

# Alterations in hepatic protein metabolism the acute

## Alterations in hepatic protein metabolism: the acute-phase protein response

The liver and skeletal muscle together account for >50% of daily body protein turnover. Skeletal muscle has a large mass but a low turnover rate (1-2% per day), whereas the liver has a relatively small mass (1.5 kg) but a much higher protein turnover rate (10-20% per day). Hepatic protein synthesis is divided roughly 50:50 between renewal of structural proteins and synthesis of export proteins. Albumin is the major export protein produced by the liver and is renewed at the rate of about 10% per day. The transcapillary escape rate (TER) of albumin is about 10 times the rate of synthesis, and short-term changes in albumin concentration are most probably due to increased vascular permeability. Albumin TER may be increased threefold following major injury/sepsis. In response to inflammatory conditions, including surgery, trauma and sepsis, proinflammatory cytokines, including IL-1, IL-6 and TNF  $\alpha$  and in particular IL-6, promote the hepatic synthesis of positive acute-phase proteins, e.g. fibrinogen and C-reactive protein (CRP). The acute-phase protein response represents a 'double-edged sword' for surgical patients as it provides proteins important for recovery and repair but only at the expense of valuable lean tissue and energy reserves. In contrast to the positive acute-phase reactants, the plasma concentrations of other liver export proteins (the negative acute-phase reactants) fall acutely following injury, e.g. albumin. However, rather than representing a reduced hepatic synthesis rate, the fall in plasma concentration of negative acute-phase reactants is thought principally to reflect increased transcapillary escape, secondary to an increase in microvascular permeability.

**Summary box 1.6**  
Hepatic acute-phase response

Following surgery or trauma, postoperative hyperglycaemia develops as a result of increased glucose production combined with decreased glucose uptake in peripheral tissues. Decreased glucose uptake is a result of insulin resistance, which is temporarily induced within the stressed patient. Suggested mechanisms for this phenomenon include the action of proinflammatory cytokines and the decreased responsiveness of insulin-regulated glucose transporter proteins. The degree of insulin resistance is proportional to the magnitude of the injurious process. Following routine upper abdominal surgery for example, insulin resistance may persist for approximately 2 weeks but this period will extend with prolonged sepsis. Postoperative patients with insulin resistance behave in a similar manner to individuals with type 2 diabetes mellitus. In intensive care, the mainstay of management of insulin resistance is intravenous insulin infusion, which is used to keep blood glucose level within reasonable limits on the basis that this will reduce both morbidity and mortality. However, unduly tight control can increase the risk of significant hypoglycaemia. It should be noted that patients with diabetes whose glycaemic control has been poor prior to their critical illness pose a particular challenge.

The hepatic acute-phase response represents a reprioritisation of body protein metabolism towards the liver and is characterised by:

- Positive reactants (e.g. CRP):

plasma concentration Negative reactants (e.g. albumin): plasma concentration

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