

# ASCCA INTERCHANGE

AMERICAN SOCIETY OF CRITICAL CARE ANESTHESIOLOGISTS

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## President's Message

### Healthy, Wealthy and Wise: The State of the Society



Todd Dorman, M.D.  
ASCCA President

As an international organization, we strive for our society to meet the three simple words in the title of this article. The Board works hard all year, hopefully utilizing collective wisdom to steer the organization through calm and rough waters. We analyze the past, looking for important trends and we try to learn from our mistakes and our successes. We dutifully prognosticate the future, knowing that doing so is next to impossible, and then we hold ourselves accountable for our interpretation of the tea leaves.

#### Health

I am happy and proud that presently the ASCCA is healthy! Our annual meeting attendance was robust. We surpassed 200 attendees, which by volume is more than a third of membership numbers. Our support for the resident mentor program was greatly appreciated by FAER and more importantly by the resident and medical student attendees. Our membership is the highest it has been in more than five years and exceeds 580 members. Our Web site is seeing over 4,000 unique hits per month. Our Residents' Guide is now for sale and download. This *Interchange*, our quarterly newsletter, has been revamped and is very well received. The critical care

track at the ASA Annual Meeting is one of the best attended tracks, and our panels at the ASA, IARS and SCA continue to be well attended and to receive excellent evaluations.

Being healthy is important, but staying healthy is equally valuable. Growth in medical student and educational memberships is a marker for a healthy future. Obviously these numbers will not fully translate into new members, but they increase the likelihood of growth in the future. We have already identified and appointed a new editor for the next version of the Residents' Guide. During this next cycle, we will utilize the strategy we have used for the *Interchange*, which is to establish an editorial panel with seasoned leadership and a plan for transitions. An enhanced Resident Mentor program will be launched at this year's Annual Meeting in New Orleans on October 16. We will continue to attend resident component meetings and are working on the details of a new membership drive.

The ASA is looking to improve support and interactions with subspecialty societies. Thus, our Society is partnering with the Critical Care Committee within ASA on several projects, including working with the AHA to craft an anesthesiologist-focused CPR course. In addition, ASA is now working with us to review and consider several legislative-oriented issues, like billing and documentation requirements. The ASCCA is indeed healthy.

#### Wealth

I am happy and proud that presently the ASCCA is wealthy! Well, in today's world, wealth is truly a matter of perspective. The ASCCA is financially stable and well positioned. A history of conservative investment strategies has enabled us to withstand the downturn better than most. Yes, our investments lost just like every investor, but we lost at a lower rate than the average investor. We continue to provide annual support for APSF and FAER as evidence of ongoing commitment to safety and research. Our two-year research grant in partnership with FAER has again received funding from Hospira. Given the

tough economic times, the continued support from Hospira for this important training grant is noteworthy and greatly appreciated. The Residents' Guide is now available and will generate some additional revenue as well.

So the ASCCA has weathered the first wave of the economic crisis well. How well we weathered the second part of this storm is not yet known. All organizations are at risk of losing members as individuals struggle to decide what they can afford. Attendance at meetings is predicted to fall. Some members are experiencing furloughs and others are at risk of losing employment. Everyone is struggling. It is during such a time that we as an organization must intensely re-evaluate all expenditures and seek new approaches to revenue. With this in mind, the Board of Directors has approved a new joint membership with IARS that will have a reduced total fee. The Board has also entered into a contract with a meeting services company to try to increase the grant and exhibitor support for the upcoming Annual Meeting.

The leadership is also working hard to increase the value you receive for your membership. Next year's Annual Meeting will be bigger and better than ever. The new enhanced *Interchange* is bringing you information on how to improve your practice. We will add a Letters to the Editor section this year so that you will have a forum to express your views and concerns. The *Interchange* will be repurposing and launching some of its material to the critical care blog at [www.criticalcareblog.org](http://www.criticalcareblog.org). This will bring you important information in a new format and facilitate greater interaction between members. We will continue to invest conservatively. So, in my humble opinion, we are indeed wealthy.

#### Wisdom

I believe that the collective wisdom and a lineage of such keep us wise! The present ASCCA leadership

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### Membership

Membership in ASCCA is open to all anesthesiologists and residents in approved anesthesiology programs. Membership applications may be obtained by contacting ASCCA at (847) 825-5586 or through the ASCCA Web site at [www.ascca.org/shop/index.php](http://www.ascca.org/shop/index.php).

### ASCCA Dues

Dues are \$150 for active and international members; \$100 for affiliate members and free for residents/fellows. Dues may be paid online at [www.ascca.org/shop/index.php](http://www.ascca.org/shop/index.php) by credit card or by mailing payment to the ASCCA office at 520 N. Northwest Highway, Park Ridge, IL 60068.

Remember, payment of your dues allows you to enjoy the full privileges of ASCCA membership.

### Web Page

You may visit the ASCCA Web site at:

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## EDITORIAL NOTES

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## PRO: Recombinant Activated Factor VII Should Be Used Early After Cardiac Surgery



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Cardiac surgery is often associated with a significant disruption of the coagulation system due to both the exposure of blood to extracorporeal circuits and to the hemodilution associated with cardiopulmonary bypass (CPB). These factors lead to high rates of excessive bleeding in this patient population.<sup>1</sup> The resultant coagulopathic state can result in clinically significant bleeding requiring massive transfusions and/or surgical re-exploration in up to 20 percent of cases.<sup>2</sup> Each of these interventions has been linked to increased morbidity and mortality for cardiac surgical patients and should be avoided whenever possible.<sup>3,4</sup> Strategies to limit bleeding in the operating room and during the immediate postoperative period include the administration of hemostatic agents as both prophylaxis and treatment, tight control of anticoagulation, and blood product transfusions, which play a pivotal role in both correction and resuscitation of patients who experience clinically significant intractable bleeding.

Recently, recombinant activated factor VII (rFVIIa) has been utilized in conjunction with blood product transfusions for the treatment of refractory bleeding in cardiac surgery patients.<sup>5</sup> rFVIIa administration results in a “thrombin burst” at the site of injury via two mechanisms (a tissue factor mediated pathway and a tissue factor independent mechanism through inter-

action with activated platelets) resulting in a potent thrombogenic effect. This agent is approved for the treatment of bleeding in hemophilic patients with inhibitors to either factor VIII or IX; however, over the past decade, rFVIIa has been utilized in an off-label fashion for the treatment of refractory bleeding in a variety of patient populations, including cardiac surgery. The obvious advantages of rFVIIa include limiting the amount of blood product exposure (which has recently been associated with an increased risk of adverse outcomes) and avoiding the need for surgical re-exploration (also well known to increase both morbidity and mortality).

The available data addressing the efficacy and safety of rFVIIa in the cardiac surgical population are somewhat limited, and the bulk of published data consists of case reports/series, institutional experience and registry reports. One of the most recently published reviews, the comprehensive Canadian review, outlines the results associated with rFVIIa in cardiac surgery in that country.<sup>5</sup> This study evaluated 503 patients who received rFVIIa at an average total dose of 62 mcg/kg following cardiac surgery in 21 centers across Canada. rFVIIa was clearly successful in slowing, if not halting, bleeding altogether in this study as evidenced by the dramatic decrease in blood product transfusions necessary following administration of this drug. There was a slightly increased rate of thromboembolic events associated with rFVIIa administration, but it is unclear at this point if this is associated with rFVIIa directly or is an artifact of the higher acuity population selected via the study design. As a result of these findings, the authors concluded that rFVIIa can be used in the treatment of refractory bleeding following cardiac surgery in the setting of adequate amounts of circulating coagulation factors and called for adequately powered randomized clinical trials to confirm their findings.

Few such trials have been completed in order to adequately assess the safety and efficacy of rFVIIa in the cardiac surgery population. Recently, a phase II trial was completed, and the results were presented at the American Heart Association meeting in November 2008; however, the results have not yet been published.<sup>6</sup> This trial enrolled patients who had undergone cardiac surgery requiring CPB and had been admitted to a postoperative care environment (ICU) for at least 30 minutes. The patients were random-

ized if they met a pre-specified bleeding rate based upon chest tube drainage to either placebo or rFVIIa at either 40 mcg/kg or 80 mcg/kg. This study demonstrated similar results as the Canadian registry review. Although the trial was not powered for efficacy, bleeding appeared to be significantly decreased as evidenced by a decrease in chest tube drainage, transfusion requirements and need for re-operation. However, there was also a numerical increase in the number of serious adverse events.

rFVIIa has been demonstrated to effectively control refractory bleeding in patients following cardiac surgery. Unfortunately, the appropriate place in therapy and the optimal dose to maximize benefit and limit adverse events are not known. It should, however, be utilized early as an aggressive therapy to limit further patient exposure to harmful blood and blood product transfusion and to prevent patients from undergoing emergent surgical re-exploration. In essence, it becomes a matter of determining which clinical scenario presents the greatest risk to each individual patient; continued blood loss, subsequent blood product transfusions, and potential re-exploration or administration of rFVIIa, which carries an as-of-yet undetermined risk of thromboembolic events. Regardless, a comprehensive, individualized assessment of the risk versus benefit for each case prior to rFVIIa use should factor in these multiple, complex interactions.

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## CON: Recombinant Activated Factor VII Should Only Be Used as Salvage Therapy After Cardiac Surgery



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Recombinant activated factor VII (rFVIIa) (Novo-seven, Novo Nordisk, Bagsvaerd, Denmark) is the recombinant form of a naturally-occurring coagulation factor approved for use in the United States to treat life-threatening hemorrhage in patients with hemophilia A or B who have developed antibodies (inhibitors) to other replacement factors (Factor VIII or IX). Since its introduction more than 20 years ago, it has been used in various off-label situations where “life-threatening, intractable” hemorrhage has occurred irrespective of the underlying cause.<sup>1</sup>

Cardiopulmonary bypass (CPB) induces a significant coagulopathy through the activation of a series of pro-thrombotic and anti-thrombotic reactions within the hemostatic and fibrinolytic pathways, as well as inducing dilutional and consumptive thrombocytopenia.<sup>2</sup> As a result, severe perioperative hemorrhage requiring massive resuscitation and transfusion of large amounts of red blood cells, platelets, plasma and cryoprecipitate can occur. rFVIIa may seem to be an ideal agent to treat this type of “intractable hemorrhage” following CPB. This off-label use of rFVIIa, however, has never been appropriately studied – or more appropriately stated – has never been published in an open peer-review process. Additionally, significant concern remains about the

safety of this agent, especially in light of the fact that this agent has never been associated with an improvement in mortality, regardless of the population, and despite any improvements in estimated blood loss, transfusion requirements or re-exploration.

While numerous case reports describe the “miraculous” reversal of coagulopathy and cessation of bleeding associated with rFVIIa administration following CPB, the efficacy of rFVIIa in this setting has not been fully studied, and each patient’s individualized potential benefit from this therapy cannot therefore be easily defined. In fact, a surprisingly large amount of the data reported in the literature come from case reports, case series or retrospective chart analysis.<sup>3</sup> These types of analyses, by their very nature, are prone to significant publication and observer bias, especially when therapies are used in an off-label manner and potential complications can be life- and/or limb-threatening. Additionally, published systematic reviews evaluating the efficacy of rFVIIa in this setting have, unfortunately, also relied on case reports and case series for their data. They, therefore, also suffer from the same biases in their analysis, and any conclusions drawn from this data, whether positive or negative, should be viewed with appropriate skepticism.

To date, there is only one published adult, randomized, controlled trial that has attempted to evaluate the efficacy of rFVIIa in patients undergoing cardiac surgery.<sup>4</sup> In this pilot study, 20 patients were randomized to receive either rFVIIa (90 mcg/kg) or placebo following CPB and protamine reversal of systemic heparinization following complex non-coronary artery bypass surgery. Using an intent-to-treat analysis, the authors were not able to demonstrate a reduction in either transfusion prior to the ICU, transfusion in the ICU, total transfusion (whole study duration) or mediastinal chest tube output.

Additionally, there is only one randomized, controlled trial (and the data remain unpublished) that has attempted to evaluate the safety of rFVIIa in patients undergoing cardiac surgery.<sup>5</sup> In this study of 172 patients that were randomized to one of three arms (placebo, low (40 mcg/kg), or high (80 mcg/kg) dose rFVIIa) for patients undergoing cardiac surgery requiring CPB. The investigators reported (although it is unclear whether through an intent-to-treat anal-

ysis) a small but statistically significant improvement in *median* volume of transfusion at 24 hours and five days after dosing (but with unclear clinical significance, as the authors evaluated mL rather than units of transfused blood). More importantly, the investigators reported an increase in fatal adverse events (placebo=5.9%, low=11.4%, high=8.7%), in critical adverse events (placebo=7.4%, low=14.3%, high=11.6%) and thromboembolic adverse events (placebo=1.5%, low=8.6%, high=5.8%).

At this time, and until more data become available, rFVIIa should be used extraordinarily cautiously, if at all, in cardiac surgery. Every patient’s individualized risk and benefit should be evaluated when rFVIIa is considered. At best, it should only be used for severe, life-threatening, intractable hemorrhage, as “prophylactic” or “routine” administration of rFVIIa is not associated with improved outcome and may place patients at undue risk for thromboembolic complications. Aggressive post-treatment monitoring for thrombosis-related complications is also recommended.

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## PRO: Start the Drip!



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While acute renal failure has been studied as an amalgam, not all nephropathies are alike. Acute tubular necrosis and prerenal azotemia don't necessarily share pathophysiologies, nor do they share mortalities. Non-oliguric renal failure and diuretic responsive renal failure may represent clinical syndromes that are unique and perhaps forgiving. The different renal outcomes between oliguric and non-oliguric ARF support the possibility of variant etiologies.

As the diagnoses within ARF vary, so would the treatments. At best, the treatments of ARF share one truth: avoid nephrotoxins. Beyond this, universalities are few. Volume loading has its role in rhabdomyoly-

sis and contrast nephropathy, but it lacks a prospective study with other forms of ARF. Studies supporting bicarbonate for contrast nephropathy suggest pH and tonicity may be more important. Vasopressors are not the "renal nooses" their reputations once held. In the appropriate clinical scenarios, vasopressors can restore urine output as much as they can take it away. Ultimately, avoidance of volume loading (vs. volume "restoring") may be most beneficial. ARDSnet demonstrated that a restrictive IV strategy reduces ICU days and the need for RRT, without an increase in organ failure.

If a volume load cannot be avoided, the recourse to a negative fluid balance is either diuresis or dialysis. Disregarding the data of RRT and mortality, subjecting a patient to dialysis access lines carries more immediate harm than a dose of furosemide. Regarding efficacy, on one hand, studies reinforce a lack of renal benefit from pharmacologic intervention (diuretics, "renal dose" dopamine, natriuretic peptides,

etc.). On the other, dialysis has not proven effective, even with dialyzable substances (e.g. contrast).

Of course, renal outcomes are secondary to ultimate outcomes, and for survival, alveoli may need to lean on nephrons for a while. While loop diuresis may exacerbate prerenal azotemia, the consequent uremia and elevated creatinines may define "acute renal success" (Thurau et al. 1976) rather than an irreversible injury. In moderated doses, furosemide improved renal outcomes in a rat model.

Studies about ARF reliably define mortality risks associated with increasing severities of ARF. The pathophysiologies of ARF/ARI/AKI are as varied as the definitions used to study them. Meta-analyses fail to reliably demonstrate a harmful effect of furosemide in critical illness. Loop diuretics hold a theoretical benefit in renal outcomes after reperfusion. Non-oliguric renal insufficiency may not be a red flag for loop diuretics, it may be a green light.

## CON: Avoid the Loop!



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Aggressive use of furosemide in the ICU pushes patients into statistical categories of poor outcomes. Furosemide has never been proven to improve renal function, and creatinine elevations, even transient ones, increase mortality, ICU stays, and dialysis requirements.

Definitions of renal dysfunction are varied: mild/moderate/severe (Bagshaw et al. 2006) or exposure to CVVH (Morgera et al. 2002). Whatever they are, they all correlate with increased mortality (1 year, or 1, 2, and 5 year). Using RIFLE classifications, Uchino et al. established the association with mortality to include in-hospital stay. This includes R score (increased Cr x 1.5 or GFR decrease >25%) patients whom furosemide overuse can easily create.

The purported benefits of furosemide in non-oliguric AKI include "flushing" effect in the tubule, improved renal hemodynamics, and attenuated

ischemia-induced apoptosis. Data for its benefit are lacking while risk resonates. In meta-analysis of loop diuretics in 2006, Ho, et al. showed no difference in hospital mortality, need for renal replacement therapy, or number of dialysis sessions needed. Instead they found a risk of temporary deafness and tinnitus in patients treated with high doses of furosemide. In an observational study from 2002, Mehta et al. showed that loop diuretics in AKI was associated with significantly increased risk of death or non-recovery of renal function. Although a subsequent larger multicenter study failed to find a statistically significant association between diuretic use and increase mortality, the odds ratio for death was still on the side of harm. This begs for additional studies, but at this stage furosemide does not have a proven benefit to the kidneys or mortality.

Diuretics may have a role in volume overload; however, they do not have a role in treating oliguria. For the patient already demonstrating renal insufficiency, avoid the furosemide. Do not fall for the false reassurance of a full Foley.

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## Concise Review



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### Review of Proposals for Health Care Reform:

On Friday, March 13, 2009 members of the American Society of Anesthesiologists (ASA) received an e-mail message from the ASA President regarding health care reform. The message discussed some of the proposals for health care reform and directed the reader to the appropriate links for getting more detailed information.<sup>1</sup> This was a timely message in view of the revived interest in health care reform by the current administration.<sup>2</sup> The ASA President's message indicated that the Obama Administration is interested in comprehensive health care reform. In view of this renewed interest in health care reform, it might be useful to review the types of proposals that have been presented for such reform. These proposals have, in general, sought incremental or comprehensive reform.

#### A. Incremental Reform Proposals:

**1) Employer Mandates:** This proposal calls to mandate all employers above a specified size to offer health insurance to their employees, with or without subsidies or tax credits to the employer.

**2) Subsidies for the Uninsured:** This proposal calls to provide Individual Tax Credits to purchase insurance in the individual market.

#### 3) Expand/Build on Medicare and Medicaid:

This proposal calls to raise the income level for eligibility for Medicaid, and/or to lower the age for eligibility for Medicare, in order to increase the number of people covered. An example of such proposal is H.R. 676, which is sponsored by the Physicians for a National Health Program (PNHP).<sup>3</sup>

**4) Health Savings Accounts (HSA):** This proposal calls for the provision of favorable tax treatment (subsidy) for the creation of individual HSAs. The increased awareness of health care cost by the consumers in this program is expected to decrease utilization, increase competition and encourage healthy behavior.<sup>4</sup>

**5) Managed Competition:** This proposal would require employers to offer a choice of plans and would provide employees with tax exemption only for the value of the low-cost plan.<sup>5</sup>

**6) Quality Incentives:** This proposal would provide financial incentives for measures that are thought to improve quality such as pay for performance (P4P) or electronic medical records (EMRs).<sup>6</sup>

#### B. Comprehensive Reform Proposals:

**1) Personal Mandates and Subsidies:** This proposal would mandate all individuals to have health care insurance while providing governmental subsidies depending on the need of the person. Most versions of this proposal call for the maintaining of the three current forms of financing health care (employer-based, means-tested Medicaid, and Medicare), while few call for their eventual substitution. The Massachusetts health care reform plan that was enacted in April 2006 and went into effect in July 2007 is an example of such a proposal.

**2) Single-Payer Proposals:** This proposal calls for Medicare-like coverage for all individuals plus coverage for dental services, long-term care, prescription drugs, and mental health care. Funding for hospitals would be provided by an annual budget that is fixed in advance. Reimbursement of physicians would be via fee-for-service or salary. The best-known version of this proposal is that of Physicians Working Group (PWG) for Single-Payer National Health Insurance.<sup>7</sup>

**3) Health Care Voucher (HCV) System:** This proposal calls for the provision of HCVs to every person under the age of 65 years to purchase health insurance from a qualified insurance company or health plan. These HCVs would provide coverage for basic health services on top of which the recipients may purchase additional coverage with their own after-tax dollars. The HCVs would replace (phase

out) employer-based insurance, means-tested programs (Medicaid) and eventually Medicare. Most proposals call for keeping the health care delivery mostly private and non-governmental. One example of the HCVs proposals is that presented by Emanuel EJ and Fuchs VR.<sup>8</sup> Specific details of their proposal include funding by an earmarked value-added tax (VAT) and creating two governmental administrative institutions: the Federal Health Board (FHB) and the Institute for Technology and Outcomes Assessment (ITOA). The FHB would be modeled on the Federal Reserve System with regional boards, and its functions would include defining and modifying the basic benefits package, contracting with health plans, informing participants about their health care options, reimbursing health plans, collecting data related to patient satisfaction and quality of care, calculating risk and geographic adjustments for payments, and regularly reporting to Congress on the health care system. The ITOA's functions would include conducting research to assess the effectiveness and value of interventions and treatment and disseminating information about outcomes of treatments.

Legislative proposals may contain elements of different proposals, and implementation of any proposal would likely generate further calls for reform.

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## Literature Review I



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### Article:

Beattie WS, Karkouti K, Wijeyesundera DN, Tait G. Risk associated with preoperative anemia in noncardiac surgery: a single-center cohort study. *Anesthesiology*. 2009; 110:574-581.

### Review:

The well known Transfusion Requirement in Critical Care (TRICC) study<sup>1</sup> was criticized for not resolving the effect of preoperative anemia from that of transfusion. Applying the TRICC-based guidelines implies lumping together patients, based solely on Hb. Imagine four hypothetical patients: One with normal preoperative hemoglobin who has a major procedure that requires transfusion; another who did not get transfused; a third and fourth who started out anemic and who either did or did not receive blood. Moreover, even invoking these four hypothetical "patients" is an oversimplification. Real patients are anemic for any number of reasons: hematopoietic, renal, nutritional, toxic, endocrine, immunologic, etc. Indeed placing such a diverse population into just two binary TRICC categories based on Hb alone, to understand mortality, is not very illuminating.

The anemia leading to transfusion is a separate and important issue, one that has been inadequately examined in the literature. In the March 2009 issue of *Anesthesiology*, Beattie and colleagues<sup>2</sup> address the issue of risk of mortality independently associated with preoperative anemia in patients undergoing noncardiac surgery.

The design of the study bears mentioning: an observational, retrospective, longitudinal, single-center cohort. Cohort studies are widely considered the best kind of observational epidemiologic studies. They are well-suited for efficiently studying a wide range of "exposure-disease" or "condition-disease" associations. Retrospective cohort studies are also inexpensive and less time-consuming but have almost all the advantages of prospective ones, and some of their own. In fact, retrospective cohort studies are insensitive to attrition.

The authors collected data on 7,759 consecutive noncardiac surgical patients at the University Health Network, Toronto General Hospital, between 2003 and 2006. Anemia thresholds for men (13 g/l) and women (12 g/l) were defined, and logistic regression and propensity analysis were used to assess the relationship between preoperative anemia and mortality.

Independent variables were height, weight, age, sex, history of CAD, CHF, cerebrovascular disease, renal disease, COPD, platelet count, perioperative transfusion, type of surgery, time spent in hospital before surgery, and medications. The primary dependent variable was mortality within 90 days of surgery. A Pearson correlation matrix of variables was used to identify predictive variables, and the model's fit was assessed with the Hosmer-Lemeshow test.

Of the 7,679 patients included, 3,047 (39.7%) were anemic, 39.8% of men and 39.5% of women. Transfusions were given to 18.6% of all patients, and were three times more likely in anemic versus nonanemic patients (30.4% versus 10.6%).

The unadjusted odds of perioperative death is higher in anemic than nonanemic patients (odds ratio [OR], 4.74; 95% CI, 3.3-6.7;  $P < 0.0001$ ). The authors point out that the threshold for increased mortality falls within the 95% confidence intervals for the WHO definition of anemia.

Adjusting for confounders of postoperative mortality (with the method of logistic regression) showed that preoperative anemia was still strongly associated with increased mortality (OR, 2.36; 95% CI, 1.57-3.41;  $P < 0.0001$ ). Other factors independently associated with increased odds of death were: age over 70 years, history of CHF, transfusion of RBC (dose-dependent), height under 155cm (61 inches), inpatient status more than five days prior to surgery, and serum creatinine greater than 176 mM (1.99 mg/dl).

A method called propensity score matching was then used to match 2,090 anemic patients with nonanemic ones, leaving the only difference between them the preoperative and discharge hemoglobin levels. This technique allowed the authors to distinguish the effect of transfusion from the effect of preoperative anemia, because the matched pairs had the same number of RBC units transfused. Once again, the anemic patients had higher mortality than nonanemic ones (OR, 2.29; 95% CI 1.45 to 3.63;  $P < 0.0001$ ).

In summary, in this large retrospective study, one third of patients (men and women alike) presenting for nonemergent surgery were found to be anemic. After adjusting for confounders, *especially RBC transfusion*, anemic patients were more than twice as likely to die within 90 days of surgery. The mortality difference was significant within 14 days of surgery and remained so to and beyond 90 days.

The main strength of the study is that it is large and appears to resolve the two separate and important risks of preexisting anemia and RBC transfusion. One limitation is that emergent, cardiac, and transplant surgeries were excluded. Another is that the retrospective nature of the study makes establishing causation impossible, meaning that anemia and mortality may be mere epiphenomena. Neither limitation greatly diminishes the weight of the study's findings.

### References:

1. Hebert PC, Wells G, Blajchman MA, et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. *N Engl J Med*. 1999;340:409-417.
2. Beattie WS, Karkouti K, Wijeyesundera DN, Tait G. Risk associated with preoperative anemia in noncardiac surgery: a single-center cohort study. *Anesthesiology*. 2009; 110:574-81.

## Literature Review II



Rachel Idowu, M.D., PGY-4  
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Lisa Weavind, M.D.  
Associate Professor of  
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### Article:

Ho PM, Peterson ED, Wang L, Magid DJ, Fihn SD, Larsen GC, Jesse RA, Rumsfeld JS. Incidence of death and acute myocardial infarction associated with stopping clopidogrel after acute coronary syndrome. *JAMA*. 2008 Feb 6; 299(5):532-9. Erratum in: *JAMA*. 2008 May 28; 299(20):2390.

### Background

Individuals who are hospitalized for acute coronary syndrome (ACS) may receive therapy which requires use of an anti-platelet agent, such as clopidogrel. This agent could be part of a “medicine-only” or a “percutaneous intervention” (PCI) treatment regimen. Previously published research and clinical experience has demonstrated that clustering of deleterious thrombotic events may occur if anti-platelet agents, such as aspirin, are discontinued suddenly. This group of researchers sought to identify whether this clustering of thrombotic events (TEs), a so-called “rebound effect,” would be similarly observed in patients who discontinued clopidogrel after experiencing an ACS. The TEs of interest were listed as all-cause mortality or acute myocardial infarction (AMI).

### Research Questions

Specifically, Ho Peterson et al. sought to investigate:

1. What is the incidence of TEs after discontinuing clopidogrel in medically-treated ACS patients?
2. What is the incidence of TEs after discontinuing clopidogrel in PCI-treated ACS patients?
3. Does an association exist between the duration of time on clopidogrel and the TE event rate?

### Methods

This retrospective chart-based evaluation was conducted through the Department of Veteran Affairs (VA) on patients who were admitted and treated for ACS between 2003 and 2005. The researchers monitored the charts for evidence of TEs after discontinuation of clopidogrel through the year 2007. They focused their evaluation on patients who received clopidogrel on individuals who were admitted under the diagnostic code of acute myocardial infarction or unstable angina. Patients who experienced TEs while on clopidogrel were transferred to the VA from another hospital, and those who experienced a bleeding adverse event were excluded from the review. They used several sophisticated statistical and analytical methods; these are clearly detailed in the methods section of the paper. Most interestingly, they sought to delineate: 1) the unadjusted and adjusted incidence of TEs in the medically-treated ACS patient, what effect the duration of clopidogrel therapy had on the occurrence of TEs and 2) what effect the length of time elapsed since clopidogrel was discontinued had on the occurrence of TEs.

### Results

The highest rate (60.8%,  $n = 163$ ) of TEs occurred in the first 90 days after discontinuation of clopidogrel. The length of time the patient took clopidogrel did not affect the clustering of TEs. The majority of patients took clopidogrel for at least three months, but less than nine months (median = 310 days; range = 120-417 days). Seventeen percent of the patients in this study population experienced one of the TEs (mortality or AMI). The research group felt that the patients in this study cohort demonstrated reasonable medication adherence because they tied patient-initiated pharmaceutical refill records to another common post-ACS medication, statins.

Their findings were similar when they examined PCI-treated ACS patients who were discharged on clopidogrel. Fewer total TEs (7.9%,  $n=124$ ) occurred in the PCI-treated patients, but the median length of time on clopidogrel was similar. As with the medical-only treatment group, the highest rate (58.9%,  $n=73$ ) of TEs occurred in the first 90 days after discontinuation of clopidogrel.

### Comments

This research group attempted to adjust for possible factors that might influence the occurrence of TEs. While the greatest limitation of their study design (inability to definitely demonstrate that patients took the medication as prescribed) could always be highlighted, they expended reasonable effort to ensure the likelihood of patient compliance by examining another drug regimen for adherence (use of statins) in the same patient population. Based on the reported results, it appears that providers who find it necessary to stop clopidogrel therapy in their ACS patients (medical or PCI-treated) or patients who self-discontinue their use of clopidogrel must be wary of the high risk of TEs occurring in the first three months after the last dose.

Further analysis in this article could have included an investigation as to the most common reasons for discontinuing clopidogrel, and whether there was any attempt by the clinical provider to “taper” or “bridge” the patient in order to ameliorate the TE risk.

For the surgeon, the greatest implication of this (and similar studies related to aspirin) is the ever-present question of whether to allow a patient to continue his or her antiplatelet agent through the perioperative period. Much of the answer to this question depends on the elective versus semi-urgent versus emergent nature of the operation, in question, and whether there is any reasonable evidence that bridging maneuvers such as high-dose aspirin or clopidogrel tapering could safely attenuate the TE risk during the first 90 days after stopping clopidogrel. Additionally, if the researchers were to have examined the reasons that clopidogrel was discontinued, an interesting sub-group analysis might have been to study those patients for whom “bleeding” led to discontinuation and assess whether those bleeding events were perioperative or traumatic.

Based on this study, it seems wisest to advise a patient: “once on Plavix, always on Plavix.”

## Literature Review III: Exploring Intensive Insulin Therapy In-Depth



Scott Ahlbrand, M.D.  
Fellow, Division of Critical Care Medicine  
Stanford University  
Department of Anesthesiology  
Stanford, California

### Article:

Lipshutz AKM, Gropper MA. Perioperative glycemic control. *Anesthesiology*. 2009; 110:408-421.

### Review:

For years now, the adverse effects of hyperglycemia have been described in a variety of clinical settings. Recently however, much attention has been given in the literature to the benefits and risks of tight glycemic control. There has been no greater debate over its utility than that found in the intensive care unit (ICU) setting. Navigating one's way through the numerous publications pertaining to this topic is confusing to say the least. That is until now. In

the most recent issue of *Anesthesiology*, Drs. Lipshutz and Gropper, from the University of California, San Francisco, present an excellent evidence-based review of the latest and most influential papers pertaining to the topic of glycemic control. If previously confused about whether or not tight glycemic control is beneficial for your patient, this article will provide greater clarity over what data exist to support or deny your claim.

The article begins with a brief history describing how the search for answers about perioperative glycemic control came about. The authors cite the first Leuven study by Van den Berghe et al. in 2001 and detail what patients were included and what they used as their endpoints. They go on to cite how the second Leuven study contradicted the data gathered from the first in order to illustrate exactly how mixed the data are on this subject. They move on to describe in their "Materials and Methods" section that all the information presented is drawn from easily accessible articles published between the years 1999 and 2008 and found within the Cochrane Library and Medline search engine.

What makes this review article so helpful in deciphering this confusing topic is the manner in which the individual studies are presented. The authors first describe the effects of intensive insulin therapy (IIT) by patient population. For example, they return to the Van den Berghe study and identify that it was surgical ICU patients who benefitted from intensive therapy. They then go on to describe additional studies from Vriesenorp et al. and Krinsley et al. to include the benefits and risks to medical ICU patients suffering from septic shock in order to show how varied the results have been between populations.

Drs. Lipshutz and Gropper also pose a new question, something not often found in review articles, and attempt to answer whether or not IIT is more beneficial in diabetics versus non-diabetics. They admit there is not yet a prospective study specifically aimed at comparing these two populations. Instead, they pick apart data that are already published, namely the Van den Berghe et al., Rady et al. and Doenst et al. studies and conclude that, to date, the only point which can be suggested is that ideal glucose levels of critically ill patients may differ by diabetic status.

The article even goes into the evaluation of which appropriate glucose targets should be used for IIT as well as comparing how blood glucose is measured, how difficult implementation of ICU protocols can be, and the overall cost-effectiveness of implementing these kinds of protocols. These are important factors to consider when deciphering this data, as they may change what conclusions can be drawn and what changes are made in our daily practices.

A review article should be a concise summary of a central subject. But at the same time, with that summation should follow additional questions posed by the author and reader as a reflection of presenting the aforementioned data in a different manner. This is what we have here. An excellent presentation of a conflicting group of data presented in a way that is easy to understand, easy to follow and easy to generate new questions from. Although the issue of IIT is not yet resolved, I strongly recommend this review article to anyone who has uncertainty about what data exist regarding who can benefit, and when, from intensive insulin therapy.

## Healthy, Wealthy and Wise: The State of the Society

*Continued from page 1*

recognizes that an organization thrives if it builds upon the shoulders of those who have gone before. Consequently, our present collective wisdom is anchored by a history of wise leadership in the past. We are happy to be doing well but will not rest upon past successes. The leadership will continue to work to improve the ASCCA, and we recognize the impor-

tance that each and every member plays in the health and wealth of a society. We welcome your comments, suggestions and advice. We are here to serve you!

So, I think it is safe to say that the ASCCA is Healthy, Wealthy and Wise...and with your help, we will work hard to stay that way!

## Fellowship Review I: Yale University Department of Anesthesiology Critical Care



Stephen Luczycki, M.D., F.C.C.P.  
Assistant Professor  
Yale University School of Medicine  
Department of Anesthesiology  
New Haven, Connecticut

### General Overview:

The Critical Care Fellowship at Yale represents a truly multidisciplinary approach to training in critical care medicine. While the overall structure of the program is designed to meet the ACGME requirements for critical care medicine, each fellow is allowed flexibility in tailoring the training experience to fulfill individual interests. The basic structure provides for a total of nine months of ICU experience and allows for three months of elective time. Previous fellows have enjoyed success in both academic and private practice careers in critical care medicine.

### Diverse Experience

Fellows begin training in our Yale-New Haven Hospital (YNHH) surgical intensive care unit (SICU) where they are exposed to a patient population including trauma (YNHH is a Level I Trauma Center), transplant (liver, pancreas, kidney), surgical oncology, gynecologic oncology, emergency general surgery, endocrine surgery, otolaryngology, orthopedics, vascular surgery, thoracic surgery and neurosurgery. The SICU is staffed by attendings and fellows with primary training in anesthesiology, surgery and emergency medicine. This staffing model allows each fellow to be immersed in a multidisciplinary environment at the outset. Fellows are expected to fully participate in and eventually direct daily rounds. They also supervise and assist in the education of residents, medical students, physician assistants and nurse practitioners.

Each rotation is for a duration of one month. While the majority of clinical time occurs in the SICU with its diverse patient population, rotations also include the Medical Intensive Care Unit and may include the Cardiothoracic Intensive Care Unit, Pediatric Intensive Care Unit and Neuro Intensive Care Unit. Elective time can include additional rotations in any of these ICUs as well as in the burn unit at Connecticut's only American Burn Association-verified burn center at Bridgeport Hospital.

### Broader Horizons

The ACGME allows for the inclusion of three months of elective time. Subject to approval by the program director, this time can incorporate a broad range of experiences. Clinical rotations can be ar-

ranged in any medical specialty, including cardiology (including echocardiography), radiology, nephrology and infectious disease. Many of our faculty serve on the editorial boards of major journals and have often invited fellows to participate in various writing projects. Research opportunities abound at Yale, and fellows are encouraged to explore their particular interests and will be assisted in finding a laboratory virtually anywhere within Yale University. Arrangements can also be made to extend the fellowship to include more robust research time for applicants with strong interests in ongoing projects.

### The Future

Yale-New Haven Hospital is currently constructing a new cancer hospital that is scheduled to open in 2009-2010. This new pavilion will include new ICUs, which will further broaden the fellowship experience and increase our capability to educate exceptionally prepared critical care physicians.

### Contacts:

For further information, please contact the fellowship program director:

Stanley Rosenbaum, M.D., F.C.C.M.  
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333 Cedar Street, TMP-3  
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## Medical Director Needed at Birmingham VA

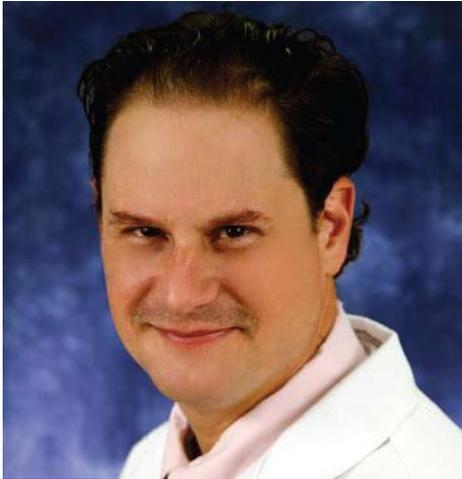
The Veterans Administration Medical Center at Birmingham, Alabama invites applications for Medical Director of the Surgical Intensive Care Unit. The applicant should be a critical care board-certified anesthesiologist. Applicants with an interest in a flexible model of covering the SICU and performing anesthesia for general and cardiothoracic surgical cases and wishing to teach residents are particularly sought. Applicants who have completed subspecialty training in critical care medicine or echocardiography also are particularly sought. Great compensation and benefits package (very close to private practice compensation with much better quality of life).

### Qualified candidates should contact:

Dr. Yasser Sakawi, Chief of Anesthesia  
Birmingham VA Medical Center  
700 South 19<sup>th</sup> Street  
Birmingham, AL 35233.  
(205) 212-3919  
[Yasser.Sakawi@va.gov](mailto:Yasser.Sakawi@va.gov)

Please attach a resume to your e-mail. The Department of Veterans Affairs is an equal opportunity, affirmative action employer.

## Fellowship Review II: Columbia University



James Orsorio, M.D.  
Assistant Professor of Anesthesiology and  
Critical Care Medicine  
Weill Cornell Medical College  
New York, New York

As a former fellow, I write with great enthusiasm about my experience and developments that shape the Critical Care Fellowship Program today at Columbia University College of Physicians & Surgeons at New York Presbyterian Hospital.

The Fellowship is approved for seven positions in a 12-month ACGME-accredited program. Since the increase was granted in 2007, all seven positions have been filled each year and candidates for the 2010-2011 year are currently being interviewed. The curriculum is designed to take the Fellows through increasing levels of experience and responsibility and prepare them for Board Certification in Anesthesiology Critical Care Medicine (ACCM).

The Fellows' year is divided into 13 four-week blocks, concurrent with the residency program. Sequential rotations include Surgical Intensive Care Unit (SICU), Cardiothoracic Intensive Care Unit (CTICU), Consults and Electives. Fellows spend about 50 percent of their time as a key member of the ICU team on the SICU (16 beds) and CTICU (21 beds).

Combined, the two units average about 2,200 admissions per year, and the variety and extent of the clinical exposure is excellent. The SICU receives about 100 liver transplant patients a year, as well as patients undergoing pancreatic transplant or major thoracic, vascular and pancreatic surgery, or any patient undergoing complicated general or obstetric surgery. The CTICU takes care of about 90 heart transplant, 50 lung transplant and 60 VAD patients each year, together with both routine and challenging cardiac surgical procedures.

About 25 percent of the time is spent providing consultation outside the ICU, in the OR, PACU, step down units, and floors. About 25 percent of the time is spent on elective rotations tailored to the individual Fellow's interests. These include Medical ICU, Coronary Care Unit, Neuroscience ICU, Pediatric ICU as well as optional rotations with the Nephrology (dialysis), Infectious Disease, Nutritional Support and Liver Transplantation services. In addition there is instruction and hands-on experience in transesophageal and transthoracic echocardiography throughout the year.

Academic and administrative activities are integrated into the Fellowship program. Wednesday is "Fellows' Day," and includes three hours of teaching: an echocardiography tutorial by the Chief of Cardiothoracic Anesthesiology, a weekly Journal Club on seminal critical care articles presented by the Fellows, and a didactic lecture given by a faculty member (that might be a nephrologist, pulmonologist, etc). As they gain experience and confidence, the Fellows start to participate as lecturers in the "ICU 101" program for medical students, residents, physician assistants and nurse practitioners conducted three times a week. Fellows are responsible for coordinating our monthly Morbidity and Mortality Rounds. During the year, Fellows, together with an ICU faculty mentor, present at Department of Anesthesiology Grand Rounds and at Critical Care Grand Rounds.

Our Fellows are encouraged to attend major critical care meetings such as the American Society of

Critical Care Anesthesiologists (ASCCA) or the Society of Critical Care Medicine (SCCM). The Department of Anesthesiology provides funding to help support academic activities for each Fellow.

Fellows are encouraged to participate in ongoing research projects and are given all available assistance in setting up their own research projects. Funding is obtained through grants approved by the Department of Anesthesiology and outside funding agencies. Through the Columbia University Office of Clinical Trials, Fellows obtain certification in Good Clinical Practice and attend an annual course at the Irving Center for Clinical Research on clinical research protocol design and statistics.

It is possible for Fellows to undertake the Critical Care and Adult Cardiothoracic Anesthesiology (ACTA) Fellowship Programs in sequence (24 months). However, the programs are separately run and require individual application and acceptance. Once an applicant has been accepted by both programs (and we have had at least one fellow a year who has done this), we do try to help to co-ordinate academic activities across the two-year continuum.

## Fellowship Review III: Johns Hopkins Critical Care Fellowship

Samuel M. Galvagno Jr., D.O.  
Fellow in Multidisciplinary Surgical Critical Care  
Johns Hopkins Medical Institutions  
Baltimore, Maryland

Critical care medicine has a long and proud history at the Johns Hopkins Hospital. The first intensive care unit (ICU) in the country, a postoperative neurosurgical unit, was developed at Johns Hopkins in 1928 by Walter Dandy, M.D. Thirty years later, in 1958, Johns Hopkins Bayview Medical Center, then named the Baltimore City Hospital, opened the first fully-staffed ICU in the country. Today, the Johns Hopkins Hospital operates seven adult ICUs, a pediatric ICU and a neonatal ICU. These units have received both regional and international acclaim for their excellence, especially regarding efforts to improve patient safety.

Many fellows come to the department with extensive previous training, including advanced graduate degrees and board certification in multiple specialties. The Division of Adult Critical Care Medicine offers a one-year critical care fellowship program that meets all certification requirements of the American Board of Anesthesiology. The program is accredited by the Accreditation Council for Graduate Medical Education. An overriding principle behind the fellowship is that one does not specialize but “generalizes” in critical care medicine. This multidisciplinary tenet resounds through all levels of the program, and each rotation reflects the department’s cross-disciplinary perspective. Hence, while rotating in the ICUs, attending physicians come from a variety of disciplines, including anesthesiology, trauma surgery, pulmonary medicine and emergency medicine.

The mission of the Department of Anesthesiology and Critical Care Medicine is to provide an educational environment optimized for the development of clinician/basic science leaders in multidisciplinary

critical care medicine. Fellows are expected to develop mastery in the diagnosis and management of complex problems in critically ill patients and necessarily develop an appreciation for the depth and breadth of the specialty. Early in the fellowship, fellows are provided with a mini-course on evidence-based medicine conducted by national leaders in the field. The principles of study design and statistical analysis are further honed during bi-monthly, formal journal club presentations with close faculty mentorship. Fellows play an active role in resident, medical student and departmental education with monthly morbidity and mortality conferences, case conferences and presentations on selected topics. During and upon completion of the fellowship, ample opportunities exist for clinical and basic science research at one of the many affiliated research groups at the Johns Hopkins Medical Institutions.

Throughout the fellowship, opportunities exist to work with faculty members of the Johns Hopkins Center for Innovation in Quality Patient Care. Headed by Peter Pronovost, M.D., Ph.D., the Center was created in 2002 to facilitate patient-centered revamping of health care delivery systems and to institute innovative care delivery models at Johns Hopkins Medicine. The Center helps coordinate the efforts of interdisciplinary teams of physicians, nurses and managers throughout the Johns Hopkins Medical Institutions to gather data, evaluate changes, and recommend and implement best practices. In addition to supporting Johns Hopkins’ patient safety efforts, the Center has worked with various hospitals in the U.S. and internationally.

Fellows receive an appointment to the School of Medicine upon matriculation. The program is integrated with the Department of Surgery’s Critical Care Medicine Fellowship, and rotations are centered in a surgical care environment. A wide variety of patients are admitted from all of the surgical specialties, in-

cluding transplant surgery. Additional no-call elective rotations are provided in the medical, pediatric, neurosciences, burn and oncology ICUs as well as rotations on other services such as infectious diseases, nephrology and pulmonary medicine.

Nine fellows are accepted each year. Combined fellowships for cardiothoracic anesthesia or other subspecialties are available. Fellows receive four weeks of vacation and a generous educational allowance for books, national meetings and other expenses. For further information, including information regarding the application process, the program director is Theresa Hartsell, M.D., Ph.D. Dr. Hartsell can be contacted via e-mail at [tharsel@jhmi.edu](mailto:tharsel@jhmi.edu). The Department of Anesthesiology and Critical Care Medicine hosts a Web page with a full description of the curriculum, faculty, educational schedule and ongoing research [www.hopkinsmedicine.org/anesthesiology/Education/fellowship/critical\\_care.cfm](http://www.hopkinsmedicine.org/anesthesiology/Education/fellowship/critical_care.cfm). For any specific questions about a typical day in the life of a critical care fellow at Johns Hopkins, feel free to e-mail me at [sgalvag1@jhmi.edu](mailto:sgalvag1@jhmi.edu).

# Plan to attend the ASCCA 22nd Annual Meeting and Critical Care Update



*Friday, October 16, 2009*  
*Hilton New Orleans Riverside*

## *Call for Abstracts*

The American Society of Critical Care Anesthesiologists invites submission of abstracts for presentation at the ASCCA 22nd Annual Meeting, which will take place on October 16, 2009, in New Orleans. Abstracts will be graded competitively on the basis of scientific merit and will be selected for poster presentation. Your abstract presentation at the ASCCA Annual Meeting will not conflict with or preclude presentation at the ASA 2009 Annual Meeting, which immediately follows the ASCCA Annual Meeting.

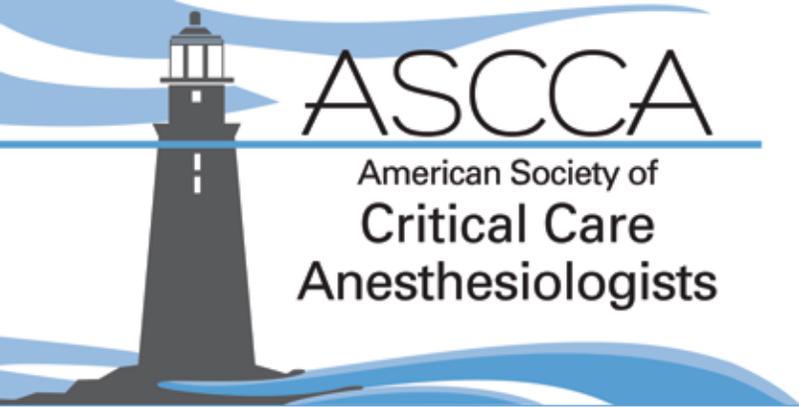
Visit the Society's online submission form at [www.ascca.org](http://www.ascca.org).  
The abstract submission deadline is June 19, 2009.

## *Young Investigator Award*

This award is presented annually to the resident or fellow whose research exemplifies the Society's mission to educate anesthesiologists in the care of critically ill patients and to foster the knowledge and practice of critical care medicine by anesthesiologists. The recipient of the Young Investigator Award will be asked to make an oral presentation of his/her work at the ASCCA Annual Meeting. Please indicate your interest to be considered for this award by checking the respective box on the online submission form.

Please contact the ASCCA office at (847) 825-5586 or [c.dionne@asahq.org](mailto:c.dionne@asahq.org) if you have any questions.  
We look forward to receiving your submission.





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