American Journal of Clinical Nutrition, Vol. 85, No. 1, 167-172, January 2007

ORIGINAL RESEARCH COMMUNICATION

Interorgan amino acid exchange in humans: consequences for arginine and citrulline metabolism[1,2,3]

Marcel CG van de Poll, Michiel PC Siroen, Paul AM van Leeuwen, Peter B Soeters, Gerdien C Melis, Petra G Boelens, Nicolaas EP Deutz and Cornelis HC Dejong

[1] From the Department of Surgery, Nutrition and Toxicology Institute Maastricht, Maastricht University and University Hospital Maastricht, Netherlands (MCGvdP, PBS, NEPD, and CHCD), and the Department of Surgery, VU University Medical Center, Amsterdam, Netherlands (MPCS, PAMvL, GCM, and PGB)

Background: The liver plays a central role in amino acid metabolism. However, because of limited accessibility of the portal vein, human data on this subject are scarce.

Objective: We studied hepatic amino acid metabolism in noncirrhotic fasting patients undergoing liver surgery.

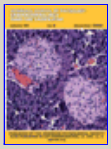
Design: Twenty patients undergoing hepatectomy for colorectal metastases in a normal liver were studied. Before resection, blood was sampled from a radial artery, portal vein, hepatic vein, and renal vein. Organ blood flow was measured by duplex ultrasound scan.

Results: The intestine consumed glutamine and released citrulline. Citrulline was taken up by the kidney. This was accompanied by renal arginine release, which supports the view that glutamine is a precursor for arginine synthesis through an intestinal-renal pathway. The liver was found to extract citrulline from this pathway at a rate that was dependent on intestinal citrulline release ($P < 0.0001$) and hepatic citrulline influx ($P = 0.03$). Fractional hepatic extractions of citrulline (8.4%) and arginine (11.5%) were not significantly different. Eighty-eight percent of arginine reaching the liver passed it unchanged. Splanchnic citrulline release could account for one-third of renal citrulline uptake.

Conclusions: This is the first study of hepatic and interorgan amino acid metabolism in humans with a normal liver. The data indicate that glutamine is a precursor of ornithine, which can be converted to citrulline by the intestine; citrulline is transformed in the kidneys to arginine. Hepatic citrulline uptake limits the amount of gut-derived citrulline reaching the kidney. These findings may have implications for interventions aimed at increasing systemic arginine concentrations.

Key Words: Glutamine • citrulline • arginine • gut • liver • kidney • interorgan amino acid exchange • humans

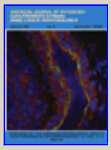
This article has been cited by other articles:



Am. J. Physiol: Endocrinology and Metabolism HOME

Y. C. Luiking, M. M. Hallemeesch, M. C. van de Poll, C. H. C. Dejong, W. J. de Jonge, W. H. Lamers, and N. E. P. Deutz
Reduced citrulline availability by OTC deficiency in mice is related to reduced nitric oxide production
Am J Physiol Endocrinol Metab, December 1, 2008; 295(6): E1315 - E1322.

[Abstract] [Full Text] [PDF]

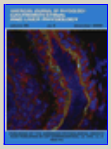


Am. J. Physiol: Gastrointestinal and Liver Physiology HOME

M. C. G. van de Poll, G. C. Ligthart-Melis, S. W. M. Olde Damink, P. A. M. van Leeuwen, R. G. H. Beets-Tan, N. E. P. Deutz, S. J. Wigmore, P. B. Soeters, and C. H. C. Dejong
The gut does not contribute to systemic ammonia release in humans without portosystemic shunting
Am J Physiol Gastrointest Liver Physiol, October 1, 2008; 295(4): G760 - G765.
[Abstract] [Full Text] [PDF]

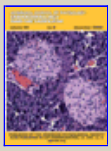
The American Journal of CLINICAL NUTRITION HOME

G. C Ligthart-Melis, M. C. van de Poll, P. G Boelens, C. H. Dejong, N. E. Deutz, and P. A. van Leeuwen
Glutamine is an important precursor for de novo synthesis of arginine in humans
Am. J. Clinical Nutrition, May 1, 2008; 87(5): 1282 - 1289.
[Abstract] [Full Text] [PDF]



Am. J. Physiol: Gastrointestinal and Liver Physiology HOME

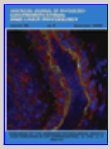
R. Thibault, S. Welch, N. Mauras, B. Sager, A. Altomare, M. Haymond, and D. Darmaun
Corticosteroids increase glutamine utilization in human splanchnic bed
Am J Physiol Gastrointest Liver Physiol, February 1, 2008; 294(2): G548 - G553.
[Abstract] [Full Text] [PDF]



Am. J. Physiol: Endocrinology and Metabolism HOME

J. C. Marini, A. Erez, L. Castillo, and B. Lee
Interaction between murine spf-ash mutation and genetic background yields different metabolic phenotypes
Am J Physiol Endocrinol Metab, December 1, 2007; 293(6): E1764 - E1771.

[Abstract] [Full Text] [PDF]

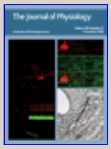


Am. J. Physiol: Gastrointestinal and Liver Physiology HOME

C. Rouge, C. Des Robert, A. Robins, O. Le Bacquer, C. Volteau, M.-F. De La Cochetiere, and D. Darmaun
Manipulation of citrulline availability in humans
Am J Physiol Gastrointest Liver Physiol, November 1, 2007; 293(5): G1061 - G1067.
[Abstract] [Full Text] [PDF]

Journal of Parenteral and Enteral Nutrition HOME

G. C. Ligthart-Melis, M. C. G. van de Poll, C. H. C. Dejong, P. G. Boelens, N. E. P. Deutz, and P. A. M. van Leeuwen
The Route of Administration (Enteral or Parenteral) Affects the Conversion of Isotopically Labeled L-[2-15N]Glutamine Into Citrulline and Arginine in Humans
JPEN J Parenter Enteral Nutr, September 1, 2007; 31(5): 343 - 350.
[Abstract] [Full Text] [PDF]



The Journal of Physiology

M. C. G. van de Poll, G. C. Ligthart-Melis, P. G. Boelens, N. E. P. Deutz, P. A. M. van Leeuwen, and C. H. C. Dejong

Intestinal and hepatic metabolism of glutamine and citrulline in humans

J. Physiol., June 1, 2007; 581(2): 819 - 827.

[Abstract] [Full Text] [PDF]