
بسم الله الرحمن الرحيم

Gastrointestinal prophylaxis in critically ill patients

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Conflict of Interest

I did not receive any financial support from the pharmaceutical companies whose medications were mentioned in this presentation.


Critical illness - Definition

A critical illness or injury acutely impairs one of more vital organ systems with a high probability of imminent life threatening deterioration in the patient's condition.

Messmann H. Crit Care Med 2013; 15(2):139-43.

Early, specific signs of GI complications are rarely present.

Because of late or missed diagnosis, morbidity and mortality related to these complications can be high.

Martin B. Adv Crit Care 2007; 18(2):158-66.

Preventive measures

- ↓ Cost.
- ↓ Stay.
- ↓ Morbidity.
- ↓ Mortality.

Strategies related to GIT

- Stress Ulcer.
- Gastric Overdistension.
- Nutritional Support.

Stress ulcer

Stress-related mucosal disease (SRMD)

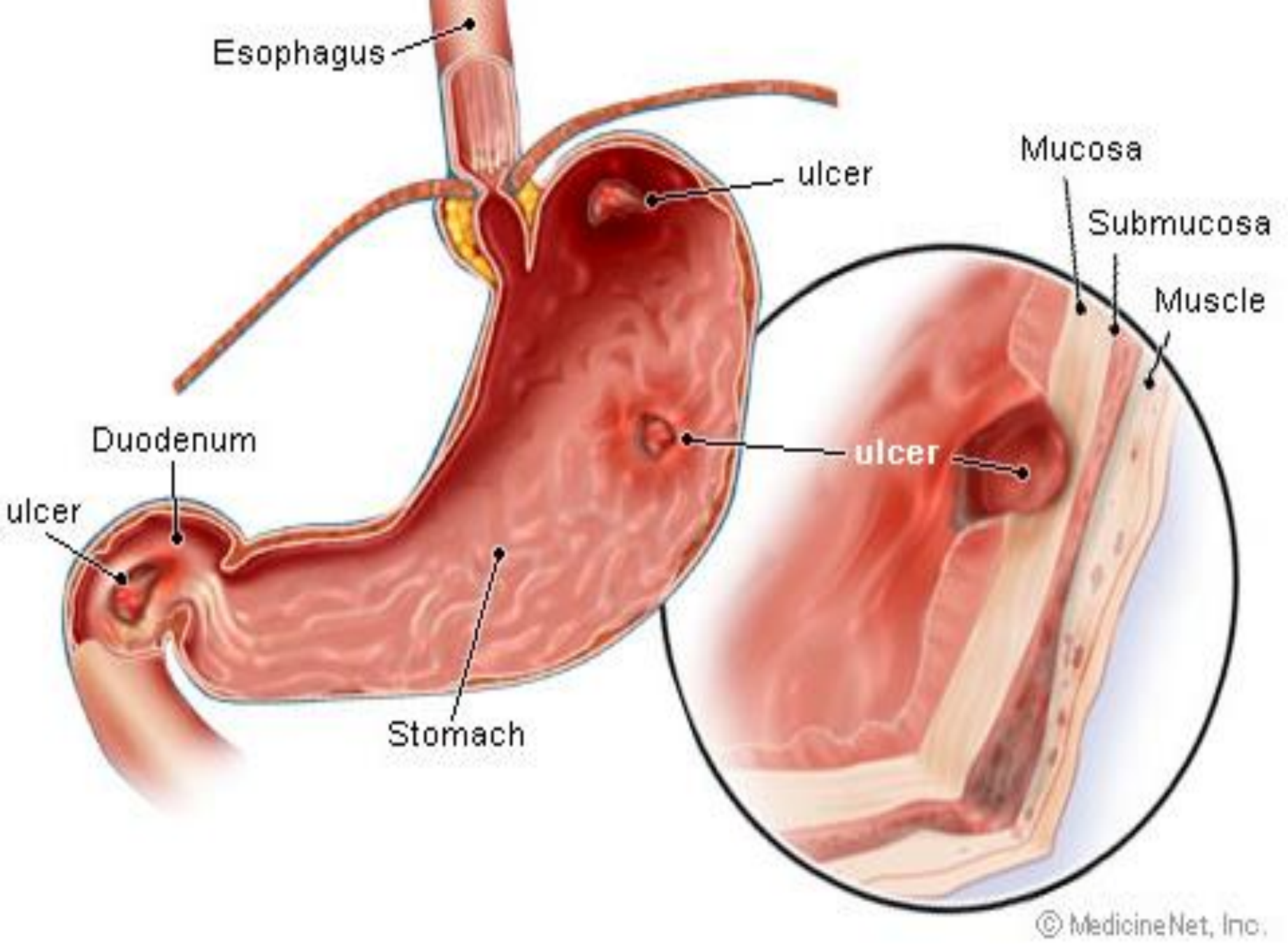
Outline

- Definition
- History
- Epidemiology
- Pathophysiology
- Guidelines
- Agent Selection & Administration
- Complications

Definition

- **Gastrointestinal mucosal injury related to critical illness.**
  - **Stomach**
  - **Duodenum**
  - **Ileum**
  - **Jejunum**
- **Macroscopic bleeding**

ASHP Therapeutic Guidelines on Stress Ulcer Prophylaxis. 2009; 15(2):139-43.


Esophagus
ulcer
Mucosa
Submucosa
Muscle
Duodenum
ulcer
ulcer
Stomach
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History

- 1842: Curling described series in burn patients
- 1932: Cushing reported ulcers with surgery and trauma
- 1970s: Development of H2 receptor antagonists

Maton PN. Aliment Pharmacol Ther. 2005 Dec;22 Suppl 3:45-52.

History

- 1990's: Dr. Cook and the Canadian Critical Care Trials Group perform landmark trials on ICU usage of H2 receptor antagonists.

- 1990s to 2000: Proton Pump inhibitors make more efficient gastric alkalinization possible.

Maton PN. Aliment Pharmacol Ther. 2005 Dec;22 Suppl 3:45-52.

Epidemiology

- Up through the 1970, stress ulcers were much more common (>30% of ICU patients)

- Today, less than 5% of ICU patients have stress ulcers with macroscopic bleeding

Del Valle J. Peptic Ulcer Disease and Related Disorders , 2010.

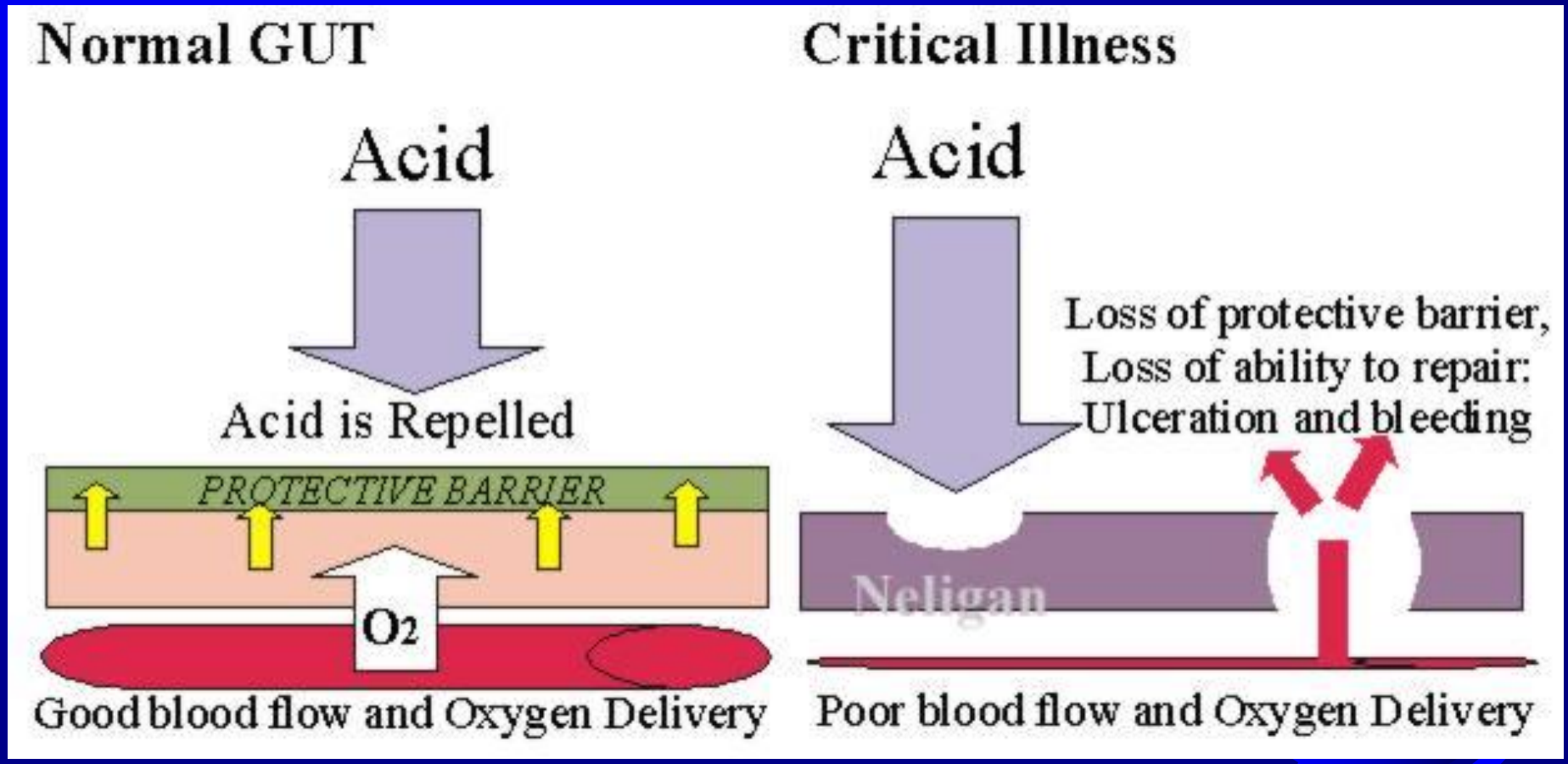
Pathophysiology

- Etiology is complex
  - Decreased Gastric pH
  - Ischemia
  - Decreased mucus production

- Usually occur within 24-48 hours of trauma/stress

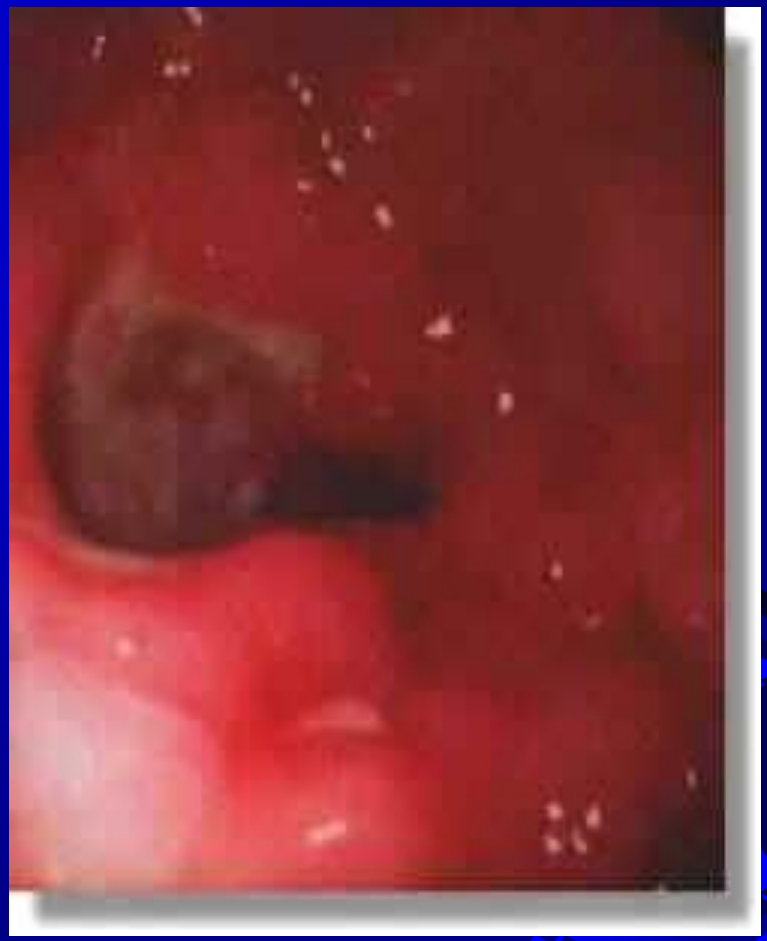
Del Valle J. Peptic Ulcer Disease and Related Disorders , 2010.

Pathophysiology



Pathophysiology

- Absent mucosal barrier + gastric acid =



Guidelines

- American Society of Health-system pharmacists (ASHP) Therapeutic Guidelines on Stress Ulcer Prophylaxis

Key Guideline Points – The Big 3

1. Coagulopathy
   - Platelet count of <50,000mm
   - INR>1.5
   - PTT of >2 times the control
2. Mechanical Ventilation
   - Longer than 24 hours
3. Recent GI ulcers/bleeding
   - Within 12 months of admissi

ASHP Therapeutic Guidelines on Stress Ulcer Prophylaxis, AJHP 1999;56(4): 347-379.
Pathophysiology and prophylaxis of stress ulcer in ICU patients. J Crit Care. 2005 Mar;20(1):35-45.

Key Guideline Points – The Little 4

- **2 or more of the following:**
  1. **Sepsis**
  2. **ICU>1 week**
  3. **Occult Bleeding within 6 days**
  4. **High dose corticosteroids**
     - **250mg Hydrocortisone**
     - **50mg Methylprednisone**

ASHP Therapeutic Guidelines on Stress Ulcer Prophylaxis, AJHP 1999; 56(4): 347-379.
Pathophysiology and prophylaxis of stress ulcer in ICU patients. J Crit Care. 2005 Mar;20(1):35-45.

Prophylaxis

- Antacids
- Sucralfate
- Histamine$_2$ receptor antagonists
- Prostaglandin analogues
- Proton pump inhibitors
- Enteral feeding

Prophylactic Options

- **Antacids:**

- **Neutralize acid.**
- **Must be given frequently and in larger volumes to be effective.**

Prophylactic Options

- **Sucralfate:**

- Adheres to epithelial cells and “restores” a cytoprotective barrier.
- Binds bile salts
- Stimulates prostaglandin synthesis
- Stimulates local epidermal growth factor

Goodman & Gilman’s Pharmacological Basis of Therapeutics. 2011.

Prophylactic Options

- **H2 Blockers:**

- Inhibit acid secretion in a dose-dependent competitive manner.

- Reduce volume of gastric acid and [H+]

- Well absorbed with half life of 2 to 3 hours.

- Most trials show lower risk of significant GI hemorrhage.

Shuman, RB. Ann Int Med 2006; 106: 562-8.

Prophylactic Options

- **Prostaglandin analogues:**

- PGE 2 and PGI 2 inhibit acid secretion and increase mucus and bicarbonate.

- **May have a more useful role in patients who are dependent on NSAIDS.**

Goodman & Gilman's Pharmacological Basis of Therapeutics. 2011.

Prophylactic Options

- **Proton pump inhibitors:**

- **The final mediator of acid secretion is the H+, K+ -- ATPase pump unique to the parietal cell.**

- **PPIs are prodrugs that are activated by protonation and covalently bind to a cysteine residue and inactivate the ATPase enzyme.**

Goodman & Gilman's Pharmacological Basis of Therapeutics. 2011.

Prophylactic Options

- NUTRITION

In multiple burn studies, enteral nutrition alone had a significantly lower GI hemorrhage when compared to H2 Blockers.

Raff, T. Burns 1997; 23:313

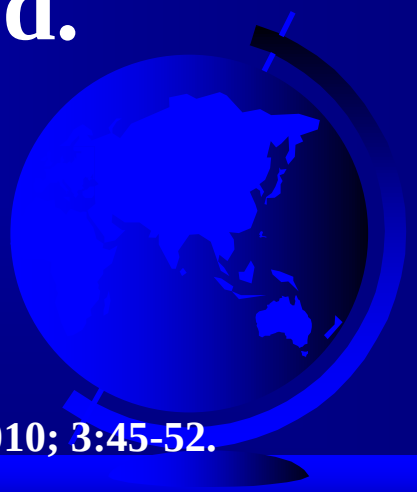
Agents and Dosing

- **IV Agents**
  - **Pantoprazole 40 mg (Q12-24h)**
  - **Ranitidine 50mg (Q8h)**

- **Oral Agents**
  - **PPI 40mg (Q24h)**
  - **Ranitidine 150mg (Q12h)**
  - **Sucralfate 1-2 grams 4 times per day**

Management Strategic Healthcare Group and the Medical Advisory Panel 2010; 39: 48-55.

Proton pump inhibitors are at least as effective as histamine 2 receptor antagonists, as a large number of clinical trials have demonstrated.



Maton PN. Aliment Pharmacol Ther. 2010; 3:45-52.

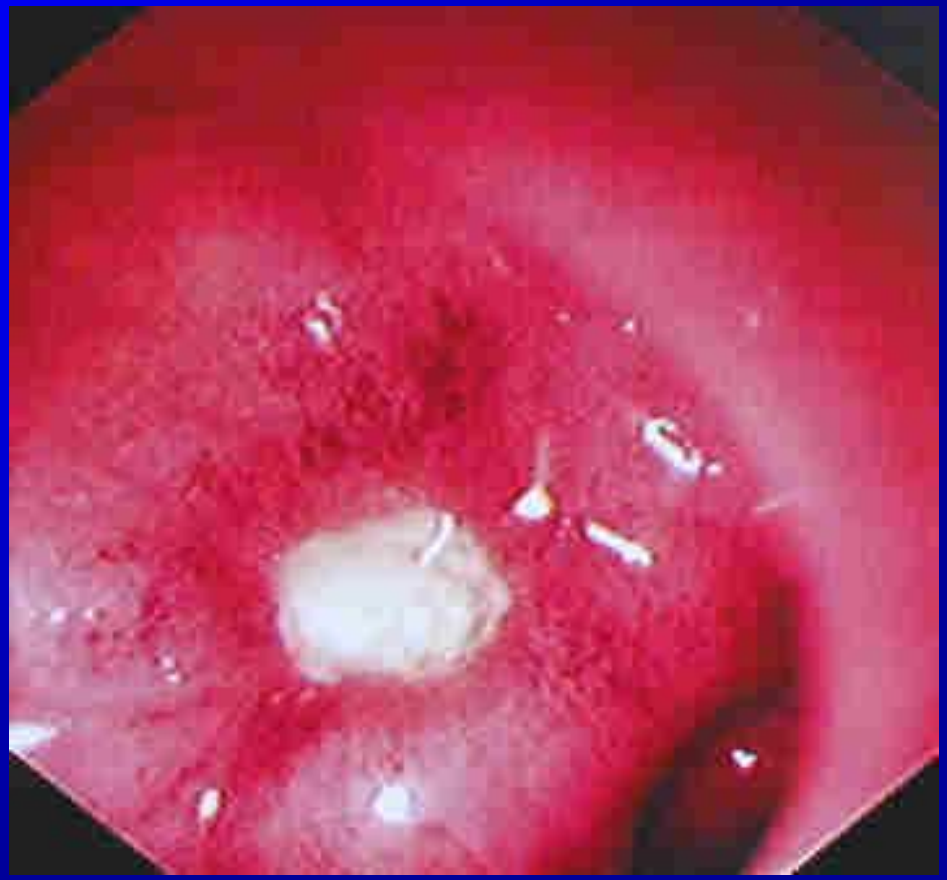
New data suggest that PPI inhibitors suppress acid production more completely in critically ill patients.

Stollman N, Metz DC. J Crit Care. 2012; 20(1):35-45.

Negative Health Outcome
Risks Associated With Acid Suppression

- Hospital Acquired Pneumonia(HAP).
- C. Difficile.
- Osteoporosis & Hip Fractures.

1. Herzig HJ et al, JAMA 2009;301(20):2120-2128
2. Dial, S, Delaney, AC, Barkun AN, et al. JAMA 2005;294(3):2989-2995
3. Yang et al. JAMA 2006:296(24):2947-2953
4. Targownik, LE et al. CMAJ 2008:179(4):319-326



This patient with no Helicobacter infection got this ulcer during a period of severe somatic stress due to a heart disease.

Gastric overdistension

Mechanical ventilation in critically ill patients is theoretically associated with a number of gastrointestinal complications, including stress ulcers, hypomotility and diarrhoea.

Other aspects of critical illness or the therapies used to treat it may further affect gastrointestinal function.

Crit Care Resusc 2010; 12: 182–185

Although gastrointestinal dysfunction is not a priority in the critically ill, intestinal hypomotility may lead to:

- **Malabsorption.**
- **Vomiting.**
- **Aspiration pneumonia.**
- **Bacterial overgrowth.**
- **Endotoxaemia.**

Crit Care Resusc 2010; 12: 182–185

Acute gastrointestinal (GI) dysfunction and failure have been increasingly recognized in critically ill patients.

A. R. Blaser et al., Intensive Care Med 2012; 38:384–394

The international Working Group on Abdominal Problems (WGAP) of the European Society of Intensive Care Medicine (ESICM) developed the definitions for GI dysfunction in intensive care patients.

A. R. Blaser et al., Intensive Care Med 2012; 38:384–394

Acute gastrointestinal injury (AGI) is a malfunctioning of the GI tract in intensive care patients due to their acute illness.

A. R. Blaser et al., Intensive Care Med 2012; 38:384–394

- **AGI grade I =**
  Risk of developing GI dysfunction or failure
  (a self-limiting condition).

- **AGI grade II =**
  GI dysfunction
  (a condition that requires interventions).

- **AGI grade III =**
  GI failure
  (GI function cannot be restored with interventions).

- **AGI grade IV =**
  Dramatic GI failure with severe impact on distant organ function
  (a condition that is immediately life-threatening).

AGI grade I

AGI grade I (risk of developing GI dysfunction or failure).

Transient and partial impairement GI function.

AGI grade I

Examples :

- Nausea and vomiting after abdominal surgery.

- Postoperative absence of bowel sounds.

- Diminished bowel motility in the early phase of shock.

AGI grade I

Management :

- **Fluid replacement by IV infusions.**

- **Early enteral feeding, 24–48 h after the injury.**

- **Limitation of drugs impairing GI motility (e.g. catecholamines, opioids).**

AGI grade II

AGI grade II (gastrointestinal dysfunction)

The GI tract is not able to perform digestion and absorption adequately.

There are no changes in general condition of the patient related to GI problems.

AGI grade II

Examples:

- Gastroparesis with high gastric residuals or reflux.

- Paralysis of the lower GI tract.

- Intra-abdominal hypertension grade I. (IAP = 12–15 mmHg).

- Visible blood in gastric content or stool.

AGI grade II

Management:

- Prokinetic therapy.

- Enteral feeding should be started or continued.

- Initiation of postpyloric feeding in patients with gastroparesis.

AGI grade III

AGI grade III:

Loss of GI function, where restoration of GI function is not achieved despite interventions and the general condition is not improving.

AGI grade III

Examples:

- Feeding intolerance is persisting despite treatment.

- High gastric residuals, persisting GI paralysis.

- Progression of IAH to grade II (IAP 15–20 mmHg).

- Low abdominal perfusion pressure (APP) (below 60 mmHg).

AGI grade III

Management:

-Undiagnosed abdominal problems (cholecystitis, peritonitis, bowel ischaemia) should be excluded.

- The medications promoting GI paralysis have to be discontinued as far as possible.

- Challenges with small amounts of EN should be regularly considered.

AGI grade IV

AGI grade IV:

GI failure with severe impact on distant organ function.

AGI has progressed to become directly and immediately life threatening, with worsening of MODS and shock.

AGI grade IV

Examples:

- Bowel ischaemia with necrosis.

- GI bleeding leading to haemorrhagic shock.

- Ogilvie's syndrome.

-Abdominal compartment syndrome (ACS) requiring decompression.

Ogilvie syndrome

acute pseudoobstruction and dilatation of the colon in the absence of any mechanical obstruction in severely ill patients.

Abdominal compartment syndrome

- The abdomen becomes subject to increased pressure.

- Cause: sepsis and severe abdominal trauma.

- Increasing pressure reduces blood flow to abdominal organs and impairs pulmonary, cardiovascular, renal, and GI function, causing MODS and death.

AGI grade IV

Management:

Condition requires laparotomy or other emergency interventions.

There is no proven conservative approach to resolve this situation.

Nutritional support

Critical illness increases nutrient requirements as well as alters metabolism.

Patients in the ICU are unable to nourish themselves orally.

Jeejeebhoy KN. Nutr Rev. 2012 Nov;70(11):623-30.

ICU patients rapidly become malnourished unless they are provided with involuntary feeding either:

- Enteral nutrition (EN): through a tube inserted into the GI tract, or

- Parenteral nutrition (PN): directly into the bloodstream.

Jeejeebhoy KN. Nutr Rev. 2012 Nov;70(11):623-30.

Between the 1960s and the 1980s, PN was the modality of choice which led to overfeeding regimens called hyperalimentation.

Later, the dangers of overfeeding, hyperglycemia, fatty liver, and increased sepsis associated with PN became recognized.

Acosta E scribano J Med Intensiva, 2011 Nov;35 Suppl 1:77-80.

In contrast, EN was not associated with these risks and it gradually became the modality of choice in the ICU.

Hence, the balanced perspective has been reached of using EN when possible but avoiding underfeeding by supplementing with PN when required.

Acosta E scribano J Med Intensiva, 2011 Nov;35 Suppl 1:77-80.

Early EN is superior to delayed EN in the critically ill

The expert committee, however favours that critically ill patients, who are haemodynamically stable and have a functioning gastrointestinal tract, should be fed early (< ৬৫ h), if possible.

EN in critically ill patients

During the acute and initial phase of critical illness, an exogenous energy supply of ๒๐–๒๕ kcal/kg BW/day is needed.

During recovery (anabolic flow phase), the aim is to provide ๒๕–๓๐ total kcal/kg BW/day.

Protein requirement

- ๑.๕ g/kg/day.
- ๒ g/kg/day in patients with trauma, severe burns, and head injury.
- ๒.๕ g/kg/day in adult patients treated with continuous renal replacement therapy (CRRT).
- nutritional support can only limit the loss of the body's protein and calorie stores.
- The goal is to administer sufficient nitrogen to provide a positive or neutral nitrogen balance.

Lipid requirements

- 0.5 – 1 g/kg/d [20-40% of energy]
- Lipid clearance is reduced in stressed patients due to decreased activity of lipoprotein lipase.
- infusion rate should not exceed 0.12 g/kg/hr to avoid the development of elevated TG levels.
- Source of essential FA , fat soluble vitamins.
- Avoid Omega 6 [linoleic is a precursor of arachinodic acid].

Parenteral nutrition

Indications:

- In patients who cannot be fed sufficient enterally.

- Intolerant to EN

Complications of PN

- PN associated with a more pronounced proinflammatory response than EN.

- Complications of excess dextrose infusion
  - hyperglycemia
  - hypertriglyceridemia
  - hepatic steatosis,
  - respiratory decompensation
  - depression of immune function

SUMMARY

Acute gastrointestinal injury (AGI) is a malfunctioning of the GI tract in intensive care patients due to their acute illness.

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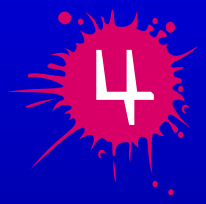
Guideline Summary

- **Big 3**
  1. **Coagulopathy**
  2. **Mechanical Ventilation**
  3. **GI Bleeding within 12 months**



- **Little 4 (2 or more)**
  1. **Sepsis**
  2. **ICU>1 week**
  3. **Occult Bleeding within 6 days**
  4. **High dose corticosteroids**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