TABLE II. Response of Male, Female, and Castrated Rats to Rations Deficient in Vit. B_{12}.

Ration	2 weeks' gain			
	Uncastrated males, g	Castrated males, g	Uncastrated females, g	Castrated females, g
Ration 1 (basal ration)	46.7 (10)*	47 (10)	43.8 (10)	42 (6)
Ration 2 (ration 1 + 25 μg vit. B_{12} per kilo ration)	57.7 (10)†	60 (10)†	63 (10)†	64.4 (6)†
Ration 3 (ration 1 + 2% 1:20 liver concentrate powder)	69.2 (10)†‡	64.4 (10)†	62.2 (10)†	71.3 (6)†

* Numbers in parentheses are number of rats fed that ration.
† Indicates differences compared to basal ration were significant at 1% level of probability.
‡ Difference between gains of uncastrated males fed ration 3 and those fed ration 2 was significant at 5% level of probability.

present in liver concentrate and not identical with vit. B_{12} is suggested.

Appreciation is expressed to Merck and Co., Rahway, N. J., for the crystalline vitamins and vit. B_{12}, to Lederle Laboratories Division, American Cyanamid Corp., Pearl River, N. Y., for folic acid, to Wilson and Co., Chicago, Ill., for liver concentrate, and to the Cerophyl Laboratories, Kansas City, Mo., for iodinated casein (Protamone).

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Metabolism of Plasma Substitute I. Dextran (Macrodex). (18870)

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The fate of dextran, unexcreted after intravenous infusion, is still undetermined. Bull and coworkers(1) report that it is not broken down by various animal tissues *in vitro*. Engstrand and Arberg(2) also have stated that dextran is not affected by tissue extracts, but is destroyed upon incubation with feces. They were able to recover 28% of infused dextran from the alimentary canal of the cat and 9% in the rabbit. We have attempted to confirm their results in 3 anesthetized dogs prepared as follows: (a) cannulae were placed in the bile duct and pyloric sphincter; (b) the upper end of the duodenum was tied off and a cannula placed in the lower end; (c) the upper end of the jejunum was tied off and a cannula placed in the ileo-caecal junction. The fluid from these areas was aspirated every 2 hours for 24 hours and each 2-hour sample was analyzed for dextran by the method of Hint and Thorsen(3). Less than 0.1% of 200 ml of 6% solution in physiologic saline infused, was found in any one of the regions cannulated. Failure to account for unexcreted dextran in the gastrointestinal tract led to study of the fate of this substance in the phlorizinized starved dog(4) to determine possible *in vivo* breakdown to dextrose.

Method. Mongrel dogs of both sexes were starved except for water. After 3 days, daily subcutaneous injections of 1 g of phlorizin suspended in 10 ml of olive oil, were begun and continued for the duration of the experiment (13-15 days). The animals were kept in metabolism cages and the urine collected every 24 hours. Complete collection was assured by catheterization. Dextrose in urine

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2. Engstrand, L., and Arberg, B., *Lancet*, 1950, v258, 1071.

3. Hint, H. C., and Thorsen, G., *Acta Chem. Scand.*, 1947, v1, 808.

4. Lusk, G., The Elements of the Science of Nutrition, 4th ed., Philadelphia, W. B. Saunders, 1928.

TABLE I. Changes in D/N Ratio after Infusion of 200 ml of 6% Solution of Dextran in Physiologic Saline.

Dog No.	Pre-infusion Avg	Range	24-48 hr post-infusion D/N
2	1.47	1.29-1.64	3.75
7	2.26	1.70-2.56	3.66
13	3.15	3.07-3.37	4.89
20	2.86	1.98-3.64	3.94
33	2.67	2.09-3.04	4.20
41	3.26	2.98-3.59	5.54*

* This figure represents the D/N ratio for 48-72 hr period following infusion.

was determined by the method of Fister(5). Dextran does not interfere with this test. The non-protein nitrogen was measured by micro-Kjeldahl digestion of a tungstic acid treated aliquot of the urine. When the dextrose/nitrogen (D/N) ratio became constant, (usually after 4-5 days of phlorizin), 200 cc of 6% dextran solution in normal saline (Macrodex) was infused intravenously, and studies were continued for 3 days.

Results and discussion. The results are summarized in Table I. In each instance there is a marked increase in the D/N ratio beyond the limits of the average value for the control period. In the starved animal, protein is being utilized as a source of energy by conversion to dextrose. When phlorizin is administered, resorption of the dextrose is prevented and a point of stabilization is reached where the ratio of dextrose in urine to non-protein nitrogen in urine becomes constant. If a substance is then administered that will alter nitrogen or glucose metabolism, the D/N ratio will be changed. The increase in D/N ratio 24-48 hours after the infusion of dextran, may be explained by one of the following mechanisms: (a) breakdown of dextran to glucose; (b) mobilization of glycogen to yield glucose; (c) conversion of the plasma protein to glucose.

Conant and coworkers(6), working with starved rats, showed that in 24 hours, liver glycogen decreased from 0.9% to 0.1%. Matthee(7), with phlorizinized rats and rabbits has shown that the glycogen very soon disappears from the liver. Lusk(8) has shown only 0.4 g liver glycogen in a meat-fed phlorizinized dog. It is therefore unlikely that the mobilization of glycogen could cause increase in D/N ratio in our phlorizinized animals.

The administration of dextran causes a decrease in plasma protein concentration(1,8). If the decrease of plasma protein is caused by dilution of the protein through the plasma expanding properties of the dextran(9), there should be no alteration in the D/N ratio. On the other hand, if this is a real loss of plasma protein, it should be metabolized similarly to the other tissue proteins and there should still be no change in the D/N ratio from the preinfusion value. It is concluded, therefore, that the change in D/N ratio we have measured in the phlorizinized dog following infusion of dextran, is due to the breakdown of dextran to dextrose.

Summary. Indirect evidence is presented to show that a portion of infused dextran ("Macrodex") is broken down to dextrose in the phlorizinized starved dog.

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