showing reaction at the interphase after 20 minutes was taken as the end point.

Results. As can be seen in the accompanying tables, the rate of destruction of the homologous antibody (Table I) and the heterologous antibody (Table II) was markedly different and fell within the ranges described by Glenny and Hopkins(3). There was no difference between the irradiated and the control animals. The anti-human serum titers were determined primarily to check the efficacy of this irradiation method and dosage in inhibiting antibody formation. Results in the 3 irradiated rabbits were positive in antigen dilutions of 1:5, 1:10, and 1:10 respectively; the 3 control animals were all positive in 1:1000 antigen dilution.

Summary and conclusions. X-irradiation in dosage of 300 r had no effect on the rate of destruction of passively transferred homologous or heterologous antisera given intravenously to rabbits 24 hours after irradiation. This x-ray dosage was sufficient, however, to decrease, but not totally prevent, the formation of antibody to the heterologous serum proteins.

Received September 20, 1950. P.S.E.B.M., 1950, v75.

Influence of Fasting on the Effect of Insulin on Glucose Oxidation.* (18238)

DOUGLAS R. DRURY, ARNE N. WICK AND EATON M. MACKAY.
From the Scripps Metabolic Clinic, La Jolla, and the Department of Physiology, University of Southern California, Los Angeles, Calif.

It has generally been believed that insulin increases the immediate oxidation of glucose and this is frequently stated in text books(1). However as Soskin and Levine(2) point out in their monograph, "this is without basis in fact." There has been no good experimental evidence that insulin will increase the oxidation of glucose until recently(3) when by using carbon^{14}-labeled glucose it was found that the old assumption is correct. Insulin actually does increase the oxidation of glucose by the extra-hepatic tissues to carbon dioxide and water. This report concerns the influence of fasting on the effect of insulin on glucose oxidation by the extra-hepatic tissues.

Experimental. The general plan of the experiments and the details of the methods used have been given elsewhere(3-6). After varying periods of fasting male rabbits (average weight 2 kg after evisceration) were eviscerated(7) and given an injection of a priming dose of carbon^{14}-labeled glucose so as to make the specific activity of the body glucose the same as the glucose to be used for the constant injection. With the aid of frequent blood sugar determinations the blood sugar was maintained at a normal level (70-130 and as near 100 mg % as possible) for 8 or more hours by the constant injection of carbon^{14}-labeled glucose. Ten units of insulin† were given intravenously each hour. Collection of the expired carbon dioxide was commenced immediately after the injection of the radioactive glucose.

Results. The data in Fig. 1 were calculated

* This investigation was supported in part by a research grant from the Division of Research Grants and Fellowships of the National Institutes of Health, U. S. Public Health Service.

1. Best, C. H., and Taylor, N. B., The Physiological Basis of Medical Practice. The Williams & Wilkins Co., Baltimore, 1943, p972.

2. Soskin, S., and Levine, R., Carbohydrate Metabolism. University of Chicago Press, p181.

3. Wick, A. N., Drury, D. R., Bancroft, R. W., and MacKay, E. M., *J. Biol. Chem.*, in press.

4. Wick, A. N., Drury, D. R., and MacKay, E. M., *Am. J. Physiol.*, 1950, v163, 224.

5. Drury, D. R., Wick, A. N., and MacKay, E. M., *Am. J. Physiol.*, in press.

6. Drury, D. R., Wick, A. N., Bancroft, R. W., and MacKay, E. M., *Am. J. Physiol.*, in press.

7. Drury, D. R., *Am. J. Physiol.*, 1935, v111, 289.

† We are indebted to Eli Lilly and Co. for generous supplies of (Iletin) insulin.

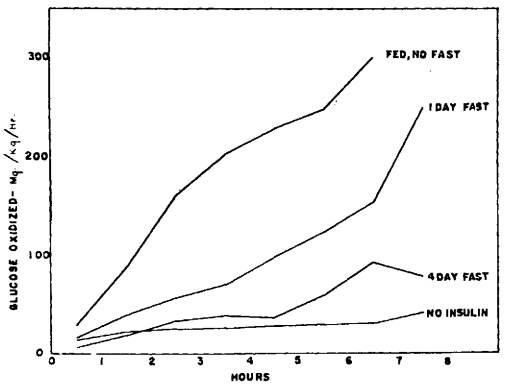

FIG. 1.

Influence of fasting on effect of insulin on glucose oxidation in the eviscerated rabbit. Three of the rabbits were given insulin. The rabbit which received no insulin had been fasted for one day.

from the specific activity (radioactive counts per minute per mg carbon) of the expired CO_2 and injected glucose. The rate of glucose oxidation increases rapidly with time after the completion of the evisceration and the simultaneous beginning of insulin administration. It is obvious that a single day of fasting greatly reduces the extent of insulin action on the rate and amount of glucose oxidized. A 4-day fast reduces the insulin action still more so that except for the last 3 of the 8 hours of observation the oxidation of glucose is little greater than when no insulin is given. When insulin is not given fasting has relatively little influence on the rate of glucose oxidation. The average glucose oxidation for the 8 hours of observation was with insulin and no fast, 199; 1-day fast, 114; 4-day fast, 52 and without insulin 30 mg per kg per hour. The usual effect of fasting(7,8) on glucose disappearance ("utilization") is noted. Glucose "utilization" with insulin and no fast was 660; 1-day fast, 540; 4-day fast, 258 and without insulin 112 mg per kg per hour.

Discussion. The literature on the influence of fasting and/or the diet upon sugar tolerance and the action of insulin is well reviewed by Lundbaek(9). Drury(7) and Bergman and Drury(8) have demonstrated the influence of fasting on the glucose "utilization" (glucose required to keep the blood sugar normal) of the eviscerated rabbit. Since these animals had no pancreas this would seem to dispose of the theory of Best, Haist and Ridout(10) who believe that the insulin content and output of the pancreas was decreased by fasting or dietary carbohydrate deprivation. Himsworth(11-13) first suggested that the decreased glucose tolerance and insulin sensitivity resulting from fasting or a low carbohydrate diet was due to the reduced production of a normal activator of insulin. Later experiments led him to conclude(14) that the effect of fasting was due to the increased production of an inhibitor of insulin which presumably arises in the anterior pituitary. There is other evidence however(15-18) which suggests that the hypophysis is unnecessary for the effect of diet and fasting on sugar tolerance and insulin sensitivity.

Insulin action may be studied with much greater certainty through its effect on the *oxidation* of glucose. The influence of the hormones of the anterior pituitary and adrenal cortex in this connection would be of much interest in relation to fasting.

Summary. Insulin increases the rate of glucose oxidation in the eviscerated rabbit. The influence of insulin upon glucose oxidation is most marked in the non-fasted fed animal. It is less effective after a day's fast prior to evisceration and the effect is greatly decreased by a still longer fasting period.

8. Bergman, H. C., and Drury, D. R., PROC. SOC. EXP. BIOL. AND MED., 1937, v37, 414.

9. Lundbaek, K., *Vale J. Biol. and Med.,* 1948, v20, 533.

10. Best, C. H., Haist, R. E., and Ridout, J. H., *J. Physiol.,* 1939, v97, 107.

11. Himsworth, H. P., *Clin. Sci.,* 1933, v1, 1.

12. Himsworth, H. P., *J. Physiol.,* 1934, v81, 29.

13. Himsworth, H. P., *Clin. Sci.,* 1935, v2, 67.

14. Himsworth, H. P., and McNair Scott, D. B., *J. Physiol.,* 1938, v91, 447.

15. Foglia, V. G., and Potick, D., *Rev. Soc. argent. de biol.,* 1941, v17, 289.

16. Heinbecker, P., Somogyi, M., and Weichselbaum, T. E., PROC. SOC. EXP. BIOL. AND MED., 1937, v36, 804.

17. Haist, R. E., *J. Physiol.,* 1940, v98, 419.

18. Samuels, L. T., Reinecke, R. M., and Ball, H. A., PROC. SOC. EXP. BIOL. AND MED., 1942, v49, 456.

Received September 15, 1950. P.S.E.B.M., 1950, v75.