PATHWAYS OF RIBONUCLEIC ACID PENTOSE BIOSYNTHESIS
BY LYMPHATIC TISSUES AND TUMORS*

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(Received for publication, June 3, 1957)

There are two well established pathways leading to the biosynthesis of pentose from glucose. The first of these involves the participation of the enzymes, transketolase and transaldolase (Fig. 2). By this pathway, 2 molecules of fructose 6-phosphate and 1 molecule of glyceraldehyde phosphate may be converted anaerobically to 3 molecules of pentose phosphate (1, 2). The second pathway is the hexose monophosphate shunt, or direct oxidative pathway. In this case, glucose 6-phosphate can be oxidized in the presence of two triphosphopyridine nucleotide-linked dehydrogenases to ribulose phosphate. The aldehyde carbon of glucose is converted to CO₂ although glucose carbon atoms 2 to 6 give rise, respectively, to carbon atoms 1 to 5 of the pentose.

It has previously been shown that, in lymphatic tissues and tumors, glucose-1-C¹⁴ is oxidized to C²¹⁴O₂ considerably more rapidly than glucose-2-C¹⁴, glucose-6-C¹⁴, or uniformly labeled glucose (3, 4). It was estimated that 2 to 5 times as much pentose was synthesized from exogenous glucose by way of the direct oxidative pathway by the tumors as by normal lymphatic tissues. These results prompted an investigation of the contribution of the transketolase-transaldolase pathway as compared with the direct oxidative pathway in the synthesis of ribonucleic acid (RNA) ribose. Glucose-1-C¹⁴, glucose-2-C¹⁴, or glucose-6-C¹⁴ was incubated in vitro with normal or tumor cell suspensions and the specific activity of the ribose isolated from the purine nucleotides of ribonucleic acid was determined. The results suggest that a substantial proportion of the RNA ribose may be synthesized by way of the transketolase-transaldolase pathway (5).

Methods

Tissues and Incubation Procedure—Cell suspensions of rat thymus, mouse spleen, rabbit appendix, lymphatic leukemia LL-5147, and the Gardner lymphosarcoma were prepared as previously described (6). The tumors were transplanted subcutaneously by trochar and the animals

* Aided in part by grants from the American Cancer Society and the Leukemia Society, Inc.
killed 14 to 20 days later. Ascites tumor cells (E-9514A) were harvested 7 to 10 days after intraperitoneal inoculation.

Incubations were carried out in 15 cc. Warburg vessels for 2 hours at 38°. The contents of the flasks were as follows: 20 μmoles of either glucose-1-C¹⁴, glucose-2-C¹⁴, or glucose-6-C¹⁴ (approximately 2.5 μc.), 5 μmoles of glutamine, 5 μmoles of serine, 5 μmoles of deoxycytidine, normal or tumor cells equivalent to about 25 mg. of dry weight of tissue, and modified Krebs-Ringer-phosphate-bicarbonate buffer (6) to bring the total volume to 2.45 cc. In those experiments in which other components were added to the incubation medium, the volume of the buffer was correspondingly reduced. Glycerol-1-C¹⁴ (3.27 μmoles, 957,000 c.p.m. per μmole) was used as substrate in place of glucose in some experiments. Glycerol-1-C¹⁴ and glucose-1-C¹⁴ were purchased from the Nuclear Corporation, Inc., and glucose-2-C¹⁴ and glucose-6-C¹⁴ were obtained from Tracerlab, Inc., and Volk Radiochemical Company.

Isolation and Purification of RNA-Purine Nucleotide Ribose—At the conclusion of the incubation, the contents of the Warburg flasks were decanted into centrifuge tubes containing ice-cold trichloroacetic acid (TCA). The nucleoprotein precipitate was extracted three times with ice-cold 5 per cent TCA, three times with cold ethanol, three times with a 3:1 mixture of ethanol-ether (65° for 5 minutes), and once each with ether and a mixture of petroleum ether-ether-acetone (6:3:1).

To the nucleoprotein, 1 cc. of 1 N KOH was added and the mixture was kept at 35° for 18 hours (7). The deoxyribonucleic acid (DNA) and protein were reprecipitated by the addition of ice-cold hydrochloric acid. The soluble fraction was adjusted to 1 N HCl and heated for 1 hour in a steam bath to hydrolyze the RNA purine nucleotides to free ribose. After cooling, the pH was adjusted to about 2 to 3 and 200 mg. of acid-washed Norit A were added to remove unhydrolyzed nucleotides. The Norit suspension was centrifuged and the supernatant fluid was passed through a 3 X 0.9 cm. Dowex 50-H¹ (200 to 400 mesh) cation exchange resin to remove inorganic cations, free adenine, guanine, or amino acids.

The eluate from the cation exchange resin was next lyophilized in a VirTis freeze dryer (The VirTis Company, Yonkers, New York). The lyophilized sample was extracted with excess methanol and the methanol solution evaporated to dryness. The residue was dissolved in a known volume of water and the ribose content determined on an aliquot of the solution (8). Aliquots were also used for paper chromatography (phenol-water (72:28) or butanol-acetic acid-water (4:1:5)). Guide strips containing aliquots of the solution and carrier ribose plus glucose were run simultaneously. The papers were dried at room temperature for 24 hours and developed with an ethanol solution of aniline hydrochloride-phthalic
acid (1.3:1.6 gm. per 100 cc. of ethanol). The ribose was eluted into stainless steel planchets and, after drying, was assayed for radioactivity.

In some instances, alanine, serine, and glycine were isolated from the TCA extracts of the tissues (9). The radioactivity attributable to the carboxyl carbon was determined after decarboxylation with ninhydrin and the β-carbon of serine or the α-carbon of glycine was assayed as the dmedon derivative of formaldehyde (10–12).

RESULTS AND DISCUSSION

Association of Radioactivity with Ribose—When cell suspensions of normal or malignant lymphatic tissues were incubated with glucose-1-C\textsuperscript{14}, glucose-2-C\textsuperscript{14}, or glucose-6-C\textsuperscript{14}, significant radioactivity was incorporated into the ribose of the RNA purine nucleotides. That this radioactivity was attributable to ribose rather than to contaminating radioactive compounds seems likely for the following reasons: (1) as shown in Fig. 1, most of the radioactivity of the paper chromatograms was found in the area of the paper containing ribose; (2) when the ribose was eluted from the paper and rechromatographed with butanol-acetic acid-water as the solvent, significant radioactivity was found only in the ribose area of the paper; (3) alternatively, the ribose which had been extracted from the paper chromatograms was subjected to paper electrophoresis. Again, significant radioactivity was found only in the ribose area of the paper; (4) if the cells were killed with trichloroacetic acid at the start of the incubation, there was no incorporation of C\textsuperscript{14} into RNA ribose.

Inhibition of Incorporation in Presence of Non-Labeled Adenosine—As a further control, the following experiments were performed: Tumor cells or rat thymus cells were incubated with radioactive glucose in the presence or absence of non-labeled adenosine. In the presence of adenosine, incorporation of labeled glucose into RNA ribose was markedly inhibited (Table I). Presumably, the added adenosine diluted the RNA ribose precursor pools at the level of adenylic, inosinic, or guanylic acid. On the other hand, the addition of non-labeled cytidine or deoxyadenosine did not alter significantly the conversion of labeled glucose to the ribose of the purine nucleotides of RNA. A slight reduction of incorporation was, however, observed when ribose 5-phosphate (5 µmoles per flask) was added to the incubation medium. The fact that more marked inhibition was not obtained is probably attributable to the slow penetration of the ribose 5-phosphate through the cell membrane.

Experiments were also carried out in the presence and absence of glucuronic acid or glucuronolactone. The latter additions did not alter the incorporation of glucose-1-C\textsuperscript{14} into RNA ribose. This result and the fact that there is a preferential oxidation of glucose-1-C\textsuperscript{14} rather than of
glucose-6-C\textsuperscript{14} to C\textsuperscript{14}O\textsubscript{2} (3) suggest that a metabolic pathway involving the conversion of glucose to glucuronic acid and the decarboxylation of the latter to the pentose compound (13) is not of quantitative significance in the synthesis of the ribose of the purine nucleotides of RNA by lymphatic cells. Bernstein (14, 15) came to the same conclusion with respect to

![Graph](http://www.jbc.org/)

**Fig. 1.** Paper chromatography or paper electrophoresis of radioactive ribose solution obtained from the purine nucleotides of ribonucleic acid.

the synthesis of liver RNA ribose in the light of degradation studies of the labeled ribose.

**Comparative Incorporation of Glucose-1-C\textsuperscript{14}, Glucose-2-C\textsuperscript{14}, or Glucose-6-C\textsuperscript{14}—**When normal or malignant lymphatic tissues were incubated with glucose-1-C\textsuperscript{14}, glucose-2-C\textsuperscript{14}, or glucose-6-C\textsuperscript{14}, significant radioactivity was found in the RNA ribose of each of the tissues (Table II). As much or more radioactivity was incorporated when glucose-1-C\textsuperscript{14} was the substrate as when glucose-6-C\textsuperscript{14} was the substrate, whereas the incorporation of C\textsuperscript{14} from glucose-2-C\textsuperscript{14} exceeded that from either glucose-1-C\textsuperscript{14} or glucose-6-C\textsuperscript{14}.
The conversion of glucose to RNA ribose was also studied as a function of time and of initial glucose concentration. Table III shows that the incorporation of labeled glucose increases with time though not linearly.

**Table I**

*Effect of Adenosine on RNA Ribose Synthesis from Glucose-C\(^{14}\)*

The values are given in micromole of C\(^{14}\) incorporated per micromole of ribose.

<table>
<thead>
<tr>
<th>Experiment No.</th>
<th>Tissue</th>
<th>Substrate</th>
<th>Control</th>
<th>Plus adenosine</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>E-9514A</td>
<td>Glucose-1-C(^{14})</td>
<td>0.025</td>
<td>0.004</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glucose-6-C(^{14})</td>
<td>0.019</td>
<td>0.005</td>
</tr>
<tr>
<td>2</td>
<td>Gardner</td>
<td>Glucose-1-C(^{14})</td>
<td>0.012</td>
<td>0.004</td>
</tr>
<tr>
<td>3</td>
<td>Rat thymus</td>
<td>Glucose-6-C(^{14})</td>
<td>0.020</td>
<td>0.009</td>
</tr>
</tbody>
</table>

*Adenosine concentration, Experiments 1 and 3, 2 mmole; Experiment 2, 0.8 mmole.*

**Table II**

*Incorporation of Labeled Glucose into RNA Ribose of Lymphatic Tissues and Tumors*

The values are given in micromole of C\(^{14}\) incorporated per micromole of ribose.

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Glucose-1-C(^{14})</th>
<th>Glucose-2-C(^{14})</th>
<th>Glucose-6-C(^{14})</th>
</tr>
</thead>
<tbody>
<tr>
<td>LL-5147</td>
<td>0.017</td>
<td>0.031</td>
<td>0.014</td>
</tr>
<tr>
<td>E-9514A</td>
<td>0.011</td>
<td>0.016</td>
<td>0.010</td>
</tr>
<tr>
<td>Gardner</td>
<td>0.016</td>
<td>0.024</td>
<td>0.012</td>
</tr>
<tr>
<td>Spleen</td>
<td>0.015</td>
<td>0.025</td>
<td>0.015</td>
</tr>
<tr>
<td>Appendix</td>
<td>0.026</td>
<td>0.046</td>
<td>0.019</td>
</tr>
<tr>
<td>Thymus</td>
<td>0.012</td>
<td>0.022</td>
<td>0.014</td>
</tr>
</tbody>
</table>

**Table III**

*Conversion of Labeled Glucose to RNA Pentose As Function of Time*

The values are given in micromole of C\(^{14}\) incorporated per micromole of ribose.

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Incubation time</th>
<th>Substrate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Glucose-1-C(^{14})</td>
</tr>
<tr>
<td>Appendix</td>
<td>1 hrs.</td>
<td>0.0069</td>
</tr>
<tr>
<td></td>
<td>2 hrs.</td>
<td>0.010</td>
</tr>
<tr>
<td></td>
<td>3 hrs.</td>
<td>0.016</td>
</tr>
<tr>
<td></td>
<td>4 hrs.</td>
<td>0.021</td>
</tr>
<tr>
<td>E-9514A</td>
<td>45 min.</td>
<td>0.012</td>
</tr>
<tr>
<td></td>
<td>90 hrs.</td>
<td>0.019</td>
</tr>
<tr>
<td></td>
<td>3 hrs.</td>
<td>0.025</td>
</tr>
</tbody>
</table>
The conversion of glucose-1-C\textsuperscript{14} to RNA ribose compared favorably with that of glucose-6-C\textsuperscript{14} at all time points.

The conversion of labeled glucose to RNA pentose was greater at high glucose concentrations than at low glucose concentrations (Table IV). At low glucose concentrations, somewhat more radioactivity was found in the pentose when glucose-6-C\textsuperscript{14} was the substrate, but at higher glucose concentrations the reverse was observed.

### Table IV

**Effect of Glucose Concentration on Conversion of Labeled Glucose to RNA Ribose**

The substrate was given as micromole of C\textsuperscript{14} incorporated per micromole of ribose.

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Glucose concentration</th>
<th>Substrate</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mm</td>
<td>Glucose-1-C\textsuperscript{14}</td>
<td>Glucose-6-C\textsuperscript{14}</td>
</tr>
<tr>
<td>Appendix</td>
<td>3.3</td>
<td>0.0076</td>
<td>0.0086</td>
</tr>
<tr>
<td></td>
<td>8.2</td>
<td>0.0094</td>
<td>0.0088</td>
</tr>
<tr>
<td></td>
<td>15.0</td>
<td>0.012</td>
<td>0.011</td>
</tr>
<tr>
<td>LL-5147</td>
<td>3.3</td>
<td>0.0049</td>
<td>0.0079</td>
</tr>
<tr>
<td></td>
<td>8.2</td>
<td>0.0091</td>
<td>0.0096</td>
</tr>
<tr>
<td></td>
<td>11.4</td>
<td>0.014</td>
<td>0.013</td>
</tr>
</tbody>
</table>

### Table V

**Conversion of Glycerol-1-C\textsuperscript{14} to Purine Nucleotide Ribose of RNA**

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Micromole of C\textsuperscript{14} incorporated per micromole of ribose</th>
</tr>
</thead>
<tbody>
<tr>
<td>E-9514A</td>
<td>0.012</td>
</tr>
<tr>
<td>Thymus</td>
<td>0.0008</td>
</tr>
<tr>
<td>Gardner</td>
<td>0.0005</td>
</tr>
<tr>
<td>Spleen</td>
<td>0.0012</td>
</tr>
</tbody>
</table>

Several experiments were performed with glycerol-1-C\textsuperscript{14} as substrate (Table V). The incorporation into the ribose of RNA was poor compared with glucose, except in the case of ascites tumor, E-9514A.

The reactions leading to pentose synthesis via the transketolase-transaldolase pathway are schematically represented in Fig. 2. Fig. 2 also indicates that, as a result of the reactions of glycolysis, glucose carbon atoms 1 and 6 give rise to the $\beta$-carbon of glyceraldehyde phosphate while glucose carbon atoms 2 and 5 are converted to the $\alpha$-carbon of glyceraldehyde phosphate. The molar specific activity of the glyceraldehyde phosphate formed from glucose-1-C\textsuperscript{14}, glucose-2-C\textsuperscript{14}, or glucose-6-C\textsuperscript{14}
should therefore be one-half that of glucose. As a result of the reactions catalyzed by transketolase and transaldolase (Fig. 2), carbon atoms 1 and 2 of glucose are converted, respectively, to pentose carbon atoms 1 and 5, and 2 and 4. With glucose-1-C\textsuperscript{14} as the substrate, pentose carbon 5 should have one-half as much radioactivity as carbon 1, and, with glucose-2-C\textsuperscript{14} as substrate, pentose carbon 4 should have half as much radioactivity as carbon 2. It is assumed that the triose phosphate formed in Reaction III, Fig. 2, equilibrates with the triose phosphate formed in Reaction I, Fig. 2. Carbon 6 of glucose is a precursor of carbon 5 of pentose.

As a result of the reactions of the direct oxidative pathway, glucose carbon atom 1 is lost as CO\textsubscript{2}, while glucose carbons 2 and 6 give rise, respectively, to carbons 1 and 5 of pentose. Thus, glucose carbon 6 gives rise to pentose carbon 5 by both pathways. Glucose carbon 2 is converted to pentose carbon 1 via the direct oxidative pathway and to pentose carbons 2 and 4 as a result of the transketolase-transaldolase pathway.

The data of Table II may be examined in the light of the above discussion. When glucose-1-C\textsuperscript{14} was used as substrate for tumor, E-9514A, 0.0107 \(\mu\text{mole}\) of labeled carbon was incorporated per micromole of ribose. The theoretical incorporation of labeled carbon into triose phosphate would be one-third of this, or 0.0036 \(\mu\text{mole}\), while approximately 0.0071 \(\mu\text{mole}\) would have been incorporated due to the transfer of carbons 1 and 2 of fructose 6-phosphate (Fig. 2). The incorporation of labeled triose phosphate derived from glucose-6-C\textsuperscript{14} should be approximately equal to that due to glucose-1-C\textsuperscript{14}. Some C\textsuperscript{14}-tetrose phosphate derived from glucose-6-C\textsuperscript{14} should also be incorporated, but the amount of this incorporation is not known. Assuming that tetrose phosphate incorporation is small compared with triose phosphate incorporation, then the difference between the total glucose-6-C\textsuperscript{14} incorporated (0.0095) and the C\textsuperscript{14}-triose phosphate incorporated (0.0036) provides a rough estimate of the incorporation of glucose-6-C\textsuperscript{14} via the hexose monophosphate shunt (0.0059). This latter value is of course an overestimation if significant C\textsuperscript{14} from tetrose phosphate is incorporated into the ribose. The sum of the incorporation of C\textsuperscript{14} from carbon atoms 1 and 2 plus the estimated incorporation via the hexose monophosphate shunt is thus 0.0071 + 0.0059 or 0.013 \(\mu\text{mole}\) of labeled carbon per micromole of ribose. The estimated incorporation via the hexose monophosphate shunt is thus about 45 per cent of the total. Theoretically, the total C\textsuperscript{14} incorporated from glucose-2-C\textsuperscript{14} should be the sum of the triose phosphate units plus the carbon atom 1 and 2 units plus the incorporation via the shunt, or 0.0036 + 0.0071 + 0.0059, or a total of 0.0166 \(\mu\text{mole}\) of C\textsuperscript{14} per micromole of ribose. The observed incorporation of glucose-2-C\textsuperscript{14} was 0.0162 (Table II), which agrees reasonably well with the above estimate. By similar calculations it can be estimated that
the incorporation of labeled glucose to RNA ribose via the hexose monophosphate shunt was 44 per cent of the total in the case of tumor LL-5147, and 39, 50, 37 and 54 per cent, respectively, in the case of the Gardner tumor, spleen, appendix, or thymus cells.

The above calculation can be regarded only as a very rough first approximation for the following reasons: (1) As mentioned previously, it is not known to what extent glucose carbon 6 is converted to pentose by way of Reactions II to IV of Fig. 2. (2) Carbon 1 of glucose may be converted to carbon 6 of fructose 6-phosphate, due to the reversal of the aldolase reaction and the hydrolysis of fructose diphosphate to fructose 6-phosphate (Fig. 2, Reaction I). (3) The carbons of the glucose substrate may be randomized to the various carbons of fructose 6-phosphate. This could take place if the ribulose phosphate, which had been formed via the direct oxidative pathway, were utilized for the resynthesis of hexose phosphate by a reversal of the transketolase and transaldolase reactions. The formation of sedoheptulose diphosphate from erythrose phosphate and dihydroxyacetone phosphate, the hydrolysis of sedoheptulose diphosphate to sedoheptulose 7-phosphate, and the conversion
of the latter to pentose phosphate and to hexose phosphate would also tend to randomize the carbon atoms of the glucose substrate.

In connection with these possibilities, the ribose in some cases was degraded by the periodate reaction. The formaldehyde formed from carbon 5 of ribose was isolated as the dimedon derivative. When glucose-1-C\textsuperscript{14} was the substrate, about 31 per cent of the ribose radioactivity was attributable to ribose carbon 5, whereas, when glucose-6-C\textsuperscript{14} was the substrate, approximately 79 per cent of the radioactivity was found in ribose carbon 5. This agrees fairly well with theoretical expectations but leaves open the possibility that some randomization takes place between carbon atoms 1 and 6 of the hexose phosphates. By comparison, Hiatt has reported that the ribose isolated from the RNA of human tumor cells (HeLa) grown in tissue culture in the presence of glucose-1-C\textsuperscript{14} contained 54 and 34 per cent of the radioactivity in carbons 1 and 5, respectively (16).

The free amino acids, glycine, serine, and alanine, were also degraded. With each of the glucose substrates, the carboxyl group carbon atoms of the three amino acids contained approximately 1 to 3 per cent of the radioactivity. When glucose-1-C\textsuperscript{14} or glucose-6-C\textsuperscript{14} was used as substrate, no formation of labeled glycine was detectable by the methods used (12). However, approximately 70 to 80 per cent of the radioactivity of serine was recovered in the \(\beta\)-carbon of that amino acid. With glucose-2-C\textsuperscript{14}, the \(\beta\)-carbon of serine contained 7 to 8 per cent of the total serine radioactivity, while virtually all the radioactivity of glycine was found in the \(\alpha\)-carbon of that amino acid. These results suggest that an extensive randomization of the isotope among all 6 carbon atoms of the glucose substrate did not take place under these experimental conditions. The radioactivity found in the \(\beta\)-carbon of serine in the experiments with glucose-2-C\textsuperscript{14} could be attributable to the oxidation of that substance to ribulose phosphate via the direct oxidative pathway, the conversion of ribulose phosphate to 1,3-C\textsuperscript{14}-fructose-6-phosphate by a reversal of Reactions IV, III, and II of Fig. 2 (1, 2), and the conversion of 1,3-C\textsuperscript{14}-fructose-6-phosphate to serine (12). The carboxylation of 1-C\textsuperscript{14}-ribulose-phosphate to 3-C\textsuperscript{14}-phosphoglyceric acid could also lead to formation of serine-3-C\textsuperscript{14} (17). There is a third possibility, namely that some of the glucose-2-C\textsuperscript{14} might have been converted by glycolysis to phosphoenol pyruvate-2-C\textsuperscript{14}. The carboxylation of the latter substance to oxalacetate, the conversion of the oxalacetate to succinate, and the resynthesis of phosphoenol pyruvate from the succinate could then lead to the labeling of the phosphoenol pyruvate on the \(\alpha\)- and \(\beta\)-carbons. From this compound, \(\beta\)-labeled serine could arise (12).

The pattern of labeling of the amino acids is similar to that observed in lactate by Villavicencio and Guzman-Barrón (4) after they had incubated
appendix cells or Gardner lymphosarcoma cells in the presence of radioactive glucose. With glucose-2-$^{14}$C as substrate, 94 to 95 per cent of the radioactivity was found in the $\alpha$-carbon of lactate and approximately 3 to 4 per cent in the $\beta$-carbon. With glucose-1-$^{14}$C as substrate, only 0.8 to 0.9 per cent of the radioactivity was found in the carboxyl carbon of lactate.

It is of interest to compare the results reported in this paper with those of other investigators. Evidence has been presented that the ribose of *Escherichia coli* or yeast RNA is derived primarily by way of the direct oxidative pathway (18-20). On the other hand, in the fasted rat or chick, $^{14}$CO$_2$ was incorporated into liver RNA pentose by combination of C$_2$ and C$_3$ units (14, 15). Both the transketolase-transaldolase pathway and the direct oxidative pathway operate to a significant extent in the synthesis of (a) ribose phosphate by Ehrlich tumor cell suspensions (21), (b) of RNA pentose of human tumor cells (HeLa) grown in tissue culture (16), and (c) of the ribityl portion of riboflavin in the mold, *Ashbya gossypii* (22).

In experiments in vivo, Schmitz et al. (23) found a striking incorporation of glucose-1-$^{14}$C into the ribosyl portion of nucleotides isolated from the Flexner-Jobling tumor, and Marks and Feigelson (24) have shown that both carbon atoms 1 and 2 of glucose contribute to the synthesis of RNA pentose of rat liver.

**SUMMARY**

Ribose was isolated from the purine nucleotides of ribonucleic acid (RNA) of normal or malignant lymphatic cell suspensions which had been incubated in the presence of glucose-1-$^{14}$C, glucose-2-$^{14}$C, or glucose-6-$^{14}$C. With each of the tissues, the incorporation of $^{14}$C was highest when glucose-2-$^{14}$C was the substrate, although as much radioactivity was incorporated from glucose-1-$^{14}$C as from glucose-6-$^{14}$C. Approximately 31 and 79 per cent of the radioactivity was due to carbon atom 5 of ribose when glucose-1-$^{14}$C and glucose-6-$^{14}$C were the respective substrates. With these substrates as well as with glucose-2-$^{14}$C, only 1 to 3 per cent of the radioactivity of free serine, alanine, and glycine was due to the carboxyl carbon atoms. The results suggest that both the transketolase-transaldolase pathway and the direct oxidative pathway may be of importance in the synthesis of the ribose moiety of RNA by lymphatic cells and tumors.

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