerulus epithelium. The following experiments affirm this result.

Experiment 2 (July 12).

The same solution as used in experiment 1.
Reduction (0,1 c c) urine of right kidney 0,2125%.
Reduction (0,1 c.c.) urine of left kidney 0,215%.
Retained by right kidney $0,21-0,2125 = \mathbf{0}$.
Retained by left kidney $0,21-0,215 = \mathbf{0}$.

Result: *No* laevulose retained by the glomerulus epithelium.

Experiment 3 (July 13).

Experiments 1 and 2 were repeated with fresh solution.
Reduction 0 1 c.c. of solution passed 0,18%.
Reduction 0,1 c.c. urine of right kidney 0,18%
Reduction 0,1 c c. urine of left kidney 0,18%,

Result: *No* laevulose retained.

Experiment 4 (July 14).

The same solution passed as in experiment 3.
Reduction 0,1 c.c. urine of right kidney 0,1825%.
Reduction 0,1 c.c. urine of left kidney 0,1825%.

Result: *No* laevulose retained.

It has probably not escaped attention that the laevulose solution used above causes about twice as strong a reduction as a glucose solution of 0.1% viz. 0.18% on an average. Where it could be possible that a solution with a so much larger reductive capability could, just in connection with that fact, be allowed to pass by the glomerulus epithelium, we experimented with a solution in which there was 0.05% laevulose instead of 0.1%.

Experiment. 5 (July 15).

RINGER's solution in which 0,05% laevulose has been dissolved.
Reduction 0,1 c.c. of perfusion liquid 0,095%.
0,1 c.c. urine of right kidney: 0,5 c.c Iodine solution; reduction 0,095%.
0,1 c.c. urine of left kidney: 0,52 c.c. Iodine solution; reduction 0,1%.
0,1 c c. urine of right kidney: 0,52 c.c. Iodine solution; reduction 0,1%.
Retained by right kidney $0,095-0,095 = 0$.
Retained by left kidney $0,095-0,1 = \mathbf{0}$.
Retained by right kidney $0,095-0,1 = \mathbf{0}$.

Result: The diluted laevulose solution also passes completely through the glomerulus epithelium.

It seemed interesting to investigate whether laevulose could influence the retention of glucose.

In order to ascertain whether the circumstances, as regards the manner in which we had formerly worked with glucose, had indeed remained unaltered, several experiments were made with glucose alone.

B. Glucose and a mixture of Glucose and Laevulose.

Experiment 6. (July 18).

Perfusion liquid in which there was 0,1% glucose.
0,1 c.c. of solution, reduction 0,0975%.
0 1 c.c. urine of right kidney: 0.3 c.c Iodine solution; reduction 0,045%.
0,1 c.c. urine of left kidney: 0,31 c.c Iodine solution; reduction 0.0475%.
Retained by right kidney: 0,0975—0,045 = **0,0525%**
Retained by left kidney: 0,0975—0,0475 = **0,05%**.

Experiment 7 (July 18).

The same perfusion liquid as in experiment 6.
0,1 c.c. urine of right kidney: 0,26 c.c. Iodine solution; reduction 0,035%.
0,1 c.c. urine of left kidney: 0,29 c.c. Iodine solution; reduction 0,0425%.
Retained by right kidney: 0,0975—0,035 = **0,0625%**.
Retained by left kidney: 0,0975—0,0425 = **0,0550%**.

Experiment 8 (July 20).

Perfusion liquid contains 0,07% glucose.
Reduction by 0,1 c.c. of solution passed 0,065%
0,1 c.c. urine of right kidney: 0,22 c.c. Iodine solution; reduction 0,025%
0,1 c.c. urine of left kidney: 0,22 c.c. Iodine solution; reduction 0,025%.
Retained by each kidney: 0,065—0,025 = **0,04%**.

Experiment 9 (Sept 20).

At the same time an experiment was made in which the perfusion liquid contained 0,2% glucose.
Reduction 0,1 c.c. of this solution 0,22%.
Reduction by 0,1 c.c. urine of right kidney 0,095%.
Reduction by 0,1 c.c. urine of left kidney 0,1125%.
Retained by right kidney: 0,22—0,095 = **0,1250%**.
Retained by left kidney: 0,22—0,1125 = **0,1075%**.

From these experiments it follows that now, as formerly, a quantity of glucose is retained, which is physiologically present in the blood of the frog. A remarkable contrast thus exists between the permeability of the kidney to glucose and to laevulose.

With this marked difference it appeared to be of importance to ascertain whether laevulose was perhaps capable of altering the permeability to glucose.

Both these substances were therefore dissolved in the perfusion liquid.

Experiment 10 (Sept. 20).

The perfusion liquid contains 0,1 % glucose and 0,05 % laevulose.
Reduction 0,1 c.c. of solution passed 0,205 %.
0,1 c.c. urine of right kidney: 0,58 c.c. Iodine solution; reduction 0,1175 %.
0,1 c.c. urine of left kidney: 0,60 c.c. Iodine solution: reduction 0,12 %.
Retained by right kidney: 0,205—0,1175 = **0,0875 %**.
Retained by left kidney: 0,205—0,12 = **0,085 %**.

Experiment 11 (Sept. 20).

The same perfusion liquid as in experiment 9.
Reduction 0,1 c.c. urine of right kidney 0,155 %.
Reduction 0.1 c.c. urine of left kidney 0,1575 %.
Retained by right kidney: 0,205—0,155 = **0,05 %**.
Retained by left kidney: 0,205—0,1575 = **0,0475 %**.

Experiment 12 (Sept. 20).

The perfusion liquid contains a mixture of glucose and laevulose
Reduction of solution passed 0,205 %.
Reduction 0,1 c.c. urine of right kidney 0,115 %.
Reduction 0,1 c.c. urine of left kidney 0,12 %.
Retained by right kidney: 0,205—0,115 = **0,09 %**.
Retained by left kidney: 0,205—0,12 = **0,085 %**.

Experiment 13 (Sept. 21).

The perfusion liquid contains 0,07 % glucose and 0,05 % laevulose.
Reduction 0,1 c.c. of this solution 0,175 % (average of 3 homonymous experiments).
0,1 c.c. urine of right kidney: 0,63 c.c. Iodine solution; reduction 0,1275 %.
0,1 c.c. urine of right kidney: 0,62 c.c. Iodine solution; reduction 0,125 %.
0,1 c.c. urine of left kidney: 0,65 c.c. Iodine solution; reduction 0,1325 %.
Retained by right kidney: 0,175—0,1275 = **0,0475 %**.
Retained by right kidney: 0,175—0,125 = **0,05 %**.
Retained by left kidney: 0,175—0,1325 = **0,0425 %**.

Experiment 14 (Sept. 21)

The same perfusion liquid as in experiment 13.
0,1 c.c. urine of right kidney: 0,64 c.c. Iodine solution; reduction 0,13 %.
0,1 c.c. urine of left kidney: 0,64 c.c. Iodine solution; reduction 0,1275 %.
Retained by right kidney: 0,175—0,13 = **0,045 %**.
Retained by left kidney: 0,175—0,1275 = **0,0475 %**.

It is apparent from these experiments that the glomerulus epithelium which, as we have seen, is completely permeable to laevulose, has held back a quantity of glucose, which was also retained when the solution perfused contained glucose alone. The laevulose while passing itself does not or hardly influence the retention of glucose. With a little exaggeration one might this say that *the kidney separates the glucose from the laevulose by means of filtration.*

C. Galactose.

Experiment 15 (July 18).

The perfusion liquid contains 0,09% galactose.
Reduction (0,1 c.c.) of solution passed 0,07%.
0,1 c.c. urine of right kidney: 0,35 c.c. Iodine solution; reduction 0,055%.
0,1 c.c. urine of left kidney: 0,33 c.c. Iodine solution; reduction 0,052%.
Retained by right kidney: 0,07 – 0,055 = **0,015%**.
Retained by left kidney: 0,07— 0,052 = **0,018%**.

Experiment 16 (Aug. 22).

The perfusion liquid contains 0,1% galactose.
Reduction 0.1 c.c. of solution passed 0,07%.
0,1 c.c. urine of right kidney: 0,3 c.c. Iodine solution: reduction 0,045%.
0,1 c.c. urine of left kidney: 0,28 c.c. Iodine solution; reduction 0,04%.
Retained by right kidney: 0,07—0,045 = **0,025%**.
Retained by left kidney: 0,07 – 0,04 = **0,03%**.

Experiment 17 (Aug. 23).

Reduction 0,1 c.c. of perfusion liquid 0,055%.
0,1 c.c. urine of right kidney: 0 25 c.c. Iodine solution; reduction 0,0325%.
0,1 c.c. urine of left kidney: 0,15 c.c. Iodine solution; reduction 0,0325%.
Retained by each kidney 0,055—0,0325 = **0,0225%**.

Experiment 18 (Aug. 23).

The same perfusion liquid as in experiment 17.
0,1 c.c. urine of right kidney: 0,25 c.c. Iodine solution; reduction 0,0325%.
0,1 c.c. urine of left kidney: 0,25 c.c. Iodine solution; reduction 0,0325%.
Retained by each kidney: 0,055 – 0,0325 = **0,0225%**.

All these experiments show that the kidney retains a slight quantity of galactose.

We shall now record a few experiments with a perfusion liquid the reduction of which approximately agrees with that of 0.1% glucose.

Experiment 19 (Aug. 23).

The perfusion liquid contains 0,15% galactose.
Reduction 0,1 c.c. of perfusion liquid 0,0975%.
0,1 c.c. urine of right kidney: 0.4 c.c. Iodine solution; reduction 0,07%.
0,1 c c. urine of left kidney: 0,4 c.c. Iodine solution: reduction 0,07%.
Retained by each kidney: 0,0975 – 0,07 = **0,0275%**.

Experiment 20 (Aug. 23).

The same perfusion liquid as in experiment 19.
0,1 c.c. urine of right kidney: 0,33 c.c. Iodine solution; reduction 0,0525%.
0,1 c.c. urine of left kidney: 0,32 c.c. Iodine solution; reduction 0,05%.
Retained by right kidney: 0,0975—0,0525 = **0,045%**.
Retained by left kidney: 0,0975—0,05 = **0,0475%**.

Here again it becomes clear that some galactose is retained. In the last experiment (20) the quantity is even comparatively large.

That galactose is retained is efficient in the same way as is the case with glucose. While glucose is a source of energy for muscular contraction; *galactose helps in the formation of the cerebrosides.*

As has been remarked earlier, frogs often present not inconsiderable differences in their capacity for retaining glucose. The time of year also has some influence. Therefore experiments were again made with frogs that had lived under the same circumstances as those of the experiments described above.

Experiment 21 (Aug. 24).
The perfusion liquid contains 0,1% *glucose.*
Reduction 0,1 c.c. of perfusion liquid 0,10%.
0,1 c.c urine of right kidney· 0,24 c.c. Iodine solution; reduction 0,03%.
0,1 c.c. urine of left kidney: 0,22 c.c. Iodine solution; reduction 0,025%.
Retained by right kidney: 0.10—0,03 = **0,07%**.
Retained by left kidney: 0,10—0 025 = **0,075%**

Experiment 22 (Aug. 24).
The same perfusion liquid as in experiment 21.
0,1 c.c. urine of right kidney: 0,25 c.c. Iodine solution; reduction 0,0325%
0,1 c.c. urine of left kidney: 0,22 c.c. Iodine solution; reduction 0,025%.
Retained by right kidney: 0,10—0,0325 = **0,0675**%.
Retained by left kidney: 0,10—0,025 = **0,075** %.

It is clear that these frogs, which were placed in the same circumstances as those of experiments 16—20, retained *a much larger quantity of glucose than of galactose.*

It now seemed desirable to investigate whether the retention of galactose although this occurred in a much smaller degree than was the case with glucose, was governed by the same conditions as regards the composition of the Ringer-solution, as had formerly been found to apply to glucose. For this reason the following Ringer's solution was used: NaCl 0,7 %, **$NaHCO_3$ 0,02** %, KCl 0.01 %, $CaCl_2$ 0.0075 %. With the application of this solution glucose was at the time retained *to a maximum* of 0.03 %. Only when the quantity of $NaHCO_3$ was increased above 0.09 % on account of which the urine was no longer acid, there could be retained much more sugar; the urine could then even be free from sugar.

What would now be the result with galactose if the Ringer's solution also in this case contained 0,02 % *$NaHCO_3$ only?*

Experiment 23 (Sept. 14).
The perfusion liquid with only 0,02% $NaHCO_3$ contains 0,1% galactose.
Reduction of 0,1 c.c. of perfusion liquid 0,08%.
0,1 cc. urine of right kidney: 0,42 c.c. Iodine solution; reduction 0,075%.
0,1 c.c. urine of left kidney: 0,43 c.c. Iodine solution; reduction 0,0775%.
Retained by right kidney: 0,08—0,075 = **0,005%**.
Retained by left kidney: 0,08—0,0775 = **0,0025%**.

Experiment 24 (Sept. 14).
The same perfusion liquid as in experiment 23.
0,1 c.c. urine of right kidney: 0,43 c.c. Iodine solution; reduction 0,0775%.
0,1 c.c. urine of left kidney: 0,44 c.c. Iodine solution; reduction 0,08%.
Retained by right kidney: 0 08—0,0775 = **0,0025%**
Retained by left kidney: 0,08—0,08 = **0.**

We see thus that with galactose as well as with glucose, the quantity of $NaHCO_3$ in the perfusion liquid is of great importance for the permeability of the glomerulus epithelium. A solution containing a small quantity of $NaHCO_3$ causes galactose to pass in toto; if the perfusion liquid contains a physiological quantity of $NaHCO_3$ (0,285 %) then on an average 0.025 % galactose is retained. We say on an average, as frogs present individual differences.

Here follows a table which gives a summary of a series of other experiments with galactose in which however the quantity of $NaHCO_3$ was, accidentally, 0.2 % instead of 0.285 %. As had also formerly been found with glucose such a modification was of very little importance.

Retention capability of kidney for galactose.

Reduction perfusion liquid, containing ± 0.1 % galactose	Reduction urine of right kidney	Retained by right kidney	Reduction urine of left kidney	Retained by left kidney
0.0825 %	A 0.05 / 0.0475 } 0.049	**0.033** %	A 0.0525 / 0.0475 } 0.050	**0.0325** %
	B 0.0775 / 0.08 } 0.078	**0.038** "	B 0.0825 / 0.0825 } 0.0825	**0** "
	C 0.0675 / 0.065 } 0.0663	**0.0163** "	C 0.0675 / 0.0675 } 0.0675	**0.015** "
0.0725 "	D 0.05	**0.0225** "	D 0.0525	**0.02** "
	E 0.045	**0.0275** "	E 0.048	**0.0245** "
	F 0.047	**0.0250** "	F 0.045	**0.0275** "

When we make a study of this table it becomes clear;

1. that there is a difference in the power for retaining galactose in the various frogs A, B, C, D, E, and F.
2. that the individual differences range between 0 and 0,033%.
3. that the power of retention is more or less the same for the right and the left kidney of the same frog.

Here again as in the former experiments it is clear that galactose *does not, like laevulose, pass through the kidney altogether, but is generally retained to a slight degree.*

This indicates in any case that galactose is used in the body. We know indeed that lactose is built up from dextrose and galactose and an article of ELSE HIRSCHBERG [1]) from WINTERSTEIN's laboratory has just appeared in which a certain affinity, that is wanting in laevulose, becomes clear between glucose and galactose in connection with the spinal cord.

We repeat, that the amount of galactose retained is in all the experiments *expressed in the percentage of glucose.* This is also the case with other sugars.

D. Mannose.

Experiment 25 (Aug. 20).

In the suitable perfusion liquid consisting of NaCl 0,5%, $NaHCO_3$ 0,285%, KCl 0,01% and $CaCl_2$ 0,02%, 0,1% mannose is dissolved.

0 1 c.c. perfusion liquid: 0,45 c.c. Iodine solution; reduction 0,0825%.

0,1 c.c. urine of right kidney: 0,48 c.c. Iodine solution; reduction 0,09%.

0,1 c.c. urine of left kidney: 0,46 c.c. Iodine solution; reduction 0,085%

Retained by right kidney: 0,0825—0,09 = **0**.

Retained by left kidney: 0,0825—0,085 = **0**.

Experiment 26 (Aug 20).

The same perfusion liquid as in exp. 25.

0,1 c.c. urine of right kidney: 0,45 c.c. Iodine solution; reduction 0,0825%.

0,1 c.c. urine of left kidney: 0,44 c.c. Iodine solution; reduction 0,08%.

Retained by right kidney: 0,0825—0,0825 = **0**.

Retained by left kidney. 0,0825—0,08 = **0,0025%**.

Thus also in this experiment no mannose was retained.

Experiment 27 (Aug. 21).

0,1 c.c. perfusion liquid: 0,35 c.c. Iodine solution: reduction 0,0575%.

0,1 c.c. urine of right kidney: 0,37 c.c. Iodine solution; reduction 0.0625%.

0,1 c.c. urine of left kidney: 0.35 c c. Iodine solution; reduction 0,0575%.

0,1 c c. urine of right kidney: 0,35 c c. Iodine solution; reduction 0,0575%.

In this exp. also *no mannose is retained.*

Experiment 28 (Aug. 21).

The same perfusion liquid as in exp. 27.

0,1 c.c. urine of right kidney 0,36 c.c. Iodine solution; reduction 0,06%.

0,1 c.c. urine of left kidney: 0,36 c.c. Iodine solution; reduction 0,06%.

Retained by each kidney 0,0575—0,06 = **0**.

In this experiment the Kidneys have also passed all the mannose.

From these experiments we may draw the conclusion that the glomerulus epithelium is totally permeable to mannose.

We shall now report some experiments made with *mutually isomeric disaccharides*: saccharose, maltose and lactose.

[1]) ELSE HIRSCHBERG. Zeitschr. f. physiol. Chemie, **100**, (1918).

These experiments seemed of importance because, amongst other reasons, their molecules are larger than those of the monosaccharides already considered. If the permeability was in connection with this size it would probably appear that the glomerulus epithelium was impermeable to the dissacharides.

E. Saccharose.

To estimate the quantity of saccharose in the perfusion liquid and in the urine, 0.1 cc. of the liquid was heated to 37° C. during 1½ hours with 0.15 cc. hydrochloric acid 1 : 1 and the reduction of the solution thus obtained determined.

Experiment 29 (July 17).
The perfusion liquid contains 0,1 % cane sugar.
After inversion it causes a reduction of 0,1275 %.
0,1 c.c. urine of right kidney after inversion causes 0,13 % reduction.
0,1 c.c. urine of left kidney after inversion causes 0,1325 % reduction.
Retained by right kidney; 0,1275—0 13 = **0.**
Retained by left kidney: 0.1275—0,1325 = **0**

Result: all the cane sugar has passed through.

Experiment 30 (July 17).
The same perfusion liquid as in exp. 29.
Reduction 0,1 c.c. urine of right kidney after inversion 0,1125 %.
Reduction 0,1 c.c urine of left kidney after inversion 0,095 %.
Retained by right kidney: 0,2275—0,1125 = **0,015** %.
Retained by left kidney: 0,1275—0,095 = **0,032** %.

Here follows a table in which several experiments are summarised.

There can be no doubt that the glomerulus epithelium has retained saccharose, either as such or in the form of glucose which has then been formed through the splitting of saccharose in the glomerulus epithelium, while the laevulose has passed into the urine. This latter alternative is of no great probability.

F. Maltose.

Experiment 35 (July 16).
In the suitable perfusion liquid with 0,285 % $NaHCO_3$, 0,15 % maltose is dissolved.
0,1 c.c. perfusion liquid: reduction 0,0825 %.
0,1 c.c. urine of right kidney: reduction 0,07 %.
0,1 c.c. urine of left kidney: reduction 0,07 %.
Retained by each kidney: 0,0825—0,07 = **0,0125** %, thus hardly any at all.

Experiment 36 (July 16).
The same perfusion liquid as in exp. 35.
0,1 c.c. urine of right kidney: reduction 0,0875 %.
0,1 c.c. urine of left kidney: reduction 0,0625 %.
Retained by right kidney: 0,0825—0,0675 = **0,015** %.
Retained by left kidney: 0,0825—0,0625 = **0,02** %.

Retention capability of kidney for saccharose.
Experiments of September 17—23 1918.

Reduction perfusion liquid containing ± 0.1 % saccharose		Reduction urine of right kidney		Retained by right kidney	Reduction urine of left kidney		Retained by left kidney
Previous to inversion	after inversion	Previous to inversion	after inversion		Previous to inversion	after inversion	
Frog A 0.01 %	0.13 %	0.0325 %	0.09 %	**0.043 %**	0.025 %	0.0825 %	**0.0475 %**
" B "			0.08	**0.05**		0.0775	**0.0525**
Frog A 0.015	0.125	0.02	0.0925	**0.0325**	0.02	0.0925	**0.0325**
" B "		0.04	0.0925	**0.0325**	0.03	0.0925	**0.0325**
Frog A 0.025	0.14	0.03	0.1025	**0.0325**	0.03	0.10	**0.04**
" B "	"		0.0875	**0.0525**		0.0825	**0.0575**
" C "	"		0.09	**0.05**		—	—

Experiment 37 (Sept. 26).
The perfusion liquid contains 0,15% maltose.
0.1 c c. perfusion liquid: reduction 0,095%.
0,1 c c. urine of right kidney: reduction 0,105%.
0,1 c c. urine of left kidney: reduction 0,11%.
Retained by each kidney: *nothing.*

Experiment 38 (Sept. 26).
The same perfusion liquid as in exp. 37.
0,1 c.c. urine of right kidney: reduction 0,1%.
0,1 c.c. urine of left kidney: reduction 0,105%
Retained by each kidney: *nothing.*

Experiment 39 (Sept. 26).
The same perfusion liquid as in exps. 37 and 38.
0,1 c c. urine of right kidney: reduction 0,0625%.
0,1 c c. urine of left kidney: reduction 0,0625%
Retained by each kidney: 0,095—0,0625 = **0,0325**%.

Experiment 40 (Sept. 27).
0,1 c c. perfusion liquid: reduction 0,08%.
0,1 c.c. urine of right kidney: reduction 0,065%.
0,1 c.c. urine of left kidney: reduction 0,0625%.
Retained by right kidney: 0,08—0,065 = **0,015**%.
Retained by left kidney: 0,08—0,0625 = **0,0157**%.

It is clear from all these experiments that the quantity of maltose retained is in any case extremely small, notwithstanding the fact that *this dissaccharide is built up from two molecules of glucose, and that the glomerulus epithelium is permeable to glucose to a very slight degree.*

G. Lactose and a mixture of glucose and lactose.

Experiment 41 (July 3).
0,2% Lactose is dissolved in the perfusion liquid.
0,1 c.c. of perfusion liquid: reduction 0,14%.
0,1 c.c. urine of right kidney: reduction 0,1375%.
0,1 c.c. urine of left kidney: reduction 0,14%.
Retained by right kidney: 0,14—0,1375 = **0,0025%**.
Retained by left kidney: 0,14—0,14 = **0**.

Experiment 42 (July 3).
0,1 c.c perfusion liquid: reduction 0,11%.
0,1 c.c. urine of right kidney: reduction 0,11%.
0,1 c.c. urine of left kidney: reduction 0,1075%.
Retained by right kidney: 0,11—0.11 = **0**.
Retained by left kidney: 0,11—0,1075 = **0,0025%**.

Here again the kidney has retained no, or very little, lactose.

Experiment 43 (July 3).
The same perfusion liquid as in exp. 42.
0,1 c.c. urine of right kidney: reduction 0,1075%:
0,1 c.c. urine of left kidney: reduction 0,1075%.
Retained by each kidney: 0,11—0,1075 = **0,0025%**.

Here again neither of the kidneys retained lactose.

Experiment 44 (Juli 4).
0.1 c.c. perfusion liquid: reduction 0,14%.
0,1 c.c. urine of right kidney: reduction 0.1450%.
0,1 c.c urine of left kidney: reduction 0,1325%.
Retained by right kidney: 0,14—0,1450 = **0**.
Retained by left kidney: 0,14—0,1325 = **0,0075%**.

Lactose has thus been retained by neither of the kidneys.

From this we may draw the conclusion that the glomerulus epithelium allows the lactose to pass altogether, although it is built up from glucose and galactose, of which compounds the former is retained to a large degree, and galactose as well, although less.

From a theoretical as well as from a clinical point of view it seemed of importance to investigate how the kidney would behave towards a mixture of lactose and glucose.

From these experiments we learn that the retention of glucose by the kidney is not influenced by lactose. The latter is passed while glucose is retained to the same degree as when there was no lactose present.

This result is in accordance with the use which for a

Retention capability of kidney for a mixture of 0.1 % glucose and 0.1 % sacch. lactis (lactose).
Experiments of September 24—26.

Reduction perfusion liquid	Reduction urine of right kidney	Retained by right kidney	Reduction urine of left kidney	Retained by left kidney
Frog A 0.1575 / 0.16	0.0825 / 0.0825	**0 0765 %**	0.0825 / 0.0825	**0.076 %**
Frog B „	0.09 / 0.095 } 0.0925	**0.065 „**	0.095 / 0.095 } 0.095	**0.065 „**
Frog C „	0.09	**0.0675 „**	0.0925	**0.065 „**
Frog D „	0.1	**0.06 „**	—	—
Frog A 0.16 %	0.096	**0.064 „**	0.104	**0.056 „**
Frog B „	0.10	**0.06 „**	0.10	**0.056 „**
Frog C „	0.104	**0.056 „**	0.094	**0.066 „**
Frog D „	0.096	**0.064 „**	0.10	**0.060 „**

considerable time has been made of lactose for clinical use to estimate the validity of kidneys and which is founded on the consideration that the healthy kidney easily passes lactose.

We thank Mr. R. ROELINK for his able assistance during this research.

Summary and Conclusion.

1. The fact, now again affirmed, that, when we pass a RINGER'S solution to which glucose has been added, through the kidney, this is retained by the glomerulus membrane, while salts, which are also crystalloids, are allowed to pass, has raised the question to what this contrast must be attributed.

2. In the first place we can think of the circumstance that glucose possesses a so much larger molecule, which could then impede the passage. If this hypothesis be correct then the disaccharides such as saccharose, maltose and lactose, which possess a still larger molecule ($C_{12}H_{22}O_{11}$) than glucose ($C_6H_{12}O_6$), would certainly not pass through. Experiments have however proved that the glomerulus epithelium is *permeable* to a large degree to these sugars, *even to raffinose* ($C_{18}H_{32}O_{16}$).
The permeability to lactose is perfect.

3. *Where the cause for the retention of glucose cannot be ascribed to the size of its molecule, we are bound to consider its structure or configuration.* There is the more occasion for doing this because its isomerics, laevulose and mannose, are allowed to pass altogether and galactose to a large degree, as has been proved by the experiments under discussion.

4. Glucose therfore occupies a unique position among the monosaccharides in regard to the glomerulus membrane. In other words *the glomerúlus membrane can distinguish glucose from the other monosaccharides in a manner that reminds of the relation of sugars and ferments*, in connection with which EMIL FISCHER used the well-known simile of a *lock and key*.

In any case these experiments are again *a new illustration of the doctrine of stereoisometrics*, but now not as has thus far been the case, through facts of chemical but of *physiological nature*, belonging to permeability.

5. Not without theoretical and clinical importance seems the fact that the capability for retention of glucose is not modified when glucose and laevulose are simultaneously present in the perfusion liquid. The two sugars are simply separated as by a filter: the glucose remains behind, the laevulose is passed. This also appears to be the case with a mixture of lactose and glucose: the lactose passes completely into the urine and the glucose is retained by the glomerulus epithelium to the same degree as when there was no lactose present.

Groningen, September 1918. *Physiological Laboratory.*