STANFORD ANESTHESIA NEWS

FOR THE ALUMNI AND FRIENDS OF THE
Department of Anesthesia
STANFORD UNIVERSITY

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Inside this Issue: Research Update • Simulation-based Training at Stanford
International Medical Missions: No Act Too Small • Interview with Dr. David M. Gaba

FROM THE EDITOR

I am delighted to present this year's issue of Stanford Anesthesia News. I want to thank the Stanford Anesthesia News staff for conceiving the table of contents, writing articles, taking photographs, staying within budget, and crafting the layout. Some of our pieces stay the same every year – like the Residency Update and the Chairman's Letter (please read the wonderful interview with Dr. Pearl) – and provides structure to this publication. Other content changes year-to-year. For example, this time we choose to highlight simulation-based training, because simulation is a major theme within the department and within the Medical School. In fact, I still remember taking an early Crisis Resource Management course at the Palo Alto VA as a first-year anesthesia resident in 1991. That remains my single most valuable day of learning. Calling for help early, delegating tasks, avoiding fixation errors, and making communicating with OR staff a high priority are tools I use everyday in the OR.

We also have other interesting articles that showcase the breadth and depth of our activities in education, medical missions, and research. Finally, please take a look at the biography of Ellis N. Cohen, one of the original leaders of Stanford Anesthesia. Some of the articles have been specifically written for this publication, while other articles originally appeared in other publications and have now been reprinted here. It is not possible to cover everything in one issue, so please let me know if you have requests for future topics. I am looking forward to hearing from you.

Best wishes the remainder of 2005!

Alex Macario MD, MBA
Editor

Alex Macario

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Ron Pearl

Chairman's Letter - Ronald G. Pearl, MD, PhD

An interview with Stanford Anesthesia News

As chairman of the Department of Anesthesia, what activities take up most of your time?

I still continue my clinical activities as a cardiac anesthesiologist and intensivist. On days when I am not in the OR or the ICU, I usually have ten hours of scheduled meetings with anesthesia faculty, hospital administrators, and medical school personnel. We deal with clinical issues, financial analyses, problems common to all the departments, long-range planning, etc. However, the most valuable time I spend is the unscheduled interactions with faculty and residents, which occur in our breakfast/lunch break room.

What is the last book you have read?

I try to read for 30-60 minutes each day and enjoy general fiction and science fiction. I am intrigued by the sociological implications in modern science fiction books and by the lyricism of good fiction. The last book I read was About Grace by Anthony Doerr, a novel where the protagonist flees his life when he has visions he will drown his baby.

How did you end up choosing medicine as a career and anesthesia as a specialty?

I was initially a math major in college but found I wanted a career that involved people more than blackboards. I do not remember my personal statement when I applied to Medical Scientist Training Programs, but I assume it mentioned the standard reasons of enjoying science, the excitement of scientific discovery, and helping people. I began medical school anticipating a career in psychiatry and did my PhD research in neuropharmacology (mechanisms of tolerance to amphetamines). However, during the clinical years I became intrigued by internal medicine and therefore came to Stanford for medicine residency. Intensive care was the most exciting rotation as a medicine resident (Mike Rosenthal was my attending) so I continued with a critical care medicine fellowship and then joined the medicine department at Stanford. After several years as a faculty member, I recognized that the anesthesiologists not only were better at critical care medicine but also enjoyed it more. The rest is history.

What was the first music record you bought?

I don't remember, but it would have been a 45 rpm rock and roll single.

Where is anesthesiology, the specialty, going to be in five to ten years?

Despite all the debate on this topic, I do not think anyone truly knows. Although changes have never occurred faster than today, five years is a relatively short time in medicine. Just one decade ago we had predictions that our specialty would quickly die out and that there would be no jobs for anesthesiologists by 2005. Since then we have survived a major excess followed by a major shortage of anesthesiologists. I anticipate that anesthesiology in five years will look similar to anesthesiology today. There will be incremental changes such as an increase in ambulatory surgery (including many surgeries that require inpatient stays today) but also an increase in the complexity of inpatient surgery. In contrast, twenty years from now the specialty will likely be radically transformed. With continuing advances in technology and the development of safer anesthetic agents, physician anesthesiologists will no longer be needed for

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The Department of Anesthesia at Stanford Cordially Invites You to Attend the Alumni Reunion Reception

LOCATION TO BE ANNOUNCED

October 23, 2005

6:00 - 8:00 pm

Please RSVP to Renee Grys, grys@stanford.edu or 650-723-5439

PLEASE INFORM YOUR COLLEAGUES

Chairman's Letter - Ronald G. Pearl, MD, PhD

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many of the simpler ambulatory procedures. Although we will continue to be required for the complex inpatient procedures, these cannot support the continuing advancement of the specialty. Hopefully, anesthesiologists will expand into roles as perioperative physicians, intensivists, and pain management physicians. The ten-year question is the pivotal one, since the survival of our specialty will depend upon whether we are able to begin our transformation by that time.

What are your goals for the department?

I have two sets of goals for the department. First, the department is the sum of the faculty, residents, and administrative staff, so my goals are to help each individual identify his or her goals and achieve them. Individual faculty may have goals focused on any combination of clinical care, teaching, scholarship, and administration. The diversity of faculty in the department usually allows the department to achieve its goals while also fulfilling each individual's goals. The second set of goals I have for the department is in the category of strategic leadership, of ensuring that the department looks far enough into the future to identify and work towards achieving our long-range goals. The governance committee retreat we held this June was a step in this process, and throughout this year we will continue working on the issues that were identified.

How many emails do you get a day? And how many do you answer?

Not counting all the spam, which is filtered and never seen, I receive about 60 e-mails a day and try to answer all of them.

Please tell us about your family.

My beautiful wife, Mary, is a teacher whose other activities include soul line dancing at Stanford and hiking (40-50 miles a week). Our older son, Jeremy, is a senior at UC San Diego and is applying to medical school. Our younger son, Nathan, is a senior at Gunn High School and still has baseball dreams.

What is the most important lesson you've learned during your time as chairman?

The importance of taking the time to listen to the concerns of each member of the department.

What do you like to do in your "free time"?

I try to spend as much time as possible with my family. For "fun" activities, I enjoy running, reading, travel, and sometimes just watching TV.

Who would you like most to switch places with for a day?

I would like to switch places with President Bush, simply because afterwards I would decide that being chair of an anesthesia department is a relatively simple job.

What is your favorite vacation spot?

We have vacationed in Kauai almost every other year. It is less developed than the other large Hawaiian Islands but has the same tropical climate. We swim, hike, and try to surf.

What has been your favorite moment as chairman?

During my second year as chair, our faculty salaries were not competitive, and we had several faculty move into private practice. Any additional faculty losses could have created a crisis where we would not have been able to cover the operating room. Several of the other clinical chairs, especially surgery and pediatrics, met with the dean and we were then able to increase salaries and retain faculty. The support that the other chairs demonstrated for our department and for my role as chair emphasized the community that exists among the chairs and made me realize that it is not always lonely at the top (or in the middle).

What is your favorite sport (to play or to watch)?

My favorite sport has always involved watching my sons play basketball (Jeremy) and baseball (Nathan). The emotions involved in high school sports far exceed those at professional games.

When Koko the Gorilla needs a Checkup, Stanford Docs Swing into Action

Courtesy of Stanford Report, written by Mitzi Baker

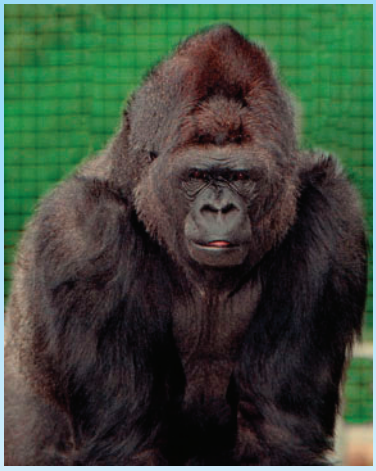

Photo: Courtesy of Ron Cohn, The Gorilla Foundation

On Aug. 8, Mihm and a team of Stanford colleagues reported to the nearby Woodside abode of Koko, the 33-year-old low land gorilla famous for her ability to communicate through American Sign Language.

The medical team's visit was prompted by an aching tooth. Using the gesture for pain and pointing to her mouth, Koko recently told her handlers that her level of pain was an eight or nine on a scale of 10. The Gorilla Foundation contacted Mihm – who has consulted with the San Francisco Zoo for years and has anesthetized lions, tigers, giraffes and elephants in addition to gorillas – about joining a team of veterinarians and dentists to treat Koko's painful tooth.

The use of anesthesia can be a risky proposition for animals, so it is used only when deemed essential, Mihm said. Because the dental surgery required anesthesia, doctors felt it would give them the perfect opportunity to take an in-depth look at Koko's overall health. Gorillas suffer from many of the same maladies as humans, Mihm said, so it makes sense for veterinarians and medical doctors to collaborate.

Shown here are anesthesia professor Fred Mihm, right, who often consults for the San Francisco Zoo, and Parag Mathur, an anesthesia resident. Also in the operating room at the Gorilla Foundation were dentist Bob Turner and, at left, Koko's caregiver Tierra Wilson.

For Koko's complete examination, Mihm recruited a team of physicians who were thrilled to volunteer their time for their legendary patient.

"This was an opportunity of a lifetime," said assistant professor of obstetrics and gynecology Bertha Chen, MD. Because Chen's research focuses on the anatomy and structure of the pelvis and many such studies are done in primates, it was a particularly appealing proposition for her. "Koko presents a unique opportunity for us to learn about gorillas. It was fascinating for me to see the similarities and differences in the primate and how close they are to us."

Koko has told her handlers over the years that she would like to have a baby, so Chen – performing her first non-human gynecologic exam – was asked to determine whether biological reasons were preventing Koko from conceiving with her partner of 11 years, Ndume. After a battery of blood tests to check hormone levels and a physical exam, which included ultrasound to look for fibroid tumors, Chen found no obstacles to Koko becoming a mother. Menopause comes very late in life for gorillas, according to Chen, and in captivity they can live into their 50s.

Like humans, gorillas are susceptible to thickening of the arteries and heart disease, so cardiologist David Liang, MD, checked out Koko's heart. Liang has previously participated in other gorilla examinations with Mihm at the San Francisco Zoo and is continually amazed at the similarities between gorillas and humans.

"The outside may be very different, but the inside is so much like humans," said Liang, assistant professor of medicine in the division of cardiology. "Other than proportion, everything is similar." In fact, he said, another doctor seeing the images taken of Koko would not be able to tell that the heart wasn't human.

During the five-hour medical workup, Koko underwent an echocardiogram; X-rays; ultrasounds; dental work, including removal of an abscessed tooth; orthopedic, gynecologic and dermatologic exams; colonoscopy and bronchoscopy. Mihm plotted out the details of the procedure with Koko's veterinarian John Ochsenreiter, along with assistant professor of anesthesia Ethan Jackson, MD, and senior anesthesia resident Parag Mathur, MD. Other members of the Stanford team involved in the medical workup included otolaryngologists Jim Koch, MD, and Nick Blevins, MD.

The only problem encountered was periodontal disease, which was treated by the dental consultants. Mihm reported that Koko woke up from the anesthesia quickly and was soon moving about, making a purring sound that he interpreted as a sign she was OK.

According to the Gorilla Foundation, Ndume watched Koko's entire procedure from a window and behaved like a nervous boyfriend, pacing and calling out to her until it was clear that she was fine. They report that she is currently taking it easy and enjoying special meals, such as a "gorilla ice cream sundae" consisting of soy ice cream and chocolate sorbet on a bed of soft tofu.

Koko, the 33-year-old who lives at the Gorilla Foundation in Woodside, got a medical workup Aug. 8 during a dental procedure required after she complained - using American Sign Language - of tooth pain. The workup pronounced the gorilla healthy except for periodontal disease. The multidisciplinary workup and treatment was conducted by dentists, veterinarians and a Stanford faculty team including cardiologist David Liang, OB/GYN specialist Bertha Chen, and otolaryngologists James Koch and Nikolas Blevins. Stanford physicians donated services.

Note: The Gorilla Foundation's mission is to bring interspecies communication to the public in order to save gorillas from extinction and inspire our children to create a sustainable future for all great apes. Their programs are supported primarily through private donations. To learn more visit www.koko.org.

RESIDENCY UPDATE

By John G. Brock-Utne, M.D.

This year's chief residents were Pat Bolton (second from right) and Barry Waddell (second from left). With great support of their wives they have been most enthusiastic, loyal and hard working. They have both been proactive, upbeat and smiling, despite the impossible task of pleasing everybody.

Another year has flown by, and, again, it has been memorable and enjoyable. We have had our share of fun and laughter but also serious times and many long working hours. Janine Roberts and Nuvia Pacheco, our Residency Program coordinators, have been outstanding. They are always willing to help, no matter how hard the task, and are instrumental in making our residency program as good as it is. I thank them for their unfailing support.

This year, eleven out of fifteen residents opted for private practice. This is different from last year when eleven out of sixteen residents chose academics/fellowships. Most of residents this year are married. Hence, one can speculate that important issues for this group were financial, family, and work conditions.

Patrick Bolton – private practice, Phoenix AZ
Jason Cooney – academic, Stanford University, CA
Francesca Dyrud – private practice, Honolulu, HI
Jonathan Fox – private practice, Walnut Creek, CA
Jenifer Henrie – private practice, Chico, CA
Kjell Hult – private practice, Pasadena, CA
Parag Mathur – academic, Stanford University, CA
Mauricio Michales – private practice, Santa Rosa, CA
Khanh Ngo – private practice, Monterey, CA
Suma Ramzan – academic, Stanford University, CA
Zed Reagan – private practice, Bend, OR
Rachael Scheuring – private practice, Santa Clara, CA
Joanna Staunton – private practice, Bay Area, CA
Stephen Ternlund – private practice, Walnut Creek, CA
BarryWaddell – academic, Santa Clara Valley Med. Ctr, CA

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RESIDENCY UPDATE

By John G. Brock-Utne, M.D.

John Brock-Utne

The following ten residents went on overseas trips to provide anesthesia care in underdeveloped countries.

Vietnam – Barry Waddell

Venezuela – Jason Cooney

Columbia – Kjell Hult, Parag Mathur, Karin Klika and Cynthia Weller (all at different times)

Peru – Brigdet Phillips with attending Andrew Patterson

Bangdelash – Suma Ramzan with attending Fred Mihm (Suma besides being an excellent anesthesiologist speaks the language and was invaluable to the team)

Mexico – Jonathan Fox

Jamica – Heidi Witherell with attending Michael Chen

This is one of the highlights of our program. We are still looking for organizations to take our residents to far away places. If you know of any groups that would be interested in having enthusiastic well-trained residents participate, please let me know. (brockutn@stanford.edu)

Again the most popular resident rotations were Cardiac Anesthesia at the Veteran's Administration Hospital in Palo Alto and Regional Anesthesia at Stanford.

I want to also recognize the 7th Edition of the popular Stanford Anesthesiology Resident Guide edited by Fred Mihm, Michael Chen, Larry Chu, Geoff Lighthall and John Calabrese. This pocket sized handbook gets better and better. It is a real little gem.

Our residents work hard, but they also play. In January, Kelly Yeh (fellow in pediatrics) organized the first Stanford Anesthesia wine tasting at the Wine Club in Santa Clara. Twelve wines were poured from four different prices ranges.

WARC (Western Anesthesia Resident's Congress) was hosted by University of California, Irvine. The department was represented by the following residents: Neetu Ahluwalia, Shawn Hodge, Matthew Kolz, Kelly Yeh and Anthony Stanzi. Larry Saidman and I represented the "oldies". It was a good meeting, and our group did very well. We all had a great time investigating downtown Disney on Saturday night. We lost some people on the way, but Ed Mariano (former chief resident and pediatric fellow now working in San Diego) joined in with great gusto and so did Matt, Kelly and Anthony. We all enjoyed Brennan's Jazz Bar immensely. The music was great, and we made a lot of friends….

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RESIDENCY UPDATE

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At the Disney superstore, we arranged races with our radio-controlled, flashing robot DOGS, against the security guards. We beat them every time, GO STANFORD. We arrived back in the hotel in one piece. Lovely party.

Neetu Ahluwalia organized the annual February weekend skiing trip for residents. My thanks to the faculty, in all the three hospitals, that covered for the residents.

The third annual Stanford Anesthesia Golf Tournament was held on April 24th. It was a great success. The winning team consisted of Scott Rudy (chief resident 05-06), David Gaba, Deanna Mann and I. Michael Champeau, who was showing his son, Andrew, how this game is played, won the closest to the pin on the eighth. Drinks and a lot of different snacks were enjoyed under the trees near the eighteenth green. We had a great time, and if you are interested in playing next year, please let me know via e-mail at: brockutn@stanford.edu.

We are still fortunate to have so many alumni come back and visit us. Most of them come and work in the OR with our residents. The residents really do appreciate the teaching and of course the networking. We are grateful to you all for taking the time and effort to contribute to the education of our residents.

In conclusion, I have a most wonderful job. Eager, enthusiastic and happy residents surround me. They work hard. I believe that when they leave us they are the very well trained.

I am happy to say that we are very proud of them and will sorely miss them when July comes around.

Adjunct Clinical Faculty this past year:

John Ahlering
Eric Amador
David Arakaki
Rhett Atkinson *(Oral Exams)*
David Berger
Gregory Botz
William Brose *(Pain Clinic)*
Heinz Brinks
Robert Buechel
Michael Champeau *(Oral Exams)*
Edward Foreman
Gordon Haddow
Maeve Hennessy
Brian Hershey
Terri Homer
Jeffrey Lee
Freddie McClendon
Dan McFarland *(Oral Exams)*
Lonnie Merrick
David Newswanger *(Oral Exams)*
Suma Singh *(Pediatrics only)*
Mark Singleton *(Pediatrics only)*
Clinton Warne

Research Update

Figure 1: **Annual research funding in the Department of Anesthesia is currently over 6 million dollars.**

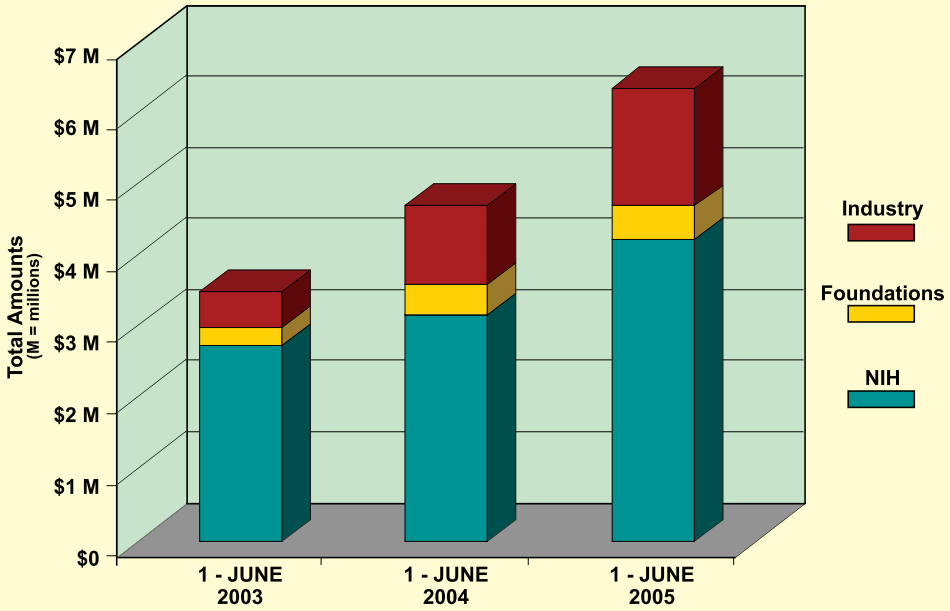
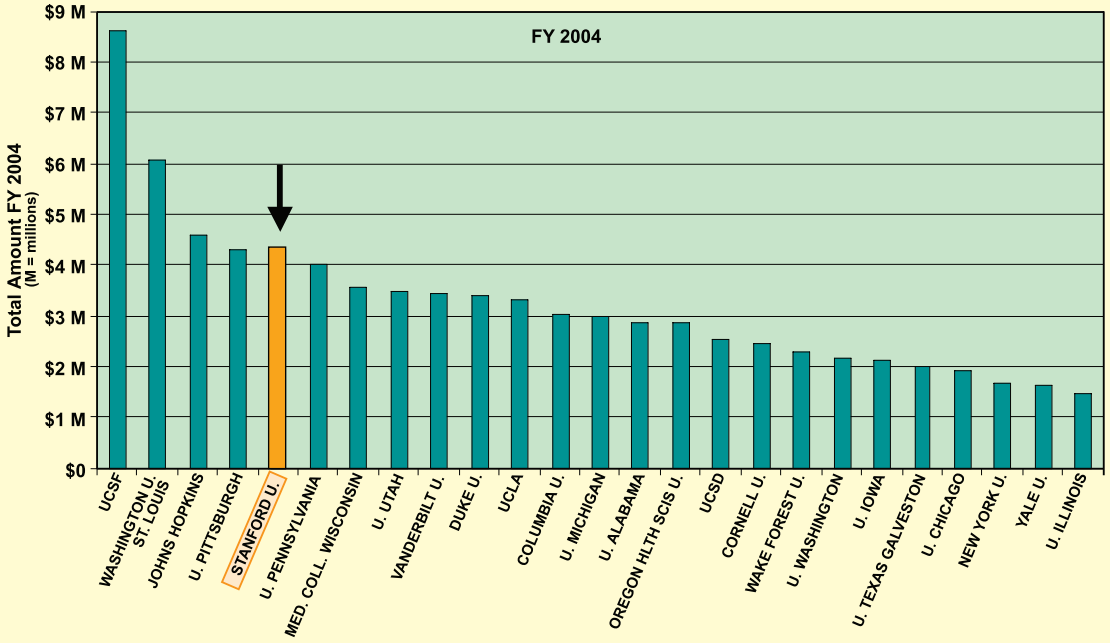


Figure 2: **NIH Awards to Anesthesiology Departments**

Stanford Anesthesiology Department now ranks 5th in the country in NIH Awards.



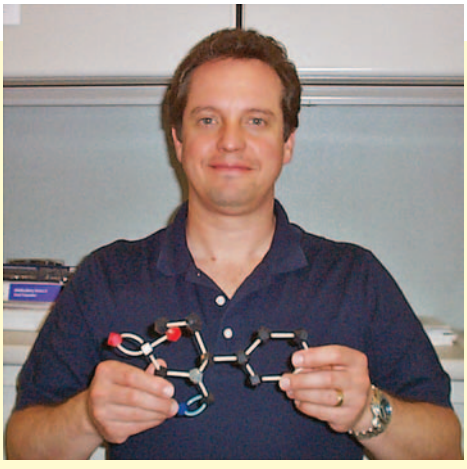
(Figures 1 & 2 courtesy of Nancy Federspiel)

Research Update 1
by M. Frances Davies, PhD, Director of Faculty Development

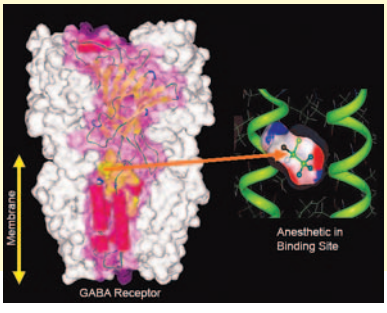
Anesthetic Interaction with Membrane Proteins
Jim Trudell, PhD, and Edward J. Bertaccini, MD

At the turn of the 20th century, the Meyer-Overton relationship was proposed relating anesthetic potency to the fat solubility of the anesthetic. This relationship fueled a large academic effort to find whether the site of anesthetic action was the lipid layer of the plasma membrane. Might anesthetics perturb this lipid bilayer? However, while some of the characteristics of anesthetic action were explained, there were also many deficiencies. Attention then shifted to the lipid-protein interface.

Recently, most research has centered on anesthetics directly interacting with membrane proteins causing a change in their function. Unfortunately, anesthetics do not have a high enough affinity for proteins to study the interaction using classical biochemical means. Since the anesthetic site of action was elusive, researchers became inventive, bringing in computational chemistry to develop molecular theories of anesthesia.



Edward J. Bertaccini



PHOTOGRAPH: Halothane sitting in a pocket within the GABA receptor. A computer generated space filling depiction of the GABA receptor illustrates that the anesthetic sits in a pocket in between alpha helices that span the lipid membrane

Drs. Jim Trudell and Ed Bertaccini have been using bioinformatics, structural biology and computational chemistry to build 3-dimensional models of the various multi-subunit ligand-gated ion channels through which anesthetics are thought to mediate their effects. Much of their work has been focused on the glycine and GABA receptors found in the brain and spinal cord. Trudell and Bertaccini have mapped out the binding site so as to determine the chemical requirements for anesthetic binding. In collaboration with molecular biologists, site-directed mutations in these ion channels have been performed. The original models are then tweaked to include the modification of the protein sequence and the binding pocket is reexamined. Molecular modeling of these channels is used to visualize the effects of mutations. This information will be used to further refine the 3-D structure of the protein.

The results of this work are best seen with the computer images of the receptor model with and without anesthetics. Trudell and Bertaccini found a binding pocket in the midst of the protein where there is room for the anesthetic to sit. The anesthetic is held there by weak forces exerted by lipophilic and hydrophilic amino acid residues. If the amino acids within that pocket were modified to make them bigger they could either mimic or block the action of an anesthetic. Even more intriguing: if the subunits of the receptor are allowed to move in the model, the effect of the anesthetic on the ion channel pore becomes apparent.

Knowing exactly how anesthetics work may make it possible to design better anesthetics - ones with more selective and specific actions or ones that are more readily reversible.

Research Update 2
by M. Frances Davies, PhD, Director of Faculty Development

Gene Therapy for Stroke
Rona Giffard, PhD, MD

Stroke is the third leading cause of death and the most common cause of disability in the United States. Cardiac arrest affects more than 300,000 people per year in the US, and the long-term survival rate is only 10%. One of the main problems encountered in these patients is neurological impairment due to cerebral ischemia. With the aim of developing drugs to improve neuronal survival, enormous energy has been spent on understanding the effects of ischemia on neurons. This does not take into account the important role astrocytes play in neuronal survival and function.

Rona Giffard

Astrocytes are the most numerous cell type in the brain and are involved in normal and pathophysiological situations such as ischemia and stroke. They supply substrates for energy metabolism, take up neurotoxic agents, modulate synaptic transmission, and support brain antioxidative defense. Therefore, damage to astrocytes could have dramatic consequences for brain function. Although astrocytes are usually considered less easily injured by ischemia than neurons, recent data from Dr. Rona Giffard's laboratory suggests that in some settings the astrocytes may be injured first. The aim of her current studies is to follow up these observations by investigating the activity and function of astrocytes after ischemia and reperfusion both in cultured brain cells and animal models of stroke while also studying ways to protect the brain from ischemia.

Dr. Giffard's group found that several different heat shock proteins and interacting proteins could protect astrocytes from succumbing to ischemia. As their name implies, the expression of these proteins are induced by heat as well as other stresses. Heat shock proteins act as molecular chaperones and interact with proteins that are either unfolded or have not yet acquired their native conformation. When cultured astrocytes were forced to express the inducible heat shock protein Hsp70, their ability to survive ischemic insults was increased. Mice that over-express Hsp70 show a reduction in infarct volume. Since normally there is little of the inducible heat shock protein in brain, how could the astrocytes and neurons in the brain be coaxed into making increasing extra stress proteins as a protective strategy?

One way is through gene therapy, in which a piece of DNA encoding the desired gene is introduced into cells, allowing them to make the protein. Another way would be to give the protein directly as a therapy. Large proteins do not cross the blood-brain barrier, so there are limitations in giving the whole protein. By studying portions of the gene using different mutants of the protein, Dr. Giffard's group is beginning to define the ischemic protection importance of different regions within the protein. They have found that a part of the protein, approximately half of the gene, is sufficient for protection. Future studies may show that even smaller lengths may be effective, getting into a range of size that may be able to be administered. The goal of course is to engineer a therapy for patients following cardiac arrest or stroke.

Research Update 3

Working at the interface between clinical and basic science, neuroscience, pharmacogenomics and molecular biology.

Tim Angelotti, MD, PhD,

How did you end up in medicine?

Being the son of two chemists, a career in science chose me. I initially felt that I would have to choose between graduate and medical school. Fortunately, I was counseled to consider a dual degree program to prepare for a career as a clinician scientist. I entered the University of Michigan School of Medicine and was accepted into the Medical Scientist Training Program ultimately deciding to pursue a PhD in Pharmacology.

How did you choose anesthesiology?

Clinically, I planned to pursue subspecialty training in critical care medicine, and I felt that training in anesthesiology would lend the best interface between medical and surgical critical care. Scientifically, I felt that anesthesiology was an open book, not tied to a single organ system like many other specialties. This unique feature would free me to study integrated physiological systems, such as the sympathetic nervous system and its effector organs.

Your training has taken you many places. How has this benefited you?

Upon completion of my medical internship, a Humboldt Fellowship allowed me to pursue eighteen months of post-doctoral training at the Institute for Pharmacology and Toxicology, Technical University in Munich, Germany. I chose to segment my post-graduate training in this way to avoid a six-year period away from research. Professionally, I consider my time abroad to be one of the most formative periods of my training and, personally, one of the most rewarding. Upon returning to the United States in January 1997, I began residency in anesthesiology at Duke University. Following completion of my anesthesiology residency in 1999, I moved to Stanford for a clinical fellowship in critical care medicine. At that point, I decided that I would like to stop moving, and I settled in at Stanford as a junior faculty member in the Department of Anesthesia.

What is your area of scientific inquiry?

Whereas much neuroscience research in anesthesia centers on the brain or spinal cord, my research focuses on the peripheral nervous system, specifically the sympathetic nervous system. The sympathetic nervous system integrates multiple vital functions, such as heart rate and contractility and vascular tone. In fact, my belief is that much of what we control in the operating room and ICU is disordered sympathetic responses. Despite much research on the central nervous system, less is known about the peripheral nervous system. It is not simply a scaled down version of the CNS.

What are you working on currently?

I initially pursued a transgenic mouse project involving beta1 and beta2 adrenergic receptors. I received a FAER New Investigator Award for this project; however the transgenic mice failed to reveal an expected phenotype. I then decided to return to my neuropharmacology roots and shifted projects towards an analysis of alpha2 adrenergic receptor function in the sympathetic nervous system. The alpha2 adrenergic receptors are activated by the catecholamines and activation acts as ‘brakes’ to decrease further release of neurotransmitter. Interestingly, the body has two genetically-related alpha2 adrenergic receptors (e.g. alpha2A and 2C) that have overlapping, but distinct functions. We use sympathetic neuron cultures, combined with molecular and cellular techniques to probe the differences between these two proteins. Presently, there are no drugs that can discriminate between these two receptors. We need to determine if there really would be any role for such a drug. One interesting offshoot is the recent finding that certain genes have been linked to pain, specifically the alpha2C

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Research Update 3 - Tim Angelotti

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receptor. Further understanding of the pharmacological and physiological differences between these receptors may be important not only for understanding the body's response to stress, but also pain.

It would appear I have an affinity for anything "alpha2," since my other research interest is in a protein component of the calcium channel, the alpha2-delta subunit. I started work on this protein while in Germany, at a time when it was believed to be merely a structural protein that held the channel complex together. Recent work has shown that it is site of action of the drug gabapentin and pregabalin, two very important drugs for chronic pain. To date, no one has exactly figured out how these drugs work. However,
evidence suggests that they also modulate neurotransmitter release.
I find it really interesting how my two independent lines of research have actually come together under the theme of neurotransmitter release regulation.

Tim Angelotti

What do you see as the career development challenges for junior faculty?
Balancing clinical responsibilities with academic interests, whether they are bench-based or translational science. The time when academic institutions could afford to float the academic career of early stage junior faculty has passed; the time line for success has been shortened. By front-loading my career with my research training, I was able to overcome many of the obstacles. However, I am dependent upon external grant funding such as NIH, and times are tight from the added demands to the federal budget. With proper mentoring, another limited asset, these problems can be overcome, but it requires dedication and discipline.

On a personal note, what do you like to do in your "free time"?
I like getting my saxophones out of their cases and getting back to playing. I also enjoy athletics, either as a spectator (I am a faithful Notre Dame alum) or as a participant (e.g., sea kayaking and golf).

What is the best book you've read?
I prefer non-fiction, since there are enough strange stories in the real world. I do not know if I can name a single "best book." Recently, I read "The Devil in the White City" by Erik Larson, concerning this country's first serial murderer from the Chicago's World Fair of 1893. I also recently finished "Catch 22," since I never had read it before, and it is such a classic. However, in terms of a book that changed how I view my world, I would recommend "The 48 Laws of Power" by Robert Greene and Joost Elffers. Similar to Machiavelli, this book annotates various power plays with real historical context. It taught me much about how people use power to their own advantage.

What was the first music record you bought?
The first album I ever purchased was the original Decca recordings of Count Basie and his orchestra from the 1930's and 1940's. Being a sax player, I am attracted to big band and swing. My parents had the early recording of Benny Goodman and his famous, jazz-altering Carnegie Hall concert of 1938. However, my favorite swing band is Jimmie Lunceford, who died way too young. He would have been bigger than the Duke or Count Basie. I search old record stores to find his original albums, of which I have two.

What is your favorite vacation spot?
Though I love Hawaii, my favorite vacation spot would have to be old Europe. I greatly enjoyed my travels there during my time in Germany. I can achieve a relaxed feeling in almost any old city, sitting at a sidewalk café; a feeling that is much more difficult to achieve in our busy, overly-wired country.

Research Update 4

Interview with David Yeomans

David Yeomans, PhD, Director of Pain Research

Danielle deLeon (Dd): What areas of research are you involved with currently?

David Yeomans, (DY): I am interested in: 1) gene therapy for chronic pain. We use viral vectors to selectively alter the genome of pain-sensing neurons, thus decreasing pain in a regionally limited area; 2) physiology of pain-sensing neurons. We focus on the differences (in animals and humans) in the anatomy, physiology, and pharmacology or pain evoked by the activation of different types of these neurons; and 3) The involvement of different sodium channel types in different pain states. We dissect which of the ten known type of sodium channels are involved in which types of pain (inflammatory, neuropathic, etc.), which, in turn, serves to validate these channels as targets for drug development or gene therapy.

Other collaborative research at Stanford includes studies with: 1) Martin Angst and Wendye Robbins to examine human interstitial fluid or skin biopsies for biomarkers that may be diagnostic of pain conditions or predictive of success of potential pain therapies; 2) Sean Mackey examining differences in spinal cord and cortical activity induced by activation of different types of pain-sensing neurons; and 3) Dave Clark of rodent skin for biomarker molecules, which coincide with skin wounding and hypersensitivity.

I have four NIH grants, a grant from Stanford's Office of Technology Licensing, and was recently asked by the liaison officer at Johnson and Johnson to submit a grant application to fund some of my ongoing research.

Dd: What do you enjoy most about your work?

DY: I love bringing people together and building synergies - finding someone you think is doing great work but has not thought of the application of what they do to something in another field. For example, someone may be working on memory. A lot of circuitry and biochemical similarities exist between memory and chronic pain. A lot of the same processes happen and with the same neurotransmitters. Something that possibly inhibits memory, which you do not normally want to do, might work well on inhibiting pain. On the other hand, something that promotes pain might promote memory. If putting those two together works, it is a beautiful thing. One plus one is more than two.

I still also get a huge thrill when there is a result that is unexpected or that is really amazing - one of those Eureka moments. I still have a very active laboratory. And I still enjoy teaching the post docs.

Dd: What is the Working Group in Pain?

DY: The Working Group in Pain (WGP) is one of several working groups within the Neuroscience Institute at Stanford (NIS). Other groups center on Parkinson's, Alzheimer's, and Epilepsy, for example. Membership in the WGP is open to anyone at Stanford interested in pain research and management.

Dd: When was it created and by who?

DY: A little background first. I was hired in September of 2000 to coordinate pain research, foster collaborations, and help some of the less-experienced faculty within our department with their research efforts in pain. The department under [chairman] Ron Pearl's leadership had decided to focus on pain research as a growth area for Anesthesia. I was brought in to boost that.

I also started getting myself involved with the neuroscientists here. Bill Mobley [MD, PhD, director of the NIS, and chair of neurology] had been working with Dick Tsien [PhD, professor of molecular and cellular physiology] and Gary Steinberg [MD, PhD, Lacroute-Hearst Professor, and neurosurgery co-director,] and wanted to form a group to encourage interactions between the clinicians and basic neuroscientists. It was called the Stanford Brain Research Center (SBRC) to start; this is now the NIS. They sent out letters asking for people who wanted to be involved and, of course, I jumped at it. I was asked to be on the SBRC steering committee, partly as a liaison towards the clinical scientists.

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Research Update 4 - David Yeomans

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David Yeomans

The idea was to bring in money, have space and faculty lines, and build up certain areas of neuroscience. We called these areas of concentration Working Groups. Initially there were four Working Groups, pain being one of the areas.

Dd: What is your role within the WGP?

DY: Sean Mackey and I serve as co-directors of the WGP. Our mission is to foster collaborative research to translate pain investigation performed in the laboratory to patient care. We also intend to enhance professional pain education, fundraising, and outreach to the community to raise awareness of pain.

Dd: What are the initiatives of the WGP?

DY: Dave Clark, Martin Angst, Sean Mackey, and I have worked with Bob Parsons, a community speaker for the Stanford Neuroscience Institute, to develop a layman's talk to be given at community gatherings (e.g., the Cupertino Senior Center, Little House in Menlo Park, and other bay area senior groups), Rotary clubs, Stanford alumni, and targeted companies. Typically, Bob is our spokesman, but sometimes one of us goes along to help. For example, Bob and I are giving a presentation on "Understanding Pain" at the Stanford Health Library. Something I try to impress upon the audience is that pain is not just a nasty feeling. It has profound effects.

For example, adequately treating cancer pain halves the rate of metastasis and halves the rate of tumor growth. You are actually treating the disease by treating the pain. Pain is a huge stressor that inhibits the immune system, the first line of defense against cancer. It makes sense, but you do not normally think about pain like that. Pain is perceived as something you have to "deal with" - grit your teeth. We want to promote a greater understanding of pain and why it is important to treat pain.

Second, we have initiated a pain science speaker series, supported by the NIS, with the idea of increasing Stanford and outside community understanding of the challenges of pain. Continuing education credits will be awarded.

Third, we are developing a relationship with Amgen, the world's largest biotech firm, to develop forums for an open exchange of ideas between Amgen and the WGP, with substantial support from Amgen for our human pain research work.

Dd: What are the major challenges so far?

DM: Our biggest challenges are to develop a cohesive set of major initiatives agreed upon by the WGP membership and to find financial support. For example, WGP members focus on diverse areas of pain research. These foci have been dictated by the researcher's experience, expertise, and, most importantly, by the availability of (usually NIH) funding. Thus, it takes a mind shift for independent investigators to come together to work upon an overriding, agreed-upon, research goal. The goal might be pain pharmacogenetics allowing customization of drug therapy to the genetics of a patient; or, it might be gene therapy for chronic pain. The difficulty of having many successful ongoing projects is figuring out what to put resources behind and encourage communal efforts on. The best way to do this is to bring in substantial donor funding. It is easier to obtain this funding if we have a cohesive group goal. On the other hand, a donor may bring their specific interests and goals to the table, which could, again, redirect efforts.

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Research Update 4 - David Yeomans

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Another major challenge is to expand the efforts of the WGP to be more inclusive of others who are early in their research careers or who are primarily clinicians but who wish to become more knowledgeable in pain research. Thus far, a few, fairly accomplished and senior, clinical and basic pain scientists have done much of the effort. We need to bring in others with the goal of furthering their careers.

Dd: What are your goals for the WGP?

DY: We hope to attract enough donor funding to develop translational pain research and pain education at Stanford. We already have a unique situation here, where clinicians and the basic scientists interact toward common goals. This is unusual in the pain research world. Our capacities to do human pain research are quite unique and should allow more rapid progress toward therapies. Part of this goal will involve acquisition of new research space within the soon-to-be built Stanford Institutes of Medicine building and recruitment of additional pain scientists with an interest in translation. In addition, we hope to initiate a new physician-scientist fellowship tract. The typical pain fellowship is one year, heavily clinical, with minimal opportunity for research. We would develop a second, two-year tract, wherein physicians wishing to develop as scientists will get time to do research.

In order to facilitate translation, we hope to develop long-term commitments from existing industries as well as with venture capitalists and the Stanford Office of Technology Transfer. We hope to provide sustaining funds and bring new pain treatments, developed at Stanford, to broad use.

Dd: On a more personal note, if you have any, what do you do in your free time?

DY: Not much. I have four children. My oldest is graduating from culinary school, my second oldest will be going to college, my third will be a high school sophomore, and my fourth is in seventh grade. I enjoy working on and racing my car (a 1995 BMW M3), scuba diving, and fishing and hiking with my wife and kids.

I am also in the process of starting two companies. Both of these are based on technologies we developed at Stanford and will be licensed through the [Office of Technology Licensing]. The first of these involves viral vectors that enable the possibility of gene therapy for chronic pain patients. The second involves a unique means of applying certain analgesic drugs to the trigeminal nerve complex for the treatment of dental pain, migraine, and temporomandibular joint pain.

Research Update 5

Stanford to Test Effects of Drug Widely Used for Pediatric Hypertension: Work Fills Gap Left by Pharmaceutical Industry

(Courtesy of Stanford University Office of Communications and Public Affairs)

STANFORD, Calif. – The National Institutes of Health awarded the Stanford University School of Medicine a $4.3 million contract to test whether a drug commonly used to treat hypertension in pediatric patients actually works safely and effectively in children. It's the second contract under a federal program established to address the pharmaceutical industry's failure to study certain drugs in infants and children both at the time the drugs were approved for use in adults and specifically after the drugs' patents have expired.

The Stanford researchers will study a hypertension drug commonly used in pediatric surgery and pediatric intensive-care settings. The work is needed because the company that invented the drug some 30 years ago never studied its effects in pediatric patients. And after the drug's patent expired, its price dropped so low that no company will invest further resources studying it.

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Greg Hammer

Research Update 5 - Greg Hammer and David Drover

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"We should know as much about the science of how drugs work in children as is known in adults," said Greg Hammer, MD, professor of anesthesia and pediatrics and associate director of the pediatric intensive-care unit at Lucile Packard Children's Hospital at Stanford. "These studies will provide that information." Hammer is principal investigator on the contract.

"Unfortunately, pediatric patients aren't just small adults," said David Drover, MD, assistant professor of anesthesia and co-investigator of the study. Kids respond to drugs differently and also break down and excrete drugs differently from adults. And drugs have different toxicities in neonates, infants, children and adults.

Historically, companies avoided testing in pediatric populations either because they didn't want to risk injuring children or didn't want to risk finding out that drugs deemed safe and effective in adults weren't so safe or effective in kids, said Drover.

"The truth may be that by not studying drugs in children, young patients have been left vulnerable to inappropriate or unsafe treatments," he said. "Clinicians are using trial and error on a case-by-case basis around the world – exposing kids to more risk than if the companies just did the studies in the first place."

After a few drugs approved for adults were shown to be toxic in children, pediatricians pressured the Food and Drug Administration and Congressto mandate drug studies in children. In 2002, Congress passed the Best Pharmaceuticals for Children Act. For drugs still under patent, the law offered companies a patent extension if they would conduct specified studies in kids.

But for drugs with expired patents (so called "off-patent" drugs), another solution was needed. "Drugs that are off-patent have no value for big pharmaceutical companies," said Drover. "The profit margins are extremely low. And that means someone else now has to pay for the investigations that the companies never did in the pediatric population."

Under the 2002 law, that "someone else" is the federal government. Thus far, the FDA has created a list of 25 off-patent drugs needing clinical testing and has issued nine written requests asking pharmaceutical companies if they will do the work. When the companies decline, as they are almost certain to do, the NIH's National Institute of Child Health and Human Development steps in to fund the work. So far research contracts have been granted for just two drugs.

David Drover

Under the contract awarded to Stanford, Hammer and Drover will spend three years conducting clinical and laboratory tests to determine the safety and effectiveness of sodium nitroprusside. This drug works to control blood pressure during anesthesia and in the intensive-care unit. The FDA listed it for testing because it is known to produce cyanide – the toxin people associate with suicide pills.

"There are early reports from years ago of patients dying of cyanide poisoning," said Drover. "So we know about the risk, but no one has ever really measured the drug's toxic effects in kids." The study will aggressively record cyanide levels in the blood of pediatric patients given nitroprusside.

According to Hammer, "It may be difficult to appreciate whether certain adverse changes are attributable to the drug rather than the underlying illness or another drug being given at the same time. That's why nitroprusside needs to be studied in a systematic fashion."

In addition to testing the drug's toxicity, the study will determine the right starting dose for infants and children of different ages and sizes, how much a particular dose affects blood pressure levels and whether it's safe to use the drug in pediatric patients for more than 12 or 24 hours.

"The competition for this contract was stiff," said Drover. In fact, Stanford wasn't the only winner – Duke University will study nitroprusside as well.

Hammer and Drover plan to write proposals for additional off-patent drug contracts in the future. "It's going to be a long, slow process catching up with these drugs that have been long out of patent," said Drover.

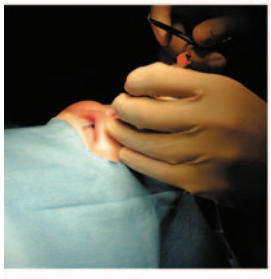
International Medical Missions: No Act Too Small

By Danielle DeLeon

No act of kindness, no matter how small, is ever wasted.
Aesop (620 BC - 560 BC), The Lion and the Mouse

In an effort by physicians in the Department of Anesthesia to contribute on a global scale, many international medical missions are dispatched yearly to underdeveloped countries in the hopes of improving, and often saving, the lives of the indigenous populations. Two faculty actively involved are Drs. Andrew Patterson and Dr. Alice Edler.

Andrew (Drew) Patterson, MD, PhD, assistant professor, volunteers for three organizations: Hospital de la Familia, Medical Missions for Children, and Interplast. These organizations provide a range of free surgical care throughout the world for children and adults who would otherwise not be able to get help. For example, based in Massachusetts, Medical Missions for Children (MMFC), Inc. is a nonprofit organization. The emphasis is to provide reconstructive surgical and dental care to children with severe congenital deformities. MMFC also focuses on education of health care professionals both here and abroad. All MMFC volunteers (surgeons, medical specialists, dentists, and nurses) are licensed and certified.



Cleft lips and palates, which are easily repaired in the United States, can lead to malnutrition, delayed speech development, and ostracism in many third world nations. In some countries, there are superstitions that if a pregnant woman sees a child with a cleft palate or lip, her child will be born with a cleft. Patterson adds, "Little kids with cleft palates, especially in these countries, can not eat well. Since they can not take adequate nutrition, their growth may be stunted. Eventually they may be too small to work. A cleft palate repair gives these kids a chance in life."

Sometimes, however, there are limits to what can be done. On one trip to a village in the jungle highlands of northern Guatemala, a woman presented 24-weeks pregnant in active labor with a breech presentation. Obstetricians working with Patterson and his team delivered the baby, but there was nothing they could do to save him. "We just had to hand the baby over to the mother and the baby died. Life is different in those places. In the United States, he would have gone to the neonatal intensive care unit, and he might have survived. In rural Guatemala, that just does not happen."

But for those who can be helped, the contribution is lasting. Patterson tells of a man who had his cleft palate repaired. "He eventually moved to the United States, became a physician, and is now a plastic surgeon. These kids can contribute to the world."

International Medical Missions: No Act Too Small

Patterson has been going on medical missions since the mid 1990s, but he had wanted to participate since high school after seeing a *60 Minutes* special focusing on Interplast. He is soon to embark on his seventh mission, this time in rural Guatemala with Hospital de la Familia. The team will perform gynecology surgeries, general surgeries, facial plastic and burn surgeries, and ophthalmology surgeries. Pediatricians with the team will also see patients in a makeshift primary care clinic.

Patterson traveled with Bridget Philip (pediatric anesthesia fellow) and Peji Ghanouni (medical student) to Cusco, Peru with Medical Missions for Children in 2004. Three Stanford ICU nurses, as well as Santa Clara Valley plastic surgeon, David Kaufman, completed the medical team.

During this trip, the team performed approximately thirty operations, running two surgeries simultaneously in one large room within a hospital in Cusco. This is the oldest city in the Americas, filled with history and roaming llamas around every corner. "It was amazing to witness the appreciation in the eyes of the Peruvian people who took such good care of their children with the very little that they had to their name," said Dr. Philip. "One mother actually carried her child four to five hours to reach the hospital. Another mother and her child were flown out from the jungle by an oil company that had recently tapped into an oil supply close to their village. This experience was one of the most special things I did during my training at Stanford. I learned more in one week than in probably one month of residency!"

On average, Patterson participates in medical missions once a year for up to three weeks. As always, he will bring a student and a Stanford Anesthesia resident. This year, Jeremy Pearl (son of Dr. Ron Pearl) will be the student, and Dr. Amy Evers will be the resident.

Alice Edler, MD, Assistant Professor, focuses on Sub-Saharan Africa where, in conjunction with the American Society of Anesthesiologists (ASA), she volunteers in any capacity that she is needed. From painting black boards in order to teach anesthesiology, to erecting stop signs to reduce medical emergencies caused by traffic accidents, to negotiating with the Minister of Health about financial assistance for the medical schools, Edler is well known for her contributions. She adds, "If you call the ASA and you lose my name, just ask them for the lady who goes to Africa." One of Edler's past triumphs included convincing the Minister of Health to aid the only MD anesthesia provider trained in Africa. "There are approximately seven or eight anesthesiologists in Sierra Leone, and all of them had come from France. I negotiated with the Minister of Health to get the guy from Sierra Leone out during the war so that he could train. That was difficult."

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International Medical Missions: No Act Too Small

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Edler's other challenges lie simply in recruiting enough people to go with her - each mission is a month long. She and her teams also face a drastic lack of resources. Without adequate sterile supplies, needles get reused in an area with a high incidence of HIV/AIDS. One of Edler's best friends there died a year and a half ago. "The part that is really hard is watching my friends die." Edler, who specifically went back to school to earn a Masters in Public Health, is a strong advocate for health awareness efforts and trains anesthesiologists about blood borne pathogen safety.

Despite the hardships, Edler values her trips and the friendships she has built. "Families are an incredible stabilizing factor in Sub-Saharan Africa and most African cultures. Learning that and being able to apply that to home is really important." She is entering her sixteenth year of service and will be continuing her valuable work in January of 2006 by going to Rwanda to finalize an agreement with the Minister of Health and open a teaching program at Kigali Institute of Health (the site of the residency program in Rwanda). This is a joint project with the Minister of Health Rwanda, the ASA, and the Canadian Society of Anesthesiologists.

The Rewards Outweigh the Risks

It is no surprise that assistance is urgently needed in many places. Third world nations are in most dire need, especially war torn areas where resources and/or the trained physicians are scarce. Many of the areas that Patterson, Edler, and their teams travel to are unsafe and sometimes require military protection. But both agree that the risks pale in comparison to the rewards.

Andrew Patterson: *"You are working really hard, but when you turn around and see 163 people whose lives have been changed, you realize that it makes a dramatic difference. Just a small effort on your part, two weeks of your vacation, committed to doing something good for somebody, can really change the world. I do not think anybody comes back from these trips who does not feel that every minute invested is worth the effort."*

Alice Edler: *"Women do not get tied to tables for C-sections anymore because of anesthesia. Kids do not have to live with congenital anomalies and be shunned. It just makes me realize that anesthesia is not this very isolated specialty where all you do is go to the operating room but that it has a much broader context."*

Gaba Heads New Initiative for Simulation-based Learning

By Danielle deLeon

On July 1st, 2004, Dr. David Gaba, professor of anesthesia, was named associate dean for Immersive and Simulation-based Learning (ISL). In this role, he defines how the School should use immersive and simulation-based technologies to support Stanford's clinical, research, and educational missions. The School's new initiative will integrate the efforts of the VA Palo Alto Health Care Systems Simulation Cente with the Center for Advanced Pediatric Education (CAPE), Stanford University Medical Media and Instructional Technology (SUMMIT), and the Department of Surgery's Center for Simulation in Medicine (CSIM).

David Gaba

Danielle deLeon (Dd): Why was the Immersive and Simulation-based Learning initiative created?

Dave Gaba (DG): The apprenticeship system we have used for many years in medicine is immersive, but it is limited, inefficient, and not optimized for learning. It is not systematic; there are gaps in the training. For example, many conditions are diagnosed and treated rarely. Inexperienced people receive less and less hands-on experience in taking care of the patients fully because we need to protect patients by having the more experienced people doing the work. Yet how are the inexperienced people going to become experienced? Also, our training focuses on individuals, not on teams, yet we know that teams are most important in safely taking care of patients.

We believe ISL can help fill these gaps. It is not a panacea but a set of techniques. We can allow people to make errors, and we can let those errors play out to their ultimate conclusion without having to intervene and protect the patient. That, too, maximizes a certain type of learning goal.

Stanford has a rich heritage of simulation – nearly twenty years. The intent of the School of Medicine Initiative on Immersive and Simulation-based Learning is symbolic of the School's recognition of the importance of these techniques.

Dd: Describe for me the transitions you had to make from professor to associate dean.

DG: Well, I had to get an office at Stanford - for the first time! I now have a very nice office in the Medical School Office Building. The biggest change was that previously I had a "parochial" view of simulation - interested in "whole patient," "mannequin-based" simulation on teamwork-oriented and crisis-management-oriented issues for interns and residents rather than students. Now, I have a much broader view on simulation, best contained in the article, "The future vision of simulation in health care" in Quality and Safety in Health Care [October 2004]. I am now interested in immersive and simulation-based learning for all the cells of the 11 dimensional space of simulation - ranging from K-12 to professional school students (including medical students, nursing students, etc.) - for a variety of applications, in a variety of domains and disciplines, using a variety of modalities.

For Stanford, this will include (but is not limited to):

- Encounters with virtual and standardized patients for medical students
- Training on basic procedural skills for medical students
- Minimally invasive surgery training for interns/residents and experienced surgeons new to MIS
- Training fellows on new endovascular interventions and technologies

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Gaba Heads New Initiative for Simulation-based Learning

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- Anatomic visualization for medical students
- Combined training of medical students, nursing students, and allied health professions students on patient care processes and settings
- Crisis management and teamwork training for combined teams of experienced personnel (including interns and residents) in settings like the OB, ICU, ED, or OR
- Simulation of actual specific cases for surgical case planning and preparation of teams for novel or tough situations

I was not that interested in some of these applications, but now I am.
Also, I go to a lot of meetings now, many more than I used to.

Dd: What are the current initiatives of the new department?

DG: We aim to conduct formal analyses on the clinical curriculum for medical students and where there are gaps that might reasonably be filled through ISL techniques and on the financial and administrative mechanisms governing funds-flows related to simulation applications across the different target populations of the School and major affiliate hospitals. We also want to educate interested faculty about what ISL can do for them. We aim to subsidize faculty who have not attended simulation scientific conferences and to conduct an annual ISL symposium. Developing new ISL curricula and applications is also important. We plan on fostering the "deployment" into the regular medical student and house staff curricula of key ISL applications.

Dd: What are the goals of the ISL?

DG: The main goals are to revolutionize the training and practice of health care using simulation as a key technology - occupying many of the "cells" in the 11 dimensional space of simulation in health care. We want to embed these techniques in the system as a regular part of the fabric of what we do. This includes routine, continuing training for everyone, regardless of seniority or hierarchy.

On a smaller basis, this means finding the gaps in what we currently are doing in terms of education, training, and practice, and figuring out where ISL can readily fill these gaps. This includes the ability to teach things that we have always thought as important but have never had the means to.

Also, we want to engage interested faculty. The same goes for students. We want them to learn and practice more and better but also to have more fun in the process.

Finally, we want to be able to create the organizational structures and practical infrastructure to make these activities sustainable long term.

Dd: On a more personal note, how do you spend your free time?

DG: I travel a lot - mostly on business, but with some nice side trips tacked on occasionally. I read a lot - mostly physics (for fun, believe it or not), current events, science fiction, etc. I follow the space program quite closely, both space science and the manned space program.

Sports-wise, I play golf about once a week - my wife plays 3-4 times per week! We are members at the Stanford Golf Course. We used to ski and scuba dive, but golf has pretty much taken over our joint recreational activities. I have recently taken up fencing (foil) - the third set of beginning fencing lessons in my life. I am finding it interesting, fun, and good exercise. Also, we go to about one to two SF Giants game a month and watch games on TV.

Simulation-based Training at Stanford

By Danielle deLeon

For decades, industries with major respnsibilities for human health and safety, such as commercial aviation, nuclear power production, and the military, used simulation-based training as an essential part of teaching. Those "hazardous domains" industries recognize that crisis management need not be learned as one goes along. Emergency scenarios can be recreated in a safe, practice environment.

A newcomer to using these techniques is medicine. Thanks to the work of Drs. David Gaba, Steven Howard, Geoffrey Lighthall, Lou Halamek, Steve Lipman, and many others, healthcare at Stanford is also reaping the benefits of simulation-based training.

At Stanford, two simulation facilities are in operation: one at the Veterans Administration (VA) Hospital of Palo Alto and one at the Center for Advanced Pediatric Education (CAPE) in the Johnson Center at Lucile Packard Children's Hospital. A third facility, the Center for Simulation in Medicine, is under construction.

David M. Gaba, MD: A pioneer of medical simulation

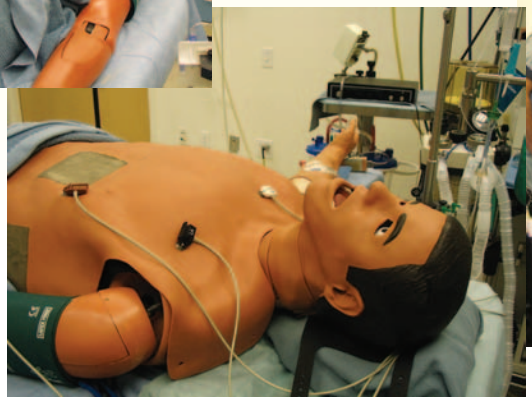
Simulation-based training is not a replacement for the current apprenticeship system, but it is, however, designed to become integral to the everyday work environment. Based on the successes of high reliability organizations, it would seem that the benefits of such training would be obvious, and yet measuring those benefits remains difficult.

David M. Gaba

Dr. David Gaba, professor of anesthesia and, now, associate dean for Immersive and Simulation-based Learning, felt the need to utilize simulation-based training in the mid-1980's. After reading "Normal Accidents," by Charles Perrow, a book about the accident at Three Mile Island, he was struck by the similarities between the power plant or the OR. In both places, accidents often were the result of faulty decision-making and communication breakdown between staff.

Traditional decision-making studies in medicine were not particularly helpful – most were about "static" decision-making settings rather than the dynamic environment of the OR - or the ICU or ED. Gaba understood that patient simulators were suited to challenge and probe clinicians in these environments. Doctors would be able to make decisions based on theoretical situations and work on the next best thing to "actual" patients.

Patient simulation started at the VA Hospital of Palo Alto in 1986 by Gaba and one of his students, Abe DeAnda Jr. The first pre-prototype



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Simulation-based Training at Stanford

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patient simulator was assembled out of a modified head and neck intubation mannequin. They used an off-the-shelf waveform simulator - the kind that biomedical engineers use to test monitoring equipment - to generate ECG waveforms, and an in-house stimulator (donated by the device manufacturer) to send signals to a pulse oximeter.

Gaba also created a "virtual blood pressure cuff" that behaved like the actual instrument by sending it information from a computer. The virtual instrument displayed readings just as if blood pressure were actually being measured. This simple simulator was enough to do a trial scenario and collect data on how an anesthesiologist dealt with a critical event. The current mannequin models are more advanced, with details such as dilating pupils, and dual "computer-controlled lungs." Some mannequins have the ability to bleed as with massive hemorrhaging.

For the same reasons a teacher does not divulge the answers before a pop quiz, current scenarios are confidential. Gaba did, however, describe a "ruptured abdominal aortic aneurysm," a life threatening bleed from the aorta. In the scenario, the patient is brought from the ED directly to the OR. The surgeon, anesthesiologist, and nurses, all arrive at the OR at the same time. They rush to get the patient anesthetized, with IV access for large-volume fluid resuscitation. The surgery gets under way quickly. Gaba says, "We often let multiple members of the anesthesia team in the room all at once, because learning how to manage many helpers at one time is a key skill." In addition to the OR, there are also simulator scenarios for the ED and ICU cases.

Steven Howard

Steven Howard, MD: Teaching teamwork in crisis management

Dr. Steven Howard, associate professor of Anesthesia, and Gaba's academic partner and office neighbor, is also associate director of the Patient Simulation Center of Innovation (PSCI) and Simulation Center of VA Palo Alto. Howard, along with Gaba, teaches Anesthesia Crisis Resource Management (ACRM) which focuses on the teamwork/communication/leadership aspects. In a crisis situation, there is no time to stand aside and teach a medical student what to do; a more experienced doctor must step in and the student has to learn by "osmosis." In contrast, in the simulated environment, students can lead or participate in an entire emergency situation and learn how to respond without the risk of harming a patient. Howard also uses the simulators to research the effects of fatigue on performance.

The first ACRM course was taught in Fall of 1990 to a dozen residents. Training involved lectures on human factors and dynamic decision-making, videotaped training using the simulator (done in a real OR since there was not a dedicated simulator center yet), and then debriefing. The scenarios were similar to what is run today, each one lasting 20-40 minutes, typically involving a major crisis situation.

Four years later, Howard teamed up with Gaba and Kevin Fish, MSc, and published a textbook, *Crisis Management in Anesthesiology*, focusing primarily on the mind of the anesthetist - nurse or physician - and how to understand, prepare for, and manage the complex decisions demanded in crisis situations. A second edition is in the works for next year. The still very popular first edition has been translated into Japanese, German (by colleague Dr. Marcus Rall), and Russian.

The current course has been whittled down from a two-day course involving twelve students to a one-day course involving four or five students and reflects a more integrated and sensible format that better captures the key teachings of the textbook. This type of training has been adopted at other centers in North America, Europe, and Australia, and the goals of PSCI are the same as when they started: Continue to innovate, educate, train, perform cutting-edge research, and collaborate both in this country and abroad.

Geoffrey Lighthall, PhD, MD: ICU simulation ongoing

Dr. Geoffrey Lighthall, Assistant Professor, first got into simulation-based training as part of his residency at Stanford. Lighthall reflects. "I remember when I was interviewing here for residency, they talked about simulation training and the significance did not quite click. After I became a resident and

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Simulation-based Training at Stanford

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Geoffrey Lighthall

learned that you can harm a patient, this training seemed indispensable. You learn the pitfalls of your own practice and make corrections before real problems occur. I could not stop thinking, 'this is something great and has great applications for critical care.'"

Once Lighthall joined the faculty, he contributed to the ICU crisis simulation course already in place. He has since started a monthly, ongoing "nuts and bolts" class for medicine residents on ICU rotations on how to manage different types of clinical emergencies. A course for medical students on the ICU service also exists.

Lighthall is also developing a medical emergency team that will expedite the care of patients on the ward who are deteriorating (e.g., patients who have low blood pressure, high heart rates, unclear diagnoses, uncontrolled pain, changes in mental status, etc). Simulation training will be used as a way of developing a "playbook" as to what this team will do in each emergency type.

Lighthall talks about the future, "I would like to see us continue to grow and lead critical care education and simulation.Getting more research projects going, looking at different ways of showing the good and bad of educational and training methods, and trying to apply the best clinical practices to make sure people are doing things right are all important areas in which we can contribute."

Lou Halamek, MD: A pioneer in pediatric/ obstectric simulation training

Dr. Lou Halamek, associate professor of pediatrics in the Division of Neonatal and Developmental Medicine, developed the Center for Advanced Pediatric Education (CAPE), which is the world's first simulation center dedicated to pediatrics/obstetrics. Halamek's interest in simulation can be traced back to a lifelong fascination with the space program and his experiences as a college athlete. These events intersected with his career in medical education in 1995 when, at a meeting in Colorado, he listened to a discussion about OR simulation and noticed similarities between the OR and the delivery room where he was working as a neonatologist. The speaker was none other than Dr. Dave Gaba.

Halamek quips, "I traveled 1,300 miles to Colorado to hear someone that I could have traveled twenty minutes down the road to talk with." That began a continuing collaboration with Drs. Gaba and Howard, in developing a pediatric and obstetric simulation program.

The first program in 1997 was run out of the VA Hospital basement, but, due to proximity issues, the program was moved to CAPE in 2002. Halamek explains, "The reason we call it CAPE is because it is a direct reference to Cape Canaveral and the aerospace program. We are paying homage to the people who have been doing this for fifty years and set the stage for those of us in medicine to follow their lead."

Halamek - in collaboration with Sue Flanagan, COO, LPCH, Paul Sharek, MD, director of patient safety, LPCH, Sandy Trotter, quality assurance, LPCH, and Lisa Wise, head of the Parent Advisory Group at LPCH - is also working on training directed at healthcare professionals who must speak with patients, parents and families when unintended consequences of therapy arise. This unique program will be tailored for different areas of the hospital; the first will involve the hematology-oncology floor. Their pilot program will be presented to a national audience at the annual meeting of the National Association of Children's Hospitals and Related Institutions.

CAPE offers an array of additional training programs to medical professionals (physicians, nurses and allied healthcare personnel) at all levels of experience (students, residents, fellows, faculty and community practitioners) including neonatal resuscitation, pediatric resuscitation, delivering bad news, and ECMO (extracorporeal membrane oxygenation). Registration is available at http://www.cape.lpch.org.

The overall goal of Halamek's team at CAPE is to be the world's first and foremost training center in fetal, neonatal, pediatric, and obstetric simulation. While being the world's leader is a motivator, it is not the main driving force. In a recent speech at the public launch event for the Immersive and Simulation-Based Learning initiative, Halamek stated, "The reason we do this is not about the technology. We do not do this because of the methodology and all the wonderful human-performance research we can do. We do this because of our patients. We do this for you, for your kids, and for your families."

Simulation-based Training

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Steven Lipman

Steven Lipman, MD: ObSim update & high-risk obstetric database

In an article in last year's *Stanford Anesthesia News*, Steve Lipman, MD, clinical assistant professor, said, *"Since the performance of the team (nurses, physicians, and technicians) is critical to patient outcome in a crisis, team-oriented simulation training makes sense."* Lipman was referring to NeoSim, a simulation-based, crisis management training program focusing on neonates and created by Dr. Lou Halamek. NeoSim has been used since September 2003 to certify every anesthesia resident as a Neonatal Resuscitation Provider (NRP), the neonatal version of advanced cardiac life support (ACLS).

ObSim: Teaching team work in obstetric crisis

Building on the success of NeoSim training for the residents, Lipman, along with Leslie Andes, MD (OB anesthesia fellow), Kay Daniels, MD and Kim Harney, MD (obstetrics), Julie Arafeh, RN, MSN, Andrea Puck, RN, MSN, Ann Ronayne, RN, BSN, and Gloria Santos, RN, BSN, MN (labor & delivery), Kim Yeager, RN, BSN, Allison Murphy, MD and Lou Halamek, MD (neonatology), and Maurice Druzin, MD (maternal fetal medicine) are close to launching ObSim, a new simulation-based training program oriented to obstetric crises. ObSim differs from NeoSim in that both the mother and baby are focal points.

The Labor and Delivery Ward at Lucile Packard employs approximately eighty different nurses and technicians. Six different private obstetrician groups, a County service, and a University service all have privileges there, and there are over 5,300 deliveries per year. The volume, acuity, and multiple personnel result in a dynamic domain.

ObSim requires care providers from obstetrics, nursing, neonatology, and anesthesiology to communicate, triage, and act while contending with stressors such as time pressure, auditory overload, task saturation, concerned family members, high stakes, and the technical and ethical problems associated with caring for two patients. The course integrates elements of maternal ACLS, NRP, and fetal monitor interpretation. The goal is to simulate a sick fetus inside of a sick mother being cared for by the obstetric team. The sick fetus is then delivered, and the pediatric team then assumes care of the neonate. All of the individuals (obstetrician, maternal-fetal medicine specialist, obstetric anesthesiologist, labor and delivery nurses, pediatrician, neonatologist, and neonatal nurses) on these teams must work together to deliver integrated care to these two patients. This represents the first and only program in the world that offers this type of high fidelity team training.

ObSim has been difficult to develop because of its scope and the associated logistical problem of getting so many people together on a regular basis. Indeed, one major difficulty often found in responding to obstetric emergencies is that many individuals from multiple medical disciplines are present and have to work together despite different priorities and often little previous team exposure.

For example, a "stat" cesarean for a fetal deceleration in a patient with a non-reassuring airway is an example of how best care for the unborn baby may place the mother at risk. In order to render best care, the team must quickly communicate, and formulate a plan, and act - precisely the purpose of training.

ObSim training for the residents will begin this Fall, 2005. The trainees will be among a small group in the nation who receive simulation training in adult, obstetric, and neonatal crises during their residency. Eventually, ObSim will be offered to both private and academic practitioners.

High-risk obstetric database: Optimizing patient safety

Lipman is also working on a high-risk obstetric database. The system will also be used to create material to drive ObSim. He has been collecting data from the obstetric anesthesia service since 2001. However, managing the data became overwhelming using the paper-based format. For example, Lipman could tell you how many parturients required disposition to the critical care unit, but if you wanted to know if there was an association between advanced maternal age and such disposition, he would have to leaf through hundreds of pages.

As a result, he went to Nancy Federspiel, PhD, director of strategic research development, who put him in contact with Susan Weber, a programmer for Stanford University School of Medicine working in the systems development and data management group in the Department of Information Resources and Technology. Together, they are designing a structured data entry and reporting system for obstetric anesthesia encounters that is fully HIPAA compliant.

The core of the application is an eight-page input form incorporating approximately three-hundred distinct factors used to create the record of a single high-risk patient encounter. Both patients and encounters, once created, can be located and edited independently. All encounter data is available as an exported Excel spreadsheet, one encounter per row, for final analysis.

Airway Management Training: An Interview with Dr. Vladimir Nekhendzy

by Danielle deLeon

Proper airway management - providing adequate oxygenation and ventilation for the patient - is the most crucial aspect of anesthesiology. Failure to do so, for even a brief period of time, can be disastrous. In fact, excluding dental damage, the single largest category of anesthetic-related injury is respiratory events.

Vladimir Nekhendzy

Danielle deLeon (Dd): What is your background in airway management training?

Dr. Vladimir Nekhendzy, clinical associate professor of anesthesia and otolaryngology (VN): I started formal airway education for the residents in 1997, during the brief Stanford-UCSF honeymoon, when I organized a combined Stanford-UCSF difficult airway (DA) workshop with the emphasis on fiberoptic intubation. That workshop was conducted mostly by the UCSF faculty, with me serving as one of the instructors. I did my anesthesia residency training at UCSF and was keenly aware of how residents benefit from that learning experience.

In 1998, with the advice and encouragement of Dr. Jay Brodsky [professor], I became in charge of the ENT anesthesia service at Stanford. I developed a comprehensive, structured curriculum for the residents, including many elements of rational difficult airway management, focusing on developing dexterity with different airway devices.

These early efforts gradually progressed to a more specific, detailed, difficult airway training curriculum, which we tailor to the individual skills and expertise of the anesthesia resident who rotates through what has now become a required, combined ENT/DA rotation.

In 2002, I initiated an annual teaching workshop on fiberoptic intubation for the first-year residents, and, starting last year, we added a DA management workshop for senior residents. Comprehensive teaching of DA management and successful conductance of the workshops has been greatly facilitated by the arrival and clinical expertise of Dr. Jeremy Collins [clinical instructor]. Reflecting major expansion of the surgical ENT department, our ENT/DA group currently includes two additional designated anesthesiologists, both highly skilled in DA management: Dr. Cosmin Guta [clinical assistant professor] and Dr. David Drover [assistant professor]. We also have an additional pool of actively involved instructors at our workshops: Drs. Martin Angst [assistant professor], Richard Jaffe [professor], Fred Mihm [professor], and Leland Hanowell [associate professor].

Dd: Why is airway management so important?

VN: When taking care of the patients in the OR, anesthesiologists frequently perform a variety of highly specialized procedures (e.g., placement of intra-arterial catheters, securing central venous access, performing transesophageal echocardiography, etc). However, our expertise in these areas is not unique. Surgeons may be equally skilled in performing invasive procedures, and cardiologists are proficient in transesophageal echo.

Airway management remains the single, indispensable skill that separates us from other healthcare professionals. Airway management is "show time" for the anesthesiologist. What happens after the patient's airway is secured, and how the rest of anesthesia is conducted, usually remains a mystery for the surgeons and the OR personnel. Like it or not, the skill and manner with which the anesthesiologist manages the patient's airway, especially the difficult airway, frequently sets the stage for judging our overall expertise.

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Airway Management Training: An Interview with Dr. Vladimir Nekhendzy

by Danielle deLeon

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Dd: What's the greatest challenge when it comes to dealing with the difficult airway?

VN: There are three general scenarios, each with its own challenges.

The first scenario is when the patient's airway is known to be difficult, before the patient is anesthetized. In this situation, most anesthesiologists would choose an awake fiberoptic intubation as a gold standard. The biggest challenge then would be, while administering judicious sedation to the patient, to meticulously and in a non-hurried manner perform 100% adequate topical anesthesia of the airway. Everything should be done gently to maximize patient comfort and facilitate patient compliance.

The second scenario deals with the situation when the airway was either not recognized as difficult or the awake fiberoptic intubation was not feasible. This means you will have to deal with the difficult airway when the patient is already anesthetized. The greatest challenge in this situation is to be fully prepared. You should have clearly devised back-up plans and all the necessary difficult airway management equipment available. This way, you can move from one intubation plan to another smoothly without creating unnecessary havoc in the OR.

The third scenario is when you are called to help another anesthesiologist. This is probably the most difficult situation - many intubation attempts have already been made, and there is usually blood in the airway, which renders fiberoptic intubation difficult. Everyone is alarmed and upset. You have to quickly assess the situation and find the most acceptable airway management technique. A proper combination of confidence and humility works best.

Dd: Describe the training.

VN: When the resident comes to the ENT/DA rotation, we ask them about their difficult airway management skills. Most residents on the rotation are second or third years and have already been exposed to certain airway management techniques and devices. We perform a "reality check" of their declared competence and, if it is adequate, immediately start teaching alternative techniques.

We always emphasize proper use of "simple intubating aids", which include the gum elastic bougie and the Trachlight™. They are relatively easy to use and will bail you out in many difficult situations. Recently, in view of the studies detailing an indispensable role of the Intubating LMA in difficult airway management, we have started placing major emphasis there.

Each resident has a "checklist" of airway management techniques. How many the resident will be able to learn (or at least get exposed to) depends on the types of the ENT surgical procedures performed during that particular month, the resident's prior expertise and learning curve, and, to a certain extent, the resident's enthusiasm.

Dd: What are your future goals for the program?

VN: I would like to continue to improve the teaching curriculum, with the emphasis on mainstream difficult airway techniques. When they practice in the future, we want Stanford residents to be confident leaders in difficult airway management. Also, we need to identify clinical research projects and get residents involved in them. Finally, we would like to take our expertise outside the department: to create teaching/research projects with the Stanford Emergency Department and Life Flight program, for example. We also aim to conduct an annual difficult airway management workshop for private practice anesthesiologists.

Ellis N. Cohen, MD, MS, Stanford University, Professor Emeritus (1963-1984): One of the Original Leaders of Stanford Anesthesia

By Jay B. Brodsky, MD

Editor's note: Biographies of many emeritus faculty are on our website (http://med.stanford.edu/anesthesia/people/faculty.html#anchor182676)

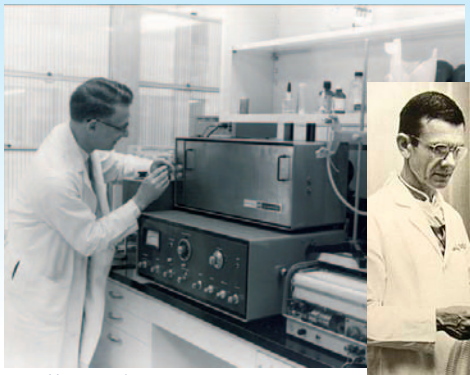
In our library are three bound volumes entitled "Departmental Publications, 1960-1972". Each is filled with papers written by Ellis N. Cohen. Much of the early success our department experienced after its establishment in 1960 can be attributed to one man, Ellis Cohen.

Ellis Cohen was born on June 5, 1919 in Des Moines, Iowa. He graduated from the University of Minnesota in 1941 and entered an accelerated medical school program receiving his MD degree in 1943. He then began a nine-month rotating internship at Detroit Receiving Hospital, which he completed January 1st, 1944. He had only a very brief interval between the end of internship and his scheduled entrance into active army service, and two of these days were spent working in the anesthesia department. He now recalls that this was the start of his anesthesia career.

He served in the Pacific Theatre during the Second World War, rising to the rank of major in the medical corp. He was a battalion and then regimental surgeon, and, along the way, earned "a couple of Purple Heart medals" as he modestly recounted to me.

Upon discharge from active service in February 1946, he returned to the University of Minnesota where he hoped to pursue a career in ophthalmology. There were no openings in the ophthalmology residency program until that July. Ralph Knight who was chairman of the anesthesiology department offered him a position as an anesthesia resident, and he began his formal anesthesia training in April 1946. After completing the two-year residency, he elected to take a third research year and earned a Master of Science degree for work on the broncho-dilatory properties of isoproterenol.

During that year, Henry Beecher, chairman of the anesthesia department at the prestigious Massachusetts General Hospital, visited and lectured at the University of Minnesota. Dr. Beecher met Dr. Cohen, recognized his potential and invited him to come to Boston as a Research Fellow. Ellis accepted and moved to Boston in 1950 to study narcotics and acid/base balance. He shared a laboratory with another promising young anesthesiologist – John Bunker – a man who would have a major impact on his career many years later.



Ellis Cohen, 1964

C. Whitcher and Ellis Cohen

After one year in Boston Dr. Cohen returned to Minnesota as director of the Department of Anesthesiology at the Charles T. Miller & Children's Hospitals in St. Paul.

Under his direction the practice of anesthesia at that hospital changed dramatically. When he arrived all anesthesia services were provided by CRNAs. He recruited only physicians trained in the relatively new specialty of anesthesiology and within a short period physicians provided all major anesthesia services at his hospital. In 1951 at the nearby Mayo Clinic, John Lundy created the first recovery room and intensive care units dedicated to the care of surgical patients. Dr. Cohen recognized the importance of these units and that same year established his own post-anesthesia care and intensive care units in St. Paul.

Even though he was in a busy private practice working in the operating room, recovery room and intensive care units, and providing obstetrical anesthesia, he continued with his research activities. His partners were more than happy to allow him a reduced clinical workload (and less income) so that he could pursue his research.

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Ellis Cohen: One of the Original Leaders of Stanford Anesthesia

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At that time in the early 1950s, Caesarians were performed under local anesthesia. He read an article on recommending cyclopropane and the muscle relaxant d-tubocurare for obstetrics. He modified this technique using thiopental for anesthetic induction, followed by nitrous oxide/oxygen anesthesia and curare. This technique was performed without the benefit of an endotracheal tube. In a paper published in 1953, Dr. Cohen and his colleagues reported no differences in patient morbidity or mortality between this technique and Caesarian section under local anesthesia. In hindsight, general anesthesia and muscle relaxants in non-intubated patients may now sound foolhardy, but at the time there was total acceptance by obstetricians and patients of this technique.

In 1960, the Stanford Medical School, then located in San Francisco, was searching for a Director of Anesthesia. The first two candidates for the position, one of whom was Bill Hamilton who later became chairman at UCSF, turned it down because the school refused to create an independent department of anesthesia. This issue was finally resolved and the third candidate John Bunker, Ellis Cohen's friend and former laboratory associate at the MGH, was appointed the first chairman of the new Department of Anesthesia at the Stanford University School of Medicine.

Dr. Bunker invited Dr. Cohen to visit Stanford with the goal of recruiting him to join the department. Dr. Cohen did not want to do clinical work preferring to devote all his time to research. They negotiated a compromise and Ellis Cohen was appointed Associate Professor. His clinical commitment was one day a week leaving four days for research. In 1960, Dr. Cohen left Minnesota and brought his wife Sylvia and their 3 young children to California.

Initial growth of the department was slow. After three years, in 1963, the Department of Anesthesia consisted of three full-time faculty members, John Bunker, Ellis Cohen and J. Belleville. Chuck Whitcher (shown in photo with Ellis Cohen) would soon join as the fourth member.

In 1963 the medical school laboratories moved to their present location in the Grant Building. The Department was given expanded research space on the second floor. Technicians were hired and the department's first full-time research laboratory was opened. Dr. Cohen pursued his interest in the muscle relaxant curare. He first developed a spectro-photometric assay to accurately chemically measure curare and its properties, replacing the bioassay "rabbit head-drop test". He then developed a fluorescent assay that increased the sensitivity of the spectro-photometric test ten-fold. Following that, he labeled curare with the radioisotope tritium and increased the sensitivity of measurements 100-fold. He was actually able to localize and photograph radioactive curare at the motor end-plate and motor nerve terminals, thus identifying the site of action of the drug.

As Ellis recently related to me, the department was fortunate to have "lots of federal government grant money". Program Project Awards were federal government grants in amounts greater than $3 million that were initially awarded for research in the fields of surgery and radiology. Manny Papper, the chairman of anesthesiology at Columbia University in New York spent a sabbatical leave at the National Institutes of Health in the mid 60s educating health officials to the importance of the new field of anesthesiology. Because of Papper's efforts, research in anesthesia was added to the medical fields covered by this program. Dr. Papper's department was the first, Robert Dripp's department the second, and Stanford became the third anesthesiology department awarded a grant under this program.

After Dr. Papper stepped down, Ellis Cohen was appointed to the Program Project Awards committee in Washington, and for many years he was the only anesthesiologist among the 20 physicians on that committee.

With grant money available, the department acquired important capital equipment including a gas chromatograph and a mass spectrometer; the latter was the first of these instruments within the entire medical school.

In 1956, the first modern halogenated anesthetic, halothane, was introduced into clinical practice. A severe, often fatal, form of liver dysfunction soon was associated with this drug. Ellis Cohen and his colleagues identified an impurity, dichlorohexafluorobutene, that was present in halothane. In their report published in Anesthesiology in 1965, they postulated that this impurity could be the cause of "halothane hepatitis". The manufacturer subsequently removed the impurity, so we will never know if dichlorohexafluorobutene was the actual the cause of halothane hepatitis. Dr. Cohen served as a consultant on the famous "National Halothane Study" co-authored by two other Stanford anesthesiologists, John Bunker and Bill Forrest.

He continued his research interests on the uptake and distribution of curare and halothane. His laboratory was growing, and the department needed research assistance.

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Ellis Cohen: One of the Original Leaders of Stanford Anesthesia

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Ellis called Stanford chemist Carl Djerassi (the inventor of the birth control pill) who sent several of his post-doctoral candidates to work in the anesthesia department. Winslow Brewer was the first followed by Jim Trudell who was Dr. Cohen's first full-time research associate. Jim is still active in our department. Joan Kendig at first worked as John Bunker's research associate, and then collaborated for many years with Dr. Cohen. Joan recently retired. Joan, Jim and Ellis Cohen published many original papers on the metabolism and distribution of volatile anesthetics.

In 1969 Dr. Cohen spent a sabbatical year in Sweden where he continued his auto-radiographic studies, using radioisotopes to label a variety of drugs (curare, diethyl-ether, halothane). He was able to demonstrate that curare did not pass the placental or blood-brain barriers, that it was eliminated by the kidneys, and for some still unknown reason, that injected curare localizes in the inter-vertebral spaces. When he returned to Stanford the following year, he continued these studies using primate brains. In the 1970s, collaborating with cardiac surgeons Norm Shumway and Ed Stinson, he used radioactive halothane to study its uptake, distribution, and metabolism within various organs of cardiac donors.

In the early 1970s while attending a medical conference in Yugoslavia, Dr. Cohen heard a presentation that associated an increased rate of miscarriages with exposure to general anesthetics. This prompted him to begin his own investigations on the effects of waste-anesthetic gas exposure on health.

After comparing anesthesiologists and operating room nurses (who were exposed to very high concentrations of waste anesthetic gases) with non- exposed pediatricians and nurses, he found a statistically significant increase in pregnancies that ended in miscarriage. That study, published in Anesthesiology in 1971 became the most referenced medical publication of that year.

This study was criticized because other factors, such as the difference in working conditions and stress between physicians and nurses of different specialties, might account for the findings. So Dr. Cohen then turned his attention to dentists and dental technicians. Unlike anesthesiologists who are all exposed to a variety of anesthetic gases (nitrous oxide, halothane, enflurane, cyclopropane), dentists used only nitrous oxide. By comparing dentists who were exposed to nitrous oxide with other dentists who did essentially the same work and were subject to the same job stresses but who did not use nitrous oxide, he again demonstrated a significant increase in miscarriages in the exposed group. This work led to many modern anesthetic practices to reduce pollution in the operating rooms, including the now routine use of gas scavenging systems.

Ellis N. Cohen was as comfortable and competent in the operating room as in the research laboratory. At Stanford, he became the anesthesiologist other physicians requested when they or their family needed surgery. He devoted himself to clinical care and teaching with the same enthusiasm that he brought to his research.

In 1977, when I arrived here after spending two years in the army, I was undecided as to what I wanted to do. Stanford was to be a temporary stop while I considered private-practice opportunities in the Bay Area. Ellis Cohen became my mentor and friend. He got me involved with his occupational exposure studies, and I became hooked on an academic career. I am still at Stanford almost 29 years later because of Ellis Cohen.

After Dr. Bunker left, Dr. Cohen was offered the chairmanship but declined. Although he felt he could be an effective and successful leader, he enjoyed what he was doing and did not want the headaches of running the department.

Dr. Cohen retired, or at least attempted to take early retirement at age 60 in 1979 after suffering from a series of transient cerebral ischemic attacks. He was appointed Professor (Emeritus), but was invited to return to active status. He served as the department's interim chair after C. Philip Larson, Dr. Bunker's replacement, stepped down in the early 1980s. During his time as interim chair, he appointed me, still a junior member of the faculty, as section chief and "scheduler" for the general operating room. I have served in those positions continually since then, so, besides my career in academics, I can also attribute my gray hair and stress ulcers to Dr. Cohen.

Dr. Cohen eventually was able to actually retire in 1984. Since then, he has devoted his time to Sylvia, his three children, and his five grand children. He proudly pointed out that not only his children but each of their spouses have PhD degrees. He and Sylvia live in the Bay Area and occasionally are able attend departmental functions. We continue to recognize his many and unique contributions to this department with the Ellis N. Cohen Award, presented at our resident graduation ceremony each June to a faculty member who has demonstrated the kind of outstanding achievement associated with the name Ellis N. Cohen.

STANFORD ANESTHESIA NEWS

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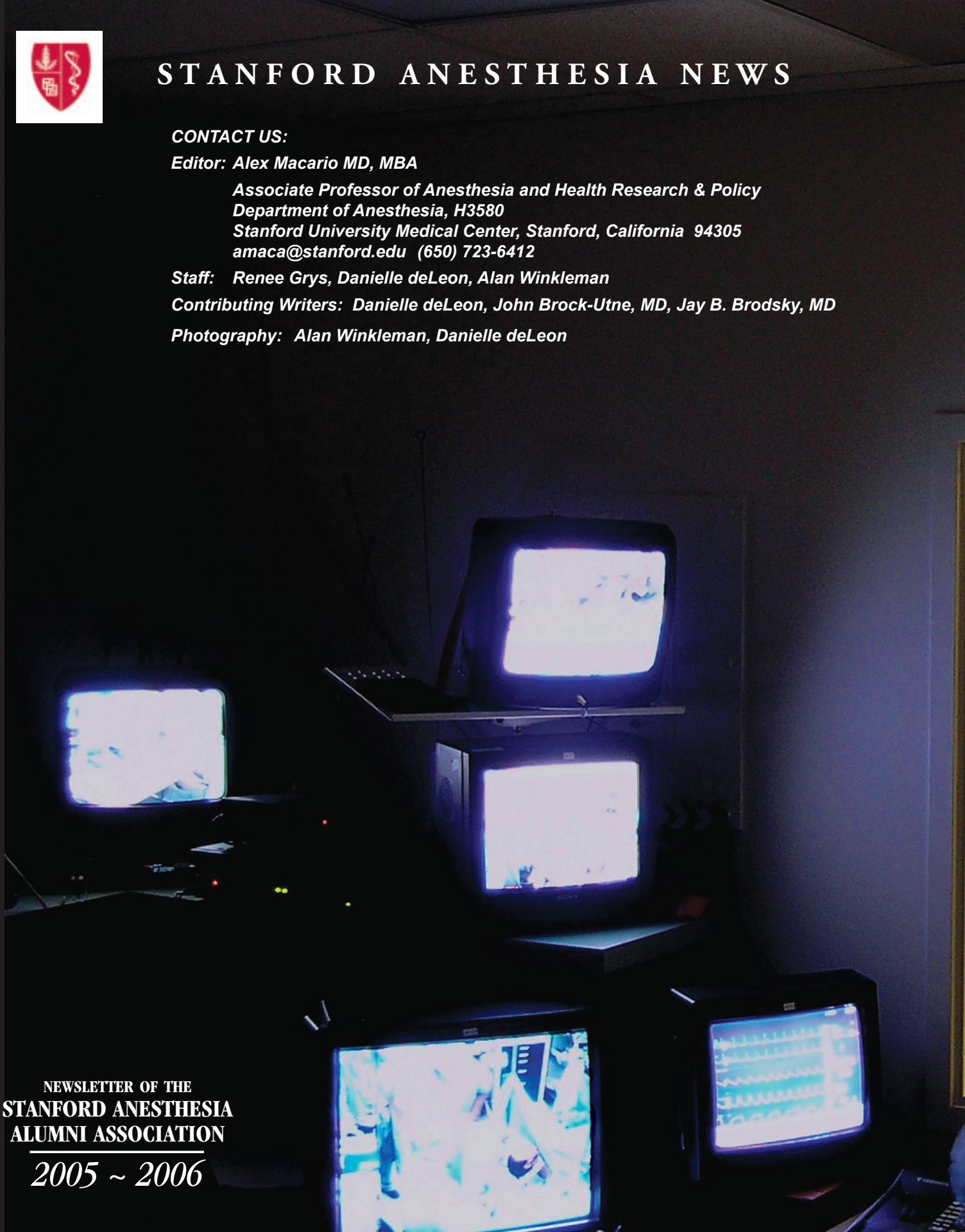

NEWSLETTER OF THE
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