

metabolism of *o*-aminophenols. Further studies are required to settle this point. If *o*-aminophenols are further oxidized within the cell through the mechanism suggested by the present experiments, an appreciable fraction of the generated *o*-quinone imines might be expected to bind free functional groups of protein side chains in a manner analogous to *o*-quinones⁹.

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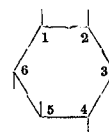
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Metabolism of 2-¹⁴C-*myo*-inositol in the rat*

Several workers have demonstrated the conversion of *myo*-inositol to glucose in the rat^{1,2,3,4}, and a recent report has indicated that kidney extracts are capable of converting inositol** to DL-glucuronic acid⁵. The availability, in our laboratory, of 2-¹⁴C-*myo*-inositol*** has made it possible further to investigate the metabolic pathways involved.

"Physiological" doses of 2-¹⁴C-inositol (0.7 to 3 mg, 0.86 to 3.7 · 10⁶ counts/min, < 1/10 of the normal daily intake) were injected intraperitoneally into well-fed, adult male rats. Useful activity (1.5 to 3% of the dose) could be recovered from the liver glycogen 8 to 12 h after the injection. The glycogen, isolated from liver and muscle by the method of STETTEN AND BOXER⁶, was hydrolyzed to glucose, and this was degraded carbon by carbon *via* *Leuconostoc* fermentation⁷. The results are shown in Table I.



myo-Inositol

TABLE I

¹⁴C DISTRIBUTION IN GLUCOSE FROM GLYCOGEN AFTER
INJECTION OF 2-¹⁴C-*myo*-INOSITOL

All samples were counted as barium carbonate after plating on copper planchets. The figures are corrected for self-absorption.

	Counts/min/mmol/C		
	Expt. 1		Expt. 2
	Liver	Muscle	Liver
Whole glucose	429	210	2457
Carbon 1	1285	633	6800
Carbon 2	89	95	691
Carbon 3	62	34	612
Carbon 4	84	62	590
Carbon 5	87	83	818
Carbon 6	1339	478	5262

In all cases, whether the glucose was derived from liver or from muscle glycogen, over 80% of the radioactivity was found in positions 1 and 6, which were about equally labeled. These results parallel those of POSTERNAK *et al.*², who found that 2-²H-*myo*-inositol was converted to 6-²H-D-glucose by a phlorizinized rat. The appearance of label in the 1-position of the glucose is, however, a new finding. No deuterium was found there by the Swiss workers; presumably carbon destined for this position lost its deuterium in the conversion process.

The present data are consistent with the hypothesis that 5-¹⁴C-D-glucuronic acid, formed by cleavage of the inositol between carbons 1 and 6, is an intermediate in the conversion to glucose. According to the scheme of BURNS AND KANFER⁸, 5-¹⁴C-D-glucuronic acid would be converted to 5-¹⁴C-D-xylulose. This,

after phosphorylation, would yield 3-¹⁴C-3-phospho-D-glyceraldehyde, which would account for the label in position 6 of the glucose, and for a good deal of that in position 1. The exact amount would depend on the degree of isomerization of the triose phosphate. If L-glucuronic acid is

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** Whenever the term "inositol" is used, the *myo*-isomer is implied.

*** The synthesis will be described in a later publication.

formed from inositol *in vivo* as *in vitro*⁵, this metabolite might also contribute to the labeling of the 1 carbon atom of glucose. The metabolism of L-glucuronic acid is totally unknown.

In order to obtain evidence about the participation of glucuronic acid in the inositol-glucose conversion, we examined 24-h urines, which contained about 2 % of the radioactivity administered to the rats. A radioactive, orcinol-positive, AgNO₃-reducing material was isolated from the acidic fraction of the urines by chromatography on Dowex-1 formate. It was identified as glucuronic acid by comparison with authentic samples in 4 different paper-chromatographic systems⁶, one of which distinguishes between glucuronic and guluronic acids.

The carbons of urinary glucuronic acid purified by ion-exchange and paper chromatography had an average specific activity of 17,000 counts/min/mmmole; the specific activity of carbon 6 was 10,000. Since the average specific activity of the glucuronic acid carbon is 7-fold greater than the maximal corresponding value for glycogen, and since the distribution of the label is clearly different, the glucuronic acid is not entirely an oxidation product of glucose. It must, in part, be derived more directly from the administered inositol. Experiments are under way to determine the enantiomorph composition of the urinary glucuronic acid, and to investigate the label distribution in the pentose metabolites.

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Induced recovery of DNA synthesis in bone marrow from irradiated guinea pigs

After an intravenous injection of bone-marrow cells into an animal subjected to total-body irradiation, a hastened recovery of haematopoiesis and lowered mortality takes place¹. It has been shown that the injected cells survive and multiply in the irradiated host², but it is not excluded that the injected marrow can stimulate the recovery of the host's own tissue by means of a humoral factor³.

To test this hypothesis, we performed some experiments *in vitro*, with bone marrow from irradiated animals. In these experiments, the rate of DNA synthesis was used as a criterion of the effects of irradiation and of recovery factors.

The bone marrow was obtained from guinea-pigs 2-72 h after total-body irradiation with 600 R of X-rays. Bone-marrow cells were incubated 6 h in a medium containing Na₂H³²PO₄. The rate of DNA synthesis was determined after isolation of DNA-P by the method of Schmidt-Thannhauser.

In every experiment, the bone-marrow suspension from an irradiated animal was divided into two portions; one was incubated with the material to be tested, the other served as the control.

Samples of each portion were incubated in 3-5 test tubes, each tube being analysed separately. At the same time, the marrow from non-irradiated animals was worked up.

In eleven experiments, it was established that the specific activity of the DNA-P of normal, non-irradiated marrow after 6 h incubation was $(6.0 \pm 0.42) \times 10^{-3}$ times that of the activity of acid-soluble P. The DNA synthesis in irradiated bone marrow falls at different intervals after irradiation to 35-13 % of the normal value (Table I).

We tried to enhance the DNA synthesis in irradiated marrow in two different ways: (1) by addition of cellular material and (2) by means of cell-free extracts or of pure compounds.

The results of the first group of experiments showed that the addition of a small amount (2-2.5 %) of non-irradiated marrow to irradiated marrow caused an increase in the DNA synthesis