Critical illness is characterized by a uniform dysregulation of all hypothalamic-anterior pituitary axes, long known to contribute to the high risk for morbidity and mortality. It is now clear that the neuroendocrine responses to acute and prolonged critical illness are substantially different.

In the acute phase of critical illness, the pituitary is secreting prolactin, which is physiologically secreted in a pulsatile and diurnal pattern, and is presumed to have immune-enhancing properties. Physiologic control of prolactin secretion largely is under the control of dopamine, but several other prolactin-inhibiting and -releasing factors can modulate prolactin secretion.

The acute phase of critical illness

- Acute physical stress, such as surgery or myocardial infarction, brings along an immediate fall in the serum levels of testosterone, even though LH levels are elevated. This suggests an immediate suppression of androgen production by Leydig's cells, which as put forward by experimental studies, PRL levels rise in response to acute physical or psychologic stress. Factors possibly involved are vasomotor hypoxia, oxytocin, and dopaminergic pathways, but again cytokines or as yet uncharacterized factors also may play a role. The rise in PRL levels after acute stress is believed to contribute to the vital activation of the immune system early in the disease process, but this remains speculative.

The prolonged phase of critical illness

- More dramatic changes develop within the male gonadal axis with prolongation of the disease, and hypogonadism ensues. The circulating levels of testosterone become extremely low and often even are undetectable, in the presence of suppressed mean LH concentrations and pulsatile LH release.

- Total estradiol levels also are relatively low but the level of bioavailable estradiol probably is maintained in view of the simultaneous decrease in sex-hormone-binding globulin. Alternately, a remarkable rise in estrone levels is observed in other studies - As testosterone is the most important endogenous androgen steroid, the abnormalities in the gonadal axis could be important with regard to the catabolic state of critical illness.

- The pulsatile fraction of PRL release becomes suppressed in patients in the prolonged phase of critical illness. It is unclear whether or not the blunted PRL secretion contributes to the immunosuppression or increased susceptibility to infection associated with prolonged critical illness.

The acute phase of critical illness

- Growth hormone (GH) is secreted by the somatotropes in the pituitary and is essential for linear growth and growth in childhood but serves many important functions throughout life.

- The regulation of the physiologic pulsatile release of GH, consisting of peak serum GH levels alternating with virtually undetectable trough levels, is important for its metabolic effects.

- Hypothalamic GH-releasing hormone (GHRH) stimulates, and somatostatin inhibits, the secretion of GH.

- GH exerts direct and indirect effects, the latter mediated by insulin-like growth factor-I (IGF-I).

The acute phase of critical illness

- During the first hours to days after an acute insult, the GH profile changes dramatically. The pulse frequency is increased, peak GH levels are elevated, and interpulse concentrations are high.

- Concomitantly, a state of peripheral GH resistance develops, triggered in part by cytokines, such as tumor necrosis factor a and interleukin-6.

- Despite the clearly enhanced GH secretion, serum concentrations of IGF-I decrease - Physiologically, this may enhance the direct lipolytic and insulin-antagonizing effects of GH, resulting in elevated fatty acid and glucose levels in the circulation, whereas indirect IGF-I-mediated somatotropic effects of GH are attenuated. As a result, costly anabolic processes, which are largely mediated by IGF-I is decreased during the struggle for survival.

The prolonged phase of critical illness

- In prolonged critically ill patients, when recovery does not occur within a few days, a different GH secretion pattern arises.

- The pulsatile release of GH becomes suppressed, whereas the nonpulsatile fraction of GH release remains somewhat elevated. A strong positive correlation is found between the pulsatile fraction of GH release and circulating IGF-I levels, which suggests that the loss of pulsatile GH release contributes to the low levels of IGF-I in prolonged critical illness.

- This chronic GH deficiency, resulting from lack of pulsatile GH secretion, could contribute to the pathogenesis of the wasting syndrome that characterizes prolonged critical illness.

- Administration of pharmacologic doses of GH, inspired by the assumption of sustained GH resistance in the prolonged phase of critical illness, unexpectedly increases morbidity and mortality.

- Initial trials studying administration of high doses of glucocorticoids clearly show that this strategy is ineffective and perhaps even harmful. In contrast, studies using subphysiologic, low-dose glucocorticoid replacement therapy for relative adrenal insufficiency report beneficial effects, at least in patients who have septic shock.

- It remains controversial whether or not administration of thyroid hormone to patients who are critically ill is beneficial or harmful.

- There is no conclusive clinical benefit demonstrated for androgen treatment in prolonged critical illness.

General

Thyroid hormone is essential for normal development and growth, and maintains metabolic homeostasis and regulatory functions, including the regulation of the hypothalamic-pituitary-thyroid axis. The thyroid hormones, triiodothyronine (T3) and thyroxine (T4), are produced by the thyroid gland and are involved in numerous physiological processes, including the regulation of energy metabolism, brain development, and cardiovascular function.

- The thyroid hormones exert their effects through the activation of thyroid hormone receptors, which are found in virtually every tissue in the body. These receptors bind to specific DNA sequences in the cell nucleus, leading to the regulation of gene expression and the production of various proteins.

- The thyroid hormones are regulated by a complex feedback system that involves the hypothalamus, pituitary gland, and thyroid gland. This system helps to maintain the proper levels of thyroid hormones in the bloodstream.

- In general, the thyroid gland adjusts its production of thyroid hormones in response to changes in the body's needs. For example, during times of increased metabolic demand, such as in response to stress or illness, the thyroid gland produces more thyroid hormones to support the body's overall metabolic rate.

- Conversely, during periods of reduced metabolic demand, the thyroid gland reduces its production of thyroid hormones to conserve energy.

- The thyroid hormones, T3 and T4, are converted to active forms in the peripheral tissues, with T3 being the more active form.

- T3 is involved in the regulation of cellular metabolism, energy production, and growth and development.

- T4 is involved in the regulation of body temperature, energy expenditure, and cardiovascular function.

- The thyroid hormones also play a role in the regulation of the immune system, with T3 being known for its immunosuppressive effects.

- The regulation of thyroid hormone levels is maintained through a negative feedback system, where the hypothalamus releases thyrotropin-releasing hormone (TRH), which stimulates the pituitary gland to release thyroid-stimulating hormone (TSH). TSH, in turn, stimulates the thyroid gland to produce thyroid hormones.

- The feedback system is sensitive to changes in the levels of thyroid hormones, with TSH production increasing in response to low thyroid hormone levels and decreasing in response to high thyroid hormone levels.

- However, in some cases, the feedback system may fail, resulting in either insufficient or excessive thyroid hormone production. This can lead to various thyroid-related conditions, such as hypothyroidism (low thyroid hormone levels) and hyperthyroidism (high thyroid hormone levels).

- Hypothyroidism can cause symptoms such as fatigue, weight gain, cold intolerance, and depression, while hyperthyroidism can cause symptoms such as weight loss, rapid heartbeat, and increased nervousness.

- The treatment of thyroid hormone disorders typically involves the use of thyroid hormone replacement therapy, which is administered to restore normal thyroid hormone levels in the bloodstream.

- In conclusion, the thyroid hormones play a critical role in regulating various physiological processes, and their levels are tightly controlled by a complex feedback system. Disruptions in this feedback system can lead to thyroid-related conditions that require medical intervention.