

Update

Fall 2017

President's Column: AUA Strategic Planning Update



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The AUA Council developed the current AUA Strategic Plan in an October 2016 planning session. The Council developed several goals as a priority for the Association:

1. Institute succession planning in the AUA leadership structure to achieve more organizational continuity.
2. Increase coordination among the Council, Educational Advisory Board (EAB) and Scientific Advisory Board (SAB).
3. Review the format, structure, and content of the Annual Meeting and make improvements as indicated.
4. Review criteria for AUA membership and make any changes deemed warranted.
5. Increase the participation of AUA members in the activities of the Association.
6. Increase opportunities for junior academic anesthesiologists, fellows and residents interested in careers in academia to become involved in the Association.
7. Increase AUA's visibility and improve its image in the academic and scientific community.
8. Conduct advocacy activities on behalf of academic anesthesiology.

Since that time, the AUA Council, Committees, and staff have engaged in efforts to achieve the objectives underlying the plan goals.

During the October 2017 AUA Council Meeting, Council President, Dr. Jeanine Wiener-Kronish reported on the successful alignment of the AUA and International Anesthesia Research

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Society (IARS) meetings. Dr. Wiener-Kronish reported that the attendance was very high for both meetings and the presentations were exceptional. Records indicate that in 2017, 135 attendees of the AUA Annual Meeting also attended the IARS Annual Meeting. In 2016, 136 attendees attended both the AUA and IARS Annual Meetings. In 2015, 44 attendees went to both the AUA and IARS Annual Meetings. The alignment of the AUA and IARS meetings is an important strategy to increase the participation of AUA members in Association activities and increase opportunities for early-stage academic anesthesiologists to advance their careers and receive exposure to AUA and its activities.

In 2015, the Active Members voted to add a new AUA membership category, Associate Member, to create an opportunity for individuals earlier in their careers to be involved in the AUA, and provide a transition path to Active Member for those early-career individuals upon meeting the requirements of Active membership. Associate Members receive the same benefits as Active Members except voting rights. AUA was pleased to welcome more than 20 new Associate Members since December 2016. At the October 2017 AUA Council Meeting, Dr. Wiener-Kronish reported that AUA membership and meeting participation has expanded substantially through the inclusion of Associate Members, young faculty with funding (including T32, FAER or institutional grants) and increased numbers of international members. As of the October 2017 meeting, there were a total of 75 Associate Members.

The AUA Council will continue to evaluate and consider the goals and objectives outlined the Strategic Plan to ensure that the work outlined is aligned with the mission of the AUA of advancement of the Art & Science of Anesthesiology by the encouragement of its members to pursue original investigations in the clinic and in the laboratory; through the development of the method of teaching (anesthesia) and provide a forum for free and informal interchange of ideas.

Visit www.auahq.org for more information.

A Tale of Many Cities: Hurricanes Katrina, Harvey and Irma

Hurricane Katrina: Recollections of a Program Director



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Hurricane Katrina struck New Orleans on Aug 29, 2005, and with it followed a national disaster of unprecedented proportion. Eighty percent of Orleans Parish flooded and 1500 people lost their lives. Graduate Medical Education in the New Orleans area was heavily impacted. At Ochsner Clinic Foundation, we were able to meet our commitments to anesthesiology residency education without skipping a beat. Our program became even more robust in the aftermath of the hurricane and flood.

There were several factors that accounted for our success. First, our institutional graduate medical education department was strong; disaster processes and communication plans were already in place. Redundancy in water and power supplies at the hospital allowed us to continue to operate even after the infrastructure of the city was destroyed. Campus ground security was visibly maintained, including a substantial National Guard presence. Operating room activities never ceased, although case volume was literally decimated for several weeks. Anesthesia Team A (2 staff and 2 residents) officially provided coverage for about 10 days although energetic volunteers appeared on campus within 48 hours. The Program Director was on site during the hurricane and the immediate aftermath. Team B carried on for another 10 days. During that time, the formality of the training environment was relaxed until everyone was allowed to return to campus about 3 weeks later. For instance, dress was more relaxed because AC was not available in most areas of the hospital for 11 days. Games, “movie nights” and other fun activities were permitted in the Anesthesia Study Area to enhance morale. Impromptu barbecues were held in the parking lot while hospital food services were heavily taxed. Fortunately, the ACGME communicated that training programs would be allowed 5 weeks of interruption of usual processes; we made absolutely sure that everyone knew that it was “training as usual” by the end of those 5 weeks.

Virtually all anesthesiology staff returned to campus to resume work. All scheduled conferences resumed within 5 weeks. We immediately hosted a Journal Club in one of the local restaurants that remained open. Although operative volumes were down, we made sure that all residents were assigned cases daily. Interestingly, there was greater acuity and variety of cases as time went on because we were for many months one of the two hospitals, among over 20 area hospitals, that remained continuously operational. In fact, we had sufficient case volume to accept 3 residents as transfers from area hospitals that were closed. Only one resident chose to transfer from our program.

Recruitment in the subsequent few years was afforded special attention. A special Power Point presentation was created emphasizing our status as a continuously operating hospital and that we actually took on several additional transfers in the aftermath of Katrina. We emphasized the many unique features of our famous city. A special “Meet and Greet” session was initiated by the residents who weathered the storm in place. For this event, all residents and the recruits attended an informal “wine and cheese” session at a resident’s home. It allowed recruits to meet current residents who remained very enthusiastic about their training experience and assured recruits of the sustained quality of their experience. This event proceeded the recruitment dinners traditionally attended by a small group of residents.

Probably the most significant feature that allowed us to continue our appeal as a training program was the ability to maintain the organization of the training environment. Significantly, in early months after the storm, institutional leadership convened all physician staff to debrief after the disaster and to provide a vision for the future. The community was stabilized by the Ochsner Clinic Foundation taking ownership of many of the closed area hospitals. A new health system was born and with it an even greater residency training enterprise.

Hurricane Harvey: Crisis and Compassion at the Department of Anesthesiology at UTHealth



Elise H. Sullivan, MD



Sam D. Gumbert, MD



Holger K. Eltzschig, MD, PhD



William H. Daily, MD

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Figure 1: Severe flooding of the Texas Medical Center, with water levels surpassing a major bridge and overflowing adjacent streets. Photo courtesy of Raphael Keegan, August 27, 2017.



Figure 2: Further images of severe flooding. Photo courtesy of UTHealth.

In an era of modern medicine where much is anticipated, trialed, and tested, there is a solemn and earnest call to charge felt when a community is thrust into unpredictable circumstances. Recent years have seen many such public emergencies, from natural disasters to crises of violence. The role of anesthesiologists in trying times has become an important field of research and process improvement^{1,2} that should be discussed internally in whatever manner deemed best by each institution. As much as can be learned from issues that arise during these demanding times, there is merit to celebrating the successes also met therein. Here, we are sharing our experience during Hurricane Harvey, a disaster which ravaged the communities in and around Houston, Texas.

Hurricane Harvey was a Category 4 hurricane that made landfall in Texas on August 25, 2017. Harvey's flooding has caused one of the most financially devastating and widespread weather disasters in United States history, with 70 percent of

Houston and areas of southeast Texas flooded by more than 1.5 feet of water. Wind speeds reached up to 130 miles per hour and the flooding totaled an estimated 27 trillion gallons of water.³ Our affected communities were stricken with estimated 90 deaths, over 1,000 rescue evacuations from homes and businesses, and conservative estimates of \$70-90 billion of damage.^{4,5,7} The public health and immediate medical care implications, coupled with physical citywide inaccessibility, created a state of emergency that none of us will soon forget. Our Department of Anesthesiology at the University of Texas McGovern Medical School provided care at Harris Health's Lyndon B. Johnson Hospital (LBJ) and Memorial Hermann-Texas Medical Center before, during, and after the hurricane.

Although Hurricane Harvey was of a magnitude previously unseen to Houston, Memorial Hermann-TMC and LBJ Hospitals did have the advantage of experience. In June 2001, Tropical Storm Allison struck with 43 mile per hour winds and widespread rainfall that peaked at 40 inches. It resulted in 41 deaths, an estimated \$5 billion damage, and left a devastating impact on Houston's Texas Medical Center.⁶ Although this storm was in some ways less consequential than Hurricane Harvey, it did cause extensive flooding at the medical center and exposed substantial weaknesses that had left our hospitals vulnerable. Most notably, all power generators - including emergency back-up generators - were at that time located on the basement level of the hospital. All power was lost. Every ventilator, phone, monitor, and computer became unusable for clinical care. Groups of individuals were assigned the task of relaying messages from floor to floor. All critically ill patients were manually ventilated for hours. Hundreds of patients were evacuated from the medical center, many patients requiring teams to physically carry them through stairwells to safety. Thus, many of the vulnerabilities susceptible to unexpected flooding had been remediated through prior tribulation. This experience also brought to the forefront the importance of communication through crisis - a valuable resource that was taken away with the loss of power.

Prior to Harvey's landfall, senior members of the Department of Anesthesiology were in close consultation with Harris Health and Memorial Hermann-TMC. Each hospital established a 24-hour command center. A comprehensive disaster plan was devised, focusing on staffing, safe access to hospitals, and availability of resources. Hospital personnel were grouped into duplicate Ride Out teams alternating in 12-hour shifts to ensure continuity of patient care. In the Department of Anesthesiology, faculty and resident teams were informed to be prepared with food and clothing to sustain 24-36 hour shifts. The relief shifts would arrive as conditions allowed. A previously developed departmental phone tree was distributed at Memorial Hermann-TMC to ensure clear lines of communication among members of the Department of Anesthesiology with other perioperative service lines. Communication and strategic planning were maintained amongst hospital and University leadership in the days prior to Harvey's landfall.

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Figure 3: One of our Memorial Hermann-TMC anesthesiology teams, still smiling after 48 hours of service. Photo courtesy of Daniel Shoham, August 27, 2017.

August 25th arrived with moderate wind and heavy rain. On Saturday morning, roads were largely passable and hospital operations were unaffected. Late Saturday afternoon, conditions rapidly deteriorated when the rate of rainfall exceeded citywide drainage capacity. Widespread flooding gripped the Houston metroplex, making travel impossible (Figures 1 and 2⁷). As the storm intensified, Houston and its surrounding communities received up to 56 inches of rain. Over 20 inches of rain fell in an area greater than the size of West Virginia, and over 40 inches of rain struck an area the size of Delaware.⁸ Faculty, residents, and staff worked throughout the night.

On Sunday morning, despite substantial flooding, several faculty, residents and anesthesia assistants (CAA) braved the elements to get to Memorial Hermann-TMC. These members of our department overcame great obstacles to serve patients in need and give respite to hard-working colleagues. One faculty anesthesiologist walked three miles through thigh-high floodwaters, while another CAA walked two miles through the storm to help relieve the anesthesia Ride Out team. On the north side of Houston, LBJ hospital and those who staffed it found themselves in an even more difficult situation. As the water rose, LBJ became an island and was utterly inaccessible for nearly three days. Like the extraordinary efforts of anesthesia team members at Memorial Hermann-TMC, one nurse anesthetist (CRNA) rode his bicycle until the water was too deep, at which point he flagged down a boat maneuvering the flooded streets and was able to reach LBJ. Eventually, Harris Health officials utilized high water vehicles and fire trucks to transport relief personnel from the Texas Medical Center. Some of those relieved had given 64 hours of service. The efforts of these incredible individuals ensured that the citizens of Houston were cared for and operating rooms were functional during the emergency state of Harvey (Figure 3).

During those grueling hours trapped at LBJ, our team faced many challenges. The most salient of these was the case of a

patient who presented emergently with subdural hematoma status post ATV collision, requiring emergency craniotomy for neurosurgical decompression. LBJ is a Level III trauma center that provides comprehensive surgical care, but it does not have a neurosurgical service. It is not staffed by neurosurgeons and does not stock the standard equipment necessary for craniotomies. Since the austere weather precluded transport by land or by air, Dr. Erik Askenasy, a colorectal general surgeon, was the only surgeon available to intervene. A detailed conversation was held with the patient's family and the decision was made to operate, the patient altered and declining.⁹ With neither standard staffing, nor supply, faculty anesthesiologist Dr. Vladimir Melnikov prepared for LBJ's first ever craniotomy. His close anesthetic care helped to keep this patient alive through these extraordinary circumstances. When wind and rain cleared enough for adequate visibility, the patient was post-operatively transported via lifeflight to Memorial Hermann-TMC for continued care.¹⁰

Through tumult and tribulation, the esprit de corps of the Department of Anesthesiology at UTHealth was truly remarkable. The days after Harvey were filled with active outreach and communication amongst department members to evaluate personal safety and home damage. Post-emergency scheduling was created with consideration given to those affected by the storm and to those who staffed the hospitals during the state of emergency. Calls and shifts were covered because of the selfless efforts of our team members.

Outside of the added in-hospital coverage, faculty and residents volunteered at the George R. Brown Convention Center to assist those in the shelters. Department members opened their homes to each other and to people in shelters, as well as donating and distributing food, water, clothing, and diapers to those in need. One faculty, a member of the National Guard, was called upon to assist bravely in helicopter rescue missions in Beaumont, Texas.

Unfortunately, several of our own department members lost their homes, possessions, and automobiles. It is estimated that the damages suffered by our departmental members exceeded \$3 million. An effort was initiated to raise funds for those affected within our department. Within one week, we raised almost \$32,000 of support for those affected by the storm. One resident did not accept the department's contribution as she felt there were others who needed it more. The generosity and camaraderie within the department was not limited to financial aid – we supported each other in any way we could. For example, following notification of one faculty's flooded house, departmental members quickly arrived with crowbars, hammers, and saws to begin the work of pulling up water-damaged flooring and drywall.

The outreach also extended from beyond our city. The Texas Society of Anesthesiologists offered to refund members their registration fee if they were unable to attend the annual meeting on September 7, 2017. With incredible empathy towards the financial struggles in which some of our members found themselves, The Anesthesia Foundation offered 0% interest loans to any residents impacted by the hurricane.

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Finally, UTHealth provided assistance to those dealing with the emotional trauma of the storm.

The devastation caused by Harvey was immense, but out of this disaster an outpouring of kindness, bravery, and community was realized. Private individuals in boats and canoes set out to rescue anyone trapped by high water. A sense of appreciation and togetherness was demonstrated in the cafeteria at Memorial Hermann-TMC as administrators served complimentary food to all who staffed the hospitals during this trying time. All the while, the call to action for our patients and for each other drove uninterrupted care and coordinated efforts to support impacted faculty and staff. Hurricane Harvey was an unprecedented event which will remain in our memories for many years to come and from which recovery will take decades. As a department, we are both proud of and strengthened by the preparation, communication, and teamwork that all members of our department displayed in order to continue our compassionate care. Our experience with Hurricane Harvey proved once again the vital role of the anesthesiologist in states of emergency, not only to the safe outcomes of patients and communities in need, but also to the well-being of one another.

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Hurricane Irma



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The weather on September 5th in Tampa, Florida was a typical sunny day when news of a Category 5 hurricane out in the Atlantic ocean broke. Having not seen a major hurricane in the area since 1921, (when a category 3 storm brought winds over 140 mph and 10-12ft storm surge) everyone

believed that there was nothing to be concerned about and went about their day. The storm was being watched as it was unprecedented that a Category 5 hurricane out in the Atlantic would continue to remain as such for over 3 days. Of all the models out there, everyone one of them showed that the storm would miss the West coast of Florida save one, the European model. We watched with trepidation as the storm came through the Caribbean and followed the path of the European model predicting that the storm would indeed come up the west coast of Florida.

With the storm now predicted to come up the west coast, people started to panic. Gas was in short supply, water in most stores were bought up within a few hours after being delivered. Houses were being boarded up in preparation for one of the most devastating storms predicted to hit us.

Johns Hopkins All Children's hospital started to gear up with plans to deal with the patients already in house and potential patients we may receive from outlying facilities as soon as they could be transported after the storm.

The Anesthesia department held meetings to determine what the best strategy would be to weather the storm. The new building built in 2009 is able to withstand a Category 5 storm such as the one that was predicted to hit us so everyone knew that there was adequate shelter. The generator could provide us with power for up to two weeks if need be. The most pressing concern was how many providers would be required to stay? For how long? Who would come to relieve them and when? Where would they sleep?

On a typical weekend call day we usually have three anesthesiologists on call. One general, one cardiac and one back up. We anticipated that the work load during the actual storm would probably not be significant since our surgeons would not operate unless absolutely necessary. The individuals that were on call on the day the hospital was going on lock down were the people assigned and classified as Team A. We also opened up the doors for Team A's families if they so chose. This would allow our people to focus on their patients and not have to worry about the safety of their loved ones. The individuals that were on call on the day the lock down was supposed to end were classified as team B. They were responsible for relieving Team A once the

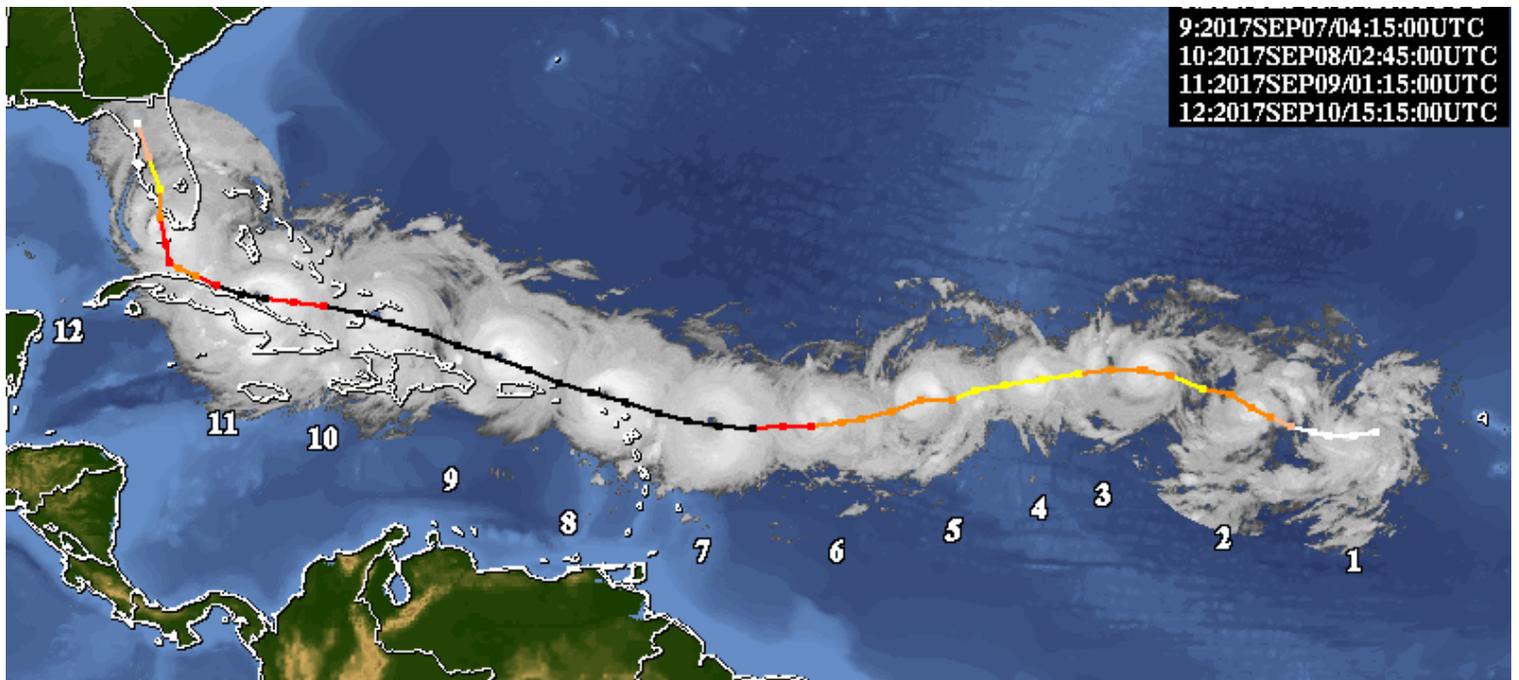
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NASA's land Sat-8 satellite images, before and after Irma.



Satellite montage of Irma using GOES IR images and NHC advisories. Courtesy of UW CIMMS.

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roads opened. This created the dilemma of where should Team B go and what about their families? As a group we made a decision to also allow team B to stay in house if they had nowhere safe to go and asked other personnel not assigned to try to make it back to the hospital as soon as they could. This is so that the personnel already in house could be relieved, and in anticipation of a significant volume of transfers and trauma after the storm once the roads and airspaces opened up.

Bracing for the storm the hospital went on lock down on 7 am September 9. Only 2-3 cases were done during the lockdown. The reminder of the time was spent entertaining oneself and watching the news wondering how the hospital would fare. As

Irma barreled down the west coast of Florida, it made a last-minute turn which resulted in Tampa experiencing hurricane category 1 winds as opposed to a category 5 storm. The lockdown ended without incident and without significant storm surge and damage. Team B was able to get in without incident.

This storm taught us that enough time should be given for families to prepare and evacuate. Enough space needs to be secured for the families of the staff that are slotted to stay if they cannot evacuate. Systems need to be in place if the electronics fail, and more than one team should try to get back to help as soon as the roads open and the lockdown ends.

From AUA, eSAS, FAER, IARS and SOCCA: An Exciting Collaborative Research Initiative for Anesthesiology Clinical and Translational Science: a Call for Letters of Intent



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Introduction

We are pleased to inform you about an important new collaborative approach to Anesthesiology clinical and translational research. For several years, colleagues in Europe, Australasia

and Canada have successfully conducted multicenter clinical trials in Anesthesiology, including perioperative medicine, pain management, peri-partum care, and perioperative critical care. These studies have enabled our field to address questions that are important to Anesthesiology and society, and have greatly advanced the quality of care we provide on a daily basis. Currently, no such clinical trials network exists in the United States. To remedy this, a consortium of academic anesthesiology organizations has launched an initiative. This effort has been conceptualized and endorsed by organizations, which have as a common goal the advancement of knowledge in Anesthesiology and the enhancement of care in perioperative medicine, critical care, pain management, and peri- and post-partum care. These organizations include the Association of University Anesthesiologists (AUA), Early Stage Anesthesiology Scholars (eSAS), Foundation for Anesthesia Education and Research (FAER), International Anesthesia Research Society (IARS), and Society of Critical Care Anesthesiologists (SOCCA). We have consulted with several program officers representing NIH institutes, and they have unanimously expressed enthusiasm regarding the process we have conceptualized. The proposed clinical trials network could naturally collaborate with other existing international networks.

The Process of Grant Selection

In order to launch this process, and to establish a proactive and dynamic agenda, we are embarking on a program to solicit, select, and refine clinical research proposals that will have a high probability of receiving support from the National Institutes of Health or another funding agency. We are therefore extending an invitation to investigators to submit letters of intent for pragmatic clinical trials in perioperative medicine. The trials could focus on any or all of the following areas: preoperative care/optimization, operating room management, postoperative management, perioperative critical care, peri- and post-partum care, and pain management. Outcomes should be clinically relevant and important to society. Letters of intent should no more than 2 pages in length, with 1 page being the Specific

Aims Page. They should be single spaced, minimum of size 11 font (Arial or Times New Roman) with minimum borders of 0.5 inches.

- 1) Please send your letters of intent as Microsoft® Word or PDF documents to Vivian Abalama, CAE (vabalama@iars.org) up to the deadline of December 31, 2017.
- 2) A study section has been established for this process, comprising representatives of the following organizations: AUA, eSAS, FAER, IARS, and SOCCA. Members of the study section will review the letters of intent, triage the proposals, and, on January 15, 2018, solicit expanded research proposals (specific aims page and 5 pages for research plan) from a subset of meritorious LOI submissions.
- 3) Expanded research proposals must be received by March 15, 2018.
- 4) The three selected grants will be announced on April 15, 2018.

The Process of Peer Feedback

On May 1 2018, following the AUA, SOCCA and IARS meetings, there will be a symposium in Chicago to launch this exciting initiative. This meeting will be advertised and will be open to those interested in anesthesiology-related clinical and translational science. The IARS has kindly offered to provide meeting space and information technology support for this event. The principal investigator or another representative of each of the three winning proposals will present their grants to peers, who will provide constructive feedback and suggestions. This will be a structured process in the form of a “Science Garage” or “Grant Boot Camp” and will serve two important functions. First, it will inform the community about the trials, and allow colleagues to become energized about the studies and sign up their sites for participation. Second, it will help to harness the collective intellectual expertise of members of the perioperative research community in order to refine and enhance the grant applications. Apart from the “Science Garage,” there will be input from an NIH representative on the importance of this initiative and of the potential to work closely with NIH institutes in advancing this exciting agenda. Representatives of FAER and the IARS will present how such initiatives could provide opportunity to early stage Anesthesiology scholars, wishing to pursue clinical and translational research paths. Finally, organizations that could serve as data coordinating centers and provide other “core” support to clinical trials (e.g., Duke Clinical Research Institute [DCRI], Multicenter Perioperative Outcomes Group [MPOG]) would be invited to make brief presentations outlining how they could provide support to the perioperative clinical trials group and provide discussion of resources (and estimation of costs) available to assist in trial conduct.

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An Exciting Collaborative Research Initiative

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The Process of Grant Refinement

The Association of University Anesthesiologists (AUA) has generously earmarked \$45,000 to provide seed funding to the three chosen grants (\$15,000 each) so that the grants can be refined, strengthened and streamlined prior to submission to an NIH institute or another appropriate funding agency (e.g., PCORI). These funds can be used to obtain statistical analysis review, preliminary data, grant writing support, or fill any specific need identified by the proposal PI. It has been clearly recognized that steps must be taken to ensure that this venture serves as a unifying force in our field, and supports academic Anesthesiology across the United States, as well as other countries. As such, participation in this endeavor does not require that principal or co-investigators must hail from specific institutions or that their trial will utilize any specific existing infrastructure. However, by participating in and conducting their research through one or several established network/s or institute/s, investigators will have access to additional expertise and resources, which will prove a massive boost to any clinical trial. Indeed a major emphasis for the NIH is that clinical research should be conducted efficiently, and utilizing existing reliable infrastructures and registries is viewed as a priority. Clinical Trial Support Units (CTSUs, CTCs, CTSCs, CRSUs, CRUs, CTUs, CTIUs, CTSIs, CRTUs) have been established at multiple academic centers and in the private sector, and conceptually allow investigators to focus on the science instead of the administrative tasks when conducting clinical trials. Brief information is provided below on the DCRI and MPOG. More information on these can be obtained from their websites, and information on other trial support mechanisms can often be obtained from research offices at academic institutions. It is our hope that at least one (if not all) of the three selected grants will be successful in garnering federal (or equivalent) funding.

Duke Clinical Research Institute (DCRI)

The inception of the DCRI dates from 1969 and the formation of the Duke Databank for Cardiovascular Disease, from this humble beginning, the DCRI has grown to be the world's largest academic research organization. The DCRI's mission is to develop and share knowledge that improves the care of patients around the world through innovative clinical research. The DCRI has a rich history of clinical trial experience and success, with completion of over 1,000 phase I-IV clinical trials, outcomes, comparative effectiveness, and implementation studies. These studies have enrolled over 1.2 million patients in 37,000 distinct sites. DCRI's faculty includes scientists, statisticians, and practicing physicians who see patients each day. Together with the DCRI's experienced and knowledgeable operations teams, clinical trial investigators can design and implement innovative clinical trials grounded in the realities of patient care. The DCRI expands the impact of clinical research beyond regulatory approval by designing trials that advance our fundamental understanding of health and disease and inform efforts to improve the quality of care.

The DCRI's faculty and operational team's passion is setting new standards for clinical innovation that changes the way healthcare is delivered.

Every day, the DCRI works to address the challenges faced by patients, physicians, government agencies, and research sponsors. The DCRI achieves this by changing the way clinical trials are conducted, by putting knowledge into practice, and by designing educational programs that inspire and prepare the next generation of clinical researchers. Everything the DCRI does is based on collaboration. The DCRI researchers and operational teams work closely with each other and with peers and partners around the world. As an academic research organization associated with the Duke University School of Medicine, the DCRI is able to challenge conventional approaches and explore innovative ways to accelerate the translation of scientific discovery into better care for patients everywhere. What makes the DCRI unique from other clinical research organizations is that it is a non-profit research organization, focused solely on creating and implementing new knowledge in perioperative care and other disciplines. This includes a long history of successful large perioperative trial work.

The DCRI offers the following specific services to investigators:

- Full integration and close collaborations among diverse trial primary investigators at many sites and clinical trial operational leaders/coordinators
- Scalable and Fit-for-purpose trial design support and operations
- Collaborative approach to academic leadership
- Mature North American site investigator networks that can be leveraged for high-quality enrollment
- Streamlined data collection (including EMR based data collection) and adverse event reporting
- Focused, risk-based monitoring and predictive modeling to minimize costs of trial conduct
- Emphasis on study drug/procedure compliance and complete follow-up
- Shared endpoint adjudication activities
- Long-standing clinical research education and fellowship opportunities to train the next generation of perioperative clinician-scientists
- DCRI commitment to cover upfront costs of clinical trial submission and planning by providing expert grant-writing assistance, budget creation, study manual of operation creation, site contracting and study material generation for the perioperative trial network

A key feature of the DCRI resource is that a clinical trial or trials network can use as much or as little of DCRI's many components as is needed. This can truly be tailored to an individual study or network's needs. This can include utilization of only data management, only clinical coordinating center resources, statistics, regulatory, or any other key trial support functions alone or in combination as needed. The

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An Exciting Collaborative Research Initiative

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DCRI has a rich experience in coordinating research networks such as the Perioperative Clinical and Translational Science Initiative described in this call for proposals. This includes a history of coordination of 34 distinct networks including the > 110 million patient record PCORnet, The NIH Health Care Systems Research Collaboratory, The Federally Funded Pediatrics Trial Network, and The NIH CTSA Trials Innovation Network.

The DCRI has recognized that there is a strong need to enhance perioperative clinical and translational research in the U.S. and around the world. For this reason, the DCRI recently recruited a Professor of Anesthesiology, Dr. Paul Wischmeyer, to be its Director of Perioperative Research. Dr. Wischmeyer is a highly accomplished clinical and translational researcher, and can be contacted by e-mail at: paul.wischmeyer@duke.edu. More information on the DCRI can be found at www.dcri.org/about/who-we-are/ and www.dcri.org/our-approach/.

Multicenter Perioperative Outcomes Group (MPOG)

MPOG is a group of passionate individuals from more than 50 hospitals across 18 states and 2 countries, working together to improve care for patients undergoing surgery. MPOG has evolved organically as a labor of love within Anesthesiology, and is committed to advancing the field academically and to providing growth opportunities for future leaders in Anesthesiology. MPOG's members include clinicians, quality improvement experts, software developers, statisticians, researchers, and administrators. Over the last decade, MPOG has built a comprehensive perioperative patient registry based on electronic healthcare data to improve quality of care, conduct research, educate caregivers and guide healthcare administration. MPOG is a collaborative venture that was made possible by the transition in hospitals to electronic medical records. Collaborating institutions contribute electronic data to MPOG, which the MPOG administrative team checks, cleans, and homogenizes. MPOG's mission is to benefit Anesthesiology and society through the generation of knowledge obtained from this valuable data repository. MPOG has a rotating Executive Board, which includes its Executive Director, Research Director, its Quality Improvement Director and 9 elected chairs, representing Anesthesiology departments in the United States and Europe. MPOG has a track record of successful and high impact observational research in perioperative medicine.

To increase the clinical impact of the existing infrastructure, MPOG founded a quality improvement initiative known as ASPIRE (Anesthesiology Performance Improvement and Reporting Exchange) three years ago, with more than \$2M of external annual funding. ASPIRE sites work together to build quality measures, review best practices, exchange ideas on how to improve patient outcomes. ASPIRE delivers measure performance information to participating sites via the ASPIRE dashboard and regular, automated provider-specific feedback emails.

The logical next step for MPOG is the establishment of IMPACT (Initiative for Multicenter Perioperative Clinical Trials) as an arm that supports and empowers perioperative clinical and translational research. As a stepping-stone to prospective, pragmatic clinical trials, MPOG recently embarked on an enhanced observational study. Chosen through a competitive process, the University of Utah and University of Virginia led a study conducted across 12 US and European medical centers focused on the Acute-to-Chronic pain transition in patients undergoing major surgery. Over the span of just 2 weeks in September 2017, more than 1100 patients were enrolled, consented, and phenotyped using robust, peer-reviewed pain, mood, affect, and opioid use instruments. Follow up 1- and 3-month phone calls have begun. A robust configurable electronic case report form (eCRF) tool, center-specific patient enrollment dashboard, registry-eCRF linkage, and competitive grant administration process have all been created to enable prospective enhanced observational studies and pragmatic randomized controlled trials.

MPOG can be contacted by email: anes-mpog@med.umich.edu. More information on MPOG can be found at mpog.org/about/.

Conclusion

We look forward to receiving letters of intent from a diverse range of investigators with projects spanning the many areas of perioperative medicine, critical care, and pain management. If you have questions regarding this initiative, please write to Vivian Abalama (vabalama@iars.org), and she will direct your query to an appropriate person on the ad-hoc coordinating committee.

This article / call for letters of intent has been endorsed by representatives of the following organizations:

- Association of University Anesthesiologists (**AUA**)
- Early Stage Anesthesiology Scholars (**eSAS**)
- Foundation for Anesthesia Education and Research (**FAER**)
- International Anesthesia Research Society (**IARS**)
- Society of Critical Care Anesthesiologists (**SOCCA**)

SAB Report: Can Anesthesiologists Optimize Brain Waste Removal?



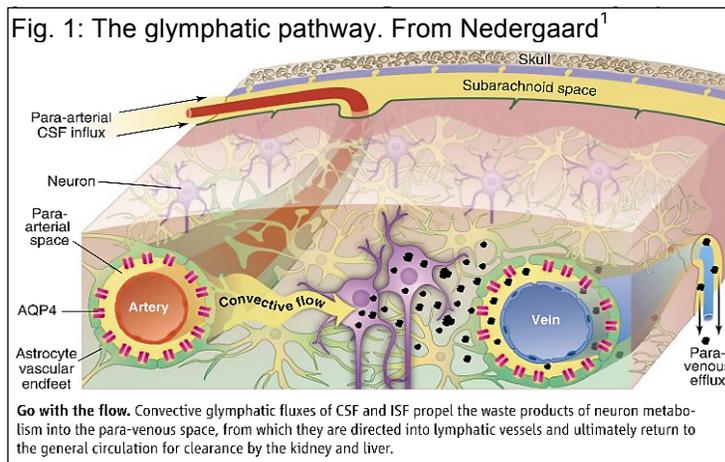
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In most of the body, the lymphatic system facilitates clearance of metabolic waste products and excess fluid. The brain parenchyma, however, is different. Devoid of authentic lymphatic vessels, the fundamental process by which waste generated in the brain is effectively removed has remained unclear. Recently, a previously underappreciated but unique component of the brain vasculature, the peri-vascular space, was discovered to function as the “front end” for a toxic waste clearance process now known as the “glymphatic pathway.”¹ At present, anatomy of the “glymphatic pathway” is complex and only partly understood. The outer perimeter is defined by glial endfeet with high expression of aquaporin 4 (AQP4) water channels that facilitate convectively-driven CSF movement into the interstitial fluid space (Fig. 1). Continuous propulsion of CSF from the peri-vascular space into the interstitial fluid (ISF) compartment helps drive soluble metabolic waste products including amyloid beta ($A\beta$) and tau peptides into peri-venous conduits for downstream removal.² Ultimately, peri-venous exit pathways for brain waste drain into authentic lymphatic vessels recently discovered in the meninges³ as well as lymphatic vessels along cranial nerves.

The main driving forces behind waste clearance via the glymphatic pathway include subtle intra-cranial pressure differentials (e.g. body position), vascular pulsatility, respiratory effort, glia endfeet AQP4 channel density and ISF volume. The link between ISF volume and brain waste removal, in particular, is very intriguing. Recent rodent studies have



shown that cortical ISF volume increases by 40% or more during slow wave sleep when compared to the awake state, and that the slow wave sleep state is associated with better brain waste clearance.⁴ Importantly, the sleep-induced enhancement of waste clearance can be mimicked by drugs that decrease arousal, in particular those that lower central norepinephrine tone.⁴ Several clinical research studies support the existence of a sleep-dependent CSF-ISF metabolic waste removal system in the human brain including: 1) circadian variation in the CSF concentration of $A\beta$ and tau;⁵ 2) increases in CSF $A\beta$ ⁶ with chronic sleep deprivation; and 3) an association between greater $A\beta$ burden and shorter sleep duration and poorer sleep quality in the elderly.⁷

Emergence of the glymphatic pathway has revived the scientific field of CSF fluid dynamics and is currently under intense investigation due to potentially wide-ranging physiological implications. Several clinical conditions are likely to disrupt glymphatic brain function including disease states that disturb intracranial pressure, conditions that damage the vascular system, and/or disorders that interfere with sleep mechanisms. Neurodegenerative diseases are of particular interest because they may arise, at least in part, as a consequence of glymphatic system dysfunction. Preclinical as well as translational clinical studies are now focusing on the role of the glymphatic pathway in development or progression of neurodegenerative diseases including stroke, brain injury, concussion and Alzheimer’s disease (AD). For AD in particular, recent data demonstrating a significant loss of peri-vascular expression of AQP4 channels in brain tissue obtained from AD patients represents a major step toward understanding the implications of glymphatic pathway function in pathogenesis of the disease.⁸

Because sleep is associated with improved brain waste clearance when compared to wakefulness, a common view has been that all drug-induced low arousal/sleep states will promote brain waste clearance.⁴ However, the basis for sleep-induced enhancement of glymphatic transport appears to be

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SAB Report: Can anesthesiologists optimize brain waste removal?

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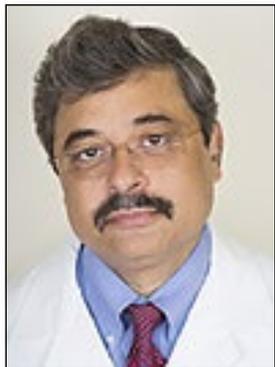
most closely linked to central norepinephrine tone/activity. In agreement with this concept, we recently showed that rats receiving dexmedetomidine (which blocks norepinephrine release from the locus coeruleus) in combination with low-dose isoflurane exhibit a 30% higher glymphatic transport function relative to rats receiving isoflurane alone.⁹ We were encouraged by this finding because in the clinical setting dexmedetomidine reduces other anesthetic agent requirements, and is used as an adjunct for sedation and for general anesthesia. One could speculate that dexmedetomidine or other drugs that reduce central norepinephrine signaling may have the added benefit of improving “brain waste removal” during anesthesia and surgery thereby enhancing brain health. In this context it is noteworthy that several clinical papers have advocated the use of dexmedetomidine prophylactically as a means to decrease the incidence of postoperative delirium¹⁰ possibly by improving perioperative sleep quality. While the underlying mechanism for this effect of dexmedetomidine remains unclear, ultimately enhanced brain waste removal may play a role.

Undoubtedly, upcoming research studies on the glymphatic pathway, sleep and its role in A β clearance from the human brain may in the future support targeting good sleep habits as a strategy for healthy brain aging and AD prevention. In addition, optimizing brain waste clearance in the peri-operative period might become a new therapeutic anesthesia objective for prevention of delirium and post-operative cognitive dysfunction.

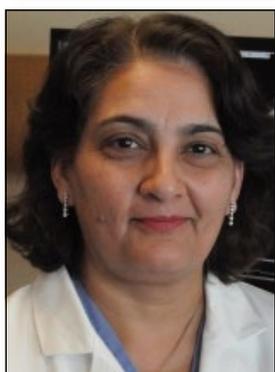
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EAB Report: Point of Care/Perioperative Ultrasound Training – Evidence of Outcome or Common Sense?



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In the last few years there has been an exponential growth in the clinical applications of perioperative ultrasound. These applications cross specialty lines and include the use of ultrasound as a diagnostic and monitoring tool and as a procedural adjunct. This is not the first time that a procedure/technique has established its clinical value prior to development of practice guidelines for clinical use. To address this dilemma, multiple specialties have taken on broad training initiatives and created guidelines for applications of ultrasound within their scope of practice. These efforts are not limited to defining the end points but also specifically delineate the pathways to achieve them. The level of expected knowledge, manual dexterity and proficiency for various training levels has been clearly established.¹⁻³ These organizations have chosen to raise basic proficiency at the grass roots level and establish readiness to perform rather than following a “top down” approach of creating certification without a clear pathway to achieve it.⁴

Specific to anesthesiologists, the perioperative uses of ultrasound are as a monitoring and diagnostic tool e.g. transthoracic (TTE) and transesophageal (TEE) echocardiography, abdominal and chest wall ultrasound, and as a procedural adjunct e.g. vascular access, regional anesthesia. Perioperative TEE was the first well-established use of perioperative ultrasound,^{5,6} followed by TTE, chest wall and abdominal ultrasound, vascular access and regional anesthesia. Of the above, there are well-established pathways for achieving certification status

only for TEE, TTE and abdominal and chest wall ultrasound after accredited fellowship training. Despite availability of these advanced pathways for establishing expertise, there is no general ultrasound education curriculum to prepare trainees for the aforementioned specific applications. Recognizing this knowledge gap, the American Board of Anesthesiology has increased the ultrasound related content in board certification examinations. Accredited training programs have responded by improving ultrasound education for residents.⁷ However, delineation of specific mandatory milestones in proficiency in perioperative ultrasound are lacking and there is a wide variation in the quality of ultrasound education during anesthesia training.⁸

Simultaneously, a large number of practicing anesthesiologists are faced with widespread adoption of a technology for which they were not specifically trained. Fiscal and logistic constraints make “on the job” training the only option available to enhance knowledge and proficiency. The current landscape of proficiency in perioperative ultrasound amongst practicing anesthesiologists ranges from advanced users to ultrasound-naïve faculty. The specialized applications are practiced in isolation with minimal crossover of skills. Due to lack of organized training efforts, ultrasound-naïve anesthesiologists are at risk of being excluded from this ultrasound revolution. The prevailing continuing medical education (CME) model is episodic, didactic and unsuitable to ensure en masse learning. Universal adoption and recognition of proficiency in ultrasound as a necessary skill set requires concerted efforts at multiple levels. Individual practitioners must recognize this training gap and be motivated to enhance their technical skills. Anesthesia departments should facilitate provision of meaningful training opportunities and create mechanisms to ensure continued clinical use of ultrasound technology by faculty to maintain skills once established.

This variation in proficiency in ultrasound is not without consequences. The quality of clinical care is impacted and the experience of trainees is unpredictable due to differences in proficiency level of supervising faculty. Other specialties have dealt with challenges of technology introduction with initiation of “practice pathways.” For example, emergency medicine has established a very well defined pathway to achieve competency in ultrasound use for qualified practitioners.² Various focused ultrasound education courses are available for practicing anesthesiologists as well. However, in addition to the time commitment and subspecialty focus, attendance of such courses is associated with fiscal and logistic hardship. A well-structured educational program for faculty should be multi-modal in content delivery, integrative with practice and repetitive to minimize attrition. To be sustainable, it has to be a value-added proposition to the individual (CME credits, improved skills), the department (improved education) and patients (enhanced quality of care). There should be pre-defined endpoints, ability

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to track progression of skills and built-in quality assurance and improvement metrics.

Universal adoption of similar programs would help in recognition of proficiency in ultrasound as an ubiquitous skillset for anesthesiologists and establish anesthesiologists as the experts in perioperative ultrasound. The “top down” approach of education that is only aimed at setting certification standards and criteria to establish expertise is an unsatisfactory option for achieving this goal.⁴ On the contrary, the desirable program should take a “bottom up” approach that is geared to imparting basic proficiency and establishing readiness for clinical use and not expertise.⁴ Establishing a broad proficiency will possibly obviate the need for establishing a specific certification for proficiency in clinical use of perioperative ultrasound.

The use of ultrasound has contributed to improvements in quality and value, specifically in regard to procedural safety, timeliness of care, diagnostic accuracy, and cost reduction. In the current era of technological advancements, ultrasound fulfills the concept of “staged imaging” where its use can first answer important clinical questions accurately and expeditiously without the expense, time or side effects of advanced imaging or invasive procedures. Whereas advanced clinical use will require specialized training, a basic level of understanding can and should be imparted to all anesthesiologists. An analogy can be drawn between the expectation of basic interpretation of electrocardiograms and chest radiographs by all clinicians and advanced level interpretation requiring expert training and certification. Handheld ultrasound systems are being introduced into medical school curricula as the modern stethoscope. It may be difficult to demonstrate improvement in patient outcome as a metric of success with widespread adoption of perioperative ultrasound. However, it is implied logic that performing an invasive procedure under direct vision rather than blindly should be safer.

Anesthesiologists have been at the forefront of innovations in patient safety. The 10-fold reduction in anesthesia-related mortality over the decades have been attributed to adoption of clinical practices and technologies over time that incrementally enhanced patient safety. This was also based on inferential implied logic and common sense rather than rigid controlled trials of outcome benefit. We believe incorporation of ultrasound into our daily practice qualifies as a similar patient safety initiative. It would be unjust to subject this obvious safety practice to the litmus test of a randomized, controlled trial.⁹⁻¹⁰ This recognition will most likely improve outcome and prevent a large number of anesthesiologists from becoming disenfranchised. Our desire as a specialty for adoption of perioperative ultrasound as an ubiquitous skill set is both a challenge and an opportunity. To keep pace with the technology is a challenge and introduction of innovations in education and training is a real opportunity. If we wait for randomized trials to give us the evidence for universal adoption we may miss the bus; let us have common sense prevail.

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The Renin Angiotensin System and the Brain: New Developments



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The classic renin-angiotensin system (RAS) is described as a process of renin splitting inactive angiotensinogen to angiotensin-1 (Ang-1). Angiotensin -1 is then converted by angiotensin -1 converting enzyme (ACE) to angiotensin II (Ang-II). The discovery of additional brain RAS components or alternate RAS such as angiotensin III (Ang-III), angiotensin IV (Ang-IV), and newly discovered member with seven amino acids Ang-(1-7), has enhanced our understanding of RAS functions in the brain.¹

Ang-IV effects occur via the AT₄ receptor, which is widely distributed in the brain like in neocortex, cerebellum, anterior pituitary, and many more brain areas. The AT₄ receptor has been recognized as Insulin Regulator Aminopeptidase (IRAP). IRAP is a member of the M1 family metallopeptidases that also contains aminopeptidases. IARP splits the N-terminal amino acid from peptides such as vasopressin, oxytocin, somatostatin, eNOS and many others. IRAP also inhibits intracellular insulin-responsive glucose transporter 4 (GLUT4) in the pyramidal cell of the hippocampus and cerebral cortex. Ang IV is a natural inhibitor to IARP. Therefore, Ang IV helps to improve the brain glucose uptake and the availability of peptides essential to memory and cognition like oxytocin and vasopressin. In addition, it enhances the availability of eNOS which is essential for the brain blood flow.^{2,3,4} Of note, exenatide the glucagon-like peptide -1 receptor (GLP-1 R) agonist that increases glucose-level-dependent insulin secretion has shown to improve the motor and cognitive functions in Parkinson's disease patients. Exenatide enhances insulin in the brain therefore it inhibits IRAP.⁵ In addition, the use of liraglutide another GLP-1 R agonist in non-diabetic patients with mood disorders has improved their cognitive functions.⁶ Angiotensin converting enzyme inhibitors (ACEIs) such as captopril or perindopril that are capable of crossing the blood-brain barrier decreased the occurrence of Alzheimer's disease. Moreover, it enhanced memory function in patients with mild-to-moderate Alzheimer's disease. Secondary analysis of data from the Systolic Hypertension in Europe (SYST-EUR) trial⁷ with enalapril and the Perindopril Protection Against Stroke Study (PROGRESS) trial⁸ showed that use of ACEIs reduced dementia and cognitive decline. Of note, candesartan angiotensin II receptor 1 (ATR1) antagonist diminished the incidence of non-fatal stroke. In addition, it showed trend towards improved cognitive function.⁹

Amenta et al,¹⁰ in a review of clinical trials that examined the outcomes of hypertensive medications on cognitive

functions, concluded that the use of ACEIs resulted in improved cognitive function and a reduction in the vascular dementia following hemorrhagic or ischemic cerebrovascular events. The harmful effects of the classic RAS in the brain like hypertension, inflammation, increased oxidative stress, blood brain barrier disruption and neurotoxicity are mainly produced by the actions of AngII via ATR1. In contrast stimulation of ATR2 by AngII, Ang-III or Ang-(1-7) results in enhancing the repair of damaged DNA, nitric oxide (NO) production and brain development. It was therefore unsurprising the ATR1 blocker (ARB) valsartan protected against ischemic brain injury after middle cerebral artery occlusion in mice given non-hypotensive doses of valsartan.¹¹ The treatment of patients with Parkinson's disease using the ACEI perindopril has improved their motor responses to the dopaminergic precursor 3,4-dihydroxy-L-phenylalanine.¹² The harmful effects of Ang-II and AT1 in dopaminergic neurons are usually balanced by anti-inflammatory, neuroprotective and anti-oxidative functions of ATR2. Therefore, in aged rats a reduction of ATR2 expression promotes inflammation and increased incidence of Parkinson's disease. Angiotensin converting enzyme -2 (ACE2) converts the octapeptide Ang-II into the heptapeptide angiotensin - (1-7) [Ang-(1-7)]. Ang-(1-7) exerts its effects mainly via Mas receptors and lesser extent via ATR2. Those effects include learning, memory, and neuroprotection. The action of Ang-(1-7) via Mas receptors augments NO production through neuronal NOS (nNOS) activation in the brain. The production of neuronal NO is considered an essential step for object recognition memory and long-term potentiation (LTP) in the hippocampus and amygdala. Ang-(1-7) could have a neuroprotective effect by enhancing the production of both nNOS and eNOS while it reduces the production of inducible of NOS (iNOS). Moreover, the antioxidant effects of the ACE2/Ang-(1-7) and Mas axis help maintaining normal endothelial function in cerebral vessels. The ACE2 and Ang-(1-7) axes have been identified in human retina glial cells.¹ The administration of Ang-(1-7) in the vitreous decreases the intraocular pressure in rabbits. Furthermore, the administration of ACE2 genes intraocularly in diabetic rats protect against diabetic retinopathy. Ang-(1-7) plays a very critical role in maintaining baroreceptor reflex and normal blood pressure. Therefore, with aging brain tipping the balance in favor of Ang-II could result in hypertension and impaired autonomic control of cardiovascular system.

Advances in understanding the functions of the RAS in the brain have opened new venues for improving perioperative care. The prophylactic effect of RAS antagonists against stroke and Alzheimer's disease may help in our research against stroke and Alzheimer's disease, in addition it may help in our research for new neuroprotective agents in the perioperative period. But in the meantime, the use of RAS antagonists as cardiovascular and pulmonary therapeutic agents will continue to attract interest.

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The Renin Angiotensin System and the Brain: New Developments

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Why Did They Do That? The FDA and the Evolution of Drug Regulation in the U.S.



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The Food and Drug Administration is responsible for the safety of pharmaceuticals, cosmetics, medical devices, and our food supply. The Charter of the Agency says it best – “To Protect the Public Health.” In this essay, I hope to briefly review the evolution of the regulation of pharmaceutical compounds from 1840 until 2017. I will speak to congressional oversight, political pressures, lobbying efforts by the pharmaceutical industry and the Agency’s repeated efforts to eliminate clear bias from the analysis of new drug compounds.

Also, I would like to use the rather dramatic release of a MedWatch Warning in December 2016 relating to all general anesthetic agents and their use in children under age three as an example of the complexities of the drug regulation process.

Anesthesiologists should be aware of the activities of the FDA and consider how this federal agency affects the practice of medicine. During my professional life, the Agency has been called to question regarding the perioperative use of droperidol, the toxicity of general anesthetic agents, the use of benzodiazepines to sedate patients during medical procedures, the liabilities associated with widespread use of opioids, the use of steroid compounds in central and peripheral nerve blocks and the toxicities of local anesthetics. Recently the FDA considered the risks and benefits of sugammadex as an agent to reverse the effects of neuromuscular blocking agents for several years before allowing it to be released on the American Market to the consternation of the pharmaceutical industry and the anesthesiology community.

Pharmaceutical Regulation: Does the Benefit Outweigh the Risk?

Briefly stated, the process of bringing a drug to market is time-consuming, complicated and very expensive. Perhaps one compound in one hundred or more that begins the development process is subsequently found to be effective to treat a particular disease, and fewer still are found to be a substantial improvement over currently accepted therapy. Modern science has improved the likelihood that some drugs will make it through the development process by drastically increasing the number of molecules that are assessed. Molecular pharmacology, improved knowledge of cellular receptors, their chemistry and anatomy, and advances in our understanding of the basis of disease all play a role.

The American public has high expectations of government and particularly the FDA. Americans want safe drugs, they want effective drugs, and they want safe, effective treatments fast. Unfortunately, the requirements for efficacy are not tied inexorably to the safety of the compound that is being evaluated. Because safety does not necessarily follow from efficacy, this slows the drug evaluation process. (Many medications that are quite effective have been found to be unsafe after marketing. Think thalidomide!) It is because of this feature of the regulatory process that the authority of FDA has increased dramatically in the 20th and 21st centuries.

How can we know from the initial studies provided by the pharmaceutical industry that newly marketed medicines are indeed safe? The answer is that comprehensive analysis is impossible with premarketing studies alone. These studies relate to hundreds or thousands of patients, and in many cases, the drug will be distributed to millions of patients from populations never considered by the drug sponsor. Hence, post-marketing studies, though expensive and difficult to produce, are critical to the long-term public health.

The Balance of Safety and Efficacy

Consider the risk of opioids. There is an obvious public health problem associated with prescription analgesics in the U.S. in 2017. Thousands have died during the last fifteen years because of the risks related to the use of these medications. But opioids are our most effective analgesic and have relieved pain for millions of patients for hundreds if not thousands of years. Pharmaceutical science is exploring other options, but we are at least five years out from a reliable, safe, and effective analgesic that can be used widely. In the interim, how do we balance the overarching requirement for the safety of the public with the needs of patients to receive treatment for painful conditions in circumstances where opioids have been found to be efficacious? Enter the Federal Advisory Committee Process.

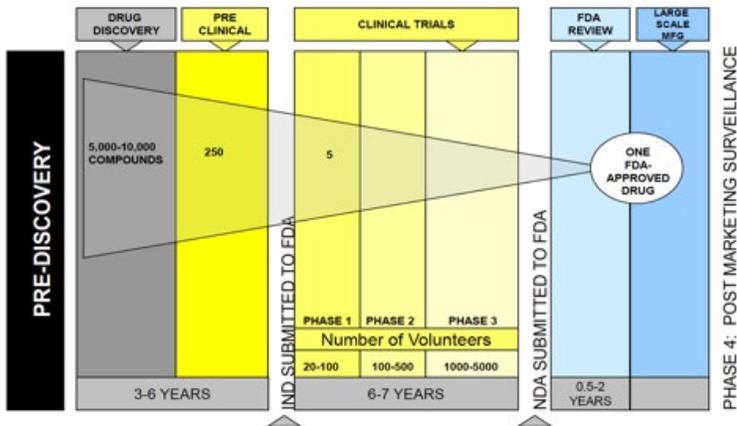
The FDA has for many years utilized the training and expertise of acknowledged experts to supplement the staff at the Agency when difficult questions need to be answered. These Advisory Committees are chartered by Congress and those chosen become Special Government Employees; a vehicle used to enforce the confidentiality of the massive amounts of industry and Agency data that are utilized in the analysis of drugs. There are individual committees for all classes of drugs, and there is a rigorous investigation into conflicts of interest within the group which is ongoing during the entire time that board members are impaneled. The questions that are asked of panels are consequential to the outcome of the analytical process, and the Agency carefully scrutinizes the discussions that come forth as well as the results of votes. In the life or death struggle to keep small pharmaceutical companies financially healthy, a poor presentation at one of these meetings can be a disaster.

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Why Did They Do That? The FDA and the Evolution of Drug Regulation in the U.S.

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R & D Process



public health. Thus, many opioids have been released that the public and outside experts have questioned. The fact that there are multiple layers of regulatory and statutory requirements for the Agency to deal with may obscure what would seem to be a straightforward decision.

What External Pressures Interfere in the Regulatory Process

In a scientific pursuit, the risk of external forces affecting the outcome of analysis should be meager, right? In fact, there is constant interference, some of which is not subtle. The industry uses every sort of information laundering, paying of experts, publishing or not publishing studies, and lobbying the Agency to affect the outcome. Congress controls the overall budget of the Agency and uses this power to attempt to move regulation in one way or another depending on the interests of individual legislators. Some high-ranking congressmen have been known to call middle management at the Agency to change an outcome.

Does the Agency Always Make the Right Choice?

It is important to understand that it is not the role of the Agency to establish winners and losers within the pharmaceutical industry. In general terms, the FDA as a component of the Federal Government strives for a healthy economy and Congress has tried to assure that over-regulation of the industry is not inhibitory to the research and development of drugs. In some cases, however, the release of a drug on the market runs the risk of exacerbating an established public health crisis. Such is the case with opioids. Unfortunately, the Agency is enjoined from denying a drug its place in the market unless it is shown to be ineffective or a genuine risk to the

The Drug Regulation Process – Present and Future

The regulation of pharmaceuticals is an evolving process. Significant changes follow disasters; small changes reflect the progression of science and technology. The process will never be perfect, but the Agency has moved recently to reduce the effect of external influence and to be inclusive and transparent in the development of regulations. The economic impact on industry of decisions by the Agency will continue to reduce total clarity. But the overall regulatory process has improved the lives of Americans and is considered to be the best in the world.



Nate Beeler; Columbus Dispatch, Columbus, Ohio

DACA Health Professionals' Letter Urging Congressional Action

DEFERRED ACTION *for* CHILDHOOD ARRIVALS

AUA was pleased to sign on and join 36 other higher education associations on an Aug. 28 letter to President Trump urging the administration to keep Deferred Action for Childhood Arrivals (DACA) intact until a permanent solution can be reached.

The letter urged Congress to pass legislation allowing health professionals and students who are undocumented to continue their employment, education, training, and research in the United States.

The AUA Council felt that signing this letter demonstrated a united stance from our community similar to other industries that have spoken up.

September 14, 2017

The Honorable Mitch McConnell
Majority Leader, United States Senate
Washington, DC 20510

The Honorable Chuck Schumer
Minority Leader, United States Senate
Washington, DC 20510

The Honorable Paul Ryan
Speaker, United States House of Representatives
Washington, DC 20515

The Honorable Nancy Pelosi
Minority Leader, United States House of Representatives
Washington, DC 20515

Dear Majority Leader McConnell, Speaker Ryan,
Minority Leader Schumer, and Minority Leader Pelosi:

On behalf of the undersigned health professions organizations, we urge you to ensure that all members of the health care workforce with Deferred Action for Childhood Arrivals (DACA) status are able to continue their employment, education, training, and research, with passage of a permanent legislative remedy, such as the bipartisan, bicameral Dream Act of 2017 (S. 1615, H.R. 3440). By providing a legal pathway to permanent residency for undocumented Americans brought to the U.S. as children, Congress can help our country produce a diverse and culturally responsive health care workforce to meet the needs of underserved populations, improve cultural awareness, and promote health equity.

With the nation's population growing and becoming increasingly diverse, it is crucial that the health professions workforce respond to the changing demographics of the country to mitigate racial, ethnic, and socioeconomic health disparities. Research demonstrates that diversity in the health professions leads to improvements in access to care for underserved communities, and some studies have shown that patients report greater satisfaction with clinical care when they are treated by providers from the same racial/ethnic background.

Diverse health professions school classes also enhance the ability of the entire workforce to provide culturally competent care to individuals regardless of their background. Higher education research shows that diversity in the classroom produces a more enriched learning environment. Diversity contributes to increased exposure to divergent perspectives, enhances cognitive complexity, promotes civic engagement and facilitates more inclusive teaching and educational content. Diversity in teams has contributed to greater productivity, creativity and innovation that has significant implications for advancing science and health care.

Health professions students who are undocumented encompass a diverse, multiethnic population, who are often bilingual and more likely to practice in underserved communities. For a narrow cohort of undocumented students that meet specific criteria, legislation like the Dream Act of 2017 would grant lawful presence in the U.S., work authorization, and in many cases state identification and driver's licenses, all of which make attending health professions school and residency training possible.

Our organizations are dedicated to promoting a culturally competent, diverse, and prepared health and biomedical workforce that leads to improved care and health equity. A permanent legislative remedy would help us achieve this goal. We urge congressional leadership to advance legislation before health professionals participating in DACA lose their lawful status and are unable to continue their employment, education, training, and research.

Sincerely,
Academic Consortium for Integrative Medicine & Health
Academy on Violence and Abuse
The Addiction Medicine Foundation
Alliance for Academic Internal Medicine
American Academy of Dermatology Association
American Academy of Family Physicians
American Academy of Hospice and Palliative Medicine
American Academy of Neurology
American Academy of Pediatrics
American Association of Anatomists
American Association of Chairs of Departments of Psychiatry
American Association of Child and Adolescent Psychiatry
American Association of Colleges of Nursing
American Association of Colleges of Pharmacy

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DACA Health Professionals' Letter Urging Congressional Action

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American Association of Colleges of Podiatric Medicine
American Association of Directors of Psychiatric
Residency Training
American Board of Medical Specialties
American College of Physicians
American Congress of Obstetricians and Gynecologists
American Dental Education Association
American Geriatrics Society
American Medical Association
American Medical Student Association
American Nurses Association
American Organization of Nurse Executives
American Physiological Society
American Psychiatric Association
American Psychological Association
American Society for Clinical Laboratory Science
American Society for Microbiology
American Society for Pharmacology & Experimental Therapeutics
American Society of Transplantation
Americas Hepato-Pancreato-Biliary Association
Asian Pacific American Medical Student Association
Association for Prevention Teaching and Research
Association of Academic Health Sciences Libraries
Association of American Medical Colleges
Association of American Veterinary Medical Colleges
Association of Anatomy Cell Biology and Neurobiology Chairs
Association of Bioethics Program Directors (ABPD)
Association of Chairs of Departments of Physiology
Association of Departments of Family Medicine
Association of Family Medicine Residency Directors
Association of Graduate Departments of Biochemistry
Association of Nurses in AIDS Care
Association of Psychologists in Academic Health Centers

Association of Schools and Colleges of Optometry
Association of Schools and Programs of Public Health
Association of Schools of Allied Health Professions
Association of University Anesthesiologists
Association of University Professors of Neurology
Association of Women's Health, Obstetric and Neonatal Nurses
Council of Emergency Medicine Residency Directors
Council on Social Work Education
Emergency Medicine Residents' Association
GLMA: Health Professionals Advancing LGBT Equality
Heart Failure Society of America
HIV Medicine Association
Infectious Diseases Society of America
Institute for Healthcare Improvement
Latino Medical Student Association
Medical Group Management Association
National Association of Hispanic Nurses (NAHN)
National Association of Nurse Practitioners in Women's Health
National Council of Asian Pacific Islander Physicians
National Hispanic Medical Association
National League for Nursing
National Organization of Nurse Practitioner Faculties
North American Primary Care Research Group
Physician Assistant Education Association
Pre-Health Dreamers
Society for Academic Emergency Medicine
Society of Academic Associations of Anesthesiology and
Perioperative Medicine
Society of Emergency Medicine Physician Assistants
Society of General Internal Medicine
Society of Surgical Chairs
Society of Teachers of Family Medicine
Student National Medical Association



In Memoriam

Edmond “Ted” Eger, II, MD by Steve Shafer, MD

Dr. Edmond “Ted” Eger, II, the anesthesiologist and scientist who pioneered development of modern inhaled anesthetics, died peacefully at his home in Tiburon, California, on August 26, 2017, one week shy of his 87th birthday. Dr. Eger’s research is the basis for the safe use of modern inhaled anesthetics administered to more than 300 million patients every year. His death was due to pancreatic cancer.

Working at the University of California, San Francisco, Dr. Eger methodically characterized the effects of drugs used in anesthetic practice. This work began with halothane and methoxyflurane in the 1960s and extended to enflurane and isoflurane in the 1970s, and to desflurane in the 1990s. Early in his career, Dr. Eger recognized the need for a fundamental unit of anesthetic potency, and introduced the concept of “MAC” for “minimum alveolar concentration” of anesthetic required to prevent movement in patients in response to surgery. MAC provided an immensely powerful research and clinical tool and became a standard for all studies of anesthetic action. It remains the standard dosing unit used by practicing anesthesiologists to this day. Dr. Eger also identified the processes governing the onset, uptake, and distribution of inhaled anesthetics into the lungs and body tissues, including the brain, and how quickly anesthetics are removed at the end of anesthesia. This provided precise guidance on how to administer inhaled anesthetics safely and effectively during surgery. Dr. Eger developed these concepts for the anesthetics available in the 1960s, and then used these concepts to identify new drugs meriting commercial development: isoflurane, sevoflurane, and desflurane. These three drugs are the mainstays of modern anesthetic practice.

Edmond I Eger II was born Sept. 3, 1930, in Chicago, the son of an advertising executive. The young Ted Eger received ether anesthesia at ages 6 and 10, experiences that would haunt him

and guide him into a career to improve anesthesia care. In both cases, he felt restrained, suffocated, and drawn into a black vortex as consciousness disappeared.

Dr. Eger graduated from Hyde Park High School at the age of 15, having led his school checker team to two consecutive victories in the All-Chicago Checker Championship. He graduated in the lower 20 percent of the class, however, and after his first (and only) day of selling women’s shoes, he resolved to improve his study habits. He enrolled in Roosevelt College and was able to transfer to the University of Illinois one year later, from which he graduated *Phi Beta Kappa* with a major in chemistry and a minor in mathematics. Later that year, he enrolled in Northwestern Medical School, from which he graduated in 1955. He had expected to pursue a career as a general internist, when an epiphany during an externship directed him to a career in anesthesia instead: assisting with the care of a patient receiving the anesthetic thiopental by infusion, the patient’s breathing gradually slowed and finally stopped, whereupon Eger discovered that he could move air in and out of the patient’s lungs by squeezing the anesthesia breathing bag, thus keeping him alive. This power of controlling a person’s breathing with his hands, coupled with the haunting memory of his own sense of suffocation during anesthesia, inspired him to embark on a career in anesthesiology. He was determined to improve on what he had experienced as a child.

Following a one-year internship at St. Luke’s Hospital in Chicago, Dr. Eger began residency training at the University of Iowa with a new baby and wife, Dollie Ross Eger, in tow (after 25 years of marriage, they divorced in 1983). Under the leadership of Iowa’s Dr. Stuart Cullen, Dr. Eger began publishing his first research papers and also began working with another anesthesia resident, Dr. John Severinghaus, who successfully challenged Dr. Eger’s initial notions about the physiology of uptake and distribution. Dr. Eger followed him to UCSF to work as his research fellow and spent the next 50 years applying



Dr. Eger is survived by his wife of 21 years, Dr. Lynn Spittler.

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In Memoriam

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precise mathematical detail to answer the questions that Dr. Severinghaus had posed while they were residents.

Dr. Eger's research, with numerous collaborators, led to more than 500 peer-reviewed publications, including nine of the 100 most highly cited anesthesia-related publications. His research trainees include the editors-in-chief of *Anesthesiology* and *Anesthesia & Analgesia*; two medical school deans; four recipients of the Distinguished Service Award from the American Society of Anesthesiologists; four recipients of the Excellence in Research Award from the American Society of Anesthesiologists; and 24 chairs of departments of Anesthesiology. Dr. Eger has received numerous awards for his research and leadership roles in anesthesia, including the Distinguished Service Award and the Excellence in Research Award from the American Society of Anesthesiology, and is an Elected Fellow of the Royal College of Surgeons, London.

Dr. Eger is the author, co-author, or co-editor of seven books. The first, *Anesthetic Uptake and Action*, published in 1975, remains the definitive description of the principles of anesthetic pharmacology. The last, *The Wondrous Story of Anesthesia*, edited with Lawrence Saidman and Roderick Westhorpe, provides a definitive history.

Fifty-five years ago, Dr. Eger founded and subsequently supported the Western Anesthesia Residents Conference, an annual meeting hosted by departments of anesthesia located in the western US inviting Anesthesia Residents to present results of their research. This conference has thrived and grown over the years to a vibrant annual meeting well-attended by residents, department chairs, and anesthesia research faculty. The conference recently honored Dr. Eger by naming an annual lectureship after him.

Dr. Eger spent his final two decades as an investigator pursuing an answer to how inhaled anesthetics work. This is one of the oldest mysteries in pharmacology, resisting solving by all of the tools of modern molecular biology. Dr. Eger discovered tantalizing clues about how fundamentally different various anesthetics are, while also proving that anesthetics have less person-to-person variability than do other drugs. He showed that modern inhaled anesthetics can anesthetize any animal at doses similar to those in humans, that plants and even the most primitive forms of life, blue-green algae, can be anesthetized. No other drug behaves like this. But despite these clues and decades of work, the puzzle of exactly how anesthetics work remains unsolved.

An avid lover of nature, Dr. Eger hiked throughout the Sierra Nevada and completed the entire John Muir Trail three times; one of his favorite places was Yosemite's Half Dome, which he last climbed on his 75th birthday with his entire family. Dr. Eger is survived by his wife of 21 years, Dr. Lynn Spitler; four children, Cris Cadence Waste, Dr. Doreen J. Eger, Edmond Eger III, and Dr. Renee R. Eger; two step-children, Dr. Diane Anderson and Paul Spitler; seven grandchildren, six stepgrandchildren, and a half-brother, Larry Eger.

We invite you to submit your reflections about Ted Eger, at: ucsfanesthesianews@ucsf.edu. [Click here](#) to read his

obituary published by the *New York Times*, "Dr. Edmond Eger II, 86, Dies; Found Way to Make Anesthesia Safer."

A memorial symposium, dedicated to Dr. Eger, will be held in January 2018. Please keep an eye on our [Anesthesia Events](#) section for details.

Finally, we are hoping to raise funds in Dr. Eger's name to encourage Anesthesia residents and fellows to pursue careers in research typified by his extraordinary success. To support this endeavor, please contact Allison White at Allison.white@ucsf.edu or 415.502.5868.

Resources:

Anesthesia QI Reporting	UCSF Email
Adult Critical Care M&M	UCSF Box
ZSFG QI Reporting	PagerBox
APeX	Events
CaseView	Internal Resources
ICU List	News
IT Help	Quality & Safety
MyAccess	# Twitter
Schedule	

Richard J. Kitz, MD, MGH by Warren Zapol, MD

Dear Colleagues,

With great sadness we share that Richard J. Kitz, MD, MGH emeritus anesthesiologist-in-chief, died Tuesday, Sept. 19, at the age of 88. Dr. Kitz led the MGH Department of Anesthesia, Critical Care and Pain Medicine from 1969 to 1994, building and shaping it into one of the largest and most respected international clinical, research and training centers for anesthesiology and its associated sciences. An innovative, thoughtful and highly effective administrator, Dr. Kitz pushed the boundaries of the discipline of anesthesia, understanding the value of integrating technology and expertise from other fields to advance knowledge and improve the quality of care for patients.

Dr. Kitz recruited to MGH a significant portion of the next generation of leaders in anesthesia and intensive care medicine, including a robust cadre who, over the following decades, became chairs of more than 20 major anesthesia departments in the United States and abroad. A beloved colleague, friend and mentor, Dr. Kitz was known for his warmth and loyalty toward the staff and especially residents, who he always considered part of his extended family.

Dr. Kitz's brilliance was apparent immediately upon his arrival at MGH at the age of 39. He focused on the hospital's existing strengths, including the first respiratory intensive unit in the nation, established in 1961 under Henning Pontoppidan, MD, and on building vital areas, including a blood-gas laboratory, led by Myron B. Laver, MD; a pediatric anesthesia team under John Ryan, MD; and the first U.S. cardiac anesthesia team under Dr. Laver, followed by Edward Lowenstein, MD.

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In Memoriam

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Dr. Kitz's own basic organic chemistry research, which began at Columbia University College of Physicians and Surgeons and proceeded to the Karolinska Institute in Sweden, focused on neuromuscular pharmacology, pain management and the action of drugs. As head of an MGH research laboratory, he was integral to the project that discovered the popular short-acting muscle relaxant, Mivacurium, which was one of the two first MGH inventions that brought significant royalties to the department and hospital. He also launched a research effort that aimed to better understand the fundamental processes that occur during anesthesia and the mechanisms behind controlled unconsciousness and reactions of the central nervous system. This work, which continues today, shines an important light on the brain under anesthesia, enabling anesthesia delivery to be more tailored and more targeted.

Dr. Kitz was the author or co-author of more than 100 scholarly publications and was an author of the MGH Anesthesia Department's landmark volume *Clinical Anesthesia Procedures of the Massachusetts General Hospital*. The success of this widely regarded work led the department to publish two subsequent books. He also served as editor of an historical compendium "This is No Humbug!" *Reminiscences of the Department of Anaesthesia at the Massachusetts General Hospital*, published in 2002. Passionate about the history of the MGH – specifically the story of the first public demonstration of anesthesia at the MGH in 1846 – Dr. Kitz helped endow a permanent anesthesia exhibit in the MGH's Russell Museum.

Dr. Kitz was a strong advocate for patient safety. He brought into the department bioengineers, including Ronald Newbower, PhD, Jeffrey Cooper, PhD, and Nathaniel P. Sims, MD, who could gather data, identify risk factors, apply mathematical models, and look systemically to improve anesthesia processes and practices. He created an environment in which engineers and clinicians worked hand in hand with a common goal of safer delivery of anesthesia. With this increased knowledge about anesthesia risks came the testing and adoption of oximeter technology from Japan that enabled better, noninvasive ways to monitor oxygen saturation, as well as new methods to measure exhaled carbon dioxide levels and track subtle changes in vital signs, and led to safer ways to deliver intravenous drugs. Indeed, Dr. Kitz and his team were at the leading edge of a transformational time in anesthesia safety, re-defining the clinical practice nationally in a way that has, no doubt, saved thousands of lives.

Dr. Kitz was the second Henry Isaiah Dorr Professor of Research and Training in Anesthesia at HMS – the first ever endowed U.S. anesthesiology chair. He also served as principal investigator for both the Harvard Anesthesia Research Center, the Basic Science Research Training in Anesthesiology Program from 1969 to 1993, and directed the Anesthesia Residency Program at MGH from 1969 to 1994. Dr. Kitz was appointed Faculty Dean for Clinical Affairs at HMS in 1994, a position he held until 1999 in which he oversaw the changing relationships between patient care, research and educational efforts of the HMS clinical faculty.

Among his many accolades, Dr. Kitz served as a board member of the American Board of Anesthesiology from 1974 to 1986, including one year as its president. He was chairman of the American Board of Medical Specialties' Committee on the Study of Evaluation Procedures, was elected to Institute of Medicine of the National Academy of Sciences (now the National Academy of Medicine) and was the founding editor-in-chief of the *Journal of Clinical Anesthesia*. In 2000 he received an honorary doctor of science degree from his alma mater, Marquette University, was an honorary fellow in the Faculty of Anaesthetists of the Royal College of Surgeons of Ireland, and a Fellow of the Royal College of Anaesthetists of England. In 1997, Harvard Medical School established the Richard J. Kitz Professorship of Anesthesia Research in his honor.

Dr. Kitz was born on in Oshkosh, Wisconsin, Oct. 25, 1929. After teaching a cadaver lesson for a class of occupational therapists-in-training that included a young lady in a red plaid skirt, he married Jeanne Marie Hogan in 1953. They had a daughter, Anne Marie Kitz, now a theological scholar. He earned his medical degree from Marquette University in 1954, and then served as a surgical intern at Columbia University College of Physicians and Surgeons (CUCPS) at the Presbyterian Hospital. He loved to play baseball growing up in Oshkosh, and he snuck onto the best team in town, the Navy team, by joining the Navy at 16 years old. Although he was shortly discovered to be under age, he kept his assigned (low) Navy serial number, which gave him the seniority to run a Marine Corps base in Japan as chief medical officer for two years. He then returned to CUCPS to complete his two-year residency in neurosurgery and anesthesiology in 1960. He served as associate professor of anesthesiology there until 1969, when he came to the MGH and Harvard Medical School – and began the remarkable journey that has left a legacy on the institutions he loved and the discipline he shepherded.

Dr. Kitz loved sailboat racing and won many races, often with fellow MGH physicians as crew members. In 1981, he served as race chairman for the Marion to Bermuda race.

On behalf of a grateful hospital that is so much richer for Dr. Kitz's many contributions and leadership, we extend heartfelt condolences to his family and friends. A memorial service is being planned for a later date.

Peter L. Slavin, MD
MGH President

Timothy G. Ferris, MD, MGPO, CEO

Jeanine Wiener-Kronish, MD, MG
Anesthetist-in-Chief

SAVE THE DATE! APRIL 26 - 27, 2018

AUA 65th Annual Meeting

Hyatt Regency Chicago, Chicago, Illinois

Hosted by Northwestern University Feinberg School of Medicine
and University of Chicago School of Medicine



FOR MORE INFORMATION,
VISIT AUAHQ.ORG.

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