

# Spontaneous hypoglycaemia in critical illness – an underappreciated emergency

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Critical illness is characterised by impairment of glucose homeostasis. Activation of the hypothalamo-pituitary-adrenal axis causes hepatic insulin resistance, increased hepatic gluconeogenesis and reduced skeletal muscle glucose uptake. The resulting stress hyperglycaemia is a widely understood sequela of critical illness. Less well recognised is the association of critical illness with spontaneous hypoglycaemia which, while less common, is associated with a far poorer prognosis. Here we present three cases encountered in our hospital in a 12 month period and discuss the underlying pathophysiological mechanisms.

## Case history #1

**Patient:** 51 year old female  
**Presentation:** Fever and leg pain  
**1° diagnosis:** Necrotising fasciitis  
**Details:** Initial treatment with i.v. antibiotics and analgesia for presumed cellulitis was followed by rapid deterioration over the subsequent 8 hours with development of shock hyperlactataemia (serum lactate 10.0mmol/L) and metabolic acidosis. With onset of reduced Glasgow Coma Score, capillary blood glucose was measured at 0.8mmol/L. Plasma cortisol was abnormal for the clinical situation at 169nmol/L. Despite aggressive resuscitation and circulatory support, she deteriorated further and died 18 hours after admission. A post-mortem revealed bilateral adrenal haemorrhage.

## Case history #2

**Patient:** 43 year old male  
**Presentation:** Respiratory distress  
**1° diagnosis:** Viral pneumonia  
**Details:** Admitted to ED Resus with marked type 1 respiratory failure following a viral prodrome. Initial investigations revealed evidence of DIC and acute kidney and hepatic injuries. Shortly after admission he became diaphoretic and aggressive, then entered PEA cardiac arrest. A capillary blood glucose was 0.8mmol/L. Following ROSC, he was transferred to the ICU but deteriorated further and died 8 days later of multiorgan dysfunction.

## Case history #3

**Patient:** 49 year old female  
**Presentation:** Fever, abdominal pain and vomiting  
**1° diagnosis:** As yet undiagnosed systemic inflammatory syndrome  
**Details:** Background of 3 admissions to ICU in the preceding 12 months with febrile illness and multiorgan dysfunction. Within the first 24 hours of this admission, developed purpura, metabolic acidosis and acute hepatic and kidney injuries. With the onset of acute confusion capillary blood glucose was measured at 1.8mm. Cortisol was appropriately elevated (1261nmol/L). Following treatment with antibiotics and steroids, she made a full recovery and remains under investigation for a systemic inflammatory pathology.

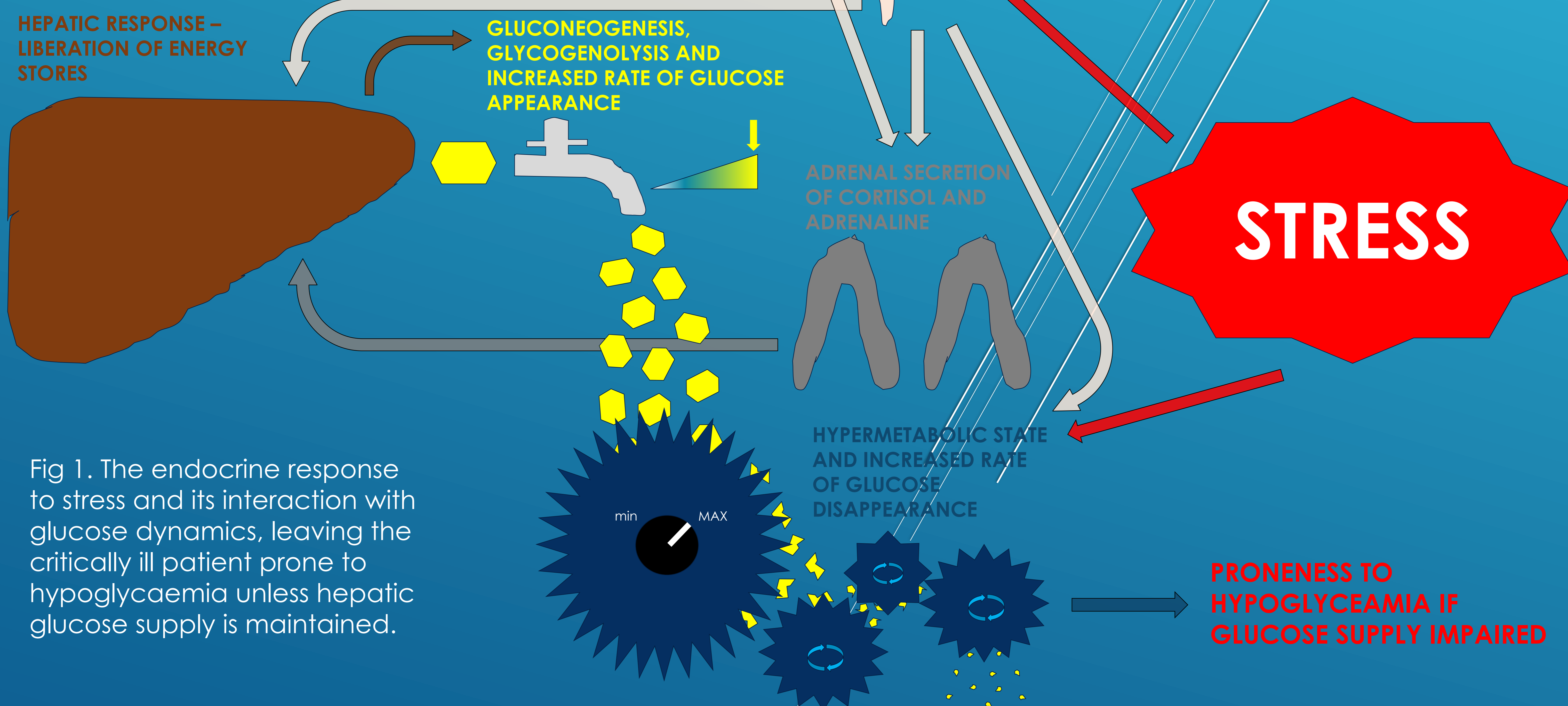


Fig 1. The endocrine response to stress and its interaction with glucose dynamics, leaving the critically ill patient prone to hypoglycaemia unless hepatic glucose supply is maintained.

Critical illness is characterised by an increase in the rate of plasma glucose disappearance due to elevated energy utilisation and an increase in non-insulin dependent flux of glucose into hypermetabolic cells. The hypothalamo-pituitary and sympathetic response results in production and liberation of adrenaline and cortisol, inducing hepatic glycogenolysis and gluconeogenesis to ensure that the rate of plasma glucose appearance at least matches this. However, the critically ill patient remains susceptible to hypoglycaemia should this response fail or be limited in some way. Spontaneous hypoglycaemia is most often encountered in patients with liver injury and the failure of liver glucose production, or with bilateral adrenal haemorrhage and the failure of hepatic stimulation. Few data on the prevalence of spontaneous hypoglycaemia in critical illnesses exist, though it is not rare. In one study of 7820 patients with acute MI, 136 (1.7%) experienced spontaneous hypoglycaemia (mean glucose 2.5mmol/L), which was associated with a doubling of mortality<sup>1</sup>. Blood glucose monitoring of all patients with illness that may become critical should be routine to allow early detection of both hyper and hypoglycaemia.

<sup>1</sup>Kosiborod M, et al. JAMA. 2009;301(15):1556-1564