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Dietary Induction of Liver Glucose-6-Phosphate Dehydrogenase in the Rat.* (30688)

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It has recently been reported that the enzyme glucose-6-phosphate dehydrogenase (G-6-P DH) decreases in the liver during starvation and increases to a peak activity several times the level of non-starved controls 72 hours after refeeding a high glucose diet‡ (1,2). The present experiment was designed to determine which dietary ingredient is serving as the inducer of this enzyme.

Materials and methods. 48 Sprague-Dawley rats weighing 365 ± 25 (S.D.) g were used in this experiment. These animals had been previously fed Purina Rat Chow. At zero time, 36 animals were started on total starvation plus water *ad libitum* while 4 animals were started on the control diet of the following composition: casein 20, methionine 0.5, glucose§ 69.78, corn oil 5.0, salt mix 4164(2) 4.0, vitamin premix in casein(2) 0.5, α-tocopheryl succinate 0.02, vitamins A and D 0.10 (to provide 1500 I.U. vit A and 100 I.U. vit D/100 g diet). After seven days of starvation, 12 starved animals were sacrificed and the remaining 24 were divided into 3 groups of 8 rats each, which were refed *ad libitum* the following three diets: Group 1 control diet as above, Group 2 the same diet with starch replacing glucose and Group 3 a diet in which all carbohydrate was omitted and replaced by fat (hydrogenated vegetable oil‖) at a level to give a diet of essentially the same calorie/protein ratio as in the carbohydrate containing diets of Groups 1 and 2. The composition of this diet is as follows: casein 31.92, methionine 0.82, hydrogenated vegetable oil‖ 59.54, salt mix 6.55, vitamin premix in casein 0.82, α-tocopheryl succinate 0.04, vitamins A and D 0.15, choline chloride 0.16.

The food intakes of these animals were such as to give approximately 75 cals per day for Groups 1 and 2 and approximately 90

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§ Cerelose, Corn Products Co., New York.

‖ Crisco.

TABLE I. Liver G-6-P DH Induction by Refeeding Different Diets G-6-P DH in Units* Per mg Protein.

	No. of rats	Units
Starved rats	12	36.7 ± 5.7†
Non-starved control rats	4	87.9 ± 6.0

	Refed rats			
	6 hrs after refeeding		72 hrs after refeeding	
Group	No. of rats	Units	No. of rats	Units
1	4	40.1 ± 2.7	4	500.7 ± 58.6
2	4	28.3 ± 3.7	4	472.3 ± 28.6
3	4	31.0 ± 2.9	4	46.3 ± 12.6

* One unit of enzyme activity is defined as the amount of enzyme in a one ml sample which at 25°C in a 3 ml assay mixture changes the OD 340 of TPNH by 0.001/min(5).

† Standard deviation.

cals per day for Group 3 and provided approximately 4 g per day proteins for Groups 1 and 2 and approximately 4.5 g per day for Group 3. There was little variation in these figures from day to day for the 3 days of refeeding except that intake of the glucose diet was lower the first day of refeeding (50 cals).

Four animals of each group were sacrificed 6 hours after refeeding and the other 4 from each group 72 hours after refeeding. The 12 control animals were sacrificed 48 hours after refeeding had been started on the experimental groups.

The livers of all animals were analyzed for G-6-P DH by the method of Löhr and Waller (3). Protein was determined by the method of Warburg and Christian(4).

Results and discussion. The results summarized in Table I clearly show the very marked increase of G-6-P DH level 72 hours after refeeding the carbohydrate-containing diets (Groups 1 and 2). That this induction may reflect new enzyme (protein) synthesis has been previously indicated by Potter and Ono in experiments using puromycin(1). It is also clear that refeeding with a carbohydrate-free diet did not cause induction of this enzyme and, in fact, the specific activity of the enzyme was lower than that in the control animals maintained on the glucose-containing ration.

The present data appear to eliminate energy *per se*, fat and protein as inducers of liver G-6-P DH and to demonstrate glucose as inducer. A requirement for an adequate amino acid pool for this rate of protein synthesis has been shown previously(2).

The 72-hour lag in attaining maximal induction of G-6-P DH in the presence of adequate dietary protein may suggest required synthesis of a precursor molecule induced by glucose or may indicate an indirect effect due to damage incurred during the 7-day starvation.

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