Sahli (100 = 14.5 gm. per 100 cc.). R. B. C. 2.24 million, W. B. C. 5,800. Smear showed anisocytosis with many macrocytes, considerable poikilocytosis, no obvious reduction of platelets. The plasma bilirubin was not increased above normal. Reticulocytes 0.7%. The gastric contents showed no free hydrochloric acid.

Diagnosis: Pernicious anemia, with subacute combined degeneration of spinal cord and moderate anemia, with cord symptoms progressing more rapidly than the anemia. The course under treatment with kidney diet is best shown in Fig. 2. The kidney was given for a period of 27 days, during which time the red cell count rose from 2.2 to 3.8 millions, the hemoglobin from 65 to 79%. The leucocytes increased from 5,800 to 10,000 per cu. mm. The percentage of reticulocytes began to increase on the 3rd day and reached a maximum of 7% on the 7th and 8th days, reaching normal again of the 17th day of the diet. As the reticulated cell count fell the total red cell count rose. During the course of observation the spinal cord symptoms grew worse, if anything, though the general condition of the patient improved.

Two patients with pernicious anemia had remissions induced by giving a diet with 250 gm. of kidney daily. The relative values of kidney and liver feeding can be determined only on comparison of a long series of cases.

[1] Whipple, G. H., and Robscheit-Robbins, F. S., *Am. J. Physiol.*, 1925, lxxii, 395, 408, 419, 431; 1927, lxxix, 260, 271.

[2] Minot, Geo., and Murphy, Wm. P., *J. Am. Med. Assn.*, 1926, lxxxvii, 47; *Bost. Med. and Surg. J.*, 1926, cxcv, 410.

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Influence of Epinephrine on Carbohydrate Metabolism of Fasting Rats.

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A brief report[1] has been made concerning the influence of epinephrine injections on the utilization of ingested glucose in rats, and of other experiments which dealt with the metabolic changes brought about by epinephrine in post-absorptive rats, rich in glycogen. In both the sugar fed and the post-absorptive rat, there was a diminution in muscle glycogen, which indicates that epinephrine has also

a point of attack in the peripheral tissues. The present experiments were made on rats fasted previously for 24 hours. After such a fasting period, the glycogen content of the rats is very constant, a point which has been established in previous work. It is also important to mention that the glycogen of the rat undergoes only a slight diminution, between the 24th and the 48th hour of fasting. This is shown in the following table, which has been calculated from previous experiments:

Glycogen Content (in mg. per 100 gm. rat)

	liver	body	total	
24 hour fasting	7	136	143	(average of 16)
48 hour fasting	10	111	121	(average of 21)
Difference	+3	—25	—22	

The present control series, which is included in the above average, showed the following values:

glycogen in liver (mg.)	3.0,	4.2,	9.9,	7.1.
glycogen in body (mg.)	123.0,	129.8,	144.1,	114.9.

In the experimental rats the average R. Q. of a 3 hour metabolism fore period, was 0.715. After the subcutaneous injection of 0.02 mg. of epinephrine, there was no perceptible rise in the R. Q., the average for a 3 hour period being 0.715. The O_2 consumption rose markedly in each experiment, with an average increase of 18.1%. The rats were killed 3 hours after the injection (after the same fasting period as the control rats) and the glycogen was determined in the liver and the rest of the body. The following values, calculated per 100 gm. of body weight were obtained:

glycogen in liver (mg.)	28.4,	50.2,	45.9,	43.1,	32.6,	51.8.
glycogen in body (mg.)	58.4,	81.9,	69.5,	76.5,	62.8,	77.2.

It will be seen from a comparison of these values with the values obtained on merely fasted controls, that there is a marked increase in the liver glycogen in every experiment. At the same time, the glycogen in the body is found to have decreased, on an average, a little more than the liver glycogen has increased (—57 mg. against +36 mg.).

An increase in liver glycogen, after epinephrine injections into fasting rabbits, has been observed by Pollak[2] and by Kuriyama.[3] In the latter author's work are included some determinations of muscle glycogen. On an average, the muscle glycogen in his injected rabbits is lower than in the controls.

The possibility suggests itself that the glycogen mobilized in the peripheral tissues (mainly muscles), has been deposited as liver glycogen. If the disappearing muscle glycogen (57 mg.) were oxidized, the R. Q. would be between 0.73 and 0.74. It is now definitely known, especially from Mann's[4] work on dehepatized dogs, that muscle glycogen does not contribute blood sugar after epinephrine injections or under any other conditions. When muscle glycogen is split, the presence of the glycolytic ferment causes an immediate change of the split products into lactic acid (Lohmann[5]). The course of events, in 24 hour fasting rats, would then be that epinephrine mobilizes muscle glycogen, and that lactic acid enters the blood stream and is carried to the liver, where it is deposited as glycogen. (In post-absorptive rats, which are rich in glycogen, the muscle glycogen mobilized by epinephrine is almost completely oxidized.)

Before considering this assumption further, it was necessary to determine whether lactic acid is able to form liver glycogen. 3.5 cc. of a 6% solution of d-lactic acid* (unneutralized) was fed by stomach tube to 24 hour fasting rats. The animals showed neither toxic symptoms, nor lesions of the stomach and intestines. They were killed after 3 hours and the liver glycogen and absorption was determined. The following values (calculated per 100 gm. of body weight):

glycogen in liver (mg.) 57.2, 50.8, 32.1, 24.0, 59.9, 34.3,

reveal that liver glycogen is deposited during d-lactic acid absorption. One possible obstacle in the explanation here proposed has therefore been eliminated. An older observation on rabbits[6] gains special significance in the light of the present work. It was found that epinephrine injections caused a strong increase in blood lactic acid. An increase has also been found, to a lesser extent, in cats and in the rats used for the present investigation.

Though the explanation here proposed seems well supported, the possibility cannot be excluded that the liver glycogen accumulating during epinephrine action is derived from non-carbohydrate (protein) sources. If this were the case, one would have to assume that the glycogen disappearing in the rest of the body, is oxidized. The combination of the 2 processes (anabolic and catabolic) would also result in the R. Q. actually observed.

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* For the preparation of d-lactic acid, we are indebted to Dr. Peterson of the College of Agriculture, University of Wisconsin.

[1] Cori, C. F., and Cori, G. T., PROC. SOC. EXP. BIOL. AND MED., 1927, xxv, 66.

[2] Pollak, L., *Arch. exp. Path. u. Pharm.*, 1909, lxi, 166.

[3] Kuriyama, S., *J. Biol. Chem.*, 1918, xxxiv, 269.

[4] Mann, F. C., and Magath, T. B., *Am. J. Physiol.*, 1925, lxxii, 629.
[5] Lohmann, K., *Biochem. Z.*, 1926, clxxviii, 444.
[6] Cori, C. F., *J. Biol. Chem.*, 1918, xxxiv, 269.

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Urea and Creatinine Concentration in the Blood; a Statistical Study.

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The relationship between the accumulation of urea and creatinine in the blood has held considerable interest since Myers[1] reported evidence which tended to show that in nephritis urea increased in the blood before creatinine did. It seemed probable that data obtained in a clinic where most of the patients were undergoing treatment for chronic diseases might show some relationships between these compounds which would be of value. Results obtained over a period of eight years were therefore tabulated and studied. All cases where analyses of both compounds in the same sample of blood were available were utilized. Such studies were not made on all patients, but blood was obtained from most of those in whom the presence of renal insufficiency was suspected. During the greater part of the period creatinine determinations were done on all specimens where a urea nitrogen concentration greater than 20 mg. per 100 cc. was found, but were generally omitted when the concentration was lower than this figure. During the earlier part of the period both substances were determined in most specimens submitted. The method of Folin and Wu[2] was used for the creatinine determination. During the last two years an unpublished method of Folin and Sumner was used for determining the urea nitrogen; before that time the technique recommended by Van Slyke and Cullen[3] was followed.

The average results are given in the table. The two halves of the table are alike except that in the right hand portion normal and slightly increased values are given at smaller intervals than in the left hand part. It is evident that, except when the urea nitrogen concentrations were low, the urea and creatinine values tended to vary together. Holbrook and Haskins[4] have recently reported similar findings in a series of selected cases. When the urea nitrogen concentration was slightly increased the ratio between creatinine and urea was approximately the same as when the urea was mark-