

## ON THE UTILIZATION OF GLYCINE FOR URIC ACID SYNTHESIS IN MAN

Sirs:

Sonne *et al.*<sup>1</sup> and Buchanan and Sonne<sup>2</sup> have recently reported on the origin of the carbon atoms of uric acid in the pigeon. They find that glycine or a metabolic derivative is probably the precursor of carbon atom 4 of uric acid. In experiments already reported<sup>3</sup> we fed glycine labeled with N<sup>15</sup> to a male human adult; uric acid was isolated from 24 hour urine

66 gm. of glycine containing 32.4 atom per cent N<sup>15</sup> excess were fed to a male human adult for 3 days and urinary uric acid isolated on subsequent days.

Days from start of feeding	N <sup>15</sup> concentration, atom per cent excess			
	Uric acid nitrogen, position No.			
	Total nitrogen, 1, 3, 7, 9	1 and 3	7	9*
1	0.078	0.028	0.241	0.015
4	0.459	0.178	1.38	0.100
9	0.308	0.144	0.800	0.144
14	0.251	0.143	0.590	0.128
39	0.095			

\* These values are calculated from the isotope concentration of the total uric acid and nitrogens 1, 3, and 7.  $C_{N9} = 4C_{N1,3,7,9} - (2C_{N1,3} + C_{N7})$ . These values, being the difference of two comparatively large numbers, must have a considerable error associated with them.

specimens in order to study its rate of synthesis and the sources of its nitrogen atoms. The results obtained demonstrate that in man the nitrogen atom in the 7 position of uric acid arises directly from the amino group of glycine and that probably the carbon atom 5 is derived from the  $\alpha$ -carbon atom of glycine. Although uric acid metabolism differs in some respects in the pigeon and in man, the results here reported, in conjunction with those of Sonne and his collaborators, indicate that both species directly utilize glycine for the synthesis of uric acid by a mechanism whereby the atoms in glycine enter into the 4, 5, and 7 positions in uric acid.

Estimations of N<sup>15</sup> concentration were carried out on uric acid. The average value for the nitrogen atoms 1 and 3 was obtained by degradation

<sup>1</sup> Sonne, J. C., Buchanan, J. M., and Delluva, A. M., *J. Biol. Chem.*, **166**, 395 (1946).

<sup>2</sup> Buchanan, J. M., and Sonne, J. C., *J. Biol. Chem.*, **166**, 781 (1946).

<sup>3</sup> Shemin, D., and Rittenberg, D., *J. Biol. Chem.*, **166**, 627 (1946).

of uric acid to alloxantin,<sup>4</sup> that for the nitrogen atom 7 by the degradation of uric acid to glycine<sup>5</sup> (isolatee as the *p*-toluenesulfonyl derivative). Hydrolysis of uric acid by concentrated hydrochloric acid at 185° for 24 hours results in the formation of ammonia, carbon dioxide, and glycine. That the amino group of the isolated glycine is indeed the nitrogen 7 of uric acid has been shown by the isolation of sarcosine from 7-methyl uric acid and glycine and methylamine from 9-methyl uric acid.<sup>6</sup> The isotope concentrations found in the alloxantin and glycine, and the calculated value for position 9, are given in the table. It is clear that the nitrogen atom at position 7 has a source other than that of the others; whereas those at positions 1, 3, and 9 seem to be derived from nitrogen liberated by the oxidative degradation of amino acids in general, that at position 7 arises specifically from glycine.

*Department of Biochemistry*  
*College of Physicians and Surgeons*  
*Columbia University*  
*New York*

DAVID SHEMIN  
D. RITTENBERG

Received for publication, January 20, 1947

---

<sup>4</sup> Nightingale, D., *Organic syntheses*, New York, **23**, 6 (1943).

<sup>5</sup> Strecker, A., *Z. Chem.*, **4**, 215 (1868).

<sup>6</sup> Fischer, E., *Ber. chem. Ges.*, **32**, 435 (1899).