



Fig. 1.—Ferrous-ferric exchange:  $x$ , radioactivity of ferrous fraction;  $x_{\infty}$ , equilibrium value;  $T_{1/2} = 44 \pm 4$  sec.

mary of the data obtained is given in Table I. All runs were made at room temperature  $23 \pm 2^{\circ}$ . The results indicate that catalysis by traces of chloride was not an important factor in determining the rate; possible effects of other undetected impurities are, of course, not eliminated. The change of half-time with iron concentration shows the reaction to be second order, presumably first order in ferric and in ferrous iron, in which case the rate constant in  $0.4 f$  perchloric acid is  $16 \text{ mole}^{-1}\text{-l.-sec.}^{-1}$  at  $23^{\circ}$ .

Experiments on the various factors which affect the rate are being continued.

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### THE *IN VIVO* SYNTHESIS OF LABILE METHYL GROUPS

Sir:

In the course of an investigation into the metabolism of amino acids, evidence has been obtained which can best be explained on the assumption of an *in vivo* synthesis of labile methyl groups in the rat. These methyl groups may be derived from the  $\alpha$ -carbon of glycine, directly, or indirectly through the  $\beta$ -carbon atom of serine, or both, and therefore from serine itself. This is contrary to the belief that labile methyl groups cannot be synthesized in the animal organism but must be provided in the diet.<sup>1,2</sup>

Serine labeled in the  $\beta$ -position with  $C^{14}$  was synthesized according to the method of King.<sup>3</sup> A total of 20.1 mg. of DL-serine- $\beta$ - $C^{14}$  in 10 ml. of water was given intraperitoneally to

(1) du Vigneaud, Cohn, Chandler, Schenck and Simmonds, *J. Biol. Chem.*, **140**, 625 (1941).

(2) du Vigneaud, *THIS JOURNAL*, **72**, 1049 (1950), did demonstrate the incorporation of methyl groups from methanol into choline; methanol, however, is not a normal dietary constituent.

(3) King, *ibid.*, **69**, 2738 (1947).

a 150-g. male rat in divided doses twice daily over a period of five days. The rat was kept on the ordinary stock diet. The serine contained a total radioactivity of 2.8 microcuries. The rat was sacrificed and the choline in the liver isolated as the reineckate, then purified through the chloroplatinate, degraded to trimethylamine, which was precipitated as the chloroplatinate and recrystallized, all according to the method of du Vigneaud, *et al.*<sup>1</sup> Radioactivity was found in the methyl groups from the choline.

SPECIFIC ACTIVITY PER MILLIMOLE IN COUNTS PER MIN.  
(Platinum, %)  
Calcd. Found

DL-Serine	$2.2 \times 10^7$		
Choline chloroplatinate	$2.3 \times 10^4$	31.7	31.5
Trimethylamine chloroplatinate	$1.3 \times 10^4$	37.0	37.0

Confirmation of these findings was obtained with another animal.

That all of the choline radioactivity is not in the trimethylamine fraction indicates that serine, at least in part, has been converted to ethanolamine; this is additional support for the findings of Stetten.<sup>4</sup>

There is reason to believe that pteroylglutamic acid and possibly vitamin B<sub>12</sub> may be involved in these transformations.

The finding of radioactivity in the choline methyl group demonstrates the *in vivo* synthesis of labile methyl groups from the  $\beta$ -carbon of serine and hence<sup>5</sup> from the  $\alpha$ -carbon of glycine.

The authors wish to thank Dr. Louis DeSpain Smith for his valuable advice.

After this work had been completed we became aware of a report by Sakami<sup>6</sup> and Welch and Sakami<sup>7</sup> on the incorporation of the methyl group of acetone and of formate into methionine and choline methyl groups. We have obtained similar results with radioactive formaldehyde.

(4) Stetten, *J. Biol. Chem.*, **144**, 501 (1942).

(5) Sakami, *ibid.*, **178**, 519 (1949).

(6) Sakami, *Federation Proc.*, **9**, 222 (1950), abstract.

(7) Welch and Sakami, *ibid.*, **9**, 245 (1950), abstract.

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### THE SYNTHESIS OF THE METHYL GROUPS AND ETHANOLAMINE MOIETY OF CHOLINE FROM SERINE AND GLYCINE IN THE RAT<sup>1</sup>

Sir:

In an investigation of the mechanism of formation of the phospholipid bases it was found that L-serine is a source not only of the ethanolamine portion of choline, but also of its methyl carbon atoms. When L-serine labeled with  $N^{15}$  in the amino group and  $C^{14}$  in the  $\beta$ -carbon atom was

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