Systemic response to surgery

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Abstract

The direct traumatic injury of surgery initiates a chain of physiological events via the endocrine, metabolic, cardiovascular and immune systems. The unregulated stress response can lead to systemic inflammatory response syndrome (SIRS), but alternatively if we were able to totally obliterate the response then this would predispose to infection and failure of the recovery process. To an extent the response is protective. This article will outline the components of the interlinked endocrine, metabolic, immune and haemodynamic responses and discuss the ways in which the various components of the response can be modified in order to optimize postoperative recovery and aim to reduce complications.

Keywords SIRS; stress response; systemic response

Introduction

The systemic response to surgery refers to a series of interlinked physiological changes that occur in response to a surgical insult. These are a mixture of immune, endocrine, metabolic and haemodynamic responses and many of these overlap.

Cuthbertson classically identified the response as a distinctly biphasic 'ebb' and 'flow' process.[1] A period of reduced metabolic activity lasting for 2–3 days (ebb phase) may be seen initially, followed by a more prolonged catabolic and hyper-metabolic phase (flow) lasting over a week depending on the recovery process. Current evidence suggests that the two phases defined by Cuthbertson are, in reality, less clearly defined.

Similar physiological changes may also occur as a result to injuries of other kinds, for example non-penetrating trauma, burns or infection. Whether the response is to surgery or any other insult the term systemic inflammatory response syndrome (SIRS) may be used. SIRS was first defined in 1992 at the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference[2] (Box 1). SIRS is diagnosed if two or more of the criteria in Box 1 are met.

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Systemic inflammatory response syndrome (SIRS)

SIRS is confirmed by the presence of two or more of the following features:

- Heart rate: >90 beats per minute
- Body temperature: <36°C or >38°C
- Respiratory rate: >20 breaths per minute
- White cell count $<4 \times 10^9$ cells/litre or $>12 \times 10^9$ cells/litre

Box 1

This article aims to discuss the elements of the surgical stress response and the different ways of modulating them to ensure the best outcome for the surgical patient.

The endocrine pathway

In response to direct tissue injury, there is a surge in afferent stimuli via the somatic and autonomic pathways from the affected area. These stimuli activate both the sympathetic nervous system and the hypothalamus, leading to a variety of hormones being released from the pituitary.

High volumes of stress hormones are released during this response, principally adrenaline and cortisol, but levels of other hormones such as glucagon, growth hormone, antidiuretic hormone (ADH) and aldosterone are also increased.

The sympatho-adrenal response

Increased catecholamine release: activation of the sympathetic autonomic nervous system leads to release norepinephrine and epinephrine from the adrenal medulla and local release of norepinephrine from the presynaptic nerve terminals causing hypertension and tachycardia.

The sympatho-renal response

Activation of the renin–angiotensin–aldosterone axis: this is a key component of the surgical stress response in terms of sodium retention. Renin is released from the kidneys in response to sympathetic activation, initiating the conversion of angiotensin I to angiotensin II, which in turn, stimulates aldosterone release from the adrenal cortex. This results in an increase in sodium reabsorption in the distal convoluted tubules and an increase in vascular tone.

The hypothalamic–pituitary–adrenal axis

Increased adrenocorticotropic hormone (ACTH) and cortisol: ACTH is the principal hormone released by the anterior pituitary in response to surgical stress. ACTH stimulates secretion of glucocorticoid from the adrenal cortex. In turn the adrenal cortex exhibits an exaggerated response to ACTH and there is a supranormal release of cortisol. In addition to the initially raised cortisol levels, significant blunting of the normal negative feedback mechanisms leading to continuing raised cortisol production also occurs. This has significant implications on the metabolism of carbohydrate, fat and protein; an overall effect to increase blood glucose levels as well as a potent anti-inflammatory effect.

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Increased growth hormone (GH): GH is released from the anterior pituitary in proportion to the degree of tissue injury. The principal effect of this is to increase glycogenolysis within the liver, increasing blood glucose. There is also a marked increase in insulin resistance.

Increased ADH release: ADH is released from the posterior pituitary gland and stimulates the insertion of aquaporins into the walls of the renal collecting ducts. This permits the reabsorption of free water down its concentration gradient back into the renal medulla and reducing urine output.

Insulin and glucagon

Reduced insulin secretion and insulin resistance: insulin is the key anabolic hormone. Protein catabolism and lipolysis are inhibited by insulin. The sympathetic nervous system exerts an effect on the pancreas via α2-adrenergic receptors which cause an early reduction in insulin secretion. At a later stage there is a delayed reduction in sensitivity of target cells to insulin, further reducing its effectiveness and leading to relatively unopposed catabolism.

Increased glucagon release: sympathetic activation of the pancreas results in increased glucagon levels. Although glucagon does stimulate lipolysis, gluconeogenesis, and hepatic glycogenolysis it has not been found to be a major player in the development of postoperative hyperglycaemia.[3]

Other hormonal responses: although most exert a negligible effect on the overall function in the context of the stress response there are elevated levels of prolactin and reduced levels of testosterone, thyroxine (T4), and tri-iodothyronine (T3) returning to normal after several days.

The metabolic effects (Figure 1)

The net result of the endocrine responses that have been discussed can be viewed of in terms of several metabolic entities, as follows.

Catabolism and substrate mobilization: in the immediate postoperative period, an initial period of low metabolic activity may be seen. However, following this, the overwhelming response to major surgery is the development of a hypermetabolic and catabolic state. Mobilization and production of glucose substrate occurs from glycogen stores in the liver and from proteolysis and lipolysis of skeletal muscle and fat reserves respectively.

Hyperglycaemia and insulin resistance: in response to the supra-normal levels of cortisol, glucagon and GH, there is increased catabolism to provide substrate for cortisol-regulated gluconeogenesis in the liver. The glycogenolysis leads to elevated blood glucose levels. GH also induces an insulin resistance which further compounds the hyperglycaemic effect. This not only affects wound healing but also has an impact on fluid homoeostasis and recovery.

Salt and water retention: fluid retention, reduced urine output and accumulation of extracellular fluid are commonly seen after surgery. This is due to the up-regulation of the renin–angiotensin–aldosterone axis in combination with the increased release of ADH.

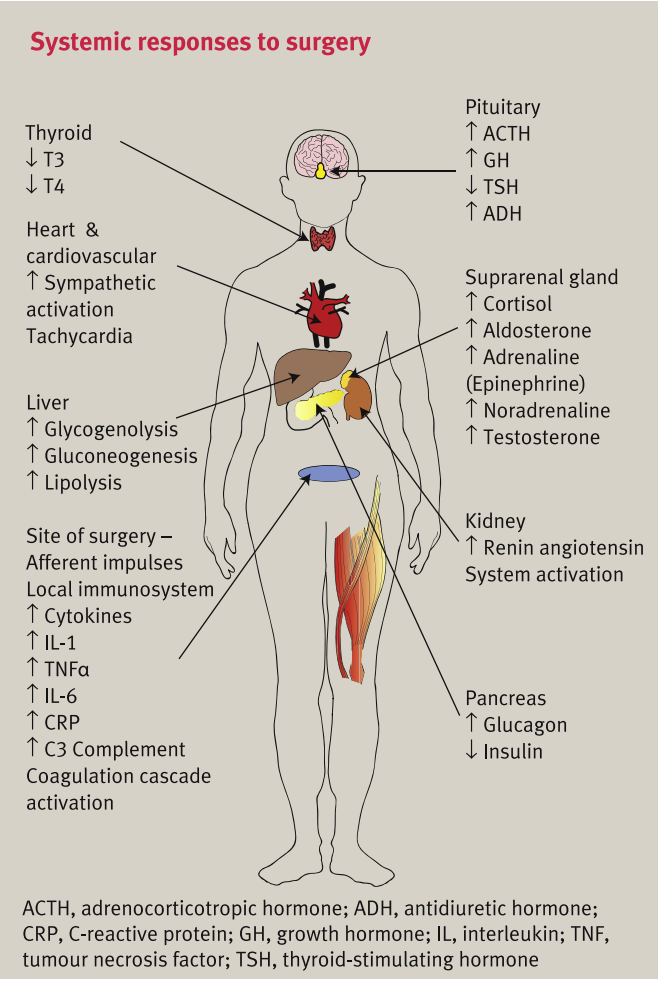

Figure 1

The immune response

The immune response is complex and multifactorial but involves the release of a series of both pro-inflammatory and anti-inflammatory cytokines. In addition, a cell-mediated response occurs. The severity of the immune response is proportional to the extent of trauma but also depends on other factors such as nutritional status, co-existing infection or the background disease requiring surgery (e.g. cancer).

Cell-mediated response

Trauma activates both the innate and adaptive immune systems. Initially the surgical insult leads a cascade of responses including activation of the complement system and recruitment of granulocytes to the site of injury. Later on, natural killer (NK) cells, neutrophils and monocytes all undergo a degree of suppression.

In addition there is a relative increase in T-helper 2 lymphocytes (Th2) which are considered to be anti-inflammatory compared to T-helper 1 (Th1) cells which are essentially pro-

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