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, $AgNO_3$-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 systems[5], 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/mmole; 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 enantiomorphic 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 place[1]. It has been shown that the injected cells survive and multiply in the irradiated host[2], but it is not excluded that the injected marrow can stimulate the recovery of the host's own tissue by means of a humoral factor[3].

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 $Na_2H^{32}PO_4$. 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

TABLE I

THE INFLUENCE OF THE ADDITION OF NORMAL MARROW CELLS ON DNA SYNTHESIS IN IRRADIATED BONE-MARROW SUSPENSIONS

Number of expts.	*Time after irradiation (h)*	*Relative rate of DNA synthesis* $= \frac{\text{sp. act. of DNA-P}}{\text{sp. act. of acid-sol. P}} \times 10^3$	
		control irradiated marrow	*irradiated marrow with 2–2.5% normal cells added*
6	2	1.9 ± 0.14*	2.9 ± 0.36*
6	6	2.1 ± 0.11	3.9 ± 0.08
4	18	0.9 ± 0.41	2.5 ± 0.70
3	72	0.8 ± 0.14	3.6 ± 0.57

* S.E. of the mean.

in irradiated marrow at all intervals studied. The DNA synthesis was increased to 42–62 % of the mean value in non-irradiated marrow (Table I).

The addition of normal, but heat-killed marrow was without any effect. The addition of normal living cells to the marrow of an animal irradiated with a high dose (1200 R) was likewise without any effect.

On the basis of these results, we concluded that the non-irradiated bone marrow contains or produces some compounds that enhance the DNA synthesis in irradiated tissue. We therefore tried to obtain similar results by means of cell-free tissue extracts or simple compounds. The bone marrow was taken from guinea-pigs 6 h after total-body irradiation with 600 R. In these experiments, the specific activity of the DNA-P was compared with that of the inorganic phosphorus in the incubation medium.

These experiments showed that the DNA synthesis in the irradiated bone marrow was stimulated, *in vitro*, by a fresh chick-embryo extract. This stimulating activity was not destroyed after the extract was heated for 3 min at 70°. However, a three-weeks old embryonal extract was without any effect. All the activity of the chick-embryo extract was in the nucleotide fraction. The fraction containing compounds not bound by a OAL-formate column (OAL is a strong-base anion exchanger) had no such effect; on the contrary, it impaired the DNA synthesis. The effect of the embryonal extract or its nucleotide fraction was very marked; the synthesis of DNA reached 90 % of its normal value.

Nucleotide-containing extracts from spleen or yeast had no effect on DNA synthesis in irradiated marrow, but they enhanced the DNA synthesis in non-irradiated marrow.

The effect of ATP was similar; it stimulated the DNA synthesis in non-irradiated marrow (167 % of the control value without ATP), but its stimulating effect in the irradiated marrow (114 % of the irradiated control value without ATP) was not statistically significant.

The most marked effect in irradiated marrow was given by some deoxyribonucleotides. Deoxyadenylic and similarly deoxycytidylic acid caused a 2.5–9 times higher rate of DNA synthesis compared with the irradiated control. After addition of these nucleotides, the DNA synthesis in irradiated marrow reached in some experiments up to 240 % of the mean value observed in non-irradiated marrow. However, these deoxyribonucleotides did not enhance the incorporation of ^{32}P into the DNA in the normal, non-irradiated bone marrow.

The results show that the normal tissue contains or produces some metabolites necessary for DNA synthesis. These metabolites seem to be absent in irradiated tissue. As the effect of normal bone-marrow cells and of some cell-free material is very similar, we may conclude that similar compounds are responsible for a part of the therapeutic effect of bone-marrow transplants in radiation sickness. Deoxyribonucleotides appear to be most effective.

Further experiments on the effects *in vivo* and those concerning the question of cells utilizing and producing these compounds are in progress.

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