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STUDIES IN GLYCINE-2-C^{14} METABOLISM IN MAN. II. TISSUE DISTRIBUTION [1]

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In a previous communication describing the pulmonary excretion of $C^{14}O_2$ in patients following the intravenous administration of 100 microcuries of glycine-2-C^{14} it was demonstrated that approximately 83 to 92 per cent was excreted via the lungs and that approximately 3 to 5 per cent was excreted within the urine in the first 10 days (1).[2] At that time preliminary autopsy data on one patient disclosed that about 10 per cent of the C^{14} was retained in compounds having a longer turnover time than the slowest component of excretion in the breath, namely the 7- to 14-day component. Since the publication of this paper three additional patients who were given C^{14} labeled glycine for the study of the life span of the red blood cell in leukemia and polycythemia vera have come to autopsy. The present paper reports the tissue C^{14} levels found in these patients.

METHODS

The patients had been given 100 microcuries (8.2 mg.) of glycine-2-C^{14} (methylene labeled) as described previously. Autopsies were carried out as soon as possible and in no case later than 12 hours after death. Samples of fresh tissue were taken in Patients 1, 3, and 4. In Patient 2 the samples had been placed in formalin for five to 10 minutes before the blocks were recut and tissue taken. The tissue was cut into approximately one gram samples and dried in vacuo. The bone sample was taken from the body of the sternum. The dried tissue was then combusted to carbon dioxide using a chromic-sulfuric acid oxidizing mixture (3). The carbon dioxide was precipitated as barium carbonate, the radioactivity of which was measured by the use of a vibrating reed electrometer and a 100 cc. ionization chamber operating at atmospheric pressure (4, 5).

RESULTS

The specific activity of the tissues is presented in Table I. Figure 1 shows the specific activity of the lungs, the myocardium, the kidney, and the liver of the four patients plotted on semilogarithmic paper as a function of time.

DISCUSSION

The table shows that within 57 days after administration the tissue concentrations in Patient 1 ranged from 0.04 dis./min./mg. of barium carbonate in the fat to 0.74 dis./min./mg. of barium carbonate in the spleen. If the fat is excluded from consideration, the range of specific activities in this patient was from 0.12 to 0.74 dis./min./mg. $BaCO_3$, or an approximately sixfold variation. It is interesting to note in this patient that the specific activity of the bone is near the average of all the tissues and that there are several tissues, particularly the myocardium, skeletal muscle, and the spleen, in which specific activity was considerably higher than that of the bone. In Patient 2 only five tissues were available, and these had been previ-

TABLE I

Tissue specific activities in dis./min./mg. $BaCO_3$

Autopsied at.....	Patient 1 57 days	Patient 2 105 days	Patient 3 152 days	Patient 4 526 days
Aorta	0.24		0.077	
Ilium	0.12		0.14	
Bone	0.37	0.15	0.35	0.038
Pancreas	0.40			0.038
Adrenal	0.30		0.103	0.02
Lung	0.44	0.300	0.129	0.044
Spleen	0.74		0.21	0.041
Liver	0.45	0.18	0.101	0.018
Bone marrow	0.33		0.137	0.047
Lymph node	0.27		0.123	
Kidney	0.42	0.25	0.087	0.026
Fat	0.04		<0.02	0.021
Myocardium	0.73	0.332	0.099	0.031
Skeletal muscle	0.614		0.42	0.081
Trachea			0.083	
Skin			0.014	0.179*
Stomach			0.045	0.043
Tumor				0.041
Bladder				0.041
Blood				0.078
Urine				0.005

* This result may be spurious; sufficient material to rerun this sample was not available.

[1] This study was supported by the Atomic Energy Commission.

[2] This has recently been confirmed by Hellman and associates (2).

ously slightly fixed in formalin so that although the data are probably reliable, the specific activities may be low. The tissues from this patient also show a comparatively small range of specific activities. The third patient shows a range of specific activities from a tissue in which no specific activity could be determined, the fat, to one in which the specific activity was 0.42 dis./min./mg. $BaCO_3$. Here also the skeletal muscle was the tissue with the highest specific activity. In Patient 4, who was autopsied 526 days after administration of the C^{14} labeled glycine, it is interesting to note that there is still a measurable amount of C^{14} present. It should be pointed out, however, that with the exception of skeletal muscle and the whole blood, the tissues are all close to the limit of resolution for the method of measurement of C^{14} which is employed (4, 5). Nevertheless, in each instance there was present a small, definite, and measurable quantity of activity; however, the actual numerical values are subject to considerable error at this level, and the value should not be regarded as highly precise.

Because all of these patients had lost considerable weight during the terminal phases of their illnesses, it is somewhat difficult to determine the precise amount of C^{14} present at autopsy; but in Patient 4 it can be estimated that approximately 1–2 per cent of the dose had been retained as late as 526 days. Figure 1 shows that for the four organs from which samples are available from all patients there appears to be a common component of elimination of C^{14}. As can be seen from the data on Patient 4, the values anticipated by extrapolation from the first three patients are considerably lower than those actually obtained at 526 days. This would indicate that there is another component of elimination having a half-time longer than 50 days.

From the data on the elimination of C^{14} in the breath, it was postulated that there should be another component of elimination from the body with a half-time of at least 90 days. Study of the long-term urinary C^{14} excretion shows that there is a component of urinary C^{14} excretion with a half-time of approximately 50 days (6). This is in close agreement with the anticipated value found from the tissue studies reported here and would indicate that instead of a fourth component of respiratory elimination of 90 days or greater there is present a renal excretory component of elimination having a half-time of 50 days. In addition, components representing approximately 2 per cent of the administered dose must be present having a half-time of elimination much greater than 50

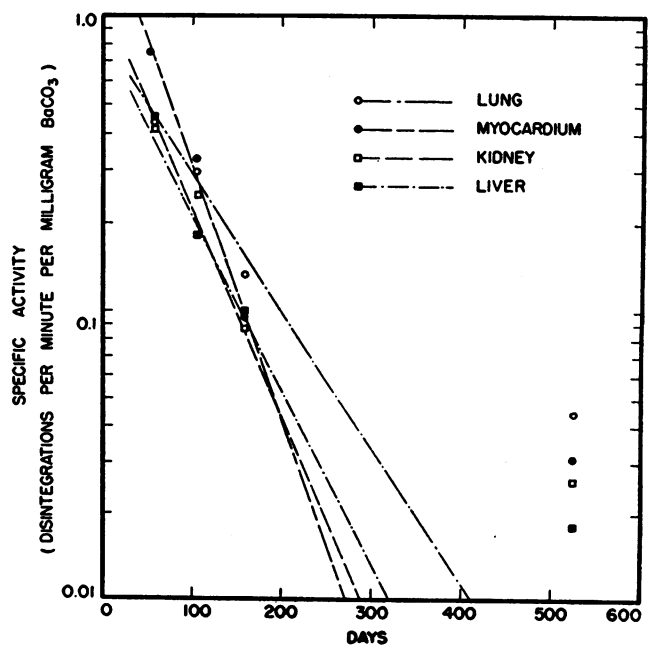

FIG. 1. SPECIFIC ACTIVITY OF LUNG, MYOCARDIUM, KIDNEY, AND LIVER

days. The mode of elimination of this 2 per cent may be either renal or pulmonary, but the specific activities are too small to measure with the instruments in current use.

SUMMARY AND CONCLUSIONS

1. The autopsy data on four patients given glycine–2–C^{14} are presented.

2. It has been shown that there is no marked concentration of the glycine–2–C^{14} in the bone and that with the exception of fat, which is very low in concentration, the tissue concentrations do not differ markedly.

3. There is a half-time of C^{14} elimination from the tissues which is approximately 50 days.

4. Autopsy of the fourth patient 526 days after administration indicates that there is at least one other component of elimination slower than 50 days.

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