the largest dose employed by Korányi and Szent-Györgyi. A slight decrease in ketonuria appears when only 7.55 mg. of glucose is given while a dose of 37.8 mg. caused an average decrease of acetone-bodies in the urine from 33.7 mg. per 100 gm. rat in the control tests to 19.4 mg. There was no evidence of diarrhea in any experiments nor of other toxic effects ascribable to the succinic acid. It is concluded that succinic acid is ineffective in preventing the ketonuria in fasting rats previously fed a high fat diet when this acid is administered in amounts far in excess of the quantity of glucose required to bring about a marked lowering in the excretion of the ketone bodies.

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Effect of Feeding and Fasting on Sugar Utilization of Eviscerated Rabbits.

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In an earlier paper by one of us[1] it was shown that the eviscerated rabbit utilizes glucose at a rate that is quite definite and fairly constant for a given animal. The rate varies, however, between different rabbits. The suggestion was made in that paper that this variation was due to the differences in the degree of fasting to which the different animals had been subjected prior to operation and that the effect of fasting is to reduce the utilization rate of the eviscerated animal. The work here reported was planned to investigate this relationship. The same technique was used as in the previous work. Essentially this consisted of measuring the rate at which glucose had to be administered to the eviscerated rabbit to maintain the blood sugar at a constant normal level.

Frequent blood sugar determinations served as a guide to the injection rate; if the blood sugar level rose the rate would be diminished, and *vice versa.* The determination was started 3 hours after completion of the operation and continued for 4 hours thereafter. Only those animals that sat up in normal posture and had normal righting reflexes after operation were used. The animals were also tested for kidney function by injecting phenol red after the opera-

[1] Drury, D. R., *Am. J. Physiol.*, 1935, **111**, 289.

TABLE I.
Rate of Utilization of Glucose in mg. per kilo per hour.

Fasted	Fed
70	137
81	175
85	191
97	205
110	208
110	209
112	221
133	228
138	236
166	246

tion. Any animals not secreting this dye were eliminated from the series. Ten rabbits were used in each of the two groups—one group fed to the time of operation, and the other fasted 4 to 6 days prior to operation. The glucose utilization rates are given in Table I.

The rates are given for the period between the 3rd and the 7th hours after operation. In this way we could be sure that we were not getting any anesthetic effect. However, the rate varies very little, as is shown in the previous paper.

The last 3 animals of the fasted group had rates of less than 110 mg. during the first 5 hours, after which they increased. They had excreted phenol red by that time so we felt they should be included in the series although kidney action may have stopped at that time. Despite the inclusion of these, there is undoubtedly a difference in the rate of the two types of preparation. The average for the fed group is 206 and that for the fasted 110. There is overlapping of individual rates in the two groups in just one case.

Is this difference due to insulin? It is reasonable to suppose that in a fed animal the islet tissue is more active than in a fasted one and although the operation involves complete removal of the pancreas there would probably be more insulin circulating in the fed than in the fasted, immediately after operation. It seemed necessary, therefore, to determine the duration of action of insulin in the eviscerated preparation and we investigated this in a separate series of animals. After evisceration we determined the glucose utilization rate. We then injected insulin intravenously and redetermined the utilization rate during successive periods thereafter.

The following is a typical protocol:

Rabbit *fasted 6 days prior to operation.*

9:45 A.M.	Operation completed.
11:15-12:16	Glucose utilization rate 101 mg. per kilo per hr.
12:40	0.025 U insulin intravenously.
12:55-1:31	Glucose utilization rate 172 mg. per kilo per hr.
1:31-2:34	" " " 97 " " " " "
2:34-3:58	" " " 69 " " " " "

This procedure was carried out on 9 other rabbits. The results are given in Table II.

TABLE II.

Days Fasted	Utilization rate before insulin	Dose of insulin units	Utilization rate immediately after insulin	Utilization rate later	Time after insulin of 2nd determination hrs.
5	110	.10	170	133	2
4	94	.10	185	138	3½
5	82	.10	188	108	6½
6	67	.050	150	111	2
4	107	.050	229	144	3½
6	53	.050	143	80	2
5	—	1.00	249	150	4½
Not fasted	211	.10	357	242	4½
’’ ’’	176	.10	285	174	2½

It is apparent from these results that the effect of these doses of insulin is largely over in 3 or 4 hours. The higher glucose utilization rates which we obtained in fed animals for 7 hours after operation could not have been due to insulin which was in the body at the time of operation. The main effect would have worn off long before that. It might be claimed that a very large amount of insulin was present in the fed animals at the time of operation; but this would have given a very high utilization rate in the first 2 hours after evisceration. To test this we injected 5 units into such a rabbit and obtained a utilization rate of over 600 mg. per kilo per hour during the first 2 hours after injection. As stated previously in this paper and as shown in the previous article[1] the utilization rate in fed animals immediately after evisceration is not that high but is the same as that shown 5 to 7 hours after that. We cannot then explain this high rate of glucose utilization by fed rabbits after evisceration as an insulin effect.

It is more probable that the difference between the glucose utilization of the fasted and fed animals is due to action of some other gland such as thyroid, pituitary or adrenal. There is much experimental work which suggests that the secretions of these glands have an action on glucose metabolism and that their action is more lasting than insulin. Thus Greeley[2] finds that the increased utilization of glucose in hypophysectomized rabbits does not occur until 20 hours on an average after removal of the gland. This would suggest a glucose-utilization inhibiting hormone of the pituitary which has quite a prolonged action.

2 Greeley, P. O., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 1070.

We may conclude then that glucose metabolism is constantly modified by at least 2 hormonal mechanisms. The agent of the first of these is insulin, powerful but acting relatively a short time (2 to 3 hours for a given medium dose). The other is a mechanism having a longer duration. The insulin mechanism may be considered as taking care of immediate needs, responding very quickly to eating of food or rise in blood sugar but having a relatively transitory effect for one given dose. The other mechanism is more slowly produced but acts during a prolonged period.

Summary. The rate of utilization of glucose by the eviscerated preparation is affected by feeding and fasting prior to operation. The tissues of the fed animals utilize glucose at a rate double that of the fasted.

This increase cannot be due to insulin.

We wish to acknowledge our appreciation to the Eli Lilly Company for the gift of insulin used in these experiments.

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Recovery from the Anemia Caused by a Diet Deficient in Vitamin K.

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The purpose of this investigation was to ascertain whether the restoration to normal of the clotting time of chicks on a diet deficient in Vitamin K was accompanied by a cure of the existing anemia. This anemia has been observed by Dam,[1] and Holst and Halbrook,[2] but thus far no extensive investigations on the regeneration of hemoglobin have been made. The changes toward normal produced by the administration of minute quantities of a Vitamin K concentrate were so rapid that it seemed desirable to report our results.

The chicks used in our experiments were one-day-old white Leghorns hatched from eggs laid by hens which had been fed a diet relatively free from Vitamin K. They were raised in battery brooders and had free access to food and water. The basal diet used in these experiments was that of Almquist[3] with only minor

[1] Dam, H., *Biochem. Z.*, 1929, **215**, 475.

[2] Holst, W. F., and Halbrook, E. R., *Science*, 1933, **77**, 354.