Glutamine and alanine metabolism in lungs of septic rats

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SUMMARY

1. The metabolism of glutamine and alanine in the lung was studied in rats made septic by a cecal ligation and puncture technique.

2. The blood glucose concentration was not significantly different in septic rats, but blood pyruvate, lactate, glutamine and alanine concentrations were markedly increased as compared with sham-operated rats. Conversely, blood ketone body and plasma cholesterol concentrations were significantly decreased in septic rats. Both plasma insulin and plasma glucagon concentrations were markedly elevated in response to sepsis. Sepsis resulted in a negative nitrogen balance.

3. Sepsis increased the rates of production of glutamine (52.5%, $P<0.001$), alanine (38.9%, $P<0.001$) and glutamate (48.6%, $P<0.001$) by lung slices incubated in vitro.

4. Sepsis increased lung blood flow by 27.6% ($P<0.05$). Blood flow and arteriovenous concentration difference measurement across the lung of septic rats showed an increase in the net exchange rates of glutamine (142.5%, $P<0.001$), alanine (129.4%, $P<0.001$), glutamate (100.9%, $P<0.001$) and ammonia (138.0%, $P<0.001$) as compared with sham-operated control rats.

5. Sepsis produced significant decreases in the lung concentrations of glutamine (26.8%), glutamate (20.8%), 2-oxoglutarate (64.8%) and AMP (18.3%). The lung concentrations of alanine (95.9%), ammonia (67.7%) and pyruvate (89.7%) were increased.

6. The maximal activities of glutamine synthetase (20.4%, $P<0.05$), phosphate-dependent glutaminase (18.9%, $P<0.05$) and alanine aminotransferase (25.5%, $P<0.05$) were increased, but there was no marked change in that of glutamate dehydrogenase, in the lungs of septic rats.

7. It is concluded that there are enhanced rates of production of glutamine and alanine from lungs of septic rats (both in vitro and in vivo). This may be due to changes in efflux and/or increased intracellular biosynthesis of both glutamine and alanine; these suggestions are discussed.

Key words: alanine, glutaminase, glutamine, glutamine synthetase, lung, metabolism, sepsis.

INTRODUCTION

Clinical sepsis may develop after major trauma such as burns or abdominal surgery, and is associated with enhanced muscle proteolysis, increased nitrogen flux, increased nitrogen loss and changes in carbohydrate and lipid metabolism (for reviews, see [1–5]). The resulting septic complications lead to a condition described clinically as a failure of the major organ systems.

Glutamine and alanine transport about 60% of the amino acid nitrogen exported by muscle [2, 6]. Although glutamine is not considered to be a dietary essential amino acid, it has several important metabolic roles (for reviews, see [7, 8]): in the gut, glutamine is known to be a major source of energy [9], in the kidneys, it supports renal ammoniagenesis [10], in the brain, it may function as a local store of neurotransmitters (e.g. glutamate, γ-aminobutyrate) [11], and its utilization and oxidation are essential for cells of the immune system (for reviews, see [6, 12]). Alanine is utilized primarily by the liver for hepatic gluconeogenesis (for a review, see [13]). Skeletal muscle has been shown to produce glutamine [see, 2, 6] and unlike other amino acids produced or utilized by skeletal muscle, glutamine does not undergo reversible transamination, instead its net production by muscle is controlled by the balance of the flux through glutamine synthesis and degradation [14, 15]. Skeletal muscle is the major site of endogenous formation of both glutamine and alanine in normal and catabolic disease states (for reviews, see [2, 6]). Recent work both in humans [16] and experimental animals [17–19] has demonstrated that the lungs contribute to the production of glutamine and alanine in normal and catabolic states. To date, there have been no detailed studies on the adaptive changes in the