

Integrate Our International Anesthesia Research Potential

To the Editor:—As a junior faculty member committed to becoming an anesthesiology physician scientist, I read the article by Schwinn and Balsler¹ on recruiting and training more of my own with great interest. However, one issue not touched upon either in the article¹ or in the accompanying Editorial View² is that a large portion of recent anesthesiology graduates, including myself, do not hold US citizenship or a green card, but came to the country on a J-1 visa.³ If they manage to obtain a visa to stay on after graduation, this visa will not allow them to pursue research training fellowships, to work part-time to make room for research, or to apply for research training or research starter grants through the National Institutes of Health, because green card status is required for all of the aforementioned pathways. But among these non-American recent graduate anesthesiologists, many are keen to embark on a research career, not

least because it will enhance their prospects to eventually obtain a waiver of the home return requirement inherent in the J-1 visa under which they completed their anesthesia training. We would miss out as a specialty if we do not tap this potential, e.g., by extending the Accreditation Council for Graduate Medical Education accredited fellowships to include an additional mandatory research year (that would hence be covered by a J-1 visa extension) and by lobbying for visa waivers for research trainees in anesthesiology.

Michael H. Andreae, M.D., The University of Medicine and Dentistry of New Jersey, Newark, New Jersey. michael@andreae.org

References

1. Schwinn DA, Balsler JR: Anesthesiology physician scientists in academic medicine: A wake-up call. *ANESTHESIOLOGY* 2006; 104:170–8
2. Knight PR, Wartier DC: Anesthesiology residency programs for physician scientists. *ANESTHESIOLOGY* 2006; 104:1–4
3. Grogono AW: Resident numbers and graduation rates from residencies and nurse anesthetist schools in 2004. *ASA Newsletter* 2004; 68:11

(Accepted for publication May 30, 2006.)

This exchange is accompanied by an Editorial View. Please see: Warner MA, Hall SC: Research training in anesthesiology: Expand it now! *ANESTHESIOLOGY* 2006; 105:446–8.

Anesthesiologist Scientist: Endangered Species

To the Editor:—We should be grateful to our four distinguished colleagues^{1,2} for starting the debate regarding the future of physician scientists in our specialty. The idea to increase the duration of our residency from 4 to 5 yr and to redesign these 5 yr to increase exposure of residents to research is attractive. In Canada and many European countries, the anesthesiology residency is 5 yr. Do we have the basis to think that our residents are smarter than Europeans or Canadians? Or that we as teachers are so much better than Canadian or European teachers that we can teach our future anesthesiologists in a shorter period of time? I don't think so. If we as a society make this decision and try to implement it, the implementation would be associated with some problems. The first one that comes to mind is a financial and political problem: How will the additional year be financed?

An increase in the duration of Accreditation Council for Graduate Medical Education–approved fellowships is also attractive. This suggestion may be risky in some cases: We already have a very low number of applicants to anesthesiology-based critical care fellowships. An increase in the duration of this fellowship by another year might decrease the number of fellows further and may lead to a decrease in our role in overall critical care medicine.

There is another potential problem with extension of residency and fellowship programs. I believe that in the future (maybe in a decade or two), our overall educational system will change. The residency as well as fellowships may become much shorter because of conversion from a structure-based (certain number of years in residency or fellowship) to a competency-based system (certain knowledge and set of skills). The latter may be partially judged by using sophisticated simulators. In that case, if this occurs in the future, the number of years in residency or fellowship would become irrelevant. Still, at that time, we as a community should insist on exposure of the trainees to research.

Exposure of residents and fellows to research is crucial. We are all born with urges to eat, drink, and do other things, but we are not born with the

urge to do research. Only exposure to research and “seduction” by mentors and role models can, and I hope will, increase the number of anesthesiologists who devote their life to a career in science.

I personally believe that despite these and other difficulties and problems, and unavoidable “growing pains,” we should bite the bullet and go for it.

I agree with the authors that we do not have enough mentors and role models.^{1,2} I would add, though, that we do not have enough “mentees.” I am afraid that a relatively large proportion of medical students applying to residencies in anesthesiology are motivated by reasons that do not necessarily promote the desire to become a physician scientist. These reasons include a certain lifestyle, a combination of a very exciting specialty and a shorter residency (compared with surgery, for example), and relatively good income even in academia. The latter is illustrated by the recent Association of American Medical Colleges data* showing, for example, that the average instructor in anesthesiology received an annual salary of \$217,000 and the average assistant professor received \$250,000, whereas in pathology, these numbers are \$135,000 and \$145,000, respectively, and in internal medicine, they are \$128,000 and \$145,000, respectively.

More importantly, I believe that a psychological profile of an anesthesiologist is characterized by the need for immediate gratification rather than gratification from long-term efforts which may seem relatively fruitless for a certain period of time. Based on the above, I would suspect that one of the ways to confront this problem is to develop our specialty into perioperative medicine. Several departments in the country have already changed the names of their departments, but this is not enough. We have to become experts in perioperative medicine. It would take time. And when we are there, I believe it would help to attract more young people to our specialty, offering them a variety of psychologically different work that would incorporate treatment of patients throughout the whole perioperative period.

This is not to replace what our distinguished colleagues offered,^{1,2} but just to supplement their suggestions and to continue the debate they started so timely and effectively.

Simon Gelman, M.D., Ph.D., Harvard Medical School and Brigham and Women's Hospital, Boston, Massachusetts. sgelman@partners.org

Anesthesiology 2006; 105:625-6

Copyright © 2006, the American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc.

Royal College Recommendations to Improve Academic Anesthesia in the United Kingdom: How They Compare with United States Proposals

To the Editor:—Of relevance to the recent editorial¹ and article² on academic anesthesiology in the United States, the Royal College of Anaesthetists in the United Kingdom published in December 2005 its *National Strategy for Academic Anaesthesia* ("the Pandit Report").* There are similarities (and differences) between our own conclusions and comments made in the two articles.

Many of the pressures on academic anesthesia are clearly similar in the two countries. Funding problems are common: United States anesthesia receives only 0.6–0.9% of National Institutes of Health grants annually²; United Kingdom anesthesia receives only approximately 0.3% of Wellcome Trust/Medical Research Council funding annually.* A small number of clinical faculty seem committed to research: Schwinn and Balsler recognize that many faculty have little or no subspecialty or academic experience beyond residency²; the Pandit Report estimates that a maximum of 15% of United Kingdom clinical anesthesia faculty express any academic interest.* There is fragmented academic training and mentoring.^{8,12}

Schwinn and Balsler's main solution is to establish an increase in subspecialty fellowships that incorporate at least 1 yr of research.² However, Knight and Wartier propose instead establishing dedicated "physician scientist pathways" focused more on those trainees identified early as having academic potential,¹ and many of their suggestions are echoed in the Pandit Report.* Our proposed mantra—to "catch them early and treat them well"—is similar to Knight and Wartier's sentiment that "Graduates of MSTPs [Medical Scientist Training Programs] (M.D.–Ph.D. programs) represent a pool of future academicians . . ." Knight and Wartier's proposals for increased flexibility in the training of those with both M.D. and Ph.D. degrees and personal mentoring of these individuals is mirrored exactly in our own recommendations.*

It is important to emphasize that we came to this conclusion not because we alone thought it was a good idea but because in the United Kingdom, "the Walport Report" has established a new, dedicated training pathway for clinical academics.† This is now distinct from the

References

1. Schwinn DA, Balsler JR: Anesthesiology physician scientists in academic medicine: A wake-up call. *ANESTHESIOLOGY* 2006; 104:170–8
2. Knight PR, Wartier DC: Anesthesiology residency programs for physician scientists. *ANESTHESIOLOGY* 2006;104:1–4

(Accepted for publication May 30, 2006.)

conventional clinical training pathway. Trainees in this new academic pathway can of course specialize in any branch of clinical medicine, including anesthesia. Both clinical and academic pathways are now overseen at the national level by a single body, the Postgraduate Medical Education and Training Board‡ (its closely related institution, the United Kingdom Clinical Research Collaboration, specifically oversees academic trainees§). The Walport Report incorporates many of the suggestions independently made by Knight and Wartier, specifically emphasizing models of training that incorporate 50% research time in clinical programs.†¹ One important thrust of the Pandit Report is to help ensure that as many United Kingdom anesthesia trainees as possible enter the new academic pathway described in the Walport Report.*

The Postgraduate Medical Education and Training Board sets generic standards for all specialties equally and assesses training programs within each specialty against these standards. Therefore, the duration and broad content of training do not differ for United Kingdom anesthesiology as compared with, say, United Kingdom internal medicine or surgery. All of this seems very different in the United States, where it seems that specialties have more flexibility to modify their training programs to influence the balance of applicants into the specialty.³ We cannot exercise this option in the United Kingdom, given the regulatory environment as it is managed by the Postgraduate Medical Education and Training Board/United Kingdom Clinical Research Collaboration.

Schwinn and Balsler rightly emphasize the need to publish in high-impact factor journals and obtain National Institutes of Health grants. However, these are aims rather than solutions. Simply identifying the aims is not sufficient. It is necessary to agree on how to achieve them. A large part of the Pandit Report is about how, in the United Kingdom context and given the constraints, the desired ends can best be achieved. The main solutions include remapping United Kingdom anesthesia training to engage more closely with the new clinical academic (Walport) training pathway; refocusing funding within the specialty to support such training, and establishing mechanisms for a more cooperative approach to supporting academia from the various anesthetic specialist societies in the United Kingdom.*⁴ I am optimistic that these recommendations will be successful because (1) we have identified clear benefits for organizations that participate in the strategy; (2) we have engaged with national nonanesthetic organizations that manage biomedical science in the United Kingdom (e.g., the Wellcome Trust and the Medical Research Council); and (3) the proposals we make are essentially cost-neutral, requiring only reorganization of current funding rather than injection of new capital.

Regardless of which solutions are chosen by United States anesthesia (i.e., whether these are close to those suggested by Schwinn and Balsler² or closer to those of Knight and Wartier¹), it is clear that a pragmatic strategy to introduce the agreed-upon changes will be necessary. I would be interested to know how this strategy will deal with any obstacles to implementation. One obstacle is usually cost. Super-

Dr. Pandit was Academic Strategy Officer for the Royal College of Anaesthetists, London, United Kingdom, and in this capacity coordinated the project that led to the "National Strategy for Academic Anaesthesia." The views above are his own and do not reflect official policy of the Royal College.

* The Royal College of Anaesthetists: A National Strategy for Academic Anaesthesia (the Pandit Report). December 2005. Available at: www.rcoa.ac.uk. Accessed May 31, 2006.

† Modernising Medical Careers, UK Clinical Research Collaboration: Medically and dentally-qualified academic staff: Recommendations for training the researchers and educators of the future (the Walport Report). March 2005. Available at: <http://www.academicmedicine.ac.uk/resources/development.aspx>. Accessed May 31, 2006.

‡ Postgraduate Medical Education and Training Board. Available at: <http://www.pmetb.org.uk/>. Accessed May 31, 2006.

§ UK Clinical Research Collaboration. Available at: <http://www.ukcrc.org/>. Accessed May 31, 2006.

ficially, the suggestions of Schwinn and Balsler seem more expensive (requiring increasing the duration and expense of training for a larger cohort of trainees), whereas the proposals of Knight and Wartier require a funding effort more focused on preidentified trainees. However, one danger is that Knight and Wartier's model creates an "academic elite," and elites are rarely popular in any community. Schwinn and Balsler's proposals, on the other hand, might do more to change the culture and acceptability of academia within the specialty by exposing a larger number of anesthesiologists to research. Knight and Wartier point out that other medical specialties have introduced fast-track Physician Scientist Training Pathways or Physician Scientist Development Programs, and this suggests that the cost issue is not insurmountable.

Finally, both articles hint at other obstacles within the specialty in the United States that seem to concern questions related to the prevalent (perhaps negative) attitudes to academia. I wonder whether

these are due in part to various conflicts created by (or the need to maintain income from) the clinical service. However, it is difficult for me to speculate further on this aspect in the United States.

Jaideep J. Pandit, M.A., D.Phil., F.R.C.A., John Radcliffe Hospital, Oxford, United Kingdom. jaideep.pandit@physiol.ox.ac.uk

References

1. Knight PR, Wartier DC: Anesthesiology residency programs for physician scientists. *ANESTHESIOLOGY* 2006; 104:1-4
2. Schwinn DA, Balsler JR: Anesthesiology physician scientists in academic medicine: A wake-up call. *ANESTHESIOLOGY* 2006; 104:170-8
3. Pellegrini CA, Warshaw AL, Debas HT: Residency training in surgery in the 21st century: A new paradigm. *Surgery* 2004; 136:953-65
4. Pandit JJ: The National Strategy for Academic Anaesthesia: A personal view on its implications for our specialty. *Br J Anaesth* 2006; 96:411-4

(Accepted for publication May 30, 2006.)

Anesthesiology 2006; 105:626-7

Copyright © 2006, the American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc.

Image Not Living Up to Goal

To the Editor:—The article by Schwinn and Balsler¹ and the accompanying editorial by Wartier and Knight² succinctly and persuasively emphasize a current problem within the specialty of anesthesiology. The number of trained and committed physician scientists entering our academic workforce is diminishing, resulting in a "brain drain" of sorts. There can be little argument with the statement of the problem, but, as suggested by the different solutions offered, there is a variety of responses. Schwinn and Balsler suggest that mandatory research training at the end of residency would hook some on the research fever, while Knight and Warner suggest a more integrated approach: mix the research experience with the clinical training, especially for those emerging from combined degree programs. Both of these approaches hold merit, and some combination should be tried, depending on the institution and circumstances. Creativity will be paramount.

But we offer another, longer range solution to what we view to be a substrate deficiency. We simply must face up to the fact that the image we have created for our specialty does not reflect our commitment to cutting-edge science, where we seek to understand pharmacology, neuroscience, biophysics, cardiovascular science, or health services research. Our image is of the fast track to financial security. No wonder our trainees are not interested in investing the additional time it takes to become a scientist. This also presents the possibility that adding a mandatory research component to the clinical fellowship will have the unintended consequence of decreasing enrollment in clinical fellowships; certainly this would be counterproductive. We therefore believe that our efforts would have a greater impact earlier in the educational pathway, at the undergraduate level and early in medical school. For example, it is likely that your associated university has a research fair of some kind, intended to link work/study and other interested undergraduates with a job in research—be it patient-oriented or laboratory research. Upon attending such a research fair at the University of Pennsylvania, we were astonished by the level of interest in our work and also the underrepresentation from other School of Medicine departments. This is a huge opportunity to get our science, our questions, our unique environment, and our skills to a potential group of recruits very early, which can only serve to disseminate more and better information and improve our image. Early integration into the medical school curricula can be of benefit as well. For example, members of our faculty teach epidemiology, cardiovascular medicine, pulmonary medicine, neurosciences, bioengineering, and doctoring, in addition to the required and elective clinical

rotations in anesthesiology, pain, and critical care. Another example of early involvement is medical simulation, a rapidly growing educational tool to which all medical students will be exposed. Anesthesiology is a clear choice for leading such efforts. By exposing those students to the vast expertise and research experiences of anesthesiologists earlier in the course of their education, students with research interests and experience may recognize the opportunities to ask and answer questions that might not traditionally be considered "anesthesiology" but that certainly fit within those fields many of us believe can be advanced through our work. Similarly, anesthesiologist investigators must speak to diverse audiences. Present your research to surgeons, neurologists, and pulmonologists as well as those in the basic sciences. Join graduate groups and attend student retreats. During a recent neuroscience graduate group retreat, a student asked us, "So what does anesthesia have to do with neuroscience?" Having an opportunity to educate such poorly informed views should enhance our ability to recruit the "right stuff." Of course, achieving these goals requires that your best people be involved in the instruction and that successful teachers be incentivized along the lines of the most productive clinicians. The benefits are less tangible and longer term, but no less important.

Finally, our trainees across the board (medical students, residents, fellows) are not blind to what goes on around them. They see and hear faculty struggling with grants and papers, and they read the news regarding National Institutes of Health funding and government budgets. Therefore, many view the physician scientist route as a difficult one. It is essential that they see the benefit, not only in terms of intellectual satisfaction, but in terms of what they contribute to the future of the discipline, and how they are treated and valued by their colleagues and the department leadership.

In summary, this is not a simple problem of adding a year to the educational continuum, or of assigning mentors to our residents or junior faculty. This will require a recalibration of what we value in our discipline; how we reward those involved in lower-financial-yield areas of education and research; and, most of all, portraying anesthesiology, pain management, and critical care as a vibrant, intellectually stimulating, and challenging field that can impact areas beyond those traditionally taught by the anesthesiologists in the first 2 yr of medical school.

Lee A. Fleisher, M.D.,* Roderic G. Eckenhoff, M.D. *University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania. fleishel@uphs.upenn.edu

References

1. Schwinn DA, Balsler JR: Anesthesiology physician scientists in academic medicine: A wake-up call. *ANESTHESIOLOGY* 2006; 104:170-8

2. Knight PR, Wartier DC: Anesthesiology residency programs for physician scientists. *ANESTHESIOLOGY* 2006; 104:1-4

(Accepted for publication May 30, 2006.)

Anesthesiology 2006; 105:627-8

Copyright © 2006, the American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc.

Academic Anesthesia and M.D.-Ph.D.s

To the Editor:—Having read Dr. Knight and Wartier's editorial,¹ as well as Dr. Schwinn and Balsler's article,² in the spirit of their request for additional dialogue, I would like to offer an extended commentary on some of the issues they raise. Although it is nearly impossible to disagree with the premise in both articles, that academic anesthesia is facing a crisis, the conclusion drawn by those articles, that the solution to our problems lie with increasing our recruitment of persons to academic anesthesiology, is fallacious. I would also draw attention to an editorial written by Douglas R. Bacon, M.D. (Editor), in the June 2005 issue of the *ASA Newsletter*.³ In this editorial, Dr. Bacon also takes the position that recruitment of additional academicians is sorely needed to solve our "crisis." The combination of these three articles in less than 1 yr seems to represent a critical mass of concern on the part of leaders in our specialty. This is, of course, an excellent and welcome development, and while I welcome Drs. Knight and Wartier's proposal that a paradigm shift is needed in dealing with the issues confronting academic anesthesiology, careful reading of the Bacon editorial and the January 2006 *ANESTHESIOLOGY* article and editorial makes clear that a consensus opinion on both causes and solutions is a fair distance away. Although I am no expert in education and have no leadership role in our specialty, I do have both an M.D. and a Ph.D. degree and, up until recently, was a fully engaged and productive academic anesthesiologist. It is from this perspective that I offer my thoughts on these three articles.

In recounting three idealized resident trajectories, Dr. Bacon makes clear his lament about losing talented residents to careers that he finds noncontributory to his vision for the future of our specialty. Dr. Bacon offers very detailed commentary on what value he thinks each resident has or could potentially have on our specialty, and then offers up an argument that, although not originating with him, seems to be *de rigueur* these days. The argument, that academic anesthesia is in trouble, in part due to the failure of the specialty to capture academic trainees in sufficient numbers to maintain our research and teaching mission, is, in my opinion, confusing the cause of our problems with their effect. Dr. Bacon writes,³

. . . He [resident No. 2] had the potential to make a major contribution in his chosen subspecialty area of anesthesiology. For the next 30 yr, his ability to teach others this specialized knowledge both in the operating room and in the press and use the training his two degrees conferred upon him could have changed anesthesiology. With this decision, all of his efforts in obtaining the two advanced degrees, his "potential" and society's investment in him, seem wasted.

Three issues present themselves after reading these words. First, do any of us have an obligation to pursue careers based on our "training" so as not to squander any "potential" we may have to impact society? Second, why would a resident like the one singled out by Dr. Bacon choose to pursue a nonacademic career? Last, what is the relation between this idealized resident's decision and the current condition of academic anesthesia?

For the first question, I suggest that by Dr. Bacon's reasoning, many anesthesia residents and practitioners would need to revert back to jobs in fields in which they had originally trained: the former nurse, engineer, state department linguist, surgeon, small business owner, basketball player, psychiatrist, Olympic medalist, or marathoner. Such

people are all now anesthesiologists and, I think, making a valuable contribution in the world, albeit not in the manner they were originally trained to. I worry that Dr. Bacon is troubled by the fact that these people are no longer doing what they were trained to do, and perhaps even at a high cost to society.

I believe, however, that education is an end to itself and that being better educated, better read, and better informed simply makes you a better person, and more able to contribute to the discourse of a modern society. A cogent argument could be made that, by reaching such a noble state, these people will eventually find their own way of contributing to society, irrespective of their individual training. We as a society have made a decision that education is personal, not utilitarian. We learn because we want to, not because society dictates to us what we study, based on a perceived need. Every parent who has ever tried to get his or her child to be interested in something and subsequently failed knows very well the false security that results from vesting in preordained career paths. Sometimes, despite much training and planning and hard work, people are just drawn to other pursuits or passions. For this reason, a physician, instead of providing cures for cancer, gave us great novels about a character named Holmes. A dentist who was curious about the effects of sulfuric ether, instead of extracting teeth, taught a surgeon about painless surgery, and a patent office clerk who wanted time to think gave the world the theory of relativity. What can we infer about the value of having practicing anesthesiologists who have pursued science but no longer are active "scientists"? Perhaps it is simply that scientific training greatly enhances intraoperative thinking. Or to quote Nietzsche,⁴

Science furthers ability, not knowledge. The value of having for a time pursued a rigorous science does not rest especially in its results: for in relation to the sea of worthy knowledge, these will be but a negligible little drop. But it brings forth an increase of energy, of deductive ability, of persistence; one has learned to gain one's purpose purposefully. To this extent, in respect to all one does later, it is very valuable to have once been a scientific man.

The goal in medicine, at least, is to improve the lives of others, and this is therefore the mission of every anesthesiologist. Many people want to make the world a better place. They may have asked themselves the question, how does a person with great talents come to exert a force on the world? In this context, Dr. Bacon's lament is even more suspect. We should be helping residents to explore answers to this question instead of demanding that they pursue some preordained path that we as academicians believe is in their, or our, best interests.

However, all of this begs the unaddressed and crucial question: Why would Dr. Bacon's lamentable resident choose a career in nonacademic anesthesia, despite his years of training and investment by others? This is also the issue at the heart of both *ANESTHESIOLOGY* articles as well. Dr. Bacon is correct on his accounting of the low numbers of M.D.-Ph.D.s that stay in academic careers. Dr. Bacon writes,³

If the crisis in academic anesthesiology is to be resolved, research, funding and mentorship need to be addressed. Finding a way to keep those individuals in whom we have heavily invested to pursue academics is just one part of the solution.

In the spirit of an ongoing dialogue about this issue, I would suggest that to help "find a way," we need to look no further than resident No.

I in Dr. Bacon's lament (a foreign-born trainee with no previous research experience or evident research interest). Despite the path that seemed most "likely" for the foreign-born trainee, he "... bonded with the new faculty member and during his senior year, a six-month research rotation was arranged."³ The tremendous power of finding a role model is crucial in one's career. However, I do not simply mean a mentor. Rather, I mean the whole environment where residents train. What do they see when they work? Do they find curious and inquisitive staff? Do they train with other residents who have pursued challenging courses of study in college, or a great internship to better prepare them for the challenges of anesthesia? Do they see their teachers finishing cases at 5:30 or do they see three handoffs to the night team in less than 1 h? Do they sense that the academic center where they are training is a genuine environment of learning and that every day, no matter how good they are, they must strive to be better still because everyone else around them is doing just that? To residents, their mental construct of anesthesia is formed in myriad ways, of which a mentor is only one. If an admired staff anesthesiologist is, however, the proverbial needle in a mediocre haystack, what should the resident conclude from this? Want to keep resident No. 2 (the M.D.-Ph.D. future academician) in academics? Show the resident what academics is, rather than just saying that he or she has an obligation to fix it.

Last, I take great issue with the now fashionable idea that academic anesthesia is in crisis, and that the problem is solvable by luring more people into that pathway. Or, as Dr. Bacon says, "... the need for their skills is acute and the crisis in academic anesthesiology is growing."³ Drs. Schwinn, Balsler, Knight, and Wartier also took this position in their writings. The crisis in academic anesthesia is growing, but luring more people to a sinking ship will only make it sink faster unless one of them brings more buckets, or fixes the leak. An objective look at the current state of affairs in academic anesthesia reveals a grim picture. By many measures, anesthesia's wish to remain an academic specialty is in serious danger. Our research dollars as a fraction of total National Institutes of Health dollars is lower than that of most major medical specialties, and more crucially, the translation of work done by anesthesiologists to the private sector or to a venue where human disease can be impacted is nearly nonexistent. At one time, the purview of academic anesthesia was broad, whereas today, our focus is much more limited and we have ceded dominance on many major medical questions to other specialties. As a specialty, one can argue that we have impacted the human condition by the increased safety of surgery in the modern era. However, I think this is primarily due to our appropriation of drugs and technology developed by other sectors and exploited in a way consistent with the goals of our specialty. In an era of shrinking availability of research dollars, a genuine squeeze on academic centers to boost clinical productivity, and the increasing demand of the National Institutes of Health for "clinically relevant research," the day will soon arrive when anesthesia will be judged for its ability to compete in this environment. By the measures cited above, we fare poorly, and a cogent argument will be made that anesthesia has no business being in research and our efforts should be

focused on training anesthesia providers and caring for patients. To ignore this scenario is akin to inviting our demise by mimicking the proverbial ostrich and its buried head. As Drs. Knight and Wartier intimate, a paradigm shift is needed because this day is coming, and this is our crisis. Recruiting more talented M.D.-Ph.D. graduates to this world is not likely to solve these problems. Those residents in anesthesia already are leaving academics for a reason, and it is my suspicion that it is because they see there are deep structural faults with the future promise of academic anesthesia. Until we as a specialty address them, talented residents will remain reluctant to jump aboard what they perceive as a sinking ship.

Drs. Bacon, Balsler, Knight, Schwinn, and Wartier are to be commended on highlighting, in a comprehensive and thoughtful manner, that our specialty is in need of some internal attention. I am concerned, however, that if we limit ourselves to the paradigm shift as outlined in their writings, we will fail to grasp to the true dimensions of our problem. If indeed others outside our specialty begin to take notice of our dismal academic performance on the field of the "grant battle," we will be at a huge tactical disadvantage. As the Chinese warrior Sun Tzu understood so long ago, the attempt to be strong everywhere results in weakness everywhere. Perhaps the paradigm shift being proffered needs to be much broader in that it not only alters the input side (trainee) of the academic training system, but also addresses the output side: which institutions should be academic, and which ones should not be. Equality of opportunity does not ensure equality of outcome, and with more than 100 academic anesthesia departments vying for research dollars, perhaps the lopsided outcomes of that competition reflect not a paucity of people to equalize the outcomes, but genuine weakness among some of the competitors. If this is true, even to a small extent, the discussion that we as a profession should be having is to which of these centers do we divert our resources—money, time, and people—to restore academic anesthesia to the place where we lament it has fallen from. Perhaps the time has come to try to stop being strong everywhere, because as of now, if the data in Drs. Bacon, Balsler, Knight, Schwinn, and Wartier's articles are accurate, we already are, in fact, quite weak everywhere.

Jason A. Campagna, M.D., Ph.D., Anesthesia Medical Group of Santa Barbara, Cottage Hospital System, Santa Barbara, California. campagna.jason@gmail.com

References

1. Schwinn DA, Balsler JR: Anesthesiology physician scientists in academic medicine: A wake-up call. *ANESTHESIOLOGY* 2006; 104:170-8
2. Knight PR, Wartier DC: Anesthesiology residency programs for physician scientists. *ANESTHESIOLOGY* 2006; 104:1-4
3. Bacon DR: From the Crow's Nest: A tale of three residents. *ASA Newsletter* 2005; 69:1-2
4. Nietzsche F: *Human, All Too Human: A Book for Free Spirits*, revised edition. Edited by Hollingdale RJ. New York, Cambridge University Press, 1996

(Accepted for publication May 30, 2006.)

Anesthesiology 2006; 105:628

Copyright © 2006, the American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc.

In Reply:—We read with considerable interest the Letters to the Editor about the Special Article by Schwinn and Balsler¹ and our Editorial View.² No single quick fix for our predicament exists. Rather, multiple plans from creative individuals in academic institutions and anesthesiology organizations must be implemented. We all share the same goal: enhancing the scientific foundation of our specialty.

Paul R. Knight, M.D., Ph.D.,* David C. Wartier, M.D., Ph.D. *State University of New York at Buffalo, Buffalo, New York. pknight@buffalo.edu

References

1. Schwinn DA, Balsler JR: Anesthesiology physician scientists in academic medicine: A wake-up call. *ANESTHESIOLOGY* 2006; 104:170-8
2. Knight PR, Wartier DC: Anesthesiology residency programs for physician scientists. *ANESTHESIOLOGY* 2006; 104:1-4

(Accepted for publication May 30, 2006.)

In Reply:—We deeply appreciate the time and effort of colleagues Drs. Andreae, Compagna, Fleischer and Eckenhoff, Gelman, Pandit, and others throughout academic anesthesiology in providing thoughtful responses to our article.¹ Only through such discourse will we make progress. In responding, we wish to emphasize, first and foremost, that we respect and appreciate the opinions expressed. It is certain that no single “turnkey” solution will singularly change the trajectory of academic anesthesiology. Above all, we are encouraged that the responses suggest broad agreement, across many perspectives, with our interpretation of the data suggesting that academic anesthesiology is indeed in crisis, and that bold steps are needed to avert the demise of our specialty as a legitimate academic discipline.

We wish to take this opportunity to respond to our colleagues while reinforcing a few key points. First, we are not recommending that the anesthesiology residency be lengthened so that every anesthesiology trainee has the opportunity to be exposed to a year of research. Indeed, we point out that most residents (in all specialties) have no interest in academic medicine, and forcing research on all clinical trainees is unlikely to be either productive or efficient. That said, our colleagues in medicine, pediatrics, and several other disciplines have used subspecialty fellowship training for this purpose, recognizing that this allows them to focus on a smaller cadre of individuals willing to commit additional time and effort to their overall training. They have, we believe, correctly identified these advanced trainees as the ideal group to groom for leadership in academic medicine.

Conversely, anesthesiology as a discipline has de-emphasized fellowship training in all respects, with only a few Accreditation Council for Graduate Medical Education (ACGME)-approved fellowships, which are largely 1-yr clinical experiences. We project a confusing picture to the public, who justifiably wonder why some centers advertise the added safety of offering providers with advanced training in cardiac and obstetric anesthesiology, while as a specialty we continue to endorse the notion that all anesthesiologists are capable of safely providing all types of care. At the same time, we also miss the opportunity to mentor a substantial number of advanced clinical trainees in the full scope of academic practice, including both research and subspecialized clinical care, in stark contrast to our colleagues in other medical disciplines.

It is difficult to argue that our generalist model has worked well, because the substandard performance of anesthesiology as an academic discipline is well documented, and the concern of the specialty is broad. Moreover, when queried, leading colleagues in other specialties will indicate that they view our 1-yr clinical fellowships as “pseudoacademic.” Further, students, residents, and faculty from within and outside anesthesiology astutely observe that our anemic commitment to fellowship training in a broad range of subspecialties is evidence that we, as a specialty, place little value on developing physician scientists, because nearly all disciplines use clinical fellowship as the time to hone these skills.

Given that our most compelling argument for not changing the number, scope, and duration of our fellowships is fear that trainees will refuse to participate, it is difficult to provide evidence that our colleagues are wrong about us. At both of our institutions, the most academically oriented M.D.–Ph.D. students usually choose specialties other than anesthesiology, not because of concern that we will require them to undergo a lengthy period of advanced training, but ironically, because we do not! It is difficult for us to argue that we have the same commitment to science as peer specialties who long ago invested in a diverse set of elite, advanced fellowship training

opportunities, all of which contain compulsory research. As a specialty, perhaps unwittingly, we project a timid commitment to academic medicine. Anesthesiology training programs, even with appended 1-yr clinical fellowships, do not have the comprehensive rigor to stand “toe-to-toe” with the advanced fellowship training programs now standard in many other disciplines.

To change course, we have proposed that anesthesiology should immediately install multiyear ACGME-approved advanced fellowship training tracks in all of its clinical subspecialties, and these should include at least 1 yr of in-depth training in either clinical or basic science research. As in all endeavors, in academic medicine, we will reap what we sow. Anesthesiology has underinvested in advanced training relative to its peers, and as such, it has underproduced individuals with a full complement of the skills needed to succeed in academic medicine, including research competency. An extensive, bold change in our expectations for advanced training, in the parlance of Dr. Compagna, is not “recruiting our fellows to a sinking ship,” but rather teaching them to swim. Data from the National Institutes of Health demonstrates that anesthesiologists who commit to serious academic research training (clinical, translational, or basic science) during an extended fellowship perform as well as those from any other medical discipline and obtain National Institutes of Health funding at the same rate.

Finally, to those who worry that expanding advanced ACGME-accredited training in our fellowships will frighten those medical students or residents who seek less rigorous training away from such endeavors, we would offer the historic examples of cardiology and gastroenterology as evidence to the contrary. Since their formation, the academic “bench” of these subspecialties has thrived by any standard, with excellent National Institutes of Health funding performance, despite highly attractive private practice compensation opportunities outside academic medicine, and despite an extensive portfolio of training requirements required for competency and safety in the clinical procedures required by these practitioners. Both require extended research periods during their ACGME-approved fellowship training programs, and across the country, these fellowship training programs are oversubscribed; further, we are not aware that many internists, or their subspecialty-trained cardiologist or gastroenterologist colleagues, are having difficulty finding employment despite similar fears at the time these subspecialties were formed. It is also noteworthy that in forming substantial fellowship training programs with ACGME accreditation, and by including extensive research and clinical educational requirements, these subspecialties were able to establish the high moral ground to justify, to the public, third-party payers, and healthcare service providers, that they deserve priority in providing consultative advice, complex clinical services, and leadership in developing the scientific and educational priorities of their disciplines.

By establishing a solid framework of advanced training in subspecialty anesthesiology, including all areas of perioperative medicine, we will advance our image in a manner that enables us to recruit the best young minds to the discipline. Although exposing gifted M.D.–Ph.D. students to research will always have an impact, as proposed by Drs. Knight and Warltier, students are unavoidably perceptive. We must exhibit the values and commitment of our peers toward advanced training, in both clinical care and research, to make long-term, consistent progress in recruiting the best and brightest medical students into anesthesiology.

We wish to thank the anesthesiology community for engaging with us in this discussion.

Jeffrey Balsler, M.D., Ph.D., Debra A. Schwinn, M.D.*
 *Duke University Medical Center, Durham, North Carolina.
 schwi001@mc.duke.edu

Reference

1. Schwinn DA, Balsler JR: Anesthesiology physician scientists in academic medicine: A wake-up call. *ANESTHESIOLOGY* 2006; 104:170-8

(Accepted for publication May 30, 2006.)

Anesthesiology 2006; 105:630

Copyright © 2006, the American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc.

Nitrous Oxide and Preconditioning

To the Editor:—We read with interest the recent report by Weber *et al.*¹ demonstrating that brief, repetitive administration of 60% nitrous oxide before prolonged coronary artery occlusion and reperfusion did not protect myocardium against infarction in rats. These findings concur with previous results from our laboratory indicating that administration of 70% nitrous oxide before and during a 15-min coronary artery occlusion failed to improve and, in fact, exacerbated the functional recovery of postischemic, reperfused ("stunned") myocardium as compared with 70% nitrogen in barbiturate-anesthetized, acutely instrumented dogs.² The results of Weber *et al.* further demonstrated that nitrous oxide exposure did not produce phosphorylation of ϵ isoform of protein kinase C (PKC- ϵ) and Src protein tyrosine kinase or cause sarcolemmal translocation of PKC- ϵ . Our investigation was conducted several years before the prosurvival signaling mechanisms responsible for anesthetic-induced myocardial protection against reversible and irreversible ischemic injury were discovered. Myocardial stunning and infarction most likely represent a continuum of ischemic damage, and it is clear that activation of PKC- ϵ plays a central role in volatile anesthetic-induced preservation of myocardial function and integrity during these processes, respectively.³⁻⁷ Src protein tyrosine kinase has also been implicated in anesthetic-induced preconditioning against infarction,^{1,6} but whether this enzyme also mediates the beneficial actions of volatile agents in stunned myocardium is unknown. The current results¹ indicating that a clinically relevant concentration of nitrous oxide does not cause preconditioning are not entirely unexpected based on our previous findings,² but they nevertheless provide new molecular insight into the observation that this anesthetic gas does not produce cardioprotection in ischemic myocardium.

Nitrous oxide may also fail to produce preconditioning as a result of adverse effects on myocardial oxygen supply *versus* demand relations. Nitrous oxide was previously shown to produce epicardial coronary artery vasoconstriction as assessed using angiography.⁸ These data suggested that nitrous oxide may theoretically compromise perfusion of ischemic myocardium.⁹ We demonstrated that 70% nitrous oxide did not affect coronary collateral perfusion or alter the ratio of endocardial to epicardial blood flow measured using radioactive microspheres in a canine model of ischemia and reperfusion, but we did not specifically examine the influence of nitrous oxide on epicardial coronary artery diameter in our investigation.² Rats have been shown to possess little if any coronary collateral blood flow,¹⁰ but the actions of nitrous oxide on transmural myocardial perfusion and epicardial coronary dimension were not quantified, nor was the potential impact of the anesthetic gas on myocardial oxygen supply considered in the current study.¹ Nitrous oxide has been shown to directly activate the sympathetic nervous system¹¹ and stimulate the release of norepinephrine from sympathetic efferents innervating vascular smooth muscle.¹² These actions increase left ventricular afterload,¹³ an important determinant of myocardial oxygen consumption. As a consequence, nitrous oxide may precipitate a relatively greater ischemic burden by increasing myocardial oxygen consumption before the onset of coronary artery occlusion. Heart rate and mean aortic blood

pressure remained unchanged during nitrous oxide preconditioning, suggesting that alterations in myocardial oxygen consumption did not occur during administration of the anesthetic gas in rats.¹ Nevertheless, the current results should also be qualified because other hemodynamic determinants of myocardial oxygen consumption were not evaluated (*e.g.*, myocardial contractility, left ventricular preload), nor was myocardial oxygen consumption directly calculated by measurement of arterial and coronary venous oxygen tensions.

Paul S. Pagel, M.D., Ph.D.,* David C. Warltier, M.D., Ph.D. *Medical College of Wisconsin, Milwaukee, Wisconsin. pspagel@mcw.edu

References

1. Weber NC, Toma O, Awab S, Fräsdorf J, Preckel B, Schlack W: Effects of nitrous oxide on the rat heart *in vivo*: Another inhalational anesthetic that preconditions the heart? *ANESTHESIOLOGY* 2005; 103:1174-82
2. Siker D, Pagel PS, Pelc LR, Kampine JP, Schmeling WT, Warltier DC: Nitrous oxide impairs functional recovery of stunned myocardium in barbiturate-anesthetized, acutely instrumented dogs. *Anesth Analg* 1992; 75:539-48
3. Toller WG, Montgomery MW, Pagel PS, Hettrick DA, Warltier DC, Kersten JR: Isoflurane-enhanced recovery of canine stunned myocardium: Role for protein kinase C? *ANESTHESIOLOGY* 1999; 91:713-22
4. Uecker M, da Silva R, Grampp T, Pasch T, Schaub MC, Zaugg M: Translocation of protein kinase C isoforms to subcellular targets in ischemic and anesthetic preconditioning. *ANESTHESIOLOGY* 2003; 99:138-47
5. Novalija E, Kevin LG, Camara AK, Bosnjak ZJ, Kampine JP, Stowe DF: Reactive oxygen species precede the epsilon isoform of protein kinase C in the anesthetic preconditioning signaling cascade. *ANESTHESIOLOGY* 2003; 99:421-8
6. Ludwig LM, Weihrach D, Kersten JR, Pagel PS, Warltier DC: Protein kinase C translocation and Src protein tyrosine kinase activation mediate isoflurane-induced preconditioning *in vivo*: Potential downstream targets of mitochondrial adenosine triphosphate-sensitive potassium channels and reactive oxygen species. *ANESTHESIOLOGY* 2004; 100:532-9
7. Obal D, Weber NC, Zacharowski K, Toma O, Dettwiler S, Wolter JI, Kratz M, Mullenheim J, Preckel B, Schlack W: Role of protein kinase C- ϵ (PKC- ϵ) in isoflurane induced cardioprotection: Low, but not high concentrations of isoflurane activate PKC- ϵ . *Br J Anaesth* 2005; 94:166-73
8. Wilkowski DA, Sill JC, Bonta W, Owen R, Bove AA: Nitrous oxide constricts epicardial coronary arteries without effect on coronary arterials. *ANESTHESIOLOGY* 1987; 66:659-65
9. Philbin DM, Foex P, Drummond G, Lowenstein E, Ryder WA, Jones LA: Postsystolic shortening of canine left ventricle supplied by a stenotic coronary artery when nitrous oxide is added in the presence of narcotics. *ANESTHESIOLOGY* 1985; 62:166-74
10. Maxwell MP, Hearse DJ, Yellon DM: Species variation in the coronary collateral circulation during regional myocardial ischaemia: A critical determinant of the rate of evolution and extent of myocardial infarction. *Cardiovasc Res* 1987; 21:737-46
11. Ebert TJ, Kampine JP: Nitrous oxide augments sympathetic nervous system outflow: Direct evidence from human peroneal nerve recordings. *Anesth Analg* 1989; 69:444-9
12. Rorie DK, Tyce GM, Sill JC: Increased norepinephrine release from dog pulmonary artery caused by nitrous oxide. *Anesth Analg* 1986; 65:560-4
13. Eisele JH Jr: Cardiovascular effects of nitrous oxide, Nitrous oxide/N₂O. Edited by Eger II EI. New York, Elsevier, 1985, pp 125-56

(Accepted for publication April 25, 2006.)

In Reply:—We thank Drs. Pagel and Wartier for their comments on our work and for drawing our attention to their previous article in 1992.¹ In that work, 70% nitrous oxide given before and during ischemia and then continued for 15 min during reperfusion impaired the functional recovery of “stunned” myocardium after a brief coronary artery occlusion (15 min) and reperfusion period of 3 h in open-chest, barbiturate-anesthetized dogs. This study thus addressed a combined effect of preischemic, intraischemic, and postischemic treatment, whereas our study addressed the effects of nitrous oxide on the defined mechanism of preconditioning. For this purpose, the gas was administered only during 3 × 5 min before ischemia² as a preconditioning stimulus followed by a washout before ischemia. We could show that nitrous oxide provided no cardioprotection by anesthetic preconditioning and that it did not interfere with the cardioprotection by isoflurane preconditioning.²

Siker *et al.*¹ investigated regional hemodynamics, myocardial tissue perfusion, and myocardial oxygen consumption in an animal model with myocardial collateral circulation. Their endpoint was the functional recovery of stunned myocardium. In contrast, we used an *in vivo* rat model and assessed lethal cell damage, *i.e.*, infarct size as the classic endpoint of ischemia-reperfusion injury. In addition, we were mainly interested in the molecular mechanisms involved.² The results clearly demonstrated that nitrous oxide in a clinically relevant dose does not produce any preconditioning effect on the heart and that none of the most discussed molecular targets, such as protein kinase C- ϵ and Src kinase, are affected by nitrous oxide—in contrast to the volatile anesthetic isoflurane.² Therefore, our study showed for the first time that nitrous oxide is, until today, the only inhalational anesthetic that offers no myocardial protection by preconditioning. It is difficult to directly compare both studies, because they are looking at different phenomena of myocardial ischemia-reperfusion injury in different experimental settings using different administration protocols; *e.g.*, as pointed out in the letter, in our study hemodynamic determinants of myocardial oxygen consumption such as myocardial

contractility or left ventricular preload were not measured. In our experimental setting, these regional hemodynamics might not be as relevant as in the study from Siker *et al.* because the preconditioning stimulus (3 × 5 min of nitrous oxide inhalation) was ended 5 min before ischemia-reperfusion and, in addition, did not alter global hemodynamics as the longer administration protocol during ischemia-reperfusion in the study of Siker *et al.* Therefore, we cannot conclude that similar hemodynamic effects as previously demonstrated by Siker *et al.* in their dog model of myocardial stunning are relevant for our rat model investigating myocardial preconditioning.

In conclusion, although addressing different topics, at least both studies demonstrated that nitrous oxide is—in contrast to volatile anesthetics and the inert gas xenon^{3,4}—the only inhalational anesthetic without myocardial protective effects in an ischemia-reperfusion situation.

Nina C. Weber, Ph.D., Benedikt Preckel, M.D., D.E.A.A., Wolfgang Schlack, M.D., D.E.A.A.* *University of Amsterdam, Amsterdam, The Netherlands. w.s.schlack@amc.uva.nl

References

1. Siker D, Pagel PS, Pelc LR, Kampine JP, Schmeling WT, Wartier DC: Nitrous oxide impairs functional recovery of stunned myocardium in barbiturate-anesthetized, acutely instrumented dogs. *Anesth Analg* 1992; 75:539–48
2. Weber NC, Toma O, Awab S, Fräsdorf J, Preckel B, Schlack W: Effects of nitrous oxide on the rat heart *in vivo*: Another inhalational anesthetic that preconditions the heart? *ANESTHESIOLOGY* 2005; 103:1174–82
3. Weber NC, Toma O, Wolter JI, Obal D, Müllenheim J, Preckel B, Schlack W: The noble gas Xenon induces pharmacological preconditioning in the rat heart *in vivo* via induction of PKC-epsilon and p38 MAPK. *Br J Pharmacol* 2005; 144:123–32
4. Weber NC, Toma O, Wolter JI, Wirthle NM, Schlack W, Preckel B: Mechanisms of xenon and isoflurane induced preconditioning: A potential link to the cytoskeleton via the MAPKAPK-2 HSP27 pathway. *Br J Pharmacol* 2005; 146:445–55

(Accepted for publication April 25, 2006.)

Perianesthetic Management of Hypertrophic Cardiomyopathy

To the Editor:—The Clinical Concepts and Commentary titled “Hypertrophic Cardiomyopathy” (HCM) by Poliac *et al.*¹ provides a detailed update on the disease, its clinical significance, and its anesthetic management. Recognition that HCM is not so “rare” and that most patients are undiagnosed significantly expands our understanding of the perianesthetic implications of HCM. However, there are two aspects of perianesthetic management upon which I wish the authors had expanded. First, despite an excellent discussion of the choice of volatile agent and avoidance of histamine releasing or vagolytic relaxants, no mention is made of induction techniques. Should the vasodilating myocardial depressant propofol be avoided in favor of etomidate? Is catecholamine-releasing ketamine contraindicated? Second, the authors are concerned “that a not inconsequential subset of HCM patients will present for surgery and anesthesia without an established diagnosis.” However, only limited diagnostic clues are provided. I suspect that I am not the only anesthesiologist whose preoperative cardiac examination does not include having the patient stand or Valsalva in an effort to produce a systolic ejection murmur. If 75% or more have an abnormal 12-lead electrocardiogram, what findings on an intraoperative 3-lead or 5-lead electrocardiographic moni-

tor might cause me to delay induction until a more formal 12-lead electrocardiogram or echocardiogram is obtained? Dr. Maron is certainly aware that HCM is the most common cause of sudden death in young American athletes.² Corrado *et al.*³ have shown that identification of young athletes with HCM can reduce their incidence of sudden death. The opportunity for anesthesiologists to make a potentially lifesaving diagnosis should not be missed.

John D. Gallagher, M.D., Dartmouth Medical School, Hanover, New Hampshire. john.d.gallagher@hitchcock.org

References

1. Poliac LC, Barron ME, Maron BJ: Hypertrophic cardiomyopathy. *ANESTHESIOLOGY* 2006; 104:183–92
2. Maron BJ: Sudden death in young athletes. *N Engl J Med* 2003; 349:1064–75
3. Corrado D, Basso C, Schiavon M, Thiene G: Screening for hypertrophic cardiomyopathy in young adults. *N Engl J Med* 1998; 339:364–9

(Accepted for publication May 5, 2006.)

In Reply:—We thank Dr. Gallagher for his insightful comments regarding our review of hypertrophic cardiomyopathy (HCM),¹ and we are pleased to learn of his opinion that understanding the perianesthetic implications of HCM have been extended. The points raised by Dr. Gallagher are important and fundamental to the practice of anesthesiology, and we wish that we could have elaborated on some of those issues in our article, although space limitations did not allow us to touch on all aspects of perioperative care. The question remains: How can the practicing anesthesiologist preoperatively identify a complex disease such as HCM, which at the time of presentation for anesthesia and surgery may be unsuspected by the medical team as well as the patient? As pointed out by Dr. Gallagher, the study of Corrado *et al.*² showed that a mass screening program in Italy of young competitive athletes (based largely on clinical history, physical examination, and 12-lead electrocardiogram) was an efficient means of detecting cardiac abnormalities, and ultimately led to the diagnosis of hypertrophic cardiomyopathy in an important minority of patients. Certainly, if such detailed preoperative examination was a standard part of the preoperative anesthetic examination, an increased number of HCM patients would be probably diagnosed before arrival in the operating room. To what extent the Italian athlete screening data, *i.e.*, the use of routine electrocardiograms, can be extrapolated to the general anesthesia population remains a difficult and unresolved issue, although this additional diagnostic test would permit anesthesiologists to make a potentially lifesaving diagnosis, as Dr. Gallagher has suggested.

In addition, clinical examinations, which include maneuvers to provoke the murmur of left ventricular tract obstruction (such as standing), characteristic of HCM, would be potentially helpful for diagnosis. The possible disastrous consequences of overlooking a preoperative diagnosis of HCM should heighten the index of suspicion and clinical vigilance on the part of the anesthesiologist in this regard.

With respect to the choice of induction agents, our article states: "The possibility of drug-induced hypotension or increased sympathetic activation upon initiating anesthesia should be considered when

choosing an induction agent, and slow titration of these drugs should be used."¹ More specifically, when inducing patients with diagnosed HCM, the anesthesiologist should consider the potential for global myocardial dysfunction besides focusing on the possibility of provoked left ventricular outflow tract obstruction. For example, an agent such as etomidate would be preferable to others (*e.g.*, propofol, ketamine) because of its relatively stable action on the cardiovascular system. Propofol produces direct myocardial depression and both arterial and venous dilatation, which potentiates systemic hypotension. Ketamine has cardiovascular-stimulating properties secondary to direct activation of the sympathetic nervous system and increases arterial blood pressure and heart rate, thereby negatively affecting the balance between myocardial oxygen supply and demand.

Etomidate produces minimal cardiac depression even in the presence of intrinsic myocardial disease and consequently would be considered the induction agent of choice for patients with HCM. Of note, etomidate does not effectively blunt the sympathetic response to laryngoscopy and intubation, and therefore, adjuvant methods (lidocaine, inhalational agents) should be considered to avoid an exaggerated sympathetic response during initiation of anesthesia.

The consideration (raised by Dr. Gallagher) regarding use of intraoperative 3- or 5-lead electrocardiogram does not seem particularly relevant to the potential identification of HCM. The diagnostic strategy of choice would be a 12-lead electrocardiogram obtained *before* induction.

Liviu C. Poliac, M.D.,* Michael E. Barron, M.D., Barry J. Maron, M.D. *University of Miami, Miller School of Medicine, Miami, Florida. lpoliac@med.miami.edu

References

1. Poliac LC, Barron ME, Maron BJ: Hypertrophic cardiomyopathy. *ANESTHESIOLOGY* 2006; 104:183-92
2. Corrado D, Basso C, Schiavon M, Thiene G: Screening for hypertrophic cardiomyopathy in young athletes. *N Engl J Med* 1998; 339:364-9

(Accepted for publication May 5, 2006.)

David C. Wartier, M.D., Ph.D., served as Handling Editor for this exchange.

Efficacy of Epidural Block during General Anesthesia

To the Editor:—When searching for possible advantages of epidural-general anesthesia compared with general anesthesia as has been attempted recently,^{1,2} it is important to know whether antinociception and blood pressure control during the procedure are accomplished by the epidural local anesthetic or by other adjuvants such as β -adrenergic blockers, opioids, or sodium nitroprusside. Epidural dose requirements vary widely and are unpredictable. When reviewing this variability, it becomes apparent that weak local anesthetic solutions, set infusion rates, and infusions based on the patient's weight will result in occasional inadequate blocks during prolonged procedures.

We simplified a previously described method³ to assess the adequacy of epidural block during general anesthesia using pupillometry while stimulating selected dermatomes. Our study population consisted of children aged 3.5 ± 2.2 yr, a group that others have found difficult to assess with pupillometry.⁴ After institutional approval, we induced anesthesia with sevoflurane. Tracheal intubation was performed after administration of rocuronium bromide and fentanyl, and

sevoflurane concentrations were set at 1.7–2% end-tidal. Three-second pupillary scans were alternatively measured (fig. 1) after tetanic stimulations (800 ms duration, 100 Hz, 140 mA) of the L4 and C5 dermatomes with a handheld Neuroptics pupillometer (Neuroptics Inc., Irving, CA)⁵ connected to a Fisher-Paykel nerve stimulator (Fisher and Paykel Healthcare Inc., Panmure, Auckland 6, New Zealand) and surface electrocardiograph pad electrodes. Injection of 1 ml/kg bupivacaine, 0.25%, was administered either caudally or into the lumbar epidural space at time zero. As shown in figure 2, dilations were abolished after stimulation at the L4 dermatome but not after stimulation at the C5 dermatome. The latency of block onset was highly variable but averaged 8.7 ± 2.0 min, slightly longer than previously reported with 0.5% bupivacaine in awake subjects (5.8 min).⁶ We conclude that in this group of subjects, in whom the epidural is placed after induction of general anesthesia and is often difficult to assess even after emergence, loss of pupillary dilation after dermatomal stimulation indicated the onset of epidural block.

Pupillary dilation during general anesthesia is a parasympathetic reflex and is not confounded by antihypertensives that alter sympathetic func-

Support was provided solely from institutional and/or departmental sources.

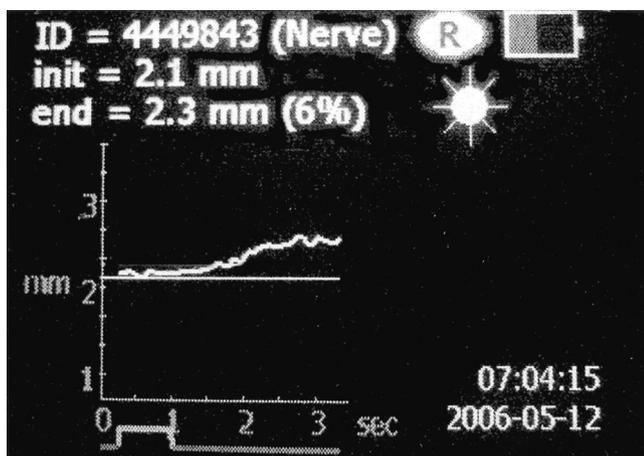


Fig. 1. The face of the pupillometer displays the 3-s scan, the percent dilation, and the time and date. The 800-ms stimulus is delivered during the square wave, shown below the x-axis. Pupillary reflex dilation is locked to the stimulus with a long latency.

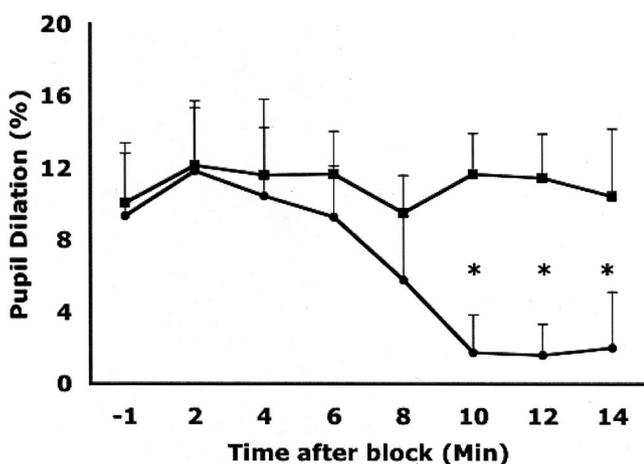


Fig. 2. Average pupillary reflex dilations from L4 and C5 stimulation sites for all 20 subjects. **Black squares** are dilations after C5 stimulation, and **black circles** are dilations after L4 stimulation. The data point for -1 min represents measures taken before injection. With one subject, the L4 dilations were not blocked. * $P < 0.001$ compared with percent dilation at C5, two-way analysis of variance.

tion. This method avoids the previously described cumbersome technique of using steel needles and a laptop computer to synchronize the pupillary measurement to the stimulus. It works just as effectively in adults but should not be used in unparalyzed patients and is unreliable if dopamine 2 antagonists or large doses of opioids have been administered. In actual practice, it is not necessary to repeatedly stimulate and assess different dermatomes; absence of dilation two segments above the anticipated skin incision predicts an ongoing effective local anesthetic block. A neutral stimulation site (such as C5, or a trigeminal location) serves as a control to confirm that the pupil will dilate.

With strict research protocols, many studies have failed to observe short-term advantages of epidural-general over general anesthesia, and this may be a valid conclusion for many operations. However, other studies, using stronger local anesthetic concentrations, have demonstrated reduced pain and improved functional capacity several weeks after hospital discharge,^{7,8} and this benefit might outweigh the added risks involved in placement and maintenance of epidural catheters. Furthermore, an effective epidural block before emergence from general anesthesia assures, with few exceptions, a pain-free emergence without the need for neuraxial or intravenous opioids and their related side effects.

Merlin D. Larson, M.D.,* Randolph S. Fung, M.D., Andrew J. Infosino, M.D., Atsuko Baba, M.D. *University of California, San Francisco, California. larsonm@anesthesia.ucsf.edu

References

- Norris EJ, Beattie C, Perler BA, Martinez EA, Meinert CL, Anderson GF, Grass JA, Sakima NT, Gorman R, Achuff SC, Martin BK, Minken SL, Williams GM, Traystman RJ: Double-masked randomized trial comparing alternate combinations of intraoperative anesthesia and postoperative analgesia in abdominal aortic surgery. *ANESTHESIOLOGY* 2001; 95:1054-67
- Hansdotir V, Philip J, Olsen MF, Eduard C, Houltz E, Ricksten SE: Thoracic epidural versus intravenous patient-controlled analgesia after cardiac surgery: A randomized controlled trial on length of hospital stay and patient-perceived quality of recovery. *ANESTHESIOLOGY* 2006; 104:142-51
- Larson MD, Sessler DI, Ozaki M, McGuire J, Schroeder M: Pupillary assessment of sensory block level during combined epidural/general anesthesia. *ANESTHESIOLOGY* 1993; 79:42-8
- Emery J, Ho D, MacKeen L, Heon E, Bissonnette B: Pupillary reflex dilation and skin temperature to assess sensory level during combined general and caudal anesthesia in children. *Paediatr Anaesth* 2004; 14:768-73
- Du R, Meecker M, Bacchetti P, Larson MD, Holland MC, Manley GT: Evaluation of the portable infrared pupillometer. *Neurosurgery* 2005; 57:198-203
- Bromage P: *Epidural Analgesia*. Philadelphia, WB Saunders, 1978
- Gottschalk A, Smith DS, Jobes DR, Kennedy SK, Lally SE, Noble VE, Grugan KF, Seifert HA, Cheung A, Malkowicz SB, Gutsche BB, Wein AJ: Preemptive epidural analgesia and recovery from radical prostatectomy: A randomized controlled trial. *JAMA* 1998; 279:1076-82
- Carli F, Mayo N, Klubien K, Schricker T, Trudel J, Belliveau P: Epidural analgesia enhances functional exercise capacity and health-related quality of life after colonic surgery: Results of a randomized trial. *ANESTHESIOLOGY* 2002; 97:540-9

(Accepted for publication April 19, 2006.)

Tumor Lysis Syndrome Induced by Dexamethasone

To the Editor:—Acute tumor lysis syndrome is being reported with increasing frequency by many hematologic units worldwide, and it deserves greater familiarity and awareness on the part of anesthesiologists and critical caregivers. It occurs when rapidly dividing large volume tumors, such as highly aggressive lymphomas and acute leukemias, are treated with cytotoxic agents. It is characterized by the rapid development of hyperkalemia, hyperuricemia,

hyperphosphatemia, hypocalcemia, and lactic acidosis and may terminate in renal failure if not considered early enough in the differential diagnosis.

A 42-year-old female patient with no previously known malady was admitted to our Ear Nose and Throat Department for investigation of bilateral parotid gland enlargement accompanied by multiple enlarged cervical lymph nodes. Initial laboratory investigations revealed a normal complete blood count and normal blood coagulation and biochemistry profiles, apart from an increased lactate dehydrogenase value of 937 U/l.

Support was provided solely from institutional and/or departmental sources.

Table 1. Laboratory Results

	Prebiopsy Data	Day 1 Postbiopsy Data	Day 6 Postbiopsy Data
Lactic acid dehydrogenase (N = 240.0–480.0 U/l)	937 U/l	7,237 U/l	940 U/l
Phosphor (N = 2.6–4.5 mg/dl)	3.0 mg/dl	14.4 mg/dl	3.6 mg/dl
Potassium (N = 3.3–5.1 mm)	3.7 mm	5.6 mm	3.92 mm
Uric acid (N = 2.4–6.0 mg/dl)	2.3 mg/dl	35.9 mg/dl	3.0 mg/dl
Calcium (N = 8.6–10.3 mg/dl)	9.2 mg/dl	7.1 mg/dl	9.2 mg/dl
Urea (N = 10.0–45 mg/dl)	13 mg/dl	142 mg/dl	10.8 mg/dl
Creatinine (N = 0.5–0.9 mg/dl)	0.65 mg/dl	2.45 mg/dl	0.56 mg/dl
Platelet count (N = 150–350 × 10 ³ /mm ³)	260	52	147

On the prebiopsy day, she underwent an excisional biopsy of a cervical lymph node under a short general anesthesia. At the end of this procedure, she was given an intravenous injection of 20 mg dexamethasone as an antiemetic.

On day 1 after biopsy, she developed symptoms of general weakness, nausea and vomiting, and a reduced urinary output. Laboratory results on this date showed evidence of metabolic acidosis, hyperphosphatemia, hyperuricemia, increased blood urea and creatinine values, a lactic acid dehydrogenase value of 7,237 U/l, and a significant reduction in the platelet count.

The patient was transferred to the intensive care unit. A computed tomography scan of the neck, chest, and abdomen revealed the presence of a mediastinal mass of 8 × 12 cm, bilateral pleural effusions, pericardial effusion, and cervical and abdominal lymphadenopathy. A diagnosis of acute lymphoblastic lymphoma (leukemia) was suspected and confirmed by bone marrow aspiration, which demonstrated 50% of T-cell acute lymphoblastic leukemia blast cells, together with one of acute tumor lysis syndrome.

Treatment with intravenous fluids, 500 ml/h, intravenous allopurinol, and intravenous furosemide was commenced together with 3 mg intravenous rasburicase. A bone marrow biopsy was performed, which showed a marrow infiltration of small lymphocytes.

The following day, day 1 after biopsy, the patient continued to receive intravenous fluids of 0.9% saline at a rate of 125 ml/h; low-dose intravenous dexamethasone was commenced with oral allopurinol, 100 mg once daily. In addition, cytotoxic agents (vincristine and cyclophosphamide) were commenced in preparation for a high-dose chemotherapy course to start after 3 days.

The laboratory values are shown in table 1.

The entity of acute tumor lysis syndrome is characterized by the rapid development of hyperkalemia, hyperuricemia, hyperphosphatemia, lactic acidosis, and acute renal failure in a patient who may have a hematologic malignancy. The mechanism that may precipitate this catastrophic cycle of events is often the initiation of cytotoxic chemotherapy inducing cell death of malignant tissue, leading to rapid release of intracellular substances that lead to these metabolic abnormalities.

Several reports from oncologic centers attest to the occurrence of acute tumor lysis syndrome in aggressive hematologic neoplasms such as Burkitt lymphoma, lymphoblastic lymphoma, and acute leukemia, usually when treatment with cytotoxic chemotherapy is commenced and rapid death of a large volume of neoplastic cells takes place.^{1,2}

The use of a single dose of preoperative intravenous dexamethasone has been reported to significantly decrease the overall incidence of postoperative nausea and vomiting in children undergoing adenotonsillectomy and as an antiemetic in adults undergoing chemotherapy.^{3,4} The exact mechanism of its antiemetic action remains unclear, but recent studies suggest a central antiemetic action through activation of the glucocorticoid receptors in the bilateral nucleus tractus solitarius in the medulla.

In our hospital, we have used intravenous dexamethasone routinely to prevent postoperative tissue edema and as an antiemetic, and have not been aware of its possible relevance in causing the tumor lysis syndrome in patients suspected of harboring a lymphoma.

Although tumor lysis syndrome may occur spontaneously before the administration of therapy, it most commonly presents after the initia-

tion of cytotoxic chemotherapy. Predisposing factors for its development include tumors with a high proliferative rate, a relatively large tumor burden, and a high sensitivity to cytotoxic agents.

Glucocorticosteroids have a known lympholytic effect and are therefore commonly used as part of combination chemotherapy protocols for the treatment of lymphoid malignancies. The mechanism of steroid action is through the induction of growth arrest and apoptosis in treated lymphocytes. Although widely used, there are only a few case reports of tumor lysis syndrome in patients with aggressive tumors treated solely with steroids.⁵ Nevertheless, empiric therapy with steroids is usually avoided in patients suspected of having a lymphoid malignancy.

The best approach in the prevention of tumor lysis syndrome, especially in high-risk patients, is by the induction of a high urine output, prevention of urate production with the xanthine oxidase inhibitor allopurinol, and more recently, by the conversion of urate to allantoin with the recombinant urate oxidase rasburicase.^{6,7} Urine alkalization remains controversial.

In the case we currently report, a diagnosis of aggressive lymphoma was highly suspected before the operative procedure of excisional biopsy. Although there were no markers for an increased risk of tumor lysis syndrome before the operation, the erroneous empiric use of intravenous steroids led to clinically significant manifestations of this syndrome. We suggest that in patients suspected of having a high-grade lymphoproliferative disorder, corticosteroid therapy should be withheld before the establishment of a precise diagnosis. In addition, preventive measures including fluid volume replacement and perhaps the use of allopurinol and rasburicase should be considered before the operation.

Michael Chanimov, M.D., Ph.D., Maya Koren-Michowitz, M.D., Mathias L. Cohen, M.B., Ch.B., Semion Pilipodi, M.D., Murat Bahar, M.D.* *Assaf Harofeh Medical Center, Zerifin, Israel. fredricag@asaf.health.gov.il

References

- Vaisban E, Zaina A, Braester A, Manaster J, Horn Y: Acute tumor lysis syndrome induced by high-dose corticosteroids in a patient with chronic lymphatic leukemia. *Ann Hematol* 2001; 80:314-5
- Cohen LF, Balow JE, Magrath IT, Poplack DG, Ziegler JL: Acute tumor lysis syndrome: A review of 37 patients with Burkitt's lymphoma. *Am J Med* 1980; 68:486-91
- Pappas AL, Sukhani R, Hotaling AJ, Mikat-Stevens M, Javorski JJ, Donzelli J, Shenoy K: The effect of preoperative dexamethasone on the immediate and delayed postoperative morbidity in children undergoing adenotonsillectomy. *Anesth Analg* 1998; 87:57-61
- Jones AL, Hill AS, Soukop M, Hutcheon AW, Cassidy J, Kaye SB, Sikora K, Carney DN, Cunningham D: Comparison of dexamethasone and ondansetron in the prophylaxis of emesis induced by moderately emetogenic chemotherapy. *Lancet* 1991; 338:483-7
- Lerza R, Botta M, Barsotti B, Schenone E, Mencoboni M, Bogliolo G, Pannacchiulli I, Arboscio E: Dexamethasone-induced acute tumor lysis syndrome in a T-cell malignant lymphoma. *Leuk Lymphoma* 2002; 43:1129-32
- Cairo MS, Bishop M: Tumor lysis syndrome: New therapeutic strategies and classification. *Br J Haematol* 2004; 127:3-11
- Trifilio S, Evens A, Gordon L, Singhal S, Tallman M, Mehta J: Low-dose recombinant urate oxidase (rasburicase) is effective in treating hyperuricemia in patients with hematologic malignancies (abstract). *Blood* 2005; 106:3123

(Accepted for publication April 27, 2006.)

Tongue Necrosis and Cleft after Prolonged Transesophageal Echocardiography Probe Placement

To the Editor:—Tongue injury is a relatively uncommon complication in the perioperative period. It is usually attributed to prolonged orotracheal intubation. Here, we report a case of necrosis of the tongue resulting in a permanent cleft that occurred after prolonged cardiac surgery during which a transesophageal echocardiography probe was placed for monitoring.

A 61-yr-old Asian Indian man was scheduled to undergo elective mitral, aortic, and tricuspid valve replacement surgery. Significant medical history included mitral valve replacement 8 yr previously for rheumatic heart disease, congestive heart failure, chronic atrial fibrillation, diabetes mellitus, and hypothyroidism. Medications included aspirin (discontinued 8 days before surgery), warfarin (stopped 2 days before surgery and replaced by low-molecular-weight heparin), digoxin, glipizide, and levodopa. The results of routine investigations were normal.

In the operating room, the patient was intubated atraumatically on the first attempt using a 7.5-mm-ID endotracheal tube, and the tube was taped at 24 cm at the level of the teeth. Anesthesia was maintained with isoflurane–narcotic technique. The transesophageal echocardiography probe (6-T multiplane transesophageal transducer; GE Healthcare, Milwaukee, WI) was placed atraumatically. Cardiopulmonary bypass was initiated and maintained without complications. An initial attempt to wean off bypass was unsuccessful because of bleeding and oozing. After the coagulopathy was corrected, weaning was successful after a total of 315 min cardiopulmonary bypass time. The patient was subsequently transferred to the surgical intensive care unit on standard dose ranges of multiple pressors (epinephrine, vasopressin, dobutamine) and placed on a ventilator. Total surgery and anesthesia times were 549 and 650 min, respectively.

Swelling of the tongue was noticed immediately on admission to the surgical intensive care unit, and it was not associated with concomitant facial or neck edema. A midline partial necrosis of the tongue became apparent on postoperative day 2. Notably, the midline position of the tongue injury was away from the endotracheal tube, which was positioned at the right lateral side of the tongue and was taped to the right side of the mouth. Planned tracheostomy was postponed because of severe adult respiratory distress syndrome, coagulopathy, and hemodynamic instability that required multiple inotropic and vasopressor support. Multiple bedside tongue débridements and routine oral care did not improve the patient's condition. Tracheostomy was performed on postoperative day 18, and local care of the tongue continued with marked improvement. A photograph taken 10 days after tracheostomy is shown (fig. 1).

The patient was then transferred to a long-term care facility with the tracheostomy in place. Six months later, the tongue had healed with a residual median linear cleft. The trachea was subsequently decannulated. This resulted in a significant improvement in articulation, and the patient recovered with only a minor functional deficit.

Tongue injury is an infrequent but potentially severe complication of prolonged orotracheal intubation. It has been reported from the use of endotracheal tubes, laryngeal mask airways, and esophageal–tracheal Combitubes.¹

The pathophysiologic mechanisms of the injury include prolonged glossal compression with venous congestion, edema, and ischemia that lead to the tongue necrosis.² The main reason for the swelling seems to be a compression of the glossal blood vessels, especially the lingual veins. Other causes include sublingual hematoma³ and obstruction of the submandibular duct.⁴ The position of the patient may also contribute to this problem. Massive tongue edema after spinal surgery has been reported, attributed to the flexed thoracic–cervical position required.⁵ Lingual nerve injury has been associated with orotracheal intubation and may contribute to this problem because of sensory deprivation.⁶



Fig. 1. Aspect of the tongue on postoperative day 10 showing superficial necrosis and medial clefting.

Yamamoto *et al.*⁷ reported a case of edema of the tongue after intraoperative monitoring by a transesophageal probe, and in this report, the tongue returned to normal size 1 day after surgery. In our patient, prolonged (540 min) contact with the transesophageal echocardiography probe might have contributed to edema that progressed to necrosis. The natural prominence at the base of the tongue and midline position of the probe favor this explanation as being the likely cause of the injury. It is unlikely that midline tongue injury could have been caused by endotracheal tube placement, because it was positioned more laterally in the mouth.

When edema of the tongue is noted during or after general anesthesia, an attempt should be made to change the position of the endotracheal tube or other transoral devices. These simple maneuvers may prevent progression to tissue necrosis. When actual necrosis is noted, early débridement is indicated.⁸ If prolonged ventilatory support is anticipated, tracheostomy should be performed as soon as possible to facilitate aggressive tongue and oral care. The formation of a tongue cleft is a permanent impairment that may result in residual functional deficit.⁹

Krishnan Sriram, M.D.,* Arjang Khorasani, M.D., Kamana E. Mbekeani, M.D., M.B.A., Subhash Patel, M.D. *Stroger Hospital of Cook County, Chicago, Illinois. ksriram41@hotmail.com

References

- McGlinch BP, Martin DP, Volcheck GW, Carmichael SW: Tongue engorgement with prolonged use of the esophageal–tracheal Combitube. *Ann Emerg Med* 2004; 44:320–2
- Takasaki Y: Transient lingual ischemia during anesthesia (case report). *Anaesthesia* 2003; 58:717
- McGoldrick KE, Donlon JV: Sublingual hematoma following difficult laryngoscopy. *Anesth Analg* 1979; 58:343–4
- Heuhns TY, Yentis SM, Cumberworth V: Apparent massive tongue swelling. *Anaesthesia* 1994; 49:414–6
- Miura Y, Mimatsu K, Iwata H: Massive tongue swelling as a complication after spinal surgery. *J Spinal Disord* 1996; 9:339–41
- Teichner RL: Lingual nerve injury: A complication of orotracheal intubation (case report). *Br J Anaesth* 1971; 43:413–4
- Yamamoto H, Fujimura N, Namiki A: Swelling of the tongue after intraoperative monitoring by transesophageal echocardiography. *Masui* 2001; 50:1250–2
- Bagenyi J, Barankay A: Report of a partial necrosis of the tongue caused by an endotracheal tube. *Anaesthesist* 1975; 24:136–7
- Stauffer JL, Petty TL: Cleft tongue and ulceration of hard palate: Complications of oral intubation. *Chest* 1978; 74:317–8

Support was provided solely from institutional and/or departmental sources.

(Accepted for publication May 16, 2006.)