In such perfusion systems the true blood sugar, blood non-fermentable reducing substance, urea and ammonia nitrogen and lactic acid all increased. Both the liver glycogen and free sugar showed substantially lower values at the close of the perfusions. The blood fatty acids were constant.

In one experiment the total carbohydrate of the perfusion system increased; in 4 a decrease occurred; the rest were unaltered. The 5 double perfusions showed a marked constancy of the total carbohydrate content, all values at the close of the perfusion being within 7% of the initial value. The total fatty acids were fairly constant, 2 experiments showing an increase and 5 a reduction.

The data obtained do not substantiate the hypothesis that carbohydrate is produced at the expense of fat.

4855

Absorption of Epinephrine from the Subcutaneous Tissue of the Rat.

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In a previous investigation of the carbohydrate metabolism of rats a dose of 0.2 mg. of epinephrine per kilo was injected subcutaneously.[1] This made it desirable to find out whether such a dose produced a rise in blood pressure. The animals received amytal intraperitoneally, followed by the injection of a small amount of urethane in order to steady the blood pressure. A glass cannula was tied into the carotid artery and connected with a mercury manometer of small dimensions. Heparin was used as anticoagulant in the cannula. Intravenous injections were made into a femoral vein and were timed by the beats of a metronome. In 4 experiments of the type shown in Fig. 1 the minimal pressoric rate of intravenously injected epinephrine was established before the subcutaneous injection was made. It was found that an intravenous injection of 0.001 mg. per kilo per minute was always followed by a rise in blood pressure, while a subcutaneous injection of 0.2 mg. per kilo made shortly afterwards had no effect on blood pressure. This result permits the conclusion that the absorption of epinephrine from the subcutaneous tissue of the rat proceeds at a rate less than 0.001 mg.

[1] Cori, C. F., and Cori, G. T., *J. Biol. Chem.*, 1928, lxxix, 309, 321, 343.

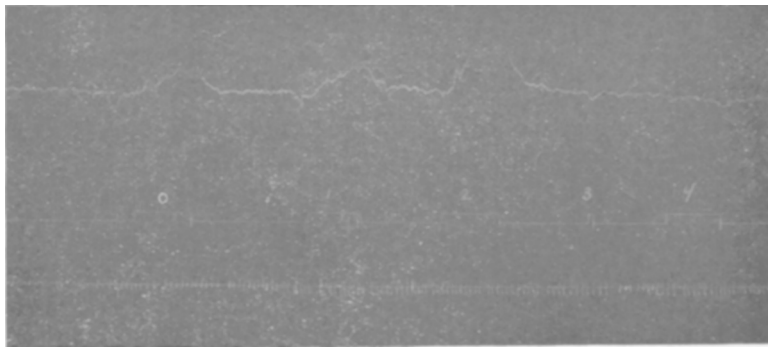

FIG. 1.

Male rat under amytal-urethane anesthesia. Weight 200 gm. Time in 5 seconds at base line of mercury manometer.

(0) 0.25 cc. of 1 to 1,250,000 injected in 1 minute or 0.001 mg. epinephrine per kilo per minute.

(1) 0.25 cc. of 1 to 835,000 injected in 1 minute or 0.0015 mg. epinephrine per kilo per minute.

(2) 0.25 cc. of 1 to 625,000 injected in 1 minute or 0.002 mg. epinephrine per kilo per minute.

(3) 0.04 mg. epinephrine injected subcutaneously.

(4) 0.25 cc. salt solution injected in 1 minute.

per kilo per minute. How much less the rate is can of course not be judged from these experiments. Since a subcutaneous injection leads to hyperglycemia and since an intravenous injection of 0.0002 mg. per kilo per minute is the smallest amount which still produces hyperglycemia in rats, the rate of absorption of epinephrine from the subcutaneous tissue must be above this figure.

In order to ascertain how long epinephrine remains in the subcutaneous tissue, chemical determinations were carried out. Rats of 250 to 300 gm. of body weight were anesthetized with amytal. A subcutaneous injection of 0.1 mg. of epinephrine was made on the dorsal side of either the hind or foreleg. At various time intervals after the injection the "depot" of epinephrine, often plainly visible in the loose connective tissue under the skin, was excised. Bleeding was avoided. The whole region of the injection was rinsed with water. After grinding and extracting the small bits of tissue in a mortar and removing traces of protein by means of the Folin-Wu precipitation, the epinephrine content was determined by means of the Folin-Cannon-Denis method.[2] Great accuracy cannot be claimed, because only 80% of the amount injected could be recovered from the subcutaneous tissue of dead animals immediately after the injection. This immediate loss may be due partly to oxidation upon exposure to air, because the injected fluid in the subcutaneous tissue

[2] Folin, O., Cannon, W. B., and Denis, W., *J. Biol. Chem.*, 1912, xiii, 477.

assumes a purplish tinge when the skin is cut. A considerable amount of epinephrine is also lost when it remains for some time under the skin of dead animals, as is shown in Table I. This indi-

TABLE I.

Recovery of epinephrine from subcutaneous tissue of rat.

0.1 mg. was injected in each case. The values are expressed in % of the amount injected.

	Immediately	Ave.	After 1 hour	Ave.	After 2 hours	Ave.	After 3 hours	Ave.
Dead rats	79; 83; 80; 78	80	65; 60; 61	62	38; 45; 40	41		
Live rats	78; 84; 81; 80	81	47; 51; 43; 58	50	32; 49; 20; 25	32	17; 18; 9; 16; 11	14

cates that the disappearance of epinephrine from the subcutaneous tissue of live animals depends not only on absorption into the blood stream but also on local destruction. The data of Table I can therefore not be used for a calculation of the rate of absorption of epinephrine into the blood stream. It is concluded from the experiments in Table I that epinephrine is still present in the subcutaneous tissue 3 hours after the injection and this direct chemical evidence agrees well with the observation that the hyperglycemia persists for at least 3 hours.

4856

The Influence of Constant Intravenous Injection of Epinephrine on Blood Sugar of Rats.

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The aim of the present experiments was a determination of the minimal rate of injection of epinephrine which causes a rise in blood sugar of rats. Similar experiments on rabbits could be made without anesthesia but this was unfortunately not possible on rats. Though amytal anesthesia has little effect on the blood sugar of rats, as may be seen in Table I, it undoubtedly lowers the carbohydrate tolerance. Animals in the postabsorptive state with a high liver glycogen content on account of previous carbohydrate feeding were used. 0.1 to 0.2 cc. of blood was withdrawn from a femoral vein by means of a syringe at the beginning and end of the injection. A