CRITICAL CARE ALERT®

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

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INSIDE

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Influenza in the ICU: Underuse of Personal Protective Equipment by Health Care Workers

ABSTRACT & COMMENTARY

By David J. Pierson, MD, Editor

Synopsis: *In this study of physicians, nurses, and respiratory therapists in the ICUs of 2 teaching hospitals, nearly 40% reported poor adherence to influenza personal protective equipment use, and more than half reported that their colleagues often failed to use such protection when caring for patients with influenza.*

Source: Daugherty EL, et al. The use of personal protective equipment for control of influenza among critical care clinicians: A survey study. *Crit Care Med* 2009;37:1210-1216.

ALONG WITH YEARLY VACCINATION, THE U.S. CENTERS FOR DISEASE Control and Prevention (CDC) recommend the use of personal protective equipment (PPE) by health care workers (HCWs) to prevent influenza infection in the ICU. Daugherty and colleagues at The Johns Hopkins Hospital performed this study to characterize the knowledge, attitudes, and behavior of ICU HCWs with respect to these recommendations. During influenza season in early 2007, they surveyed internal medicine residents, pulmonary-critical care fellows and faculty, nurses, and respiratory therapists (RTs) working in the medical and cardiac ICUs in 2 Baltimore teaching hospitals.

Surveys were distributed to 292 clinicians at the 2 study hospitals, and 256 (88%) were completed by housestaff (82), faculty and fellows (39), nurses (91), and RTs (44). Overall, 85% of respondents reported knowing when their patients were on droplet (respiratory) precautions, although nurses and RTs were less likely to report knowing this than doctors. Overall, 62% reported high adherence (> 80%) to the protection measures. However, only 63% of respondents correctly identified the equipment that would provide adequate protection, with failure to indicate that a gown and gloves were needed in 27% and 11% of HCWs, respectively. Eleven percent of respondents indicated that they did not wear a mask when patients

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were on respiratory isolation; 53% reported that their coworkers "often forget to use recommended PPE when taking care of influenza patients."

Although 80% of respondents believed that adhering to the precautions prevented the acquisition of influenza infection, about half of them considered their use inconvenient, and 21% of them said that using the recommended precautions interfered with patient care. HCWs who considered adherence to be inconvenient were less likely to report a high rate of personal adherence (odds ratio [OR], 0.42; 95% confidence interval [CI], 0.22-0.82). In all work categories, 56% indicated that they would be reprimanded by their supervisor if they did not use the precautions when caring for a patient with influenza, and those so indicating were more likely to report high adherence (OR, 2.40; 95% CI, 1.25-4.62).

The authors noted that the use of self-report via a questionnaire likely resulted in over-estimation of PPE use among the HCWs in the study. They concluded that levels of such use were suboptimal, indicating that HCWs may be at substantial risk for both acquisition and transmission of influenza and other respiratory viruses during a pandemic. Further, they concluded that both increased knowledge and modification of organizational factors would likely be required to improve respiratory virus infection control in the ICU.

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Questions & Comments

Please call **Paula Cousins,** Senior Managing Editor, at (404) 262-5468.

■ **COMMENTARY**

Even if the case fatality rate of the current influenza A H1N1 (swine flu) pandemic proves to be low, it is likely that many patients infected with this and other respiratory viruses will be cared for in the ICU, whether for virus-related or other reasons. Thus, secondary transmission of respiratory viruses in the ICU is of major concern for public health reasons and also for the health of both HCWs and other patients in the unit. The CDC recommends the use of barrier precautions — droplet (surgical mask) and standard (gown and gloves for potential contact with infectious secretions) — in the care of patients with influenza. While the optimal form of PPE in some instances remains to be established with certainty, whatever the equipment employed, it must be used to be effective. This study, carried out 2 years ago, indicates that both knowledge of and adherence to current recommendations for the prevention of nosocomial spread of influenza and other respiratory viruses are not as good as they should be.

The study included ICU HCWs in several job categories and at 2 different large general hospitals. Although there were some differences between the institutions and among physicians, nurses, and RTs on some included items, the deficits in knowledge and reported practice and in the attitudes revealed were common to both hospitals and all categories of HCWs. Importantly, both the belief that adherence to respiratory precautions was inconvenient and the assumption that non-adherence would bring reprimand by one's supervisor were significant factors in the likelihood that the individual HCW would adhere to the guidelines — making such adherence less and more likely, respectively. These findings point to areas in which efforts to improve PPE use, and hence to decrease the risk of nosocomial influenza transmission, might profitably be targeted. ■

Intensive Insulin Therapy: A Bit More Sugar May Be Nicer

ABSTRACT & COMMENTARY

By Saadia R. Akhtar, MD, MSc

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

Synopsis: *This large multicenter, randomized, controlled parallel-group trial found that intensive glucose*

management, compared to conventional (target glucose 81-108 mg/dL vs ≤ 180 mg/dL), increases 90-day mortality in both medical and surgical ICU patients.

Source: NICE-SUGAR Study Investigators; Finfer S, et al. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med* 2009;360:1283-1297.

THIS STUDY WAS DESIGNED TO DETERMINE WHETHER intensive glucose control in ICU patients reduces mortality at 90 days. Secondary outcomes included survival time during the 90 days, cause-specific death, duration of mechanical ventilation, need for renal replacement therapy, and hospital and ICU lengths of stay.

Forty-two hospitals (38 academic tertiary care centers and 4 community hospitals in Australia, New Zealand, and North America) took part in this trial of medical and surgical ICU patients. Eligible patients were expected to require ≥ 3 days of ICU care. Subjects were randomized to glucose control that was either intensive (target 81-108 mg/dL) or conventional (target ≤ 180 mg/dL, with insulin stopped once glucose < 144 mg/dL), per predefined treatment algorithms. Randomization was stratified by type of admission (operative or non-operative) and also by region. The target glucose control was continued until the patient was eating or discharged from the ICU, was resumed if the patient returned to the ICU within 90 days of randomization, and was discontinued permanently at 90 days after randomization or death, whichever came first. Severe hypoglycemia was defined by blood glucose ≤ 40 mg/dL. Usual demographic and clinical data were collected, including severity-of-illness scores and information about prior diagnosis of diabetes and recent corticosteroid use. Standard statistical methods and intention-to-treat analysis were utilized. An estimated sample size of 6100 was needed to detect a 3.8% mortality difference with a statistical power of 90% and two-sided alpha of 0.05.

Over 4 years, 6104 subjects were randomized (< 15% from North America). The 2 groups had no significant differences in baseline demographic or clinical characteristics. About one-third of the subjects in each group were operative. Median duration of study treatment was about 4 days, and mean time-weighted glucose levels were 115 mg/dL in the intensive control group vs 144 mg/dL in the conventional group. Study treatment was discontinued early due to adverse events in only 0.4% of subjects in the intensive group vs < 0.1% in the conventional group. More subjects in the intensive control group received corticosteroids.

At 90 days, the absolute difference in mortality between the 2 groups was 2.6% with a statistically significant odds ratio for death in the intensive control group of 1.14 (yielding a number needed to harm of 38); deaths from cardiovascular causes were more common in these patients. These results remained the same after adjustment for 6 predefined variables. There were no significant differences between the 2 groups in other secondary outcomes. As might be expected, severe hypoglycemia occurred more often in the intensive control group (6.8% vs 0.5%).

■ COMMENTARY

Observational prospective and retrospective studies over the past decade have clearly shown that severe hyperglycemia is associated with adverse outcomes.[1] Conversely, there is some evidence that severe hypoglycemic episodes may lead to worse ICU outcomes, including mortality.[2] Thus, although we can agree that glucose control is important, questions remain about what specific glucose level(s) we should be targeting.

Van den Berghe et al's 2001 study of intensive glucose control in a single surgical ICU sparked a huge change in clinical practice when it demonstrated a significant decrease in ICU mortality (as well as hospital mortality, infections, acute renal failure, and polyneuropathy) for patients managed with insulin drips to target glucose 80-110 mg/dL (the study achieved mean glucose of 103 mg/dL).[3] The control group's target was glucose between 180-200 mg/dL, and insulin was not started until glucose reached > 215 mg/dL (mean glucose 153 mg/dL in this group). Severe hypoglycemia occurred in about 5% of patients in the intensive glucose control group. The study was criticized for high mortality in the control group (relative to the patients' severity of illness and diagnoses). It was also unclear how the center's early, aggressive use of combined parenteral and enteral nutrition would impact the generalizability of the results. Nevertheless, the findings were striking enough to lead to implementation of tight glucose control via similar protocols in ICUs across the world, often with extrapolation to nonsurgical ICU patients.

Subsequent studies in mixed or medical ICU populations, however, have provided conflicting results (often with high rates of severe hypoglycemia). Van den Berghe's own attempt to replicate the original study in a medical ICU failed to show an overall mortality benefit of intensive glucose management. There were some other improved outcomes (earlier liberation from mechanical ventilation and earlier ICU and hospital discharge). On subgroup analysis, those patients in the intensive glucose control group with ICU length of stay ≥ 3 days did appear to have improved mortality.[4]

Meta-analyses of studies of intensive glucose control in mixed or medical ICU populations have also not demonstrated improved mortality or overall benefit.[5]

NICE-SUGAR is a well-designed and well-executed trial that sways the pendulum further away from the tight glucose control recommended by Van den Berghe et al. NICE-SUGAR differs from the Van den Berghe investigations in several ways; perhaps most notably, the target (and actual achieved) glucose in the control group is considerably lower than in the prior studies, suggesting that more modest glucose control may be the true "holy grail" of glycemic management in the ICU. It leaves us to wonder whether there truly is mortality benefit to very tight glucose control in specific ICU populations. If so, how can those patients be identified? How can intensive glucose control be beneficial in post-cardiac surgery ICU patients while at the same time increasing deaths from cardiovascular causes in mixed ICU populations receiving similar glucose management? What is the threshold glucose above and below which harm may occur? What are the potential mechanisms of such harm or benefit?

Although it may raise more questions than it answers, NICE-SUGAR is one of the most noteworthy studies of the year. It has already changed practice in the mixed medical-surgical ICUs where I work and I hope the same is happening across the world. I suggest not initiating insulin therapy in ICU patients until blood glucose exceeds 180 mg/dL; at that point, insulin should be used to target modest glucose control (140-160 mg/dL). Whether intensive glucose control (as defined by Van den Berghe et al) may be beneficial in certain post-surgical ICU patients or in any patient beyond the first 3 days of an ICU stay is uncertain. I believe there are enough questions and enough evidence of potential harm from intensive glucose control (target 80-110 mg/dL) that more modest targets should be utilized until further studies clearly replicate prior positive results. ■

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Editor's Comment

Has Tight Glucose Control Come Full Circle?

By David J. Pierson, MD, Editor

Intensive insulin therapy in the ICU is a dynamic and controversial issue that has played out in the medical literature, at the bedside, and in the offices of policy makers over the last 8 years. Amid mounting evidence that hyperglycemia is harmful to critically ill patients, the initial report of Van den Berghe and colleagues of improved mortality with tight glucose control took the critical care world by storm,[1] initiating a wave of ICU- and hospital-level policy changes and protocols as well as practice guidelines from several prestigious professional organizations and the Surviving Sepsis Campaign in support of intensive insulin therapy. That the Van den Berghe study was from a single institution, in surgical ICU patients monitored very closely and managed aggressively with mainly parenteral nutritional support, raising the possibility that perhaps not all patient populations or critical care management environments would derive the same benefits from intensive insulin therapy, was discussed at journal clubs and in editorials, but such therapy quickly became the standard of care for thousands of ICUs.

As nicely summarized by Dr. Akhtar, studies published since that initial report, extending intensive insulin therapy into wider populations of ICU patients, have been less positive, and the benefits of this therapy have become progressively less obvious. Publication of the NICE-SUGAR study, the largest clinical trial to date, which included medical, surgical, and mixed ICU patients, has increased the uncertainty, suggesting that intensive insulin therapy may actually be harmful.

The largest and most rigorous meta-analysis on this issue to date has just been published.[2] This analysis by Griesdale and colleagues at several Canadian and U.S. institutions included results of the NICE-SUGAR study. In all, it included 13,567 patients in 26 randomized controlled trials of intensive insulin therapy. Among the trials that reported mortality, the pooled relative risk (RR) of death with intensive insulin therapy compared with conventional therapy was 0.93 (95% confidence interval

[CI], 0.83-1.04). Among those that reported hypoglycemia, the pooled RR with intensive insulin therapy was 6.0 (95% CI, 4.5-8.0) — a 6-fold increase in this complication. Stratification by type of ICU suggested a benefit in surgical ICU patients, whereas no such suggestion was found in medical or mixed ICU patients.

Griesdale et al conclude as follows: "[O]ur findings do not support the guidelines of organizations such as the American Diabetes Association, the American Association of Clinical Endocrinologists, and other organizations, including the Surviving Sepsis Campaign, that recommend intensive insulin therapy for all critically ill patients. Our meta-analysis incorporates the results of the largest trial to date. We are not aware of any ongoing trial of sufficient size to affect these results; thus, we suggest that policy makers reconsider recommendations promoting the use of intensive insulin therapy in all critically ill patients."

This most recent evaluation shows that a dogmatic approach to this issue is difficult to justify using currently available data. The authors emphasize that they "cannot exclude the possibility that some patients may benefit from intensive insulin therapy, although the characteristics of such patients remain to be clearly defined; as does the effect of different blood glucose algorithms, the method of measuring blood glucose, and the influence of nutritional strategies." In the meantime, Dr. Akhtar's recommendations seem to me to be sound advice. ■

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What Should We Make of Candida Isolated from Respiratory Tract Samples?

ABSTRACT & COMMENTARY

By Andrew M. Luks, MD

Pulmonary and Critical Care Medicine, University of Washington, Seattle

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

Synopsis: *This prospective study of autopsies performed on patients who died in a medical ICU demonstrates that candida pneumonia is a very rare occurrence and suggests that antifungal therapy can be safely withheld in patients in whom* Candida *species are isolated from the respiratory tract during a fever work-up.*

Source: Meersseman W, et al. Significance of the isolation of *Candida* species from airway samples in critically ill patients: A prospective, autopsy study. *Intensive Care Med* 2009 Apr 9; Epub ahead of print.

COLONIZATION OF THE RESPIRATORY TRACT AND OTHER sites with *Candida* species is common in ICU patients but it is unclear how often these species cause pneumonia that warrants antifungal therapy. Meersseman and colleagues sought to clarify this issue by defining the incidence of candida pneumonia and the value of isolating *Candida* species from respiratory tract samples in immunocompetent and immunosuppressed individuals with evidence of pneumonia at the time of autopsy.

They conducted a prospective study of all autopsies performed on patients who died in the medical ICU over a 2-year period at a single institution. A variety of data was collected on all deceased patients including, but not limited to, *Candida* species isolated from tracheal aspirates or bronchoalveolar lavage (BAL) specimens, identification of *Candida* species from other sites ≤ 14 days before death, and antifungal treatment. Tracheal surveillance cultures were performed routinely on a weekly basis at this institution as well as in response to suspicion for pneumonia, while BAL was performed to evaluate new pulmonary opacities in immunocompromised patients. All autopsies were performed within 24 hours of death. Histologic criteria for the diagnosis of acute candida pneumonia included the presence of neutrophils in the interstitium and alveolar spaces and microscopic evidence of fungal organisms with histologic features typical for *Candida* spp. (i.e., budding yeast and pseudohyphae). Cultures were not performed on the post-mortem specimens.

During the study period 1587 patients were admitted to the ICU and 301 (19%) died. Autopsies were performed on 232 patients (77% autopsy rate), 135 (58%) of whom had histologic evidence of pneumonia. Of the patients with histologic evidence of pneumonia, 77 had growth of *Candida* species on respiratory tract samples (56 positive tracheal aspirates, 12 positive BAL samples, and 9 with growth on both) while 58 had no positive cultures for the organism. Both groups included patients on corticosteroids or with neutropenia while the group of

patients with histologic evidence of pneumonia also included 21 patients with either solid or hematologic malignancy or who had undergone solid organ transplant. Histologic evidence of candida pneumonia was not found in any of the autopsied patients. An additional 47 of the autopsied patients had growth of *Candida* species on respiratory tract samples but no evidence of pneumonia of any etiology on autopsy. Eleven patients across all study groups had candidemia, while 3 had candida peritonitis and 4 patients had candiduria. None of the patients with candida cultured from sites outside the respiratory tract developed candida pneumonia.

■ COMMENTARY

Fever is a common problem in ICU patients for which we invest considerable time and resources in attempts to identify an etiology. On many occasions, cultures fail to show a definitive explanation for the fever but do provide evidence of *Candida* species on either a BAL or tracheal aspirate. As the fevers continue this leaves many clinicians wondering whether it is worth treating the patient with antifungal therapy for a possible candida pneumonia. In fact, even though current guidelines recommend against the use of antifungal therapy when *Candida* species are isolated in BAL fluid in immunocompetent patients, 24% of ICU physicians report prescribing antifungal agents under these circumstances.[1]

The study by Meersseman and colleagues provides useful information that should guide decisions in this situation and prevent the unnecessary use of antifungal therapy. Consistent with the results of prior studies that have examined this issue,[2] they found no evidence of candida pneumonia in a mixed population of ICU patients. Although data were collected at only a single center and the autopsy specimens were not cultured, there was a very high autopsy rate and, as a result, the chances of missing cases where candida pneumonia was present but was not detected because histologic examination could not be performed were limited.

Another strong aspect of the study was the fact that the study population included a wide array of medical ICU patients, including immunocompetent patients and those with various forms of immunosuppression such as corticosteroid use, neutropenia, organ transplantation, and solid and hematologic malignancies. While the results should be applied in the care of immunocompetent patients, we should still be cautious before applying them to all immunosuppressed patients, as the total number of such patients in the study was small and other studies have showed evidence of candida pneumonia in patients with malignancy or neutropenia.[3] More studies involving other centers and larger sample sizes are necessary before we can disregard the possibility of candida pneumonia in immunosuppressed patients.

Finally, another situation in which clinicians broach the idea of antifungal therapy is when *Candida* species are cultured concurrently from multiple sites such as the urine and respiratory tract. Eighteen patients in this study, however, had positive cultures from other sites including the blood, urine, or peritoneum, yet candida pneumonia was not subsequently identified in any of these patients. While not definitive given the low numbers of patients in this situation, this finding does suggest that antifungal therapy for pneumonia can be withheld when candida is concurrently identified in urine and respiratory tract samples and should be reserved for patients with blood stream infections or peritonitis. ■

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Patients' Bath Basins May Serve as a Reservoir for Potential Sources of Infection

ABSTRACT & COMMENTARY

By Leslie A. Hoffman, RN, PhD

Department of Acute / Tertiary Care, School of Nursing, University of Pittsburgh

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

Synopsis: *Some form of bacteria grew in 98% of samples cultured from patient bath basins obtained from three acute care hospitals, including basins from three ICUs.*

Source: Johnson D, et al. Patients' bath basins as potential sources of infection: A multicenter sampling study. *Am J Crit Care* 2009;18:31-38, 41.

THIS STUDY EXAMINED PATIENTS' BATH BASINS AS A possible reservoir for bacterial colonization and a

risk factor for subsequent hospital-acquired infections. In a prospective study involving 3 acute care hospitals, 92 bath basins were evaluated including basins from 3 ICUs (cardiac care, surgical ICU, medical ICU). The basins cultured for the study were used at least twice for whole-body bathing of patients who were hospitalized for ≥ 48 hours (mean 6.9 days). Cultures were obtained by swabbing the basins after the bath water had been emptied and the basins were allowed to air dry for at least 2 hours after bathing.

Some form of bacteria grew in 98% of the samples. The organisms with the highest positive rates of growth were enterococci (54%), gram-negative organisms (32%), *Staphylococcus aureus* (23%), vancomycin-resistant enterococci (VRE, 13%), methicillin-resistant *Staphylococcus aureus* (MRSA, 8%), *Pseudomonas aeruginosa* (5%), *Candida albicans* (3%), and *Escherichia coli* (2%). Mean plate counts, in colony-forming units, were 10,187 for gram-negative organisms, 99 for *E. coli*, 30 for *P. aeruginosa*, 86 for *S. aureus*, 207 for enterococci, and 31 for VRE. Findings suggest that bath basins may be a reservoir for bacteria and, therefore, a potential source of transmission of hospital-acquired infections.

■ COMMENTARY

Findings of this study suggest that potentially harmful microorganisms are present in bath basins in acute and critical care settings. With 2 exceptions, all cultures grew some form of bacteria, including VRE and MRSA. As part of infection control precautions, all at-risk patients who were admitted to ICUs were screened for MRSA (nares) on admission and all tested negative. Therefore, positive cultures were obtained from basins used by patients who were not previously identified as carriers. The researchers noted that all of the basins sampled were stored upright, instead of upside down, a position that allowed any water remaining in the basin to pool at the bottom. In some units, multiple basins were stacked on top of each other and basins were used for storage of incontinence cleanup items and other patient supplies, a practice that potentially created additional opportunities for contamination. In addition, nurses disposed of used bath water in sinks used for hand-washing, a practice that could result in contamination of the sink and surrounding areas.

Health care facilities have taken numerous steps to prevent nosocomial infections, including disinfection procedures, contact precautions, and education regarding the importance of adhering to protocols for gloving and hand-washing between each patient visit. Findings of this study provide strong support for the use of prepackaged bath products as a means of reducing risk for nosocomial infection. With a properly used bath pack, the same washcloth is not used to bathe the entire body, thus reducing the potential of spreading bacteria from one body area to another. Bathing requires less time and the product contains a skin conditioner that avoids the drying effects of soap and water. Prior studies have reported lower microbial counts on patients' skin after a prepackaged bath, compared to a bath given with a bath basin, although the differences were not significant. ■

Distress Contagion: Interpreting Health Care Team Response to ICU Stressors

ABSTRACT & COMMENTARY

By Leslie A. Hoffman, PhD, RN

Synopsis: *When events were assessed by one team member as highly stressful, individual distress was highly contagious, impairing performance of the entire multidisciplinary team.*

Source: Piquette D, et al. Stressful intensive care unit medical crises: How individual responses impact on team performance. *Crit Care Med* 2009;37:1251-1255.

The ICU is commonly viewed as a stressful environment. While common, stress responses are likely to vary over time, between individuals, and as a result of the context in which they occur. This study was prompted by the authors' desire to better understand factors that influence team function during the events that surround a medical crisis, defined as an event that requires the immediate response of multiple ICU team members as a consequence of acute patient instability. From interviews of ICU clinicians, the authors attempted to determine: 1) the effects of stress on individual performance during a medical crisis; 2) specific behaviors that positively or negatively impact team performance; and 3) potential strategies to manage such events more effectively.

A total of 32 participants were recruited from medical-surgical, cardiovascular, and neurosurgical ICUs in a university-affiliated institution, and interviewed using a semi-structured format. Participants included ICU attending physicians (n = 6), residents (n = 7), nurses (n = 14), and respiratory therapists (n = 5). Not

surprisingly, the need for quick decision making and the high stakes involved were cited as common stressors during a medical crisis. However, those interviewed described a number of resources available to meet such demands. Most crises were described as challenging rather than threatening, able to be brought quickly under control and, as a result, not perceived as distressful or problematic.

Several conditions were cited as leading to situations that were perceived as highly stressful. As might be expected, greater stress resulted if the patient did not respond and continued to deteriorate. High levels of stress were also reported if any member of the team appeared unable to appropriately fulfill his or her role or displayed an "emotional outburst." Such behaviors were perceived as creating a phenomenon the authors termed "disruptive contagion" because it spread rapidly, disrupting functioning of the team. To resolve this problem, participants recommended attempting to refocus on the patient-related goals and guarding against displays of excessive emotions, particularly displays of anxiety.

■ COMMENTARY

Several recent studies have commented on the high prevalence of symptoms of burnout and acute post-traumatic stress disorder (PTSD) among ICU clinicians. These findings are concerning in view of the increasing need for critical care clinicians. There are many commonly cited reasons that make the ICU environment one that exposes clinicians to high stress levels, but limited knowledge in regard to what to do to change this situation. The present study examined one aspect that may contribute to stress and burnout — ICU team response to a medical crisis.

The finding of most interest was the highly stressful consequences that were perceived to result from emotional outbursts during the management of such events. Termed "disruptive contagion" by the authors, such events triggered concerns regarding the ability (medical, nursing, or respiratory care) to provide optimal patient care, a critical factor in an environment where team members strongly depend on each other. Stress levels quickly escalated, particularly if the team leader was the one exhibiting a strong emotional reaction. This observation is important because it identifies a potentially modifiable risk factor.

For some time, anesthesia providers have used training in Crisis Resource Team Management to perfect their skills during unexpected or uncommon crisis events. Team function is stressed with participation by anesthesiologists, fellows, nurse anesthetists, and nurse anesthesia students. Implemented using high-fidelity human simulation, such training allows one to perfect skills in a safe environment with the benefit of debriefing. Key behaviors that are reinforced during such training include communication, leadership, optimal use of resources and information, and continuous reassessment to avoid inappropriate decision making. In addition to training in crisis management, such programs could be designed to incorporate actors whose behavior is designed to be profoundly disruptive with the goal of learning not only the technical skills required to adeptly manage such events, but also the behavioral skills needed to provide leadership and inspire confidence in others during such events. ■

CME / CNE 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.

CME / CNE Questions

9. Which of the following is currently recommended by the CDC when caring for a patient with influenza when contact with secretions is anticipated?

a. Surgical mask
b. Gown
c. Gloves
d. All of the above

10. What percentage of deceased medical ICU patients who underwent autopsy had histologic evidence of candida pneumonia?

a. 0%
b. 5%
c. 10%
d. 15%

11. In the study of stressors in the ICU work environment, participants reported that events during a medical crisis in the ICU were:

a. always viewed as highly stressful.
b. viewed as more stressful during night shifts.
c. rated differently in regard to stress by nurses and residents.
d. more stressful when accompanied by emotional outbursts.

Answers: 9. d, 10. a, 11. d.

PHARMACOLOGY WATCH

Supplement to *Clinical Cardiology Alert*, *Clinical Oncology Alert*, *Critical Care Alert*, *Infectious Disease Alert*, *Internal Medicine Alert*, *Neurology Alert*, *OB/GYN Clinical Alert*, *Primary Care Reports*, *Travel Medicine Advisor*.

Guidance on the Appropriate Use of NSAIDs

In this issue: NSAIDs in the elderly; managing GI and CVD risk with NSAIDs; low-dose naltrexone and fibromyalgia; treating glucocorticoid-induced bone loss; FDA Actions.

NSAIDs and dementia

Chronic use of nonsteroidal anti-inflammatory drugs (NSAIDs) in the elderly may increase the risk of dementia and Alzheimer's disease according to a new study. This is in contrast to previous studies that suggested that NSAIDs may actually be neuroprotective. The current study from Seattle looked at members of Group Health who were age ≥ 65 years (median, 74.8 years) and free of dementia. Patients were followed for up to 12 years to identify dementia and Alzheimer's disease. Of the 2736 patients studied, 351 (12.8%) were heavy users of NSAIDs at enrollment and another 107 became heavy users during follow-up. Over the course of the study 476 individuals developed dementia including 356 who developed Alzheimer's disease. Those defined as heavy NSAID users showed an increased incidence of dementia (hazard ratio [HR], 1.66; 95% confidence interval [CI], 1.24-2.24) and Alzheimer's disease (HR, 1.57; 95% CI, 1.10-2.23). The authors suggest that this study looked at an older cohort than previous studies. Decreased rates of dementia seen in the previous studies may have reflected a delay in onset of dementia, which may explain the increased incidence seen in the older patients in this study (*Neurology* 2009 April 22; epub ahead of print). ■

GI and CVD risk with NSAIDs

In a related story, the Canadian Association of Gastroenterology Consensus Group has published guidelines on use of long-term NSAIDs in patients at risk for GI bleeding and cardiovascular disease. The guideline includes the recommendation that NSAIDs should always be used at the lowest effective dose for the shortest possible duration of treatment and that patients should be evaluated for the need for gastroprotective strategies and cardiovascular risk. For patients at low GI risk but high cardiovascular risk, the group recommends naproxen because of potentially lower cardiovascular risk than other NSAIDs or COX-2 inhibitors. For patients at high risk for GI side effects and low cardiovascular risk, a COX-2 inhibitor alone or traditional NSAIDs with a PPI offers similar protection. For patients at very high risk for GI bleeding, a COX-2 inhibitor plus a PPI is the safest option. In patients with both GI and cardiovascular risks, NSAIDs should be avoided if possible, but if anti-inflammatories are needed, and the patient is already on aspirin, the recommendations included naproxen plus a PPI if cardiovascular risk is the main concern or a COX-2 plus a PPI if GI side effects are the primary concern (*Aliment Pharmacol Ther* 2009;29:481-496). ■

Low-dose naltrexone and fibromyalgia

Perform a Google search of "low-dose naltrexone"

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and you will find a myriad of anecdotal testimonies to the benefits of the drug in a wide range of diseases including fibromyalgia. Now a small study suggests that naltrexone may be of some benefit in this difficult condition. Naltrexone (not to be confused with naloxone) is an opioid receptor antagonist used primarily for treatment of alcohol dependence and opioid dependence. Because of multiple internet reports of benefit in patients with fibromyalgia, researchers from Stanford performed a single-blind, placebo-controlled crossover study of 10 patients with moderately severe fibromyalgia who were not on opioids. The dose of naltrexone used was 4.5 mg per day, which is less than 10 times lower than the dose used for addiction (50 mg per day). Patients on active treatment reported a 32.5% reduction in fibromyalgia symptoms compared to baseline vs a 2.3% reduction for placebo (P = 0.003 vs placebo). Side effects, which included insomnia and vivid dreams, were rare. Interestingly, patients with higher sedimentation rates had the greatest reduction in symptoms and best response to low-dose naltrexone. The authors hypothesize that low-dose naltrexone may inhibit the activity of microglia and reverse central or peripheral inflammation, thus reducing symptoms of fibromyalgia, although more studies are needed. They also suggest that naltrexone can be used in addition to other medications commonly used for fibromyalgia (*Pain Med* 2009 April 22; epub ahead of print). ■

Treating glucocorticoid-induced osteoporosis

For patients with glucocorticoid-induced osteoporosis, a once-yearly infusion of zoledronic acid is as effective as daily risedronate for the prevention and treatment of bone loss according to a new study from *Lancet*. In a 1-year, international, randomized, double-blind, placebo-controlled, non-inferiority study, 833 patients with glucocorticoid-induced osteoporosis were randomized to receive zoledronic acid 5 mg as a 100 mL IV infusion over 15-20 minutes on day 1 plus oral placebo or 5 mg of risedronate daily and 100 mL IV placebo infusion on day 1. Patients were allocated to a prevention or treatment subgroup depending on the duration of glucocorticoid use preceding study. Zoledronic acid infusion was non-inferior and superior to risedronate for increase of lumbar spine bone mineral density in both the treatment (P = 0.001) and prevention groups (P < 0.0001), respectively. Adverse events were more frequent in patients given zoledronic acid primarily because of increased flu-like symptoms within the first 3 days after the infusion. The authors conclude that a single 5 mg intravenous infusion of zoledronic acid is non-inferior and possibly more effective and more acceptable to patients than 5 mg of oral risedronate daily for prevention and treatment of bone loss associated with glucocorticoid use (*Lancet* 2009;373:1253-1263). An accompanying editorial suggests that once-yearly zoledronic acid seems to have obvious advantages over an oral regimen but the long-term safety is still unknown and also raises the question of whether anabolic drugs, such as teriparatide, which stimulate bone formation by acting on osteoblasts and osteocytes, might eventually be a better option (*Lancet* 2009;373:1225-1226). ■

FDA Actions

Plan B, the so-called "morning after pill" will soon be available to women age 17 and older without a prescription. Previously the FDA and the Bush administration had limited the access of the drug to women 18 and older but a U.S. district judge ruled in March that the older age limit was "arbitrary and capricious." The judge also directed the agency to evaluate clinical data to determine whether there should be any age restrictions on use of the drug. The FDA has no plans to appeal the court's decision. Duramed Pharmaceuticals must file paper work with the FDA, a process that is expected to take 30 days. Plan B is levonorgestrel in a 2-pill pack, the first to be taken within 72 hours of unprotected intercourse and the second pill 12 hours later.

The FDA has approved a new TNF-alpha blocker monoclonal antibody for the treatment of rheumatoid arthritis, active psoriatic arthritis, and active ankylosing spondylitis. Golimunab is given once a month as a subcutaneous injection in combination with methotrexate for rheumatoid arthritis. It may be used with or without methotrexate for psoriatic arthritis and as monotherapy for ankylosing spondylitis. As with all TNF-alpha blockers, the FDA is requiring a risk evaluation mitigation strategy (REMS), which includes a medication guide for patients and a communication plan for physicians regarding potential side effects. Also similar to other drugs in this class, golimumab will carry a boxed warning regarding the risk of tuberculosis and invasive fungal infections. Golimumab was developed by Centocor Ortho Biotech, a division of Johnson & Johnson. The drug will be marketed under the trade name Simponi™. ■