Anaesthesia, Analgesia and the Surgical Stress Response

Nafeesa Akhtar Nov 2020

What is it about?

- The stress response to surgery consists of two main components: neuroendocrine-metabolic and inflammatory-immune.
- After surgery, there is a state of hypercatabolism, which produces readily useable metabolic energy sources.
- Cytokine production is related to the degree of surgical tissue injury.
- Inhibition of the stress response is greatest with central neural blockade and minimally invasive surgery.
- General anaesthesia has little effect on cytokine responses as it cannot influence direct tissue trauma.

Which specialties

- Major vascular
- Major abdominal
- Joint replacement
- Cardiac Surgery using CPB

- Also consider minor surgery
- Laparoscopic, robotic

What is the stress response?

What is the stress response

- Metabolic, hormonal, haematological and immunological changes in the body in response to trauma or surgery
  - HPA and cytokine cascade
- Activation of the sympathetic nervous system
- Also psychological and behavioural changes

Neuroendocrine-metabolic response

- Sympathetic nervous system
- Paraventricular nucleus
  - Detect physiological changes, such as hypotension and inflammation
- PVN fibres project directly to the posterior pituitary and also control various anterior pituitary functions.
- Adrenaline
  - Sympathetic and hormonal responses
- Vascular smooth muscle tone
- Lipolysis, gluconeogenesis
- Cellular metabolic activity and the coagulability of blood increase.

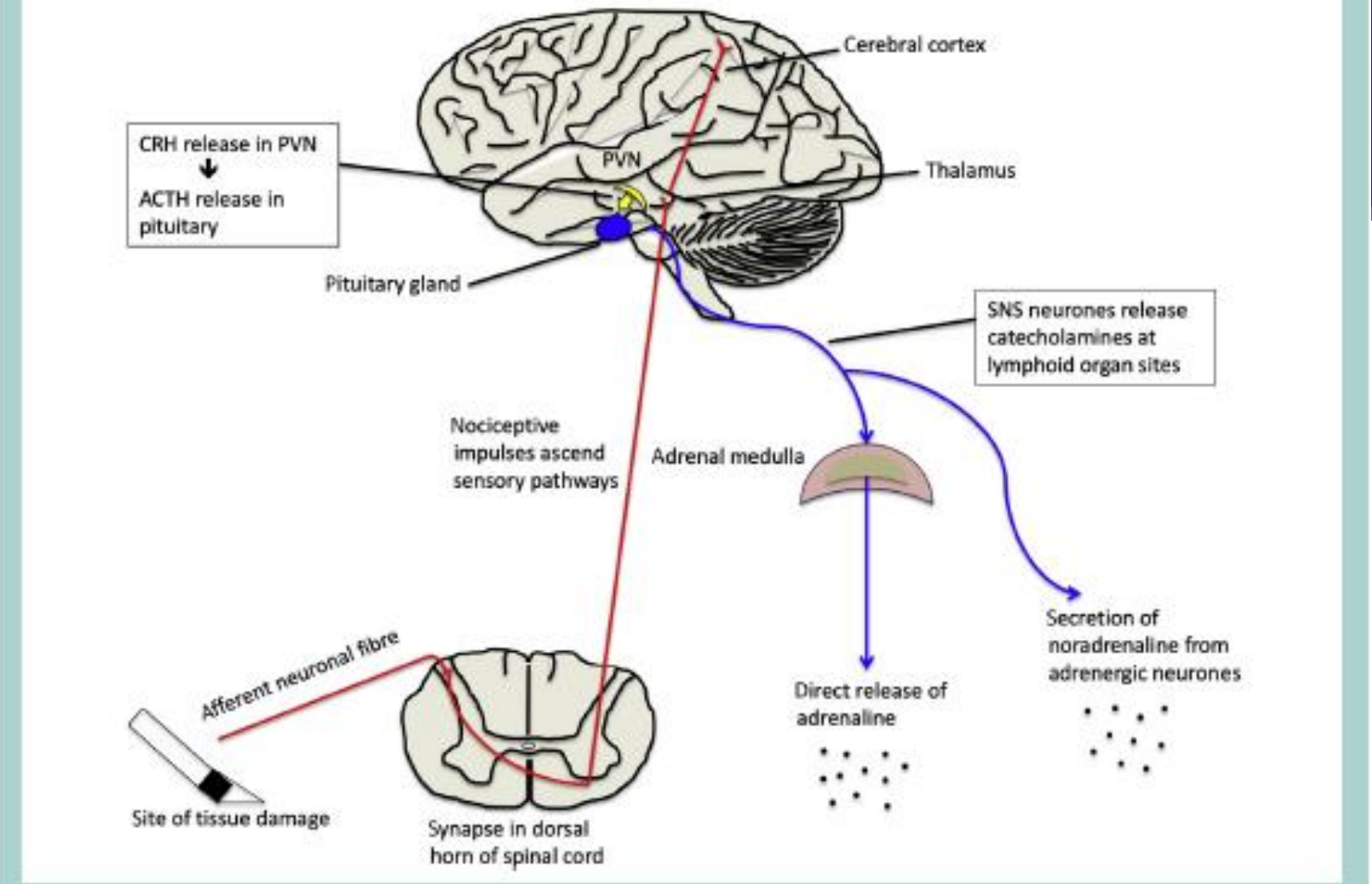


Fig 1 Hypothalamic activation of the neuroendocrine response.

Endocrine system response

- The hypothalamus both directly and indirectly coordinates the complex hormonal stress response

- HPA!!!!!!!
- WOOOOOOOOOOO

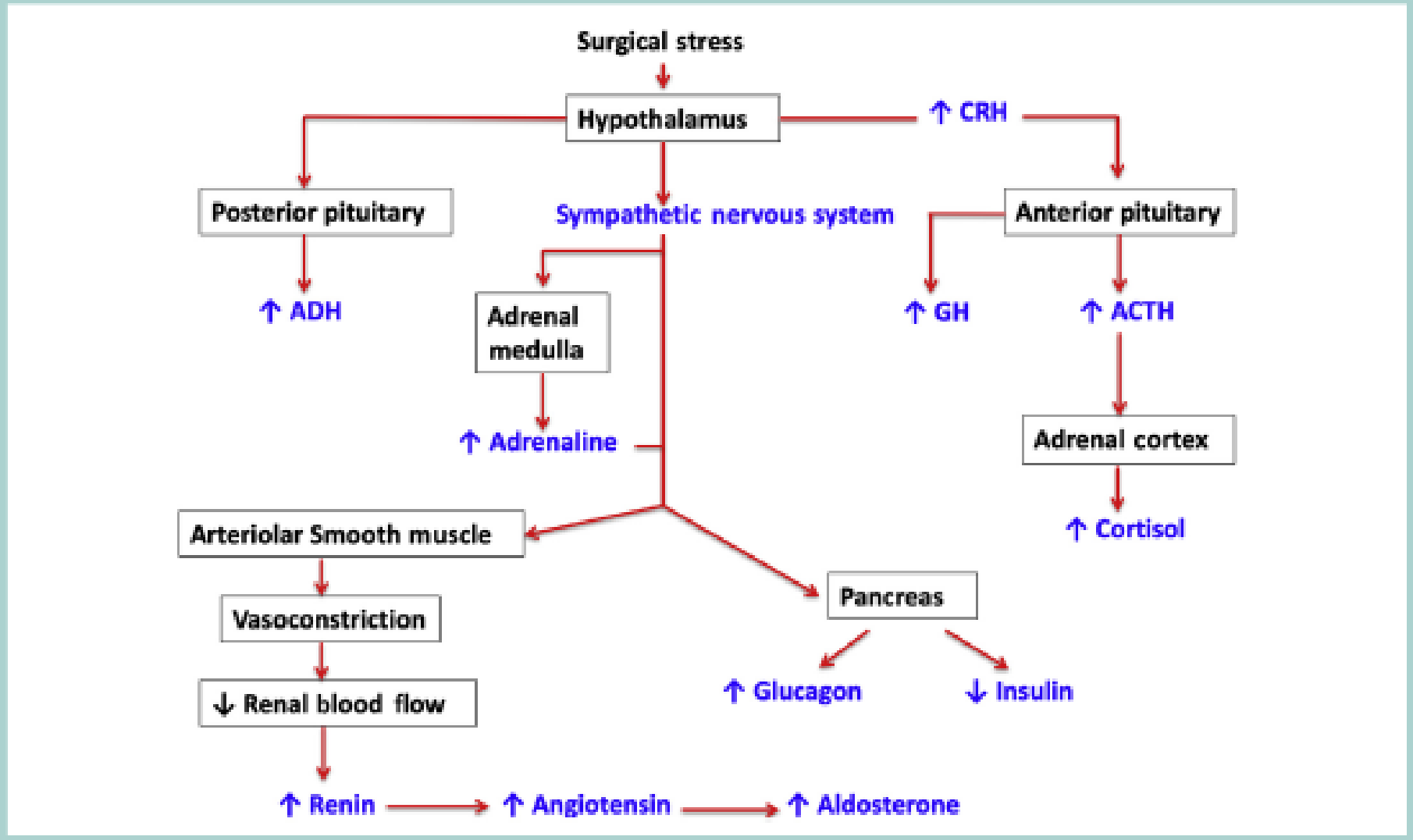


Fig 2 Integration of the stress response by the hypothalamus, sympathoadrenal, and sympathorenal responses.

Endocrine system response

- The HPA axis is a stress-responsive neuroendocrine system that adapts and responds to homeostatic challenges, such as surgery…
- Immediately after surgery, ultradian pulses in ACTH and cortisol both increase
- ACTH concentrations return to baseline within 24 h, but plasma concentrations of cortisol remain increased for ~7 days after major surgery
- Chronic activation of the HPA axis
  - Age, frailty, 'CV deconditioning', depression
- GH, ADH, (T3/T4, prolactin/testosterone)

Metabolic response

Table 1 Summary of catabolic fuel metabolism

Metabolic process	Catabolic reaction	Caused by	Effect
Hepatic gluconeogenesis	Amino acids → glucose	Increased adrenaline, glucagon, and cortisol concentrations stimulate this mobilisation of fuel stores	Increased blood glucose Protein catabolism
Hepatic glycogenolysis	Glycogen → glucose		Increased blood glucose
Lipolysis	Triglycerides → fatty acids and glycerol		Increased plasma fatty acids
Proteolysis	Protein → amino acids		Increased plasma amino acids

Overall

- Mobilisation of substrates and catabolism
  - Glycogenolysis
  - Skeletal muscle breakdown
  - Formation of acute phase proteins
  - Lipolysis
- Reduced ability to respond to and control hyperglycaemia
- Utilisation of alternative compounds, e.g. ketone bodies, as energy substrates
- Water and sodium retention
- Increased sympathetic tone

Immune-inflammatory response

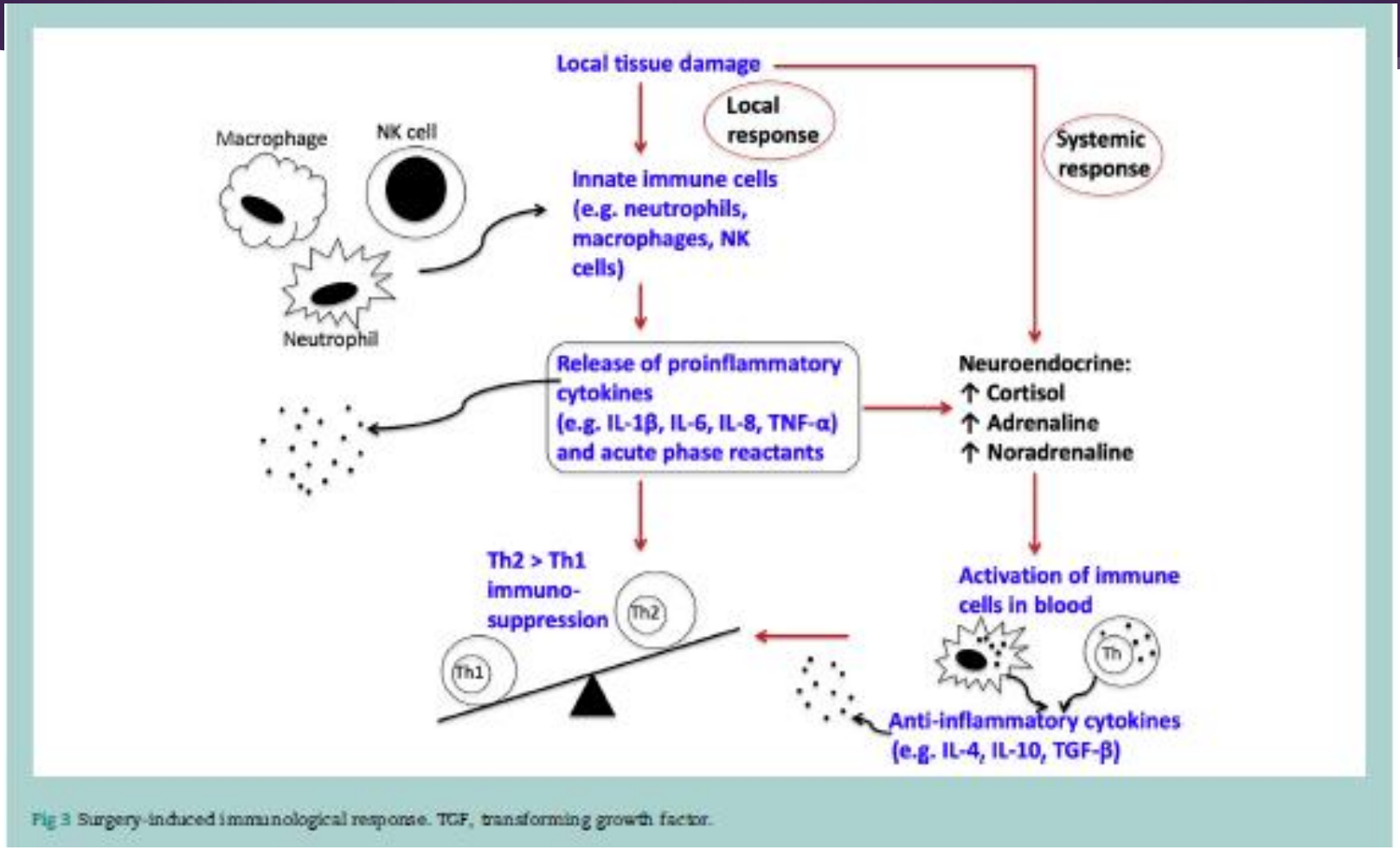


Fig 3 Surgery-induced immunological response. TGF, transforming growth factor.

Immune-inflammatory response

- Innate and cell-mediated adaptive (acquired) immune systems

- Innate
  - Non-specific, early
  - Monocytes → macrophages
  - Macrophages, NØ, NK cells → proinflammatory → cytokines → SIRS
- Acquired
  - T-lymphocytes and antigen presenting cells
  - The shift in Th1:Th2 balance causes impaired cell-mediated immunity

Stress Response

- In health focus on combating pathogens and tissue repair, whilst maintaining vital organ function
- In surgery the opposite
- Hypercoagulability and fibrinolysis occur due to the effects of cytokines and acute phase proteins on the coagulation pathway
- Immunosuppression occurs as a direct effect of cortisol secretion.

Modulation of the perioperative stress response

- Propofol
  - Single dose
  - TCI
  - Lowest proteolytic response
- Etomidate
  - inhibits synthesis of cortisol and aldosterone for up to 8 h after a single induction dose
- Thiopental and ketamine have both been shown to suppress NK immune cell activity in in vitro
- Volatiles
  - impair platelet aggregation and clot stability
  - immunosuppressive and immuno-activating effects

Modulation of the perioperative stress response

- Benzo-diazepines
  - ↓cortisol
- Alpha-2 adrenergic receptors
  - ↓sympathetic outflow
  - stimulation augments endogenous opioid release, and modulates the descending pathways
  - ↓ Cortisol, renin, cytokine
- Opioids
  - Consider BBB
  - ↓ACTH, GH
  - Immunosuppressive , cancer recurrence?

Modulation of the perioperative stress response

- Regional techniques
  - ↓HPA
  - ↓catecholamines, catabolism, hyperglycaemic response
  - Think other positives
- Surgical techniques
  - Approach and duration
- Glucocorticoid cover
  - ↓ pro-inflam. biomarkers and ↑anti-inflamm cytokines
- Nutrition and fluids management
  - Catabolism, wound healing, immune function

What do we want to achieve?

- Reduce stress response to surgery
- Optimal peri-operative management and… Enhanced Recovery
- Standardised patient centred care
- Demonstrate best clinical practice
- Constant appraisal of outcomes
- To reduce hospital length of stay

Common ERAS themes

Common ERAS themes

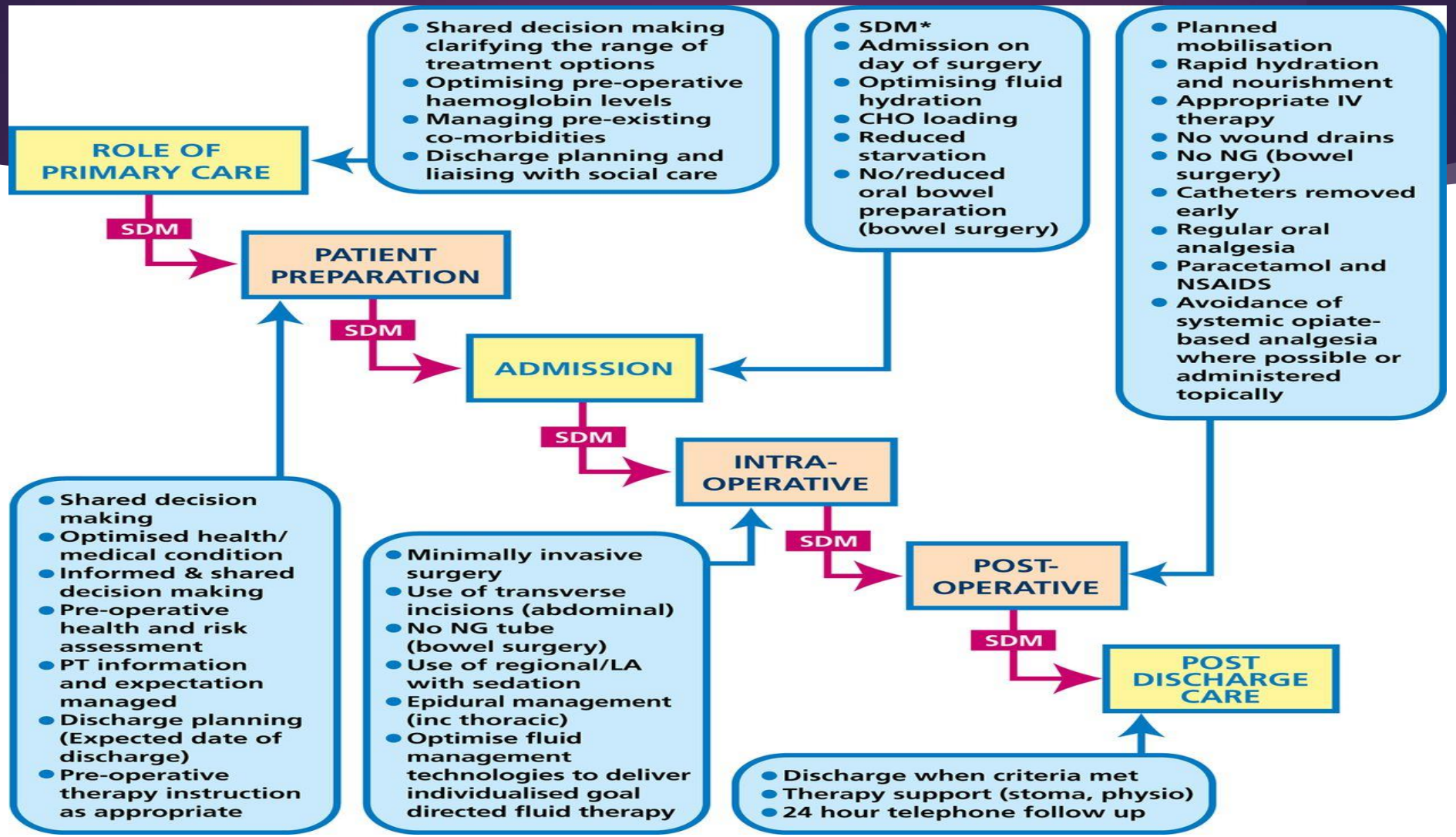
- Reduced length of stay
- Reduce perioperative stress response, catabolism, and post op complications

- Education – patient centred
- Reduce/stop smoking and alcohol intake
- Preoptimise Hb and co-morbidities
- Risk assessment (CPET)
- Prehabilitation

- Post op –
  - Early discharge
  - Telephone consults

Common ERAS themes

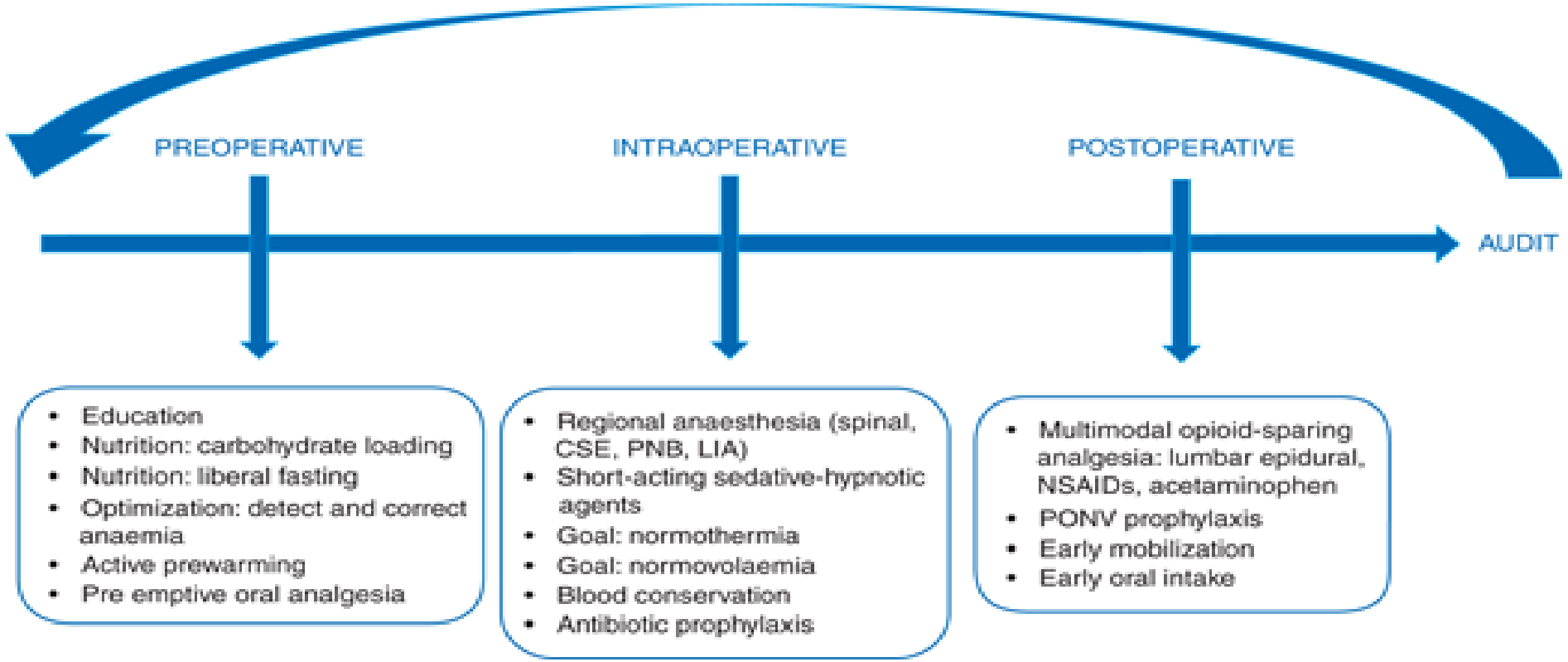
- Fluid therapy; goal directed
- Minimal fasting times, CHO loading, early enteral feeding
- Short acting anaesthetic agents (?TIVA)
- PONV prophylaxis
- Multimodal opioid sparing analgesia, simple regular analgesics
- Regional anaesthesia - Nerve blocks, ?epidurals
- Antibiotic prohylaxis
- Walking up to point of surgery, early mobilisation
- Warming
- Minimally invasive surgery
- Thromboprophylaxis


ROLE OF PRIMARY CARE
Shared decision making clarifying the range of treatment options
Optimising pre-operative haemoglobin levels
Managing pre-existing co-morbidities
Discharge planning and liaising with social care
SDM
PATIENT PREPARATION
Shared decision making
Optimised health/ medical condition
Informed & shared decision making
Pre-operative health and risk assessment
PT information and expectation managed
Discharge planning (Expected date of discharge)
Pre-operative therapy instruction as appropriate
SDM
ADMISSION
SDM*
Admission on day of surgery
Optimising fluid hydration
CHO loading
Reduced starvation
No/reduced oral bowel preparation (bowel surgery)
SDM
INTRA-OPERATIVE
Minimally invasive surgery
Use of transverse incisions (abdominal)
No NG tube (bowel surgery)
Use of regional/LA with sedation
Epidural management (inc thoracic)
Optimise fluid management technologies to deliver individualised goal directed fluid therapy
SDM
POST-OPERATIVE
Planned mobilisation
Rapid hydration and nourishment
Appropriate IV therapy
No wound drains
No NG (bowel surgery)
Catheters removed early
Regular oral analgesia
Paracetamol and NSAIDS
Avoidance of systemic opiate-based analgesia where possible or administered topically
SDM
POST DISCHARGE CARE
Discharge when criteria met
Therapy support (stoma, physio)
24 hour telephone follow up

Abdominal, colorectal

- Education re stoma care
- No bowel prep
- No NGT
- No drains
- Laparoscopic approach – i.e. minimally invasive
- Transverse incisions
- Avoid opioids; rectus sheath, TAP blocks, catheters and pumps
- Epidural or no?
  - Reduction in the duration of ileus, a reduced incidence of pulmonary thromboembolism, reduced blood loss, a reduction in postoperative chest complications, and modification of the stress response
  - Complications, poor mobilization and fluid management (to combat hypotension)

Orthopaedic basics



Orthopaedic trial ERAS

Preoperative	Intraoperative	Postoperative
Carbohydrate drinks	Spinal anaesthetic	Early oral hydration
Continue regular analgesia	Capsular LA infiltration by operating surgeon	Thromboprophylaxis
Analgesic Premed on day of surgery(paracetamol 1g/Oxycontin 10mg/Gabapentin 300mg*)	No urinary catheter	Physiotherapy on day of surgery to mobilise
Preoperative warming	Tranexamic acid 1g	Regular oral analgesia

Gynaecology

- No bowel prep
- Minimally invasive, transverse incision where possible
- Nerve blocks and PCA but also avoid excessive opioids
- Epidurals no longer preferred over above
- Goal directed fluids
- No NGT, no drains
- Early fluid and mobilisation

Urology

- Education re catheter and stoma care
- CHO loading
- High inspired oxygen
- Regional anaesthesia
- Avoid opioids/PCA
- Avoid isoflurane
- Cell salvage
- Avoid drains, and remove early
- Urine output target (if monitored) of 0.3ml/kg/hr, averaged over 4 hours

Summary

- Stress response is complex and multifactorial
  - Therefore easy to question
- Combination of neuroendocrine-metabolic and inflammatory-immune processes
- Hypothalamus controls all… ish
- Increase in sympathetic tone
- Catabolic cascade
- Overexpression of inflammatory and suppression of immune mediators

Articles to read

- Anaes, analgesia and the surgical stress response, BJA Ed, Sept 2020
- Enhanced Recovery After Surgery (ERAS), Anaesthesia Tutorial of the Week, Nov 2010
- Enhanced recovery for gastrointestinal surgery, CEACCP, Dec 2015
- Enhanced recovery from surgery in the UK: an audit of the enhanced recovery partnership programme 2009–2012, BJA Oct 2015
- DOH, Enhanced Recovery Partnership Programme March 2011
- Endocrine and metabolic response to surgery, CEACCP Oct 2004
- Enhanced recovery after surgery for primary hip and knee arthroplasty: a review of the evidence, BJA Dec 2016