
**Abstract**

Significant gaps remain in our knowledge of the pathways of amino acid catabolism in humans. Further quantitative data describing amino acid metabolism in the kidney are especially needed as are further details concerning the pathways utilized for certain amino acids in liver. Sufficient data do exist to allow a broad picture of the overall process of amino acid oxidation to be developed along with approximate quantitative assessments of the role played by liver, muscle, kidney, and small intestine. Our analysis indicates that amino acids are the major fuel of liver, i.e., their oxidative conversion to glucose accounts for about one-half of the daily oxygen consumption of the liver, and no other fuel contributes nearly so importantly. The daily supply of amino acids provided in the diet cannot be totally oxidized to CO2 in the liver because such a process would provide far more ATP than the liver could utilize. Instead, most amino acids are oxidatively converted to glucose. This results in an overall ATP production during amino acid oxidation very nearly equal to the ATP required to convert amino acid carbon to glucose. Thus gluconeogenesis occurs without either a need for ATP from other fuels or an excessive ATP production that could limit the maximal rate of the process. The net effect of the oxidation of amino acids to glucose in the liver is to make nearly two-thirds of the total energy available from the oxidation of amino acids accessible to peripheral tissues, without necessitating that peripheral tissues synthesize the complex array of enzymes needed to support direct amino acid oxidation. As a balanced mixture of amino acids is oxidized in the liver, nearly all carbon from glucogenic amino acids flows into the mitochondrial aspartate pool and is actively transported out of the mitochondria via the aspartate-glutamate antiport linked to proton entry. In the cytoplasm the aspartate is converted to fumarate utilizing urea cycle enzymes; the fumarate flows via oxaloacetate to PEP and on to glucose. Thus carbon flow through the urea cycle is normally interlinked with gluconeogenic carbon flow because these metabolic pathways share a common step. Liver mitochondria experience a severe nonvolatile acid load during amino acid oxidation. It is suggested that this acid load is alleviated mainly by the respiratory chain proton pump in a form of uncoupled respiration.(ABSTRACT TRUNCATED AT 400 WORDS)