Optimal management of stress ulcer prophylaxis requires a concerted effort among all members of the healthcare team. This article presents an overview of the epidemiology and pathophysiology of stress-related mucosal disease (SRMD), medical management of SRMD, and the role of intensive care unit (ICU) nurses in improving the care of patients at risk for SRMD.

Definition of SRMD
SRMD encompasses 2 types of mucosal lesions: (1) stress-related injury, which is diffuse, superficial mucosal damage, and (2) discrete stress ulcers, which are deep focal lesions that penetrate the submucosa, most often in the body and fundal parts of the stomach. Stress-induced lesions that are preceded by mucosal congestion often lead to bleeding in focal areas and then eventually affect multiple areas of the upper gastrointestinal tract.

Epidemiology of SRMD
Gastroduodenal lesions are a common finding in the ICU. Within the first 24 hours after ICU admission, approximately 75% to 100% of critically ill patients have some endoscopic evidence of gastroduodenal or upper gastrointestinal lesions. Clinically significant bleeding, defined as gastroduodenal bleeding associated with clinically important complications (eg, hemodynamic compromise, need for blood transfusion, need for surgery), occurs in approximately 2% to 6% of ICU patients. Schuster et al found that 6% of patients in the ICU had overt bleeding (defined as any episode of coffee-ground emesis requiring lavage, hematemesis, or melena with or without a change in hemoglobin levels or hematocrit).

Of note, the criteria used to define bleeding in clinical studies vary widely (eg, guaiac-positive stool or nasogastric aspirate, overt hematemesis, or...
the need for a blood transfusion). In one study, the mortality rate in patients with endoscopic evidence of ulcers, bleeding, or both within 18 hours of admission to a medical ICU was 57% compared with 24% in patients with either a normal mucosa, only nonhemorrhagic erosions, or petechial changes (P < .03). About 50% to 77% of critically ill patients with gastrointestinal bleeding will die, typically of the underlying medical condition or of multiple organ failure.

### Etiology and Pathophysiology of SRMD

Both the etiology and pathophysiology of SRMD appear to be multifactorial and have not been fully elucidated. Ischemia and reperfusion are thought to cause the mucosal defenses to break down, resulting in mucosal injury and ulceration. The major factors of SRMD recognized to date include reduced blood flow, mucosal ischemia, hypoperfusion, and reperfusion injury. Under normal conditions, the integrity of the gastric mucosal is maintained by several factors, including the microcirculation and the mucus layer, which nourishes the mucus and eliminates hydrogen ions, oxygen radicals, and other potentially toxic substances found in the gut lumen. The mucus layer protects the epithelial mucosal surface from hydrogen ions (including acid) and other potentially harmful substances. It also traps bicarbonate ions secreted by the mucosa to neutralize hydrogen ions. Thus, lesions develop when the mucosal barrier is unable to block the harmful effects of hydrogen ions and oxygen radicals.

Gastric hypoperfusion causes the release of nitric oxide, the production of oxygen radicals, and the reduction of prostaglandin synthesis. At normal levels, nitric oxide synthase enhances gastric mucosal integrity by maintaining blood flow and perfusion in the gastric mucosa. Elevated levels of nitric oxide synthase cause reperfusion hyperemia and cell death, an enhanced inflammatory response, and gastric and small-bowel dysmotility. Increased production of oxygen radicals and a reduced ability to clear them also cause inflammation, cell death, and further release of damaging cytokines. In addition, gastric epithelial turnover is accelerated while mucosal repair mechanisms are impaired.

Prostaglandin synthesis is decreased by gastric hypoperfusion, as well as by bicarbonate and mucus secretion, allowing back diffusion of hydrogen ions and pepsin that damage the mucosa epithelial layer. Normally, the buffering effect of bicarbonate and the mucus layer keep pH neutral even though the pH in the gastric lumen is often between 1.5 and 1.7. Additionally, upper gastrointestinal motility is slowed, a situation that reduces stomach emptying. This reduction in gastric emptying leads to prolonged exposure of the poorly defended mucosa to gastric acid, thus increasing the risk of ulceration.

Peripheral oxygen saturation levels are not an indicator of gastromucosal perfusion. In one study, critically ill patients with sepsis who required mechanical ventilation had approximately 50% less blood flow in the upper gastrointestinal tract than did patients who were undergoing elective endoscopy. Both critically ill and control patients, however, had normal peripheral oxygen saturation levels (Table 1).

### Risk Factors for Gastrointestinal Bleeding

In a landmark, prospective, multicenter cohort investigation (N = 2252), Cook et al studied the potential risk factors for stress ulceration in the ICU and the incidence of clinically important gastrointestinal bleeding. Clinically important gastrointestinal bleeding was defined as overt bleeding (in the absence of other causes) complicated by one of the following factors within 24 hours after the onset of bleeding:

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**Table 1** Gastrointestinal hypoperfusion in the intensive care unit

<table>
<thead>
<tr>
<th>Measure</th>
<th>Critically ill patients (n = 6)</th>
<th>Control patients (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure, mm Hg</td>
<td>83</td>
<td>95</td>
</tr>
<tr>
<td>Pulse, beats per minute</td>
<td>104</td>
<td>81</td>
</tr>
<tr>
<td>APACHE II score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admission</td>
<td>17.0</td>
<td>NA</td>
</tr>
<tr>
<td>Procedure day</td>
<td>16.8</td>
<td>NA</td>
</tr>
<tr>
<td>Fraction of inspired oxygen, %</td>
<td>55</td>
<td>21</td>
</tr>
<tr>
<td>Oxygen saturation, %</td>
<td>96.5</td>
<td>94.2</td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>10.3</td>
<td>14.1</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>2.0</td>
<td>1.1</td>
</tr>
<tr>
<td>Prior days on ventilator</td>
<td>12</td>
<td>NA</td>
</tr>
<tr>
<td>Complications</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; NA, not applicable. Reprinted from Spirt et al, with kind permission of Springer Science and Business Media.
Physicians were encouraged to withhold stress ulcer prophylaxis in all patients except those who had major burns, head injury, endoscopic or radiographic evidence of peptic ulcer or gastritis within the previous 6 weeks, organ transplants, or upper gastrointestinal bleeding 3 to 42 days before admission. Those patients received stress ulcer prophylaxis after admission to the ICU and were thus excluded from the study.\(^8\) The investigators found that respiratory failure requiring mechanical ventilation for longer than 48 hours and coagulopathy were strong independent risk factors for clinically important bleeding.\(^8\)

**Clinical Features of SRMD**

In critically ill patients requiring mechanical ventilation and use of a nasogastric tube, acute gastrointestinal bleeding may become clinically evident, with a bloody gastric aspirate or the appearance of material that looks like coffee grounds in the gastric aspirate. In patients without a nasogastric tube, hematemesis or melena may be the first sign of gastric bleeding. Unexplained hypotension or a decrease greater than 2 g/dL in hemoglobin level should also prompt evaluation for bleeding in the upper gastrointestinal tract.\(^23\)

**Medical Management of SRMD**

Because hypoperfusion appears to be an important factor in the development of SRMD, high-risk patients (eg, those receiving mechanical ventilation or who have coagulopathy) should be aggressively monitored and treated. In order to maintain hemodynamic optimization, frequent assessments should include determination of physiological, clinical (ie, blood pressure, skin color and appearance, skin warmth, and mental status), and laboratory (ie, hemoglobin and hematocrit levels and white blood cell counts) measures and serum electrolyte levels.

Local irritants (eg, nonsteroidal anti-inflammatory drugs or aspirin) should be avoided.\(^27\) Measures to improve hemodynamic parameters should restrict the use of vasopressors when possible because use of these agents can worsen ischemia of the gastrointestinal tract. Vasopressors do increase blood pressure, but at the expense of mesenteric perfusion.\(^24\)

If possible, early enteral nutrition should be considered in certain patients. The gastroprotective effect of enteral feedings is an area of continued debate. Overall, studies in which the effects of enteral nutrition on gastric bleeding risk were evaluated have had numerous shortcomings, including inadequate statistical power, concurrent use of pharmacological prophylaxis, lack of a consistent enteral nutrition regimen, and variable definitions of bleeding.\(^25\) In a retrospective analysis, Raff et al\(^26\) found that enteral feedings initiated within 12 hours of trauma were as effective as histamine 2 receptor antagonists (H\(_2\)RAs) and/or antacids for reducing the risk of clinically significant hemorrhage in the upper gastrointestinal tract (ie, hemoglobin reduction >3 g/dL, shock, or the need for blood transfusion or surgical intervention). In a multicenter, randomized trial comparing sucralfate with ranitidine, Cook et al\(^27\) also found that the risk of clinically important gastric bleeding was reduced in patients receiving enteral feedings. However, patients in that study were not randomized to receive or not receive only enteral feedings. Thus, the results may actually be an indica-

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**Respiratory failure requiring mechanical ventilation for longer than 48 hours and coagulopathy were strong independent risk factors for clinically important bleeding.**
tion that patients who tolerate enteral feedings are intrinsically less likely than patients who do not to have bleeding.27

Pharmacological Prophylaxis

The American Society of Health-System Pharmacists Commission on Therapeutics has developed guidelines for stress ulcer prophylaxis based on studies in which (1) clinically important bleeding was used as a study end point and (2) prophylaxis was compared with no prophylaxis. Stress ulcer prophylaxis is recommended for adults admitted to the ICU who2

- have coagulopathy,
- require mechanical ventilation for more than 48 hours,
- have a history of gastrointestinal ulceration or bleeding within 1 year before admission, or
- have at least 2 of the following risk factors: sepsis, ICU stay longer than 1 week, occult bleeding lasting 6 days or longer, and use of more than 250 mg hydrocortisone or the equivalent.

These recommendations do not apply to patients with single-system injuries such as head trauma, spinal cord injury, or thermal injury; patients with these injuries were excluded from studies in which subjects were randomized to receive prophylaxis or no prophylaxis.2 In general, few studies with clinically important bleeding as an end point have indicated significant differences between the medications used for prophylaxis. However, the sample sizes needed to detect clinically important bleeding, a relatively rare event, were insufficient to preclude a type II statistical error. Comparative studies that have shown substantial differences in bleeding rates between treatment groups have had unexpectedly high bleeding rates in one of the groups.2

Surveys28,30 indicate that approximately 86% of critically ill patients admitted to the ICU receive some form of stress ulcer prophylaxis. In 1995, when stress ulcer prophylaxis was first extensively evaluated, H2RAs were used 67% of the time.30 Sucralfate, a topically acting aluminum salt, was used in 24% of patients.30 In a more recent 2002 national survey of level I trauma centers, H2RAs and sucralfate were the preferred agents for stress ulcer prophylaxis in 71% and 25%, respectively, of institutions that had a preferred agent. In addition, omeprazole was the preferred agent at 3% of institutions.30 These data are changing with the introduction and increasing use of proton pump inhibitors (PPIs) in the ICU.

Histamine2 Receptor Agonists

H2RAs act by decreasing gastric acid secretion through reversible, competitive inhibition of histamine-stimulated acid secretion and are effective in reducing basal acid production. However, because gastrin and acetylcholine provide alternative pathways to the stimulation of acid secretion, acid suppression with H2RAs is incomplete, and H2RAs appear to be less effective than PPIs in preventing bleeding of stress ulcers.31

In addition to the lack of potency of H2RAs, dosing can be difficult because of the nonlinear kinetics and short duration of action; patients often require 3 or 4 doses a day. Tolerance develops with H2RAs as early as 72 hours after administration, a characteristic that may make these agents less effective in situations in which intragastric pH levels must be sustained for a long period.30 However, the clinical significance of this finding has not been shown. Furthermore, evidence of the clinical benefit of H2RAs exists in the form of a landmark study involving critically ill patients who required mechanical ventilation. In that study,33 significantly lower rates of clinically important gastrointestinal bleeding were reported among patients who received ranitidine than among patients who received sucralfate.

Drug interactions can occur with H2RAs, particularly with cimetidine. Cimetidine decreases clearance of warfarin, theophylline, phenytoin, lidocaine, and clarithromycin. Ranitidine interactions, though less frequent, can occur with nifedipine and cyclosporine. An additional significant disadvantage of H2RAs is the risk of neuropsychiatric effects.30 Nevertheless, H2RAs have been the agents of choice for stress ulcer prophylaxis, primarily because of their availability in an intravenous formulation.

Sucralfate Sucralfate, although less widely used than H2RAs for stress ulcer prophylaxis, is another option.30,36 It coats the gastric mucosa and creates a thin, protective layer between the mucosa and the gastric acid in the lumen.30 H2RAs and sucralfate have comparable effectiveness for preventing stress ulcers, at 10% to 25% and at 15% to 40%, respectively.11 Some researchers14,35 found an association between increased gastric pH and growth of gram-negative organisms in samples obtained via bronchoalveolar lavage, as well as an increased risk of nosocomial pneumonia in patients with higher gastric
pH. For this reason, sucralfate, which does not inhibit or neutralize gastric acid, was considered an attractive option. Cook et al., however, found no significant differences in the rates of ventilator-associated pneumonia, durations of ICU stay, or mortality rates between critically ill patients receiving ranitidine and those receiving sucralfate.

In a more recent randomized controlled trial, intravenous omeprazole 40 mg daily was compared with intravenous famotidine 40 mg twice a day, sucralfate 1 g in suspension 4 times a day, and intravenous placebo. The incidence of nosocomial pneumonia did not differ significantly among the 4 groups; however, gastric colonization was significantly greater in the groups that received agents that increased pH \( (P<.05) \). Sucralfate is available in solution and suspension and can be adminis-

<table>
<thead>
<tr>
<th>Study/treatments</th>
<th>No. of patients</th>
<th>% with bleeding</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Martin et al,37</td>
<td>65</td>
<td>14</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>H2RA (cimetidine)</td>
<td>66</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>66</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Zimmer et al,38</td>
<td>100</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>H2RA</td>
<td>100</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Antacid</td>
<td>100</td>
<td>5</td>
<td>NS vs no treatment &lt;.005 vs no treatment .005 vs cimetidine</td>
</tr>
<tr>
<td>No treatment</td>
<td>100</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Weigelt et al,39</td>
<td>61</td>
<td>5</td>
<td>NA</td>
</tr>
<tr>
<td>H2RA (cimetidine)</td>
<td>16</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Antacid</td>
<td>124</td>
<td>4.8</td>
<td>NA</td>
</tr>
<tr>
<td>Kingsley,40</td>
<td>125</td>
<td>8.8</td>
<td>NA</td>
</tr>
<tr>
<td>H2RA (cimetidine)</td>
<td>100</td>
<td>5</td>
<td>NS vs placebo</td>
</tr>
<tr>
<td>Antacid</td>
<td>100</td>
<td>5</td>
<td>NS vs placebo</td>
</tr>
<tr>
<td>Ben-Menachem et al,9</td>
<td>100</td>
<td>5</td>
<td>NS vs placebo</td>
</tr>
<tr>
<td>H2RA (cimetidine)</td>
<td>100</td>
<td>5</td>
<td>NS vs placebo</td>
</tr>
<tr>
<td>Sucralfate</td>
<td>100</td>
<td>5</td>
<td>NS vs placebo</td>
</tr>
<tr>
<td>Placebo</td>
<td>100</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Levy et al,31</td>
<td>596</td>
<td>1.7</td>
<td>.02 vs H2RA</td>
</tr>
<tr>
<td>H2RA (ranitidine)</td>
<td>604</td>
<td>3.8</td>
<td>&lt;.005 vs H2RA</td>
</tr>
<tr>
<td>Sucralfate</td>
<td>35</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>32</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>PPI (omeprazole)</td>
<td>38</td>
<td>10.5</td>
<td></td>
</tr>
<tr>
<td>Azevedo et al,41</td>
<td>38</td>
<td>9.3</td>
<td></td>
</tr>
<tr>
<td>H2RA (ranitidine)</td>
<td>32</td>
<td>0</td>
<td>NS vs H2RA and</td>
</tr>
<tr>
<td>Sucralfate</td>
<td>38</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Hastings et al,42</td>
<td>51</td>
<td>4</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>Antacid</td>
<td>49</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>51</td>
<td>4</td>
<td>&lt;.005</td>
</tr>
</tbody>
</table>

Table 2: Results of controlled trials of stress ulcer prophylaxis in high-risk patients

Findings from recent trials with high-risk patients suggest that administration of proton pump inhibitors is also an effective method of preventing stress ulcers. Findings from recent trials with high-risk patients (ie, those with coagulopathy or respiratory failure) suggest that administration of PPIs is also an effective method of preventing stress ulcers.9,31,33,37-42 (Table 2). Because PPIs inhibit the final step in acid production (the generation of gastric hydrogen ions via hydrogen potassium adenosinetriphosphatase), they provide long-lasting suppression of acid secretion. In a clinical trial in which high-risk patients were given intravenous ranitidine administered through a nasogastric tube, although administration via a tube can be labor intensive. Sucralfate decreases the absorption of ciprofloxacin, norfloxacin, theophylline, tetracycline, phenytoin, cimetidine, ranitidine, l-thyroxine, ketoconazole, and digoxin. Use of sucralfate should be avoided in patients with compromised renal function to avoid aluminum accumulation and poisoning.36
ing whereas only 6% of those given omeprazole had bleeding ($P = .01$). In recent open-label studies ($n=60$, $n=75$), no high-risk patients experienced bleeding while taking a PPI. These small-scale studies suggest that PPIs are effective for prophylaxis against stress ulcers. Additionally, their rapid onset of action, linear kinetics, longer duration of action, and lack of observed tolerance suggest that PPIs may have pharmacokinetic advantages relative to H2RAs.31,32,45 Furthermore, PPIs have been associated with relatively few drug interactions (Table 3). Additionally, PPIs are not renally eliminated, so complications associated with their use in patients with renal dysfunction are minimal.50-54

PPIs can be given via a nasogastric tube in patients unable to take medications by mouth, although the process is both time and labor intensive. For example, 30 minutes must be allotted for dissolution when omeprazole is administered via nasogastric suspension. With simplified omeprazole, lansoprazole, and pantoprazole bicarbonate suspensions, effectiveness depends on several factors: amount of the diluent, agitation, preparation time, site of delivery, size of the tube, and adherence to the syringe.55 A new immediate-release form of omeprazole recently approved in the United States for use in preventing bleeding of stress ulcers may ease enteral administration.56 However, slow gastric emptying may impair absorption and delivery of drugs administered via nasogastric tube.

With the availability of intravenous pantoprazole, and more recently intravenous lansoprazole, caregivers now have the option of an intravenous PPI. Although studies have suggested superiority of oral PPIs over H2RAs for prevention of stress ulcers, few studies have examined intravenous PPIs. A dose-response study57 is under way with intravenous pantoprazole in the ICU, and preliminary data indicate that the target pH value for preventing stress ulcers ($\geq 4$) can be consistently reached with this agent. When oral medications are tolerated, an intravenous PPI should be switched to an oral PPI preferably of the same compound, because intravenous formulations of both pantoprazole and lansoprazole are equipotent to the oral formulations.58

### Table 3  Proton pump inhibitors and drug interactions

<table>
<thead>
<tr>
<th>Drug</th>
<th>Omeprazole</th>
<th>Esomeprazole46</th>
<th>Lansoprazole</th>
<th>Rabeprazole47</th>
<th>Pantoprazole48</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>Cl $^{48}$</td>
<td>Cl $^{48}$</td>
<td>Cl $^{48}$</td>
<td>Cl $^{48}$</td>
<td>Cl $^{48}$</td>
</tr>
<tr>
<td>Diazepam</td>
<td>Cl $^{48,49}$</td>
<td>Cl $^{48}$</td>
<td>Cl $^{48}$</td>
<td>Cl $^{48}$</td>
<td>Cl $^{48}$</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Cl $^{48}$</td>
<td>Cl $^{48}$</td>
<td>Cl $^{48}$</td>
<td>Cl $^{48}$</td>
<td>Cl $^{48}$</td>
</tr>
<tr>
<td>Theophylline</td>
<td>Cl $^{50}$</td>
<td>Cl $^{48,51}$</td>
<td>Cl $^{48}$</td>
<td>Cl $^{48}$</td>
<td>Cl $^{48}$</td>
</tr>
<tr>
<td>Digoxin*</td>
<td>Cl $^{48}$</td>
<td>Cl $^{48}$</td>
<td>Cl $^{48}$</td>
<td>Cl $^{48}$</td>
<td>Cl $^{48}$</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>AUC $^{52}$</td>
<td>AUC $^{52}$</td>
<td>AUC $^{52}$</td>
<td>AUC $^{52}$</td>
<td>AUC $^{52}$</td>
</tr>
</tbody>
</table>

*Digoxin interactions may be due to decreased digoxin acid hydrolysis, increased absorption in the stomach, or an interaction with p-glycoprotein. These digoxin interactions appear to be unrelated to alterations in metabolism and would be expected to occur with all proton pump inhibitors.50,54

Abbreviations: AUC, area under the curve; Cl, clearance; C$_{\text{max}}$, maximum concentration; NT, not tested; t$_{1/2}$, half-life. Dashes indicate no interaction.
yields a solution that is stable at room temperature for 24 hours, whereas a solution made by using 50 mL of 5% dextrose in water must be administered within 12 hours. Administration of intravenous lan-
soprazole requires the use of an in-
line filter, and the product should be infused over 30 minutes. Other Prophylaxis Options
Antacids are also used for stress ulcer prophylaxis and, like sucralfate, are available in solution and suspension. They must be administered to patients every 1 to 2 hours, however, and pH levels must be constantly monitored, a situation that makes antacids cumbersome and time-consuming for nurses to administer, particularly in ICUs. Antacids have numerous adverse effects, including diarrhea, flatulence, headache, nausea, hepatic dysfunction, electrolyte abnormalities, constipation, and altered drug absorption. As a result, antacids are rarely used to prevent stress ulcers. Prostaglandin analogs such as misoprostol are ineffective for prophylaxis.

Discontinuation of Prophylaxis
Many clinicians continue stress ulcer prophylaxis until patients begin an oral diet or are transferred from the ICU. However, in a survey by Bar-
letta et al, 39% of institutions reported that approximately 50% of patients who received stress ulcer prophylaxis in the ICU were continu-
ing treatment after being discharged to non-ICU settings. Indirect evidence, such as mention of routine discontinu-
tion of prophylaxis in published studies, suggests that most experts consider the risk of clinically impor-
tant bleeding outside the ICU to be too low to justify continued prophy-
laxis. Each patient should be indi-
vidually assessed for risk factors. Cost Issues
Medications used to prevent stress ulcers are associated with costs and adverse events that should be considered when deter-
mining the duration of treatment. Cash estimated that 30 patients at high risk for clinically important upper gastrointestinal bleeding (defined as those receiving prolonged mechanical ventilation or with significant coagulopathy) would need to receive prophylaxis to prevent 1 episode of bleeding. In contrast, more than 900 patients who do not meet these criteria would need to receive prophylaxis to prevent 1 episode of bleeding. These findings suggest that stress ulcer prophylaxis is appropriate for patients at high risk but not for those at lower risk for clinically important bleeding in the upper part of the gastrointestinal tract.

Results of several studies indicate that practice guidelines for stress ulcer prophylaxis can have a positive economic impact without increasing the risk for gastrointesti-
nal bleeding. In the first study, implementation of guidelines limiting prophylaxis with cimetidine or sucralfate to trauma patients at risk for clinically important gastrointesti-
nal bleeding resulted in an 80% decrease in drug cost without an increase in bleeding. In another study, the appropriateness of prophy-
laxis (number of days meeting guideline criteria) along with the incidence of gastrointestinal bleeding and ventilator-associated pneu-
monia, drug costs, length of stay in the ICU, and duration of ventilator use were evaluated. The implementa-
tion of guidelines for stress ulcer prophylaxis increased appropriateness from 76% to 91% and decreased mean daily medication costs from $2.50 to $1.30 (Canadian). In a recent study, practice guidelines that included a treatment algorithm with famotidine and sucralfate reduced the mean percentage of days of inap-
propriate prophylaxis in a trauma ICU from 50% to 25% without compromising patients’ care (P = .005).

Acquisition costs of PPIs vary among institutions as a result of purchasing contracts and in some cases may approximate the cost of an H2RA. Although the pharmaco-
economic data on the use of PPIs for stress ulcer prophylaxis are limited, Schupp et al reported that PPIs can be cost-effective relative to H2RAs. In their study, no patients in the PPI group experienced treatment failure; whereas 5 patients in the cimetidine group did.

Future Therapeutic Interventions
As discussed, the underlying cause of SRMD is local hypoperfusion of the mucosa in the upper part of the gastrointestinal tract. Thus, early new techniques for both detecting and treating hypofusion in ICU patients are needed. A device inserted in a nasogastric tube that could continuously measure local blood flow would help detect gut ischemia. ICU nurses and physicians armed with improved methods of detecting local ischemia must then be able to treat the ischemia. Thus, new medications that selectively improve gut hemo-
dynamic parameters are necessary. Although low-dose dopamine and dobutamine are thought to improve gastrointestinal perfusion, this assumption has never been proved. Additional long-lasting agents that control pH without the development
of tolerance are important. Thus far, tolerance does not appear to develop in patients taking PPIs, but more long-term studies are needed.

Nursing Considerations

Critical care nurses with knowledge of the pathogenesis, risk factors, and prophylaxis of stress-related bleeding can have a dramatic impact on outcomes. When a new patient is either admitted or transferred to the ICU, nurses must assess the patient for any risk factors for SRMD (ie, mechanical ventilation >48 hours, coagulopathy, severe burns, multiple organ failure, neurological trauma, sepsis/septic shock, and the administration of corticosteroids). Once this assessment has been done, stress ulcer prophylaxis should be considered and then discussed with physicians. Important treatment options include early and sufficient fluid administration, aggressive stabilization of hemodynamic status, prevention or treatment of infection, adequate antisecretory therapy, and enteral nutrition. Feedings should be started early in appropriate patients because oral or enteral nutrition may improve overall outcome. Because they are keenly aware of possible limitations in the means of administering medications to a particular patient, nurses can discuss the available routes and methods of medication administration with physicians.

Once a particular regimen is started, nurses can provide continuous assessments of patients at risk for stress ulcers. Hemodynamic and laboratory values should be monitored so the ICU team can be alerted to any abnormalities. Continued assessment of renal function is necessary in patients receiving sucralfate or H2RAs. For patients receiving agents that do not affect gastric pH, such as sucralfate, monitoring is limited to detection of potential adverse events and signs of gastrointestinal bleeding. However, pH monitoring may be appropriate for patients receiving agents that neutralize gastric acid, especially antacids. Monitoring gastric pH is not routine in the clinical setting and remains controversial. In one survey, 29% of institutions reported routine use of pH paper, a pH sensor, or gastric tonometry for measuring gastric pH. In addition, pH paper and sensors do not appear to be interchangeable; the hand-held pH meters appear to be more accurate than pH paper in critically ill patients with pH readings of 4.0 or less. Endoscopy is considered the reference standard for accurate diagnosis of stress-related ulcers, although it is invasive.

Because of the need for polypharmacy in critically ill patients, nurses must also remain cognizant of potential drug interactions, encompassing both dose adjustments and serious adverse effects. Common adverse effects should be well known, so that early signs of an adverse reaction can be recognized and culpable medications can be discontinued expeditiously. Patients must also be monitored for the early signs of gastrointestinal bleeding: hypotension, tachycardia, hematemesis, hematochezia, blood material that looks like coffee grounds in the nasogastric tube, melena, or progressive anemia.

Last, nurses should be aware that patients at risk for stress-related bleeding must be routinely assessed for aspiration pneumonia because of an overall gut dysmotility, particularly with the use of antacids. Signs include rales, wheezing, decreased breath sounds, tachypnea, tachycardia, fever, hypoxemia, and changes on radiographs. In intubated patients, methods of detecting silent aspiration include checking tracheal aspirates for glucose with oxidant reagent strips.

Conclusions

Increased knowledge of risk factors and improved ICU care have decreased the incidence of stress-related bleeding. Intravenous pantoprazole appears to be effective for stress ulcer prophylaxis. Prolonged mechanical ventilation and coagulopathy are the 2 factors associated with the highest risk of stress-related bleeding. Armed with this information and effective treatments, caregivers should be able to determine which patients are at high risk for stress-related bleeding and whether prophylactic therapy is indicated.

ICU nurses play a vital role in the care of patients at risk for stress ulcers. They have the first-line knowledge of each patient’s risks and clinical condition. They should be able to recognize high-risk patients and to evaluate treatment options with physicians. This discussion should regard hemodynamic status, fluids, and pharmacology, as well as prophylactic therapy. Evidence to support the use of PPIs in these patients is increasing, and PPI use is an important topic for physicians and nurses to discuss.

Acknowledgment
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References
57. Aris R, Karlstadt R, Paoletti V, Blatcher D, McDevitt J. Intermittent intravenous pantoprazole achieves a similar onset time to pH ≥4.0 in ICU patients as continuous infusion H2-receptor antagonist, without tolerance. Paper presented at: 66th Annual Scientific Meeting of the American College of Gastroenterology; October 2001; Las Vegas, Nev.
Learning objectives:
1. Discuss the etiologies and pathophysiology of stress-related mucosal disease (SRMD).
2. Identify risk factors for gastrointestinal bleeding.
3. Discuss current therapeutic interventions for SRMD.

1. What percentage of patients admitted to the intensive care unit (ICU) have endoscopic evidence of gastrointestinal lesions within the first 24 hours?
   a. 50% to 75%
   b. 75% to 100%
   c. 25% to 75%
   d. 25% to 50%

2. Which one of the following is not a criterion used to define bleeding in clinical studies?
   a. Guaiac positive stool or nasogastric aspirate
   b. Overt hematemesis
   c. Need for blood transfusion
   d. High suspicion of bleeding

3. What was the mortality rate of patients with endoscopic ulcers or bleeding that developed within 18 hours of ICU admission?
   a. 15% to 35%
   b. 35% to 45%
   c. 45% to 55%
   d. 55% to 75%

4. Which of the following is not a major factor for development of stress-related mucosal disease (SRMD)?
   a. Altered mucosal defense
   b. Cigarette smoking
   c. Mucosal ischemia
   d. Reperfusion injury

5. Why do SRMD lesions develop in the gastrointestinal mucosa?
   a. The mucosal barrier is weakened by medications.
   b. The mucosal barrier is unable to block the harmful effects of hydrogen and oxygen radicals.
   c. The mucosal barrier secretes too much acid.
   d. The mucosal barrier is not affected by decreased blood flow.

6. Which of the following statements best describes increased risk for ulceration?
   a. Increased gastric emptying places mucosa at risk
   b. Medications that are given without food
   c. Reduced gastric emptying leads to increased exposure to gastric acid
   d. Increased pH

7. In Cook’s landmark study, criteria for clinically important gastrointestinal bleeding included overt bleeding and other complicating factors. Which one of the following was not a complicating factor?
   a. Increased systolic blood pressure of 30 mm Hg
   b. Decreased hemoglobin levels more than 2 g/dL
   c. Increased heart rate more than 20 beats per minute
   d. Decreased systolic blood pressure of 20 mm Hg

8. What 2 factors are strong independent risk factors for clinical important bleeding?
   a. Mechanical ventilation and renal failure
   b. Respiratory failure and liver failure
   c. Mechanical ventilation and coagulopathy
   d. Multiple trauma and coagulopathy

9. Which one of the following is not a sign of gastrointestinal bleeding?
   a. Hematemesis
   b. Melena
   c. Hypertension
   d. Hypotension (unexplained)

10. Which group of patients is not recommended for stress ulcer prophylaxis?
    a. Patients who are in the ICU for more than 24 hours
    b. Patients with coagulopathy
    c. Patients requiring mechanical ventilation more than 24 hours
    d. Patients with history of gastrointestinal bleeding

11. What percentage of patients admitted to the ICU receive some type of stress ulcer prophylaxis?
    a. 56%
    b. 66%
    c. 86%
    d. 37%

12. Which statement best describes how proton pump inhibitors work?
    a. Coat mucosal barrier
    b. Inhibit final step in acid production
    c. Block H2 receptors
    d. Inhibit oxygen availability for acid production

13. Which one of the following is not an important treatment option for SRMD?
    a. Early fluid administration
    b. Vasopressors to improve gastrointestinal blood flow
    c. Prevention of infection
    d. Enteral feeding

Test answers: Mark only one box for your answer to each question. You may photocopy this form.

1. a  2. a  3. a  4. a  5. a  6. a  7. a  8. a  9. a  10. a  11. a  12. a  13. a

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