Vomiting

No Digestion

Diarrhoea

NAUSEA

No Absorption

BLOATING

No Motility

Feeding Intolerance

Gut Dysfunction

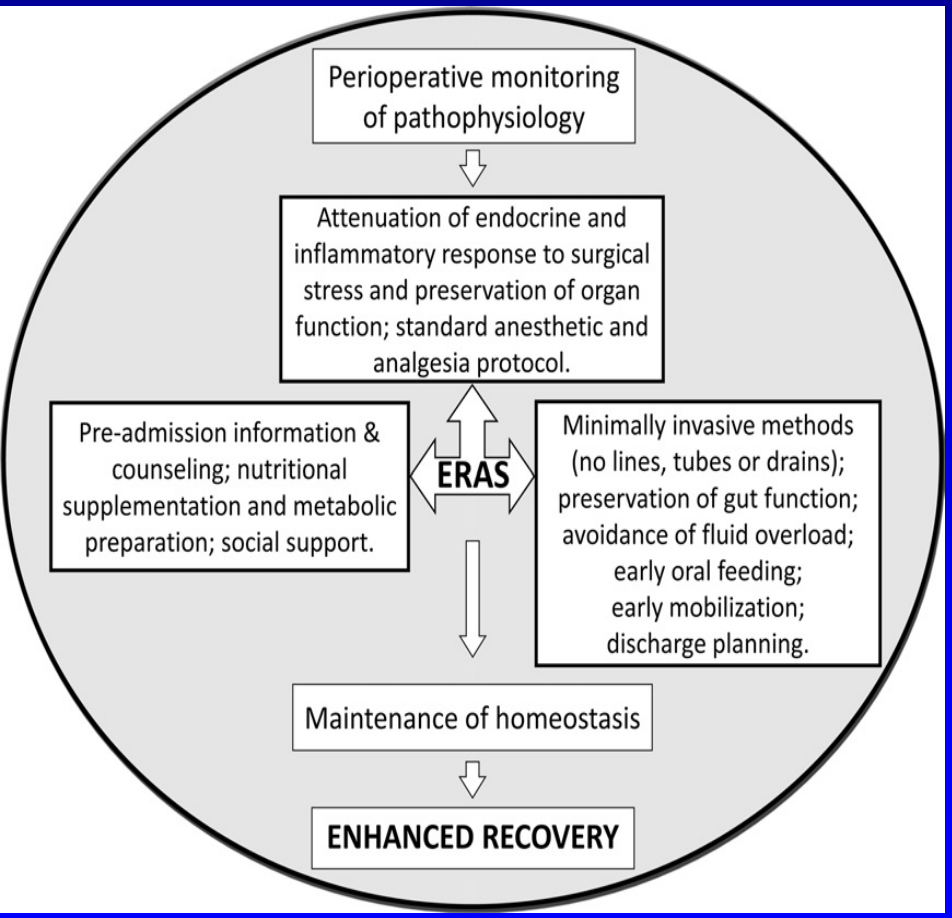
THE GUT IS ON STRIKE - INTESTINAL FAILURE

JP Pretorius
Departments of Surgery and Critical Care
University of Pretoria &
Steve Biko Academic Hospital

Elective vs Emergency Surgery or Critical Illness

Elective Surgery

Operated = Not sick



Emergency Surgery / CC

Serious systemic Illness

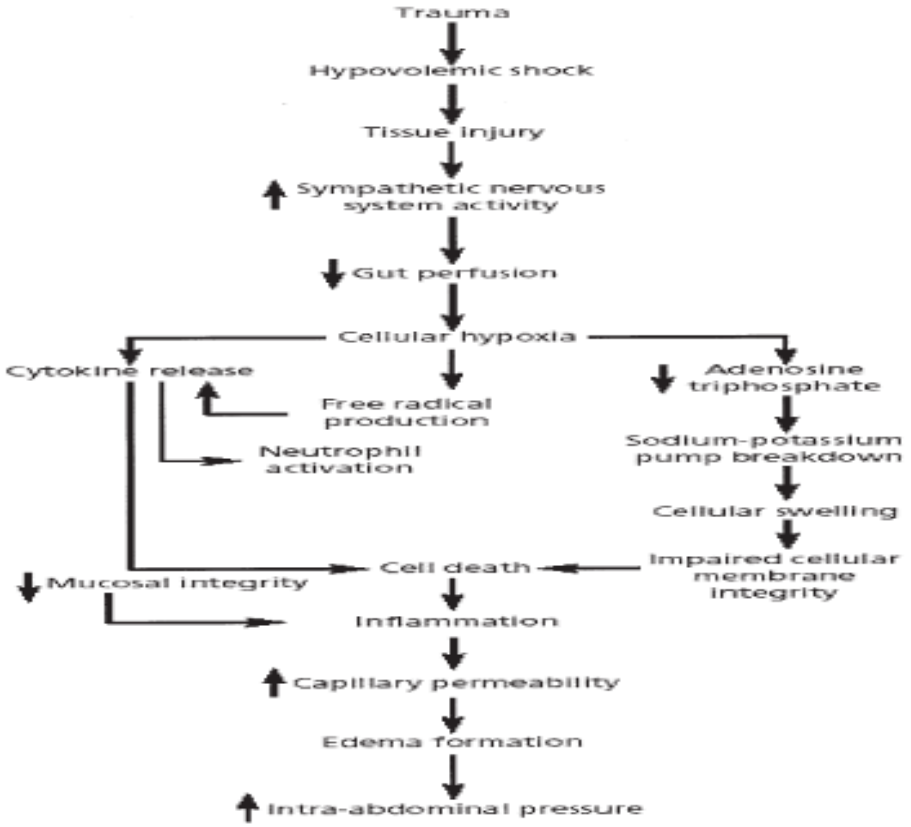


Fig 1. Pathophysiology of abdominal compartment syndrome.

Intensive Care Med (2012) 38:384–394
DOI 10.1007/s00134-011-2459-y

CONFERENCE REPORTS AND EXPERT PANEL

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Gastrointestinal function in intensive care patients: terminology, definitions and management. Recommendations of the ESICM Working Group on Abdominal Problems

Gastro-intestinal Failure ---

Differentiate post-op ileus from ileus during MODS and MOF

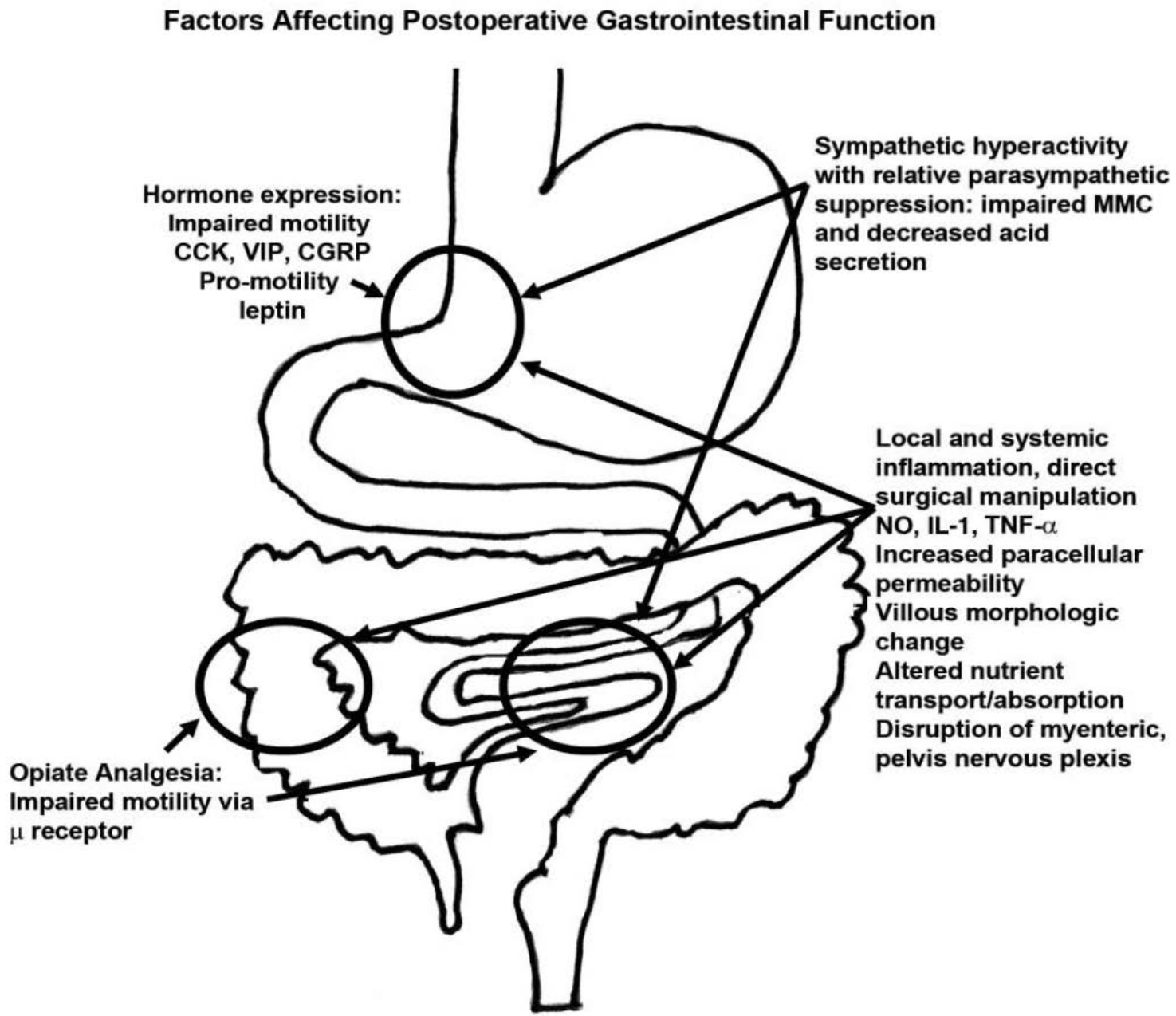
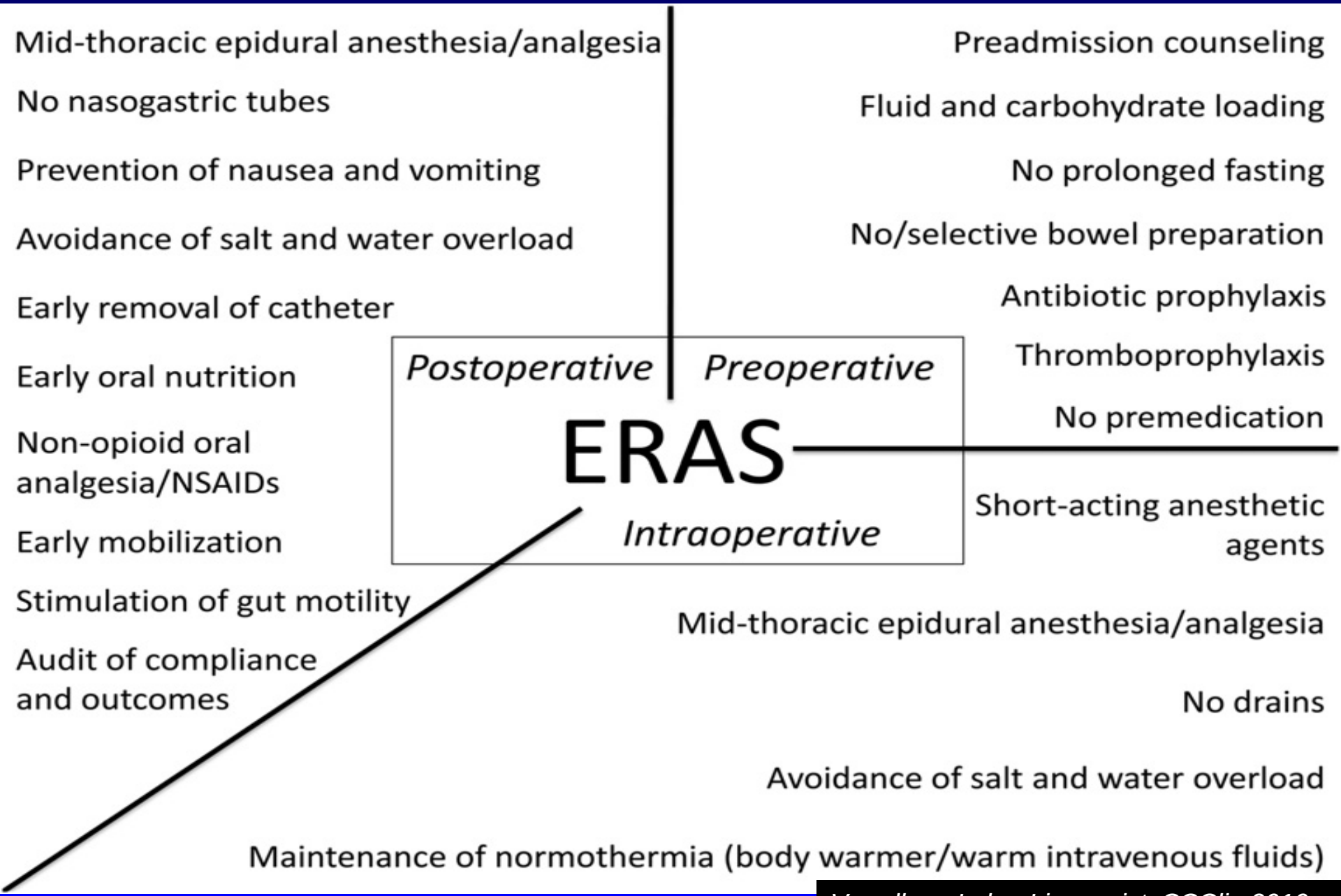


Figure 2. Factors that affect postoperative gastrointestinal function. CCK, cholecystokinin; VIP, vasoactive intestinal polypeptide; CGRP, calcitonin gene-related peptide; MMC, migratory motor complex; NO, nitric oxide; IL-1, interleukin 1; TNF-α, tumor necrosis factor α.

Components of ERAS - Prevention is better than cure



Varadhan, Lobo, Ljungqvist, CCClin 2010

The Gastro-intestinal Tract

is FAR more

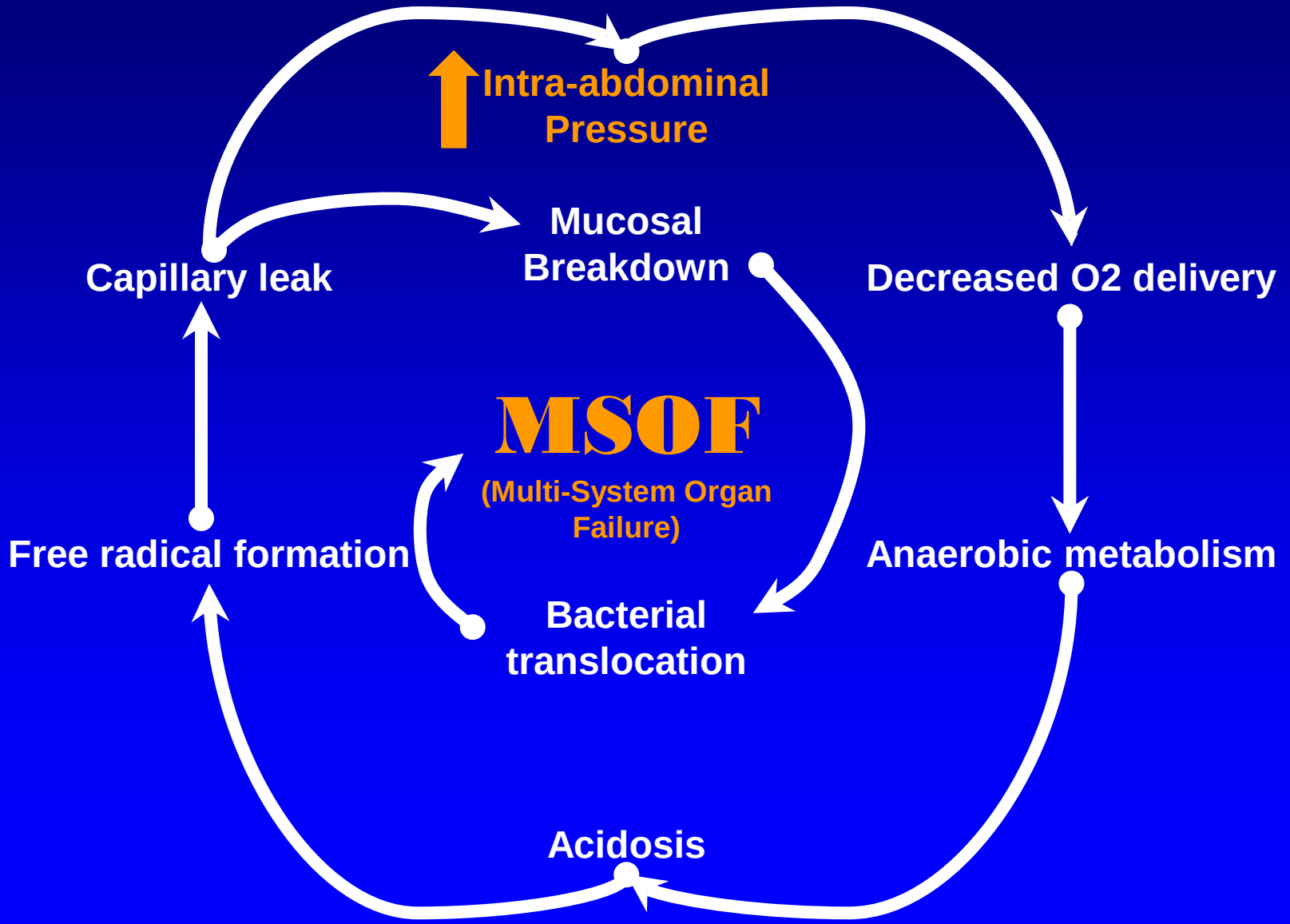
than a place to deliver and digest food!

Considering the systemic or global importance of the gastro-intestinal tract in human pathophysiology during serious illness 1.

- Carrico et al. 1985

  The gut as the “motor” of multiple organ failure

Gut as Motor of MODS - A Vicious Circle?



Considering the systemic or global importance of the gastro-intestinal tract in human pathophysiology during serious illness 2.

- Alverdy et al. 2003

  Interaction between host and bacterial pathogens lead to gut derived sepsis (at least partially independent of the pro-inflammatory response of the bacteraemia)

- Sousa et al. 2004

  Germ free mice that entirely lack commensal bacteria have an improved survival rate following intestinal ischemia/reperfusion compared with conventional animals

- Deicht et al. 2006

  Ligation of lymph duct after haemorrhagic shock prevents distant organ injury in a variety of animal species

Considering the systemic or global importance of the gastro-intestinal tract in human pathophysiology during serious illness 3.

- Reintam et al 2006:

  GIF seems to be a relevant independent clinical predictor of mortality in ICU. It significantly prolongs mechanical ventilation and ICU stay.

- Reintam Blaser, Malbrain et al 2012:

  Created a Classification for AGI (acute gastro-intestinal injury)

  - Grade 1 = Increased risk of developing GI dysfunction (self-limiting condition) [following abdominal surgery]
  - Grade 2 = GI dysfunction (condition requires intervention) [Gastroparesis, ileus, IAH]
  - Grade 3 = GI failure (Function cannot be restored with interventions) [Progression of abovementioned with persistence or worsening of MODS]
  - Grade 4 = Dramatic manifestation of GI failure (condition that is immediately life threatening) [bowel ischaemia/necrosis, GI bleed →shock, ACS, Ogilvie syndrome]

- Reintam et al 2013:

  Using the above it was not possible to develop a valid GI dysfunction score that improved the accuracy of the SOFA score.

Considering the systemic or global importance of the gastro-intestinal tract in human pathophysiology during serious illness 4.

- Full circle: Klingensmith, Coopersmith 2016:

  Again "The gut as the motor of multiple organ dysfunction in critical illness"! Crit Care Clin 32 (2016) 203-212.

  The gut is composed of - an epithelium
  - adaptive immune system
  - the microbiome

- ***All elements of the gut – the epithelium, the immune component and the microbiome – are impacted by critical illness and can in return, propagate a pathologic host response.***
- ***This may be both local and distant. Mechanisms include – alterations in homeostatic processes and defense mechanisms as well as release of toxic mediators into both the mesenteric lymph and the systemic circulation.***

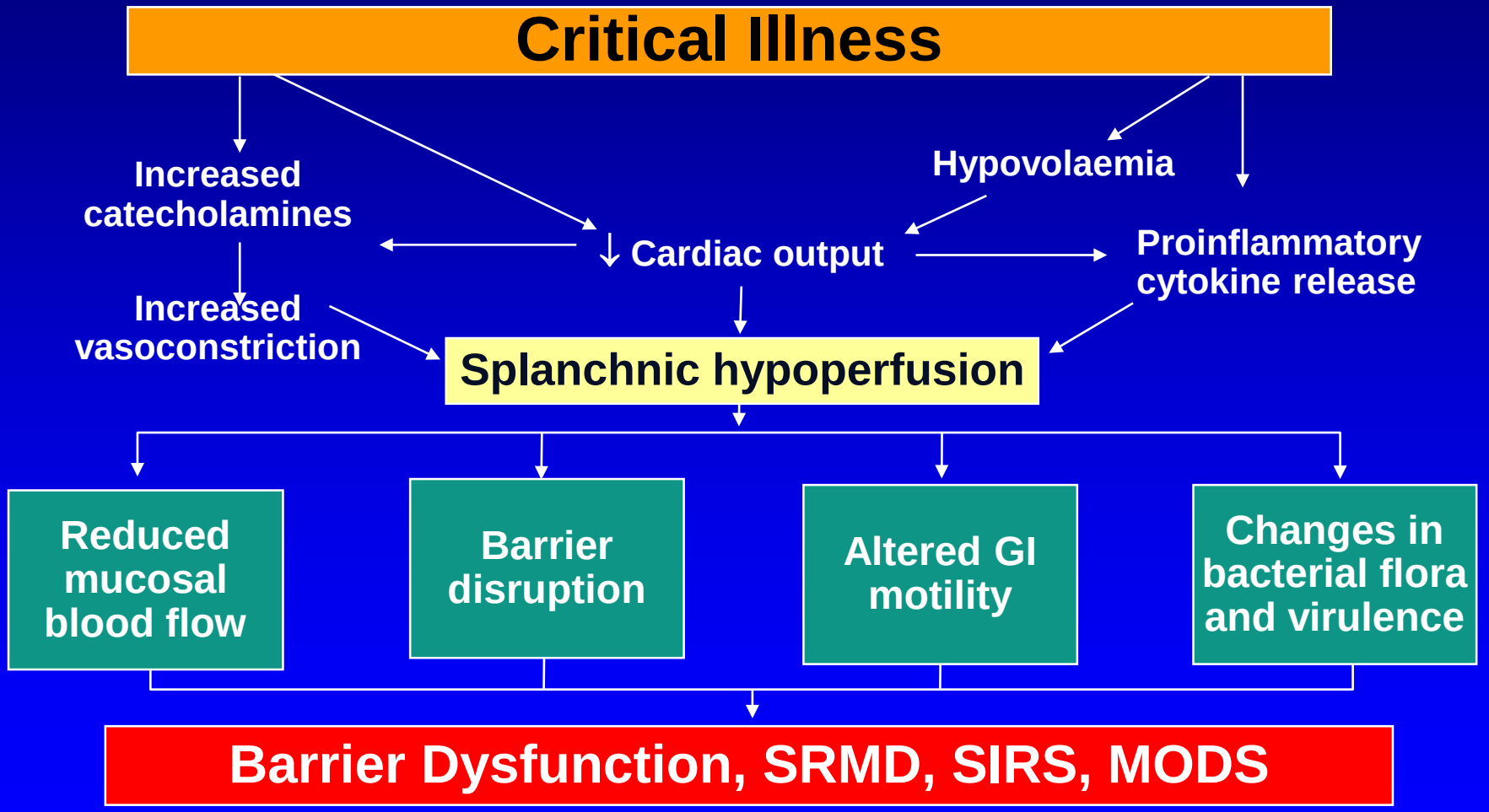
Normal gut physiology

A 3-way partnership exists between it's epithelium, immune tissue and commensal bacteria.

Each element modifies the other via "crosstalk" → this integrated result is the major determinant for survival in MODS.

Dysfunction of any element of the gastro-intestinal tract can contribute to critical illness

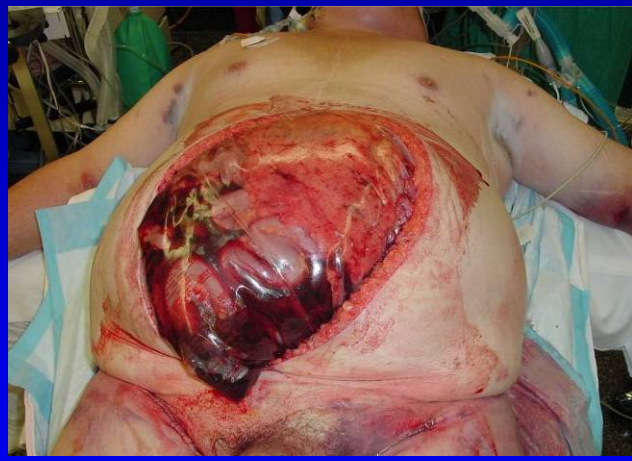
Pathophysiologic events in the GUT during Critical Illness

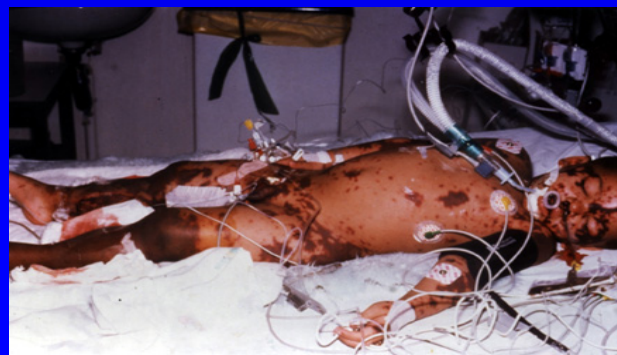


Schmidt H, Martindale R. *Curr Opin Nutr Metab Care*. 2003;6:587-591. Mutlu GM, et al. *Chest.* 2001;119:1222-1241.

GI Dysfunction in the ICU: When does it become a *"problem"* ?

- As surgeons we are very much aware of ileus. Ileus post operatively…
  during Intra-abdominal sepsis..
  post trauma…
- Mostly we regard ileus as a mere annoyance and not really a problem
- What should we be concerned about ?
  - Nausea, vomiting, bloating
- When should we "worry" ?
  - *Decreased abdominal compliance*
  - *Increased intra-abdominal volume*
  - *Setting of capillary leak*
- Why should we 'worry" ?



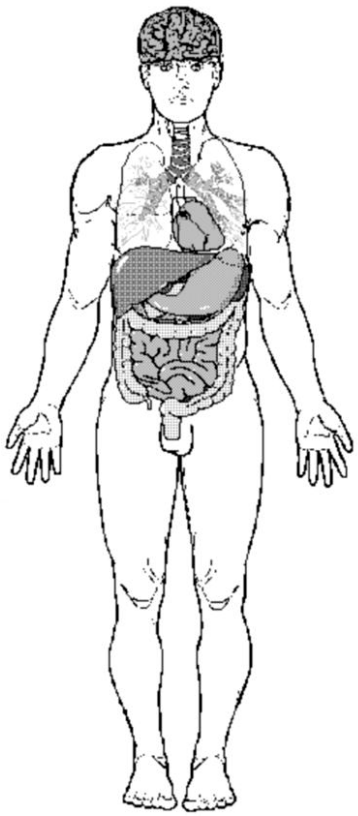


CENTRAL NERVOUS SYSTEM
Intracranial pressure ↑
Cerebral perfusion pressure↓
Idiopathic intracranial hypertension in morbid obesity

CARDIOVASCULAR SYSTEM[1]
Difficult preload assessment
Pulmonary artery occlusion pressure ↑
Central venous pressure ↑
Transmural filling pressure =↘
Intra thoracic blood volume index =↘
Global enddiastolic blood volume index =↘
Extra vascular lung water =↗
Stroke volume variation ↗
Pulse pressure variation ↗
Right ventricular end-diastolic volume =↘
Cardiac output ↓
Venous return ↓
Systemic vascular resistance ↑
Venous thrombosis ↑
Pulmonary embolism ↑
Heart rate ↗ =
Mean arterial pressure ↗ =↘
Pulmonary artery pressure ↑
Left ventricular compliance ↓
Left ventricle regional wall motion ↓

HEPATIC SYSTEM
Hepatic arterial flow ↓
Portal venous blood flow ↓
Portocollateral flow ↑
Lactate clearance ↓
Glucose metabolism ↓
Mitochondrial function ↓
Cytochrome p450 function ↓
Plasma disappearance rate
Indocyanine green ↓

GASTRO-INTESTINAL SYSTEM
Abdominal perfusion pressure ↓
Celiac blood flow ↓
Superior mesenteric artery blood flow ↓
Blood flow to intra-abdominal organs ↓
Mucosal blood flow ↓
Mesenteric vein compression ↑
Intramucosal pH ↓
Regional CO2 ↑
CO2-gap ↑
Success enteral feeding ↓
Intestinal permeability ↑
Bacterial translocation ↑
Multiple organ failure ↑
Gastro-intestinal ulcer (re)bleeding ↑
Variceal wall stress ↑
Variceal (re)bleeding ↑
Peritoneal adhesions ↑



RESPIRATORY SYSTEM
Intrathoracic pressure ↑
Pleural pressure ↑
Functional residual capacity ↓
All lung volumes ↓
(~restrictive disease)
Auto-PEEP ↑
Peak airway pressure ↑
Plateau airway pressure ↑
Dynamic compliance ↓
Static respiratory system compliance ↓
Static chest wall compliance ↓
Static lung compliance =
Hypercarbia ↑
PaO2 ↓ and PaO2/FiO2 ↓
Dead-space ventilation ↑
Intrapulmonary shunt ↑
Lower inflection point ↓
Upper inflection point ↑
Extra vascular lung water =↗
Prolonged ventilation
Difficult weaning
Activated lung neutrophils ↑
Pulmonary inflammatory infiltration ↑
Alveolar edema ↑
Compression atelectasis ↑

RENAL SYSTEM
Renal perfusion pressure ↓
Filtration gradient ↓
Renal blood flow ↓
Diuresis ↓
Tubular dysfunction ↑
Glomerular filtration rate ↓
Renal vascular resistance ↑
Renal vein compression ↑
Compression ureters ↑
Anti-diuretic hormone ↑
Adrenal blood flow =
Abdominal wall complications in CAPD↑

ABDOMINAL WALL
Compliance ↓
Rectus sheath blood flow ↓
Wound complications ↑
Incisional hernia ↑

ENDOCRINE SYSTEM
Release pro-inflammatory cytokines ↑
(IL-1b, TNF-a, IL-6)

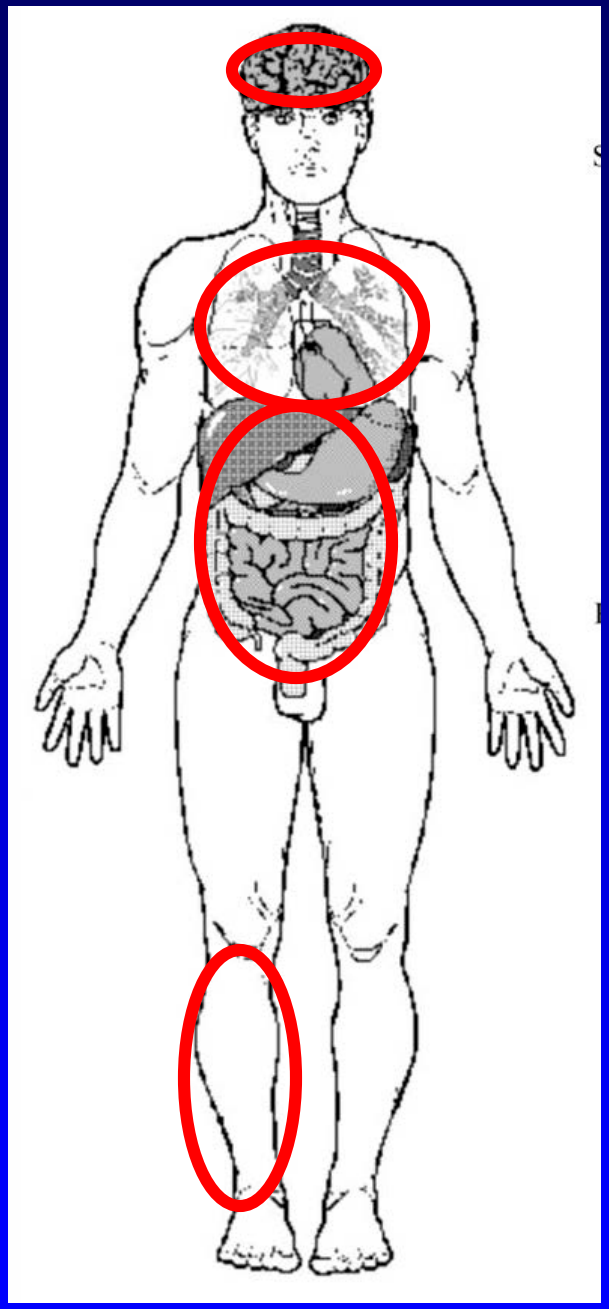
[1] Cardiovascular effects are exacerbated in case of hypovolemia, hemorrhage, ischemia and high PEEP ventilation

Wide spread pathophysiological implications of intra-abdominal hypertension on end-organ function.

?

SYMPTOMATIC OF TOTAL BODY INJURY OR DISEASE STATUS OF THE MOMENT

Malbrain: Curr Opin Crit Care, Volume 10(2).April 2004.132-145



Intracranial CS

Thoracic CS

Abdominal CS

Extremity CS

Major Compartments

Generalised Inflammatory Response

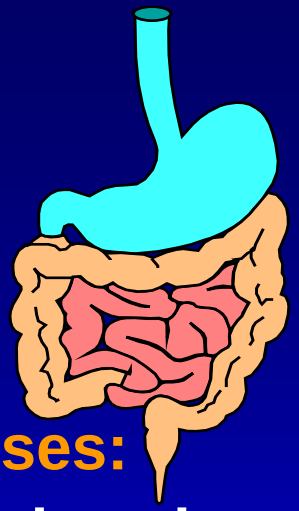
Mitchelin man?

Oedema is Dangerous!!!!!

Actually…The Polycompartment Syndrome Concept

- There are different compartments in the body: **cranium, thoracic, abdomen and extremities etc……**
- They are not independent entities but instead are intricately connected.
- ***Surgeons must recognise the existence of multi- or polycompartment syndromes***

Physiologic Sequelae of Abdominal Compartment Syndrome



Gastrointestinal:

- **Increased intra-abdominal pressures causes:**
  - **Compression / Congestion of mesenteric veins and capillaries**
  - **Reduced cardiac output to the gut**
- **The result:**
  - **Decreased gut perfusion, increased gut edema and leak**
  - **Ischaemia, necrosis, cytokine release, neutrophil priming**
  - **Bacterial translocation**
  - **Development and perpetuation of SIRS**
  - **Further increases in intra-abdominal pressure**

When the gut is on strike…..

- Continuum: Available….

  Partially available….

  Totally unavailable for nutrition

- What do we call this strike?
  - Ileus?
  - Intolerance?
  - …. Rather….Gastro-intestinal failure!

GI dysfunction is a common problem in critcally ill patients, yet it is not given the same consideration as other organ systems regarding scoring and predicting outcome in ICU.

The GUT responds to hypoperfusion / reperfusion injury in such a way that it can independently trigger and sustain SIRS or systemic sepsis.

The gut is often on strike during …..

- "Scenario's" of gut intolerance / failure / ileus
  - Post operative ileus (lesser or greater extent in almost all)
  - Short bowel syndrome / Loss of critical bowel mass
  - Proximal high output fistulae
  - Severe diarrhoea or emesis
  - Abdominal distention or intra-abdominal oedema > ACS
  - Partial or complete bowel obstruction
  - Acute colonic pseudo-obstruction
  - Sever gastrointestinal bleeding
  - Mesenteric ischaemia
  - Severe haemodynamic instability

  ….influences LOS … Impact on resource utilization … has patient implications

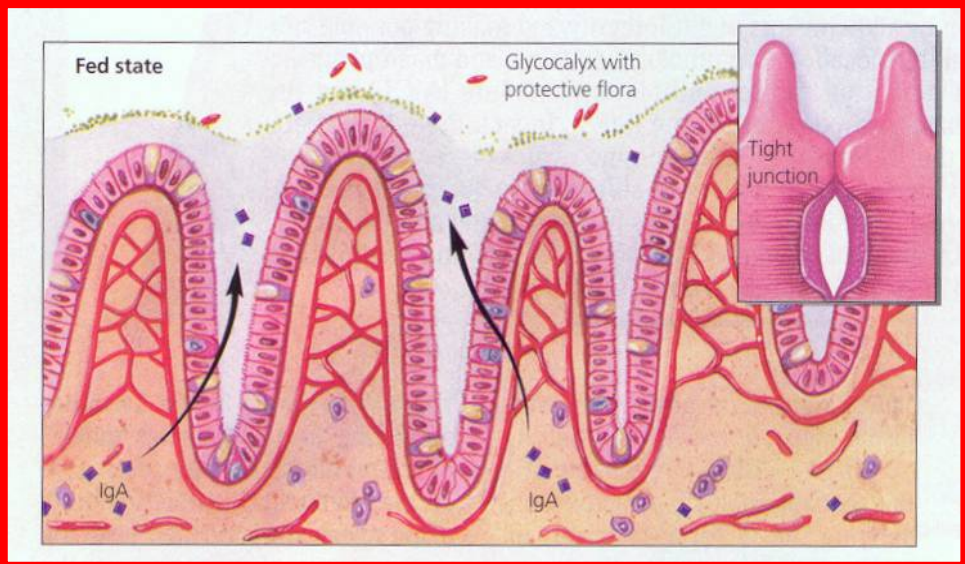
Gut anatomy
The gut is composed of 1.

1. Different types of epithelial cells
   - : Absorptive enterocytes
   - : Goblet cells (mucus production/mucin)
   - : Enteroendocrine cells (sympathetic and parasympathetic innervation)
   - : Paneth cells (defensins/AMP)
   - : Specialized M-cells(follicle associated epithelium)

- Turnover rate of epithelial cells (apoptosis to replacement): 3days - 3weeks
- Apical junctional complexes (controls paracellular movement of water, solutes and immune cells)
- Critical illness (sepsis and non-infectious inflammation) alter proliferation and apoptosis of intestinal epithelium

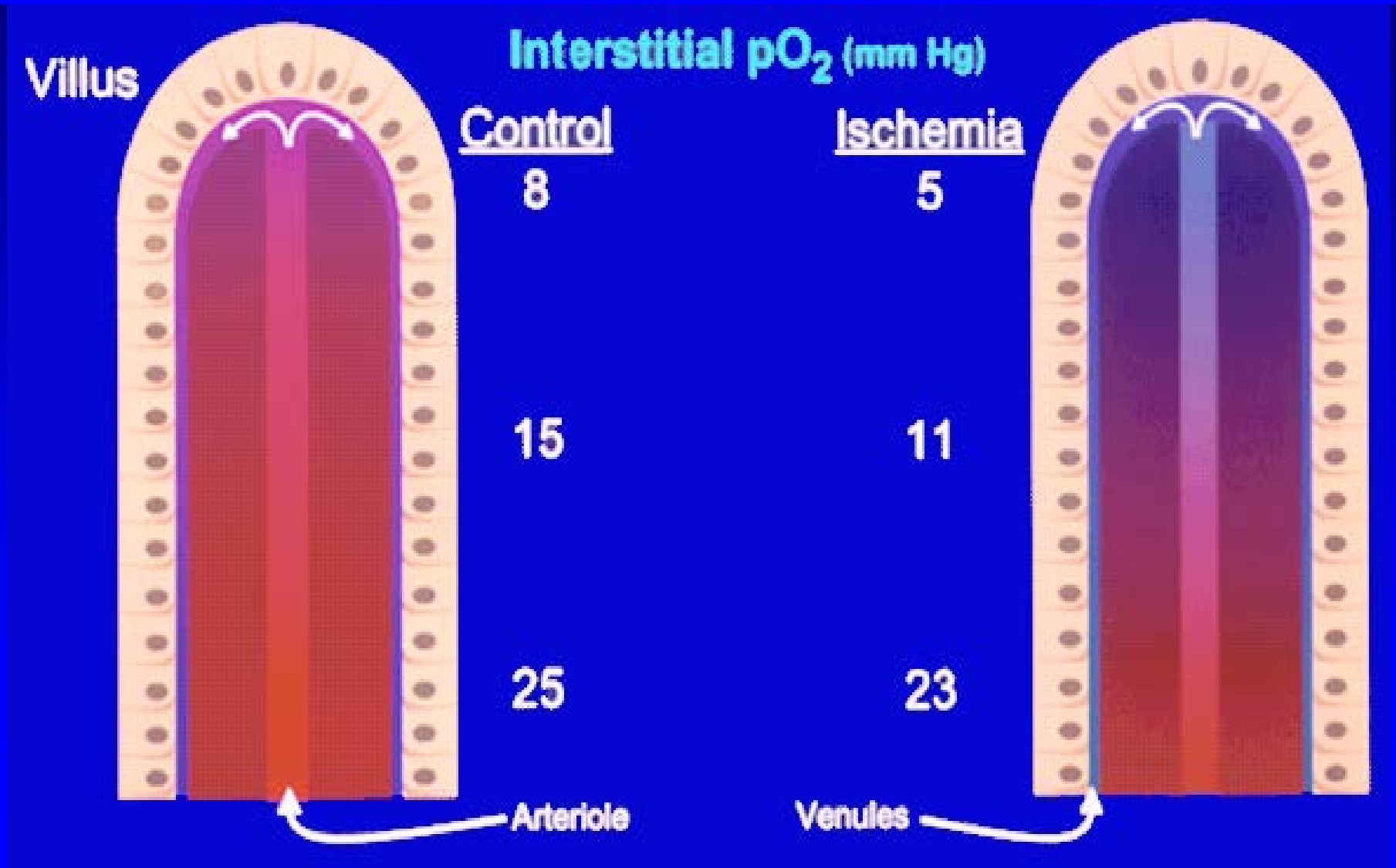
Splanchnic Hemodynamics

- GI tract receives 25% of cardiac output (varies widely)
  - 1.25 L/min at rest, 3.0 L/min with meal, 0.5 L/min with exercise
  - Segmentally dilates to nutrient bolus
- Uses 33% of total 0_2 consumption at rest
- Small intestine receives nearly 50% of arterial blood flow to splanchnic bed (uneven distribution)
- Villous tips are at highest risk



Blood flow (ml/min*100g)	
Splanchnic	*50*
Kidneys	*400*
Brain	*55*
Skeletal Muscle	*3*
Heart	*80*

Cells at the villus tips are exposed to greater hypoxic stress during ischemia.



Essential Information for Successful Nutrition

- Metabolic response to injury
- Autophagy
- The GIT microbiome, GIT physiology and metabolomics
- Nutritional assessment
- Planning (Requirements, Formulas, BMI)
- Available Nutritional Drugs – enteral & parenteral
- Elective surgery vs Emergency surgery or Acute injury (ERAS vs Nutrition in the acute phase of critical illness)
- Route of administration - TPN vs TEN
- Enteral access
- Total Fluid Management & Fluid balance
- Monitoring

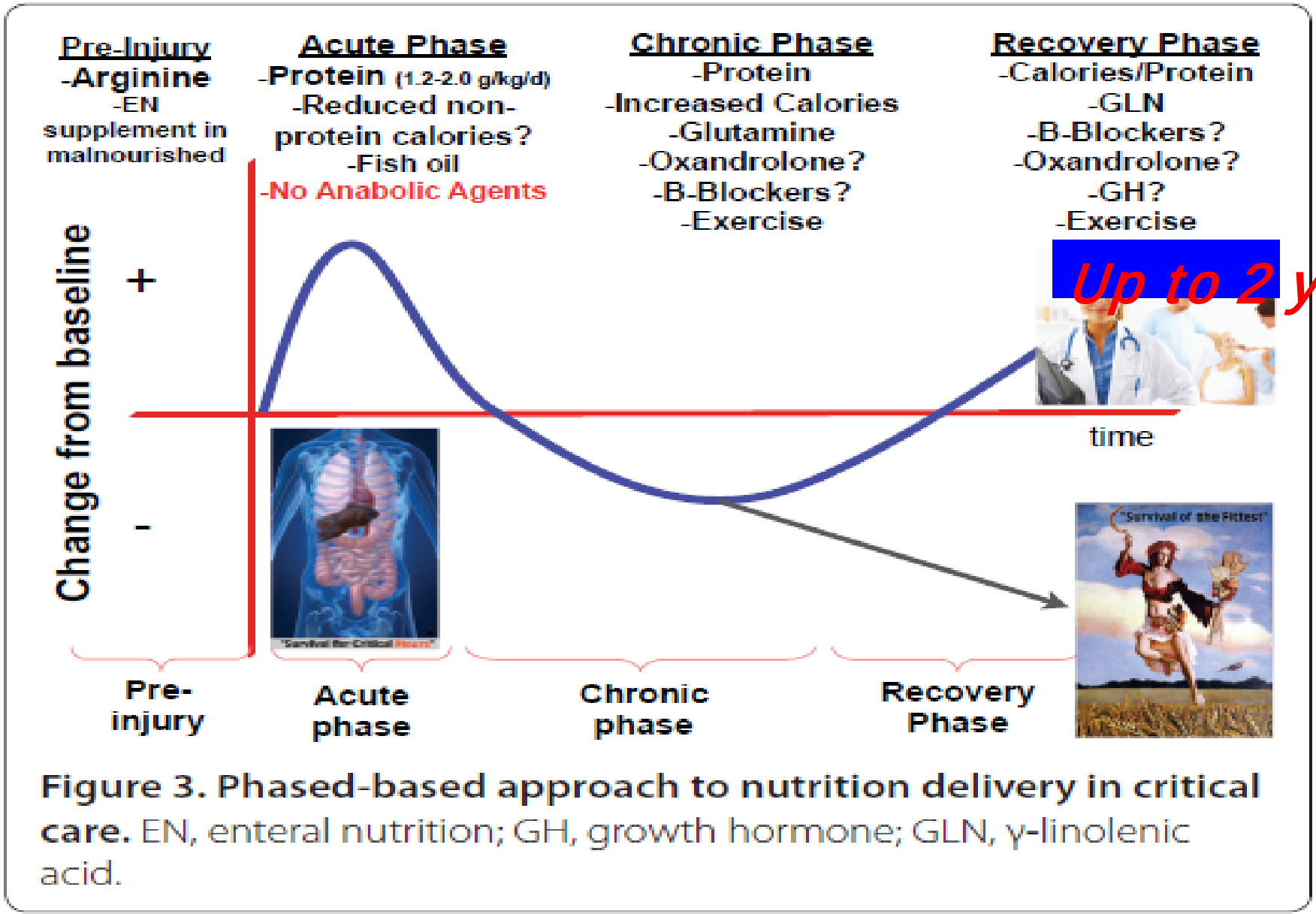


Figure 3. Phased-based approach to nutrition delivery in critical care. EN, enteral nutrition; GH, growth hormone; GLN, γ-linolenic acid.

Adequate Protein Delivery….
THE KEY TO OPTIMAL NUTRITION IN THE ICU ?

WHAT DOES THIS MEAN FOR OUR MODERN ICU PATIENTS?

We may need to provide more aggressive protein resuscitation,
or feeding in the acute and chronic phases of injury

When should we be concerned?

Signs & symptoms: nausea, vomiting, bloating, diarrhoea

- Adynamic ileus:
  1. Myogenic -
  2. Neurogenic -
  3. Humoral mechanisms
- Bloating & distension: common physical findings, but clinical significance still poorly defined. Frequently used to hold or discontinue tube feeds – individualise
- Pathophysiology:
  1. Subjective sensation of bloating
  2. Objective presence of abdominal distension
  3. The volume of intra-abdominal contents

TRIAD: Patient with ileus on abdominal radiograph + abdominal distension o/e + lack of bowel sounds = EN intolerance

BUT: Use at least "Trickle/Trophic Feeds" in cases with small bowel access

Nutrients **2013**, *5*, 162-207; doi:10.3390/nu5010162

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Review

Nutrition of the Critically Ill—A 21st-Century Perspective

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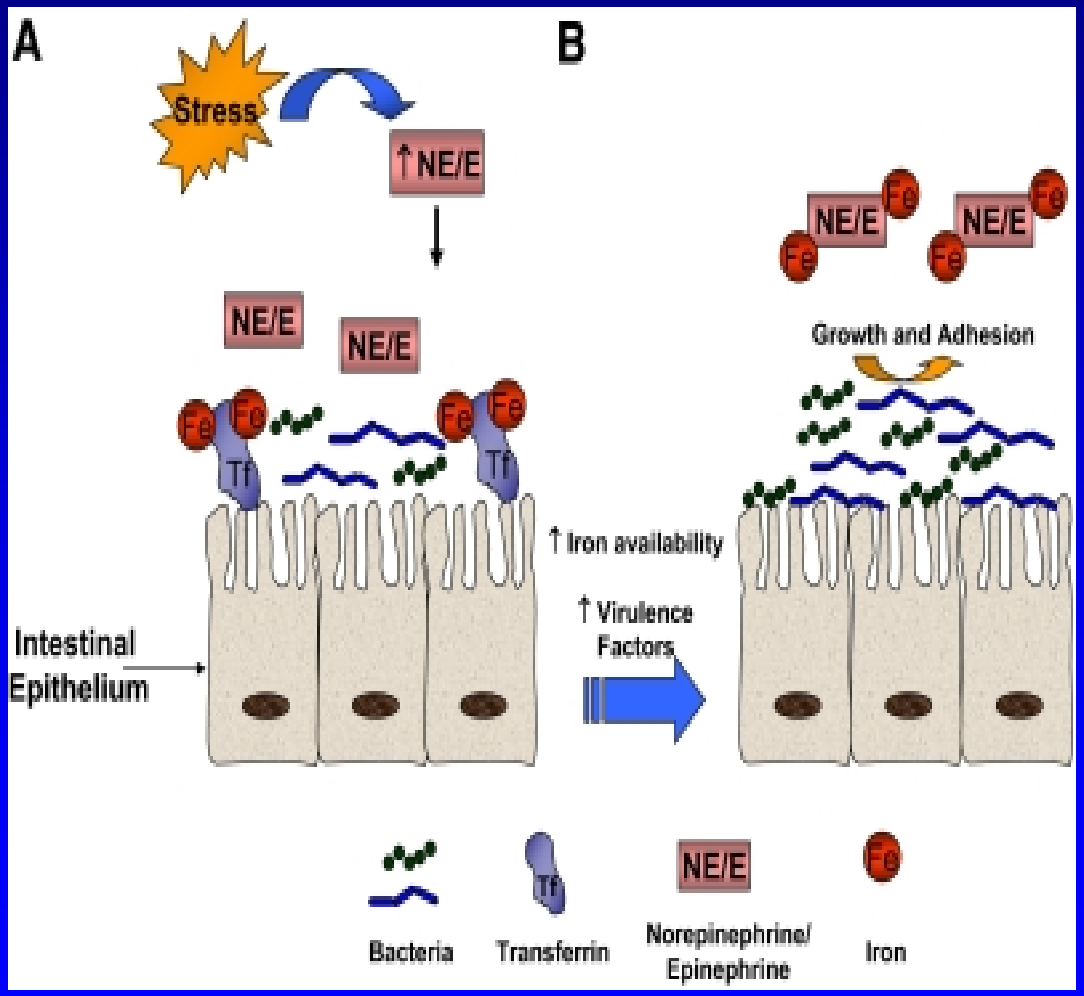
- *The present knowledge, as obtained from extensive research, especially in recent years, suggests that good health and well-being, in addition to regular physical exercise, good sleep and control of stress/spiritual harmony is strongly associated with the food we eat, and its influence on bodily functions, particularly microbiota.*
- *It is unfortunate that the sickest patients are more or less in constant stress, cannot exercise, and receive the worst nutrition. The modification of these conditions should be a highly prioritized challenge.*

Neuro-endocrine Function



Mechanism for gut derived sepsis

- Transferrin affinity normally prevents free iron availability in the gut (iron poor environment).
- Traumatic stress → increases NE/E in the intestinal lumen
- NE/E acts as a “magnet” to mediate sequestration of iron (iron rich environment)
- Bacteria plus free iron → siderophores → ↑ bacterial growth and virulence
- Commensal bacteria becomes pathogenic

Neuro-endocrine function

- Recent advances in neuro-immunology have identified a direct link between the neuroendocrine and immune systems (cross talk)

Radek et al. 2010

Journal of Leucocyte Biology

Small bouts of stress → **enhances** immune system

Prolonged periods of stress → excess production of neuroendocrine-derived mediators **dampens** immune response to invasive pathogens (stress induced **immune modulation**)

→ exacerbate epithelial inflammatory disease

Intestinal Alkaline Phosphatase (IAP)

- Irrigation of abdominal cavity with IAP reduced the SIRS response + remote organ damage, and increased the survival rate in mice with fecal peritonitis.
  Ebrahimi et al. J Gastrointest Surg 2011
- IAP is a gut mucosal defense factor maintained by enteral nutrition
  Goldberg et al. 2008 Nat Acad of Sciences USA
- Brush border enzyme IAP
  - has the ability to detoxify LPS (dephosphorylation of lipid A moiety in LPS → endotoxin)
  - and prevent bacterial invasion across the gut mucosal barrier.
  - IAP expression and function is lost by starvation.
  - Is expressed exclusively by villus-associated enterocytes.
  - Is an excellent marker for crypt-villus differentiation
  - Intra-peritoneal irrigation with IAP could be a novel therapy for intra-abdominal sepsis
  - Irrigation of the peritoneal cavity with IAP for mice with intra-abdominal sepsis, had a similar survival rate as mice with intra-abdominal sepsis treated with systemic antibiotics

Intestinal Permeability Changes

- ***Alterations in intestinal epithelial permeability (Increased in critically ill patients)***
  - *Multiple proteins are necessary for the assembly and function of tight junctions*
  - *Nitric Oxide (NO) and/or Peroxynitrite ($ONOO^-$) are involved in the regulation of tight junction protein expression and function*
  - *NO-dependent changes in Na^+, K^+-ATPase activity can affect tight junction assembly and function*
  - *Functional iNOS expression is essential for LPS-induced alterations in intestinal permeability in mice*
  - *Endotoxemia is associated with derangements in ileal mucosal tight junction protein localization*
  - *Surgical stress leads to systemic absorption of gut-derived toxins*

Fink 2007 Mechanisms of sepsis-induced organ dysfunction and recovery

Gut anatomy
The gut is composed of 2.

2. Adaptive immune system

- *Prevent pathogens from penetrating epithelium*
- *Prevent uptake of foreign antigens*
- *Controls the intensity of the immune response against luminal bacteria and antigens (prevents a pathological response)*

GALT: (gut associated lymphoid tissue)

- largest lymphatic organ in the body

- composed of : Peyer Patches

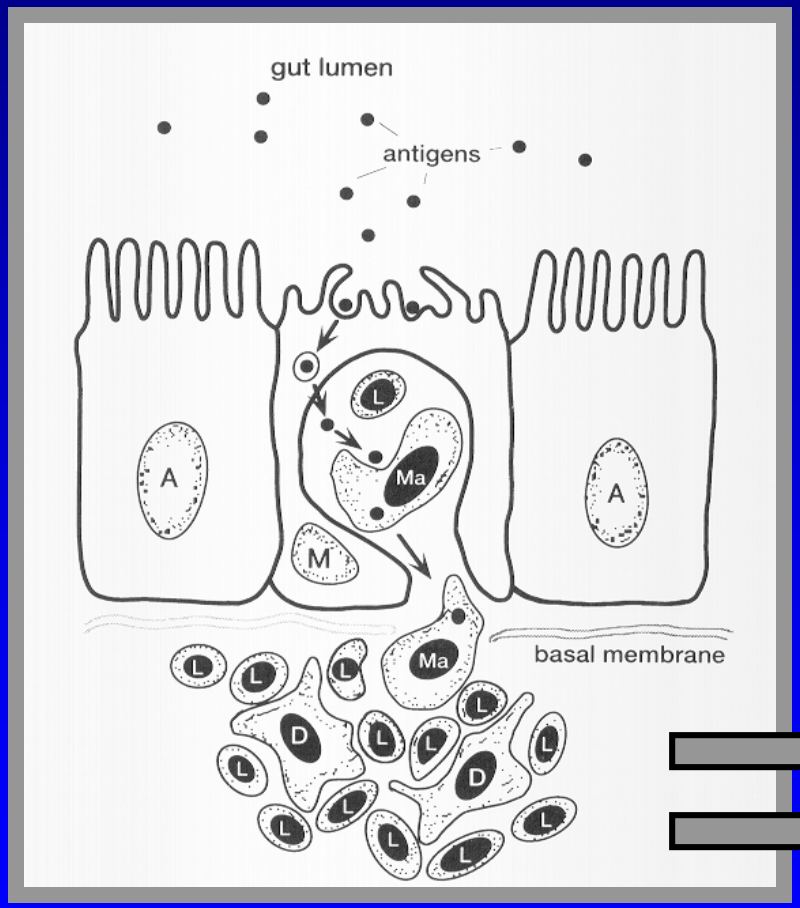
: Mesenteric lymph nodes

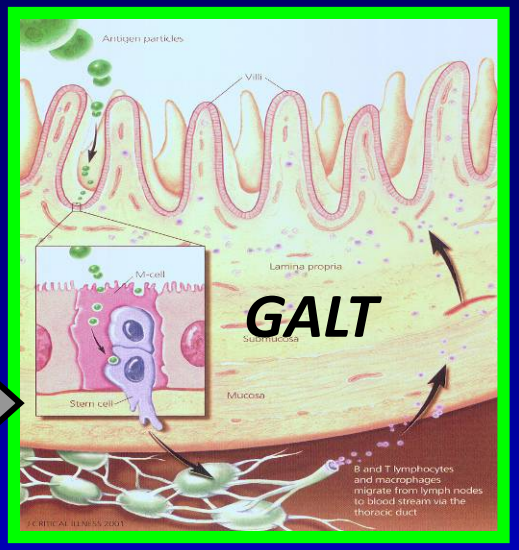
: Lamina propria (CD4 andCD8 T-cells/B-cells)

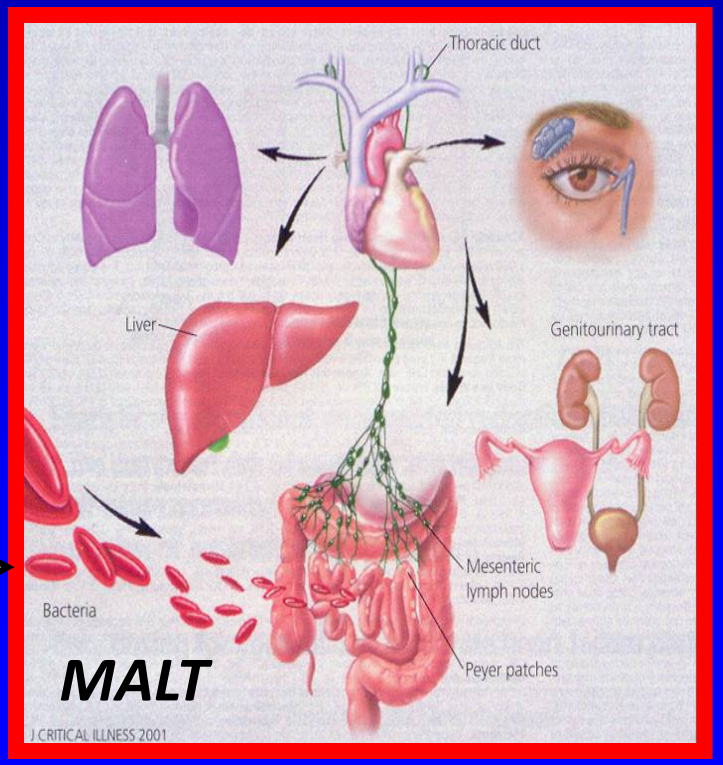
: Intra-epithelial lymphocytes and macrophages

COX inhibitors increase lymphocyte apoptosis and suppress macrophage response

Feeding Maintains GALT / MALT







Gut anatomy
The gut is composed of 3.

3. The microbiome

- Human intestine is home for 100 trillion bacteria (500 – 1000 species)

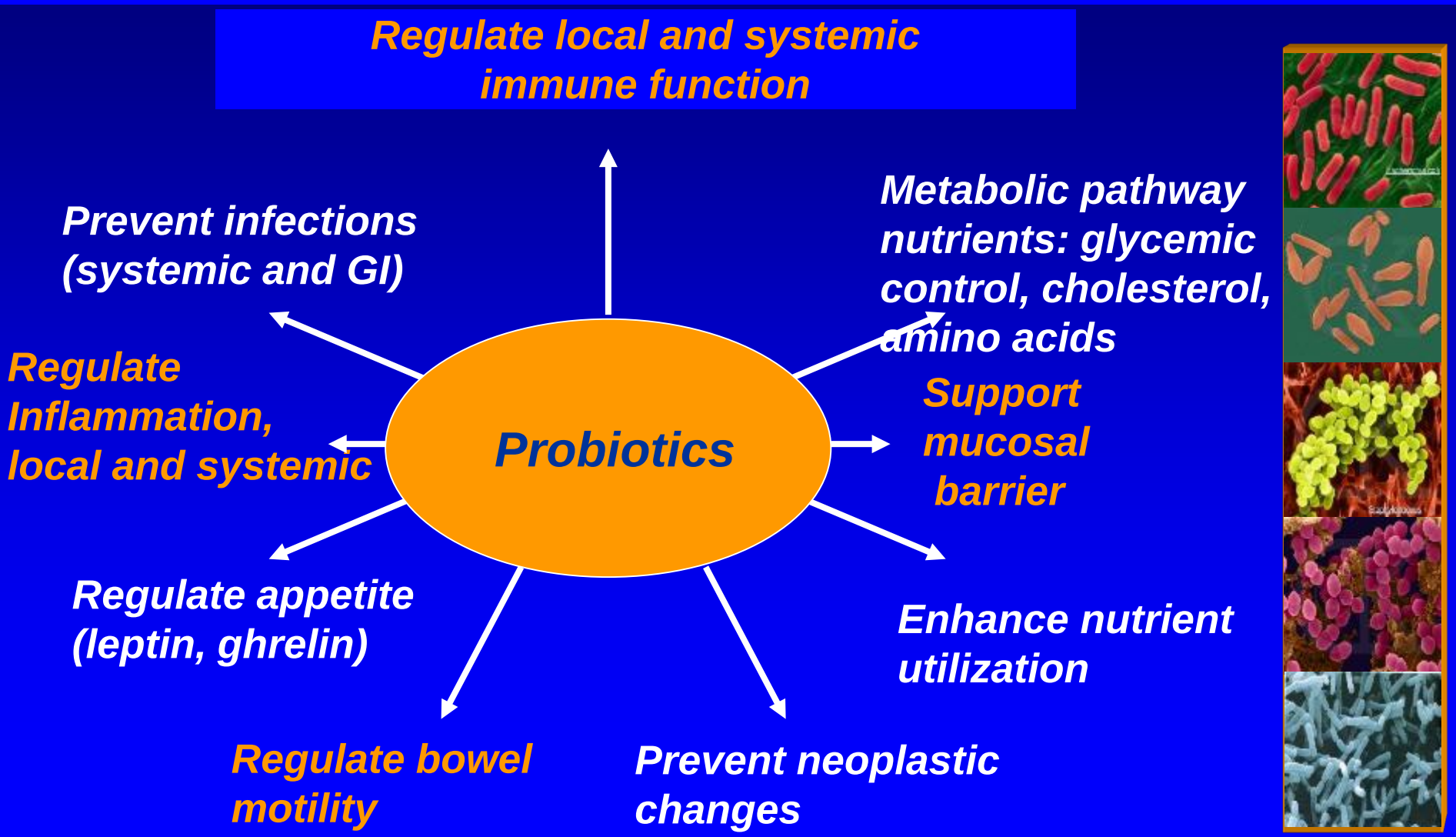
  This is 10x more bacterial cells than human host cells.
- Normally there is a well-tolerated symbiotic relationship between the human host and its microbiome.
- The microbiome can alter its behaviour on environmental cues. The ability of bacteria to sense host stress, their own environment and surrounding bacterial density and alter their virulence in response has profound clinical implications.
- Preventing bacteria from becoming virulent or reprogramming them to a non-virulent phenotype may REVOLUTIONIZE the treatment of gut-derived sepsis
- Outside of enteral nutrition no treatment targeting the gut is currently widely used in ICU.

32. Restoring Microbiota—Key to Success?

Studies of the critically ill, especially those with systemic inflammatory reaction syndrome (SIRS), report severe dysbiosis. When compared with healthy volunteers, they often have 10,000 times fewer total anaerobes, including the "beneficial" Bifidobacterium and Lactobacillus, and 100 times more "pathogenic" bacteria, such as Staphylococcus bacteria. The content in the gut of organic acids, in general, but butyric and propionic acids, in particular, are severely reduced. Recent studies report the production of "mucosa-tightening" butyric acid as almost extinct (from 16.6 ± 6.7 to 0.9 ± 2.3) [72–74].

The incidence of organ failure and ICU mortality is reported to be significantly higher in patients with profound reductions in size and diversity of microbiota, especially when associated with a massive presence of enterococci and with the use of antibiotics, especially clindamycin [186]. Information like this provides strong support to efforts to prevent dysfunctioning microbiota, "dysbiosis" and, when needed—as it always is for critically ill patients—strong and forceful efforts to restore homeostasis in microbiota, the ideal state of balance being called "eubiosis". Recent cutting-edge results from the supplementation of synbiotics to postoperative and critically ill patients as discussed earlier, support recommendations to routinely supplement specific LAB and fibers (synbiotics) to a wide group of patients undergoing major medical or surgical treatments or suffering from polytrauma or medical emergencies such as acute pancreatitis or myocardial infarction. For patients who cannot tolerate enteral feeding, administration of synbiotics by enemas with live LAB may be a treatment option. It is important to remember that most patients do not die of their disease but from a disordered physiology caused by either the disease or, as often happens, by the treatments.

Probiotics: Exploring the Mutually Beneficial Effects of Bacteria and their Substrates in the Human Host



Approaches to Maximizing Gut Function in Critical Illness 1
= decrease the duration of the strike

- Maintain visceral perfusion
- Source control
- Enhanced recovery pathways (ERAS)
- Strict glycaemic control
- Correction of acidosis and electrolyte abnormalities
- Early nutritional support
    - Enteral preferred
    - < 24 (48) hours
    - Use specific nutrients to attenuate metabolic response
- Mechanical : laparoscopic surgery (mainly elective surgery)

Adapted from Martindale 2007

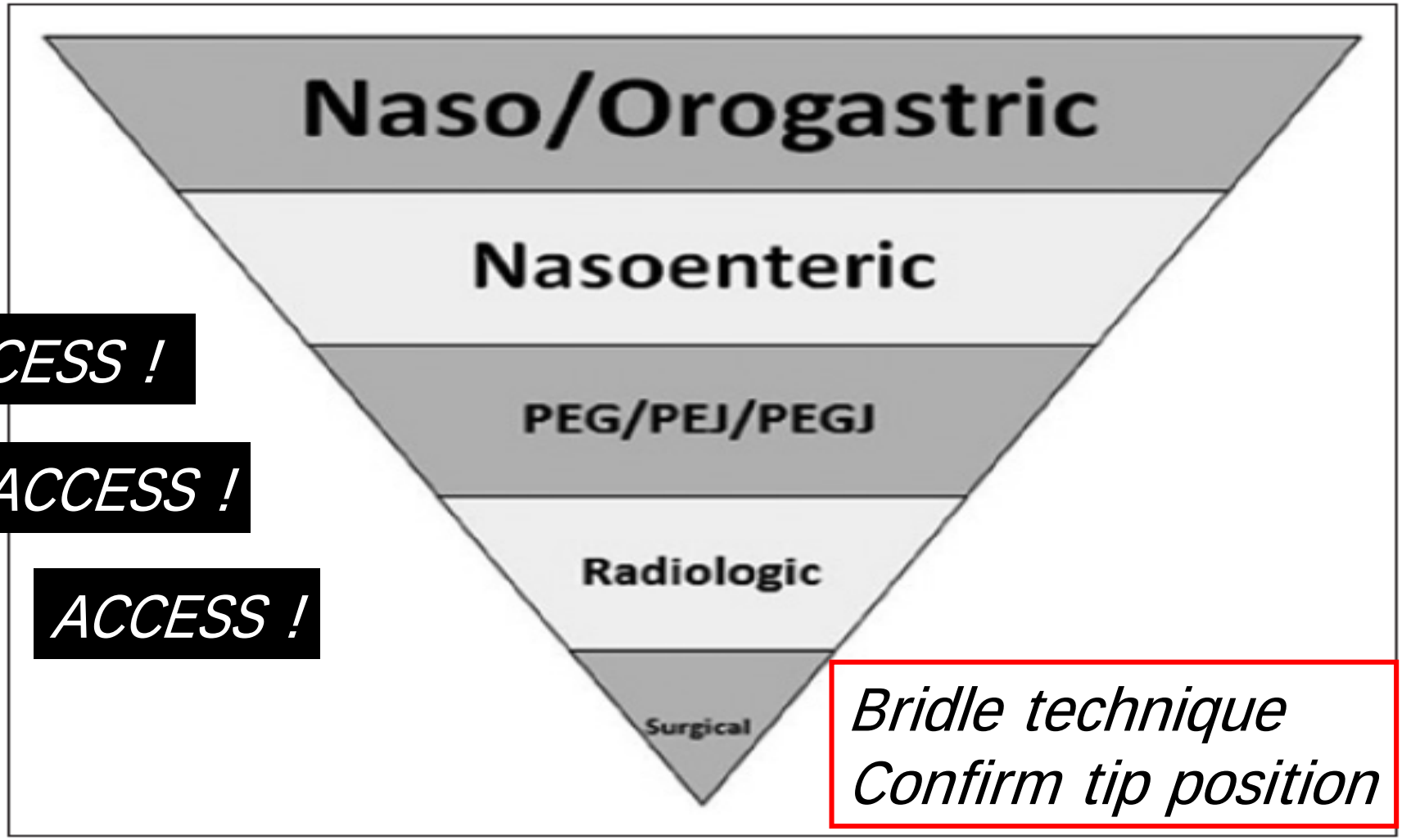


Figure 1. Most patients are amenable to less complex enteral access strategies. However, as clinical complexity increases, a small subset of patients will require more invasive measures to achieve appropriate enteral access. PEG, percutaneous endoscopic gastrostomy; PEGJ, PEG with jejunal extension; PEJ, percutaneous endoscopic jejunostomy.

Approaches to Maximizing Gut Function in Critical Illness 2
= decrease the duration of the strike

- Pharmacological interventions
  - Chewing gum: simulation of cephalic-vagal axis
  - Prokinetics
    - Metoclopramide, Erythromycin, Neostigmine
  - Anti-secretory attempts
    - Octreotide?, Cimetidine
  - Selective peripheral antagonism of μ-opioid receptors
    - Alvimopan – novel breakthrough
  - Minimize medications that alter GI function
    - Anticholinergics, Narcotics, Vasopressors
  - Neely and Catchpole regimen: Sympathetic-parasympathetic imbalance
    - IV volume, alpha blocker, parasympathomimetic

The Gastro-intestinal Tract plays

a CENTRAL role

in critical illness of any origin

It is astonishing with how little reading a doctor can practice medicine,

BUT ....

it is not astonishing how badly he may do it..... Sir William Osler


creature comforts
"They look so good 'cause they eat so good"

Martindale Proposes Gut Dysfunction in Critically Ill Patients Develops due to:

- **Mucosal barrier disruption**
  - **Visceral hypoperfusion**
  - **Absence of biliary and pancreatic secretions**
  - **Changes in luminal bacteria and bacterial products**
- **Altered motility**
  - **Bowel edema**
  - **pH / electrolyte abnormalities / hyperglycemia**
  - **Excessive opiates**
  - **Inhibitory neurotransmitters / peptides (NO*, VIP†, substance P)**
  - **Excess sympathetic tone**
  - **↑ Inflammatory mediators into muscularis (iNOS‡, COX-2)**
- **Mucosal and GALT§ atrophy**
  - **No luminal delivery of nutrients**

*NO=nitric oxide; †VIP=vasoactive intestinal peptide; ‡iNOS=inducible nitric oxide synthase; §GALT=gut associated lymphoid tissue.

Treatment of GI failure (Gastrokinetics)

- Metoclopramide (Maxolon):
  # Suggested dose: 10mg q6h IV
  # $5HT_4$ agonist → stimulate gastric and duodenal motility
  #Disadvantage: 1. Effect of drug diminishes rapidly over 3 days (only 20% effective by day 3)
  2. Not effective in brain injury patients
  3. Long term or high dose treatment → irreversible tardive dyskinesia.
- Erythromycin:
  # Suggested dose: 3mg/kg → 250mg q6h IV (Doses as low as 70mg can stimulate bowel!)
  # Stimulate high amplitude antral contractions that spread to the duodenum
  # Effective in patients with high gastric residual volumes
  # Reduced efficacy by day 4(down regulation of motilin receptors)
  # Concerns: AB resistance, potential cardiac arrhythmias

Treatment of GI failure (Gastrokinetics)

- Opiate antagonists:

  Enteral Naloxone → reverses high GRV and aspiration pneumonia*

  (given during opioid treatment)

- Combination therapy:

  Metoclopramide plus Erythromycin

- Acupuncture (WGAP)

- Neostigmin for small intestine or colon dilation (WGAP)

* Meissner et al, CCM 2003;31:776-780

Other agents to treat GI failure

- Potential new agents:

  1. **ABT-229**: synthetic derivate of Erythromycin with no antibiotic effect → 7-40 fold more potent than erythromycin in accelerating gastric emptying.*

  2. CCK antagonist : **Loxiglumide** → Study 1997 Saito et al. : Loxiglumide had no effect on gastric emptying and intestinal transport activity in mice.*

  3. Agonists of other hormones: **Ghrelin** → stimulate motility of bowel and promote anabolic metabolism via Growth hormone secretion.**

  4. TENS – transcutaneous electrical nerve stimulation. Gate theory in spinal cord. Set according to individual experience.

*Arzneimittelforschung.1997 Dec; 47(12) 1375-82.

** Peeters TL. J Physiol Pharmacol. 2003 54(suppl 4); 95-103.

*Cowles et al.
J Pharm and Experimental Therapeutics; 2000: Vol 293, 1106-1111.

The goal is successful nutrition!

- Mostly start with early gastric feeding (communicate with operating surgeon)
- If laparotomy is done – place feeding tube distal to Treitz when at all possible – for all patients in need of post op HC or IC – my personal bias to ensure early EN
- Use TPN only if targets are not met by 72h in critically ill patients – I start even earlier with TPN based on the patient's nutritional history / status, pathology, diagnosis, or surgery.
- EN *is* preferable,… but *TPN still has indications*

Recommended Approach to Nutritional support in ICU

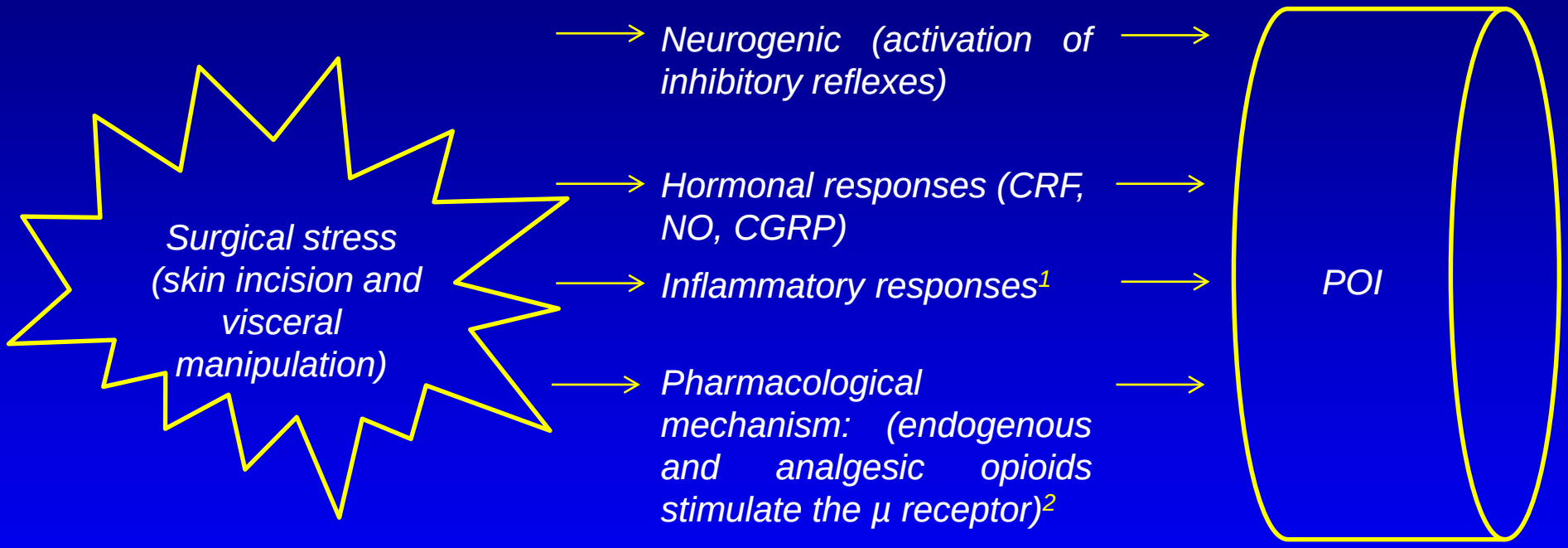
- Obtain history of past nutrition and assess patient's status
- Consider pathophysiology, procedures or surgery involved
- Assess resuscitation status
- Consider possibility of re-feeding or over feeding
- Assess the % availability of the gut – striking or not?
  - 1st choice always the gastrointestinal tract
  - In critically ill patients: 85-90% EN vs 10-15% TPN
- Persistence of intolerance – start TPN early
  - ASPEN 2009 * in general: start TPN <7 days = indication for TPN
    * with protein-energy malnutrition on admission to ICU, and the gut on strike – start TPN without delay
  - ESPEN 2009 * start <3 days

To Catch the BUS -

- ***DO NOT GIVE UP ON THE GUT!!!***

- *My practice:*
  - *Follow the recommendations*
  - *But:* AT THE SAME TIME at least try to utilize the accessible or available part of the gut in addition,… on an on-going daily basis until tolerance returns.
  - *This = Combine TPN and EN*

AUGESTAD KM et al. Postoperative ileus (POI), recent advances and future perspectives



Pathogenesis of postoperative ileus. *[1]Laparoscopic surgery decreases the surgical stress and inflammatory response. 2Primarily exogenous opioids, e.g. morphine, binding to μ-receptors in the GI tract, which results in disorganized and non propulsive and, thus, prolongs ileus. In addition, activation of opioid receptors, which occurs following major abdominal surgery , inhibits acetylcholine release, reduce gastrointestinal motility, and has been demonstrated to play a key role in POI regulatory pathway. Alvimopan inhibits this effect by blocking the pheripheral opioid μ receptor.*

Postoperative Ileus

- Definition: Consensus Conference 2006
  - "transient cessation of coordinated bowel motility after surgical intervention, which prevents effective transit of intestinal contents or tolerance of oral intake"
- Primary POI: …such cessation occurring in the absence of any precipitating complication
- Secondary POI: …that occurring in the presence of a precipitating complication (infection, anastomotic leak)
- Selectively affects stomach, small bowel or colon
- Endpoint for GI recovery: composite of "time to first tolerance of solid food and time of first bowel movement"

The Food Fight 1

- Parenteral nutrition
- Enteral stimulation
- Gut-derived mucosal immunity

Nutritional support is an integral concept of modern patient care, ***BUT,*** is there evidence of nutrition-altered mucosal immunity in humans?

1.Human studies…lowered mucosal IgA…reduced resistance to infection (? Immune tipping point)

2. Neonatal studies…convincing…populating the gut with immunoglobulin-producing cells + intraepithelial GALT cells depend on enteral nutrition

3. In adult humans?

Hermsen, Sano, Kudsk 2009 Langenbecks Arch Surg

The Food Fight 2

4. Decreases in LP-GALT cells in colon-CA patients nourished preop with TPN vs patients allowed oral intake
5. Wijesinha: loop ostomies: found more GALT cells present in proximal limbs exposed to nutrient stream vs distal limbs where nutrient stream was diverted
6. Buchman: no biopsy changes in human volunteers on TPN. Question about extent of examination possible in acutely ill hospitalized patients

Conclusion:

Certainly, nutritional support matters but remains difficult to study and exceedingly difficult to quantify

Studies and debate on how, when, how much, what kind for how long, continue.

Hermsen, Sano, Kudsk 2009 Langenbecks Arch Surg

Managing the Gut on Strike
The GUT Bundle ?
ERICC?….. ala ERAS
Enhanced Recovery in Critical Care?

- Rx modalities = multimodal approach at present
  - Minimally invasive surgery, Pharmacotherapy, ERAS
- Optimal integration of all treatment options
- Novel suggestions
  - Probiotics, Microbiota
  - Vagal activation to reduce period of intestinal hypomotility
    - Stimulation of Vagal antiinflammatory pathway > enteral adminisration of lipids
  - Stig Bengmark – role of saliva (the breast milk of the gut) NO, IgA, lactoferrin, LDH, lysozyme, mucins etc

What is Autophagy ?

- *A normal physiological process in the body that deals with the destruction of cells in the body.*
- *It maintains homeostasis or normal functioning by protein degradation and turnover of the destroyed cell organelles for new cell formation.*
- *Upscaled and increased during cellular stress ie when there is deprivation of nutrients and/or growth factors*
- *May provide an alternate source of intracellular building blocks and substrates that may generate energy to enable continuous cell survival*

Autophagy and Cell Death

- *Kills cells under certain conditions. These are form of programmed cell death. Programmed cell death is commonly termed apoptosis.*
- *Autophagy is termed a nonapoptotic programmed cell death with different pathways and mediators from apoptosis.*
- *Maintains a balance between manufacture of cellular components and breakdown of damaged or unnecessary organelles and other cellular constituents.*
- *There are some major degradative pathways that include proteasome that involves breaking down of most short-lived proteins.*

Autophagy and Stress

- *Autophagy enables cells to survive stress from the external environment like nutrient deprivation.*
- *Allows cells to withstand internal stresses like accumulation of damaged organelles and pathogen or infective organism invasion.*
- *Seen in all eukaryotic systems including fungi, plants, slime mold, nematodes, fruit flies and insects, rodents AND HUMANS*

Nutrition of the Critically Ill

1. *Morbidity and death continue to rise in Modern Medicine*
2. *Health care associated infections do not receive enough attention*
3. *Artificial nutrition – a major contributor to sepsis*
4. *Colloid-associated morbidity often neglected*
5. *Crystalloids often enough after surgical procedures*
6. *Nutrition made to prevent deterioration of immune functions*
7. *Dysbiosis-associated over-reacting neutrophils*
8. *Efforts to reduce inflammation, neutrophil infiltration and tissue destruction*
9. *Life-threatening systemic inflammation*
10. *Numerous mechanisms to control intestinal homeostasis*
11. *Experience with pro- and synbiotics (Metabolic enchephalopathy)*
12. *It is all about inflammation*
13. *Inflammation control – Pharma and/or Probiotics*

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WHAT'S NEW IN INTENSIVE CARE

2016

P. Singer
G. S. Doig
C. Pichard

The truth about nutrition in the ICU

1: enteral nutrition, preferably as early as possible
2: avoid over nutrition
3: predictive equations for energy needs are frequently inaccurate
4: the timing to prescribe supplemental parenteral nutrition remains uncertain
5: give enough protein to fight anabolic resistance
6: glutamine is recommended in parenterally fed patients without MOF
7: give selenium in sepsis and consider fish oil in ARDS
8: blood glucose should be controlled, conventionally
9: monitoring: do not measure gastric residual volume

THE TRUTH ABOUT NUTRITION IN THE ICU - 1

Conclusions

a) Critically ill patients have become more polymorbid, aged, and complex.

*b) No studies demonstrating that **neither fasting nor starvation** benefits the critically ill. There IS a NEED to FEED.*

c) Practice has been improved by numerous studies in the field of early enteral feeding, glucose control, and preventing nutrition complications.

d) Studies are required to define the best timing for supplemental parenteral nutrition, as well as the quantity and quality of protein, lipids, and micronutrients.

THE TRUTH ABOUT NUTRITION IN THE ICU - 2

Conclusions

a) Provide adequate energy and proteins.

b) Avoid both hypocaloric AND hypercaloric feeding.

c) Prescribe nutrition according to the individual patients needs – Diagnosis – Think – Prescribe – DON'T GUESS. ***(Give one 3L bag of the white stuff)***

d) Parenteral nutrition remains a powerful tool when the gut is on strike

e) After 3-4 days of unsuccessful EN start TPN alone or in combination with EN ….. Reach the nutritional target!

f) Finally…IT IS THE PRESCRIPTION AND NOT THE ROUTE THAT IS OF IMPORTANCE !