formed per 100 gm. liver were as follows: After 2 hours, 0.52 gm.; after 3 hours, 0.68 gm.; after 4 hours, 1.36 gm. The excretion of galactose in the urine shows many striking features and needs further investigation. The percentage of the absorbed galactose that is excreted increases more and more the longer the absorption proceeds, in spite of the fact that the rate of absorption remains constant. Thus, in one hour 27 per cent of the absorbed galactose appears in the urine, in two hours 41 per cent, in three hours 51 per cent and in four hours 60.5 per cent.

SUMMARY.

1. The rate of glycogen formation in the liver during the absorption of fructose is slightly greater than during the absorption of glucose and leads to a higher glycogen maximum.
2. The liver plays a larger role in removing fructose from the blood stream than glucose.
3. Large doses of insulin almost completely suppress the glycogen formation from fructose.
4. Galactose is very slowly converted into glycogen and is excreted to a large extent in the urine.

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The influence of insulin on the tolerance for intravenously injected glucose and fructose.

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It has been found previously[1] that non-fasting male and female rats during amytal narcosis show no glycosuria, when glucose is infused at a rate between 2.2 and 2.5 gm. per kilogram per hour. Woodyatt's[2] figure for the intravenous tolerance limit of rabbits, dogs and men was only 0.85 gm. glucose per kilogram per hour.

[1] PROC. SOC. EXP. BIOL. AND MED., 1925, xxii, 127.

[2] Woodyatt, R. T., Sansum, W. D., and Miller, R. M., *J. Am. Med. Assn.*, 1915, lxv, 2067.

It seemed, therefore, of interest to investigate whether insulin would be able to raise the high intravenous tolerance of rats. It has also been shown that the maximum rate at which glucose could be absorbed from the intestine was below the maximum rate at which glucose could be infused intravenously without causing glycosuria. It seemed desirable to study if this was also true for fructose.

EXPERIMENTAL.

The method used has been fully described in our previous paper.[1] The infusions were again made into the femoral vein and were extended from 1 to 3 hours. For the present experiments only male animals were used. They were fasted for 48 hours previously. The preliminary fasting period did not change the intravenous tolerance for glucose to any larger extent, as can be seen from the following data: Four rats received glucose at a rate of 2.2, 2.4, 2.5, and 2.5 gm. per kilogram per hour and showed no glycosuria, while 2 rats which were infused at a rate of 2.6 gm. per kilogram per hour, excreted sugar in the urine.

Insulin, in doses varying from 20 to 40 units, was injected subcutaneously 30 to 45 minutes previous to the start of the infusion, and the injection was repeated at the beginning of each new hourly infusion period. In 5 experiments with insulin a rate of infusion of 2.7, 2.9, 3.0, 3.0, and 3.4 gm. glucose per kilogram per hour failed to produce glycosuria. In 8 other experiments a rate of infusion of 3.0, 3.1, 3.2, 3.2, 3.2, 3.2, 3.4, and 3.6 gm. glucose per kilogram per hour was above the tolerance.

These data indicate that the intravenous tolerance of rats which received large doses of insulin is close to 3.0 gm. glucose per kilogram per hour. It will be noted that the effect of insulin is very slight. There is obviously a limit to the amount of glucose that can be metabolized in the body. Rats, with the aid of their own insulin production, almost reach this limit and, therefore, the injection of insulin from without does not raise the tolerance very markedly. Burn and Dale[3] used decapitated cats from which all the abdominal organs including the pancreas had been removed. From the amount of glucose that had to be infused intravenously in order to prevent the blood sugar from falling, they calculated the amount of sugar removed. This was, without insulin, approximately 0.15 to 0.2 gm. per kilogram per hour. The greatest observed rate of sugar disappearance during insulin

[3] Burns, J. H., and Dale, H. H., *J. Physiol.*, 1924, lix, 164.

action was approximately 0.8 gm. per kilogram per hour. The low initial sugar tolerance would indicate that the preparations were in a diabetic condition and hence the strong effect of insulin is not surprising.

The experiments with fructose showed that the intravenous tolerance limit was at a rate of 0.35 gm. per kilogram per hour. Insulin injections had no decided influence on the intravenous tolerance for fructose. The quantitative estimations of fructose in the urine were checked in most instances by the Seliwanoff reaction. The rate of absorption of fructose from the intestine was found to be close to 0.8 gm. per kilogram per hour.[4] Fructose was not excreted in the urine even if the absorption of this sugar from the intestine was allowed to proceed for 5 hours. Obviously, the intravenous tolerance for fructose is markedly below the rate at which this sugar is absorbed from the intestine. How could this discrepancy of the tolerance, when tested by the intravenous route and by the intestinal route be explained? There is evidence that the kidney threshold for fructose is very low. If fructose is absorbed from the intestine, it passes first through the liver, before it reaches the general circulation. The liver plays a very important role in removing fructose from the circulation, as is set forth in the preceding paper. When fructose is infused into the femoral vein, the liver cannot quickly enough intercept this sugar and the fructose concentration in the blood might easily rise above the kidney threshold. In order to test this possibility, fructose was infused into a mesenteric vein. In 6 rats the tolerance by this route was close to 0.7 gm. per kilogram per hour or almost as high as the rate of absorption of fructose from the intestine.

SUMMARY.

1. The intravenous tolerance of male rats, fasted previously for 48 hours, was close to 2.5 gm. glucose per kilogram per hour.

2. Large doses of insulin raised the tolerance to 3.0 gm. glucose per kilogram per hour.

3. The tolerance for fructose, when infused into the femoral vein, was close to 0.35 gm. per kilogram per hour.

4. The tolerance for fructose, when infused into a mesenteric vein, was between 0.6 and 0.8 gm. per kilogram per hour.

5. Insulin had practically no effect on the intravenous tolerance for fructose.

[4] *J. Biol. Chem.*, 1925, lxvi, 691.