

## ENHANCED RECOVERY AFTER SURGERY (ERAS)

### ANAESTHESIA TUTORIAL OF THE WEEK 204

8<sup>TH</sup> NOVEMBER 2010

Cathryn Matthews, Derriford Hospital, Plymouth.  
Correspondence to [cathrynmatthews@gmail.com](mailto:cathrynmatthews@gmail.com)



---

### QUESTIONS

1. The stress response causes
  - a. Hepatic glycogenolysis
  - b. Insulin resistance
  - c. Increased ACTH levels
  - d. Reduced growth hormone levels
  
2. Enhanced recovery programmes include
  - a. Use of nasogastric tubes
  - b. Carbohydrate drinks on day 1 postoperatively
  - c. Transverse incisions
  - d. Fasting from midnight before surgery
  
3. Anaesthetic management of enhanced recovery patients can involve
  - a. Regional techniques
  - b. Sedative premedication
  - c. Antiemetics
  - d. Goal Directed fluid therapy

### INTRODUCTION

Enhanced recovery is a combination of elements of care for elective surgery which aims to:

- Optimise pre-operative preparation for surgery
- Avoid iatrogenic problems such as postoperative ileus
- Minimise the stress response to surgery
- Speed recovery and return to normal function
- Early recognition of abnormal recovery and intervention if necessary

The overall strategy is that patients are in the best health for surgery, have evidence based care throughout their hospital stay and have the best possible rehabilitation. They also have partnership and responsibility for their care. The principles of this approach can be used for any surgery anywhere in the world.

This approach has been used in many centres in the UK for different procedures, especially colorectal and orthopaedic surgery, and is now the focus of the Enhanced Recovery Partnership Programme (ERPP), which aims to spread the technique across the UK. Evidence is continuing to emerge about the benefits of enhanced or rapid recovery, and many other countries are incorporating it into their care; from Denmark, where Professor Kehlet first pioneered the technique, to the USA. The applications are likely to be applicable to many more situations than they are currently used for, and require the involvement of all professionals involved in the patients care, including primary care physicians, hospital consultants, allied health professionals and hospital managers.

## THE STRESS RESPONSE TO SURGERY AND TRAUMA

Surgery and trauma induce complex metabolic, hormonal, haematological and immunological responses in the body and activate the sympathetic nervous system. The initial stimulus for this response comes from cytokines, especially IL-6 and TNF, released by leucocytes and endothelial cells present at the site of injury. These lead to both local and systemic effects. Nociceptive afferent nerve fibres (A-delta and C fibres) transmit pain impulses to the central nervous system from the periphery via the spinothalamic tracts.

### Sympathetic nervous system

The sympathetic nervous system (SNS) is stimulated by:

- Hypotension via baroreceptors
- Hypoxaemia or metabolic acidosis via chemoreceptors
- Pain, anxiety and distress via the limbic system and cerebral cortex
- Autonomic afferent nerves
- Hypothalamus directly activates the SNS

The effects of increased sympathetic outflow are well known:

Alpha-1 adrenoceptors cause peripheral and splanchnic vasoconstriction, hepatic glycogenolysis, pupillary dilatation and intestinal smooth muscle relaxation. The role of alpha-2 adrenoceptors is less clear but activation is associated with platelet aggregation and sedation.

The activation of beta receptors causes an increase in cardiac contractility and heart rate, with smooth muscle relaxation resulting in peripheral vasodilation and bronchodilation. There are also widespread metabolic effects.

As a result, hypertension, tachycardia, renin and glucagon release occur. The cardiovascular effects are aimed at maintaining cardiac output and essential organ function, whilst the release of renin causes conversion of angiotensin 1 to angiotensin 2. This causes peripheral vasoconstriction and aldosterone release from the adrenal cortex, resulting in sodium and water retention. Glucagon release from the alpha cells of the Islets of Langerhans in the pancreas increases glycogenolysis in the liver and muscle, leading to increased glucose and lactate concentrations and mobilisation of free fatty acids. The metabolic effects of the sympathetic nervous system are much less important than the effects of insulin.

### Hormonal and metabolic changes

The overall metabolic changes that occur in the stress response involve protein and fat catabolism to provide energy substrates. Protein from skeletal muscle and glycerol produced from fat breakdown are utilised in gluconeogenesis in the liver. Fatty acids are metabolised into ketone bodies which can be used as an energy source by many organs.

#### *ACTH and Cortisol*

During surgery, the hypothalamus stimulates the release of pituitary hormones such as adrenocorticotrophic hormone (ACTH) leading to cortisol secretion from the adrenal cortex within minutes of the start of surgery. Negative feedback mechanisms normally acting on the ACTH/ cortisol pathway are inhibited and the levels of both remain elevated. Cortisol acts on many systems in the body, resulting in hyperglycaemia and peripheral insulin resistance. It also stimulates hepatic glycogen synthesis and has immunomodulatory and anti-inflammatory effects. Its mineralocorticoid action compounds the sodium and water retention effects of the SNS and antidiuretic hormone.

#### *Antidiuretic hormone (ADH) and growth hormone (GH)*

These hormones are secreted by the pituitary gland causing, salt and water retention and mobilisation of energy substrates respectively. The rise in GH levels is proportional to the severity of the tissue injury and metabolic effects occur via insulin-like growth factors, particularly IGF-1. This leads to

protein synthesis, inhibition of protein breakdown and promotion of lipolysis. Overall, GH acts in a protective manner on skeletal muscle acting as a brake for the protein catabolism that occurs and promoting tissue repair. Its anti-insulin effect limits glucose uptake and utilisation by cells to ensure a more plentiful supply for neurons when supply is limited. Growth hormone may also stimulate glycogenolysis by the liver.

### *Insulin*

Insulin levels do not respond appropriately to the hyperglycaemia and catabolism caused by the above changes, possibly due to sympathetic nervous system inhibition of pancreatic beta cell secretion (an alpha adrenergic effect). The severity of the hyperglycaemia is proportional to the severity of the insult and thus serum glucose levels closely mirror the catecholamine response. Insulin resistance of the peripheral tissue also occurs, reducing utilisation of the available glucose and compounding the hyperglycaemia.

### *Others*

Beta endorphin and prolactin are produced by the pituitary gland but their role in the stress response is unclear. Acute phase proteins are produced by the liver. They are inflammatory mediators, anti-proteinases and free radical scavengers, are involved in tissue repair and augment or otherwise modify the immune response.

## **Haematological and Immunological changes**

Hypercoagulability and fibrinolysis occur due to the effects of cytokines and acute phase proteins on the coagulation pathway. Leucocytosis and lymphocytosis also occur. Immunosuppression occurs as a direct effect of cortisol secretion.

### **Summary of the Stress Response to Surgery**

#### **Hormones whose levels are:**

Increased: ACTH, cortisol,  
GH, IGF-1  
ADH, glucagon

Reduced/ inappropriately low: Insulin

Mobilisation of substrates Glycogenolysis  
Skeletal muscle breakdown  
Formation of acute phase proteins  
Lipolysis

#### **Overall:**

Reduced ability to respond to and control hyperglycaemia  
Utilisation of alternative compounds, e.g. ketone bodies, as energy substrates

### **Detrimental effects of the stress response**

Overall, the multisystem effects of the stress response lead to many potentially harmful effects including:

- Increased myocardial oxygen demand, increasing risk of ischaemia
- Hypoxaemia
- Splanchnic vasoconstriction which may impact on healing of anastomoses
- Exhaustion of energy supplies and loss of lean muscle mass, leading to weakness of both peripheral and respiratory muscles if severe
- Impaired wound healing and increased risk of infections
- Hypercoagulability
- Sodium and water retention

The ERP aims to reduce these detrimental effects by reducing surgical stresses and reducing or pre-empting the metabolic changes that occur.

## **COMPONENTS OF ENHANCED RECOVERY PATHWAYS**

Enhanced recovery programmes involve changes in every step of the patient care process, from the referral from primary care through to the post-operative phases and follow-up. The majority of the evidence for ERPs comes from colorectal surgery, although these components apply equally for other applications such as gynaecological, urological or orthopaedic surgery.

### **Preoperative**

The two main areas of pre-operative care are pre-admission and pre-operative care in hospital.

#### *Pre-admission*

Pre-operative optimisation should initiate in primary care, targeting areas such as anaemia, diabetic and blood pressure control and other medical problems. Smoking cessation and advice on alcohol consumption will also be helpful in many patients as both are associated with adverse outcomes.

Formal preoperative assessment should occur before surgery, including further optimisation of medical problems and risk stratification, e.g. using cardiopulmonary exercise testing. Together with full information about the planned operation, this will assist in consent and informed decision processes by the patient. A central tenet of this approach is to make the patient a partner in their care and give them joint responsibility for their recovery. Therefore, the level of information given is very important as this will define the patients' expectations and facilitate adherence to the pathway. It is vital that specific tasks and targets, e.g. postoperative oral intake or mobilisation, are given to the patient at this stage in the pathway, ideally both in verbal and written formats.

Discharge planning should take place at this stage and full instructions given about stopping regular medication where appropriate. The purpose of pre-operative nutritional drinks and any new medication can also be explained at this time.

#### *Pre-operative care in hospital*

Key features:

- Admission on the day of surgery
- Avoidance of bowel preparations
- Avoidance of prolonged fasting
- Carbohydrate drinks
- Avoidance of sedative premedication

Admission on the day of surgery can occur as the patient has been fully prepared for surgery in the pre-hospital period of their care. Traditional pre-operative preparations, such as fasting from midnight or bowel preparation, are avoided unless there is evidence to suggest benefit from these interventions. Many of these interventions have actually been found to be harmful, rather than have the intended beneficial effect. For colorectal surgery a key factor in recovery is the return of normal bowel function, which is affected by pre-operative fasting, bowel preparation, analgesia and anaesthetic approaches as well as any complications that may develop, accordingly many enhanced recovery interventions are aimed at reducing the incidence of postoperative ileus.

Both prolonged starvation and bowel preparation have adverse effects on hydration status and electrolyte balance. There have been two large multi-centre randomised controlled trials (RCTs) which have shown no benefit from bowel preparation in colorectal surgery and there is also evidence of increased morbidity and post-operative ileus. There is conflicting data on the risk of anastomotic leak; some small RCTs have suggested an increased risk but other data indicates that there may be a protective effect for very low rectal anastomoses.

There is also very poor evidence for fasting from midnight on the night before surgery. A Cochrane review has demonstrated strong evidence to support reducing these periods to two hours pre-operatively for clear fluids in elective situations, although a six hour fast is still recommended for solid food. Within ERPs, pre-operative carbohydrate drinks are provided with the aim of minimising the protein catabolism, negative nitrogen balance and insulin resistance that occurs with the stress response, meaning that the loss of lean muscle mass is minimised.

### **Intraoperative care**

Patient care should be individualised with the use of minimally invasive techniques where possible. Laparoscopic colonic resection has been shown to reduce the length of hospital stay, initial wound complications and time to return of gastrointestinal tract function. If an open procedure is required for abdominal surgery, transverse incisions should be made preferentially to reduce postoperative pain. The use of wound drains is avoided as there is no evidence of beneficial effect for most types of colonic surgery. Nasogastric tubes are actually associated with increased morbidity and increased time to return of bowel function and should also be avoided in elective situations.

Overhydration has previously been common in the perioperative period, and comparisons of liberal and restrictive fluid regimes suggest that this may be detrimental, with prolonged time for return of gastrointestinal tract function, impaired healing and increased length of hospital admission. Fluid therapy intraoperatively can be goal directed using cardiac output monitoring such as oesophageal doppler in high risk patients to optimise cardiac output without overloading the patient. Early commencement of oral intake means that intravenous fluids can be discontinued much more quickly than has conventionally been the case. If postoperative hypotension secondary to epidural analgesia is a problem, this may be best treated with vasopressors rather than large quantities of intravenous fluids.

#### **Intraoperative care**

Short-acting anaesthetic agents

Avoid long-lasting opiates where possible

Use of thoracic epidurals for colorectal surgery

Avoid the use of drains and nasogastric tubes

Avoid overhydration

Attention to temperature control

Thromboprophylaxis

Risk stratification of PONV and aggressive prophylaxis and treatment

### **Anaesthetic factors**

Historically, high dose opioid techniques have been used to moderate the stress response. If sufficiently high doses are used, hypothalamic and pituitary secretion are suppressed. However, this is at the expense of significant sedation and respiratory depression and is not used in current practice. Alpha-2 agonists such as clonidine reduce cortisol secretion and benzodiazepines also have a modulatory effect on the stress response, possibly by a central mechanism of action. Again these are not commonly used in enhanced recovery programmes due to their sedative actions.

There is little evidence to favour one anaesthetic technique over another but the general principles of enhanced recovery support the use of medications that have minimal post-operative hang-over and effects on gastrointestinal motility. Therefore, long-acting premedications are generally avoided as they reduce the ability of the patient to achieve the immediate post-operative goals required of the programme. Short acting anaesthetic agents and analgesics should be used where possible, for example using fentanyl perioperatively in preference to morphine. Total intravenous anaesthesia can be used, including remifentanyl, or short-acting volatile anaesthetic agents.

Epidural anaesthetics are commonly used for colorectal surgery although there is no evidence that intraoperative epidural use improves outcomes in this patient group. The aim of their use is to reduce the dose of general anaesthetic needed and the stress response to surgery. If sited before the start of surgery, release of stress hormones and post-operative insulin resistance are reduced. They also provide post-operative analgesia and reduce post-operative ileus by blockade of the sympathetic nervous system when compared to opioid-based analgesic regimes. For musculoskeletal surgery regional anaesthesia can be used alone or in combination with general anaesthesia to achieve the same effect. The use of low concentration local anaesthetic mixtures (facilitate by opioids such as fentanyl) reduces motor block and therefore interference with mobilisation.

Avoidance of postoperative nausea and vomiting (PONV) is also very important. This is one of the side effects of surgery most feared by patients and can be severely incapacitating. Interruption of oral analgesia caused by PONV can cause real problems with analgesia. The ERAS (Enhanced Recovery After Surgery) Group recommends risk stratification of patients during surgery for PONV using the Apfel scoring system with prophylaxis given for patients at moderate or high risk. The risk factors used are: female sex, motion sickness or previous PONV, non-smokers and the administration of opioids postoperatively. Two risk factors constitute moderate risk and high risk patients have three or more. If PONV develops it should be treated aggressively as soon as possible. The drugs used to combat PONV will vary according to availability and local practice. A Cochrane review of antiemetic prophylaxis did not show a beneficial effect of one agent over another so drug choice is dependent on patient factors, cost and practical considerations. The ERAS group have recommended the use of dexamethasone at induction or a 5HT<sub>3</sub> receptor antagonist such as ondansetron at the end of surgery in moderate risk patients. They suggest high risk patients receive total intravenous anaesthesia, plus dexamethasone at induction and either a 5HT<sub>3</sub> receptor antagonist, droperidol or metoclopramide near the end of surgery.

## Postoperative

Post-operative care involves maintenance of hydration by encouraging the discontinuation of intravenous fluid therapy and early commencement of oral intake, including carbohydrate drinks. These can be continued beyond the return of normal intake if pre-operative nutritional status is poor. Similarly to pre-operative fasting, prolonged post-operative fasting is also detrimental as early resumption of oral intake is associated with fewer wound infections and shorter hospital admissions. Importantly oral intake must be combined with the above measures to reduce ileus.



**Figure 1.** Oral intake should be resumed early. This can frequently be in theatre recovery.

Any drains, and urinary catheters present are removed as early as possible. Multimodal analgesia is used with regular oral paracetamol and non-steroidal anti-inflammatory drugs where tolerated. Excessive intravenous opioids are avoided because of increased sedation, ileus and respiratory complications, although small doses of oral opioids for breakthrough pain are appropriate. The use of analgesic adjuncts such as gabapentin or pregabalin has been shown to have a beneficial opioid sparing effect post-operatively.

Mobilisation should occur early in accordance with the pre-operative plan agreed by clinicians and patients. The aim is to reduce skeletal muscle loss and improve respiratory function and oxygen delivery to tissues. Patients should be encouraged to achieve daily procedure specific goals which can be guided by specific day-by-day proformas to ensure all areas of care receive attention. Ideally, patients should sit out of bed for 2 hours on the day of surgery and for at least 6 hours a day until discharge. The success of this aspect of the program depends on the pre-operative setting of expectations including the concept of patients being partners in their care and taking part-ownership of post-operative rehabilitation.

The involvement of physiotherapy and rehabilitation departments is vital to help with patient motivation and safety. Best results are achieved when the whole multidisciplinary team have belief and interest in the program. This can be achieved by ensuring that all disciplines are consulted when developing an ER program.

Criteria-based rather than time-based discharge should be used with appropriate community support. Telephone follow up should occur at around 24 hours to confirm that recovery is still proceeding according to plan, identify any potential problems and answer any questions that the patients may have. A contact number is also given to patients to enable them to contact an experienced, specialty specific healthcare professional if necessary.

Finally, audit and regular reviews of the processes involved and compliance with all aspects of the pathway should be undertaken. These should ideally include comparisons between hospitals offering the enhanced recovery service to ensure equivalent levels of care are being provided in different areas. These processes are vital to detect successful or failing interventions, determine the reasons why this may be happening and identify areas of care that need reviewing or improving. They also provide

motivation for staff and patients. The enhanced recovery approach represents a major change to the way in which surgery is approached and carried out. It is therefore essential to have robust data to provide evidence of improved outcomes, which can then be used to support business cases for ongoing development of these services. Many of the traditional approaches to peri-operative care have recently been found to be detrimental and such data is important to ensure that all interventions performed have an evidence base and we do not fall into the traps of the past.

## **THE BENEFITS AND EVIDENCE FOR ENHANCED RECOVERY PATHWAYS**

There are benefits to both patients and the health service as a whole from this approach. Patients are prepared for surgery and medically optimised. If the process is started in primary care, patients can be ready for surgery more quickly, which will help to reduce waiting times. In hospital, patients receive evidence based care, have fewer changes in physiology and recover more quickly. Pain, postoperative bowel dysfunction (if undergoing colorectal surgery) and immobilisation are minimised. As a result, they spend less time in hospital and develop fewer complications or hospital associated infections. They are therefore able to return to their usual activities, including work, more swiftly.

Significant reductions in median length of stay have been achieved, which could lead to an estimated 140,000 - 200,000 patient bed days saved throughout the UK per year. Importantly, the access patients have to specialist advice and services is improved when they are discharged home. The enhanced efficiency that is present in other sections of the ERP is continued into this period meaning that it is often possible to treat minor complications by a ward visit without the need for an overnight stay. Therefore, although re-admission rates may not necessarily drop, the overall time spent in hospital is reduced and there is no evidence of an increase in the rate of serious complications. A recent meta-analysis of enhanced recovery programmes in colorectal surgery concluded that this approach reduced the length of hospital stay and the number of complications without compromising patient safety.

The partnership between clinicians and patients improves the experience of patients going through these pathways. Increased capacity for patients occurs due to the shorter time spent in hospital, reducing waiting times or reducing the number of staff required, which has secondary financial benefits to the health service and to hospitals at a local level.

Finally, there are improved relationships between primary care and hospital trusts and better multidisciplinary team dynamics within the healthcare team, which also improves patient care and the working conditions of all involved in patient care.

In the UK, the Enhanced Recovery Partnership Programme (ERPP) is the result of partnerships between the Department of Health, NHS Cancer Action Team, NHS Improvement, NHS Institute of Innovation and Improvement and the Royal Colleges. Now in the final stage of the programme, it aims to spread this approach across the whole of the NHS and to widen its applications where appropriate. It is estimated that if the ERPP is implemented across the NHS in colorectal, musculoskeletal, urological and gynaecological surgery, the financial savings could be £35-52 million pounds annually.

Sign up to receive ATOTW weekly - email [worldanaesthesia@mac.com](mailto:worldanaesthesia@mac.com)

## ANSWERS TO QUESTIONS

1. TTTF
2. FTTF
3. TFTT

## WEBLINKS

UK [Department of Health Enhanced Recovery Partnership Programme](#)

## REFERENCES and FURTHER READING

1. Desborough. The Stress Response to Trauma and Surgery. *BJA*; 2000; 85 (1): 109-17
2. Lassen, Soop, Nygren et al. Consensus Review of Optimal Perioperative Care in Colorectal Surgery. ERAS Group Recommendations. *Arch Surg*; 2009; 144 (10): 961-969
3. Roberts J, et al., Thinking differently: Working to spread enhanced recovery across England. *Current Anaesthesia & Critical Care*; 2010; doi:10.1016/j.cacc.2009.12.003 (in press)
4. Department of Health Guidance. Delivering Enhanced Recovery: Helping Patients get better sooner after surgery. Published 31<sup>st</sup> March 2010 on the Department of Health Website.