OBSERVATIONS WITH P^{32} OF THE CHANGES IN THE ACID-SOLUBLE PHOSPHATES IN THE LIVER COINCIDENT TO ALTERATIONS IN CARBOHYDRATE METABOLISM

Sirs:

Recent studies in this laboratory with radioactively labeled phosphorus on the acid-soluble phosphates of liver have yielded interesting information regarding the phosphate cycle in the intact animal. We wish to report findings which indicate the marked influence of insulin and of glucose administration on the phosphate compounds of liver.

Distribution of Labeled P in Acid-Soluble Phosphates of Liver

Treatment	No. of rats	Total acid-soluble	Inorganic	P of adenosine triphosphate		Mercury* ppt. P	Alcohol† ppt. P	Residual‡ P
				Labile	Non-labile			
Controls fasted 12 hrs.	10	177 ±12.6	77.6 ±8.3	11.7 ±2.9	3.3 ±2.4	20.2 ±5.1	44.0 ±5.1	28.6 ±4.5
Glucose (300–400 mg. intraperitoneally)	10	204.0 ±14.2	56.6 ±7.5	49.0 ±7.2	12.8 ±3.3	24.6 ±3.8	25.4 ±3.1	12.9 ±3.8
Insulin (4 units intraperitoneally)	8	244.3 ±19.2	92.5 ±9.6	41.5 ±8.1	15.6 ±4.0	21.4 ±5.6	26.2 ±7.6	14.5 ±3.1
Glucose + insulin (injected amounts same as above)	6	262.0 ±18.3	83.4 ±8.0	64.5 ±6.8	16.2 ±2.8	25.0 ±9.0	22.7 ±6.7	20.2 ±3.5

The analyses were carried out on rats sacrificed 110 minutes after administration of Na_2HPO_4 labeled with P^{32}. All values are in per cent of administered dose × 10 of the labeled P per 100 gm. of fresh liver. The measure of variability is the mean deviation from the mean.

* This fraction contains nucleotides other than adenosine triphosphate.

† This fraction consists largely of glycerol phosphate but it also contains some hexose monophosphates.

‡ This fraction consists largely of phosphoglyceric acid.

Rats weighing about 200 gm. were fasted for a period of 12 hours, given the treatment shown in the table, and then injected intraperitoneally with trace doses of $Na_2HP^*O_4$.[1] The animals were sacrificed at varying time intervals and the acid-soluble phosphate constituents were fractionated and analyzed for radioactivity. The distribution of radioactive phosphorus in the various acid-soluble fractions of the liver 110 minutes after administration of the phosphate is summarized in the table.

A maximum in the P* concentration of the total acid-soluble phosphates

[1] The chemical symbol with an asterisk is used to represent an element labeled with radioactive isotope.

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was usually attained at about 110 to 120 minutes. Glucose administration caused a marked alteration in the time relations of the labeled phosphate distribution. The peak in the radioactivity of the labile P of adenosine triphosphate of the animals given glucose occurred at 110 minutes after the injection of P*, whereas the peak in the control group was at 200 minutes. The peak in the radioactivity of the non-labile P of the adenosine triphosphate was similarly reduced from 250 to 110 minutes. The peak in the radioactivity of the P of the alcohol and the residual fractions was increased in time by glucose administration from 110 to 210 and 245 minutes respectively.

The data of the table show that both glucose and insulin produce an increase in the adenosine triphosphate P* and a decrease in the residual and alcohol P*. Insulin induces a marked rise in the total acid-soluble and inorganic P*. This confirms previous findings of Nelson and coworkers[2] that insulin causes a shift of phosphate from serum to liver. Insulin and glucose administered together produce a significantly greater increase in the radioactivity of the labile P of adenosine triphosphate than either does alone.

It was found that the injection of malonate, phlorhizin, or sodium fluoride prevented the rise in the labile P* of adenosine triphosphate following administration of glucose; iodoacetate was without effect. The dietary state of the animal was also found to have a profound influence on the distribution of the radioactive phosphate.

These results illustrate the importance of the rôle played by the organophosphates in the metabolism of the liver *in vivo*.

Division of Biochemistry
University of California Medical School
Berkeley

NATHAN KAPLAN
DAVID M. GREENBERG

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[2] Nelson, N., Rapoport, S., Guest, G. M., and Mirsky, I. A., *J. Biol. Chem.*, **144**, 291 (1942).

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Nathan Kaplan and David M. Greenberg

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