BIOCHEMISTRY OF STRESS

Stress refers to factors that alter or threaten to alter the body's internal environment. There are two types of stress generating factors viz. 1. Internal: Pain, Psychological pressure and 2. External: Cold, prolonged exercise, physical injury, environmental factors.

The most common adaptation to stress

- Increased CNS stimulation: this leads to stimulation of Hypothalmus releasing CRH, that in turn acts on anterior pituitary releasing ACTH. The ACTH acts on adrenal cortex releasing Cortisol.
- Activation of sympathetic division of autonomic nervous system causing elevation of secretion of catacholamines.
- Increased plasma concentration of prolactin and thyroid hormones.

Cortisol mediated adaptation to stress

During stress the corticotrophin releasing hormone (CRH) is released from hypothalamus that bind CRH receptors in anterior lobe of anterior pituitary releasing the ACTH.

Factors modulating the release of ACTH from Adenohyposys:

- Stress, hypoxia, hypoglycaemia.
- Nor-epinaphrin, serotonin, GABA.
- CRH, Vassopressin, Angiotensin, TRH, GnRH.

The ACTH release is inhibited by hormones glucocorticoid, Enkephalin.

The ACTH action on adrenal gland is rapid, within a minute of its release there is an increased concentration of steroids in the adrenal venous blood.

ACTH binds ACTH receptors in adrenal cortex releasing glucocorticoids (cortisol). The primary function of the cortisol is to re-distribute energy (glucose) to regions of the body that needs it most (i.e. the brain and major muscle) during the fright, flight and fight response. Apart from this, cortisol also leads to suppression of body's immune system.

Three types of glucocorticoids that are present in adrenal cortex are

- Cortisol.
- Cortisone.
- Corticosterone.

The cortisol is the most potent glucocorticoid. The precursor of cortisol is cholesterol. The cholesterol is transported in blood boud to cortisol binding globulin (CBG). Plasma half life of Cortisol is 70 minutes.

Cortisol regulates the glucose metabolism. It causes the hyperglycemia and suppress glucose utilization.

Action of cortisol:

Free cortisol molecules diffuse across the cell membrane and binds to cytosolic receptors. The cortisol receptors complex move to nucleus. Inside the nucleus the complex binds to DNA causing stimulation of some genes and inhibition of some genes.

- It enhances the elevating effect of nor-epinephrine on blood pressure thus helping to prevent fall in blood pressure.
- Stimulate gluconeogenesis and inhibit glycolysis.
- Stimulate degradation of fats and protein, increasing the plasma concentration of fatty acids and amino acids.
- Inhibits the formation of prostaglandins that are required for eliciting inflammation at the site of injury.
- Reduces antibody production (immune-suppression) and number of lymphocytes.

Adrenal medullary hormones

Two basic hormones are epinephrine and nor- epinephrine. Nor- Epinephrine is synthesized in adrenal medulla and post-ganglionic sympathetic neurons. In contrast to cortical hormones, the adrenal medullary hormones are not essential for life. The epinephrine and nor-epinephrine are primarily metabolized in liver and has plasma half life of 1-3 minutes.

Regulation of secretion:

Secretion of hormones from adrenal medulla is a part of reaction of the sympathetic nervous system to stress. Secretion is stimulated by pre-ganglionic sympathetic nerve fibers. These nerve fibers release acetyl choline that depolarises the cell membrane of the medulary cells causing the release of hormone stored in the secretory vesicles of adrenal medulary cells.

Action of epinephrine and nor- epinephrine

The action of epinephrine and nor-epinephrine allow the body to mobilize its resources in ways that are suitable for facing both physical and physiological challenges.

1. Stimulates glycogenolysis and gluconeogenesis in liver causing the elevation of plasma glucose.
2. Increase break-down of triglycerides in adipose tissues elevating the plasma fatty acid concentration.
3. Increased cardiac output and blood pressure.
4. Alteration of blood perfusion to skeletal muscle and less through the abdominal organs.
5. Enhancing alertness for preparing the animal for *fright, flight* and *fight response*.

BIOCHEMISTRY OF SHOCK

Shock refers to generalized inadequate blood flow though the body to the extent that the body tissues are damaged because of too little flow, especially due to little oxygen and other nutrients delivered to the tissue cells.

Cellular damage due to shock

1. Active transport of sodium and potassium thourgh fell membrane is greatly diminished. Sodium and chloride accumulate in cells and potassium is lost from cells. The cells begin to swell.
2. Mitochondrial activity in the cells of oliver as well as in many tissues of the body becomes severely depressed.
3. Lysozomes in the cells break open with intracellular release of hydrolases that causes further intracellular deterioration.
4. Cellular metabolism of nutrients such as glucose, eventually depressed in the last stage of shock. The action of insulin is highly depressed..

All these contribute to further deterioration of many organs of the body.

1. Liver: depression of metabolic and detoxification function.
2. Lungs: eventual development of pulmonary edema and poor ability to oxygenate the blood.

ACIDOSIS IN SHOCK

Due to decreased supply of oxygen, the cells derive the energy through aneorobic process of glycolysis that leads to production of lactic acid. In addition, poor blood flow to the tissue prevents normal removal of CO_2 that reacts with water producing carbonic acid lowering the pH.