Perioperative Myocardia Ischemia Reperfusion Injury: Nature’s Great Paradox

Although advances in anesthetic and surgical techniques currently allow the majority of patients to undergo coronary artery bypass grafting (CABG) procedures without significant mortality, more than 25% of this surgical population may still experience substantial morbidity related to adverse perioperative cardiovascular outcomes. Stroke, myocardial infarction (MI), ventricular failure, and perioperative dysrhythmias, can directly effect length of stay and cost of hospitalization, patients’ functional capacity at discharge, and can ultimately contribute to mortality.

The etiology of myocardial dysfunction following CABG is often multifactorial, yet frequently involves perioperative myocardial ischemia1. The myocardium may be particularly susceptible to ischemia during CABG surgery due to underlying coronary artery disease (CAD), perioperative hemodynamic instability, inadequate protection during cardiopulmonary bypass (CPB), coronary

A Quiet Place
by Ronald Hurley, M.D.

It’s midnight and I’m typing by gaslight at the cabin. The woodstove is doing its job well and I’m in shirtsleeves despite the cold November air. Darla, my boxer, is snoring gently on the couch. I love this — the peace, the quiet, and yes, the solitude. Please don’t get me wrong… I love my job and all my friends at the Brigham. However, one has to admit, the job can be overwhelming at times. There’s always more to do — one more e-mail to get out, one more page to answer, you all know what I mean…

Let me tell you a little about the cabin! It’s about 90 minutes west of Boston in a small town, Royalston, on the New Hampshire border. The town itself is rural (no commercial establishments of any kind!), but the cabin outdoes the town. It sits on a 10-acre lot next to Long Pond, a tributary of Tulley Lake. Most of the surrounding several thousand acres are conservation and flood control land. Travel a mile and a half, in about 15 minutes, from the paved road and you’ve arrived. There are a couple of other rarely used cabins in the neighborhood but one would be forgiven for thinking they’d traveled to remote Alaska.

The cabin has neither electricity nor running water, but does have propane. So it’s necessary to light the refrigerator, lights and stove pilots. Yes, I said light the refrigerator. When I was very young gas refrigerators were fairly common and were reputed to last much longer than electric ones. The woodstove provides the heat and, yes, there is an indoor toilet. It’s odor-free — one simply adds peat moss to one’s leavings and it all drops into a composting drum that is emptied once a year, odor-free and rich in nutrients which I gladly donate to the forest. Cell phones do not work but radios do, especially my new satellite radio — Nirvana is every baseball game listened to with perfect reception.

Folks ask what I do at the cabin. First of all, I’m not a complete hermit and do welcome company, especially my family; wife Beth and my daughters Meg and Emily. However, they have lives of their own, and while they like the cabin, they’re not quite as passionate about it as am I.
Relaxing on sun-drenched bluffs east of Long Pond (red circle marks approximate location). At right, an early morning canoe ride.
There’s a canoe and a couple kayaks, plus a rugged mountain bike trail that’s way too ambitious for me! Mostly, I just take joy in the activities of daily living — cooking breakfast, building the fire to warm the cabin, splitting some logs for the night’s campfire, hiking with Darla, napping in the hammock, listening to music and reading until I sleep. Heaven.

I’m not sure where this passion for rustic solitude comes from. My parents are mystified. I spent most of my outdoor life as a child of the 50s hauling golf clubs around a wild and woolly 9-hole course. I grew up in Newburyport, a quaint and historic tourist destination now, but a fairly depressed blue-collar town in the 50s. (They fixed it up after I left — perhaps there was a connection.) Off to Tufts Engineering because I was good in math. By graduation I’d decided that engineering was not for me, but Harvard School of Public Health sounded more people-oriented. There, a course in human physiology was offered and taught in part by Dr. David Leith, an anesthesiologist from the Peter Bent Brigham. Epiphany as David opened a new world to me…and medicine became my goal. However, there was a bit of a problem. I was missing some prerequisites (fixable at night) and had a history at Tufts of “under-achieving”, reflected in my GPA (not fixable without time travel). However, I took the needed courses, applied to U.S. schools, and was promptly rejected. Somewhat discouraged, I took a job teaching at North Shore Community College in Beverly, MA while I retook some of my lesser triumphs from Tufts.

For some reason I applied to the Royal College of Surgeons in Ireland. Fortunately, the Irish didn’t seem to understand American grading systems — I think they thought the closer to 1.0 you got, the better you’d done. Apparently, I was a star. Well, the next 3 years were some of the best of my life but I had to leave before my liver gave out and/or my new wife divorced me (she was supporting the enterprise while living with my parents in Connecticut). I transferred to UMass Medical, which was both outstanding and the bargain of the century. Tuition was $1000 per year. Senior year I met Benjamin Covino, who was leaving UMass for the new Affiliated Hospitals Center, a name they soon dropped for Brigham and Women’s.

That was 1980 and after an internship in Worcester I followed Ben to the Brigham. My Brigham career is known to most of you. I have been so fortunate with three great chiefs; Ben, Simon and now Chuck. I truly love the department and try to make it just a little bit better every year. As I say to residents working with me for a day; “Let’s 1) take care of the patient; 2) learn something from each other; and 3) have fun!”
artery embolization, and/or technical complications (i.e., incomplete revascularization, graft spasm or kinking). Although prolonged myocardial ischemia alone jeopardizes cellular structural and biochemical integrity, oxygen deprivation that is limited to less than 20 minutes is usually associated with only transiently depressed myocardial contractility. Paradoxically, the restoration of blood flow following sustained myocardial ischemia beyond 45 minutes results in a phenomenon known as myocardial ischemia reperfusion (I/R) injury, in which tissue injury is augmented in excess of that produced by ischemia alone.

Paradoxically, the restoration of blood flow following sustained myocardial ischemia...results in tissue injury in excess of that produced by ischemia alone.

During cardiac surgery, SIRS is most profoundly affected by the exposure of circulating blood to the bioincompatible surfaces of the CPB extracorporeal circuit, which results in the generation of factor XII and activation of the intrinsic pathway of the coagulation cascade via the contact system. The subsequent production of kallikrein activates the kinin-bradykinin system, leads to the generation of plasmin, and stimulates production of the complement component C5a, which is a potent anaphylotoxin, promoter of proinflammatory interleukins, and stimulator of neutrophil enzyme release. Plasmin in turn activates the fibrinolytic system, generates additional contact activation proteins, and promotes cleavage of the complement component C3 into C3a, another anaphylotoxin. The extrinsic pathway of the coagulation system is also activated in the perioperative period by the production of tissue factor from endothelium and muscle in response to surgical trauma, inflammatory stimuli and oxidative or shear stress. Thrombin produced from both intrinsic and extrinsic coagulation pathways, catalyzes the formation of insoluble fibrin from fibrinogen, which binds the platelet plug to initiate hemostasis.

The normal balance of hemostasis is often disturbed in cardiac surgical patients. The concomitant procoagulant activities of thrombin combined with the stimulation for fibrinolysis may become uncontrolled in the presence of significant vascular injury. In addition, several coagulation proteins including thrombin and Factor Xa have pro-inflammatory properties. Subsequent disseminated intravascular coagulation and microvascular occlusion may contribute to multiorgan dysfunction syndrome. Thus, the combination of endothelial cell, platelet and leukocyte activation along with circulating cytokines and pro-coagulants associated with SIRS, favors a systemic procoagulant / pro-inflammatory state.

Pro-inflammatory properties could be linked to the development of multiorgan dysfunction syndrome. Thus, the combination of endothelial cell, platelet and leukocyte activation along with circulating cytokines and pro-coagulants associated with SIRS, favors a systemic procoagulant / pro-inflammatory state which can exacerbate local I-R injury.

Myocardial I-R injury has been associated with transient reperfusion arrhythmias, myocardial stunning, and irreversible myocardial injury which can contribute to...
perioperative morbidity and mortality. It is therefore not surprising that a significant effort has been devoted toward developing novel surgical techniques and pharmacological agents aimed at reducing the generation and pathophysiological consequences of pro-inflammatory mediators involved in I-R injury. Ideally, the morbidity associated with perioperative myocardial I-R injury may be diminished by limiting the duration and severity of the initial ischemic insult and assuring timely reperfusion. However, aortic cross-clamping and CPB is still required for the majority of cardiac surgical procedures, thus subjecting patients to varying degrees of multiorgan I-R injury. Furthermore, although extracorporeal circuit modification and CABG without CPB (i.e.; OPCAB: “off-pump CABG”) may reduce inflammatory mediator generation, neither procedure guarantees that myocardial I-R and associated perioperative morbidity can be entirely prevented.

A wide variety of modifications in cardiac surgical technique have been proposed in an attempt to either reduce the duration and severity of myocardial ischemia and/or the generation of the systemic inflammatory mediators involved in I-R injury. These techniques have included the utilization of various cardioplegia recipes and delivery techniques, temperature regulation, CPB circuit modification, bilateral extracorporeal circulation, hemofiltration, leukocyte depletion, minimally invasive surgical techniques, and OPCAB. Modification of anesthetic techniques including the use of thoracic epidural anesthesia and analgesia, have also been shown to attenuate the perioperative stress response and myocardial injury following CABG.

In addition, several anesthetic agents commonly used during cardiac surgery including sodium thiopental, propofol, opioids, midazolam and volatile agents also have systemic anti-inflammatory effects.

Most of the remaining therapeutic strategies have primarily focused on preventing or treating reperfusion injury by administering pharmacological agents targeted towards the most significant pro-inflammatory mediators associated with myocardial I-R injury. Several therapeutic interventions including pharmacological preconditioning agents, adenosine and adenosine-regulating agents, ROS scavengers and antioxidants, corticosteroids, Na+/H+ exchange inhibitors, and serine protease inhibitors have been investigated in an attempt to demonstrate a positive impact on ameliorating myocardial I-R injury.

Several members of our Cardiac Anesthesia Division along with Greg Stahl, Ph.D. from the department’s Center for Experimental Therapeutics and Reperfusion Injury have been involved with translational and clinical studies involving the potential role of C5 complement inhibitors in attenuating perioperative myocardial I-R injury. Pexelizumab (Alexion Pharmaceuticals; Procter & Gamble Pharmaceuticals) is a recombinant single chain, monoclonal antibody which binds to complement component C5 to inhibit C5a and the formation of the membrane attack complex, C5b-9. In 2004, a Phase III clinical trial called the “Pexelizumab for Reduction in Infarction and Mortality in Coronary Artery Bypass Graft Surgery” (PRIMO-CABG) was conducted to evaluate the efficacy and safety of pexelizumab in reducing perioperative MI and mortality in CABG surgery. The study was a randomized, double-blind, placebo-controlled trial, including 3099 adult patients undergoing CABG surgery with or without valve surgery enrolled at 205 hospitals in North America including the Brigham and Women’s Hospital and Western Europe. Patients were randomly assigned to receive intravenous pexelizumab (n = 1553) or placebo (n = 1546) prior to CPB initiation. Compared with placebo, pexelizumab was not associated with a significant reduction in the risk of the composite end point of death or MI in 2746 patients who had undergone CABG surgery only, but was associated with a statistically significant risk reduction through postoperative day 30 days.
among all 3099 patients undergoing CABG with or without valve surgery. These clinical trials implicating a potential role for C5 inhibition in cardiac surgical patients have provided the foundation for a second recently completed Phase III trial (PRIMO CABG II), which will hopefully provide promising results for this novel therapy.

Myocardial I-R injury contributes to adverse cardiovascular outcomes following cardiac surgery. The pathogenesis of I-R injury is complex, involving the activation, coordination and amplification of several systemic and local pro-inflammatory pathways. Therapeutic considerations including preoperative risk stratification (co-morbidity; surgical complexity), minimizing initiating factors predisposing to SIRS, limiting ischemia duration and administering appropriate immunotherapy directed toward systemic and local pro-inflammatory mediators of I-R injury, should all be considered. In addition, genetic-environmental interactions are rapidly being recognized for their role in the pathogenesis of cardiovascular disease. Thus, treatment and prevention of perioperative morbidity associated with myocardial I-R will ultimately require a multifocal approach.

References:
12. Mangano D. Effects of acadesine on myocardial infarction, stroke, and death following surgery: a meta analysis of the 5 international randomized trials. JAMA 1997; 277:325-332
2005 turned out to be memorable and momentous, after all. Leaps by a few, flight by many, and gains were made by all! The department continued to reap the harvest of decades of scholarship, and of its investment in diversity, innovation and enthusiasm to break new ground. Consequently, many new programs were initiated; several others were imagined and the imaginings crystallized—all within the span of a short year.

Recommendations made by faculty members at the departmental retreat of 2004 were honored in letter and in spirit. Born out of conversation and frank dialogue were initiatives like the Mentoring program put together by the division of Faculty Development and Education under the guidance of Simon Gelman, M.D., the STAR fellowship program, the Simon Gelman fellowship program, and the inception of the division of Clinical Innovation. The Faculty Board continued to outperform itself, and its interactive monthly faculty forums have become a tradition worth savoring. Friends like Matt, Alessia, Roman and Jeff found other homes, while the rest of us continue to find our fulfillment among the known and the familiar.

2005 was also a year of natural disasters—almost as if we needed the reminder that the interdependence of nations and peoples continues to usher us to a higher calling. The freakish tsunami in Indonesia, relentless hurricanes in the Americas—in particular those along the Gulf of Mexico, the frightening mudslides of Guatemala, and then the merciless earthquake in northwestern Pakistan, all served to remind us that a higher order prevails, and that where we can, when we can, help is owed.

I extend my warm wishes for a happy holiday season to you and your families.

Naila Moghul, M.D.
Charles A. Vacanti, M.D., was elected President at the annual meeting of the Society of Academic Anesthesiology Chairs (SAAC) in Washington, D.C., in November. Dr Vacanti will serve as president-elect for one year and then as president for the following two years. Previously, Dr. Vacanti had served as an elected member of the governing council for the Association of Anesthesiology Program Directors (AAPD) for three years, from 2001–2004. He was also a member of the governing council for SAAC for 2004–2005. Additionally, from 2003–2005, Dr. Vacanti had served as the appointed representative of SAAC on the Council of Academic Societies (CAS) for the AAMC.

Charles A. Vacanti, M.D., was elected as a Continental representative for North America for the Tissue Engineering Regenerative Medicine International Society (TERMIS) in October, 2005.

Charles A. Vacanti, M.D., has been appointed to the new ASA committee on “Academic Anesthesiology” by the President-Elect of the ASA. The committee, composed of approximately 15–20 academic anesthesiologists, has another BWH faculty member, Beverly Philip, M.D., serving on it. The resident member appointed to that national committee, Brian Gelfand, M.D., is also in the Anesthesiology Department at the BWH, giving our department more representation on that committee than any other academic anesthesiology department.

2005 ASA Activities

Jill Antoine, M.D., Chair, ASA Committee on Trauma and Emergency Preparedness, Member, ASA Executive Committee Taskforce on Katrina Relief Effort. As Chair of the ASA Committee, Jill worked directly with ASA President Eugene Sinclair, M.D. and members of the ASA Executive Committee to coordinate the Katrina Relief Efforts.

Simon Body, M.D., presented a lecture on Perioperative Thrombosis: Who is at Risk?

William Camann, M.D., moderated the Sol Shneider/SOAP Obstetric Anesthesia breakfast panel: Are We Placing Our Patients at More Risk than We Care to Admit?

William Camann, M.D., gave a refresher course lecture on Current Controversies in Obstetric Anesthesia.

William Camann, M.D., was the winner of the ASA Media Award for Television, for Today Show segment Painfree Labor on Feb 17, 2005.

Dan Dedrick, M.D., attended the New England Caucus meeting Friday evening, served as a Massachusetts Delegate to the first session of the ASA House of Delegates, audited Reference Committee One as the representative of the New England Caucus, attended Refresher Courses and attended the ad hoc meeting of the ASA Committee on Residents and Medical Students, Monday afternoon attended second meeting of the New England Caucus (reporting on Ref. Comm. One), Tuesday morning again served as a Massachusetts Delegate to the second session of the ASA House of Delegates, followed in the afternoon by a special meeting on the new ACGME Residency Review Committee proposal for curriculum revisions, and finally attended the Society for Education in Anesthesiology breakfast panel.

John Fox, M.D., presented a lecture on Perioperative Echocardiographic Evaluation of the Aortic Valve.

John Fox, M.D., presented a workshop on Basic Echocardiographic Evaluation of Valvular Lesions—Aortic Valve.

Simon Gelman, M.D., Director of FAER, participated in all FAER activities including Board of Directors meetings.

Alan Harvey, M.D., Delegate, ASA House of Delegates, Anesthesia Patient Safety Foundation, Board of Director Retreat, Anesthesia Patient Safety Foundation, Education and Training Committee ASA Committee on Bylaws, ASA Section Council to the American Medical Association.

Bhavani Kodali, M.D., moderated a session on Equipment, Monitoring and Sodalime.

Beverly Philip, M.D., Organizer and Moderator, Clinical Forum on Ambulatory Anesthesia; Organizer and Moderator, panel Propofol by Nonanesthesiologists: Where Are We One Year Later, SAMBA delegate, ASA House of Delegates, SAMBA Board of Directors meeting, New England Caucus attendee, Committee meetings: Ad Hoc Sedation Credentialing Committee, Research Committee, Scientific Advisory Committee, Vice Chair, Scientific Content Subcommittee for Ambulatory Anesthesia, Annual Meeting Committee, Annual Meeting Oversight Committee, Executive Committee of the Annual Meeting Oversight Committee.

Gan TJ, Apfel C, Kovac A, Philip B, Lawson F. The NK-1 receptor antagonist aprepitant for prevention of postoperative nausea and vomiting. Poster A-769

Edgar Ross, M.D., taught at a cadaver course on sympathetic blockade.

Nicholas Sadovnikoff, M.D., participated in a panel called New and Old Therapeutics. The topic of his talk was Perioperative Steroid Replacement.

Sarin P. Philip BK. Postoperative pain control in ambulatory surgery patients: Can we be doing better? Poster A-649


Stanton Shernan, M.D., presented a lecture on Perioperative Echocardiography for Valve Surgery: Clinical Applications.

Douglas Shook, M.D., presented a lecture on Perioperative Echocardiographic Evaluation of the Pulmonic and Tricuspid Valves.

Gary Strichartz, Ph.D, Professor of Anaesthesia, Pharmacology and Biophysics and Vice Chair for Research in the Department spoke on Pharmacological Studies on Preventing or Modulating the Plastic Changes in Experimental Models of Incisional Pain at the Anesthesiology-Sponsored Symposium, Plasticity in Postoperative Pain at this year’s ASA meeting.

Lawrence Tsen, M.D., gave the Refresher Course lecture entitled Anesthesia for Cesarean Delivery at the ASA 2005.

Frederick Van Pelt, M.D., Anesthesia Patient Safety Foundation Board of Directors Workshop, The Role of Patients in the Mission of APSF.

William Camann, M.D., and Kathryn Alexander, M.A. have written Easy Labor: Every Woman’s Guide to Choosing Less Pain and More Joy During Childbirth, to be published in early 2006 by Random House/Ballantine Books. The book is designed to be the first complete and comprehensive guide to pain relief during labor and delivery. "It’s hard to imagine childbirth ever being easy, but this guide will point soon-to-be mothers in the right direction. In a straightforward manner, the authors discuss medical and non-medical approaches to dealing with pain during the most physically painful time of a woman’s life. Dr. Camann brings more than 20 years of obstetric and anesthesia experience to the task, providing invaluable advice for mothers, especially first-timers. The authors hope that by moving the focus away from the intense pain, a mother can experience the joy that comes from childbirth. Practicality is paramount, as is ample preparation prior to entering the delivery room. They assert that each woman’s decision about her labor is a personal choice, and each experience will be different—as such, they discuss all possibilities. Pain medications, water birth, natural birth and Cesarean delivery are covered in detail, as well as what to expect, what others have experienced and how to be prepared. Easy Labor will ease the fears about childbirth and prepare the expectant mother for the joy that comes with the miracle of life." —Kirkus Report. For further details see the book’s website at http://www.easylabor.net.

Academic Activities & Achievements

Stephen B. Corn, M.D., was featured in the October 17 issue of Mass High Tech for the aspect of his work focused on patient monitoring in hospital, home and other settings.

Stephen B. Corn, M.D., was featured in the Fall 2005 issue of Steps to Learning, East Meadow School District, New York. The article focused on his clinical innovation work.

TheAnswerPage.com was selected to be an educational exhibit for the fourth consecutive year at the Fourth Annual Harvard Medical School Medical Education Day Symposium on November 1. Stephen B. Corn, M.D., gave the presentation which featured content written by Drs. Corn and Segal, and several other members of our department. See the website for a full list of contributing authors.

Stephen B. Corn, M.D., was honored by Cambridge College on November 28 at their “Prescription for Success” seminar. Those attending the recognition included: Michael Dukakis, former three term governor of Massachusetts and presidential candidate in 1988, Phil Johnson, former NE Regional Director of Health and Human Services, Peter Meade, Executive Vice Present of Corporate Affairs of BC/BS of MA, Charlie Baker, President and CEO of Harvard Pilgrim Health Care, and Jim Roosevelt, President and CEO of Tufts Health Plan.

Omid C. Farokhzad, M.D., (PI, BWH, $750,000 Direct) was among the consortium of 10 MIT and Harvard scientists who successfully competed for a $20 million National Cancer Institute award forming the MIT-Harvard Center for Cancer Nanotechnology Excellence. The focus of the center, which will be directed by Robert Langer, Ph.D. at MIT, and Ralph Weissleder, M.D., Ph.D. at MGH, will be the development of novel technologies for cancer detection and treatment. Drs. Langer and Farokhzad will co-lead one of the major projects of the grant aimed at developing targeted nanoscale drug delivery vehicles for cancer therapy (press release: http://web.mit.edu/newsoffice/2005/techtalk50-4.pdf).

Easy Labor

Every Woman’s Guide to Choosing Less Pain and More Joy During Childbirth

Omid C. Farokhzad, M.D., (PI, BWH, $750,000 Direct) was among the consortium of 10 MIT and Harvard scientists who successfully competed for a $20 million National Cancer Institute award forming the MIT-Harvard Center for Cancer Nanotechnology Excellence. The focus of the center, which will be directed by Robert Langer, Ph.D. at MIT, and Ralph Weissleder, M.D., Ph.D. at MGH, will be the development of novel technologies for cancer detection and treatment. Drs. Langer and Farokhzad will co-lead one of the major projects of the grant aimed at developing targeted nanoscale drug delivery vehicles for cancer therapy (press release: http://web.mit.edu/newsoffice/2005/techtalk50-4.pdf).
Isabel Legarda, M.D., won second prize in the 10th Annual Anesthesia History Association Resident Essay Contest held in October, for her essay entitled Revival: on the eighteenth century origins of the modern code and the pioneering work of Charles Kite and James Elam. Isabel has been invited to present her essay at the AHA’s annual meeting, to be held at the Mayo Clinic next spring. The essay can be read here.

James Philip, M.D., received the Partners In Excellence Award as a member of the 11-member Intern Orientation Skills Training Task Force. This is the sixth year in a row that Dr. Philip has received a Partners In Excellence Award.

David Silver, M.D., received the Partners In Excellence Award as a member of the Intern Orientation Skills Training Task Force.

Lawrence Tsen, M.D., accepted an invitation to join the editorial board of The International Journal of Obstetric Anesthesia.

**Publications**


Memtsoudis, SG, Rosenberger, P, Lofflier, M; Eltzschig, HK; Mizuguchi, A; Shekar, P, Shernan, SK, Fox, JA; Utility of transesophageal echocardiography during intraoperative cardiac arrest. Chest, 2005


**Lectures**

Simon Body M.D., presented a lecture on Genetic Basis for Adverse Outcomes after Cardiac Surgery at a symposium entitled “Improving Outcomes in Open Heart Surgery” held in Boston on November 19.

William Camann, M.D., presented the following Grand Rounds lecture to the Obstetrics and Gynecology Department at Danbury Hospital, Danbury, Connecticut on November 14: What’s New in Obstetric Anesthesia?

Stephen B. Corn, M.D., was invited presenter at the Mass. MedTech Investors Conference held on November 1 at the Park Plaza Hotel, Boston, MA. The presentation featured the technical and clinical applications of his non-contact breathing technology.

Stephen B. Corn, M.D., was the invited visiting professor and panelist at the Medical Development Group Boston Forum on November 2. His lecture was entitled, Medical Needs: From the Physician’s View.

Dan Dedrick, M.D. and Scott Segal, M.D., attended the Fall Meeting of the Society for Education in Anesthesiology. As part of that meeting, they presented a workshop on Evidence-Based Medicine.

Omid C. Farokhzad, M.D., gave a talk titled Cancer Nanotechnology: Drug Encapsulated Nanoparticle-Aptamer Bioconjugates For Targeted Delivery to Prostate Cancer Cells at the European Cancer Conference (ECCO13) in Paris, France on November 1.

Omid C. Farokhzad, M.D., presented a talk describing the In vivo Efficacy of Nanoscale Drug Delivery Vehicles Using Mouse Models of Prostate Cancer at the European Cancer Conference (ECCO13). The press release of the conference was picked up by 120 news agencies including CNN, ABC, NBC, CBS, NY Times, Boston Globe, etc., in Europe, Asia, the Americas and Australia. The conference, which was attended by 10,000 participants,
later did a separate press release featuring the work as one of 3 most promising examples of what is on the horizon for the future of targeted cancer therapy.

_Gyorgy Frendl, M.D._, presented the following Grand Rounds lecture in the Anesthesiology Department at New England Medical Center / Tufts University School of Medicine on October 24: _The Benefits of Point-of-Care, Real-Time Ultrasound Guidance for the Placement of Central Venous Catheters._

_Ru-Rong Ji, Ph.D._, presented a lecture on _Spinal Glial Mechanisms of Neuropathic Pain_, as part of the scientific symposium Expanding Vistas in Neuropathic Pain on August 18 in Uluru, Australia, at the Pre-Congress Satellite Meeting of the World Congress on Pain.

_Ru-Rong Ji, Ph.D._, chaired the symposium _Map Kinases and Pathological Pain_, at the 11th World Congress on Pain in Sydney, Australia on August 25. He was also a speaker at this symposium, which was very well received.

_Stavros Mentsouedis, M.D._, gave oral presentations at the American College of Chest Physicians/Chest meeting in Montreal on Nov 1. The abstracts were also published in the journal _Chest._

_Beverly Philip, M.D._, participated in the 34th Argentine Congress of Anesthesiology, held in Buenos Aires on August 31-September 3. She spoke on _Ambulatory Anesthesia: Changing the Process; Recovery Issues for the Ambulatory Surgery Patient; and Inhalation Sedation/Analgesia with Sevoflurane._

_Beverly Philip, M.D._, gave the Sujit and Uma Pandit Lectureship in Anesthesiology, at the University of Michigan, Ann Arbor, on September 7-8. She presented Grand Rounds on _Fast Track Recovery_, and held a Lunch and Learn discussion on _Ambulatory Anesthesia Challenges_. Lots of "Hellos", including from Nora Naughton, who is embarking on a surgery center leadership position in that department.

_Beverly Philip, M.D._, participated in the 20th International Congress of the Israel Society of Anesthesiologists, held in Tel Aviv on Sept 27-29. She spoke on _Total Intravenous Anesthesia vs Inhalation Anesthesia for Ambulatory Patients._

_Beverly Philip, M.D._, attended the Strategic Planning Meeting of the Accreditation Association for Ambulatory Health Care (AAAHC). Dr Philip is the organization’s Secretary. The meeting was held in West Palm Beach, Florida on Sept 16–18.

_James Philip, M.D._, attended the International Congress of the Israel Society of Anesthesiologists, Tel Aviv, Israel from September 26–29. On September 27, he was the meeting’s first Plenary Speaker and presented the Charlene Kirkpatrick Memorial Lecture. The topic was _Engineering Our Way to the Future - Evolution of Clinical Monitoring_. On September 29, he presented a Refresher Course Lecture on _Kinetics of Inhaled Anesthetics_. On September 30, Dr Philip was visiting speaker at the Israel National Simulation Center, located at the Sheba Medical Center, Tel-Aviv University, Tel Hashomer, Israel. He spoke on _Learning and Teaching Inhalation Anesthesia Kinetics with Gas Man_.

_Charles Serhan Ph.D._, was informed by the World Scientific Journal that his paper _Lipid-Derived Mediators in Endogenous Anti-Inflammation and Resolution: Lipoxins and Aspirin-Trig-
ggered 15-epi-Lipoxins_ was one of the journal’s most downloaded articles.

_Stanton Shernan, M.D._, presented a lecture on _Perioperative Systemic Inflammation and Myocardial Ischemia Reperfusion Injury_ at the Medical University of South Carolina Town Grand Rounds in Charleston, SC on November 17.

_Stanton Shernan, M.D._, presented a lecture on _Perioperative Myocardial Ischemia-Reperfusion Injury_, at a symposium entitled “Improving Outcomes in Open Heart Surgery” held in Boston on November 19.

_Gary Strichartz, Ph.D._, presented a lecture on _The Role of Ion Channels in Neuropathic Pain_, as part of the scientific symposium Expanding Vistas in Neuropathic Pain on August 18 in Uluru, Australia, at the Pre-Congress Satellite Meeting of the World Congress on Pain.

_Lawrence Tsen, M.D._, gave Grand Rounds at the University of Massachusetts/Memorial Hospital, Department of Anesthesiology, with a presentation entitled: _Epidural Equinox_ on October 19.

_Lawrence Tsen, M.D._, was guest faculty at the 11th Annual Advances in Physiology and Pharmacology in Anesthesia and Critical Care Conference in Hilton Head, South Carolina, November 6–9. He presented two lectures entitled: _Do CSE’s and PCEA’s Really Make Life Easier?_ and _Dogma on Trial: Ephedrine and Oxygen in Obstetrics._

_Lawrence Tsen, M.D._, was the Panel Moderator and Lecturer for the Gertie Marx Memorial Lecture at the 59th PGA in New York on Dec 9. His presentation was: _The Effect of Neuraxial Labor Techniques on Maternal Fever and Fetal Outcome._
My Dear Sir,

Everybody wants to have a hand in the great discovery. All I will do is give you a hint or two as to names—or the name—to be applied to the state produced, and to the agent.

The state should, I think, be called *anaesthesia*. This signifies insensibility, more particularly (as used by Linnaeus and Cullen) to objects of touch. The adjective will be *anaesthetic*. Thus we might say, the *state of anaesthesia*, or the *anaesthetic state*. The means employed would be properly called the *anti-anaesthetic agent*. Perhaps it might be allowable to say *anaesthetic agent*; but this admits of question.

The words *anti-neuric, aneuric, neuro-leptic, neuro-lepsia, neuro-stasis*, seem too anatomical; whereas the change is a physiological one. I throw these out for consideration.

I would have a name pretty soon, and consult some accomplished scholar such as President Everett, or Dr. Bigelow, Sr., before fixing upon the terms which will be repeated by the tongues of every civilized race of mankind. You could mention these words which I suggest, for their consideration; but there may be others more appropriate and agreeable.

Yours respectfully,

O. W. Holmes