EDITORIAL COMMENT

STRESS, ALCOHOL METABOLISM AND BURN INJURY

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In the preceding letter, Professor Mezey (1998) proposes an alternative explanation of the observation published in this journal by Jones et al. (1997) that alcohol (ethanol) metabolism is accelerated in patients suffering from burns, namely that of stress-induced hormonally-mediated enhancement of activity of liver alcohol dehydrogenase (ADH; EC 1.1.1.1), possibly through growth hormone elevation and dihydrotestosterone depletion, as occurs in the rat immobilization stress model (for references, see Mezey, 1998). Jones et al. (1997) earlier suggested that the accelerated ethanol metabolism observed in their patients with burns may be due to an increased mitochondrial reoxidation of NADH secondary to the increased activity of the mitochondrial respiratory chain associated with the hepatic hypermetabolic state of such patients. The response of Professor A. W. Jones is that he does not disagree with Professor Mezey’s proposals, but that, because not all patients with burns are alcoholics (and certainly none of his was), NADH reoxidation must remain as a potential parallel mechanism of the accelerated ethanol metabolism in such patients.

There are several other potential explanations of why ethanol metabolism is enhanced in patients with burns. One such explanation derives from the observation by Professor Mezey’s group (Mezey et al., 1990) that adrenaline (the increase in the circulating levels of which is a major feature of stress) accelerates ethanol metabolism in isolated rat hepatocytes by increasing the rate of mitochondrial NADH reoxidation and also even of ADH activity. A second explanation is that of possible induction of activity of liver tryptophan pyrrolase (tryptophan 2,3-dioxygenase; EC 1.13.11.11), leading to increased NAD\(^+\) synthesis, by glucocorticoids, whose circulating concentrations are also elevated in stress. Thus, rats stressed by burn and other means have been shown to exhibit an increase in circulating corticosterone concentration and to possess a new hepatic glucocorticoid receptor (Hirota et al., 1985a), coined receptor ‘C’, which has been implicated specifically in glucocorticoid induction of liver tryptophan pyrrolase, but not that of tyrosine-2-oxoglutarate aminotransferase (EC 2.6.1.5), another hepatic glucocorticoid-inducible enzyme the induction of which, as well as that of tryptophan pyrrolase, is effected under normal conditions through the action of glucocorticoids on the classical receptor ‘B’ (Hirota et al., 1985b). Tryptophan pyrrolase is the first and rate-limiting enzyme of the quantitatively most important tryptophan-degradative route, the hepatic kynurenine–nicotinic acid pathway, the distal product of which is NAD\(^+\) (for a review of the functions of this enzyme, see Badawy, 1977). Glucocorticoid induction of tryptophan pyrrolase by acute administration of corticosterone to rats in the fed state, or through its endogenous release following a 24-h period of starvation, leads to increased synthesis of NAD\(^+\)(P\(^+\)) (Badawy, 1981). Provision of the oxidized forms of nicotinamide-adenine dinucleotides (phosphates) through glucocorticoid induction of hepatic tryptophan pyrrolase could therefore provide another potential mechanism by which stress can accelerate ethanol metabolism in patients with burn injury. Glucocorticoids could even accelerate ethanol metabolism by two additional mechanisms: (1) increased rate of mitochondrial NADH reoxidation secondary to enhancement of that of gluconeogenesis, as has been suggested by Clark and Owens (1966); (2) induction of ADH activity through increased gene...
expression (Wolfla et al., 1988; Majewski and Yang, 1995).

There appear, therefore, to be several potential mechanisms by which ethanol metabolism could be enhanced in patients with burn injury. Determination of the circulating concentrations of the hormones mentioned above and of intermediary metabolites reflecting the redox states of the hepatic NAD(P) couples, and also of parameters of tryptophan and related metabolism in such patients may throw light on the roles of the above potential mediators of the acceleration of ethanol metabolism in these patients.

REFERENCES