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Metabolism of Various Sulfur Compounds in Cystinuria.*†

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A cystinuric patient was kept for a period of approximately 4 months on a standard meat free diet and his urine analyzed daily for various nitrogenous and sulfur constituents. In addition the cystine sulfur was determined by both the Folin and the Sullivan[1] methods.

During experimental periods of 3 days each the following compounds were fed in the quantities indicated containing equivalent amounts of sulfur: cystine (6.4 gm.), glutathione (16 gm.), cysteine HCl (8.8 gm., neutralized) and dl-methionine (8 gm.). The experiments were carried out in triplicate except the one with glutathione which was repeated only once.

The results may be summarized as follows:

Cystine experiments showed that 94% of the extra sulfur was excreted as inorganic sulfate and that there was no rise in the excretion of cystine.

Glutathione experiments showed that 80% of the extra sulfur was excreted as inorganic sulfate and that there was a slight rise in the excretion of cystine which amounted to 9% of the extra sulfur.

Cysteine experiments showed that only 34% of the extra sulfur were excreted as inorganic sulfate while there was a large increase in the excretion of cystine, continuing for several days after the feeding, which increase in cystine excretion accounted for 66% of the extra sulfur. The analyses also indicated that additional cystine and not cysteine was being excreted.

dl-Methionine experiments showed that only 34% of the extra sulfur was excreted as inorganic sulfate while there was a large increase in the excretion of cystine, continuing for several days after the feeding, which increase in cystine excretion amounted to 47% of the extra sulfur; there was also a definite increase in the excretion

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[1] *Cf.* Brand, E., Harris, M. M., and Biloon, S., *J. Biol. Chem.*, 1930, **86**, 315.

of undetermined (non-cystine) neutral sulfur which amounted to 19% of the extra sulfur. The analyses again indicated that additional cystine and not cysteine was being excreted.

These experiments tend to show that the metabolism of cystine may be quite different from that of cysteine and that these 2 compounds are not as interchangeable in intermediary metabolism as has been assumed generally. They further show that the metabolic behavior of an amino acid may vary markedly depending upon whether it is catabolized as a free amino acid (cysteine) or in combined form as a peptide (glutathione). The experiments also indicate that methionine may be metabolized via cysteine. The experiments thus indicate the possibility of a conversion of methionine into cystine. The experiments by Jackson and Block[2] and by White and Lewis,[3] which have established a metabolic interrelationship between methionine and cystine perhaps should be interpreted in this way.

The finding that cystine is excreted following the administration of cysteine indicates the possible rôle of the kidney in the oxidation reduction mechanism of the SS-SH system.

It appears that the cystine which the cystinuric excretes in the urine may be derived, in part or in whole, from that portion of the protein sulfur which is present in the protein molecule in the form of methionine. Further experiments will be necessary to determine to what an extent cystinuria is primarily a disturbance in methionine metabolism.

The possibility of a disturbance in glutathione synthesis in cystinuria should be considered. This view would be in keeping with the aspects of intermediary protein metabolism indicated in a previous publication.[4]

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Cultivation of European Type of Typhus Rickettsia in Presence of Live Tissue.

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The cultivation of Rickettsia presents considerable difficulties. Successful cultivation, with demonstrable rickettsia in cells, has been

[2] Jackson, R. W., and Block, R. J., *J. Biol. Chem.*, 1932, **98**, 465.

[3] White, A., and Lewis, H. B., *J. Biol. Chem.*, 1932, **98**, 607.

[4] Brand, E., and Harris, M. M., *Science*, 1933, **77**, 589.