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Citrullinemia and an Alternative Urea Cycle

Letter to the Editor

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Scott-Emuakpor *et al.* (6) described a case of citrullinemia in a 33-year-old man who also had raised plasma and urine levels of lysine, homocitrulline, and homoarginine. It was therefore postulated that the patient was synthesizing urea by a late developing cycle whose intermediates were the homo-analogues of the ordinary urea cycle. We have also observed similar raised levels of these amino acids in a child with the same defect of argininosuccinic acid synthetase who died at 7 months of age [4, 8].

However, normal levels of lysine and homocitrulline were found in all the patients in nine families with disorders of the urea cycle other than citrullinemia which we have investigated. Furthermore, homoarginine could not be detected in two of the patients with hyperammonemia and four of the patients with argininosuccinic aciduria whose plasma and urine were examined for this amino acid [5]. From all of these findings it was concluded [5] that the high levels of lysine, homocitrulline, and homoarginine in citrullinemia do not necessarily indicate an alternative pathway of urea formation.

Competitive inhibition of urea cycle reactions both by lysine and by the various urea cycle intermediates is well known [4], and Hers [3] has suggested that the unexplained high levels of citrulline which have been found in saccharopinuria [1] might arise from competitive inhibition, because of the similarity in structure between saccharopine and argininosuccinic acid synthetase. The high lysine levels in citrullinemia might thus result from competitive inhibition of lysine catabolism by citrulline. Alternative utilization of lysine would then explain the high levels of homocitrulline and homoarginine, as in persistent hyperlysinemia [2]. The lysine and homocitrulline levels in a patient with hyperornithinemia [7] might be similarly explained.

References and Notes

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9. Requests for reprints should be addressed to: V. G. Oberholzer, B.A., The Charles Hayward Research Building, Queen Elizabeth Hospital for Children, Hackney Road, London, England E2 8PS.
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