Metabolism of Neoplastic Tissue. XVII

Blood Glucose Replacement Rates in Human Cancer Patients*

GEORGE A. REICHARD, JR.,† NELSON F. MOURY, JR., NORMAN J. HOCHELLA, RICHARD C. PUTNAM, AND SIDNEY WEINHOUSE

Fels Research Institute, Temple University Medical School, and the Germantown and Lankenau Hospitals, Philadelphia, Pennsylvania

SUMMARY

Kinetic methods of measuring rates of glucose turnover, utilizing C14-labeled glucose, were applied to human subjects bearing a variety of neoplasms. By measuring rates of decline of the blood glucose specific activity after a single injection of uniformly labeled glucose-C14, net turnover rates were estimated. In seventeen patients with cancer the average value of 131 ± 29 mg/kg body weight/hr was not significantly different from the average value of 120 ± 17 mg/kg/hr observed for ten cancer-free subjects. Since this procedure gives only net glucose turnover, uncorrected for glucose resynthesized from labeled 3-carbon metabolites via the Cori cycle, a new procedure was applied, based on the randomization of labeling which occurs when glucose-l-C14 is broken down to 3-carbon fragments and is resynthesized to glucose. In seven subjects with cancer “corrected” turnover rates ranged from 124 to 370 mg/kg/hr, with an average of 192 mg/kg/hr, as compared with an average of 161 mg/kg/hr for four normal subjects. Average recycling rates were 50 ± 20 mg/kg/hr for the cancerous subjects and 26 ± 6 mg/kg/hr for the normals.

The data indicate that rates of replacement and recycling of blood glucose may be higher in subjects with cancer, but the differences were not as marked as one would have expected in view of the generally high glycolytic activity of tumors in vitro.

Although a high rate of glucose utilization, with concomitant production of lactic acid (aerobic glycolysis), has long been recognized to be a characteristic feature of the neoplastic cell, and though there is some evidence that tumor glycolysis occurs in vivo as well as in vitro, little information is available concerning the magnitude of this process in vivo or its metabolic consequences to the host. If the high glycolysis displayed by tumors in vitro is typical of their behavior in vivo, a large tumor should constitute a serious drain on the carbohydrate reserves of the host. For example, on the basis of a QO2 of 10, a tumor of 100 gm. dry weight would produce about 4 gm. of lactic acid per hr. and in doing so would use up slightly more than this quantity of glucose. Previous studies of glucose turnover, with C14-labeling technics, demonstrated that a normal, fasting and resting 70-kg. human will produce and use about 7 gm. of glucose per hr., which at least 60 per cent or approximately 4 gm. will be used by the brain alone (16). Thus, a tumor of such size can be anticipated to require approximately as much glucose as the whole body in the resting state, with the exception of the nervous system. Unlike muscle and adipose tissue, whose glucose uptake is repressed by a normally impermeable membrane that requires insulin for glucose transport, the tumor cell probably utilizes glucose constantly, regardless of the dietary and hormonal state. Such a constant drain on the glucose reserves might be expected to require considerable adjustment in gluconeogenic mechanisms and thus profoundly affect the metabolic status of the tumor-bearing host.

Several recent reviews (5, 11) call attention to frequently observed “spontaneous” hypoglycemias associated with massive nonpancreatic tumors in man, and these have been attributed to a “glucose hunger” by the tumors. On the other hand, there are conflicting reports concerning the responses of cancer patients to the various glucose tolerance tests. Essentially normal responses were observed by Rohdenberg (18) to oral glucose administration, whereas Glicksman and Rawson (9) reported impaired responses associated with an increased incidence of diabetes mellitus. Marks and Bishop (4, 13) also observed impaired responses to intravenous glucose injections in patients with neoplastic diseases; however, Weisenfeld et al. (21) were unable to confirm these results and cite.

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† Present address: Smith, Kline and French Laboratories, Philadelphia, Pa.

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difficulties in methods and criteria of normality in explanation of the differences between these groups.

In recent years we and others have been employing C¹⁴-labeling procedures for measuring rates of glucose production and utilization in man (14, 16) and animals (8). These procedures have the advantage over the more traditional tolerance tests or measurements of arteriovenous differences in providing reliable estimations of turnover rates regardless of whether or not changes occur in net balance and, moreover, are applicable to subjects in a steady state.

Two procedures were employed: The first method involves the intravenous injection of a single “tracer” dose of glucose labeled with C¹⁴, following which procedure samples of blood are withdrawn at regular intervals for the assay of the levels and radioactivity of blood glucose. On the principle that labeled blood glucose is constantly undergoing replacement by new, unlabeled glucose entering the extracellular space from the liver while glucose is constantly being withdrawn by the peripheral tissues (principally the brain), the “turnover” rate may be estimated from the first-order reaction rate expression,

\[ R = \frac{2.3B \log_{10} i_s/i_t}{t} \]  

(1)

where \( R \) = turnover rate in mg/100 ml/min.,
\( B \) = the average blood glucose concentration in mg/100 ml during the interval, \( t \),
\( i_s \) = the initial blood glucose concentration at time, \( t \),
\( i_t \) = the sp. act. of blood glucose at time, \( t \).

A full description of this procedure and a discussion of the assumptions underlying its application and of its experimental limitations may be found in previous publications by ourselves (8, 15) and others (19, 23).

One limitation of this method is that it depends solely on the rate of dilution of labeled by unlabeled glucose molecules; hence, it does not give any indication of the degree to which labeled glucose carbons that are broken down to lactic acid in peripheral tissues are “recycled” by resynthesis to glucose in the liver. Although the existence of this so-called “Cori cycle” has been recognized for many years, until recently its quantitative significance in the intact animal has never been determined (17). If lactate production is high in tumor tissues, then such recycling may be expected to be of special significance in the glucose economy of the cancer patient. For our second method, a variation of the above procedure has been worked out which allows not only a determination of the magnitude of the Cori cycle but also the estimation of a corrected figure for total glucose turnover, which takes into account the resynthesis of glucose via the Cori cycle. The principles of this procedure and the experimental application in the human in the basal state have recently been published elsewhere (17). Briefly summarized, the method involves the intravenous injection of glucose-1-C¹⁴ instead of glucose-U-C¹⁴ as in the previous method, and the blood samples that are subsequently withdrawn are submitted not only to determination of blood glucose level and total radioactivity, but are degraded chemically so as to obtain estimates of the radioactivity of carbons 1 to 5 on the one hand and carbon 6 on the other. The method is based on the following well established sequence of reactions leading from lactate-3-C¹⁴: Lactate-3-C¹⁴ → pyruvate-3-C¹⁴ → malate-3-C¹⁴ → fumarate-2,3-C¹⁴ → malate-2,3-C¹⁴ → oxalacetate-2,3-C¹⁴ → phosphoenolpyruvate-2,3-C¹⁴ → glucose-1,2,5,6-C¹⁴. The equations used for calculation of the Cori cycle as well as the total glucose turnover rate are given below:

\[ \ln \left( \frac{\sigma_o}{\sigma_t - 3\sigma_o} \right) = \gamma t \]  

(2)

\[ \ln \left( \frac{\sigma_o}{\sigma_t - 2\sigma_o} \right) = \gamma(1 - \rho)t \]  

(3)

where
\( \gamma \) = fractional rate of blood glucose turnover,
\( \rho \) = the fraction of \( \gamma \) which is returned, via the Cori cycle, to each of the glucose carbons 1, 2, 5 and 6;
\( \sigma_t \) = the total radioactivity in carbons 1 to 5 of the blood glucose at time, \( t \);
\( \sigma_o \) = the total activity of carbon 6 of the blood glucose at time, \( t \);
\( \sigma_e \) = the total activity of glucose carbons 1 to 5 at 0 time.

In these equations, \( \sigma_t \) and \( \sigma_o \) are determined experimentally by a procedure described in detail elsewhere (17), and \( \sigma_e \) is obtained by extrapolation of \( \sigma_t \) to zero time (when all the radioactivity is in carbon 1). Methods of injection of labeled glucose, of collecting blood samples and assaying for glucose levels and radioactivity, and for collection and assay of respiratory CO₂ may be found in previous publications (3, 16, 19).

The subjects of this study were patients from the Germantown and Lankenau Hospitals, Philadelphia. In all cases of malignant disease, diagnosis was established by histologic examination of biopsy specimens. All patients came to the experiment after having fasted since the previous evening’s meal. Throughout the experimental period they were at rest on a cot or in a comfortable chair and were allowed water ad libitum. To avoid any undue apprehension the procedure was carefully explained beforehand. All patients were in relatively good physical condition, although, in some instances, the disease had progressed to a considerable extent. Medical histories, together with other pertinent information are listed in Table 1.

RESULTS

Glucose-U-C¹⁴ experiments.—The results of a typical experiment of the first type are shown in Chart 1. The data from this experiment will be used to illustrate the principle and calculations involved. The patient was a 68-year old woman weighing 51 kg. suffering from carcinoma of the cecum. At zero time she was given an intravenous injection of 97.5 µc. (17.6 mg.) of glucose-U-C¹⁴, and blood and respiratory samples were collected at 30-minute intervals for a total of 240 minutes. Although the blood glucose concentration remained essentially constant at 100 mg/100 ml, the specific activity of the
TABLE 1

GLUCOSE TURNOVER EXPERIMENTS OF FIRST TYPE

<table>
<thead>
<tr>
<th>Subject no.</th>
<th>Sex</th>
<th>Age (yrs.)</th>
<th>Wt. (kg.)</th>
<th>Diagnosis</th>
<th>(2) Blood glucose range (mg/100 gm)</th>
<th>(3) Pool (gm/kg)</th>
<th>(4) Space % of body wt.</th>
<th>(5) Carbon from glucose in CO₂ (%)</th>
<th>(6) Blood glucose replacement (mg/kg/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>53</td>
<td>73.2</td>
<td>Anaplastic bronchogenic carcinoma with diffuse metastases</td>
<td>100-124</td>
<td>0.46</td>
<td>41</td>
<td>25</td>
<td>96</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>50</td>
<td>55.5</td>
<td>Epidermoid carcinoma of lung with metastases</td>
<td>94-106</td>
<td>0.57</td>
<td>57</td>
<td>29</td>
<td>141</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>73</td>
<td>55.5</td>
<td>Metastatic ovarian cystadenocarcinoma</td>
<td>102-114</td>
<td>0.36</td>
<td>33</td>
<td>32</td>
<td>98</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>57</td>
<td>45.5</td>
<td>Hodgkin's disease</td>
<td>72-84</td>
<td>0.47</td>
<td>59</td>
<td>30</td>
<td>102</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>81</td>
<td>59.0</td>
<td>Chronic lymphocytic leukemia</td>
<td>91-112</td>
<td>0.53</td>
<td>53</td>
<td>40</td>
<td>151</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>83</td>
<td>57.7</td>
<td>Ovarian cancer with peritoneal metastases</td>
<td>112-122</td>
<td>0.48</td>
<td>40</td>
<td>25</td>
<td>93</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>67</td>
<td>62.0</td>
<td>Carcinoma of breast</td>
<td>108-110</td>
<td>0.28</td>
<td>26</td>
<td>35</td>
<td>116</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>63</td>
<td>51.0</td>
<td>Metastatic carcinoma of liver</td>
<td>80-100</td>
<td>0.37</td>
<td>43</td>
<td>25</td>
<td>160</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>74</td>
<td>79.1</td>
<td>Metastatic carcinoma of larynx</td>
<td>118-126</td>
<td>0.41</td>
<td>33</td>
<td>28</td>
<td>109</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>57</td>
<td>57.8</td>
<td>Hodgkin's disease</td>
<td>94-100</td>
<td>0.63</td>
<td>65</td>
<td>31</td>
<td>188</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>54</td>
<td>57.2</td>
<td>Cholangiocarcinoma</td>
<td>84-109</td>
<td>0.37</td>
<td>41</td>
<td>28</td>
<td>145</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>70</td>
<td>44.8</td>
<td>Epidermoid carcinoma of lung</td>
<td>86-100</td>
<td>0.41</td>
<td>43</td>
<td>25</td>
<td>127</td>
</tr>
<tr>
<td>13</td>
<td>F</td>
<td>68</td>
<td>51.1</td>
<td>Carcinoma of cecum</td>
<td>96-102</td>
<td>0.53</td>
<td>53</td>
<td>33</td>
<td>172</td>
</tr>
<tr>
<td>14</td>
<td>M</td>
<td>54</td>
<td>56.0</td>
<td>Cholangiocarcinoma</td>
<td>75-100</td>
<td>0.35</td>
<td>46</td>
<td>25</td>
<td>167</td>
</tr>
<tr>
<td>15</td>
<td>F</td>
<td>56</td>
<td>51.0</td>
<td>Carcinoma of breast with soft tissue metastases</td>
<td>90-100</td>
<td>0.35</td>
<td>36</td>
<td>27</td>
<td>116</td>
</tr>
<tr>
<td>16</td>
<td>M</td>
<td>66</td>
<td>77.7</td>
<td>Adenocarcinoma of colon metastatic to liver</td>
<td>88-102</td>
<td>0.54</td>
<td>54</td>
<td>25</td>
<td>172</td>
</tr>
<tr>
<td>17</td>
<td>F</td>
<td>41</td>
<td>78.0</td>
<td>Carcinoma of breast with diffuse metastases</td>
<td>94-96</td>
<td>0.24</td>
<td>26</td>
<td>25</td>
<td>79</td>
</tr>
</tbody>
</table>

Average ± S.D.  
Ten normal: Average ± S.D.

Blood glucose declined exponentially from an extrapolated initial value of 6,900 counts/min to 1,900 counts/min at the close of the experiment 240 minutes later. From equation 1 we obtained for the turnover rate during the 240-minute period,

\[ R = \frac{2.3 \times 100 \log(6900/1900)}{240} = 0.54 \text{ mg/100 ml/min}. \]

From the extrapolated zero time specific activity of 6900 it is possible to calculate the glucose pool. Since the 17.6 mg. of glucose injected had an initial specific activity of 10.6 × 10⁴ counts/min, the glucose pool was 17.6 × 10⁴ × 10⁹/6.9 × 10⁹ = 27,000 mg total or 27.0/51.1 = 0.53 gm/kg body weight. Since the glucose concentration was 100 mg/100 ml the glucose space was 27.0 liters, corresponding to 27.0 × 100/51.1 = 53 per cent of the body weight.

The change in the specific activity of the respiratory CO₂ with time is shown as the solid circle line in Chart 1A. This curve shows a rise in specific activity to a maximum value at about 90 minutes, followed by a decline paralleling that of the blood glucose. This behavior is typical of all these experiments thus far conducted and is in agreement with the theoretical considerations and the experimental data of Baker et al. (3). From the data of this curve, using equations of Baker et al. (3), we calculated that in this experiment 33 per cent of the total respiratory CO₂ carbon was derived from the oxidation of the blood glucose.

The results of seventeen such experiments carried out in cancer patients have been tabulated in Table 1. The turnover rates are given in mg glucose/kg body wt/hr, and the means, together with their standard deviations, appear at the bottom of the table. In the last line is a summary of the results of a similar study, previously reported (16) with thirteen subjects of similar age and background as the cancer patients, but who were free of obvious metabolic disorders or neoplastic disease. Blood glucose levels in the cancer patients were in the normal range in all the subjects and remained reasonably constant throughout the experimental period (column 2). A noteworthy difference from the normal subjects was a higher and more variable space (column 4) and pool size (column 3) despite the normal blood glucose levels. Column 5 shows that, within a relatively narrow range, the proportion of glucose carbon in the respiratory carbon
The patient was a 38-year-old male admitted to the hospital for treatment of a recurrent, uncomplicated duodenal ulcer. He was in good physical condition and weighed 73 kg. Following the intravenous injection of 20.4 mg. glucose-1-C14, the specific activity of carbons 1-5 ($\sigma_1$) dropped exponentially during the ensuing 4 hours, whereas the total blood glucose concentration ranged narrowly between 90 and 96 mg/100 ml. Extrapolation of the specific activity ($\sigma_t$) back to zero time gave an initial blood glucose specific activity of 32,000 counts/min. From the specific activity of the injected glucose-1-C14, 6.3 X 10^6 counts/min, and the amount injected, 20.4 mg., we estimate that 20.4 X 6.3 X 10^6/6.4 X 10^9 = 20.1 gm. represents the pool size; and from the average blood glucose concentration of 94 mg/100 ml we estimate the glucose space as 20,100/0.94 = 21.4 liters or 21.4 X 100/73.6 = 29 per cent. These values are characteristic of normal subjects reported previously (17). At the same time that $\sigma_t$ dropped exponentially, $\sigma_6$ (dotted line) rose rapidly to 300 counts/min and then slowly fell in a manner predicted from the theoretical considerations discussed earlier (17). From equations (2) and (3), we calculate a total blood glucose replacement rate, $\gamma$, of 0.84 per cent throughout the 4-hr. experimental period, with a range of 0.74-0.98 and a recycling rate ($4\rho$) of 0.12 or 12 per cent of the replacement rate. Thus, this subject was replacing blood glucose at an average rate of $94 \times 0.84 = 0.79$ mg/100 ml/min. With a glucose space of 29 per cent, this corresponds to a total replacement rate of $0.79 \times 1000 \times 0.29 = 60/100 = 138$ mg/kg/hr and, with 12 per cent recycling, a recycling rate of $138 \times 0.12 = 17$ mg/kg/hr.

Chart 1C depicts a similar experiment of the second type on a 38-year-old female with far advanced Hodgkin's disease, involving the spleen, liver, bone marrow, lymph nodes, and lungs. During 5 years of treatment, this patient received intermittent x-ray and chemotherapy and during the current admission had received nitrogen mustard 2 weeks prior to the test. There was massive enlargement of liver and spleen and diffuse infiltration of the right lung. Despite the severity of her condition, the blood glucose level was normal and remained so throughout the experiment. However, the blood glucose turnover rate was very high, as was the recycling rate. The replacement rate, $\gamma$, ranged from 1.2 to 1.8 per cent throughout the experiment, and $4\rho$ ranged from 20 to 32 per cent of the replacement rate. These values correspond to an absolute replacement rate of 370 mg/kg/hr and a recycling rate of 89 mg/kg/hr. Despite the extensive liver involvement, glucogenesis was thus proceeding at about double the normal rate; the glucose pool size, about 440 mg/kg, and the space, 41 per cent, were both at approximately normal values. Of a total of eight patients under study, only one other displayed an abnormally high blood glucose replacement rate. This was a 54-year-old woman in the terminal stages of a steady 1-year, downhill course of carcinoma of the cervix with diffuse metastases in the pelvis. She was extremely emaciated, with a weight of 41 kg, as compared with 68 kg, prior to her illness. This patient had an essentially normal blood glucose replacement rate of 0.78 per cent/min and a somewhat elevated fractional recycling rate of 28 per cent. However, the high glucose space, owing doubtlessly to her extreme emaciation, brought the absolute replacement rate on a weight basis to 244 mg/kg/hr and the recycling rate to 68 mg/kg/hr.

All the other cancer patients displayed essentially normal replacement rates, with curves essentially identical with those shown in Chart 1C. Because of the possible
TABLE 2
GLUCOSE TURNOVER EXPERIMENT OF THE SECOND TYPE

<table>
<thead>
<tr>
<th>Subject no.</th>
<th>Sex</th>
<th>Age (yrs.)</th>
<th>Wt. (kg.)</th>
<th>Diagnosis</th>
<th>Blood glucose range (gm/kg)</th>
<th>Pool space % of body wt.</th>
<th>Blood glucose replacement (mg/kg/hr)</th>
<th>Blood glucose recycling (mg/kg/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>54</td>
<td>41.4</td>
<td>Cancer of cervix with diffuse metastases</td>
<td>97-104</td>
<td>0.52</td>
<td>52</td>
<td>244</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>38</td>
<td>57.2</td>
<td>Diffuse lymphoma—probably Hodgkin's disease</td>
<td>105-113</td>
<td>0.44</td>
<td>41</td>
<td>370</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>71</td>
<td>39.1</td>
<td>Epidermoid cancer of esophagus</td>
<td>106-118</td>
<td>0.41</td>
<td>38</td>
<td>161</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>82</td>
<td>45.5</td>
<td>Epidermoid cancer of esophagus</td>
<td>98-110</td>
<td>0.37</td>
<td>36</td>
<td>124</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>84</td>
<td>56.5</td>
<td>Epidermoid cancer of neck</td>
<td>92-102</td>
<td>0.27</td>
<td>28</td>
<td>161</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>49</td>
<td>86.3</td>
<td>Carcinoma of head of pancreas with hepatic metastases. Diabetes of 2 months' duration controlled with 40 u insulin</td>
<td>350-368</td>
<td>0.72</td>
<td>21</td>
<td>134</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>68</td>
<td>67.7</td>
<td>Epidermoid cancer of esophagus, diabetes of recent origin</td>
<td>155-184</td>
<td>0.49</td>
<td>29</td>
<td>148</td>
</tr>
</tbody>
</table>

| Average | | | | | 35 ± 8 | 192 ± 66 | 50 ± 20 | |
| Four normal: Average | | | | | 36 ± 8 | 161 ± 37 | 26 ± 6 | |

The results of these experiments are summarized in Table 2. The replacement rate includes the recycled glucose, and the recycling rate, 4ρ, in this diabetic patient was 40 per cent or 54 mg/kg/hr, again a value in the normal range. Because of the high glucose pool, the curve for incorporation of activity in carbon 6 does not reach a maximum, as it does in the normal subjects, but continues to rise throughout the experimental period.

Blood glucose turnover and recycling in cancer patients.—Table 2 summarizes the results obtained with seven cancer patients in experiments of the second type. These experiments proved somewhat disappointing in that no clear-cut differences from the cancer-free subjects were observed. Except in diabetic patients the blood glucose levels were in the normal range, as were the pool sizes and spaces. In view of the fact that, in the experiments of the second type, the replacement rate includes the recycled glucose, it is not surprising that these values averaged 192 mg/kg/hr, or considerably higher than did those obtained in experiments of the first type; if one subtracts the average value for glucose recycling—namely, 50 mg/kg/hr—an average net replacement rate of 142 mg/kg/hr is obtained. This value is only slightly higher than the average replacement rate observed in experiments of the first type. Moreover, if the two highest values are eliminated, the average replacement rate would be 146 mg/kg/hr. If this is corrected by an average recycling rate of 39 in these patients, an average net replacement rate of 107 mg/kg/hr is obtained, a value well within the range observed for normal and cancer patients in experiments of the first type.

If the recycling rates are dependent, as a first approximation, on the rate of production of lactic acid, a high rate of glycolysis should lead to an enhanced recycling of glucose. Although the high average rate of glucose recycling—e.g., 50 mg/kg/hr—observed in these experiments might be construed in this manner, it is obvious that the range of variation is so great that no definite conclusions are warranted.
DISCUSSION

Although glycolysis is perhaps the most thoroughly investigated biochemical phenomenon of the neoplastic cell, there is relatively little information concerning the quantitative significance of this process during growth of the tumor in situ in the tumor-bearing host.

Several investigators, including Cori and Cori (6), Hiatt (10), and others (see the comprehensive review by Aisenberg [1]) have obtained evidence of the occurrence of tumor glycolysis in vivo. It is surprising, therefore, that, despite frequent reports of hypoglycemia accompanying the presence of tumors in man, the vast majority of such cases display no remarkable lowering of blood glucose—in fact, several investigators have reported lowered rather than increased glucose tolerance in cancer patients (4, 9, 13), though this finding is disputed (18, 21). The consensus of many clinical studies is that there is little if any elevation of blood lactate in cancer patients (22). Evidently if there is increased lactate and glucose turnover in the human cancer patient, this is not disclosed by clear-cut alterations in the levels of these substances in the blood. The more detailed explorations of glucose metabolism carried out in this study likewise reveal little clear-cut evidence of abnormalities of glucose utilization or production. The experiments of the first type demonstrate that net blood glucose replacement rates are virtually identical in cancer patients and cancer-free hospitalized subjects of the same general age group, and the data also reveal no abnormality of glucose oxidation to CO₂ in these patients. The results of the experiments of the second type are less clear. Although they do indicate that lactate production may, on the whole, be higher than that in comparable controls, the range of variation is too wide to allow any definite conclusion. Several causes may be responsible for this high degree of variation, but the most likely possibility is that the quantity of viable tumor tissue probably varies greatly. For example, the two patients with widely disseminated cancer—namely, patients 1 and 2 of Table 2—displayed by far the highest net turnover and recycling rates. It is conceivable that a more thorough investigation among a large population of cancer patients might provide some indication of a correlation between glucose recycling and the type or magnitude of cancer; but, because of the difficulty and expense of the experimental procedure, further exploration of this problem did not seem worth while.

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Metabolism of Neoplastic Tissue. XVII Blood Glucose Replacement Rates in Human Cancer Patients


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