Fourth Stage

General Surgery

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Lecture 1

What is a physiological response?

are **the body's automatic reactions to a stimulus.** the body always responds to an injury with a predictable inflammatory response, as the first step towards healing. **Redness, heat, swelling and pain** are associated with this first stage. Redness and heat are caused by increased blood flow.

Physiological responses to injury

The physiological responses to injury are how the body reacts to an injury immediately after its occurrence and how it adapts over a period of time.

The repair of injured soft tissue, such as a muscle, usually commences within 24 hours following an injury. One of the first signs that soft tissue is injured is the appearance of swelling. When the injured area starts to swell, it will feel painful. This is due to the swelling creating pressure on the nerves surrounding the damaged tissue.

The swelling occurs because the surrounding blood vessels are ruptured, allowing blood to bleed into the areas and the tissue fluid to gather around the injury site. The injured area will usually look red because the blood vessels surrounding the site dilate, which also has the effect of making the injured area feel hot.

The injured area will show a reduced function or a total inability function because of the pain and swelling. The level of the signs and symptoms will be directly related to the degree of the injury - the greater the degree, the greater the effects of inflammation. It is over a period of between 48 and 72 hours and up to 21 days that the repair is carried out with vigour by the body.

The body's clotting mechanism seals the end of the torn blood vessels so that further blood plasma cannot escape into the surrounding tissues. As the immediate effects of injury subside the healing/repair process begins. This consists of:

- **Absorption of swelling**
- **Removal of debris and blood clot**
- **Growth of new blood capillaries**
- **Development of initial fibrous scar tissue.**

After 12 hours, and for the first four days, the cells soon become active and new capillary blood vessels form and gradually grow to establish a new circulation in the area.

What is the ebb phase of trauma?

The Ebb phase develops within the first hours after injury (24–48 hours) ,It is characterized by **reconstruction of body's normal tissue perfusion and efforts to protect homeostasis**. In this phase, there is a decrease in total body energy and urinary nitrogen excretion.

In contrast, the "flow" phase occurs after resuscitation from a state of shock, which leads to an increased metabolic turnover, activation of the innate immune system and induction of the hepatic acute-phase response.

PHYSIOLOGICAL EFFECTS OF INSULIN AND INSULIN RESISTANCE IN STRESS

The decrease in the normal anabolic effect of insulin, i.e. the development of insulin resistance, is the main source of a series of reactions in response to injury and the consequent metabolic state Hinton et al. and Woolfson et al. showed the positive effects of insulin in stress metabolism 30 years ago. Insulin is the most important anabolic hormone in the body. Insulin regulates glucose metabolism to keep glucose levels on very tight limits in healthy people. Insulin provides normalization of glucose level after food intake by activating quick glucose uptake and storing it as glycogen in the liver, muscle and adipose tissue. This uptake is carried through GLUT4, which is a specific glucose transporter activated by insulin. The carriers provide active and rapid glucose uptake in these organs and in many other organs and cells, and can cause a temporary increase in glucose uptake after carbohydrate ingestion. This uptake also uses other carriers that affect glucose levels.

Insulin controls protein metabolism by primarily reducing muscle protein degradation, and supporting protein synthesis in the presence of amino acids. Insulin also controls fat metabolism by stimulating the formation of triglycerides and inhibiting their breakdown. Insulin acts at the cellular level via specific receptors, in insulin sensitive cells such as muscle and fat cells. The specific signalling pathways in insulin sensitive cells are activated to provide anabolic reactions such as glycogen storage, protein synthesis in muscle, or as to block lipolysis in fat cells.

In all major stress conditions such as major surgery, the effect of insulin increases due to secretion of stress hormones like glucagon, catecholamines, cortisol and growth hormone and the inflammatory reaction generated by cytokines. Amino acids, free fatty acids and glucose is released into the bloodstream from various tissues in stress response. The substrate metabolism also changes and fat is consumed in the body rather than glucose. These reactions can be corrected with exogenous insulin therapy after operations like colorectal surgery. It has been reported that by infusing sufficient amount of insulin to keep glucose within normal range, the remaining metabolism is normalized. In these studies, nutrition was provided by total parenteral nutrition. When nutrition is provided and the effect of insulin on the metabolism re-establishes, protein degradation, free fatty acid levels and substrate oxidation are normalized. From a clinical point of view, insulin infusion sufficient enough to normalize glucose levels can be used as the final aim to achieve these reactions. From a clinical point of view, insulin infusion can be used to achieve glucose control. Tight glycemic control will improve the outcomes of critically ill patients .Postoperative insulin resistance can be prevented in elective surgery by specific perioperative practices such as preoperative carbohydrate administration, epidural block and minimally invasive surgery .There are significant differences between short or long-term starvation and critically ill patients with trauma or sepsis in terms of metabolic changes and requirements .

Stress-hyperglycemia and insulin resistance are extremely common, especially in critically ill patients with sepsis. Multiple pathogenic mechanisms are responsible for the metabolic response. Thus, the release of proinflammatory mediators and counter-regulatory hormones that may play a role increases. Current data indicate that while insulin shows the opposite effect, hyperglycemia may enhance proinflammatory response .Cohort studies showed the relationship between intraoperative hyperglycemia during elective surgery and postoperative morbidity, and this can be used as an early stage marker of complications .

The incidence of sepsis has increased dramatically in the last decade. The reasons for this are use of immunosuppressive therapy, an increasing number of invasive procedures, and the increasing age in the population .Each year, approximately 750 thousand cases of sepsis are admitted in the United States and approximately 225 thousand of them are fatal. With the use of antimicrobial agents and advanced intensive care conditions, the mortality rate has remained at 30–40% during the past three decades .Recent data suggest that tight glycemic control with insulin can establish a balance between proinflammatory and anti-inflammatory mediators and can improve the condition of critically ill patients .

Critical illness related stress is characterized by the activation of hormonal response in the hypothalamic-pituitary-adrenal axis, cortisol is released from the adrenal gland .The release of cortisol by the activation of this axis is a major component of general adaptation to disease and stress, and contributes to maintaining cell and organ homeostasis.

In addition to the cortisol increase in stress response, epinephrine, norepinephrine, glucagon, and growth hormone also increase .Insulin levels are usually normal or decreased together with increased peripheral insulin resistance .As a result of increased activation of pancreatic alpha receptors, insulin secretion is suppressed .In addition to insulin resistance, IL1 and TNF also suppress insulin secretion. Low or normal levels of insulin, and increase in other counter-regulatory hormones result in stress hyperglycemia. When the increase in counter-regulatory hormones such as glucagon, growth hormone, catecholamines and glucocorticoids, and cytokines such as IL1, IL6 and TNF is combined with the increase in catecholamines, dextrose and nutritional support, they play an important role in relative insulin resistance

Sepsis is characterized by insulin resistance .The insulin resistance in sepsis is directly proportional to the intensity of the stress response. Alpha-2 adrenergic blockage is characterized by decreased insulin resistance in septic mice .Glucocorticoids correct insulin-mediated glucose uptake in skeletal muscle.