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Review Article

Pathophysiological Reaction of the Body to Trauma: A Review Update

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Abstract

Trauma to tissues can be of large magnitude (macrotrauma), such as the trauma that exists with crush injuries and both moderate and severe sprains or strains. The trauma can also be of small magnitude (microtrauma), such as the trauma that typically exists with stress fractures and other overuse syndromes. Regardless of magnitude, trauma exists in several forms, including physical, chemical, thermal, metabolic, and biological. Injury from any of these sources induces an inflammatory response whose magnitude largely depends on the severity of the injury and the degree of vascularization of the tissue. A local inflammatory response always occurs in relation to trauma. Severe injury or multiple trauma evoke a systemic inflammatory response. This systemic inflammatory response to major injury is caused by hormonal, metabolic and immunological mediators, and is associated with a haemodynamic response. Accidental unanaesthetised trauma is also to a larger extent associated with ischemia, ischemia/reperfusion injury, hypovolemia and the immunological reactions secondary to blood transfusion. The systemic inflammatory response is required for tissue repair and has evolved in all mammals to optimize the healing potential of an organism. In uncomplicated trauma patients the systemic inflammatory response is temporary, predictable and well balanced between pro- and anti-inflammatory mediators. If the patient is exposed to severe major trauma an initial exaggerated proinflammatory response may be observed. In this review the pathophysiological changes have been described after trauma to the body. [*Journal of Science Foundation, 2015;13(1):15-20*]

Keywords: Pathophysiological reaction; trauma; road traffic accident

1.0. Introduction

After major trauma there ensues a complex series of changes from which scarcely any tissue of the body escapes (Merrick 2002). The nervous system responds promptly with increased out-put of autonomic impulses (Bauer and Fritz 2004). There is an immediate outpouring of catecholamines from the adrenal medulla, while the other endocrine glands respond more slowly; stimulation of hypothalamus leads to an increase in adrenocortical over activity. These changes assist the injured persons to withstand trauma (Povlishock and Katz 2005). One very obvious early effect of trauma involves the circulatory system. When the trauma is severe, a state develops from which recovery

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may or may not occur; this is called shock and is characterized by inadequate perfusion of the tissue, hypotension, and depression of general metabolic activity.

2.0. Response to Injury

If the patient survives, there ensure metabolic changes that terminate in complete recovery and this is called the period of convalescence (Cernak and Noble-Haeusslein 2010). For descriptive purposes therefore it is convenient to consider the response to injury under three headings.

2.1. The metabolic changes
2.2. The circulatory changes
2.3. Shock

2.1. **The Metabolic Change:** These changes may be considered under the following headings:
2.1.1. The early, or EBB phase
2.1.2. Convalescence
2.1.2.1. Catabolic phase
2.1.2.2. Anabolic phase

2.1.1. The Early or EBB Phase

The early response to injury is termed the low flow, or ebb phase (Triplett 2000). After severe injury it is accompanied by a state of shock. This is characterized by under perfusion of tissues, a reduction in the metabolic rate, a reduced body temperature, and an increased output of catecholamines from the adrenal medulla. Catecholamines have many actions (Sharma 2011).

- They cause increased glycogenolysis in the liver, and this combined with a decrease insulin level, leads to hyperglycaemia.
- They have a lipolytic effect on the adipose tissues such that free fatty acids are released.
- Lactic acid is released from the muscles, and in addition, hypoxia of the tissues leads to the formation of lactic acid. This is converted into glucose in the liver (Cori cycle). Excess production of lactic acid leads to a metabolic acidosis.
- The effect of the catecholamines on blood vessels is complex but, in general, stimulation of the α_1 and α_2 receptors causes vasoconstriction. β_1 receptor stimulation has a positive ionotropic effect on the heart and causes coronary artery dilatation. The β_2 effect causes smooth muscle relaxation of the bronchi, intestinal muscle and selected blood vessels.

2.1.2. Convalescence

Assuming that the patient survives the initial phase and does not die of shock, there ensues a period of metabolic upset that has been termed the high-flow phase or simply the flow phase. This has two components like a catabolic phase, which is characterized by excessive protein break down and a negative balance, followed by an anabolic phase, during which the body's stores are replenished (Inamasu et al., 2003).

2.1.2.1. The catabolic phase: During the catabolic phase there is increase glucose production in the liver. This gluconeogenesis is fed by lactate, pyruvate, and alanine and other amino acids derived from muscle, which are used as substrates. The breakdown of muscle components, particularly the proteins, for use in energy generation leads to muscular atrophy and a consequent loss of weight. The nitrogen of the metabolized amino acids is excreted as urea. And the body enters a phase of negative nitrogen balance. The extent of this nitrogen loss varies according to the

severity of the trauma; it may reach 20gm (expressed as urea) daily, but usually does not exceed 10gm. Its duration varies with the extent of the trauma. The following point should be noted (Lord et al., 2014):

- The nitrogen loss cannot be abolished by increasing the protein intake; any extra protein in the diet is broken down and extra nitrogen excreted. There is therefore no point in forcing patients to ingest protein during this phase.
- The administration of carbohydrate does reduce the nitrogen loss very considerably.

During the catabolic phase there is an increased production of insulin two or three times above normal. Nevertheless, the tissues appear to be resistant to the action of cortisol. The relative lack of insulin activity is one mechanism whereby amino acids are released from muscle. There is, however, sufficient insulin activity to inhibit lipolysis, hence fatty acids are not released from the adipose tissues, and while the muscles waste as a result of protein loss, the adipose tissues remain intact. Although adrenal cortical hyperplasia occurs after injury, the increased secretion of cortisol that ensues is not the major cause of protein breakdown. The catabolic phase is accompanied by a local inflammatory reaction, and the inflammatory 'Soup' that form contains many highly active compounds. Tumor necrosis factor (TNF) is an important component. In addition there is interleukin 1 (IL-1). In the hypothalamus IL-1 leads to the production of prostaglandin E_2 (PGE_2), which changes the set-point of the heat-regulating center thereby causing fever (Vieweg et al., 2006). Pyrexia at this stage does not therefore indicate infection. In the skeletal muscles IL- also leads to the production of PGE_2, Lysosomal enzymes are activated, and the protein breakdown that result causes the release of amino acid (mostly alanine) into the blood stream; this protein loss contributes to the loss of weight.

2.1.2.2. The anabolic phase: The final stage of convalescence is characterized by a positive nitrogen balance and a re-synthesis of muscle protein. The changes noted during the catabolic phase are reversed, and the body returns to normal.

2.2. The Circulatory Changes

The changes in the circulation are seen to their best advantage following acute haemorrhage; this will therefore be described first.

2.2.1. Haemorrhage: Hemorrhage is the most dramatic of the circulatory disorders.

2.2.2. Effects of acute haemorrhage: These depend mainly upon two factors:

- The amount of blood loss.
- The speed with which the loss occurs.

The general effects are slight when less than 20% of the blood volume is lost (Vieweg et al., 2006). A sudden loss of 33% may cause death, but if the bleeding extends over a period of 24 hours, a loss of over 50% of blood volume is not necessarily fatal; however, with losses of over 50% the effects are always serious (Lier et al., 2008). The body response to acute haemorrhage may be divided into three phases.

2.3. Phase I

2.3.1. The early changes: During the first few hours the manifestations are mostly due to nervous mechanism. An immediate syncope may occur, and this is followed by important vascular changes which result in the redistribution of the remaining blood, the volume of which is considerably depleted.

2.3.2. Immediate syncope (primary shock): Syncope, at one time called primary shock, consists of a sudden loss of consciousness and it commences with yawning, sighing respiration, nausea and vomiting. This is followed by loss of consciousness, but the attack rarely lasts for more than a few minutes. The condition is characterized by a fall in blood pressure, a slow pulse, and pallor and

coldness of the extremities. The cardiac output remains unchanged, but there is a widespread vasodilatation of the muscles which results in a dramatic fall in blood pressure and a reduction in the cerebral blood flow. This leads to a loss of consciousness. Psychological factors such as fear and anxiety also play a large part. Pain is also an important factor.

2.3.3. The phase of redistribution of available blood to vital centres: Following haemorrhage the venous return to the heart fall as does the right atrial pressure. The cardiac output is reduced, and the blood pressure tends to fall. The tonic inhibitory impulses from aortic and carotid sinuses to the vasomotor centers are therefore reduced. Baroreceptors are also present in the atria. The increased activity of the vasomotor center results in and increased peripheral resistance, and the blood pressure is maintained. The blood vessels of the brain are not affected by this generalized vasoconstriction, and the coronary vessels actually dilate. There is also tachycardia. In the human, 60-70% of the blood volume is contained in the veins and venules . Constriction of these vessels can readily increase the venous return to the heart; following a 10% blood loss, contraction of the venous reservoir can prevent any change occurring in the cardiac output and blood pressure (Inamasu et al., 2003). The arteriolar constriction is selective and the blood flow to the skin, skeletal muscle, salivary glands, intestines, liver, spleen and kidneys is reduced. The skin becomes pale, clammy and cold. Salivary secretion stop, the mouth becomes dry, and thirst results. The intestine manifests impaired digestion, and water is not well absorbed- a point to remember when treating patients. The blood flow to essential organs is, however, maintained. These include the brain, heart, diaphragm and intercostal muscles. Although this selective vasoconstriction is mediated mainly by autonomic nerves, two additional mechanisms play some part:

- The adrenal medulla secretes excess adrenaline and nor-adrenalin. Both are general vasoconstrictors but adrenaline dilates skeletal muscular vessels while nor-adrenaline dilates the coronary vessels.

- There is also an increased secretion of renin by the kidneys, due to a decreased renal afferent arteriolar pressure.

These mechanisms tend to restore the blood pressure, and divert blood from the less essential organs to those of immediate importance, namely the heart and brain. With a blood loss of less than 30% the blood pressure tents to remain almost unchanged, blood pressure measurements are therefore not an accurate guide to the severity of the bleeding. If the blood loss is of such a magnitude that these compensatory mechanisms are unable to maintain an effective blood pressure, haemorrhagic shock ensues.

2.3.4. Changes in Respiration: The pulmonary blood flow is reduced pari passu with the cardiac output. There is an increase in physiological dead space due to under perfusion of the lungs. The increase in dead space ventilation in part explains the hyperpnoea which characteristically occurs after haemorrhage. The major factor causing this air hunger, however, is a fall in arterial blood p^H due to metabolic acidosis (Vieweg et al., 2006).

2.3.5. Blood Supply to The Brain: The blood flow to the brain is determined by the systemic blood pressure and the resistance of the cerebral vasculature. When the blood flow to the brain is reduced as a result of hypotension, the Po_2 of the brain tissue is reduced and the Pco_2 rises. These changes cause vasodilatation and a corresponding increase in blood flow. Any marked reduction of arterial Pco_2 due to hyperpnoea tends to impair the cerebral circulation, because the cerebral vessels are very sensitive to changes in CO_2 tension. When the flow falls below a critical level for any length of time, the cortical neurons undergo necrosis. Blindness may occasionally follow acute haemorrhage, especially gastrointestinal through the mechanism not well known; spasm of retinal arteries may be a factor (Vieweg et al., 2006).

2.3.6. Blood supply to the heart: The coronary blood flow is related to the systemic blood pressure and the duration of ventricular diastole. Tachycardia and hypotension both tend to produce myocardial ischaemia. Heart failure therefore occurs (Vieweg et al., 2006).

2.3.7. Renal blood flow: There is intense renal vasoconstriction which leads to acute tubular necrosis (ATN) with oliguria and even anuria. ADH secretion contributes to the oliguria (Vieweg et al., 2006).

2.3.8. Blood changes: The haemoglobin level and the red cell count are both normal immediately after haemorrhage. Their measurement is useful as a baseline but of no value as an immediate guide to the amount of blood lost.

2.3.9. The **platelet count** rapidly rises after haemorrhage, and may be $1000x10^9$ per liter within an hour (Vieweg et al., 2006). The **clotting time** decreases within a few minutes and the fibrinolytic system is activated.

2.3.10. The **white-cell** count rises within 2 to 5 hours, and may reach $35x10^9$ per liter (Vieweg et al., 2006). The excess cells are neutrophil leukocytes released from the stores in the bone marrow.

2.4. Phase II

2.4.1. The restoration of blood volume[15]: During this fluid is withdrawn from the tissue spaces, particularly of skin and skeletal muscle, into the blood stream. This continues until equilibrium is reached. The lost plasma proteins are replaced within 2 to 3 days (Vieweg et al., 2006). As the blood volume is restored, so the vasospasm passes off, and the capillary pressure rises. Thus, extra cellular fluid passes into the blood until the forces governing the interchanges of fluid across the capillary wall are balanced, during this phase there is progressive haemodilution, rapid at first and complete by about 2 days. Haemoglobin estimation is now of value, because they reflect magnitude of the original blood loss.

2.5. Phase III

2.5.1. The replacement of lost red cells[15]: During the dilution phase anaemia becomes apparent, and is of a normocytic normochromic type. Within 4 to 7 days the reticulocyte count reaches 5 to 15% indicating active red cell formation (Vieweg et al., 2006). The bone marrow shows normoblastic hyperphlasia, the stimulus for which is probably erythropoietin. The reticulocytosis should about after 10 to 14 day's; failure to do so suggests recurrent haemorrhage. The white-cell count should return to normal after 3 to 4 days (Vieweg et al., 2006).

3.0. Shock

Shock, or cardiovascular collapse, is the final common pathway for a number of potentially lethal clinical events, including severe hemorrhage, extensive trauma or burns, large myocardial infarction, massive pulmonary embolism, or microbial sepsis, regardless of the underlying pathology. Shock constitutes widespread hypoperfusion of tissue due to reduction in the blood volume or cardiac output or redistribution of blood, resulting in an inadequate effective circulatory volume. Incident to the perfusion deficit, there is insufficient delivery of oxygen and nutrients to the cells and tissues and inadequate clearance of metabolites (Vieweg et al., 2006). The cellular hypoxia induces a shift from aerobic to anaerobic metabolism, resulting in increased lactate production and sometimes-lactic acidosis (i.e., metabolic acidosis) while at the outset the haemodynamic and metabolic derangements are correctable and induce reversible injury to cells, persistence or worsening of the shock state leads to irreversible injury and death of cells and sometimes, unhappily, the patient. The haemodynamic derangement in the many clinical states

sometimes complicate by shock can be divided into several types, namely, hypovolaemic, traumatic, cardiogenic, septic, anaphylacitic, vasovagal, psychogenic, neurogenic and burn shock. As this study is on the trauma (i.e., blunt abdominal trauma) only haemorrhagic shock (in other word hypovolaemic shock) and traumatic shock will be described next, though possible end results of different types of shock are same. Hypovolaemnic shock is due to loss of intravascular volume by haemorrhage, dehydration, vomiting and diarrhea. Until 10-15 percent blood volume is lost; the blood pressure is maintained by tachycardia and vasoconstriction. Fluid moves into the intravascular space from the interstitial space – a 'transcapillary refill' which may exceed 1 liter in 1 hour in injured but otherwise fit patients (Fragae et al., 2010). In addition, the venous capacitance vessels constrict, pushing blood into arterial system and therefore compensating for the volume deficit. Traumatic shock is due primarily to hypovolaemia from bleeding externally (open wounds), from bleeding internally (torn vessels in the mediastinal or peritoneal cavities, ruptured organs such as liver and spleen or fractured bones) or fluid loss into contused tissue or into distended bowel. Traumatic contusion to the heart itself may cause pump failure and shock, while damage to the nervous system or to the respiratory system results in hypoxia. Several observations on experimental models show different mediators to be highly elevated in plasma in different types of shock. It has been shown that TNF-α (Tumor necrotic factor-α), IL-1 may be the ultimate and essential mediators of possibly all forms of shock. One additional putative player, in the ever-expanding cast of character in shock is myocardial depressant factor (MDF) produced in the ischemic pancreas, MDF induces splanchnic vasoconstriction, depresses myocardial contractility, and enhances membrane leakiness.

4.0. Conclusion

In conclusion it is very clear that trauma causes multiple pathophysiological reactions to the body. These may be very easily manageable; however, some condition are very life threaten. These reactions are also varied according to the type of injury with their different dimension. Proper and prompt management is essential to tackle this type of condition.

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