A study of the time course of fructose-2,6-bisphosphate production in a septic mouse model. By D. Hepburn, J. Broom and D. J. Smith, *Surgical Metabolic Unit, Department of Surgery, University of Aberdeen, Foresterhill, Aberdeen AB0 2ZB*

Where sepsis occurs in the post-surgical period, mortality rates tend to be high. In sepsis, metabolism is grossly disrupted with glucose becoming the preferred fuel for energy provision even where ketogenesis has been promoted. Glycogen stores are rapidly exhausted and body protein is wasted through proteolysis which serves to provide the gluconeogenic precursors for glucose formation in the liver (Imamura *et al.* 1975). Ketone bodies disappear from the circulation whereas circulating glucose levels are elevated and glycolytic flux is increased. This increase is thought to be strongly influenced by the recently discovered metabolite, fructose-2,6-bisphosphate (F2,6P2), which is the most effective accelerator of phosphofructokinase activity known to date (Van Shaftingen *et al.* 1980). High levels of F2,6P2 are present in the liver in the fed state whereas levels are very low in the fasted state. A previous study using a septic mouse model showed that the hitherto low levels of F2,6P2 in fasting mouse livers were greatly increased within 3 h of the septic insult (Hepburn & Broom, 1985): no such increase was noted in the fed septic animals where levels remained high despite a marked depression of glycogen stores.

The present study investigated the time course of F2,6P2 increase after inoculation with live *Escherichia coli.* Using the same septic model, control and septic fasted animals were killed at 15, 30, 60, 90 and 180 min post-inoculation and livers were rapidly freeze-clamped. Little difference between fasted control and septic animals was observed at 15 or 30 min (0·751 (SD 0·185) and 0·740 (SD 0·207) pmol/g) but by 60 min F2,6P2 levels had virtually trebled (1·763 (SD 0·478) pmol/g) and production continued to increase between 90 and 180 min post-inoculation (1·922 (SD 0·092) and 3·713 (SD 0·280) pmol/g). Thus sepsis elevated F2,6P2 production within 1 h of inoculation in contrast with the results of a study by Kuwajima *et al.* (1984) on fasting and refeeding of healthy mice where a delay of 6 h was observed before elevation of F2,6P2 levels in the liver.

A differing time scale of events occurs in sepsis compared with that of the normal state and this may be governed by activation of an existing enzyme or by *de novo* synthesis of 6-phosphofructose-2-kinase, the enzyme involved in F2,6P2 production. Sepsis might remove inhibition of enzyme activity in the fasted state, thus increasing F2,6P2 levels, whereas refeeding is perhaps associated either with *de novo* synthesis of the enzyme or with a very slow derepression of enzyme activity.

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