Metabolic control of hepatic gluconeogenesis in response to sepsis

M. SALLEH M. ARDAWI, ABDULRAHMAN A. ASHY, YASIR S. JAMAL, and SAMIR M. KHOJA
JEDDAH, SAUDI ARABIA

The regulation of hepatic gluconeogenesis was studied in rats made septic by cecal-ligation and puncture technique. Blood glucose was not significantly different in septic rats, but lactate, pyruvate, and alanine were markedly increased. Conversely, blood ketone body concentrations were markedly decreased in septic rats. Both plasma insulin and glucagon were markedly elevated in septic rats. The maximal activities of glucose 6-phosphatase, fructose 1,6-bisphosphatase, pyruvate carboxylase, and phosphoenolpyruvate carboxykinase were decreased in livers obtained from septic rats suggesting a diminished hepatic gluconeogenesis. Hepatic concentrations of lactate, pyruvate, and other gluconeogenic intermediates were markedly increased in septic rats, whereas those of fructose 2,6-bisphosphate and acetyl-CoA were decreased. The rate of gluconeogenesis from added lactate, pyruvate, alanine, and glutamine was decreased in isolated incubated hepatocytes from septic rats. It is concluded that the diminished capacity of hepatic gluconeogenesis of septic rats could be the result of changes in the maximal activities or regulation of key nonequilibrium gluconeogenic enzymes or both but do not exclude other factors (e.g., toxins). (J Lab Clin Med 1989;114:579-586)

Abbreviations: ADP = adenosine 5’-diphosphate; AMP = adenosine 5’-monophosphate; ATP = adenosine 5’-triphosphate; CoA = coenzyme A

Clinical sepsis develops after major trauma such as burns or abdominal surgery, and the septic episode is not merely limited to the bacterial insult but has been described as an acquired disease of intermediary metabolism.1,2 In humans and experimental animals sepsis causes several changes in carbohydrate, lipid, and protein metabolism.1,3,4

Hepatic gluconeogenesis has been reported to either increase or decrease7-11 after the induction of sepsis.

Such differing findings are related to several factors: source and type of sepsis, nutritional states of animals, and the stage or phase of infection or both.12

A considerable amount of work has been performed on the control of hepatic gluconeogenesis in different physiologic conditions (e.g., starvation13 and exercise14). However, limited information is available on the regulation of hepatic gluconeogenesis in response to sepsis.4,15

The present work was designed to obtain more information about the regulation of hepatic gluconeogenesis in septic rats with a cecal-ligation and puncture technique.16 This has been done by measurements of key nonequilibrium enzymes and concentration of key metabolites in the pathways of glycolysis and gluconeogenesis together with the extent of hepatic gluconeogenesis in vitro in septic and corresponding sham-operated rats. The relevance of these changes to the overall regulation of hepatic gluconeogenesis in sepsis is discussed.