CHU tivoli

ULB

Centre Hospitalier Universitaire de Tivoli

Prévention de l 'ulcère de stress aux soins intensifes (Stress Ulcer Prevention ou SUP)

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Ulcère de stress?

Ulcère de stress contexte

-En 1842 un certain chirurgien? Anglais? De nom de Curling rapportait le premier cas d'hémorragie digestive chez un patient souffrant de brûlures étendues

-En 1942, Cushing (pas harvy) décrivait les premiers ulcères de stress au cours des traumatismes

-Première vraie publication par Skillman (1969)

-5% des patients décédés d' insuffisance respiratoire, sepsis , hypotension terminale; avaient des lésions gastrique

-Depuis très nombreux publications (>580)

-Prévention de l' ulcère de stress ou Stress Ulcer Prevention ou SUP est la règle

Ulcère de stress contexte

-Incidence : entre 2 et 15% des patients admis en REA.

(N Engl J Med 1994)(Crit Care Med 1999)

-21,7% à l'admission et 88,9% àJ3 sans prévention

(Eddleston JM et al CCM,1994)

-Prolonge le séjour et augmente la mortalité

(48,5% vs 9,1% à gravité équivalente)

(N Engl J Med 1994)

(Intensive Care Med 2013)

Ulcère de stress contexte

-gastrique dans 50-75%

-Lésions superficielles et peu inflammatoires

-Souvent asymptomatique

-Gravité liée à la présence d'un saignement:

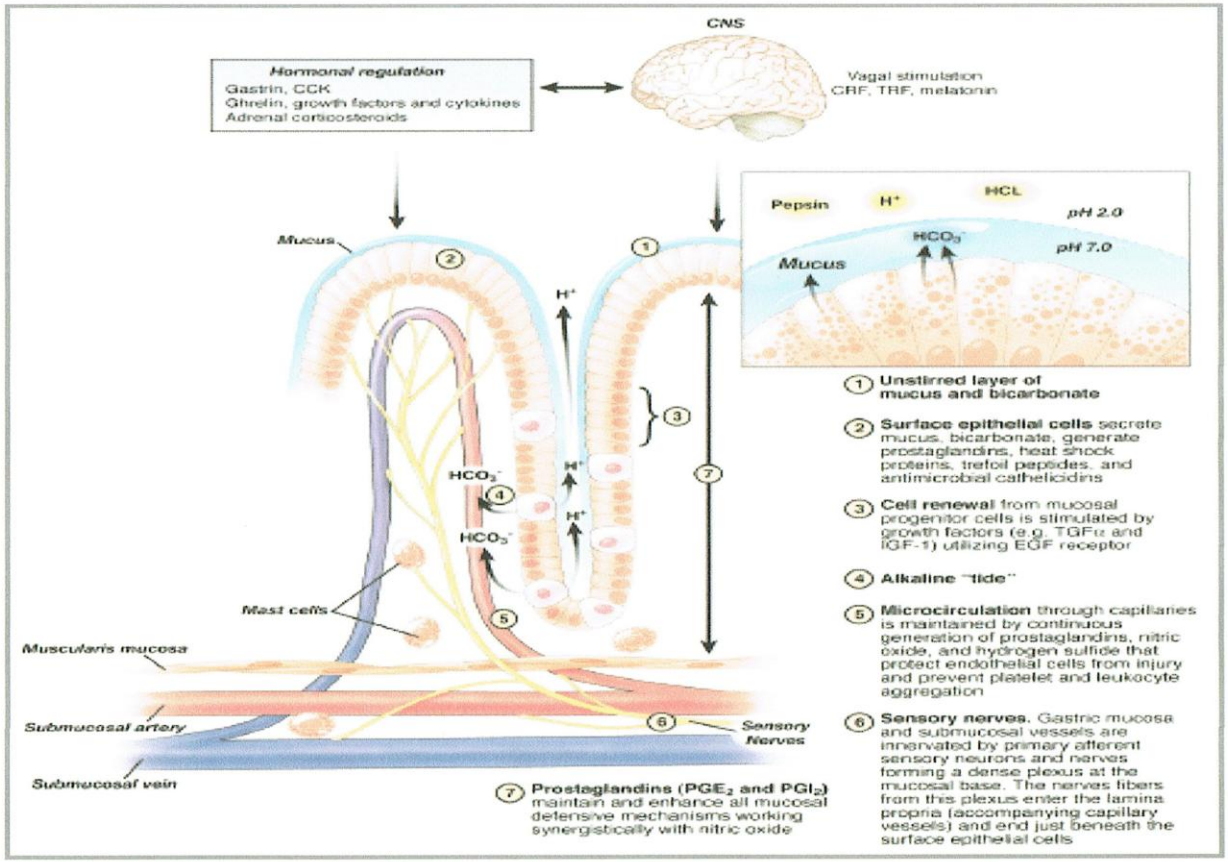
-Occulte, cliniquement évident ou cliniquement important avec trouble hémodynamique

(Ann Int Med 1994)

-Prévention =gold standard

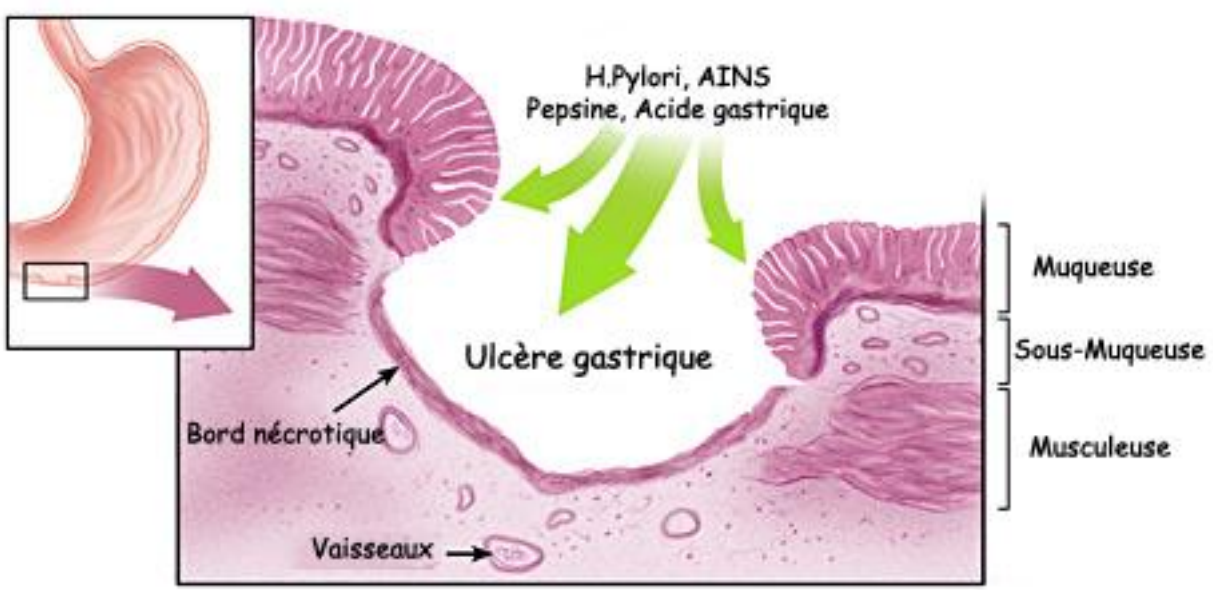
(Intensive care Med 2008)

Ulcère de stress
Physiologie fonctionnelle



Laine L. et al Gastroenterology 2008

Ulcère de stress
Physio-pathologie simple



Ulcère de stress
Physio-pathologie simple

-<u>les facteurs protecteurs:</u>

-la sécrétion de **Prostaglandines**, qui stimule la production de Bicarbonate et augmenter le flux sanguin

-la production **de mucus** de surface

-**l'intégrité** de l'épithélium de surface

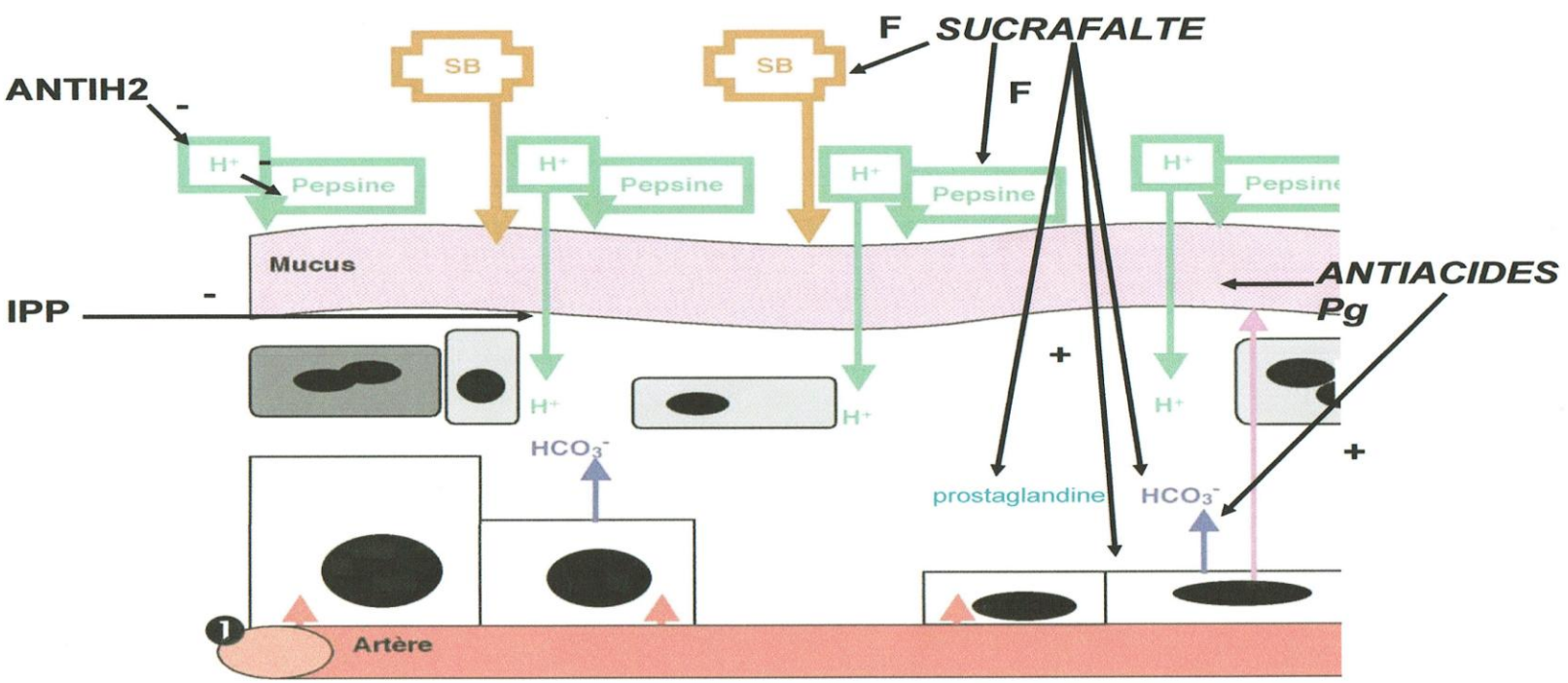
-**la vascularisation** de la muqueuse

Ulcère de stress prévention

TTT PREVENTIF MEDICAMENTEUX

1. ANTISECRETOIRES

2. ANTIACIDES



Ulcère de stress prévention

Table 3.—Randomized Trials of Stress Ulcer Prophylaxis*

Comparison	No. of Trials	Common Odds Ratio (95% Confidence Interval)
Antacids vs placebo/control		
Overt bleeding	7	0.66 (0.37-1.17)
Clinically important GI bleeding	3	0.35 (0.09-1.41)
Mortality rate	4	1.42 (0.82-2.47)
Histamine$_2$-receptor antagonists vs placebo/control		
Overt bleeding	20	0.58 (0.42-0.79)†
Clinically important GI bleeding	10	0.44 (0.22-0.88)
Pneumonia	8	1.25 (0.78-2.00)
Mortality rate	15	1.15 (0.86-1.53)
Histamine$_2$-receptor antagonists vs antacids		
Overt bleeding	16	0.56 (0.37-0.84)
Clinically important GI bleeding	10	0.86 (0.46-1.59)
Pneumonia	3	1.01 (0.65-1.57)
Mortality rate	14	0.89 (0.66-1.21)
Sucralfate vs placebo/control		
Overt bleeding	3	0.58 (0.34-0.99)
Clinically important GI bleeding	1	1.26 (0.12-12.87)
Pneumonia	2	2.11 (0.82-5.44)
Mortality rate	4	1.06 (0.67-1.67)
Sucralfate vs antacids		
Overt bleeding	10	0.97 (0.62-1.51)
Clinically important GI bleeding	5	1.49 (0.42-5.27)
Pneumonia	6	0.80 (0.56-1.15)
Mortality rate	11	0.73 (0.54-0.97)
Sucralfate vs histamine$_2$-receptor antagonists		
Overt bleeding	12	0.89 (0.63-1.27)
Clinically important GI bleeding	4	1.28 (0.27-6.11)
Pneumonia	11	0.78 (0.60-1.01)
Mortality rate	11	0.83 (0.62-1.09)

Ulcère de stress prévention

Comparison of Omeprazole and Ranitidine
for Stress Ulcer Prophylaxis
LEVY 1997 *Digestive Diseases and Sciences,*

TABLE 2. RISK FACTORS FOR CLINICALLY IMPORTANT BLEEDING*,†

	Ranitidine	*Omeprazole*
Burr		0
Coa		5
Acut		0
Majo		3
Acute renal failure	6	4
Respiratory failure	27	22
Sepsis	8	5
Shock	10	10
Trauma	11	5

TABLE 3. CLINICAL OUTCOMES*

	Ranitidine	*Omeprazole*	P
Stress ulcer bleed	11 (31%)	2 (6%)	<0.05
Nosocomial pneumonia	5 (14%)	1 (3%)	NS

* The risk factor distribution was similar in the two study groups Respiratory failure was the most common risk factor in both study groups. A few more patients with major neurologic insult. major surgery, or trauma were randomly assigned to receive ranitidine.

† $P = 0.013$.

Ulcère de stress prévention

-plusieurs études:

IPP>> que antiH2> succralfate

-effets secondaires(pneumonie,clostridium):

succralfate<antiH2<IPP

-en pratique:

antiH2 est le plus utilisé

IPP type pantoprazole 40mg est de plus en plus utilisé

Succralfate peu utilisé en Belgique

Donc…

Donc…

FAUT - IL TRAITER ?

Fagon, Intensive Care Medecine 2003 :

Etude observationnelle.
Prophylaxie vs non prophylaxie sur 2 périodes

Cause of bleeding	Prophylaxis (*n*=736)	No prophylaxis (*n*=737)
Overt gastrointestinal bleeding	1.9 (0.9–2.9)	1.6 (0.7–2.5)
Clinically significant gastrointestinal bleeding	1.4 (1.5–2.2)	1.1 (0.3–1.8)
Confirmed extradigestive bleeding	4.6 (3.1–6.1)*	9 (7–11)
Probable extradigestive blood loss	2.2 (1.2–3.2)	3 (1.8–4.2)

Kantorova, Hepatogastroenterology 2004 :

Etude monocentrique contrôlée vs placebo
n = 287 avec 4 bras
Patients sous VM ou avec coagulopathie

	Oméprazole n = 72	Famotidine n = 71	Sucralfate n = 69	Control n = 75	
HD importante	1 (1%)	2 (3%)	3 (4%)	1 (1%)	ns

Intensive Care Med (2014) 40:11–22
DOI 10.1007/s00134-013-3125-3

SYSTEMATIC REVIEW

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Stress ulcer prophylaxis versus placebo or no prophylaxis in critically ill patients

A systematic review of randomised clinical trials with meta-analysis and trial sequential analysis

Received: 30 July 2013
Accepted: 25 September 2013
Published online: 19 October 2013

Systematic review registration
The International Prospective Register of Systematic Reviews (PROSPERO), No. CRD42013004142.

Electronic supplementary material
The online version of this article (doi:10.1007/s00134-013-3125-3) contains supplementary material, which is available to authorized users.

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Abstract *Purpose:* To assess the effects of stress ulcer prophylaxis (SUP) versus placebo or no prophylaxis on all-cause mortality, gastrointestinal (GI) bleeding and hospital-acquired pneumonia in adult critically ill patients in the intensive care unit (ICU). *Methods:* We performed a systematic review using meta-analysis and trial sequential analysis (TSA). Eligible trials were randomised clinical trials comparing proton pump inhibitors or histamine 2 receptor antagonists with either placebo or no prophylaxis. Two reviewers independently assessed studies for inclusion and extracted data. The Cochrane Collaboration methodology was used. Risk ratios/relative risks (RR) with 95 % confidence intervals (CI) were estimated. The predefined outcome measures were all-cause mortality, GI bleeding, and hospital-acquired pneumonia. *Results:* Twenty trials ($n = 1{,}971$) were included; all were judged as having a high risk of bias. There was no statistically significant difference in mortality (fixed effect: RR 1.00, 95 % CI 0.84–1.20; $P = 0.87$; $I^2 = 0$ %) or hospital-acquired pneumonia (random effects: RR 1.23, 95 % CI 0.86–1.78; $P = 0.28$; $I^2 = 19$ %) between SUP patients and the no prophylaxis/placebo patients. These findings were confirmed in the TSA. With respect to GI bleeding, a statistically significant difference was found in the conventional meta-analysis (random effects: RR 0.44, 95 % CI 0.28–0.68; $P = 0.01$; $I^2 = 48$ %); however, TSA (TSA adjusted 95 % CI 0.18–1.11) and subgroup analyses could not confirm this finding. *Conclusions:* This systematic review using meta-analysis and TSA demonstrated that both the quality and the quantity of evidence supporting the use of SUP in adult ICU patients is low. Consequently, large randomised clinical trials are warranted.

Keywords Stress ulceration · Gastrointestinal bleeding · All-cause mortality · Meta-analysis · Trial sequential analysis · Stress ulcer prophylaxis

Introduction

Critically ill patients are at risk of stress-related gastrointestinal (GI) bleeding [1]. The reported incidence of GI bleeding in the intensive care unit (ICU) ranges from 2 to 15 %, however this data derives from research published 15–20 years ago [2, 3]. Intensive care practice has changed substantially over recent decades and,

This systematic review using meta-analysis and TSA demonstrated that both the quality and the quantity of evidence supporting the use of SUP in adult ICU patients is low. Consequently, large randomised clinical trials are warranted.

Prévention ulcère de stress
Risque de pneumonie?

Table 3

Community-acquired pneumonia based on proton pump inhibitor exposure

PPI exposure	Case patients	Control participants	Odds Ratio	*P* value
No PPI exposure	73 187	777 626	1	-
No PPI exposure in 30 d	3424	19 215	0.95	0.05
Current PPI exposure	3455	10 031	1.02	0.48
< 1.5 DDD	3056	9126	1	0.94
> 1.5 DDD	399	905	1.23	0.01
Duration of PPI Use (d)				
< 2	64	54	6.53	< 0.001
< 7	124	148	3.8	< 0.001

Prévention ulcère de stress
Risque de pneumonie?

AJGE 2009

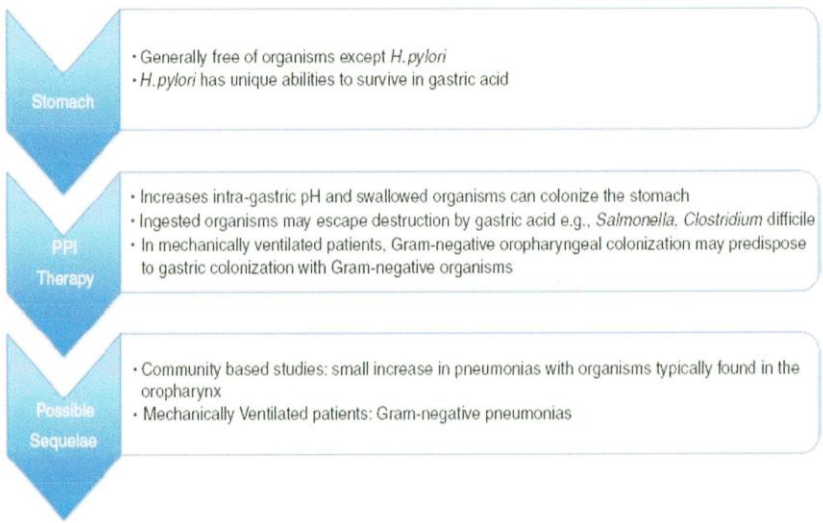

Figure 1. Potential sequence of events that may lead to pneumonia in patients taking a proton pump inhibitor (PPI).

PharmacoEconomics (2014) 32:5–13
DOI 10.1007/s40273-013-0119-5

REVIEW ARTICLE

Use of Proton Pump Inhibitors for the Provision of Stress Ulcer Prophylaxis: Clinical and Economic Consequences

Jeffrey F. Barletta · David A. Sclar

Published online: 25 November 2013

Abstract The provision of stress ulcer prophylaxis (SUP) for the prevention of clinically significant bleeding is widely recognized as a crucial component of care in critically ill patients. Nevertheless, SUP is often provided to non-critically ill patients despite a risk for clinically significant bleeding of roughly 0.1 %. The overuse of SUP therefore introduces added risks for adverse drug events and cost, with minimal expected benefit in clinical outcome. Historically, histamine-2-receptor antagonists (H2RAs) have been the preferred agent for SUP; however, recent data have revealed proton pump inhibitors (PPIs) as the most common modality (76 %). There are no high quality randomized controlled trials demonstrating superiority with PPIs compared with H2RAs for the prevention of clinically significant bleeding associated with stress ulcers. In contrast, PPIs have recently been linked to several adverse effects including *Clostridium difficile* diarrhea and pneumonia. These complications have substantial economic consequences and have a marked impact on the overall cost effectiveness of PPI therapy. Nevertheless, PPI use remains widespread in patients who are at both high and low risk for clinically significant bleeding. This article will describe the utilization of PPIs for SUP and present the clinical and economic consequences linked to their use/overuse.

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Key Points for Decision Makers

- Proton pump inhibitors surpassed histamine-2-receptor antagonists (H2RAs) as the most common agent utilized for the provision of stress ulcer prophylaxis. Several studies have demonstrated excessive use of PPIs in patients at low risk for clinically significant bleeding, in whom the benefit is likely unrecognized and could be associated with significant economic waste.
- There are no high quality randomized controlled trials demonstrating superiority of PPIs versus H2RAs. Several studies have reported a strong association of intense acid suppression with infectious adverse effects such as pneumonia and *Clostridium difficile* diarrhea. These adverse effects are associated with costs that exceed US$14,000 per patient.
- The overall cost effectiveness of PPIs will be based on the incidence of clinically significant bleeding at baseline, the observed reduction in bleeding rates with therapy and the adverse effects that occur with their use. In settings where the incidence of bleeding is low (e.g., non-intensive care unit patients), it is doubtful that PPIs will be cost effective. In settings where the incidence of bleeding is high (e.g., mechanically ventilated patients), clinicians must balance the costs avoided through the prevention of bleeding with the costs accrued through the occurrence of adverse events.

1 Introduction

Proton pump inhibitors (PPIs) are widely used for the provision of stress ulcer prophylaxis (SUP) in critically ill patients. In a recent multicenter study, PPIs were selected in 76 % of patients who were administered acid suppressive medications

Prévention ulcère de stress
Coût?

-Coût des DCI (anti H2 <IPP)

5 amp de Zantac 8,37€

1 amp de Pantoprazol 8,90€

-Complications (pneumonie, colite à clostridium)

+ou-10.000€ / patient par séjour

polémique?

Daru et al
Published online Nov 27, 2012.
Stress ulcer prophylaxis in critically ill poisoned patient

Et Alors?

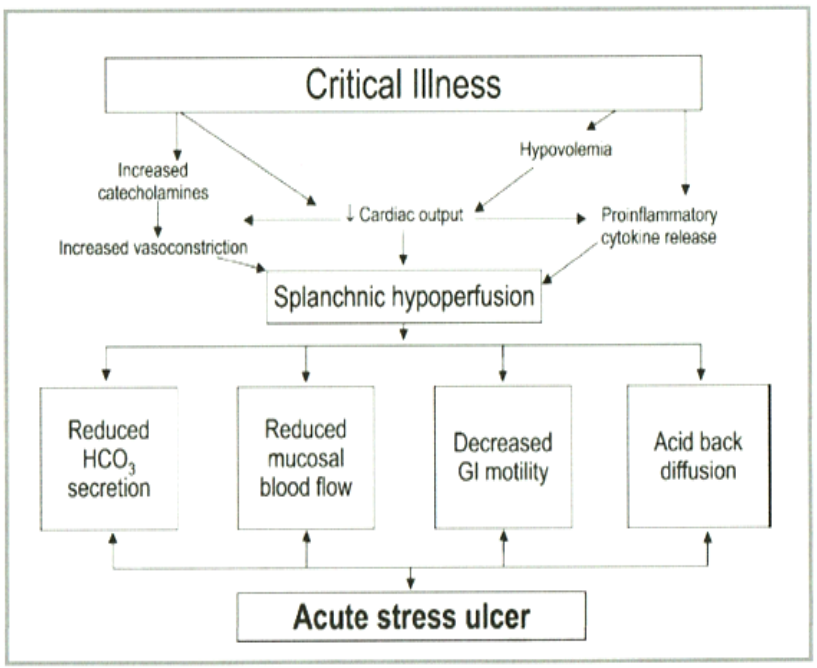
-ne plus faire de la prévention systématique?

-d'autre thérapie que les simples « anti-acides »?

-traiter le choc, la nutrition entérale ?

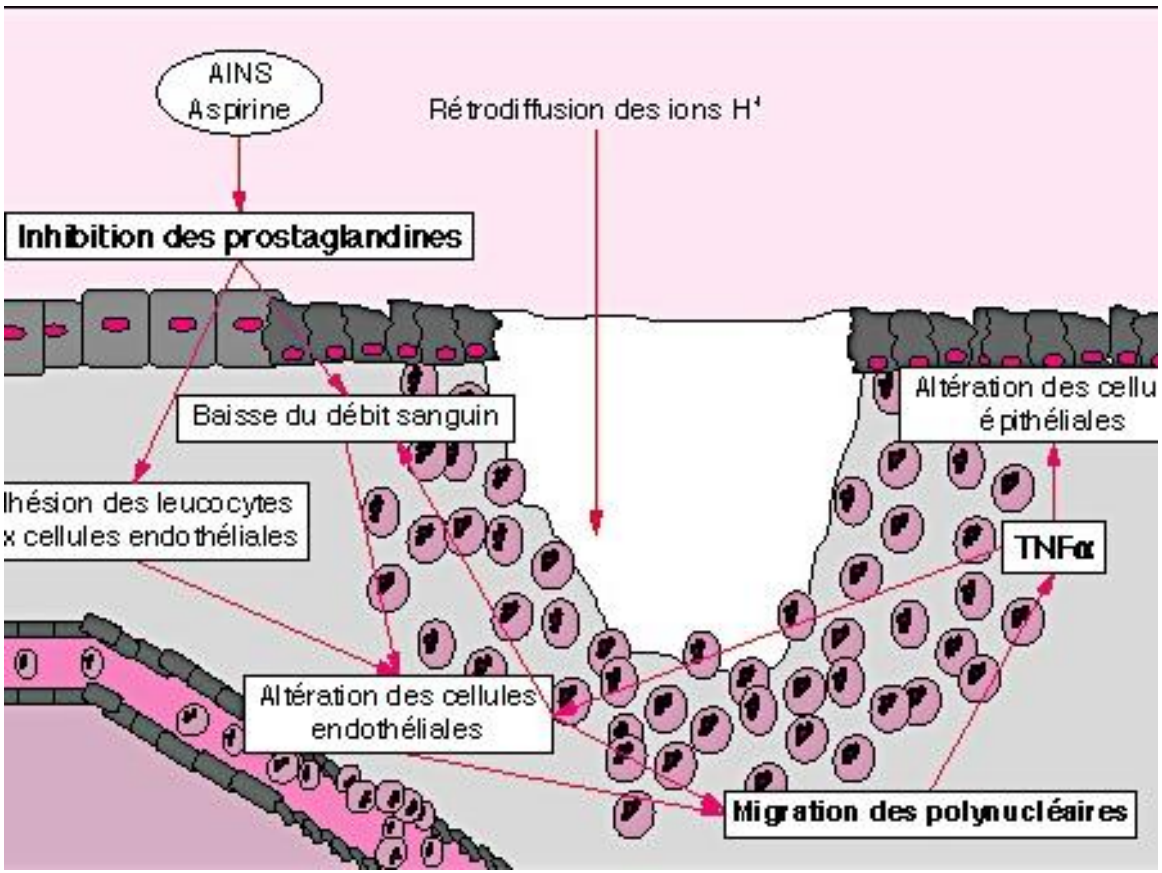
Stress-related mucosal disease

Gastrite aigue érosive



Stollman N et al JCC 2003

Prévention ulcère de stress
Physio-pathologie moins



Prévention de l'ulcère de stress

- En raison d'une meilleur prise en charge du choc; l'incidence est en diminution (2,1%)

- Plus d'hémorragie digestive haute aux soins intensifs (différent d'un ulcère de stress)

- >50% des lésions sont oesophagiennes, ou sur sonde gastrique avec une prise en charge spécifique

Prévention de l'ulcère de stress

-traitement optimale du bas débit, améliorer la perfusion splanchnique (NAD/Dobutamine)

(Critical Care Med 1999)

-Nutrition parentérale: pas de preuve formelle mais traitement adjuvent et son absence est un facteur de risque certain

(New Engl J Med 1996)

-

-éradication HP?Non

(Crit Care Med 2006)

Risk Factors for Gastrointestinal Bleeding in Critically Ill Patients

- 2252 patients inclus sur 1an, monocentrique
- 674 ont reçu une prophylaxie

Risk Factor	Simple Regression		Multiple Regression	
	Odds Ratio	P Value	Odds Ratio	P Value
Respiratory failure	25.5	<0.001	15.6	<0.001
Coagulopathy	9.5	<0.001	4.3	<0.001
Hypotension	5.0	0.03	3.7	0.08
Sepsis	7.3	<0.001	2.0	0.17
Hepatic failure	6.5	<0.001	1.6	0.27
Renal failure	4.6	<0.001	1.6	0.26
Enteral feeding	3.8	<0.001	1.0	0.99
Glucocorticoid administration	3.7	<0.001	1.5	0.26
Organ transplantation	3.6	0.006	1.5	0.42
Anticoagulant therapy	3.3	0.004	1.1	0.88

Cook D et al, NEJM 1994

Prévention de l'ulcère de stress

-Facteurs de risque :

- majeurs:
  - ventilation mécanique>48%,
  - Coagulopathie
- mineurs:
  - PAS <80
  - IRA,IHC
  - TC,Trauma médullaire, brûlures>35%SC
  - Corticothérapie à haute dose.

Et Donc

-surveillance attentive des patients sans facteur de risque
-sélection des patients bénéficiant d'une prévention:
    -VM>48h
    -coagulopathie
 mais aussi les patients avec un risque d'hypoperfusion splanchnique
-Anti-H2 plutôt que IPP
-à envisager aussi:
-nutrition entérale précoce
-endoscopie précoce?

Merci de votre attention

Et

Vous pouvez poser vos questions

Faire connaître vos remarques…

Et

Puis réveiller discrètement ceux qui dorment

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