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President's Message

Good Reasons to Attend Annual Meeting in October

Michael F. O'Connor, M.D., F.C.C.M.

There are many good reasons to come to SOCCA's Annual Meeting, including seeing old friends, making new ones, and interacting with your national and international colleagues. Here are some more reasons:

- To attend our second, expanded course on perioperative ultrasound and learn about perioperative/ICU ultrasound from Michael Wall, M.D., Danny Talmor, M.D. and the excellent faculty composed of Anne-Sophie Beraud, M.D., Thomas Comfere, M.D., Charl de Wet, M.D., Michael Hanedy, M.D., Antonio Hermandez, M.D., Benjamin Kohl, M.D., Wolf Benjamin Kratzert, M.D., Matthias Merkel, M.D., Colin F. Royse, M.B., Chad Wagner, M.D., and Michael Woo, M.D.
- To hear a debate between Richard Silverman, M.D. and Walter Boyle, M.D. about the role that mid-level practitioners might play in the ICU.
- To learn about controversies in palliative care from Rebecca Aslakson, M.D., Craig Blinderman, M.D., Allen Gustin, M.D., and Liza Weavind, M.D.
- To see the basic and clinical science presented in our scientific poster sessions, a vital and growing part of our annual meeting.
- To hear about how critical care has changed from some of the giants who founded this organization, including John Downs, M.D., Myer Rosenthal, M.D. and Jeffrey Vender, M.D.
- To seize this chance to visit Washington, D.C, capital of the greatest country in history. To visit the Smithsonian, and to break bread with old friends and colleagues at any of D.C.'s wonderful restaurants.
- Come to SOCCA's Annual Meeting to learn what your peers believe is the state of the art in your profession, what its future might hold, and how we can use the experience of our past to craft a brighter future.

The past 20 months have been an exciting time for SOCCA. I have had the good fortune to work with a terrific board of directors and executive director. I have benefited from their tireless efforts on behalf of our organization. It has been an honor to serve with such a terrific group of leaders on behalf of such a great organization.

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A Note from the Editor to SOCCA Members:

If you would like to contribute a review for a Fellowship Program at your institution in a future issue of the SOCCA Interchange, please contact Chris Dionne at **c.dionne@asahq.org**.

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PRO: Drug Shortages Compel Critical Care Physicians to Provide Evidence-based, Cost-effective Care

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Recent increases in drug shortages pose numerous problems for hospital systems, anesthesia providers and critical care physicians. The total number of drug shortages in 2005 was around 50. In 2010 there were 178 drug shortages reported to the FDA, 132 of them being sterile injectables.[1] Although sterile injectable drugs are a small percentage of the overall prescription drug market, they make up a disproportionate share of drugs in shortage. Currently, we have a shortage of important injectables such as succinylcholine, atropine, epinephrine, furosemide, etomidate, calcium chloride and diltiazem. Acquisition and administration of medications with proven patient benefit has become increasingly difficult particularly with generic medicines. Multiple classes of generic medications ranging from sedatives to chemotherapy agents offer patient benefit but little financial incentives to pharmaceutical companies. In addition, many pharmaceuticals require components only supplied by foreign drug companies, or the natural materials required to make some agents has been depleted, such as bretylium. Much has already been written about the socioeconomic and medical pitfalls to drug shortages, but there are some potential underlying benefits.

Trainee education for both residents and fellows depends upon the interplay of self-education through reading and exposure to a wide range of case presentations. Therapeutic modalities for some pathologies are predetermined, such as targeted antibiotic therapy for drug-resistant organisms. However, habitual or thoughtless prescribing is a major problem particularly when choosing "favorite antibiotics" for pneumonia or old standbys for ICU sedation when alternative therapies exist. What can be argued is that a limited availability of once indiscriminately prescribed medications can potentially foster critical thinking to determine alternate therapy options. For example, the existing thiopental unavailability and waning etomidate supplies have many practitioners concerned over patient safety. Other induction medications such as methohexital or ketamine may not have the same physiologic effects but still can be safe when used judiciously and may be preferable in some cases. Furthermore, a shortage of sedatives in the ICU like benzodiazepines and propofol may increase the use of other therapeutic modalities such as maintenance of sleep/wake cycles and patient orientation protocols. Recently, Roberts and colleagues found that an 84-percent decrease in propofol use in adult critical care units did not alter duration of mechanical ventilation.[2] The use of dexmedetomidine and narcotics for ICU sedation, as a result of benzodiazepine shortages, can positively affect mortality.[3]Overall, learning or relearning different methods for patient care can increase the educational experience of trainees while perhaps improving outcomes.

In order to secure alternative medication types and concentrations, many hospitals develop multidisciplinary committees to address shortages. The teams often consist of hospital administrators, anesthesiologists, critical care physicians and pharmacists. Fostering communication in the health care field may broaden treatment options through open discussion. In addition, patient drug safety considerations from nursing, physician, administrator and pharmacist perspectives potentially decrease complications with both drugs in shortage and drugs in good supply. This open format also helps ensure hospital-wide compliance preventing interdepartmental drug usage inconsistencies that would further worsen existing shortages and increase the likelihood of new shortages. Griffith and colleagues point out, "an effective approach should include prospectively tracking shortages and maximizing inventory by appropriately managing usage."[4] The committees maintain employee education on medication formulation, mixing and administration guidelines that help to decrease waste and increase patient safety. Also, these hospital systems have begun addressing shortages through modifying default drug choices, introducing physician disincentives for prescribing certain drugs and restricting physician's

> "Shortages have opened the door for communication not only within hospitals but on a larger national scale."

prescribing choices.[5] Inadvertently, drug shortages have increased usage of a multidisciplinary approach while helping to decrease complications, decrease further shortage and increase patient safety.

Drug shortages can help ameliorate administration of medications given historically but with minimal indication. For instance, etomidate is used as the sole amnestic in some critical care units and emergency departments for procedures. While a useful drug, etomidate does not have a completely benign side effect profile. Automatic use of etomidate may increase the likelihood of producing adrenal insufficiency in a population of patients already at risk; this is supported by the CORTICUS trial and a recent meta-analysis by Albert and colleagues.[6] Etomidate is associated with higher morbidity, including hospital length of stay, ICU days and days requiring mechanical ventilation.[7] Sodium bicarbonate usage in "code events"continues to be routine despite the fact that the American Heart Association has removed it from ACLS protocols and much hard data exist to support its disuse secondary to its affect on pH and alveolar ventilation.[8] The recent shortage of sodium bicarbonate injectable syringes helps critical care physicians reevaluate the necessity of medications in particular clinical scenarios. Such close examination of practice methods potentially decreases patient risk and decreases use of non-indicated medications in routine practice.

Drug shortages have not only drawn the attention of health care providers but also the public and the public's electorate on a national scale. The ABC News Medical Unit recently reported in April the results of an anonymous online survey conducted by the ASA of 3,063 anesthesiologists in which seven deaths were directly attributed to drug shortages.[9] However, the survey raised more questions than it answered and no causal link could be drawn between a particular scarce medication and patient mortality. One commenter on the survey asserts, "Besides the postponement or cancellation of elective surgeries and less-than-optimal outcomes, drug shortages force anesthesiologists to switch from shorter-acting to longer-acting drugs." More than half of doctors who answered the ASA survey questions said they'd altered procedures to accommodate shortages. For example, they switched from general to regional anesthesia. However, the author ignored the fact that other "long-acting" drugs are also in short supply and many patients benefit from regional anesthesia over general.

After increasing shortages of chemotherapy agents, including cytarabine, the American Society of Clinical Oncology (ASCO) has had congressional and FDA meetings throughout 2010 and 2011 focused on mechanisms to mitigate drug shortages, including establishing a pricing floor for generic drugs, mandatory proactive drug shortage reporting to the FDA and prompt review of backlogged medications awaiting generic status.[10] Congress and the president have worked in conjunction to increase the U.S. Food and Drug Administration's power in controlling drug shortages. In November 2001, President Obama issued an executive order expanding FDA reporting regulations while increasing Department of Justice oversight of potential pharmaceutical stockpiling and price gauging.[11] Thus, serendipitously, the shortages have opened discussion regarding regulatory processes concerning government, consumers and industry. This is a discussion that may lead to the prevention of countless more shortages. In 2011 alone, nearly 100 shortages were prevented secondary to the cumulative actions of patients, physicians and governmental officials. Without some shortages, multilevel discussions would have never begun.

Drug shortages will continue to be a part of medicine practice, especially as long as the health care system follows an "infinite resource" care model and drug manufacturers shun cheap agents for more profitable alternatives. However, despite a potential negative impact on health care, shortages do offer some positive aspects. They can increase trainee exposure to less utilized medications and teach flexibility in medical practice. They also can help physicians reevaluate the necessity and benefit of certain drugs. Shortages have opened the door for communication not only within hospitals but on a larger national scale. In the end, decreased access to pharmaceuticals may increase the availability of new, better drugs that are easier and cheaper to synthesize. More importantly, physicians must now think before they prescribe.

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CON: Drug Shortages Expose Patients to Harm and Leave Clinicians to Choose Potentially Unsafe Treatments for Their Patients

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Drug shortages are not a new phenomenon in medicine. Medication shortages can be traced back to the 1950s, with vaccination shortages and the influenza epidemic. As little as 20 years ago, drug shortages were an uncommon inconvenience to patients and physicians. In 1996, the FDA reported only three medications in short supply. By the year 2000, that number had billowed to 119.[1] In 2011, the FDA tracked over 250 drug shortages. The majorityof these shortages, about 60 percent in 2010, are seen in sterile, injectable medications.[2] This puts specialties such as anesthesia, emergency medicine and certainly critical care medicine in a position to be profoundly affected. Issues arising from drug shortages include, but are not limited to, patient safety, health care cost, quality control and biomedical ethics.

In a medical environment that is increasingly centered on patient safety and patient outcomes, drug shortages pose a significant threat to patient care. Shortages have affected many classes of medications routinely used in the critical care setting, including opioids, opioid antagonists, antibiotics, muscle relaxants, diuretics and blood pressure medications, among others. As pointed out by De Oliveira and colleagues, "Medication shortages may result in an environment that predisposes to an increase in the likelihood of medication errors, thus impairing patient safety."[1] Data collected by U.S. Pharmacopeia Center for the Advancement of Patient Safety highlighted 832 cases of medication errors from January 2003 through August 2004, which identified medication shortages as a major cause of such mistakes.[3] Substitution of medications with higher concentration or potency than routinely used can lead to an overdose. Good examples of this can be found in the medications fentanyl and naloxone. Both of these medications are on the shortage list, leaving physicians to use alternative doses or concentrations to cover the shortage. This puts patients at risk for overdose and can lead to life-threatening complications such as respiratory depression, respiratory arrest, cardiac arrhythmias and pulmonary edema.[1]

> "The bioethics of health care delivery is also put into play regarding drug shortages. Who has the final say as to which patients receive a scarce medication?"

Another alarming example is the medication succinylcholine. This medication is the drug of choice for rapid sequence induction in patients with full stomachs in need of emergency airway management. Unavailability of this medication would result in the use of nondepolarizing agents, possibly leading to poor intubating conditions and increased risk to patients with unanticipated difficult airways that are also difficult to mask ventilate. Additionally, rocuronium, an often-used alternative to succinylcholine for rapid sequence induction, is also on the shortage list.[1]

Antibiotics represented 13 percent of the 193 unavailable medications as of February 2011. Griffith et al. states "a tenuous supply of anti-infective agents may result in delays of effective therapy, suboptimal therapeutic selections, and incorrect substitutions."[4] Many disease states, including bacterial sepsis, bloodstream infections, nosocomial pneumonia, ventilator-associated pneumonia and community-acquired pneumonia, show increased mortality rates after delay in antibiotic therapy. Not only does timely treatment with antibiotics affect mortality, but the choice of antibiotic used for treatment does as well. This can be seen in the treatment of neurosyphilis from 1999-2000, when the drug of choice (penicillin G) was recalled owing to regulatory concerns from the FDA necessitating that physicians use "alternative" agents.[4]

The current political environment in the U.S. has placed an ever-narrowing focus on the containment of health care costs. Drug shortages have a direct affect on the cost of health care. With the majority of these sterile injectable medications being generic, overhead

for production is high and profit margin is low for manufactures. Gehrett and colleagues state: "Given the pricing structure and regulatory environment, there is no assurance of a competitive return on invested capital used for facility expansion or improvement…,"[5] i.e., manufactures have no incentive to invest in the production of these generic medications. As options for lower-cost generic medications dwindle, physicians are forced to turn to newer, more expensive therapies. Hospitals also feel the effects of the drug shortages in their overhead budget. In the face of declining resources, many institutions are forced to start stockpiling medications. Storage for these stockpiles is not free of costs, which are absorbed by the institution. Also, costs increase for pharmacy departments when they are forced to purchase drug products outside of contracts, known as "the grey market," because of shortages.

In exceptional instances, such as that which has occurred with the propofol shortage, the FDA may allow importation of "unapproved" alternative medications. The FDA allowed the temporary use of an unapproved propofol formulation, Propoven 1%, after its inspection of its manufacturing facilities and testing to evaluate safety of the product. There are concerns with medications produced overseas, as the guidelines for the safe production of these medications varies widely from nation to nation.[1]

The bioethics of health care delivery is also put into play regarding drug shortages. Who has the final say as to which patients receive a scarce medication? Dr. Annekathryn Goodman of Massachusetts General Hospital addresses these concern when she asks, "will resources be handed out on a first-come, first-served basis, or will distribution of this resource be based on age, predicted years of life remaining, and the importance of the individual to society?"[6] These are not easy questions to answer, much less attempting to implement ethical principals in a drug shortage crisis.

The effects of medication shortages and their negative impact on the global health care community cannot be overestimated. Patient safety should never be compromised, regardless of the cause. Sweeping changes are needed in the political, legal and health care venues to ensure that proven generic medications and first-line treatments are not removed from the critical care physicians armamentarium to fight disease.

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CME Question

Which of the following medications that is used as an alternative to succinylcholine for rapid sequence inductions in the emergency airway protocol is currently on the FDA drug shortage list?

A. Mivacurium
B. Cisatricurium
B. Vecuronium
D. Rocuronium

Answer: D

A Review of Current and Novel Antiplatelet Agents

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Antiplatelet agents are widely used in the prevention and treatment of thrombotic diseases. There are multiple antiplatelet agents in current clinical usage and development, and knowledge of each one's indications and potential side effects are necessary for intensivists caring for the patients on these medications.

Antiplatelet drugs are classified primarily according to the molecular mechanism through which they have their pharmacologic effect, and this article will address the indications, pharmacology and potential limitations of the agents within each category.

COX-1 Inhibitors

Drugs in this class:
Aspirin

Indication:
The secondary prevention of atherothrombotic disease.[1]

Mechanism of action:
Aspirin works by inhibiting the prostaglandin-producing enzyme cyclooxygenase, which can affect inflammation, fever, protection of gastric mucosa, regulation of renal function and platelet aggregation.[4] The platelet prostaglandin thromboxane A2 increases expression of fibrinogen receptors on platelet membranes and facilitates fibrin crosslink between platelets to form a platelet plug. COX-1 inhibition by aspirin is irreversible and regular low doses lead to more than 95 percent suppression of thromboxane A2 production.[68]

Limitations of COX-1 inhibitors:
1. Gastrointestinal bleeding or intolerance.
2. There are patients who seem to have resistance to aspirin, and recurrent vascular events are not infrequent in patients on chronic aspirin therapy, at a rate of 6-8 percent per year.[5] Whereas "aspirin resistance" is thought to be affected by compliance, cigarette smoking, hyperlipidemia and diabetes, the exact mechanism is a focus of ongoing research, especially with respect to the need for dual or multiple antiplatelet therapy.[6]

ADP Receptor Antagonists

Drugs in this class:
Ticlopidine (Ticlid), clopidogrel (Plavix) and prasugrel (Effient) are the current agents used in this class.

Indication:
MI, stroke/TIA or symptomatic peripheral arterial disease, usually used in conjunction with aspirin.

Mechanism of action:
Thienopyridines inhibit adenosine diphosphate (ADP)-dependent platelet function by irreversible modification of the platelet $P2Y_{12}$ receptor. Drug effects persist for the life of the platelet. Short-lived active metabolites are generated from the orally administered prodrug via cytochrome P450.[7] Due to the unfavorable side-effect profile of ticlopidine (diarrhea, neutropenia and aplastic anemia), clopidogrel has become the preferred thienopyridine.[8] Important differences in metabolism and efficacy exist between clopidogrel and prasugrel.

Clopidogrel, a second-generation thienopyridine, is metabolized by cytochrome P450 from prodrug to active form in a two-step process.[9] Genetic variability in metabolism exists, with poor metabolizers exhibiting higher rates of cardiovascular events. Genetic testing for cytochrome P450 2C19 (CYP2C19) polymorphisms can identify patients at increased risk for treatment failure and should be considered prior to initiating therapy in patients at high risk for poor outcomes.

Prasugrel, a third-generation thienopyridine, requires a single-step cytochrome-dependent metabolism from prodrug to active form. Unlike clopidogrel, common P450 genetic variants do not significantly affect active drug levels. Onset of action is faster than clopidogrel.

Prasugrel has been shown to generate an active metabolite more efficiently than clopidogrel, leading to higher levels of platelet inhibition.[19] The PRINCIPLE-TIMI 44 trial demonstrated that prasugrel achieved superior platelet inhibition when compared to high-dose clopidogrel.[20] In the TRITON-TIMI 38 trial, prasugrel reduced the composite endpoint of death, non-fatal MI and non-fatal stroke by 20 percent in comparison to clopidogrel.[21] However, rates of major hemorrhage were higher by 32 percent in the prasugrel group compared to the clopidogrel group. Due to the higher bleeding risk, prasugrel is recommended for those patients who are poor metabolizers of clopidogrel and in those patients at lower risk for bleeding complications.

Limitations of thienopyridines:
1. The metabolism of clopidogrel, which is a prodrug, requires two-step activation involving several hepatic cytochrome P

isoenzymes for conversion to the active metabolite.[22] This results in a delayed onset of action (6-8 hours after a 300mg loading dose) and potentially increases the risk of ischemic events.
2. Irreversible binding to $P2Y_{12}$ receptors, leading to a gradual recovery of platelet function after drug withdrawal. In the CURE study, among patients undergoing CABG, bleeding tended to be more common if CABG was performed within five days of clopidogrel administration, as evidenced by chest tube output and blood product administration.[12]
3. The broad interindividual variability in levels of platelet inhibition achieved with clopidogrel with reports showing that about 30 precent of patients experience clopidogrel "nonresponsiveness" despite appropriate dosing.[24]

Reversible ADP-receptor Antagonists

Drugs in this class:

Ticagrelor (Brilinta, oral), cangrelor (intravenous) and elinogrel (both intravenous and oral) are associated with rapid onset and offset of platelet inhibition. Of these, only ticagrelor is approved for clinical use.[25]

Indication:

Stable coronary artery disease for prevention of ischemic events or prevention of stroke or death from vascular causes

Mechanism of action:

Ticagrelor belongs to the class of drugs termed cyclopentyl-triazolo-pyrimidines. Like the thienopyridines, ticagrelor blocks the platelet $P2Y_{12}$ receptor to inhibit the prothrombotic effects of ADP.[25] Ticagrelor binds reversibly to $P2Y_{12}$ and does not require metabolic activation. It needs only 1.5-3.0 hours to reach peak plasma levels, allowing a rapid antiplatelet effect.[26,27] Ticagrelor's half-life is approximately 12 hours and its antiplatelet effect is low at 48 hours after the last dose.[28] It has a faster onset than clopidogrel and does not require conversion from a prodrug, which means there is less variability in patient responsiveness.

Limitations of reversible ADP-receptor antagonists:

1. Ticagrelor requires twice-daily dosing, raising concerns with compliance.
2. Higher incidence of hemorrhagic stroke and GI bleeding with ticagrelor compared with clopidogrel is also concerning and is a definite limitation of its use.[35]

Thrombin Receptor Antagonists

Thrombin interacts with two platelet receptors called PAR-1 and PAR-4. Protease-activated receptor 1 is the predominant receptor in humans and has a higher affinity for thrombin compared with PAR-4.[36] Two agents against PAR-1 are currently under investigation. Vorapaxar is a potent oral thrombin receptor antagonist with a half-life of 126-269 hours that inhibits platelet function for up to four weeks after discontinuation.[37,38] Two ongoing phase 3 trials are under way with vorapaxar.[38,39,40] A second oral agent, atopaxar, has recently completed phase 2 evaluation.[41]

Glycoprotein IIb/IIIa Inhibitors

Drugs in this class:

Abciximab (Reopro), eptifibatide (Integrilin) and tirofiban (Aggrastat).

Indication:

Randomized clinical trials have demonstrated that adjunctive therapy with GP IIb/IIIa antagonists decreases the combined endpoint of death, myocardial infarction and target vessel revascularization after PCI.[50,51]

This class of antiplatelet agents is associated with greatest clinical benefit in the following scenarios:

1. Conditions associated with a high likelihood of intracoronary thrombosis, such as ST-elevation and non-ST-elevation MI where an invasive strategy is planned.
2. When the anticoagulant is heparin rather than a direct-thrombin inhibitor.
3. When the patient has not been treated before PCI with a $P2Y_{12}$ antagonist.
4. In unstable ACS patients who require transfer to a PCI center.
5. To reduce the risk of stent thrombosis in a patient with ST-elevation MI (especially when there is not adequate pretreatment with a $P2Y_{12}$ antagonist).

Mechanism of action:

Abciximab is a monoclonal antibody that displays a rapid on-rate, binding to platelets in less than 1 min.[46] The dissociation (off-rate) of abciximab is measured in hours.[47] Abciximab has the greatest affinity for GP IIb/IIIa among the drugs in this class.[47] Eptifibatide and tirofiban are small molecules that exhibit a longer half-life compared with abciximab, 2.5 h and 2h, respectively.[48] Another key difference is the off-rate of eptifibatide and tirofiban which is 10-15 seconds compared with hours for abciximab.[49]

Limitations of glycoprotein IIb/IIIa inhibitors:

Oral GP IIb/IIIa inhibitors have been studied, but the results have been disappointing. Because of an increased risk of death in those treated with oral agents, further development was abandoned.[57]

Phosphodiesterase Inhibitors

Drugs in this class:

Cilostazol (Pletal) and dipyridamole (Persantine) are two commonly used agents in this class.[58,59] The combination drug of dipyridamole and aspirin is sold under the trade name of Aggrenox.

Continued on page 9

A Review of Current and Novel Antiplatelet Agents

Continued from page 8

Indication:

Intermittent claudication is a frequent consequence of peripheral arterial disease with a prevalence of 2-9 percent in individuals greater than 50 years.[59] Treatment options for this disease are limited, with surgical intervention reserved for severe or progressive cases.[60]

Pharmacotherapy is reserved for patients resistant to risk factor modification, exercise and diet changes.[60]

Mechanism of action:

The phosphodiesterase inhibitors function as both vasodilators and antiplatelet drugs. Cilostazol is a reversible type III phosphodiesterase inhibitor with vasodilator and antiplatelet effects. The inhibition of PDE-III by cilostazol results in a rise in intracellular cyclic adenosine monophosphate (cAMP) levels in PDE-III-rich cells such as platelets, vascular smooth muscle cells, endothelial cells and cardiocytes.[61] Cilostazol also inhibits adenosine uptake into cells, leading to an elevation of interstitial and circulating adenosine levels. By elevating cAMP levels and blocking calcium ion release, cilostazol inhibits contraction of smooth muscle cells and produces non-hemogenous vasodilation, especially in the femoral arteries.[62] Disease progression might be slowed through its antiproliferative effect on vascular smooth muscle.[63] *Up to 12 weeks of therapy may be required before symptoms improve.*

The phosophodiesterase inhibitor dipyridamole had previously been used as a coronary vasodilator and was later developed as platelet inhibitor acting via the ADP mechanism, showing improved efficacy in conjunction with aspirin in cerebrovascular disease.[65, 66]

Limitations of phosphodiesterase inhibitors:

1. Cilostazol is contraindicated in patients with heart failure of any severity due to theoretical concerns related to its mechanism of action and classification as a phosphodiesterase inhibitor.[59]
2. Cilostazol is metabolized extensively by the cytochrome isoenzymes CYP3A4 and CYP2C19. When known inhibitors of these isoenzymes (erythromycin, diltiazem, fluconazole, etc.) are coadministered with cilostazol, supratherapeutic levels have been observed.[64]

Summary

In summary, a multitude of clinical conditions are currently treated with antiplatelet therapy. Novel drug classes that target unique aspects of platelet aggregation are introduced here as well as a newer generation drugs in familiar classes. For the peri- and postoperative clinician, an understanding of the pharmacology and indications for each agent is crucial.

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Literature Review: The Low-Tidal-Volume Wave Rolls On

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Lellouche F, Dionne S, Simard S, Bussières J, Dagenais F. High tidal volumes in mechanically ventilated patients increase organ dysfunction after cardiac surgery. *Anesthesiology.* 2012; 116 (5):1072-82.

Since the seminal ARDSNet trial in 2000,[1] ventilation with lower tidal volumes, i.e., 4-8 mL/kg of ideal body weight, has become the standard of care in patients with acute lung injury (ALI) and acute respiratory distress syndrome (ARDS). In this population, the low-tidal-volume approach has been shown to decrease organ dysfunction and mortality, probably via reduction of ventilator-induced lung injury and resultant proinflammatory cytokine release. However, it is still debated how low the volume should be to see a benefit and whether this approach should be applied to other disease states, or even used preventatively in those at risk for lung injury. Studies evaluating the effects of different tidal volumes in various populations without ALI have produced mixed results.

It is widely believed that the development of lung injury is usually triggered by a systemic inflammatory process, which is then exacerbated by the increased mechanical stretch produced by high tidal volumes; this is referred to as the "double-hit theory." Cardiac surgery and cardiopulmonary bypass (CPB) incite a substantial inflammatory response in the body, and cardiac surgery patients are at elevated risk for pulmonary complications, such as ALI, compared to other surgical patients.[2] Therefore, if lower tidal volumes protect against developing lung injury, this effect might logically be seen in individuals recovering after cardiac surgery. One randomized controlled trial investigating this effect found that using lower tidal volumes to ventilate patients after cardiac surgery resulted in a lower proportion of patients remaining intubated six hours later and a lower rate of reintubation.[3] However, this study was relatively small and did not specifically address rates of lung injury and non-pulmonary organ dysfunction.

The latest addition to this debate is the study by Lellouche and colleagues in a recent issue of *Anesthesiology*. This paper used a prospective cohort design to examine whether higher postoperative tidal volumes were associated with greater rates of organ dysfunction in cardiac surgical patients. This study enrolled 3,434 adult patients undergoing coronary-artery bypass grafting (CABG) or valvular heart surgery with sternotomy and CPB at the Quebec Heart and Lung Institute. Patients undergoing heart transplant, mechanical circulatory support, descending aortic surgery or other infrequent procedures were excluded. After CPB, recruitment maneuvers were initiated, and patients were then ventilated using synchronized intermittent mandatory ventilation (SIMV) with respiratory rate (RR) of 10 breaths/min, positive end-expiratory pressure (PEEP) of 5 cm H2O, and FiO2 of 70-100 percent. Patients were managed via fast-track protocol: early termination of sedation, minimal analgesia and extubation as early as clinically feasible. Dedicated respiratory therapists managed ventilator weaning. There was no protocol for setting initial tidal volume, but volumes could be adjusted in the perioperative period by anesthesiologists or intensivists based on blood gas results.

The initial tidal volume on admission to the intensive care unit (ICU) was used for all analyses; while somewhat limited as a data point, this value was used for the entire course of SIMV in 84 percent of patients. Ideal body weight (IBW) was calculated for all patients. Three groups of tidal volume were defined: low (<10 mL/kg IBW), traditional (10-12 mL/kg IBW) and high (>12 mL/kg IBW). Organ dysfunction, the primary outcome, was defined as prolonged mechanical ventilation (more than 24 hours), prolonged hemodynamic instability or use of vasopressors (more than 48 hours), or increase in creatinine greater than 50 µM (0.57 mg/dL) from preoperative baseline. Secondary endpoints included duration of mechanical ventilation, length of ICU and hospital stay, and ICU, hospital and long-term mortality. In terms of statistics, group comparisons were performed with one-way analysis of variance (ANOVA) for continuous variables and the chi-square test for categorical variables.

The majority of patients underwent isolated CABG. Numerous factors were associated with use of higher tidal volumes, notably body mass index (BMI) > 30 and female sex. Emergency surgery, diabetes mellitus, hypertension, chronic pulmonary disease and postoperative intra-aortic balloon pump (IABP) use were also correlated with higher tidal volumes. In the multivariate analysis, high tidal volume was an independent risk factor for organ failure (single or multiple). The high-tidal-volume group had a rate of any organ failure of 18 percent and multiple organ failure of 6.1 percent, versus 11 percent and 2.9 percent for the low-tidal-volume group. Respiratory, hemodynamic and renal dysfunction were all more common with higher tidal volumes. High tidal volume was also an independent risk factor for prolonged ICU stay (>48 hours and >1 week). Single- or multiple-organ failure increased risk of ICU, hospital and overall mortality. Higher tidal volume itself was not shown to be a risk factor for mortality.

This paper has some provocative implications. First, it seems that high tidal volume may confer a risk for development of both pulmonary and non-pulmonary organ failure in patients at risk for ALI, with a consequent increase in ICU length of stay. This finding is plausible in light of multiple studies that have found lower rates of organ failure in patients ventilated with lower volumes. Therefore, it seems prudent to use lower tidal volumes (i.e., < 10 mL/kg of IBW) as a default setting for ventilating at-risk patients when clinically feasible. In most cases, when lung function is optimized perioperatively via recruitment maneuvers, PEEP, bronchodilators and other such therapies, this is an attainable goal.

Another interesting point made by the authors is that women and obese patients are more likely to be ventilated with potentially injurious settings. Several other studies have reported such patterns.[4,5] This should be an easily remediable problem, solved in most cases by remembering to utilize IBW, not actual body weight, when setting the ventilator. This approach should be part of standard protocol in most intensive care settings, as well as potentially in the O.R.

Nevertheless, the paper has several limitations. First, as a non-randomized observational study, there is a chance that unrecognized confounders may have affected the results; this effect is mitigated by the multivariate analysis but remains a problem for all non-randomized studies. Second, as a related matter, while this study determined an association between higher tidal volumes and organ failure, causality is more difficult to establish. For instance, when patients are developing lung injury, hypoxia and organ failure, clinicians may set higher ventilator volumes to reduce atelectasis and improve oxygenation. The paper did not include data on actual levels of PEEP and FiO2 utilized, nor rates of hypoxia, making it difficult to determine the nature of this relationship. In fact, the authors themselves cite failure to evaluate and standardize levels of PEEP as a weakness in their design. In many cases, higher PEEP and recruitment maneuvers must be used to offset the atelectasis that can otherwise result from lower tidal volumes. And while it is noted that in the majority of patients the initial tidal volume in the ICU was continued for the duration of SIMV, it is unclear what ventilator changes were instituted in the remainder of patients and how this could have affected the results.

While there was a relationship between higher tidal volumes and organ failure, the tidal volumes picked by the authors to represent "high" and "low" groups are somewhat higher than physiologic tidal volumes, and higher than what is prevalent in most recent lung-injury research. It would be interesting to know if the relationship the authors identified would have held for even lower tidal volumes that might be more in line with current best practice for ALI.

Interestingly, while this study associated higher rates of organ failure and longer ICU stays with high tidal volumes, there was no difference in mortality between different tidal-volume groups. This is despite the fact that patients with organ failure after surgery are at higher risk of death, a fact confirmed by the authors' data. It is therefore unclear why high tidal volumes would not be directly associated with increased mortality; this was not discussed in detail by the authors and may be related to relatively low rates of mortality in the study population as a whole.

In summary, this new work by Lellouche and colleagues provides further support to the idea that using lower tidal volumes is beneficial for patients who are at risk for developing lung injury, which potentially includes nearly all patients receiving intensive care. This approach may reduce ventilator-associated trauma and consequent organ dysfunction. It is especially important to pay close attention to the ventilator settings in women and the obese, who are at higher risk of over-ventilation. However, these results are not conclusive. A randomized controlled trial enrolling at-risk patients, comparing multiple tidal volumes, and collecting comprehensive data on ventilator settings, oxygenation and organ dysfunction would bring more clarity to this important issue. In the meantime, the tide of low volumes makes further inroads – apparently a good thing for the critically ill.

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Multiple-Choice Review Question

Based on the study by Lellouche et al., which of the following patients would be least likely to receive ventilation with high tidal volumes based on ideal body weight?

A. 68-year-old diabetic man with a myocardial infarction, cardiogenic shock and an intra-aortic balloon pump undergoing emergent CABG with CPB.
B. 70-year-old woman with rheumatic heart disease undergoing isolated mitral valve replacement.
C. 50-year-old obese man with hypertrophic cardiomyopathy undergoing septal myectomy.
D. 85-year-old man with chronic kidney disease and past cerebrovascular accident undergoing aortic valve replacement.
E. 73-year-old man with COPD undergoing combined CABG and mitral valve repair.

Answer: D

Literature Review: Progress in Mortality and Morbidity in the ICU: What Is the Value of an Intensivist at Night?

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Florida Gulf-to-Bay Anesthesia Associates, P.A.

Wallace DJ, Angus DC, Barnato AE, Kramer AA, Kahn JM. Nighttime intensivist staffing and mortality among critically ill patients. *N Engl J Med*. 2012; 366:2093-101.

This retrospective cohort study[1] in the May 31, 2012 *New England Journal of Medicine,* accompanied by an editorial in the same issue of the journal,[2] is one of a growing class of papers that address mortality in critically ill patients, with a view toward assessing the value of having trained intensivists, not merely internists, anesthesiologists, emergency physicians or surgeons, immediately available to care for them. Intensivists are expensive, it is posited, and even more so if they are staffed around the clock in the ICU. Is the reduction in mortality worth the expense, when the status quo (the open ICU where all are welcome to care for their patients without intensivist input) costs nothing more in human resources?

Many think so. Since the publication of the landmark paper by Rivers et al.,[3] it has become clear that in many critical illnesses, time is of the essence. In Rivers et al., a subset of patients with incipient or frank urosepsis was treated with a time- and hemodynamic-variable-constrained protocol. Those receiving the benefit of the protocol (invasive monitoring, rapid fluid resuscitation, pressor and inotrope medication, antibiotic therapy, and transfusion if needed) had a dramatic improvement in mortality compared with controls who were treated by standard methods in the ED or elsewhere.

> "Day or night, intensivist awake, intensivist asleep down the hall or asleep at home miles away, the high-intensity ICUs are better with regard to mortality. Adding the nocturnist-intensivist does not seem to improve the quality of care in the high-intensity ICU."

This study by Rivers et al.,[3] employing so-called "goal-directed therapy," suggested that if: 1) rapid diagnosis of a particular critical illness is made and 2) rapid, targeted, invasive, intervention in resuscitation and more specific therapies are instituted according to an algorithm, then improved mortality rates will occur. It was and is generally believed that the best-suited specialist to do both of these things is the intensivist. Thus the movement to staff every ICU with intensivists, perhaps even around the clock, was born and is growing.

In this paper by Wallace et al., the authors tried to determine if risk-adjusted in-house mortality figures would improve if a nighttime intensivist was added to either a low-intensity ICU (an "open" one, where intensivist care or consultation was optional) or a high-intensity ICU (a "closed" or "semi-closed" one where either transfer of care to an intensivist or intensivist consultation was mandatory).

Methods:

Unusual for this journal, the paper is a retrospective cohort study derived from surveys of coordinators of a proprietary ICU software product (APACHE 4, Cerner Corp., Kansas City, MO) at 49 different ICUs located in 25 hospitals. Data were collected on a total of 65,752 patients. The APACHE 4 coordinators were and are persons posted by Cerner who manage and revise the individual copy of the software product at each institution using it. The massive data collection capability of the software is one reason why the study could be conducted so easily and inexpensively.

Data collection amounted to having the APACHE 4 coordinator fill out a detailed survey about the clinical variables of patients on admission. The primary outcome was death in-hospital, with the primary exposure variable the nighttime presence of an intensivist in the ICU or his or her immediate availability in the hospital.

Covariates were any potential confounders that might influence mortality: age, gender, race or ethnicity, APACHE score (range 0-252 according to the numerical scale), coexisting diseases (HIV, lymphoma, myeloma, cirrhosis, liver failure, immunosuppression and metastatic cancer), where the patient was before admission to the ICU (ED, ward, home, etc.,), mechanical ventilation, and the educational status of the hospital in which the ICU was located, "minor teaching" (ratio

of residents to beds less than 0.25) or "major teaching" (ratio of residents to beds 0.25 or greater).

Statistical analysis was done by way of logistic regression to evaluate the relation between nighttime staffing and risk-adjusted hospital mortality.

Results:

When nighttime intensivist staffing was added to low-intensity ICUs, there was a significant improvement in risk-adjusted in-house mortality. (RR = 0.62, 95% CI, 0.39 to 0.97, p = 0.04) compared to the control.

When nighttime intensivist staffing was added to high-intensity ICUs, there was no improvement in risk-adjusted in-house mortality (RR = 1.08, 95% CI 0.57 to 1.07, p = 0.13).

When residents were included in the set of nighttime intensivists, the improvement in mortality was observed in both the low-intensity ICUs (RR = .42, 95% CI, 0.29 to 0.59, $p < 0.01$) and the high-intensity ICUs (RR = 0.47, 95% CI, 0.34 to 0.65, $p < 0.01$).

Discussion:

When the authors of this paper crafted their study to retrospectively "add" intensivists to both low- and high-intensity ICUs, they cannily found a way to ask and answer the question, "Do we want Rivers et al., or just their algorithm?" In other words, the high-intensity ICUs seem to operate on a different plane altogether from that of the low-intensity ICUs. Day or night, intensivist awake, intensivist asleep down the hall or asleep at home miles away, the high-intensity ICUs are better with regard to mortality. Adding the nocturnist-intensivist does not seem to improve the quality of care in the high-intensity ICU.

The low-intensity ICUs of Wallace et al., on the other hand, benefit greatly from the addition of a nocturnist-intensivist, even if it is a resident physician, according to the authors. So the powerful message here is that great and rapid progress in mortality can be made with little additional expense in these low-intensity units by hiring a nocturnist-intensivist or even just a night resident.

So it appears that the presence or absence of the intensivist in many ways is immaterial to good ICU outcomes provided three things occur: 1) The diagnostician can reliably decide that the patient has a critical illness (sepsis, acute lung injury, acute cardiac event, acute stroke, etc.); 2) A commonly accepted and efficacious algorithm (à la Rivers et al.) exists for rapid invasive resuscitation and management of the illness; and 3) The therapist can confidently insert lines, catheters, and other monitors and reliably and correctly assess the data they put out, and can feed back to the algorithm, summoning specialists from other fields as needed.

These persons need not be intensivists. For instance, ED physicians are quite capable of making the correct diagnoses and securing lines and initiating antibiotic therapy, etc.; and experienced CRNAs or ICU nurses can implement protocols or algorithms with ongoing feedback and management according to the responses to the first interventions. CRNAs in particular are familiar with insertion of lines and monitoring physiological variables, adjusting vasoactive medications and administering fluids as needed. They do this routinely in the O.R. now. It would seem that in well-run, high-intensity units overseen during the day by state-of-the-art intensivists, ICU nurses and others are doing precisely this.

If they could not, then, how could the high-intensity ICUs in Wallace et al., perform equally well with or without a nocturnist-intensivist?

Lastly, why might the addition of residents to the mix confer improved mortality in both low- and high-intensity ICUs? Though not explained by the authors, one might conjecture that the presence of residents means response times are perhaps that much shorter, and implementation of algorithms that much more timely. Other studies are needed to explore this result.

References:

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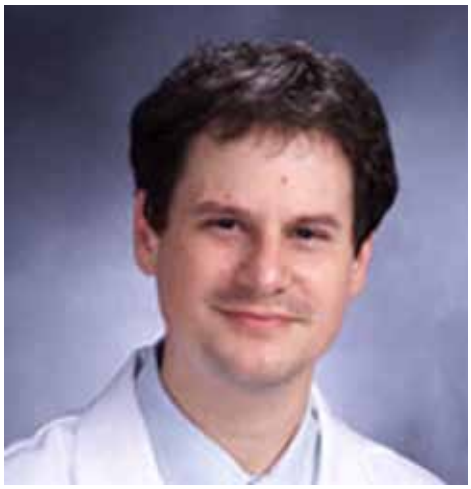
CME Question:

According to Wallace et al., which one of the following is true about the addition of a nocturnist-intensivist to the staff of an ICU?:

A. Adding a nocturnist-intensivist did not improve risk-adjusted in-hospital mortality in the setting of a low-intensity ICU.
B. Adding a nocturnist-intensivist did not improve risk-adjusted in-hospital mortality in the setting of a high-intensity ICU.
C. Adding a resident physician nocturnist-intensivist did not improve risk-adjusted in-hospital mortality in the setting of a low-intensity ICU.
D. Patients in the highest third of acute physiology scores (i.e., the sickest patients) did not have improved risk-adjusted in-hospital mortality scores when attended to by resident physician nocturnist-intensivists.

Answer: B

Fellowship Review: New York-Presbyterian Hospital/Weill Cornell Medical Center



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The Department of Anesthesiology at the New York-Presbyterian/Weill Cornell Medical Center is pleased to announce the establishment of an ACGME-accredited Anesthesiology Fellowship in Critical Care Medicine. This one-year training program, based on the ACGME guidelines for fellowship training and the institution's accreditation equivalency requirements, is approved for three fellows per year. The program is designed to prepare fellows to become specialists in critical care with a broad knowledge base involving all aspects of management of critically ill patients. Fellows will work in concert with specialists on the patient care team in the cardiothoracic, surgical, medical and burn intensive care units, neuroscience care unit and pediatric intensive care unit. The program will provide the resources necessary to facilitate clinical practice, teaching, administration and research required for successful fellows as they become leaders in the field of critical care medicine.

The Cardiothoracic Intensive Care Unit (CTICU) and Surgical Intensive Care Unit (SICU) at New York-Presbyterian Hospital / Weill Cornell Medical Center (NYPH-WCMC) compose the core training sites for fellows. In the CTICU, fellows will be exposed to a broad scope of cardiovascular pathology and will gain experience in managing the care of patients following high-risk thoracic aortic surgical procedures and complex valvular and revascularization procedures, as well as patients with ventricular-assist devices and patients on ECMO.

In the SICU, fellows will be exposed to a wide range of general surgical, vascular and urologic pathology. In addition, there is a well-established renal transplant program and growing liver transplant program. A very busy high-risk labor and delivery service at the NYPH-WCMC offers a unique opportunity to provide perioperative care for complex obstetric patients. Combined, the CTICU and SICU admit approximately 2,000 patients per year.

The fellowship program is unique in having the busiest burn management unit in the tri-state area with more the 1,200 admissions annually. This distinctive rotation will prepare fellows to manage single and multisystem organ failure in burn patients. Additionally, fellows will learn principles of hyperbaric oxygen therapy in the management of burn patients.

The Medical Intensive Care Unit (MICU), the Pediatric Intensive Care Unit (PICU) and the Neuro-Intensive Care Unit offer additional experience in the medical and postoperative management of adult and pediatric patients.

The curriculum is designed to guide fellows through increasing levels of responsibility and independent practice under the supervision of an exceptional fellowship faculty. The critical care teams are directed by attending intensivists from anesthesiology critical care, surgery critical care, medicine critical care and pediatric critical care. The critical care fellows will work closely with consultant colleagues from all fields of medicine and will be strongly supported by a team of exceptionally capable nurses, respiratory therapists, clinical pharmacists, nutritionists, physical and occupational therapists, and speech pathologists. This staffing model allows each fellow to be immersed in a multidisciplinary environment throughout the yearlong fellowship. Fellows will be directly involved in the supervision and teaching of residents, medical students and physician assistants.

Fellows will spend four months in the CTICU and two months in the SICU. Other rotations are one month in duration. Fellows will spend one month on an elective of their choice. Fellows are encouraged to design their own electives to fit their specific interests or future career goals. Faculty mentors will assist in this process. The NYPH-WCMC community has vibrant research programs, including basic science and clinical and translational research. Several faculty members have particular interests in quality improvement projects. Fellows will be encouraged to participate in ongoing research projects and pursue their own interests during fellowship training.

Interested candidates should send inquiries by e-mail to:

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(James A. Osorio, M.D.) Program Director

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(Keisha M. Brown) Fellowship Program Coordinator

Society of Critical Care Anesthesiologists
SOCCA

25TH ANNUAL MEETING AND CRITICAL CARE UPDATE

PRESENTED PRIOR TO ***ANESTHESIOLOGY 2012***

OCTOBER 11-12, 2012
RENAISSANCE WASHINGTON DC DOWNTOWN HOTEL
WASHINGTON, DC

Pre-Meeting Workshop
CRITICAL CARE ULTRASOUND WORKSHOP

Faculty

Anne-Sophie Beraud, M.D.
Thomas B. Comfere, M.D.
Charl A. de Wet, M.D.
Michael Haney, M.D., Ph.D.
Antonio Hernandez, M.D.
Benjamin A. Kohl, M.D.
Wolf Benjamin Kratzert, M.D., Ph.D.
Matthias Merkel, M.D., Ph.D.
Colin F. Royse, M.B., B.S.
Daniel S. Talmor, M.D., M.P.H.
Chad E. Wagner, M.D.
Michael H. Wall, M.D., FCCM
Michael C. Woo, M.D.

Thursday, October 11, 2012
7:45 a.m. - 5:30 p.m.

SOCCA will be conducting a full-day critical care ultrasound workshop utilizing hands-on training with live models, simulators, and state-of-the-art ultrasound equipment from several companies. This course is designed to teach the participant the fundamentals of critical care ultrasound including: standard ultrasound views for the Focused Assessed Transthoracic Echo (FATE) exam, use of ultrasound in hemodynamically unstable patients, pleural ultrasound as well as rescue transesophageal echo. The course will also utilize an audience response system for multiple case discussions and clinical decision making scenarios. ***(Limited to 40 registrants)***

Learning Objectives

Upon completion of this workshop the participants should be able to:

1. Review current experience and literature regarding the use of ultrasound for the intraoperative and ICU management of critically ill patients and those undergoing high-risk surgery;
2. Review and discuss the use of transthoracic ultrasound in perioperative cardiac evaluation, including ventricular volume and function, and valvular function;
3. Review and discuss the use of transthoracic ultrasound in thoracic assessment, including pleural effusions and pneumothorax;
4. Develop technical facility with the use of ultrasound for vascular access, cardiac evaluation, trauma and thoracic assessment.

MEETING SCHEDULE

Thursday, October 11, 2012

7:00 a.m. — **Critical Care Ultrasound Workshop Registration**

7:45 a.m. - 5:30 p.m. — **Critical Care Ultrasound Workshop**

Friday, October 12, 2012

6:30 a.m. - 5:00 p.m. — **Registration**

7:30 - 8:00 a.m. — **Continental Breakfast - Exhibits Open**

8:00 - 8:05 a.m. — **Welcome and Introduction**
Ronald W. Pauldine, M.D.
Carlee A. Clark, M.D.

SESSION I: Early Mobilization and Cost

8:05 - 8:35 a.m. — **Early Mobilization to Reduce Health Care Cost**
Dale M. Needham, M.D., Ph.D.

8:40 - 9:10 a.m. — **Cost Effectiveness in Critical Care**
Brian Cuthbertson, Ch.B., M.D., FRCA

9:15 - 9:45 a.m. — **Midlevel Practitioners in the ICU, at What Cost? - Pro vs. Con**
Richard B. Silverman, M.D.
Walter A. Boyle III, M.D., FCCM

9:50 -10:10 a.m. — **Break and Vendor Visits**

SESSION II: Controversies in Palliative Care

10:10 -10:15 a.m. — **Moderator and Introduction**
Rebecca Aslakson, M.D.

10:15 - 10:25 a.m. — **Palliative Care. Should DNR Be The Default**
Craig D. Blinderman, M.D., M.A.

10:30 - 10:50 a.m. — **Terminal Sedation And General Anesthesia For Palliative Care**
Allen Gustin, M.D.

10:50 - 11:15 a.m. — **Reaction Panel**
Liza M. Weavind, M.D.
Ronald G. Pearl, M.D., Ph.D.

11:15 -11:30 a.m. — **Young Investigator Award: Early BIS and Sedative Requirements During Therapeutic Hypothermia Predict Neurologic Outcome at ICU Discharge**
Nicholas Burjek, M.D.

11:30 - 11:35 a.m. — **Introduction of ASA President Elect**
Michael F. O'Connor, M.D., FCCM

11:35 a.m. - Noon — **ASA President-Elect Address**
John M. Zerwas, M.D.

Noon - 1:10 p.m. — **Lunch and SOCCA Business Meeting**

Session III: Malpractice in the ICU

1:15 -2:15 p.m. — **Defending Critical Care: Navigating Through a Malpractice Case Moderator and Introduction**
Neal H. Cohen, M.D., MPH, MS
Audience Response Legal Panel

2:20-2:35 p.m. — **SOCCA-FAER- Hospira Physician Scientist Award Lecture**
APOE to Sex Differences: The Circuitous Route of Science
Michael (Luke) James, M.D.

2:35 - 2:50 p.m. — **Break and Vendor Visits**

2:50 - 3:15 p.m. — **Moderated Poster Session**

3:15 - 3:45 p.m. — **"Anesthesiology Critical Care - Back to the Future" Lifetime Achievement Award Recipient Presentation**
Philip D. Lumb, M.B., B.S., MCCM

Session IV: SOCCA 25 Years Later. What's Changed?

3:50 - 4:00 p.m. — **Moderator and Introduction**
Robert N. Sladen, M.B., Ch.B., FCCM

4:00 - 4:15 p.m. — **Mechanical Ventilation**
John B. Downs, M.D., FCCP, FCCM, M.B.A.

4:20 - 4:35 p.m. — **Hemodynamic Monitoring**
Myer H. Rosenthal, M.D.

4:40 - 4:55 p.m. — **Critical Care Staffing**
Jeffrey S. Vender, M.D.

5:00 - 5:10 p.m. — **Moderator and Audience Response**

5:15 – 6:45 p.m. — **Welcome Reception**

Society of
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The host hotel for the SOCCA 25th Annual Meeting and Critical Care Update is the Renaissance Washington DC Downtown Hotel. Please secure your guest room, airline, and rental car reservations through **www.ASAHQ.org/Annual-Meeting.aspx**

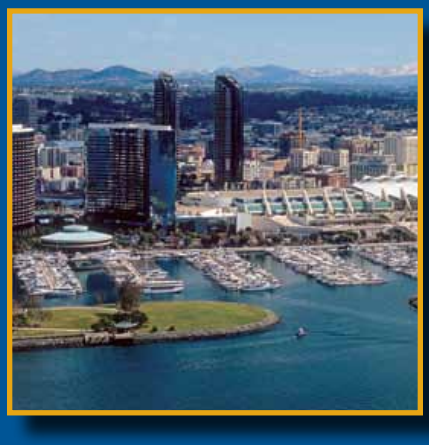
SAVE THE DATE FOR THESE FUTURE SOCCA MEETINGS

SOCCA 26TH ANNUAL MEETING AND CRITICAL CARE UPDATE

OCTOBER 10 - 11, 2013
San Francisco, California

SOCCA 27TH ANNUAL MEETING AND CRITICAL CARE UPDATE

OCTOBER 9 - 10, 2014
New Orleans, Louisiana



SOCCA 28TH ANNUAL MEETING AND CRITICAL CARE UPDATE

OCTOBER 23 - 24, 2015
San Diego, California