Regulation of Rat Liver Enzymes by Natural Components of the Diet*

NORMA PEREZ, LYLLIAN CLARK-TURRI, ELIANA RABA JILLE, AND HERMANN NIEMEYER

From the Instituto de Química Fisiológica y Patológica, Santiago, Chile

(Received for publication, October 17, 1963)

Changes in the metabolism of intact animals caused by reduction or exclusion of carbohydrates from the diet have been the subject of active research (1–3). Changes occurring in the utilization of sugars by isolated tissues of animals fed with different amounts of carbohydrates have also been studied (3–6). The problem of interpreting these facts at the molecular level emerges as an important challenge for those interested in biological adaptation and metabolic regulation. Alterations occurring in the metabolism of a cell undoubtedly reflect modifications in enzyme activity, leading to variations in the relative rates of certain reactions and metabolic sequences and to discrimination among several alternative pathways of metabolism. The occurrence of changes in enzyme activity in mammals brought about by modifications in the quality and quantity of diet seems well established. In particular, the enzyme pattern of liver is substantially modified by changing the nature and amount of food offered to the rat (7, 8). Our main efforts have been directed toward obtaining some information on the effect of carbohydrate supply on the activity of liver enzymes directly concerned with carbohydrate utilization.

In rats fed a high fat, carbohydrate-free diet, a significant decrease was observed in the activities of several enzymes: glucokinase (EC 2.7.1.2) (9, 10), α-glucan phosphorylase (EC 2.4.1.1) (11), glucose-6-phosphate dehydrogenase (EC 1.1.1.49) (9), phosphoglucone dehydrogenase (decarboxylating) (EC 1.1.1.44), (9) and uridine diphosphate (UDP) glucose-α-glucan glucosyltransferase (EC 2.4.1.11) (9). Deprivation of food produced a similar effect (0, 12). Analogous results have been obtained by other investigators working under similar conditions (13–15).

The dependence of α-glucan phosphorylase and UDP-glucose-α-glucan glucosyltransferase on dietary carbohydrate has been also evident in animals receiving maltose-dextrin as the sole source of calories; in these animals, values equal to or higher than those of rats fed a balanced diet were observed (9, 11). To our knowledge there is no information on the effect of this particular diet on the other enzymes with which this report is concerned.

Dependence on carbohydrates has been further explored by giving glucose after carbohydrate deprivation. It was shown that when α-glucan phosphorylase and glucokinase activities were diminished as a consequence of deprivation of food or feeding a high fat, carbohydrate-free diet, the administration of glucose provoked a recovery to normal values (8–11). The dehydrogenases of the pentose cycle did not recover under these conditions, but normal values could be attained in relatively short periods by feeding a balanced diet (8, 9).

The purpose of the present work was to gather more precise information on the influence of a particular constituent of diet on several liver enzymes directly involved in carbohydrate metabolism. The results indicate a pattern of changes in activity characteristic for each enzyme or group of enzymes, with carbohydrate or protein, or both, being responsible for the maintenance of normal levels of the various enzymes thus far examined.

**Experimental Procedure**

Male albino rats, weighing about 200 g, were used in all experiments. The animals were kept in experimental cages in a room maintained at 26–28° with alternating 12-hour periods of light and darkness, and were fed a milled stock diet for 2 or 3 weeks before the experiment was started. During this period the rats were frequently weighed to accustom them to handling.

All the experimental diets contained the same amounts of salts and vitamins (11) per 100 calculated calories. Intakes were restricted to be approximately isocaloric by giving 50 kcal of the diet daily. The proportions of carbohydrate (as a mixture of maltose and dextrins), casein, and fat (margarine and vegetable oil) were modified as indicated below for each experiment. Water was always given ad libitum. Animals were killed by decapitation without anesthesia, and the blood was allowed to drain. Livers were chilled in cracked ice, blotted, and weighed. Portions of 300 to 500 mg were homogenized in different media, depending on the enzyme to be assayed.

**Enzyme Assays**—A total homogenate prepared in 0.1 M potassium citrate, pH 6.5, was used for the assay (37) of glucose 6-phosphatase (EC 3.1.3.9) by the procedure of Freedland and Harper (16).

α-Glucan phosphorylase was assayed at 30° in a 10% whole homogenate prepared in 0.1 M KF, according to methods previously published (12). Inorganic phosphate was measured by the method of Lohmann and Jendrassik (17). Arginase was assayed in the same homogenate, diluted 100-fold, by the method of Cabello, Basilio, and Prajoux (18).

A 10% homogenate prepared in a medium containing 0.1 M KCl, 0.025 M glycylglycine, pH 7.5, 0.006 M EDTA, and 0.006 M MgCl₂ was centrifuged at 105,000 × g for 20 min. The supernatant fluid was used for the assay of arginase, glucose 6-phosphate dehydrogenase, phosphogluconate dehydrogenase,
glucosephosphate isomerase, and phosphoglucomutase. Glucokinase was assayed in a medium of the following final composition, which differs from that previously used: 0.1 M KCl; 85 mM glycyglycine buffer, pH 7.5; 12.6 mM MgCl₂; 100 mM glucose; 3.3 mM ATP; 1.6 mM EDTA; 0.5 mM NADP; and an excess of glucose 6-phosphate dehydrogenase (0.02 unit) and phosphogluconate dehydrogenase (0.02 unit). The reaction was followed simultaneously in a cuvette without ATP, which served as a blank. According to Víñuela, Salas, and Solà (19), there are two different liver enzymes able to phosphorylate glucose. One is referred to as glucokinase (EC 2.7.1.2) and is characterized by its high specificity toward glucose (and mannose) and by its high $K_m$ (10⁻² M). The other, similar to animal hexokinase (EC 2.7.1.1), has a low $K_m$ (10⁻⁵ M). This important discovery has been confirmed by us¹ and by other investigators (20). At the concentration used in our system (0.1 M), glucose saturates glucokinase and hexokinase. Thus both enzyme activities are measured together. For sake of simplicity we shall refer to both activities as “glucokinase.” Current experiments have permitted us to distinguish between the effects of dietary conditions on both enzymes.¹ The reduction of NADP was followed in 1-ml cuvettes at 340 mp in a Beckman spectrophotometer, model DU, provided with a Photovolt recorder and with thermostater to operate at 25° or 30°. Glucose 6-phosphate dehydrogenase and phosphogluconate dehydrogenase were assayed in a medium essentially similar to that of Glock and McLean (23), at pH 7.5, after the reduction of NADP as in glucokinase. Phosphoglucomutase (EC 2.7.5.1) was determined at 30° by the procedure of Najjar (24). Glucosephosphate isomerase (EC 5.3.1.9) was determined at 30° by following the production of fructose 6-phosphate from glucose 6-phosphate (25) with a resorcinol reaction (26).

The enzyme activities were expressed as micromoles of substrates transformed in 1 minute and were referred to 100 g of body weight. The body weight selected for reference depended on the type of experiments. As a general criterion, the weight of the animals in the last common condition was selected. Thus, in experiments in which several diets were compared, the weight of the rats on the starting day was used. When animals were given carbohydrate after a period of fasting or after being fed a carbohydrate-free diet, the body weight at the time when the carbohydrate was supplied was employed as standard of comparison. Specific activities were expressed in units per g of total liver protein. Protein was measured by the method of Lowry et al. (27), with crystalline bovine serum albumin as standard.

The following reagents were obtained from Sigma Chemical Company: ATP, NADP, glucose 6-phosphate, glucose 1-phosphate, fructose 6-phosphate, 6-phosphogluconate, and bovine serum albumin. Glucose 6-phosphate dehydrogenase was purchased from C. F. Boehringer and Soehne, GmbH, Mannheim, Germany. 6-Phosphogluconate dehydrogenase was a partially purified preparation (23).

**RESULTS AND DISCUSSION**

**Effect of Different Experimental Diets after Stock Diet**—In a first series of experiments, the activity of several liver enzymes was assayed in groups of animals that had received either a balanced diet, a high fat diet, or a carbohydrate diet for 6 days. The compositions of these diets were the following, expressed as percentage of calories supplied: balanced diet, 27% protein, 62% maltose-dextrin, 11% fat; high fat diet, 21% protein, 79% fat; carbohydrate diet, 100% maltose-dextrin. Table I shows that the various enzymes responded differently to the dietary modifications. Values obtained from rats kept on balanced diet were taken as standards of reference (±100).

Glucokinase exhibited normal values when carbohydrate was the sole exogenous source of calories, although under these conditions a net breakdown of proteins predominates, as evidenced by the decrease in total liver proteins (Table II). α-Glucan phosphorylase was also well maintained with the carbohydrate diet, as has been reported from this laboratory (11). In Table I are also included, for the purpose of comparison, data on UDP-glucose-α-glucosyltransferase from previous work (9), showing that this enzyme is also maintained at normal values with a carbohydrate diet. On the other hand, in substantiation of previous information (9–11), there was a marked decrease in the activity of the three enzymes mentioned above with a high fat diet, in which case the total protein is the same as in the balanced diet.

Glucose 6-phosphatase and phosphoglucomutase exhibited an opposite pattern, since they decreased with a carbohydrate diet and remained constant on a high fat diet (the slight increase over balanced diet is not statistically significant ($p > 0.05$)). Maintenance of glucose 6-phosphate dehydrogenase and of phosphogluconate dehydrogenase seemed to require both carbohydrate and proteins, inasmuch as a marked decrease in activity was observed when rats were fed a carbohydrate diet and also a high fat diet. Glucosephosphate isomerase maintained the same values in all diets.

Arginase was assayed as representative of enzymes not directly concerned with carbohydrate metabolism, and for which dependence on protein intake is well established (25, 29). As expected, the arginase values for rats fed on carbohydrate diet were much lower than those for animals fed on diets containing protein. It is worthwhile to point out that many liver enzymes decrease or even disappear during relatively short periods of time on a protein-free diet (29, 30).

Experiments in which rats were changed from a carbohydrate diet to a high fat diet supported the conclusions derived from those referred to above, and gave further information concerning the kinetics of enzyme changes. Fig. 1 shows the effect of putting rats on a high fat diet for 2 days after they had been fed for 6 days with a carbohydrate diet. A value of 100 is given to the enzyme levels of animals fed only carbohydrate. Glucokinase decreased to approximately the low values found in a 6-day period of high fat diet; glucosephosphate isomerase remained at the same level, while glucose 6-phosphatase and phosphoglucomutase increased about 90%. In those cases in which alteration of the enzyme activities occurred, intermediate values were observed after 1 day of the high fat diet.

**Limitation of Variables in Diets**—The fact that the high fat and the balanced diets are composed of two and three components, respectively (apart from salts and vitamins), made it difficult to define the direct contribution of protein or fat to the modification of the activity of some liver enzymes. Experiments were thus designed in which only one nutrient was given at a time or two nutrients were fed in different proportions during 6
TABLE I
Relative activity of liver enzymes from rats fed different diets for 6 days

Values for the balanced diet are taken as 100. Results are expressed as means ± standard error. Figures in parentheses indicate number of animals.

<table>
<thead>
<tr>
<th>Enzymes</th>
<th>Diet</th>
<th>Balanced</th>
<th>Carbohydrate</th>
<th>High fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucokinase</td>
<td>100 ± 9.5 (8)</td>
<td>105 ± 5.8 (5)</td>
<td>33 ± 2.1 (15)*</td>
<td></td>
</tr>
<tr>
<td>α-Glucan phosphorylase</td>
<td>100 ± 5.2 (7)</td>
<td>94 ± 4.7 (9)</td>
<td>64 ± 3.4 (7)*</td>
<td></td>
</tr>
<tr>
<td>UDP-glucose-α-glucan glucosyltransferase†</td>
<td>100 ± 4.3 (6)</td>
<td>126 ± 4.5 (7)*</td>
<td>61 ± 2.3 (8)*</td>
<td></td>
</tr>
<tr>
<td>Glucosephosphate isomerase</td>
<td>100 ± 12.2 (10)</td>
<td>96 ± 15.7 (7)</td>
<td>102 ± 2.0 (4)</td>
<td></td>
</tr>
<tr>
<td>Phosphoglucomutase</td>
<td>100 ± 6.6 (7)</td>
<td>70 ± 6.9 (7)*</td>
<td>119 ± 13.9 (4)</td>
<td></td>
</tr>
<tr>
<td>Glucose 6-phosphatase</td>
<td>100 ± 9.7 (6)</td>
<td>66 ± 5.6 (4)*</td>
<td>122 ± 2.7 (8)</td>
<td></td>
</tr>
<tr>
<td>Glucose 6-phosphate dehydrogenase</td>
<td>100 ± 8.8 (5)</td>
<td>52 ± 11.8 (4)*</td>
<td>37 ± 4.8 (5)*</td>
<td></td>
</tr>
<tr>
<td>Phosphogluconate dehydrogenase</td>
<td>100 ± 7.0 (9)</td>
<td>38 ± 5.8 (4)*</td>
<td>65 ± 6.9 (5)*</td>
<td></td>
</tr>
<tr>
<td>Arginase</td>
<td>100 ± 9.9 (5)</td>
<td>38 ± 2.5 (5)*</td>
<td>98 ± 9.0 (8)</td>
<td></td>
</tr>
</tbody>
</table>

* Differences with balanced diet are statistically significant (p < 0.001).
† Values taken from a previous report (9).

TABLE II
General characteristics of animals subjected for 6 days to diets with variable proportions of protein, carbohydrate, and fat

<table>
<thead>
<tr>
<th>Diet</th>
<th>No. of rats</th>
<th>Body weight</th>
<th>Liver weight</th>
<th>Intake*</th>
<th>Liver protein*</th>
<th>Liver glycogen†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Initial</td>
<td>Final</td>
<td>g</td>
<td>g</td>
<td>g</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>kcal/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Balanced</td>
<td>4</td>
<td>205</td>
<td>205</td>
<td>7.6</td>
<td>24.7 ± 0.6</td>
<td>0.63 ± 0.01</td>
</tr>
<tr>
<td>Carbohydrate, 100%</td>
<td>10</td>
<td>197</td>
<td>181</td>
<td>5.8</td>
<td>22.1 ± 0.4</td>
<td>0.41 ± 0.01</td>
</tr>
<tr>
<td>Carbohydrate, 80%; fat, 20%</td>
<td>3</td>
<td>207</td>
<td>184</td>
<td>5.4</td>
<td>22.3 ± 0.6</td>
<td>0.43 ± 0.04</td>
</tr>
<tr>
<td>Carbohydrate, 50%; fat, 50%</td>
<td>4</td>
<td>191</td>
<td>170</td>
<td>5.6</td>
<td>23.0 ± 0.3</td>
<td>0.46 ± 0.04</td>
</tr>
<tr>
<td>Carbohydrate, 20%; fat, 80%</td>
<td>6</td>
<td>200</td>
<td>170</td>
<td>6.0</td>
<td>21.8 ± 2.5</td>
<td>0.47 ± 0.05</td>
</tr>
<tr>
<td>Carbohydrate, 80%; protein, 20%</td>
<td>6</td>
<td>203</td>
<td>203</td>
<td>7.2</td>
<td>21.0 ± 1.1</td>
<td>0.57 ± 0.04</td>
</tr>
<tr>
<td>Carbohydrate, 50%; protein, 50%</td>
<td>9</td>
<td>198</td>
<td>198</td>
<td>6.5</td>
<td>23.9 ± 0.6</td>
<td>0.72 ± 0.02</td>
</tr>
<tr>
<td>Carbohydrate, 20%; protein, 80%</td>
<td>7</td>
<td>194</td>
<td>196</td>
<td>8.8</td>
<td>23.4 ± 1.2</td>
<td>0.82 ± 0.04</td>
</tr>
<tr>
<td>Protein, 100%</td>
<td>9</td>
<td>196</td>
<td>185</td>
<td>7.6</td>
<td>20.9 ± 0.7</td>
<td>0.79 ± 0.01</td>
</tr>
<tr>
<td>Protein, 50%; fat, 50%</td>
<td>6</td>
<td>177</td>
<td>189</td>
<td>7.0</td>
<td>25.3 ± 3.7</td>
<td>0.75 ± 0.04</td>
</tr>
<tr>
<td>Protein, 21%; fat, 79%</td>
<td>6</td>
<td>198</td>
<td>195</td>
<td>8.0</td>
<td>24.5 ± 1.1</td>
<td>0.69 ± 0.03</td>
</tr>
</tbody>
</table>

* Per 100 g of body weight on the starting day of experimental diet.
† Per 100 g of tissue, wet weight.
‡ Percentage of calories.

Days. The general characteristics of the various groups of animals used are summarized in Table II. The body weight was kept relatively constant during the 6 days on the experimental diets, with the exception of rats fed protein-free diets.

These experiments indicated the complexities inherent in attempting to elucidate the nature of specific agents controlling enzyme levels in the intact animal. The results are shown in Figs. 2 to 7. No corrections were introduced for small differences in caloric intake.

Glucokinase appeared to be the most sensitive enzyme with regard to the supply of carbohydrate, inasmuch as maximal activities could be obtained only when this nutrient was present in the diet. When proteins were the sole source of calories, a drastic reduction in enzyme activity was observed (Fig. 2). If fat was substituted in varying proportions for protein, a more accentuated diminution was attained. Fig. 2 also shows the changes in specific activity, pointing out clearly the importance of carbohydrate for glucokinase activity.

α-Glucan phosphorylase could be kept at approximately the same levels with different proportions of carbohydrate and protein (Fig. 3), thus substantiating previous information (11). However, the specific activity was about twice as high with a 100% carbohydrate diet as with the protein-fat and 100% protein diets. The substitution of fat for either carbohydrate or protein evoked a decrease in enzyme activity.

Phosphoglucomutase (Fig. 4) and glucose 6-phosphatase (Fig. 5) exhibited a common pattern. Both enzymes appeared to require a minimum supply of protein (about 20%). In fact, if carbohydrate or fat was substituted for up to 80% of the calories contributed by protein, the same levels of activity as in the livers of rats fed the 100% protein diet were observed. The specific activities remained approximately the same under the various dietary conditions, this being especially clear in the case of phosphoglucomutase.

Glucose 6-phosphate dehydrogenase (Fig. 6) and phosphogluconate dehydrogenase (Fig. 7) also depended on the protein supply. However, carbohydrates represented a valuable complement within certain limits, inasmuch as the maximal activities...
FIG. 1. Relative activities of liver enzymes ("glucokinase," glucosephosphate isomerase, glucose 6-phosphatase, and phosphoglucomutase) from rats fed a high fat diet for 2 days after 6 days on a carbohydrate diet. Values of animals fed the carbohydrate diet are taken as 100. The bars represent the mean of determinations performed on four rats. The vertical lines indicate standard error.

were observed with a diet composed of both protein (80%) and carbohydrate (20%). When fat was substituted for protein or carbohydrate, the enzyme activities reached very low levels. The specific activities of both enzymes increased as the protein content of the diet was augmented up to 80% of the calories, when the complementary nutrient was carbohydrate.

The effect of dietary protein on enzyme levels seems rather complicated. Proteins appear to be responsible for different types of action. One of these actions can be described as a nonspecific effect on total liver proteins, which increase when the amount of dietary protein is augmented. This effect may be considered as a reflection of a general activation of protein biosynthesis depending on the size of the cell amino acid pool (31). In addition, there seems to exist a more specific effect of dietary protein, acting in a discriminate manner on different enzymes.

It appears that the changes in specific activities of the enzymes may be a good indication of the specificity of the diet effect. In fact, specific activity is a measurement of the response of a given enzyme as compared with the bulk of enzyme and structural proteins.

The specific activities of phosphoglucomutase and glucose 6-phosphatase are rather constant under widely different dietary conditions (Figs. 4 and 5), suggesting that the increase in enzyme activities observed when proteins are supplied is a consequence of the nonspecific effect of protein. Few other enzymes behave similarly (29, 32, 33).

FIG. 2 (upper left). "Glucokinase" activities in liver supernatant fraction as function of diet. The circles represent the values from animals that received a mixture of carbohydrate (0 to 100% of calories) and protein to complete an isocaloric ration. The triangles indicate rats that received a mixture of carbohydrate (20 to 100% of calories) and fat to complete an isocaloric ration. The squares indicate animals that were given a mixture of fat (0 to 80% of calories) and protein, also to complete caloric supply. The vertical lines indicate standard error.

FIG. 3 (upper right). α-Glucan phosphorylase activities in whole homogenate of liver as function of diet. For significance of symbols, see the legend of Fig. 2.

FIG. 4 (lower left). Phosphoglucomutase activities in liver supernatant fraction as function of diet. For significance of symbols, see the legend of Fig. 2.

FIG. 5 (lower right). Glucose 6-phosphatase activities in liver homogenate as function of diet. For significance of symbols, see the legend of Fig. 2.
Glucose 6-phosphate dehydrogenase and phosphogluconate dehydrogenase, which are also dependent on the protein supply, behaved in a different way. There is a marked increase in the specific activities of both dehydrogenases which follows the increment in liver proteins. The specific activities of several enzymes directly involved in protein or amino acid metabolism, such as arginase and other enzymes of the urea cycle (28), threonine dehydratase (EC 4.2.1.16) (34), alanine transaminase (EC 2.6.1.2) (35), and glutamate dehydrogenase (EC 1.4.1.3) (29), also increase markedly as the protein in the diet increases. Xanthine oxidase (EC 1.2.3.2) (29, 36), urate oxidase (EC 1.7.3.3) (29), and other oxidoreductases (29, 30, 37) follow the same pattern. Thus it appears that in all these cases there is a specific action of proteins, or amino acids derived from them, on some enzymes. An inductive effect of proteins, or their derivatives, may be postulated.

Glucokinase and α-glucan phosphorylase, which seem to depend mostly on dietary carbohydrate, exhibit a good correlation between their specific activities and the proportions of carbohydrate in the diet (Figs. 2 and 3). It is a remarkable fact that the specific activities of both of these enzymes are about the same whatever carbohydrate is replaced by protein or by fat, in spite of the great difference in total liver proteins under these two dietary conditions. This indicates that the greater activity (per 100 g of body weight) observed when protein, instead of fat, is substituted for carbohydrate must be interpreted as a consequence of the nonspecific action of dietary proteins.

Supply of Carbohydrates after Carbohydrate Deprivation—A method that appears to fulfill the requirements necessary for detection of the specific effect of some dietary compounds is the administration of a single food to animals that have been stabilized in another diet not containing that particular substance. This approach seems to be especially fruitful when enzyme activities change rather abruptly.

Experiments were designed with the aim of providing better information on the dependence of some enzymes on the supply of carbohydrate, under conditions in which changes in the protein content of the liver were minimized. Animals were fed during 6 days a high fat diet and then supplied with carbohydrates alone, for periods varying from a few hours to 2 days. In the groups scheduled to be killed after 12 hours or less, a mixture of glucose (20%) and maltose-dextrin (30%) was given by stomach tube. For longer term experiments, the carbohydrate diet was given ad libitum.

Glucokinase increased very rapidly after carbohydrate administration. After 6 hours the enzyme activity was equivalent to that found in rats maintained on a balanced diet or a carbohydrate diet. A brief report on this enzyme has been published (10), and a more detailed study of the characteristics of glucokinase recovery will be presented elsewhere.

Glucose 6-phosphatase, on the contrary, decreased significantly from an initial value of 92.9 ± 2.1 to 71.1 ± 7.0 units per 100 g of body weight after 12 hours of carbohydrate administration. During the first 6 hours, no change was observed (96.7 ± 2.1 units). Phosphoglucomutase did not change during 6 hours. This enzyme was not assayed for longer periods. The activities of glucoserephosphate isomerase and of the dehydrogenases of the pentose cycle were not modified significantly by the administration of carbohydrate, thus confirming the observations made with the type of experiments presented above.

To test the dependence of the enzyme activities on the supply of carbohydrate as the sole source of exogenous energy, another group of rats was fed for 6 days with a balanced diet and then deprived of food for 48 hours, with water ad libitum. Subsequently the animals received carbohydrate for different periods before death. As in the previous experiment, when periods shorter than 12 hours were used, a mixture of glucose and maltose-dextrin was given by stomach tube. Results are presented in Table III.

Glucokinase again recovered very rapidly. Phosphorylase was not assayed, but previous results have shown that there is a slow recovery, normal values being attained after approximately 3 days of refeeding (11). Glucosephosphate isomerase, which had decreased during fasting, returned to normal values (corresponding to the balanced diet) after the third day of feeding carbohydrate. Glucose 6-phosphatase did not decrease significantly with fasting (p > 0.10), but after 24 and 72 hours of feeding the carbohydrate diet a decrease in the enzyme activity, with respect to values on the balanced diet (p < 0.02), accompanied the decrease in total liver protein. Phosphoglucomutase, glucose 6-phosphate dehydrogenase, and 6-phosphogluconate dehydrogenase, however, which had already been reduced by fasting, were not changed significantly by feeding carbohydrate. Only the transient increase observed in 6-phosphogluconate dehydrogenase in the first 6 hours after carbohydrate supply was statistically significant (p < 0.01). The slight increase in glucose 6-phosphate dehydrogenase in the same period, however, was not significant (p > 0.10). The results obtained with the
The isomerase also remains constant when animals are fed a diet consisting only of carbohydrate (Table I). The possibility can be considered that some intermediate metabolites of the glycolytic and gluconeogenic pathways, such as glucosephosphate isomerase (Table I) and glucosephosphate dehydrogenase, derivatives may act as inducers of certain enzymes. On the other hand, both dehydrogenases of the pentose cycle and degradation do not behave as a unit from the point of view of changes caused by modifications in the dietary constituents. The activities of several enzymes directly involved in carbohydrate utilization from livers of rats fed diets of different compositions were studied. The response of these enzymes to dietary changes differed widely.

**SUMMARY**

The activities of several enzymes directly involved in carbohydrate metabolism were compared in livers of rats fed diets of different compositions. The response of these enzymes to dietary changes differed widely.

**REFERENCES**
