THE OXIDATION AND DISTRIBUTION OF THE METHYL GROUP ADMINISTERED AS METHIONINE*

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It is well known that the methyl radical attached to sulfur or nitrogen in a number of important biological compounds cannot be synthesized by the animal body but must be supplied in the diet. Either methionine, choline, or betaine may serve as the dietary source of the essential methyl group (1). Not only are the methyl groups of these compounds interchangeable in the body, but, directly or indirectly, they provide the methyl groups for the synthesis of still other compounds such as anserine (2), creatine, and creatinine (3). Appreciable quantities of the latter compound are normally excreted in the urine. Thus methyl groups can be lost from the body without undergoing degradation.

Since this essential radical moves in toto (3, 4) from compound to compound within the body, and since it can leave the body in an intact form, we wished to ascertain whether the body can oxidize the methyl group to carbon dioxide and water, or whether it is quantitatively excreted in the urine and feces as creatinine and hitherto unidentified methyl compounds. Furthermore, because of the migratory properties of the labile methyl group, it was also of interest to extend our knowledge concerning the rapidity with which the methyl group of administered methionine enters into transmethylation reactions and the speed at which it penetrates into the various tissues and organs of the body.

Oxidation of Methyl Group to Carbon Dioxide

The possibility of obtaining an unequivocal answer to the question concerning the oxidation of the methyl group was provided when Melville, Rachele, and Keller (5), in our laboratory, succeeded in synthesizing L-methionine containing a high concentration of C\textsuperscript{14} in the methyl group.

In our initial experiment 200 mg. of the radioactive methionine were

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given by stomach tube to a 165 gm. rat that had previously been fed a purified diet containing 1.2 per cent methionine, 0.2 per cent choline chloride, and no cystine. The labeled methionine was given at 9.00 a.m. and the animal was placed immediately in a metabolism apparatus designed for the continuous and quantitative collection of carbon dioxide. Food was withheld during the remainder of the experiment.

The presence of radioactivity in the carbon dioxide expired during the 1st hour of the experiment demonstrated that the rat was able to oxidize the methyl group administered as methionine. At this time 0.8 per cent of the ingested methyl carbon had appeared in the expired air. The amount of methyl oxidized per hour then rose to a peak value of 2.3 per cent at the 6th and 7th hours. Thereafter the rate of oxidation declined to an average value of 0.29 per cent at the 16th to 24th hours. From this time until the termination of the experiment at 52 hours, the rate of oxidation was approximately constant at 0.23 per cent per hour.

At the end of 52 hours 32.4 per cent of the methyl groups administered as methionine had been completely oxidized to carbon dioxide and water, as indicated by the radioactive carbon dioxide present in the expired air. (This figure does not take into account the carbon dioxide that was formed from methyl groups and subsequently entered into synthetic reactions in the body.) An additional 18.7 per cent of the administered methyl groups was eliminated in the urine and feces either as methyl compounds or as oxidation products of methyl groups. The amount of methyl carbon accounted for in the expired carbon dioxide, urine, and feces on each day of the experiment is shown in Table I. A total of 51 per cent of the administered methyl carbon had left the body by these three routes during the course of the experiment. We next attempted to account for the remaining 49 per cent of the administered methyl carbon.

### Table I

<table>
<thead>
<tr>
<th>Pathway</th>
<th>0-24 hrs.</th>
<th>24-52 hrs.</th>
<th>Total for 52 hrs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expired CO₂</td>
<td>26.4</td>
<td>6.0</td>
<td>32.4</td>
</tr>
<tr>
<td>Urine</td>
<td>16.2</td>
<td>2.1</td>
<td>18.3*</td>
</tr>
<tr>
<td>Feces</td>
<td>0.03</td>
<td>0.4</td>
<td>0.43</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>42.63</strong></td>
<td><strong>8.5</strong></td>
<td><strong>51.13</strong></td>
</tr>
</tbody>
</table>

* This figure was erroneously given as 14.6 per cent in a preliminary report on the oxidation of the methyl group of methionine (6).
Anatomical and Chemical Distribution of Methyl Carbon

The intense oxidation of the methyl group during the experiment was accompanied by the ubiquitous appearance of C\textsuperscript{14} in the organs, tissues, and major chemical fractions of the body and by its entry in high concentrations into the newly synthesized creatine and choline. Analysis of fifteen tissues and organs at the end of the experiment revealed the presence of C\textsuperscript{14} in each of them. Although the oxidation to carbon dioxide of the methyl group (administered as methionine) had been constant for 28 hours, the concentration of the methyl carbon in these tissues and organs was far from uniform.

The highest concentrations of the methyl carbon were found in the kidneys, liver, and adrenals. Skeletal muscle and integument, although containing approximately 40 per cent of the total C\textsuperscript{14} present in the body, had relatively low concentrations, and brain, despite its high choline content, possessed the lowest concentration of any tissue, with the exception of the depot fat.

Since, as will be shown below, a considerable proportion of C\textsuperscript{14} in the body was present in methyl compounds, the values obtained for C\textsuperscript{14} concentration must reflect to some extent the concentrations of the administered methyl group in the various tissues and organs.

Following the removal of the small samples (approximately 70 mg. each) of organs and tissues for C\textsuperscript{14} determination, the remainder of the animal, less the blood and kidneys, was frozen in dry ice, finely ground, and subjected to solvent fractionation. Each of the resulting chemical fractions, water-soluble, fat-soluble, trichloroacetic acid-soluble, acetone-soluble, and crude protein, contained appreciable quantities of C\textsuperscript{14}. By far the highest concentration of methyl carbon was found in the water-soluble fraction. 78 per cent of the radioactivity present in this fraction was attributable to choline and creatine. 82 per cent of the radioactivity of the ether-soluble fraction was attributable to choline.

Following the isolation of choline from the ether-soluble material, the remainder of this fraction was further subdivided. The free fatty acids were only slightly radioactive. The cholesterol fraction, of particular interest because of the carbon-bound angular methyl groups, possessed a higher degree of radioactivity. However, analysis of the data showed that but 1 carbon atom in every 800 molecules of cholesterol was derived from the methyl carbon of the administered methionine. A similar degree of radioactivity was observed in the "wax" and "oil" fractions comprising the balance of the unsaponifiable material. Neither of these fractions nor the cholesterol fraction contributed significantly to the total radioactivity of the ether-soluble material.
Over-All Recovery of Methyl Carbon

The per cent of the administered methyl carbon recovered in this experiment may be calculated both from the results of the tissue and organ analyses, and the results of the chemical analyses. Estimation, on the basis of tissue and organ analyses, of the portion of the originally introduced methyl carbon retained in the rat's body gave a value of 101 mg., in terms of methionine, or 50.5 per cent of the original dose. This value taken in conjunction with the per cent of methyl carbon lost from the body in the urine, feces, and expired air (Table I) gives a total recovery of 101.6 per cent.

Estimation of the methyl carbon still present in the body, on the basis of chemical analyses (plus the C\(^14\) contained in the kidneys and blood), gave a value of 85.6 mg., in terms of methionine, or 42.8 per cent of the original dose. This is a minimum figure, since some loss of radioactive carbon present as carbonate and bicarbonate must have occurred during the trichloroacetic acid extraction. Nevertheless, the total recovery of methyl carbon calculated with this value is 94 per cent.

Participation of Administered Methyl Group in Transmethylation Reactions

37 per cent of the administered methyl carbon still present in the body at 52 hours had participated in transmethylation reactions and was present in the methyl groups of creatine and choline. The high degree of transmethylation activity of the methyl group of the administered methionine reflected by this value is appreciated when one considers that at the same time the crude protein fraction contained only 40 per cent of the administered methyl carbon still present in the body. Equally illuminating in an appraisal of the transmethylation reactions involving the administered methionine molecules is an examination of the specific radioactivity of the creatine, choline, and protein-bound methionine present in the rat after 52 hours of fasting.

In the total body creatine, 1.74 per cent of the methyl groups was derived from the administered methionine. Since approximately 4 per cent of the body creatine is synthesized in 2 days (7), and since all of the radioactive creatine must have been contained in this fraction, 44 per cent of the newly synthesized creatine was formed from the administered methionine, although the latter, immediately after its absorption, comprised at the most only 22 per cent of the total body methionine. The proportionately

1In view of the amount of methyl carbon oxidized to carbon dioxide, it is probable that part of the C\(^14\) present in the protein fraction was derived from carbon dioxide fixation and was no longer present in the methyl groups of methionine.

2The total body methionine is the sum of the administered methionine and the methionine already present in the rat at the beginning of the experiment. The latter
greater contribution of administered methionine to creatine synthesis, as compared with the methionine present in the body protein at the beginning of the experiment, is thus apparent.

Choline was isolated separately from both the water- and ether-soluble fractions. The water-soluble choline was decidedly the more radioactive of the two preparations, in conformity with previous results on rabbits obtained with deuterium-labeled methionine (2). In the present experiment 16.7 per cent of the water-soluble (free) choline molecules and 10.9 per cent of the ether-soluble (phospholipide) choline molecules had derived a methyl group from the administered methionine.

It is interesting to compare the concentrations of administered methyl groups in the two choline fractions with the concentration of labeled methyl groups in protein-bound methionine. According to the compilation of Block and Bolling (8), rat protein contains 3 per cent methionine. If it is assumed that all of the radioactivity in the crude protein fraction is resident in the methyl group of methionine (an exaggerated estimate, as has been previously mentioned), then 5.7 per cent of the protein-bound methionine molecules contained a methyl group supplied by the administered methionine. This is a lower figure than obtains for either of the choline fractions. Accordingly, transmethylation to form choline was a more active process than incorporation of the administered methyl into the total body protein, either by direct introduction of the whole methionine molecule, or by transmethylation between the administered methionine and protein-bound methionine (or homocysteine).

The over-all picture of the metabolism of the methyl group of the 200 mg. of methionine administered in this experiment is one of active participation in both degradative (oxidative) and synthetic (transmethylation) reactions. The rapid rise and fall in the rate of oxidation of the administered methyl group must have reflected a similar rise and fall in the concentration of the radiomethyl in the tissues and cells which oxidize it most rapidly. Although the process of oxidation in itself would lower the concentration, it appears from the wide-spread chemical and morphological distribution of the radiomethyl group observed at the end of the experiment that this was not the only factor involved, but that the chemical and anatomical translocations of the methyl group also contributed to the establishment at 10 to 24 hours of the steady rate of oxidation. Conversely, the establishment of a steady rate of oxidation suggests that the administered...

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Footnote:

3Preliminary experiments in vitro have shown that the methyl group of labeled methionine is oxidized by liver and kidneys but not by heart or testes.

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was calculated on the assumption that protein made up 14 per cent of the body weight and that 3 per cent of the protein was methionine (8).
methyl group, and its oxidation products, had reached at that time an equilibrium with their counterparts already present in the body, and that the assimilation of the radiomethyl group had thus been completed.

The demonstration of the oxidation of the labile methyl group administered as methionine raises a number of important questions, such as the relation between the rate of oxidation and the amount of dietary methionine ingested, the influence of dietary choline and cystine on the oxidation of the methyl group of methionine, and the relative rate of oxidation of the methyl group administered as choline, betaine, sarcosine, creatine, etc. Moreover, the identification of the intermediary products in the oxidation of the methyl groups to carbon dioxide and the determination of their roles in metabolic processes, as well as the location of the enzyme systems effecting these oxidations, become matters of considerable interest. These and related problems are now under investigation.

**EXPERIMENTAL**

*Collection of Expired Carbon Dioxide*—The metabolism apparatus used for the collection of CO₂ and illustrated in Fig. 1 was sturdy, simple, and readily assembled. Rubber tubing was used to connect the members of the assembly. All connections and joints, with the exception of the desiccator stopper and lid, were sealed with glycerol. The former was sealed with beeswax and the latter with Lubriseal.

The flow through the metabolism chamber was 1.1 liters per minute. The pressure within the chamber was approximately 8 mm. of Hg below atmospheric pressure. Except in hot summer weather, the internal temperature of the metabolism chamber, with a rat present, was generally 28° with occasional 1° fluctuations. In hot weather the chamber was held at 28° by draping it with wet towels. A fan placed at variable distances from the desiccator was directed toward it to increase evaporation.

Outward leaks from the apparatus were prevented by the slight negative pressure in the metabolism chamber and the higher negative pressure in the NaOH absorbers. The apparatus was checked for inward leaks by running it for several hours without a rat and with water replacing the alkali in the NaOH scrubbers. If leaks are present, the terminal Ba(OH)₂ solution will become cloudy.

During an experiment complete recovery of expired CO₂ was indicated by the absence of cloudiness in the terminal Ba(OH)₂ solution. This was the case after 12 hours of continuous operation without replacing the NaOH solution.

In metabolism experiments a second pair of scrubbers containing 2.5 N NaOH was connected to the 3-way stop-cocks shown in Fig. 1. By
switching from one pair of absorbers to the other, collections were made at any desired interval without the loss of expired CO₂.

The 400 ml. of 2.5 N NaOH contained in each tower were prepared from concentrated NaOH and air-free water. Following a collection, the contents of each of the two towers were poured into a 1 liter volumetric flask, each tower was rinsed with two 45 ml. portions of air-free water, and the combined solutions were then made up to volume.

**Determination of Radioactivity**—Aliquots of the solutions containing Na₂CO₃ were chosen to yield approximately 50 mg. of BaCO₃ (30 to 60 mg.). Such an aliquot was transferred to a 50 ml. Erlenmeyer flask, brought to approximately 25 ml. with air-free water, stoppered with a CO₂ absorbing tube, and heated to boiling on a hot plate. 2 ml. of 1 m BaCl₂ were then introduced rapidly and the flask was immersed in a boiling water bath. This temperature insured the formation of a coarse crystalline precipitate of BaCO₃.

The flask was cooled, and the precipitate, following the addition of 5 drops of a 1 per cent solution of Triton NE₂, was collected on a filter paper

disk of 2.32 sq. cm. area by the filtration method described by Henriques et al. (9) for benzidine sulfate. During the filtration the Erlenmeyer flask was washed three times with 10 ml. portions of water. The collected precipitate was kept covered with water until the last of the washings had been poured into the cylinder. After the last portion of wash water had been sucked through, 4 ml. of absolute alcohol were poured immediately over the precipitate, the cylinder was removed, and the precipitate and filter paper were wetted down with several drops of alcohol. The \( \text{BaCO}_3 \) disk was allowed to dry for 5 minutes at the pump under an infra-red lamp.

The \( \text{CO}_2 \) evolved from the combustion of tissues, chemical fractions, and compounds obtained from the rat was converted to \( \text{BaCO}_3 \) and made into disks by the method described above. The tissues and chemical preparations were oxidized in a combustion tube, through which there flowed a continuous stream of \( \text{CO}_2 \)-free \( \text{O}_2 \), and the evolved \( \text{CO}_2 \) was collected in carbonate-free 2.5 \( \text{N} \) \( \text{NaOH} \). This combustion method has been described by Keller, Rachele, and du Vigneaud (4).

The radioactivity of the \( \text{BaCO}_3 \) samples was measured with the use of a bell-shaped Geiger-Müller counter with a mica window of less than 2 mg. per sq. cm. and an Autoscaler scaling circuit. Samples derived from the expired \( \text{CO}_2 \), chemical preparations, and tissues were counted alternately with a standard made from the combustion of a weighed amount of the radioactive methionine used in the experiment. By comparing the counts given by an unknown sample with the counts given by the methionine standard (after correcting each for background and self-absorption), the amount of the administered methionine represented by the unknown was calculated by a simple proportion. The per cent of administered methionine, methyl group, or \( \text{C}^{14} \) (in this instance all three are identical) that had been converted to or was contained in the unknown was then calculated.

**Organ and Tissue Analysis**—At 52 hours the rat was anesthetized with sodium amytal, exsanguinated, skinned, and dissected. The intestinal tract was washed out with water. After weighing the organs, samples ranging in weight from 25 to 150 mg. were removed for combustion. The weights of the more diffuse tissues were calculated from the figures given by Donaldson (10). The weights of tissues and organs together with their \( \text{C}^{14} \) content (in terms of the 200 mg. dose of radioactive methionine) are given in Table II. The sum of these weights, 143 gm., compares favorably with the weight of the animal at the time of sacrifice, 141 gm. The concentration of \( \text{C}^{14} \), in terms of administered methionine, in the fresh tissues and organs is illustrated in Fig. 2.

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When necessary, non-radioactive \( \text{Na}_2\text{CO}_3 \) was added to the \( \text{NaOH} \) solution to provide the desired amount of carbonate for precipitation with \( \text{BaCl}_2 \).
Chemical Fractionation—The procedure followed in the solvent fractionation of the rat (less kidneys, blood, and samples taken for combustion) is illustrated in Diagram 1. Several extractions were made with each solvent. The concentration of C\(^{14}\) (in terms of administered methionine) found in each of these fractions is shown in Table III.

In addition to the fractionation shown in Diagram 1, the ether-soluble fraction was saponified in Ba(OH)\(_2\) solution and acidified. The lipides were then removed from the water-soluble components (choline, glycerol, etc.) by ether extraction. The lipide fraction was resaponified in a methanol solution of KOH and separated into fatty acids and non-saponifiable material. The fatty acids were only slightly radioactive. The ethereal solution of the non-saponifiable matter was washed twice with 0.1 N NaOH and seven times with water. It was then subdivided into sterol, wax, and oil fractions by means of fractional crystallization from methanol (11). The cholesterol fraction after two crystallizations from methanol yielded a white crystalline material composed of notched monoclinic

### Table II

**Distribution of Labeled Methyl Carbon Administered As Methionine (200 Mg.) in Organs and Tissues at 58 Hours**

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Wet weight</th>
<th>Labeled carbon*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle</td>
<td>63.5†</td>
<td>27.9</td>
</tr>
<tr>
<td>Liver</td>
<td>7.2</td>
<td>23.7</td>
</tr>
<tr>
<td>Integument</td>
<td>24.6†</td>
<td>12.6</td>
</tr>
<tr>
<td>Small intestine</td>
<td>4.3</td>
<td>5.8</td>
</tr>
<tr>
<td>Blood</td>
<td>10.0†</td>
<td>5.5</td>
</tr>
<tr>
<td>Bone</td>
<td>10.2†</td>
<td>6.35</td>
</tr>
<tr>
<td>Kidneys</td>
<td>1.3</td>
<td>5.2</td>
</tr>
<tr>
<td>Large intestine</td>
<td>3.5</td>
<td>3.2</td>
</tr>
<tr>
<td>Testes</td>
<td>3.3</td>
<td>3.1</td>
</tr>
<tr>
<td>Lungs</td>
<td>3.7</td>
<td>2.8</td>
</tr>
<tr>
<td>Depot fat</td>
<td>8.5†</td>
<td>1.2</td>
</tr>
<tr>
<td>Spleen</td>
<td>0.9</td>
<td>0.95</td>
</tr>
<tr>
<td>Pancreas</td>
<td>0.8</td>
<td>0.76</td>
</tr>
<tr>
<td>Brain</td>
<td>1.5†</td>
<td>0.5</td>
</tr>
<tr>
<td>Adrenals</td>
<td>0.025</td>
<td>0.06</td>
</tr>
<tr>
<td>Intestinal contents</td>
<td></td>
<td>1.4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>143.2</strong></td>
<td><strong>101.02</strong></td>
</tr>
</tbody>
</table>

* The labeled carbon is expressed as mg. of administered methionine.
† Calculated from the data given by Donaldson (10).
plates. The solid fraction (wax) was pale yellow and the oil fraction was red. Each of these fractions possessed approximately the same low degree of radioactivity.

Isolation of Choline and Creatine—Choline was isolated from both the water- and ether-soluble fractions as choline chloroplatinate. Creatine was isolated from the water-soluble fractions as creatinine potassium picrate (3). The platinum content of each of the choline derivatives was 31.2 per cent as compared with the theoretical value of 31.7 per cent. The creatinine potassium picrate was pure, according to the Jaffe reaction.

The creatine content of the water-soluble and trichloroacetic acid-soluble fractions (Diagram 1) as determined by the Jaffe reaction was 223 mg. and 72 mg., respectively. The choline chloroplatinate isolated from the water- and ether-soluble fractions amounted to 36 mg. and 154

Fig. 2. Concentration of the labeled methyl carbon administered as methionine in the organs and tissues at 52 hours.
Procedure for solvent extraction

Rat frozen in dry ice, ground, and extracted with absolute alcohol, hot 95% alcohol, warm alcohol-ether; and ether

Combined extracts
- Alcohol and ether removed in vacuo, extract partitioned between water and ether

Residue
- Extracted with 6% trichloroacetic acid

Water-soluble
- Dried in vacuo

Ether-soluble
- Ether removed in vacuo

Residue
- Extracted with acetone and ether; ether fraction discarded

Acetone-soluble
- Acetone removed in vacuo; residue washed with ether and dried

Crude protein
- Residue dried and ground in mill

Trichloroacetic acid-soluble
- Residual solvents removed in vacuo; extracted with ether; dried in vacuo
mg., respectively. These values were translated into the amount of water-soluble and fat-soluble choline contained in the whole animal on the basis of the choline content of the rat as given by Jacobi and Baumann (12).

The radioactivity of the choline and creatine samples was determined following their combustion. On the basis of our past experience it was assumed that all of the C\textsuperscript{14} was in the methyl groups. The C\textsuperscript{14} present in these compounds was expressed as mg. of administered methionine (Table III).

### Table III

**Distribution of Labeled Methyl Carbon Administered As Methionine in Chemical Fractions of Body\* at 52 Hours**

<table>
<thead>
<tr>
<th>Fraction</th>
<th>Dry weight</th>
<th>Labeled carbon</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>gm.</td>
<td>Amount</td>
</tr>
<tr>
<td>Water-soluble</td>
<td>2.0</td>
<td>13.51</td>
</tr>
<tr>
<td>Ether-soluble</td>
<td>10.9</td>
<td>20.48</td>
</tr>
<tr>
<td>Trichloroacetic acid-soluble</td>
<td>17.4</td>
<td>8.16</td>
</tr>
<tr>
<td>Acetone-soluble</td>
<td>1.5</td>
<td>3.90</td>
</tr>
<tr>
<td>Crude protein</td>
<td>18.0</td>
<td>30.60</td>
</tr>
<tr>
<td>Total</td>
<td>49.8</td>
<td>76.65</td>
</tr>
</tbody>
</table>

\* The kidneys and approximately one-half of the blood were not included in the fractionation.

† The labeled carbon is expressed as mg. of administered methionine.

### SUMMARY

The results of an experiment are reported in which 200 mg. of methionine labeled with C\textsuperscript{14} in the methyl group were given orally to a rat that was then fasted for 52 hours.

The ability of the animal organism to oxidize the methyl group (administered as methionine) to carbon dioxide and water at a rapid rate was demonstrated by the appearance of one-quarter of the administered methyl carbon in the expired carbon dioxide during the 1st day. Thereafter the rate of oxidation of the methyl group fell to a low but steady value.

At the same time the administered methyl group participated extensively in transmethylation reactions, as was shown by its appearance in the methyl groups of creatine plus choline in an amount equal to the quantity present in the body protein itself. Moreover, the specific activity of both the water-soluble and fat-soluble choline fractions exceeded the estimated specific activity of the protein-bound methionine. Accompanying these
chemical translocations of the administered methyl group was its widespread distribution throughout the body, as reflected by the presence of C\textsuperscript{14} in all of the major organs and tissues. However, this distribution was most uneven, by far the highest concentrations of C\textsuperscript{14} being found in the kidneys, liver, and adrenals.

These findings suggest that the chemical and anatomical distribution of the administered methyl group contributed to the fall in the initial high rate of oxidation and to the establishment of the steady rate of oxidation of this radical, and, conversely, that the establishment of this steady rate of oxidation marked the end of the major chemical and morphological translocations that brought the methyl group into equilibrium with the labile methyl pools (and their oxidation products) already present in the body.

The total recovery of the administered methyl carbon was 94 per cent when calculated from the chemical analyses of the animal plus the C\textsuperscript{14} eliminated in the respiratory CO\textsubscript{2}, urine, and feces. Similar calculations on the basis of tissue and organ analyses gave a total recovery of 101 per cent.

The authors wish to acknowledge the technical assistance of Mrs. Marion H. Wilson.

BIBLIOGRAPHY

1. du Vigneaud, V., Harvey Lectures, 38, 39 (1942-43).
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