ISSN 2073-9990 East Cent. Afr. J. surg. (Online)

The Systemic Response to Surgical Trauma – A review.

E.P. Weledji[1], J. C. Assob[2]
[1] Dep't of Clinical Sciences, Faculty of Health Sciences, University of Buea, Cameroon, W/Africa
[2]Dep't of Biomedical Sciences, Faculty of Health Sciences, University of Buea, Cameroon, W/Africa
Corresponding to: E.P. Weledji, E-mail: elroypat@yahoo.co.uk

Better understanding of the systemic response to surgical trauma will enhance the perioperative care of the patient. This will enhance recovery; reduce morbidity, length of hospital stay and cost. The new insight of enhanced recovery is based on the physiological principles of minimizing surgical stress by limiting the initiating factors. This is manifested by avoiding the stress hormones using thoracic epidural anaesthesia and minimally invasive (laparoscopic) surgery; avoiding stress-induced diabetes (hyperglycaemia) by pre-operative anabolic setting of the patient and avoiding fasting; treating hyperglycaemia with insulin; postoperative pain control with epidural analgesia and, early postoperative feeding and mobilization.Survival is determined by physiology rather than anatomy. Enhanced recovery has challenged traditional perioperative care.

Introduction

There are major and rapid physiological changes that occur during elective and emergency surgery, to maintain constancy of the internal environment *('milieu interieu'*) now termed homeostasis[1,2]. These include (a) a rapid adaptation of circulatory mechanisms to restore blood pressure and volume, (b) activation of clotting mechanisms to reduce blood loss,(c) the conservation of water and electrolytes by the kidneys and with the lungs maintenance of acid-base neutrality, (d) the adaptations of the metabolic and immunological mechanisms which includes the mobilization of aminoacids from protein for gluconeogenesis and wound repair and the mobilization of fatty acids and glycerol from fat for energy production and gluconeogenesis respectively. Claude Bernard[1] noted hyperglycaemia in haemorrhage and gave the first report on hyperglycaemia in stress.

The response to surgical stress is based on afferent stimuli mainly from altered circulatory volume and tissue injury that would stimulate a neurohumoral response of stress hormones and cytokine production. These have cardiovascular and metabolic effects[2,3,4]. The independent factors predicting length of hospital stay are (a) type of surgery (70%), (b) perioperative blood loss, (c) postoperative insulin resistance[5,6].

Surgical stress

Surgical stress occurs before, during and after an operative procedure. It is the end result of a *variety of stimuli evoked by (a) psychological stress, (b) tissue injury, (c) alterations in circulation, (d) anaesthetic agents and (e) postoperative complications. The adaptive host r*esponse to surgical stress encompasses three stress response systems: (1) endocrine responses, (2) sympathetic nervous system stimulation, (3) acute phase response. These are intimately linked to the hypothalamic-pituitary adrenal axis (neuro-endocrine axis), the stimuli being integrated in the hypothalamus. The afferent stimuli are processed in the hypothalamus. The posterior hypothalamus controls release of Adrenocorticotrophic hormone (ACTH) from the anterior pituitary which stimulates secretion of glucocorticoids from the adrenals. The paraventricular nuclei (PVN) and the supraoptic nuclei (SON) of the hypothalamus secrete the antidiuretic hormone (ADH/vasopressin) to the posterior pituitary (neurohypophysis) and thence to the circulation. The sympathetic reflex activity is regulated at the medulla and spinal cord and partially coordinated by the posterior hypothalamus. The catecholamines (adrenaline and noradrenaline) are the front-runner hormones as they play an important role in volume conservation via vasoconstrictive effects

ISSN 2073-9990 East Cent. Afr. J. surg. (Online)

on kidney and circulation. They also affect the intermediary metabolism of carbohydrates, fat and protein[2,7,8].

.

Stimuli for neuroendocrine response

The stimuli for the neuro-endocrine reflexes are:

1. Altered circulating blood volume

Volume depletion is the most important single factor that influences the systemic response to surgical trauma. Fluid loss commonly occurs as a result of haemorrhage e.g. ruptured abdominal aortic aneurysm, ectopic pregnancy, injury to a major blood vessel. Other causes include loss of extracellular fluid in vomiting, as in intestinal obstruction, severe diarrhoea, and loss of plasma as in burns. Acute haemorrhage results in the activation of the haematological, cardiovascular, renal and neuroendocrine systems.

- ***Neuroendocrine system***

As a result of decreased firing of baroreceptors from hypotension and decrease in sodium concentration, there is an increase in ADH from the posterior pituitary gland. ADH causes increased intravascular volume by resorption of NaCl and water at the distal tubule, collecting ducts and loop of Henle. There is also an increase secretion of ACTH and Growth hormone directly through central autonomic pathways.

- ***Cardiovascular system***

The decreased activation of the baroreceptors (carotid sinus, aortic arch. left atrium, pulmonary vessels) stimulate the sympathetic nervous system to increase release of noradrenaline which increase heart rate, myocardial contractility, and cause peripheral vasoconstriction. However, blood pressure alone should not be used as the main indicator for shock, especially in young people as these compensatory mechanisms prevent significant decrease in systolic blood pressure until the patient has lost 30% of blood volume. More weight should be given to pulse, respiratory rate and skin perfusion[9]. Patients taking beta-blockers may not present with tachycardia. Since young fit patients can withstand low blood pressure for surprisingly long periods, the different and controversial concept of hypotensive resuscitation has emanated[10]. The aim of resuscitation here is to maintain critical organ perfusion (of the heart, brain and kidney) but not disrupt the blood clot that has formed around the injury. Thus, fluid is not given to maintain a 'normal blood pressure' but is withheld until surgical control is achieved. Conscious hypotension and active observation is utilized.

- ***Renal system***

The sympathetic nervous system stimulates renin secretion from the juxtaglomerular apparatus through decrease renal perfusion from renal artery vasoconstriction. The renin-angiotensin system is activated. Renin cleaves circulating angiotensinogen produced by the liver to angiotensin I which is then converted to Angiotensin II by the lung and kidney. Angiotensin II is not only a potent vasoconstrictor but also a powerful stimulator of aldosterone release from the adrenal cortex. Aldosterone, in turn leads to an increase in sodium reabsorption by the kidney. This coupled with the increase in free water retention induced by ADH leads to extracellular volume expansion. The volume changesmay result in changes in plasma osmolality which further modifies the response via aldosterone and ADH to produce an isotonic absorbate.

- ***Haematological system***

There is the activation of the coagulation system and contracting blood vessels release thromboxane (TxA). An immature blood clot is formed on the bleeding source by the activation of platelets. The damaged blood vessel exposes collagen which causes fibrin deposition and formation of a stable clot after 24 hours[2].

ISSN 2073-9990 East Cent. Afr. J. surg. (Online)

2. Afferent nerve impulses

a. Pain

Pain is an important factor in the neuro-endocrine response to surgical trauma[2,7]. The pain stimuli reach the hypothalamus and stimulate the autonomic nervous system and release of the pituitary hormones.Sometimes anticipated pain by the patient may trigger impulses from the higher centres before the injury. The evidence for pain as a major factor are (1) both ACTH and GH rise within 1hr of skin incision for a laparotomy, (2) paraplegics do not respond similarly to operations below the level of cord transection, (3) spinal/epidural anaesthesia gives a delayed response. Epidural has less effect on the autonomic nervous system, thus minimizing the hypotension from peripheral vasodilatation following sympathetic blockade. (4) Laparoscopic (minimally invasive) surgery decrease the physiological response to injury and consequent decrease in hospital stay[11,12,13].

b. Wound

The inflammatory cells from tissue damage release cytokines (interleukins IL1,6) into the circulation which give an acute phase response (APR)[2,13]. The acute phase response is a systemic response to localized tissue damage. The myriad of systemic effects include fever, leucocytosis, hypothalamic-pituitary axis stimulation, immune activation and production of the acute phase proteins. The acute phase reactants are proteins mainly secreted by the liver during injury, unlike other tissues which undergo proteolysis during the metabolic response to injury. The positive reactants (α chymotrypsin, complement C3, caeruloplasmin, fibrinogen, haptoglobin and C-reactive protein (CRP) are those whose levels rise during the APR. The negative reactants (albumin, transferring) levels decline during the same period. The acute phase reactants are part of the host-defence mechanisms to injury. C3 and CRP are required by phagocytic cells for opsonization. Fibrinogen is essential for blood coagulation and proteases limit tissue damage. The serum levels rise during the first 24-48 hrs after surgery and are proportional to the severity of the injury e.g. CRP in acute pancreatitis. It falls back to normal after 48-96hrs but may remain elevated in presence of sepsis or other complications[2,14].

- ***Mutual relationship- glucocorticoids and cytokines.***

There is a mutual relationship between glucocorticoids and cytokines. Cytokines are capable of stimulating the HPA axis during stress, and glucocorticoids facilitate the elaboration of the various acute phase proteins by the cytokines. Glucocorticoids can also inhibit cytokine production. This paradoxical activity caused by the dual role played by glucocorticoids in a permissive fashion (a) initiates the host response and (b) later as it remains elevated attenuate the homeostatic response[3,4]

Systemic Inflammatory Response Syndrome (SIRS)

Cytokines are helpful towards the host response but potentially hazardous if uncontrollable or in excess. This is seen in SIRS, septic shock and multiple organ failure[2,14]. SIRS is a massive systemic reaction arising from a variety of insults, with an evolution of a cytokine cascade (tumour necrosis factor (TNF), Interleukins IL1,6,8), and a sustained activation of the reticulo-endothelial system (RES). This leads to an elaboration of secondary inflammatory mediators causing cell damage: (1) arachidonic metabolites (prostaglandins and leukotrienes), (2) nitric oxide (NO) vasodilator, (3) oxygen free radicals, (4) platelet activating factor (platelet aggregation, vasodilatation, capillary permeability). The clinical response of SIRS includes 2 or more of the following (1) temperature $<38^0$C or $< 36^0$C, (2) heart rate >90 beats/min, (3) respiratory rate >20 breathes/min, (4) white cell count (WCC) >12 or$< 4 \times 10^9 l^{-1}$ or >0.10 immature forms (bands) [Society of critical care medicine 1992] .

c. Toxic factors

Toxic factors have a modifying rather than an initiating role in the neuroendocrine response. They may be exogenous or endogenous. Exogenous factors includes (a) exotoxins secreted by Gm positive bacteria e.g.

ISSN 2073-9990 East Cent. Afr. J. surg. (Online)

Clostridium welchii causing gas gangrene (b) endotoxins elicited by Gm negative bacterial cell wall producing septic shock and initiating the metabolic process. Endogenous toxic factors include (1) fat emboli from bone fracture, (2) ATP, (3) Kinins, (4) myoglobins from crush injury causing kidney failure and myoglobinuria. Sepsis is a combination of infection and SIRS. It is an evolving process as it is a continuum of the host response to infection and other inflammatory insults. The sequelae reflect increasing severity of the systemic response to infection and not increasing severity of infection[3]. The mortality from a bacteraemia is 5%, sepsis 15%, septic shock (sepsis + hypotension/ systolic blood pressure<90mmHg) 50%, full blown SIRS 80% and multiple organ failure (MOF) 90%. A patient with full blown SIRS may require simply supportive treatment as surgical intervention may not abort the ongoing cytokine cascade.

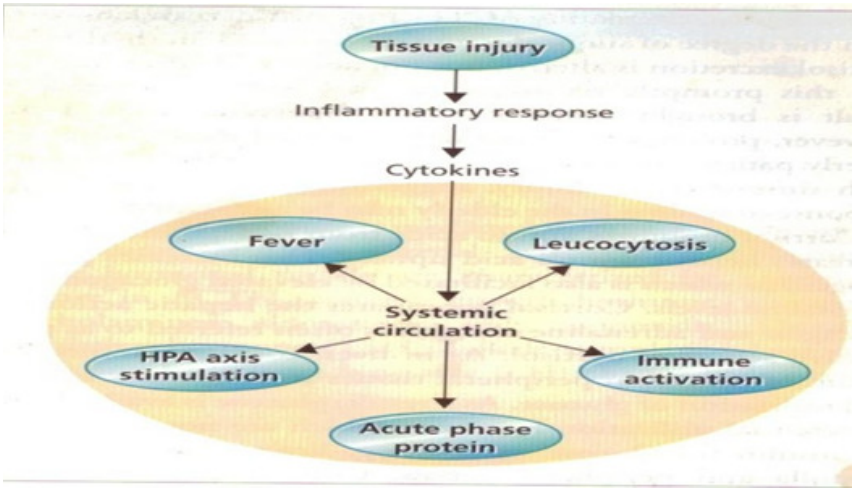

Fig.1 acute phase response [Carey et al 1999]

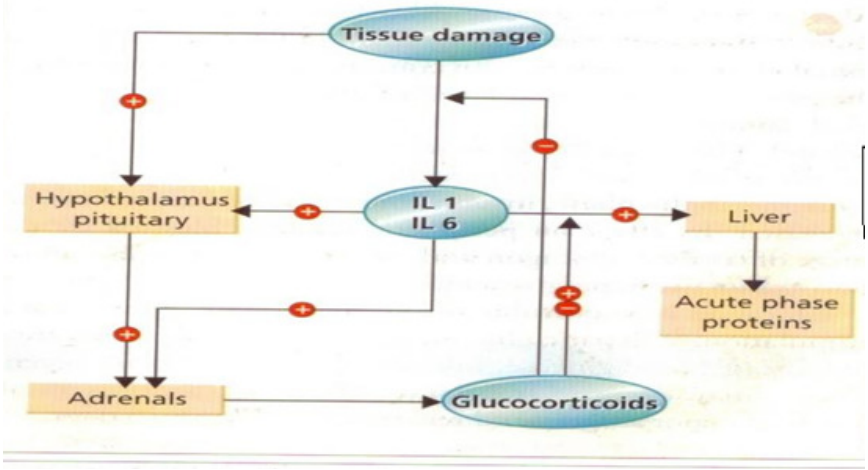

Figure 2. Glucocorticoids and cytokines- a mutual relationship

Mortality will also increase with the number of organs failed; 40% for single organ failure, 60% for 2 organ failure and 98% for 3 organ failure[9].

- **Changes in blood coagulation**

ISSN 2073-9990 East Cent. Afr. J. surg. (Online)

After injury or infection blood is initially hypercoagulable[2,14,17]. Hypercoagulation contributes to the increase incidence of deep vein thrombosis and pulmonary embolism after operation or trauma and is maximized in the first 12hrs after injury. The increased ACTH and cortisol may be responsible due to the increased number of platelets and adhesiveness, a component of the Virchow's triad for venous thromboembolism. Noradrenaline also increases coagulability. Preventive measures including prophylactic anticoagulation are obviously better than cure. Hypocoagulation often follows hypercoagulation (when clotting factors are depleted) as in disseminated intravascular coagulation (DIC) commonly due to septicaemia, haemorrhage and hypothermia. The treatment of DIC is to treat its cause and replace clotting factors.The prognosis is usually poor.

- **Immunological changes**

Despite the major impact of prophylactic antibiotics, the overall incidence of sepsis after elective surgery remains static in the region of 5-10%[2,14]. Though technical factors may play a part this residual sepsis may be a reflection of perturbation of the immune system due to surgical stress. While minor operations may stimulate the immune response the predominant effect of major surgery is immunodepression. Laparotomy down regulates MHC class II antigen on the monocytes mediated by IL-10 released by the T helper 2 cells. Defects in neutrophil chemotaxis, phagocytosis and lysosomal enzyme contents have been identified. It would be interesting to know how much of these may be the effect of the hyperglycaemia (diabetes) of injury[15].. Because many operations are accompanied by haemorrhage , the postoperative immune depression may be caused in part by blood loss and cellular hypoxia rather than surgery. Perioperative blood transfusion also contributes to immunosuppression but the underlying mechanism is largely unknown[16].

Metabolic response to operation and injury

The patient exhibits an increase in total energy requirement (hypermetabolic state)[7,17]. This manifests as a short ebb phase and a long flow phase following injury. The short ebb phase is a period of traumatic shock with a general depression of enzymatic activity and oxygen consumption that last for minutes to a few hours. If the patient survives this, the flow phase will follow. The flow phase has an initial catabolic phase that lasts for 3-8 days, and a later anabolic (recovery) phase that lasts for some weeks. In the catabolic phase the protein and fat mobilization is associated with an increased urinary nitrogen excretion and weight loss, whereas, in the anabolic phase protein and fat stores are restored and weight gained. The catabolic period of flow phase is of most concernin the management of operated or injured patient as the shorter it is the earlier the recovery[8].

- ***Factors modifying the metabolic response***

These factors affect the magnitude and duration of the response.*Severity of injury*: the greater the injury the greater the response; *Nature of injury:* burns produce a greater response because of greater heat and fluid loss from the burn area[18]; *Infection* potentiates the metabolic response. The catabolic phase persisting as long as infection remains [Carey et al 1998].*Other complications* including DVT, pulmonary embolism, compartment syndrome potentiates the response[19].. Compartment syndromes can be prevented by recognizing patients at risk and treat promptly for example by avoiding primary fascia or skin closure using a mesh or Bogota bagin extensive abdominal injury with bowel oedema[20]. *Ambient temperature* modifies the response especially in burns where there is a reduced metabolic demand after injury if the ambient temperature is increased for example from 20^0C to 30-32^0C as there is decrease energy loss from evaporation of water (latent heat). This principle is used in specialized burns units. *Corticosteroids* have a permissive role as illustrated above. A certain level of corticosteroids is necessary to produce the metabolic response, but patients on steroids have a negative feedback on the pituitary axis with resultant decrease in ACTH production. Therefore the need for an increased corticosteroid dose appropriate to the current dose and magnitude of surgery so as to prevent an Addisonian crisis[17]. A*ge and sex* has an influence as there is less metabolic response in children, women and the elderly[6,17].

ISSN 2073-9990 East Cent. Afr. J. surg. (Online)

Bowel preparation causes dehydration before surgery and further dehydration with overnight fasting. There is an increased risk for hypotension during anaesthesia and excess fluid treatment with a resultant guts oedema and reduce gastrointestinal motility[21]. Bowel preparation does not reduce the risk of complications but increases the risk of anastomotic leakage because of dehydration[22]. Avoiding bowel preparation would enhance recovery by avoiding unnecessary fasting and fluid derangements before the onset of surgery.

Anaesthesia and drugs modify the response by affecting the vascular system and hormone production. Ether stimulates catecholamines and ADH, morphine stimulates ADH, spinal/epidural anaesthesia decrease the initial response by blocking the afferent pathways. Prompt and adequate replacement of fluid loss via oesophageal Doppler monitoring of left atrial filling, stroke volume and aortic flow (goal directed fluid management) limits the liberation of catecholamines, aldosterone and ADH. It avoids the complications of fluid overloading or under-filling and thus favour faster recovery[21,23].

Surgical technique: meticulous and gentle tissue handling during operation reduces the amount of trauma and post operative metabolic demand[17]. Survival is determined by physiology rather than anatomy[19]. Damage control surgery in 'bad' injury patterns (high energy, multivisceral damage, prolonged hypotension, massive blood loss) focus on restoring normal physiology and not normal anatomy. Rapid operations to stop ongoing bleeding and contamination by packing and stapling across or tying damaged bowel ends off and returnto the abdominal cavity, followed by reconstruction 24-72 hrs later when hypothermia, acidosis and coagulopathy have been corrected is the principle[20,24]. The bloody vicious cycle (lethal triad) of hypothermia (temp < 34^0C), coagulopathy (PT >16 seconds) and acidosis (pH <7.2) from a prolonged operation is avoided[25,26]. Abdominal compartment syndrome can occur after closure or a tight abdominal closure over many packs. The intra-abdominal pressure of patients at risk including patients without abdominal injury should be measured at regular intervals by monitoring the urinary bladder pressure. At the first sign of abdominal compartment syndrome developing or persistent elevation of bladder pressures >20-25, return immediately to theatre for the opening of the laparotomy incision and tension- free re-closure over mesh or Bogota bag[19,]

Nutritional status: A well nourished patient withstands surgery better than one poorly nourished[8,27,28]. Wound healing is more efficient and resistance to infection is greater.Starvation occurs frequently after operation or injury and adversely affects convalescence.Surgery and injury impose considerable catabolic demands, and starvation adds an important component to post traumatic catabolism, particularly when continued for 3-4 days after surgery as glycogen stores are depleted. Provision of enough calories and nitrogen during the catabolic phase modifies and prevents weight loss and negative nitrogen balance especially in the undernourished, severe trauma or septic patient[7,17]. Better still, the new insight of preoperative anabolic setting of the patient should diminish the catabolic phase as compared to the traditional overnight fasting routine which has no scientific support[27.] A carbohydrate-rich drink 2hrs before anaesthesia, changes the overnight fasted state of metabolism into a fed state, improves well being perioperatively and markedly reduces the metabolic derangement and the risk of hyperglycaemia in the post operative phase[8,28]. Parenteral nutrition is only of benefit prior to surgery in a severely malnourished patient with a non-functioning gastrointestinal tract. Parenteral nutrition with its attendant risks and expense may still have other specific indications. A classic pre-operative indication for parenteral nutrition is a severely malnourished patient with dysphagia from an obstructing oesophageal carcinoma.

Two or three weeks of parenteral nutrition before operation may improve the chances of survival after oesophageal resection. Preoperative feeding gastrotomy is no longer favoured in oesophageal cancer as it interferes with subsequent surgery. Parenteral nutritionmay also be instituted for protracted ileus (no sign of peristalsis after 3 days)post surgery while the underlying cause of the ileus is determined and dealt

ISSN 2073-9990 East Cent. Afr. J. surg. (Online)

with. In some hypercatabolic states the metabolic demands are so high that parenteral nutrition should be instituted immediately [7,17]. These situations include multiple injury, major burns, severe sepsis, some patients with head injury or after certain neurological operations and tetanus. The majority of enterocutaneous fistulae will close on conservative management with parenteral nutrition in the absence of distal obstruction, or a local disease process. In general, the complications of pre-operative parenteral nutrition outweigh the benefits[29]. The intra-operative period is a relatively insulin-resistant state, and intravenous feeding is associated with hyperglycaemia and is probably superfluous[30].

The Diabetes of injury

During the metabolic response there is increase in glucose production with simultaneous increase in insulin secretion. However, due to the antagonistic effects of the stress hormones (adrenaline, glucagon, cortisol, growth hormone) there is decrease tissue sensitivity to insulin [8,17,27]. The insulin resistance developing after surgery gives rise to hyperglycaemia similar to type 2 diabetes mellitus but faster[30]. Insulin resistance rises with the magnitude of surgery (e.g. laparascopic cholecystectomy < open< major colorectal surgery)[17]. Hyperglycaemia increases complications and mortality as it overloads the mitochondria blocking glycolysis and the Kreb's cycle. Thus enhancing further inflammatory response and cytokine production leading to a vicious cycle with insulin resistance and hyperglycaemia. The organs mainly affected are the kidney, endothelia of blood vessels and heart, blood cells and neural tissue as they have an uncontrolled inflow of glucose, (glucose uptake simply dependent on glucose level) with no storage capacity. Thus the resultant overflow of oxidation and cytokine production. Meanwhile glucose uptake in muscle and fat is regulated by insulinthat has control of glucose inflow with sites of insulin resistance[15]. The early (within days) postoperative complications include infections, probable cardiac, renal failure, ventilatory support and polyneuropathy. If not reversed, the type2 diabetes mellitus will later predispose infections, cardiovascular effects, renal failure, muscle weakness and polyneuropathy[31,32,33]. The diabetes of injury responds drastically to insulin treatment as compared to ordinary patients with non- insulin dependent diabetes[30,35,].

Enhanced Recovery after Surgery

The new insight of enhancing recovery after elective surgery excludes diabetics, patients with ileus (slow motility) and reflux. It is based on the principle of reducing metabolic stress in major surgery[30,35,36]. This is manifested via firstly minimally invasive (laparoscopic) surgery, secondly, preoperative actions aimed at (a) avoiding stress hormones by thoracic epidural anaesthesia[37]; (b) preparing an anabolic setting of the patient bya preoperative carbohydrate feed and no overnight fasting. A carbohydrate load of 12.5% carbohydrate drink (400ml) and 20% glucose (800mls) iv given 2-3 hours before anaesthesia and surgery will stimulate enough insulin production to face the stress of surgery[38,29].

ISSN 2073-9990 East Cent. Afr. J. surg. (Online)

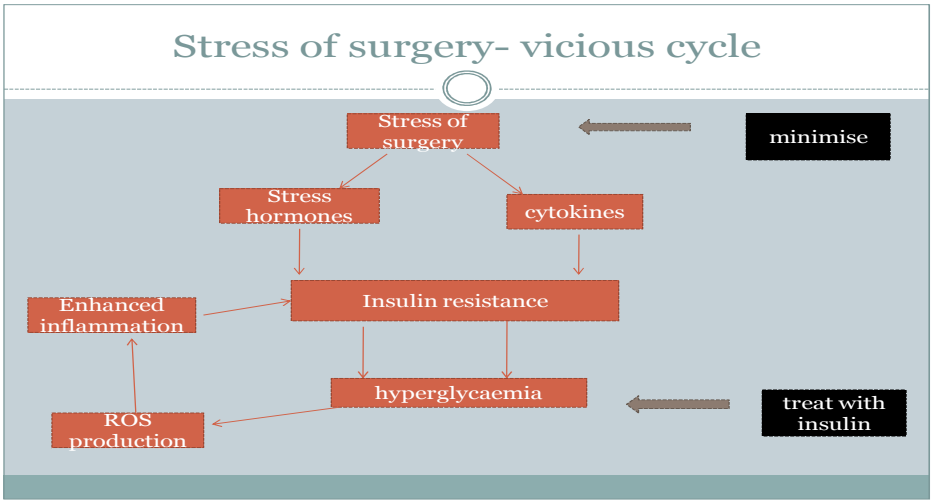

Fig.3: Stress of surgery- vicious cycle

It is safe (260 mOsm/kg water) and renders fast gastric emptying. Clear fluids do not necessarily change metabolism; (c) avoiding postoperative hyperglycaemia by preoperative carbohydrate loading or treatment with insulin[30,32,33].

Treatment with insulin has decreased the mortality in intensive care unit by 43% and mortality in hospital by 34%[34]. Insulin also reduces wound healing time by promoting wound matrix (laminin/collagen type IV) formation[16]. Thirdly, postoperative early mobilization, early enteral feeding (day1) including early use of feeding jejunostomy instituted during oesophageal or gastric resection for cancer are encouraged[40]. Intravenous fluids are stopped, nasogastric tube if inserted is removed early to promote gut motility, prevent breathing difficulties and damage to the protective nasociliary and cough mechanisms[27]. Postoperative pain control uses epidural analgesia for 48 hours and non-steroidal anti-inflammatory drug[35,37]. Opiates are avoided as they paralyze the gut thus promoting post operative ileus, affect the cardiovascular, respiratory, neurological systems and thus slow recovery. Epidural analgesia also helps nutrition by diminishing pain[27]. Prolonged length of hospital stay can be predicted by age, multiple procedures and enhanced recovery programme deviation as a result of pathology or intra-abdominal complications[6]. Failure to mobilize prompts further investigation. Enhancing recovery (perioperative care)is thus a chain of events associated with an interactive physiology as most parts interact with subsequent parts and so interdisciplinary insight and understanding is necessary.

Conclusions

The understanding of the systemic response to surgical trauma will enhance perioperative patient care, enhance recovery and decrease hospital stay. Survival is determined by physiology rather than anatomy. There is a growing realization that the exsanguinating critically ill patient may not be able to tolerate complex reconstructive surgery and therefore damage control surgery has developed. The importance of metabolic factors in the response to surgery has been emphasized, the disturbance of metabolism and insulin resistance. Hyperglycaemia should be avoided or treated. Enhancing recovery challenges traditions.The outcome of enhanced recovery are its physiological benefit that decreases morbidity and, its economic benefit that returns the patient to work earlier and decrease hospital stay costs.The basis of enhanced recovery by reducing surgical stress has benefitedthe patient, hospital and community.

References

1. Bernard C. (1877) Hyperglycaemia in haemorrhage. Paris Baillieer 210, 1877
2. Carey D.P, Manas K. Roy, Delicata R.J, AnandMahadevan (1999); Response to surgical trauma: Surgical emergencies (p25-36) (editors): Monson, Duthie.O'Malley. Blackwell publishers
3. Guillou, P.J. (1995) Adjuvant biological response modifiers after major surgery or trauma. British Journal of Surgery 1995; 82: 721-723
4. Souba, W.W. (1994) Cytokine control of nutrition and metabolism during critical illness, Current problems in Surgery Volxxxi, no7 577-652
5. Thorell A, Nygren J, Ljungqvist O. Insulin resistance, a marker of surgical stress: CurrOpinClinNutrMetab Care 1999; 2 (1):69-78
6. BoulindCE,Yeo M, Burkill C, Witt A, James E, Ewings P, Kennedy RH, Francis NK. (2012) Factors predicting deviation from an enhanced recovery programme and delayed discharge after laparoscopic colorectal surgery:Colorectal disease: Vol 14 Iss3 Ps103-110) :The metabolic response to operation and injury: Principles and Practice of Surgery1989; (p69-76), 5th edn Churchill Livingstone
7. LjungqvistO,Hausel J, Nygren J, Thorel A, Soop M in collaboration with the ERAS study group. Preoperative patient preparation for enhanced recovery after surgery.Transfusion alternatives in transfusion medicine. 2007; 9 (1): 45-49
8. Wilmore D.W et al. Care of the surgical patient. American College of surgeons/scientific American Medicine.Newyork; 1988
9. Bickell, WH. Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries. New England Journal of Medicine 2004; v331-1105.
10. Alexander- Williams, J. laparoscopy in abdominal trauma. Injury 1994; 25(9): 585-586
11. Levy B.F, Scott MT, Fawcett WJ, Rockall TA. 23-hour stay laparoscopic colectomy.Dis Colon Rectum 2009;52(7):1239-1241
12. Slim K. (2011) Fast track Surgery- the next revolution in surgical care following laparoscopy. Colorectal Disease 2011; 13 Is 5: P478-480
13. Carey D.P, Manas K. Roy, Delicata R.J. Shock: Surgical emergencies. 1999; (p11-24) editors: Monson, Duthie.O'Malley. Blackwell publishers
14. Brownlee M. Thepathobiology of diabetic complications- a unifying mechanism. Diabetes 2005; 54 (6) (2005)
15. Carton E.G, Phelan D.M (1999). Perioperative management of the emergency patient: Surgical emergencies (p37-48) (editors): Monson, Duthie.O'Malley. Blackwell publishers
16. Forrest A.P.M, Carter D.C, Macleod I.B (1989) :Parenteral nutrition in surgical patients : Principles and Practice of Surgery (p100-104), 5th edn Churchill Livingstone
17. Pierre E.J, Barrow RE, Hawkins HK. Effect of insulin in major burn injury and wound healing. J of trauma 1998: 44: 342-345
18. Desmetriades D.Abdominal compartment syndrome. Trauma 2000;2:277-281
19. Bowley DMG, Barke P, Boffard KD.Damage control surgery-concepts and practice .JR Army Med Corps 2000; 146: 176-182. A meta-analysis of randomized controlled trials of intravenous fluid therapy in major elective open abdominal surgery: getting the balance right.ProcNutrSoc 2010 Nov; 69(4): 488-98
20. Slim K, Vicaut E, Panis Y, Chipponi J.(2004) Meta-analysis of randomized clinical trials of colorectal surgery with or without mechanical bowel preparation. Br J. Surg 2004; 91: 1125-1130
21. Noblett SE, SnowdenCP, Shenton BK, Horgan AF.(2006) Randonized clinical trial assessing the effect of Doppler- optimized fluid management on outcome after elective colorectal resection. Br. J Surg 2006; 93: 1069-1076
22. Sugrue M, Jones F Janjua J et al.Temporary abdominal closure. Trauma 1998;45(5):914-921

ISSN 2073-9990 East Cent. Afr. J. surg. (Online)

23. Cannon WP. The prevention of wound shock. JAMA 1918,70:618
24. Gobler K D. The impact of hypothermia and dilutional coagulopathy. J trauma 1994; 36: 847
25. Soop M, Carlson GL, Hopkinson J, Clarke S, Thorell A, Nygren J, Ljungqvist O (2004): Randomized clinical trial of the effects of immediate enteral nutrition on metabolic responses to major colorectal surgery in an enhanced recovery protocol. Br J Surg 2004; 1138-1145
26. Ljungqvist O (2010). Insulin resistance and outcomes in surgery.J. ClinEndocrinMetab 2010; Sep;(95): 4217-9
27. Nightingale J, Woodward (2006)J: Guidelines for management of patients with a short bowel. Gut 2006; 2 55 (supplIV) :IV)-IV12
28. Ljungqvist O.L. (2010) Randonized clinical trial to compare the effects of preoperative oral carbohydrate versus placebo on insulin resistance after colorectal surgery. Br J. Surg 2010; 97 (3):327
29. Ahmed J,Lim M, Khan S, McNaught C, MacFie J. Predictors of length of stay in patients having elective colorectal surgery within an enhanced recovery protocol. International J of Surgery 2010; 8 (8): 628-632
30. Khaodhiar L, McCowen K, Bistrain B. Perioperative hyperglycaemia, infection or risk?Curr Op ClinNutrMetab 1999; 2(1): 79 -82:1999
31. Krinsley JS (2004).The effect of an intensive glucose management protocol of the mortality of critically ill adult patients. Mayo Clinic Proc 2004: 79, 992-1000.6
32. G van den Berghe, Bouillon R, Mesotten D. Glucose control in critically ill patients. N Engl. J Med 2009; 361:89-92
33. Society of critical care medicine consensus conference 1991 (1992). Critical care medicine 1991; 20(6): 865
34. Lassen K, Soop M, Nygren J, Cox PB, Hendry PO, (ERAS) group. Consensus review of optimal perioperative care in colorectal surgery; Enhanced Recovery after surgery (ERAS) recommendation.Arch Surg 2009; 144(10): 961-969
35. Uchida I, Asoh T, Shirisaka C, Tsuyi H (1988) Effect of Epidural anaesthesia on postoperative insulin resistance as evaluated by insulin clamp technique. Br J Surgery 1988; 75: 557-562
36. Nygren J (2006).The metabolic effects of fasting and surgery: Best practice& research clinical anaesthesiologyvol 2006; 20 Is3: 429-438
37. Anderson HK, Lewis SJ, Steve T (2009). Early enteral nutrition within 24hr of intestinal surgery versus later commencement of feeding.A systemstic review and meta-analysis.J of Gastrointestinal Surgery 2009;13 (3): 569-575
38. Preston S (2011). Enhanced recovery in minimal access oesophageal and gastric cancer surgery.Annual scientific meeting of Association of Upper Gastrointestinal surgeons of Gt Britain and Ireland. Belfast 15 Sep 2011