equilibrium at the same rate and hence penetrate with equal rapidity into the liver cells.

3. The muscles are less permeable for sugar than the liver. The ratio blood sugar: liver sugar : muscle sugar, 3 minutes after the injection, is of the order, 100 : 87 : 37.

4. The different sugars investigated penetrate into the muscle cells at the same rate.

2858

The tolerance of rats for intravenously injected glucose.

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It has been found that rats absorb from the intestine 1.78 grams glucose per kilogram body weight per hour without showing glycosuria. Since, also, equal amounts of sugar were found to pass from the intestine into the blood stream in equal periods of time, the absorption is comparable with a continuous intravenous infusion at a constant rate. Woodyatt, Sansum and Wilder[1] determined the glucose tolerance of normal rabbits, dogs and men by the continuous intravenous infusion method. They found that if glucose was infused at a rate of 0.85 gram per kilogram an hour, no glycosuria was produced, even if the infusion was extended over many hours. This is obviously a much lower tolerance than that observed on rats during intestinal absorption. There seemed to be two explanations possible. Either the rat has a higher glucose tolerance than rabbit, dog or man, or, the glucose tolerance, when tested by the intestinal route, is higher than when tested by the intravenous route. In order to see which of the two explanations is correct the sugar tolerance of rats was tested by the intravenous infusion method.

Experimental.

Non-fasting male and female rats were used. The experi-

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

ments could not be made without general anesthesia. Fortunately, amytal (iso-amy-ethyl barbituric acid) is a narcotic which is known to have no effect on carbohydrate metabolism, an observation which we have verified on previous occasions. A 2 per cent solution of amytal was made. Seven and five-tenths to 8 mg. per 100 gram body weight, injected intraperitoneally, produced a very satisfactory narcosis.

The infusions were made into the femoral vein. The device used to secure a constant, very slow flow of the sugar solution from the burette was that described by Burn and Dale.[2] A 10 cc. burette, graduated in 0.02 cc., was used and readings were taken every 2 minutes. The rate of infusion could be kept constant within 0.02 cc. as is shown by the following figures. Rat No. 6 of Table I was infused with an 8.2 per cent glucose solution, 4.08 cc. being delivered from the burette in 1 hour. The burette readings in cc. in 2 minute intervals, were as follows: 0.13, 0.13, 0.14, 0.13, 0.13, 0.14, 0.13, 0.13, 0.13, 0.13, 0.14, 0.13, 0.14, 0.14, 0.15, 0.14, 0.13, 0.14, 0.14, 0.14, 0.15, 0.15, 0.14, 0.14, 0.13, 0.13, 0.13, 0.14, 0.13, 0.13.

After the infusion had been kept up for 1 hour a small opening was made in the abdominal wall and the bladder pressed out gently. At the same time 0.2 cc. of blood were collected from the other femoral vein. In most instances the infusion was extended for 1 or 2 more hours.

The urine was treated with Lloyd's reagent in order to remove interfering substances and the sugar was determined by the Hagedorn and Jensen method. Rats fasted for 48 hours excrete a urine which contains 0.35 mg. reducing substances per 100 grams body weight per hour. It is doubtful whether these reducing substances are actually sugar. During the absorption of glucose from the intestine, rats excrete 1.36 mg. reducing substances per 100 gram body weight per hour and have a blood sugar ranging from 0.170 to 0.203. An excretion of more than 2 mg. reducing substances per 100 gram body weight per hour, which coincides with a blood sugar concentration above 0.200, was taken as indicating glycosuria.

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[2] Burn, J. H., and Dale, H. H., *J. Physiol.*, 1924, lix, 164.

TABLE 1.

The intravenous tolerance of rats during amytal narcosis. An excretion of more than 2 mg. of sugar per 100 gm. body weight per 1 hour indicates glycosuria.

No.	Weight and sex	Length of infusion period	Percentage of glucose solution	CC. infused	Glucose per 100 gm. body weight per 1 hour	Blood sugar	Sugar excreted per 100 gm. per 1 hour	Rate of infusion below or above tolerance
	gm.	Min			gm.	mg.	mg.	
1	F. 132.5	90	8.00	2.02	0.081	—	0.37	below
2	M. 131.4	60	7.55	1.52	0.087	—	0.57	below
		60	7.55	2.05	0.118	143	0.77	below
3	M. 146.8	60	9.35	2.15	0.137	167	0.94	below
4	M. 126.9	54	9.25	3.09	0.250	215	2.37	just above
5	F. 128.5	60	9.25	4.88	0.351	337	20.85	above
		60	Infusion was stopped			151	5.56	—
6	F. 126.6	60	8.20	4.08	0.264	254	8.87	above
		54	8.20	3.90	0.252	315	32.60	above
7	M. 152.7	60	9.30	3.87	0.235	201	1.95	below
		60	9.30	3.90	0.237	209	1.94	below
8	M. 136.4	80	9.00	4.44	0.219	—	0.99	below
9	F. 141.9	60	14.85	1.97	0.206	152	1.00	below
		60	14.85	2.61	0.272	—	14.30	above
		60	14.85	2.46	0.257	376	31.14	above
10	F. 146.2	60	15.05	2.16	0.222	—	8.88	above*
		60	15.05	2.19	0.225	266	13.95	above*
11	M. 155.2	60	15.20	1.82	0.178	147	0.77	below
12	M. 153.6	60	15.20	2.24	0.221	—	1.55	below
		60	15.20	2.12	0.210	—	1.22	below
		60	15.20	2.27	0.224	151	1.10	below

*Vaginal smears showed that this rat was at the height of oestrus.

It will be seen from Table 1 that the intravenous tolerance of rats is between 2.2 and 2.5 gram glucose per kilogram body weight per hour. This is a tolerance of about two and one half times as high as that found by Woodyatt on rabbits, dogs and men. Rat No. 10 falls out of the series. This animal was at the height of oestrous, as was revealed by vaginal smears. Whether this is a mere coincidence or whether the glucose tolerance is lowered during oestrous can only be decided after a larger number of animals has been examined.

The intravenous tolerance is a measure of the maximum rate at which glucose can be metabolized in the body. It is an interesting physiological fact that the maximum rate at which glucose can be absorbed from the intestine is markedly below the intra-

venous tolerance rate. Rats, fasted for 48 hours, absorb glucose at a rate close to 1.78 gram per kilogram per hour or 1.54 gram per kilogram per hour if based on the body weight before fasting.

Summary.

The intravenous tolerance of non-fasting rats during amytal narcosis is between 2.2 to 2.5 gram glucose per kilogram body weight per hour.

2859

Significance of change in oxygen absorption after insulin in normal rabbits.

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Respiration experiments by the closed circuit method employing an apparatus which gave perfect control checks are reported upon twenty fasting rabbits. Seventeen of these received an injection of insulin subcutaneously which reduced the blood sugar an average of 62 mg. in two hours. One of two basal periods of 45 to 60 minutes each were obtained before giving insulin, and two periods of at least 45 minutes each, in all cases, and four periods in five of the cases, were obtained after insulin. There was no rise but often a fall in respiratory quotient during the first period up to one hour after insulin. In the second period, however, the average respiratory quotient was 0.98 in contrast with the average of 0.74 in the pre-insulin period. In the third period after insulin, the respiratory quotient returns to the normal level and persists also in the fourth period. The oxygen absorption on the average rises the first hour and falls considerably below the pre-insulin level the second hour. The CO_2 elimination rises the first hour and the average for all the animals rises still farther the second hour. But the average for the five animals studied longest the CO_2 does not rise farteher in the second period, and falls