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INSIDE

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Dealing with ICU Delirium

ABSTRACT & COMMENTARY

By David J. Pierson, Editor

Synopsis: *Delirium occurred in about one-third of patients in this study of a mixed medical-surgical ICU population. It was more frequent in more seriously ill patients, and also in those with hypertension, alcoholism, and the effects of sedative and analgesic drugs.*

Source: *Ouimet S, et al. Incidence, risk factors, and consequences of ICU delirium. Intensive Care Med. 2007;33:66-73.*

Ouimet and colleagues at Maisonneuve-Rosemont Hospital in Montreal studied 820 consecutive patients admitted to their mixed medical-surgical ICU to determine the incidence of delirium, factors associated with it, and its clinical consequences. The patients were adults who stayed in the ICU more than 24 hours and survived for at least 1 day. The mean APACHE II score on admission was 16.5, and 79% of the patients were mechanically ventilated. Delirium was assessed daily using the Intensive Care Delirium Screening Checklist (ICDSC), as previously reported by the same group[1] and as summarized in Table 1. Patients were considered to have delirium if the score on the 8-point assessment screen was 4 or higher.

After patients who remained comatose throughout their ICU stay (n = 56) were excluded, delirium occurred in 243 of 764 patients (31.8%), during a mean of 5.7±7 days of data collection per patient. Patients who developed delirium had an ICDSC score of 4 or higher for a mean of 38% of their ICU stay, and 10% of them remained delirious at ICU discharge.

Comparing patients with delirium with those who did not develop it according to the ICDSC, initial APACHE scores were higher (mean 18 vs 14, $p < 0.0001$), but there were no differences in age, sex, or diagnosis. Delirium occurred with equal frequency in medical and surgical patients, and was not more frequent in those with previous neurologic illness. However, it was statistically more frequent in patients with hypertension (odd ratio, 1.88, 95% confidence interval 1.3-2.6) and alcoholism (OR 2.03; 95% CI 1.26-3.25). Delirium was more likely in patients who received sedatives and analgesics when used to induce coma (OR 3.2, 95% CI 1.5-6.8) for procedures, but not when these drugs were used in other circumstances. Patients who developed delirium while in the ICU experienced higher ICU mortality (19.7% vs

Table 1

Intensive Care Delirium Screening Checklist.[1] Delirium is considered to be present when the score on the following 8 items, assessed each nursing shift, is 4 or higher.

1. Altered level of consciousness: coma (no response) or stupor (no response to loud voice and pain).
   - No response: **No score assigned**
   - Response only to intense and repeated stimulation: **No score assigned**
   - Response to mild or moderate stimulation: **1 point**
   - Normal wakefulness or sleep with easy arousal: **0 point**
   - Exaggerated response to normal stimulation: **1 point**
2. Inattention: difficulty following conversation or instructions; easy distraction: **1 point**
3. Disorientation: any obvious mistake in time, place, or person: **1 point**
4. Hallucination, delusion, or psychosis: **1 point**
5. Hyperactivity requiring sedation or restraints, or clinically important psychomotor slowing: **1 point**
6. Inappropriate speech or mood: **1 point**
7. Sleep/wake cycle disturbance: frequent spontaneous awakening; sleeping less than 4 hrs/night: **1 point**
8. Marked fluctuation in symptoms or in the manifestations of any of the above items from shift to shift: **1 point**

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10.3%) and overall hospital mortality (26.7% vs 21.4%), as well as longer average stays in both the ICU (11.5 vs 4.4 days) and in the hospital (18.2 vs 13.2 days).

COMMENTARY

Evidence is accumulating that delirium in ICU patients is an important and detrimental phenomenon. A number of studies have found associations between the development of delirium and increased morbidity and mortality as well as with increased lengths of stay in both ICU and hospital.[2] It stands to reason that sicker patients and those with longer ICU stays would be more likely to develop delirium—just as they are more likely to develop nosocomial infections and dysfunction in other organ systems—but multivariate analyses in several studies have documented that the adverse effects of delirium persist when these things are accounted for. Thus, the prevention, prompt diagnosis, and treatment of delirium in the ICU should be prominent in the clinician's mind during the management of patients' primary illnesses.

Two assessment schemes are available for diagnosing and monitoring delirium: the ICDSC, as used in the present study[1], and the Confusion Assessment Method for the ICU (CAM-ICU), introduced by Ely and colleagues.[3] The incidence of delirium among patients in the ICU in different studies, using these techniques for diagnosis, has ranged from about 10% to more than 80%, likely reflecting differences in severity of illness, case mix, and management in addition to any differences between the methods themselves. The incidence of 32% in the present study, which excluded relatively few patients and included a broad mix of medical and surgical ICU patients, seems reasonable considering all the variables in published reports. In any event, ICU delirium is clearly both common and important, making its recognition and management high priority for all critical care clinicians.

Several other important points are brought out by the Ouimet study and its accompanying editorial. ICU delirium occurs in both "hyperactive" and "hypoactive" forms. While the former is easier to recognize and poses the obvious threats of unintended extubation and dislodgement of vascular lines, studies have shown that delirium in patients lying motionless in bed is also associated with adverse outcomes. Delirium should not be treated with sedatives and narcotics. These agents can mask its manifestations but they do not treat the underlying disorder and in fact may make it worse. The current treatment of choice is haloperidol.

Table 2, adapted in part from the editorial by Polderman[2], lists steps clinicians can take to reduce the likelihood that their patients will develop delirium in the ICU.

While few would argue with the importance of preventing a phenomenon so strongly associated with

adverse patient outcomes, at present there is little evidence that treating delirium once it is recognized improves those outcomes. Common sense tells us that treatment should help, but well-designed studies of this important aspect of ICU management are sorely needed. ■

Table 2: 10 Measures for Preventing ICU Delirium

1. Treat pain appropriately
2. Use benzodiazepines and other sedatives as sparingly as possible
3. Monitor patients for delirium (ICDSC or CAM-ICU)
4. Provide patients with cognitive stimulation
   - Frequent visits from family and friends
   - Radio; television
   - Music
   - Talking to the patient
5. Give patients their eyeglasses and hearing aids
6. Mobilize patients as early and as often as possible
7. Facilitate normal sleep; avoid repetitive awakenings
8. Reduce noise levels in the ICU
9. Avoid dehydration
10. Avoid and promptly correct electrolyte and metabolic derangements

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Diagnosing VAP: Less is More

ABSTRACT & COMMENTARY

By Uday Nanavaty, MD

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Dr. Nanavaty reports no financial relationship to this field of study.

Synopsis: *In a randomized trial to evaluate two strategies for diagnosing VAP, authors found that endotracheal aspiration was as good as bronchoalveolar lavage fluid and quantitative culture in defining the pathogens and directing therapy.*

Source: Canadian Critical Care Trials Group. A randomized trial of diagnostic techniques for ventilator-associated pneumonia. *N Engl J Med.* 2006 Dec 21;355(25):2619-30.

Ventilator-associated pneumonia (VAP) is a major nosocomial infection associated with increased morbidity and perhaps with some attributable mortality. There has been great controversy as to which is the best practical strategy to diagnose and treat VAP. Routine practice has been to evaluate endotracheal aspirates in suspected cases, and then to change the therapy based on culture results. Alternative strategies, including bronchoalveolar lavage (BAL) with quantitative cultures and protected brush specimens obtained via bronchoscopy with quantitative cultures, have been touted to be more specific and hence better than the routine practice.

In order to ascertain whether BAL with quantitative cultures is in fact a better strategy, the Canadian Critical Care Trials group performed a randomized controlled trial. Patients in 28 ICUs across Canada and the US were randomized to one of the two diagnostic strategies. The diagnosis of VAP was suspected in patients who were mechanically ventilated for at least 4 days who had new or persistent radiographic evidence of pneumonia without another obvious cause, and any two of the following features: temperature > 38º C, leukocytosis (defined as leukocyte count > 11.0 x 103 per mL) or neutropenia (neutrophil count less than 3500 per mL), purulent endotracheal secretions, potentially pathogenic bacteria isolated from the endotracheal aspirate, and increasing oxygen requirements. If patients were colonized or infected with MRSA or *Pseudomonas* species, or if they were immunocompromised, they were excluded from the study. The ICU physician or respirologist performed BAL from the area likely to be affected and also rated the pre-test likelihood of VAP as low, medium, or high. Two antibiotics with activity against pseudomonas, namely ciprofloxacin and meropenem, were administered in a randomized manner after either diagnostic strategy. One group received both agents and the other received meropenem alone. The antibiotics were continued until the culture results were available. If the culture was positive, antibiotics were narrowed according to the institutional practice. If cultures were negative, antibiotics were discontinued at the discretion of the attending physician except for the group with high likelihood of VAP. In the BAL group, if the quantitative culture had sub-threshold numbers of pathogenic organisms, the physician could elect to treat based on the clinical assessment.

The study was conducted under the auspices of the Canadian Critical Care Trials Group between May 2000 and February 2005. A total of 2531 patients were screened, and out of 1144 who were eligible, 740 patients were enrolled. Both groups were comparable including the number of patients receiving antibiotics within 24 hours prior to enrollment. The mean time between admission to the ICU and enrollment was 7.9±5.2 days. Significantly more patients in the BAL group had posi-

tive cultures (59.7% vs 51.9%). In the BAL group, study antibiotics were started approximately 8 hours after initial suspicion for VAP, as compared to 6.8 hours in the ET aspiration group ($p < 0.001$). The median duration of antibiotic treatment for VAP was 10 days. The adequacy of empirical treatment of antibiotics did not differ between the two groups in culture positive patients: 89% of the BAL group with positive cultures vs 89.5% of the ET aspirate group with positive cultures. The percentage of patients who were found not to have VAP was similar between the two groups: 13.7% in the BAL group, 17.1% in the ET aspiration group.

The 28-day mortality rate for the whole study population was 18.7% (95% confidence interval, 15.9% to 21.7%). The adjusted relative risk of death by 28 days in the BAL group as compared to the ET aspiration group was 1.01 (95% CI, 0.75 to 1.37; $p= 0.94$). In previously defined subgroups, there was no statistically significant difference in mortality with either strategy. Thus, BAL and quantitative cultures did not offer any advantage in patients who were considered highly likely to have VAP, in those with APACHE II scores more or less than 24, in patients who were in the ICU for less or more than 7 days at randomization, in those who had received antibiotics within 3 days before randomization, or in patients who were thought to have high-risk organisms (such as Acinetobacter, Methacillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas* species, or *S. maltophilia* as well as multi-drug-resistant organisms). Overall, about 60% patients were considered cured of VAP, approximately 30% had clinical failure, and the remainder 10% or so had an indeterminate outcome. Again, both groups were similar in the outcome of VAP.

COMMENTARY

VAP is unfortunately a common problem in most ICUs. One of the biggest problems in considering the incidence of VAP is the lack of a standard definition. With implementation of the "VAP bundle," many institutions have reported a VAP incidence rate of essentially 0%. I believe that although the goal rate of VAP should be 0%, it is a monumental task to achieve, and institutions that report these rates often use different definitions than that used in this study.

Once VAP is suspected, practice is highly variable. The variability exists in both the diagnostic method used and the therapies initiated for VAP. This study provides a practical starting ground for at least a fourth of the patients with suspected VAP (about 25% enrollment from the screened population).

One can use this study to standardize the diagnosis of VAP and to standardize the treatment of VAP once it is suspected. With further proof that endotracheal aspiration is as good as BAL in helping guide the management of VAP, the high cost of bronchoscopy can be avoided. In addition, because endotracheal aspiration is available at all settings that provide mechanical ventilation, one can presumably shorten the interval between the time of suspected VAP and the start of antibiotic therapy. Once the strategy to identify those patients at high risk of staphylococcal infection, especially MRSA infection, is identified, appropriate antibiotics can be started for the majority of patients with suspected VAP. Between appropriate diagnostic strategy and guidelines based appropriate antibiotic therapy, true reduction in morbidity and mortality of VAP is achievable. ■

Prevalence of Burnout Among Intensivists is High

ABSTRACT & COMMENTARY

By David J. Pierson, MD, Editor

Synopsis: *In this study of physicians working in French adult ICUs, evidence of burnout was present in nearly half. Burnout was more likely in female physicians, in those who were not married, and among those who reported strained relationships with colleagues and staff nurses.*

Source: Embriaco N, et al. *Am J Respir Crit Care Med.* 2007 (published on line ahead of print January 18: doi:10.1164/rccm.200608-1184OC)

PROFESSIONAL BURNOUT IS A PSYCHOLOGICAL syndrome in response to chronic interpersonal stressors on the job. In order to determine the prevalence of burnout among physicians working in ICUs, and to investigate associated factors, the investigators carried out a nationwide one-day survey study in the adult ICUs of 189 French public hospitals. Interns, residents, fellows, and attending physicians currently working in the ICU were surveyed. In addition to demographic information about the responding physicians, data were sought about the size and staffing of the ICU and the severity of illness of its patients. To quantitate the features of burnout, the authors used the Maslach Burnout Inventory (MBI) scale, a 22-item questionnaire used in other studies and previously shown to be reproducible and valid. The MBI uses a 7-point Likert scale (which does not include the word "burnout") to determine the frequency with which

respondents experience certain feelings related to their work during the week preceding the day of the survey. Three domains of burnout are investigated: the emotional exhaustion subscale (9 items), which assesses feelings of being emotionally overextended and exhausted by one's work; the depersonalization subscale (5 items) measuring an unfeeling and impersonal response toward those under one's care; and the personal accomplishment subscale (8 items), which assesses feelings of competence and successful achievement in one's work with people.

The study took place on March 25, 2004. Directors of 189 of the 318 potentially eligible French ICUs (59%) agreed to participate in the study, and 978 physicians (82%) completed and returned the survey instrument. Of the respondents, 54% worked in teaching hospitals, and 72% were men; 24% were interns or residents, 14% fellows, and 62% attending physicians. Using the MBI scale, a high level of burnout was identified in 46.5% of the respondents, and of the others, 23.3% had a low level of burnout and 30.2% a moderate level of burnout. Of the intensivists, 37 % recorded 10 or higher in the depersonalization domain, a score considered to be high, indicating burnout. A high level of emotional exhaustion was present in 19%, and a low level of personal accomplishment in 39%. Of the respondents, 39.6% indicated that they wanted to leave their jobs, and this intention was higher in those whose level of burnout was also high. By the Centers of Epidemiologic Studies Depression Scale, evidence of depression was found in 24% of the respondents, 81% of whom also scored high on burnout.

Intensivists reporting high levels of burnout were more likely to be women, to be single, and to be younger with less ICU experience. Severity of illness and mortality among the patients whey cared for had no relationship to the likelihood of burnout. However, high workload and interpersonal conflicts, such as with colleagues or nurses, were associated with burnout; having better working relationships with nurses and chief nurses correlated with a lower frequency of burnout. The authors suggest that, while burnout is common, affecting nearly half of the intensivists in their study, improving working conditions and relationships with colleagues might have a favorable effect on its incidence and severity.

COMMENTARY

Professional burnout is a psychological syndrome in response to chronic interpersonal stressors on the job, in which affected individuals lose concern and emotional feeling for the people with whom they work, coming to treat them in a detached or even dehumanized manner. Burnout is distinct from depression in that it is confined to the work environment, while the former affects all aspects of a person's life. In this study of physicians working in ICUs in public hospitals in France, almost half of them met accepted criteria for burnout according to one or more of the 3 domains studied.

In the only published study of burnout among intensivists in North America, Guntupalli and Fromm[1] surveyed a random sample of 248 internist members of the Society of Critical Care Medicine, using the same instrument (the MBI scale) employed by Embriaco et al in the current paper. The findings were similar in that evidence of burnout was very common. In this earlier study, one-third of the respondents scored abnormally high on the emotional exhaustion scale, nearly two-thirds had abnormally low scores on the personal achievement scale, and 20% rated high on the depersonalization scale. In their survey, which included only attending physicians (no trainees), Guntupalli and Fromm found that high levels of emotional exhaustion were associated with anticipating leaving critical care before retirement.

Although methods and results have varied somewhat, as discussed by the authors of the present article, studies to date indicate that burnout is present in somewhere between one quarter and two-thirds of physicians working in the ICU. The associations between burnout and high workload, and with the quality of working relationships with colleagues and nurses documented in the study by Embriaco and colleagues, suggest possible avenues for prevention and remediation. Whether reorganization and efforts to improve collegial working relationships can reduce the prevalence and severity of burnout remains to be seen, but would certainly seem worthwhile based on the findings of this study. ■

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Special Feature

Patient-Ventilator Dys-Synchrony During Lung Protective Ventilation

by Dean Hess, PhD, RRT

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Dr. Hess reports no financial relationship to this field of study.

In 2000, the Acute Respiratory Distress Syndrome Network (ARDSnet) reported an

unprecedented low mortality for ARDS patients ventilated with a tidal volume of 6 mL/kg of predicted body weight (and a plateau pressure ≤30 cm H_2O) compared to a tidal volume of 12 mL/kg.[1] Since then, it has been shown that adoption of a 6 mL/kg tidal volume strategy for ARDS into usual practice results in mortality similar to that of the ARDSnet study.[2] Moreover, in patients who do not have ARDS or acute lung injury (ALI) at the time of intubation, tidal volume is an important risk factor for the development of ALI or ARDS during the course of mechanical ventilation.[3, 4]

Patient-ventilator dys-synchrony occurs when gas delivery from the ventilator does not match the neural output of the respiratory center. One of the clinical observations when implementing a lung protective ventilation strategy in which tidal volume and inspiratory plateau pressure are constrained is the development of patient-ventilator dys-synchrony. For clinicians used to observing a calm patient who is passively ventilated, the emergence of patient-ventilator dys-synchrony is alarming and presents an important impediment to implementation of a lung protective ventilation strategy.[5] Although clinicians often associate patient-ventilator dys-synchrony with a low tidal volume setting on the ventilator, it is important to note that dys-synchrony has been recognized for many years—even when high tidal volumes were commonly used. The prevalence of patient-ventilator dys-synchrony with low tidal volumes, compared to high tidal volumes, is unknown.

There are 3 major categories of patient-ventilator dys-synchrony. *Trigger dys-synchrony* occurs when the effort of the patient fails to adequately trigger the initiation of the inspiratory phase. *Flow dys-synchrony* occurs when the flow or volume delivered from the ventilator does not meet the demands of the respiratory muscles. During volume-controlled ventilation, for example, flow and volume delivery are fixed. If patient demand increases, airway pressure decreases, the amount of assistance provided by the ventilator decreases, and the imposed work of breathing increases.[5] *Cycle dys-synchrony* occurs when the inspiratory phase of the ventilator does not coincide with the neural inspiratory time of the patient; in other words, the inspiratory phase of the ventilator stops prematurely or it extends into the neural expiratory time of the patient.[6]

Precise measurement of patient-ventilator dys-synchrony requires use of an esophageal balloon, but this is not practical for usual patient care. Dys-synchrony is clinically identified as use of accessory muscles, active exhalation, tachypnea, tachycardia, diaphoresis, nasal flaring, and other signs of respiratory distress. However, dys-synchrony can be subtle and not easily recognized by clinical examination.[7] Patient-ventilator dys-synchrony can also be detected by careful examination of the waveforms of pressure and flow displayed on modern ventilators.[8]

Patient-ventilator dys-synchrony is common during mechanical ventilation and patient discomfort is also common during mechanical ventilation. The extent to which dys-synchrony and discomfort are related is unknown. Because patient-ventilator dys-synchrony looks uncomfortable to the clinician, we believe that it must feel uncomfortable for the patient. And perhaps it does. However, there has been little study of the relationship between dys-synchrony, discomfort, ICU recall, and long term functional outcomes in patients with ALI and ARDS. One study suggested health related quality of life was similar for survivors of a high versus low tidal volume strategy though the level of dys-synchrony was not reported.[9]

Improving Patient-Ventilator Synchrony

The following should be considered to improve patient-ventilator synchrony.[10, 11] In many cases, selection of ventilator settings to achieve the best synchrony is a matter of trial-and-error and the settings that achieve the best synchrony may vary from time to time.

Respiratory rate: An increase in respiratory rate setting on the ventilator may entrain the patient's breathing pattern to the ventilator. In the ARDSnet study, the respiratory rate was increased as tidal volume was decreased to maintain minute ventilation constant (to a maximum of 35 breaths/min). Even higher respiratory rate settings (and thus a higher minute ventilation) may be required. Presumably this is due to the higher dead space fraction when tidal volume is reduced, requiring a higher minute ventilation to avoid hypercapnia and its resultant effect on respiratory drive. Increasing the respiratory rate setting has been shown to decrease work of breathing and increase patient comfort.[12]

Auto-PEEP: The triggers on modern ventilators are very sensitive to patient effort. Despite this, trigger dys-synchrony may occur in the presence of auto-PEEP. Accordingly, efforts should use employed to minimize the amount of auto-PEEP. Although concern has been raised regarding the potential for auto-PEEP with the

high respiratory rates used in the ARDSnet strategy, this is usually not an issue due to the low tidal volumes employed and the high elastic recoil pressures of patients with ARDS.[13]

Inspiratory flow: An increase in set inspiratory flow may better meet the flow demand of the patient. Deviation of inspiratory flow from that desired by the patient can greatly affect respiratory comfort.[14] However, a higher inspiratory flow also decreases neural inspiratory time, resulting in a greater spontaneous breathing frequency, which can worsen dys-synchrony.[15]

Inspiratory time: A shorter inspiratory time (the result of a higher inspiratory flow during volume-controlled ventilation) may improve patient-ventilator synchrony. However, if the inspiratory time setting on the ventilator is less than the neural inspiratory time, double-triggering and worsening dys-synchrony may occur.

Flow waveform: Dys-synchrony may improve with a descending flow waveform in some patients. For the same peak flow, inspiratory time is longer with a descending flow. This may achieve the goal of better synchrony due to higher flow while avoiding double-triggering due to an inspiratory time that is too short.

Pressure-controlled ventilation: Pressure-controlled ventilation achieves the goals of a descending flow waveform and an adjustable inspiratory time independent of flow. Pressure-controlled ventilation may result in better synchrony in some patients.[16, 17] Whether this is due to pressure-controlled ventilation per se or the descending flow is unclear. Likely the same effects on patient-ventilator synchrony occur with volume-controlled ventilation using a descending ramp flow waveform.[18] A potential limitation of pressure-controlled ventilation in patients with a vigorous inspiratory effort is the possibility that transpulmonary pressure (the principal determinant of ventilator-induced lung injury) may increase due to the negative intrapleural pressure swings. For the same tidal volume and inspiratory flow, work of breathing is likely the same for pressure controlled ventilation and volume-controlled ventilation.[19]

Pressure rise time: With pressure-controlled ventilation, the clinician can adjust to rate of rise in pressure at the onset of the inspiratory phase. If the pressure rises more quickly, flow is higher at the beginning of inhalation. Rise time adjustment may affect work of breathing and patient comfort.[20, 21]

Tidal volume: An increase in tidal volume, if accompanied by an increase in alveolar ventilation, decreases respiratory drive by lowering the $PaCO_2$ (chemoreceptor effect) and activating stretch receptors (Hering-Breuer reflex). It is important to note that the ARDSnet protocol allows tidal volume to be increased to 8 mL/kg in the case of patient-ventilator dys-synchrony, provided that the plateau pressure remains ≤30 cm H_2O.

Sedation: Although excessive and prolonged sedation is not recommended or appropriate, adequate sedation is necessary during mechanical ventilation, though in selected patients may be difficult to achieve regardless of ventilator settings. Despite the often voiced concern that patients require more sedation when the tidal volume is reduced, this concern has not been born out in studies that assessed sedation requirement with lung protective ventilation. Patient-ventilator dys-synchrony was reported long before lower tidal volume ventilation became acceptable; even with the use of large tidal volumes some patients require large sedative doses to ameliorate ventilator dys-synchrony. That sedative requirements were found to be similar for patients randomized to 6 ml/kg versus 12 ml/kg tidal volumes in two ARDSnet centers supports the conclusion that sedative needs may be largely determined by clinical factors other than ventilation strategy.[22, 23] Such factors may include as pain, agitated delirium, metabolic acidosis, drug withdrawal, or agitation from septic encephalopathy.

What's a Clinician To Do?

As clinicians, we should assess synchrony and comfort each time we visit the bedside of a patient undergoing mechanical ventilation.[24] If the patient demonstrates signs of dys-synchrony and discomfort, efforts should be undertaken to appropriately adjust the ventilator, and the sedative, analgesic, and other general medical needs of the patient should be addressed. However, given the demonstrated survival benefit of lung protective ventilation strategies, lung protection should remain the priority and should not be abandoned for fear of patient-ventilator dys-synchrony. That the need for lung protection may exist at end-inspiratory airway pressures previously thought to be safe; the tradeoff between lung protection on the one hand, and patient ventilator synchrony, sedative needs, and acid base homeostasis on the other remains a major clinical challenge. More study is needed to determine the prevalence of patient-ventilator dys-synchrony, its mechanism, its impact on important patient outcomes, and the optimal lung-protective strategies to avoid it. ■

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CME Questions

26. Which of the following is/are signs of delirium included in the Intensive Care Delirium Screening Checklist?
a. exaggerated response to normal stimulation
b. inattention
c. disorientation
d. inappropriate speech or mood
e. all of the above

27. Based on the study by the Canadian Critical Care Trials group:
a. The diagnosis of VAP due to staphylococci is not possible with bronchoscopy.
b. The diagnosis of VAP due to Pseudomonas species is easily achieved with endotracheal aspirate.
c. BAL and quantitative cultures do not provide any additional advantage over endotracheal aspirate in patients with VAP where staphylococci or Pseudomonas are not suspected.
d. All patients with suspected VAP should have bronchoscopy and BAL.
e. Protected brush specimens are best to diagnose VAP.

28. In the study of French intensivists, which of the following best describes the results in terms of burnout and depression?
a. Only a minority of respondents were depressed, but most of those who were suffered from burnout.
b. The majority of respondents had both depression and burnout.
c. depression was common, but burnout was uncommon.
d. respondents tended to be either depressed or burned out, but not both.
e. none of the above

29. Which of the following is a bedside sign suggesting the presence of patient-ventilator dys-synchrony?
a. use of accessory muscles of ventilation
b. active exhalation
c. tachypnea
d. nasal flaring
e. all of the above

30. Which of the following statements is most accurate with respect to patient-ventilator dys-synchrony?
a. it has been proven to occur more commonly with low-tidal-volume ventilation
b. it occurs when gas delivery from the ventilator does not match with the neural output of the respiratory system
c. it is usually a manifestation of ICU psychosis
d. its occurrence indicates a high risk for ventilator-associated lung injury
e. none of the above

Answers: 26(e); 27(c); 28(a); 29(e); 30(b)

CME / CE Objectives

After reading each issue of *Critical Care Alert*, readers will be able to do the following:

- Identify the particular clinical, legal, or scientific issues related to critical care.
- Describe how those issues affect nurses, health care workers, hospitals, or the health care industry in general.
- Cite solutions to the problems associated with those issues.

In Future Issues:

Adverse Physiological Effects of Extreme Lateral Positioning in Respiratory Failure

Supplement to *Critical Care Alert*
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CRITICAL CARE ALERT™

A monthly update of developments in critical care and intensive care medicine

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Higher HDL Cholesterol in Statin Therapy, Key to Slowing Atherosclerosis?

Aggressive statin therapy is associated with slowed progression and even regression of atherosclerosis. A new study suggests that, when monitoring statin therapy, increases in HDL cholesterol may be as important as decreases in LDL cholesterol in preventing disease progression. Researchers from the Cleveland Clinic reviewed 4 large studies from United States, North America, Europe and Australia in which 1,455 patients with angiographic coronary disease underwent serial intravascular ultrasonography while receiving aggressive statin therapy for 18 or 24 months. During therapy, mean LDL levels dropped from 124.0 mg/dl to 87.5 mg/dl, and mean HDL levels increased from 42.5 mg/dl to 45.1 mg/dl, and LDL to HDL ratios were reduced from a mean of 3 to 2.1 ($P < 0.001$ for all). These changes were accompanied by a small, but statistically significant decrease in atheroma volume as measured by intravascular ultrasound. The largest decrease in atheroma volume was associated with patients with LDL cholesterol less than the mean of 87.5 mg/dl, and percentage increases in HDL cholesterol of greater than 7.5%. The authors conclude that when treating with statins, decreases of LDL cholesterol and increases in HDL cholesterol are independently associated with regression of atheroma volume. They also note that these changes were not associated with reductions in clinical events or improved clinical outcomes and that more research is needed (*JAMA*. 2007; 297:499-508).

Citalopram Useful for Depression in CDA Patients

Major depression affects up to one quarter of patients hospitalized with coronary artery disease and these patients have a worse prognosis than non-depressed patients. A new study from Canada compares the efficacy of citalopram vs interpersonal psychotherapy in reducing depressive symptoms among these patients. The study randomized 284 patients with CAD and major depression to 12 weeks of interpersonal psychotherapy plus clinical management vs clinical management only, and a second randomization compared 12 weeks of citalopram 20-40 mg/day vs placebo. The main outcomes were scores on objective depression scales. Citalopram was superior to placebo in reducing depression scores ($P = 0.005$), but interpersonal psychotherapy was ineffective, being no better than clinical management. The authors conclude that citalopram administered in conjunction with weekly clinical management was effective in treating depression whereas there was no evidence of value for interpersonal psychotherapy. The authors suggest that citalopram or sertraline (based on previous studies) should be considered as first-step treatment for patients with CAD and major depression (*JAMA*. 2007;297:367-379). An accompanying editorial agrees that citalopram and sertraline are safe and effective for treatment of depression in patients with coronary heart disease, and suggests physicians should actively screen for signs and symptoms of depression in these patients. However, there is not yet

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any evidence that treating depression in this patient population reduces subsequent cardiac events (*JAMA*. 2007;297:411-412).

When to Stop Anticoagulation Before Surgery?

For patients on warfarin who have been bridging therapy with low molecular weight heparin (LMWH) prior to surgery, when is the best time to stop anticoagulation? A new study suggests that the evening before surgery is too late. Researchers in Ontario, Canada, looked at 80 patients who were scheduled for surgery or invasive procedures and were bridged with LMWH. All 20 patients had normal renal function and were given enoxaparin 1 mg/kg of body weight twice daily with the last dose administered the evening before surgery. Blood anti-factor Xa heparin levels were measured shortly before surgery, an average of 14 hours after the last dose. Two-thirds of patients had anti-Xa heparin levels of 0.5 U/ml or higher shortly before their invasive procedure. Patients with higher BMIs were more likely to have higher levels as were patients with lower creatinine clearances. The authors conclude that preoperative bridging with twice daily enoxaparin results in high residual anti-Xa heparin levels if the last dose is given the evening before surgery. They recommend that the last dose be given the morning on the day prior to surgery (*Ann Int Med.* 2007;146:184-187).

Drug Warnings: Ranibizumab and Bevacizumab

Both of Genentech's anti-angiogenic agents, ranibizumab (Lucentis) and bevacizumab (Avastin), have been the subject of new warnings from the company and the FDA. Ranibizumab, which is used for the treatment of neovascular (wet) macular degeneration, has been associated with increased risk of stroke in elderly patients. The drug, which is administered as an monthly intraocular injection, was found to be associated with a 1.2% risk of stroke at the recommended dose of 0.5 mg compared to a 0.3% risk associated with the lower-than-recommended 0.3 mg dose ($P = 0.02$) at an average follow-up of 230 days. Patients who had a history of stroke were at the highest risk. Bevacizumab, which is approved for treatment of non-small cell lung cancer and metastatic colorectal cancer, was recently found to be associated with increased risk of gastrointestinal perforation and potentially fatal pulmonary hemorrhage. Gastrointestinal perforation was seen as a complication of patients treated for colorectal cancer, while pulmonary hemorrhage was seen in patients receiving chemotherapy plus bevacizumab for lung cancer. Other bleeding complications seen in bevacizumab-treated patients including GI hemorrhage, subarachnoid hemorrhage and hemorrhagic stroke.

Growth Hormone Treatment, More Harm Than Good

The January 16, 2007, *Annals of Internal Medicine* includes a review of the safety and efficacy of growth hormone in the healthy elderly. The review was undertaken because growth hormone is widely recommended and sold as an anti-aging agent in this population. The authors reviewed 31 articles, which included a total of 220 participants who received growth hormone. The mean age was 69 and patients were generally overweight. Treatment duration mean was 27 weeks. Growth-hormone-treated patients compared to placebo- treated patients were noted to have decreases in overall fat mass and increases in overall lean body mass, but weight did not change significantly. Total cholesterol decreased, although not significantly, after adjustment for body composition changes. Bone density and other lipid levels did not change. Those treated with growth hormone were significantly more likely to experience soft tissue edema, and arthralgias, carpal tunnel syndrome, and gynecomastia as well as a slightly increased rate of diabetes and impaired fasting glucose. The authors conclude that growth hormone use in the elderly is associated with small changes in body composition and an increased rate of adverse events and cannot be recommended (*Ann Int Med*. 2007; 146:104-115).

FDA Actions

The FDA has warned against unsupervised use of topical anesthetic products for cosmetic procedures. The agency has received multiple reports of adverse events associated with patients applying excess amounts of topical agents containing lidocaine, tetracaine, benzocaine, and prilocaine. Two women who used topical anesthetics with lidocaine and tetracaine died after applying the creams to their legs and wrapping their legs in plastic to increase absorption. Healthcare professionals are cautioned to prescribe topical anesthetics with caution in the lowest concentration consistent with pain relief goals and to advise patients in their safe use.

The FDA has approved Roche's orlistat for over-the-counter use to facilitate weight loss. The drug, available in prescription form under the trade name "Xenical," blocks absorption of fat by inhibiting pancreatic lipase thus preventing triglyceride absorption in the small bowel. The over-the-counter version will be available as a 60 mg dose, half the prescription dosage. Orlistat over-the-counter will be marketed as "Alli." ■