Sapere Aude!
The 2009 Excellence in Research Lecture
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This essay is based on my remarks in acceptance of the American Society of Anesthesiologists Excellence in Research Award at the 2009 Annual Meeting. I used the great honor bestowed by the Society to acknowledge and thank a few—but certainly not all—of the many folks who made it possible for me to be considered for that award. I then used the opportunity to make a number of editorial and philosophical comments about certain aspects of career development that I find to be mission critical for the health and safety of our specialty. These topics are discussed here and concern mentorship and how productivity and independence relate during career development of junior faculty. The second broad area was commentary on how we, as a specialty, might think beyond the confines of our clinical horizons in terms of academic inquiry.

My comments are mainly aimed at our younger colleagues. I truly hope that the well-attended Excellence in Research session had many future recipients of the award in the audience, and that a few minutes of my musing might have sparked the imagination of at least a few.

Mentorship and Apprenticeship

If you are thinking about an academic research career, and you have decided that you wish to carve nature at the joints, what are the considerations? If you want to develop into a successful investigator, the stronger the mentor is, the greater the potential of success. I suppose that is a testable hypothesis, but for now it is a proposition based on my retrospection.

One of the canards quacking through the cosmos (a mem-

orable turn of phrase used by Mike McCurry, former press secretary for President Bill Clinton) is that you need to be some kind of “rocket scientist” to be a successful researcher. I am definitely a strong proponent of Thomas Edison’s proportions in the paraphrase, “Achievement is 1% inspiration, and 99% perspiration.” If you want to pursue a career that involves scholarly activity centering on scientific research, you do not even need research training before you start on your journey (my undergraduate major was in Germanic Languages). There is no absolute precondition for academic success—with the possible exception of mentorship. In my view, that is a sine qua non for the best outcome.

If we accept this premise, then it seems logical to start with a question or a specific topic of interest and then let that lead to choosing a mentor. However intuitive, a somewhat more nuanced approach is recommended, rather than “specific question leads to choice of specific mentor.” My advice is to first find a strong mentor who is working in your general area of interest. It is not necessary to make a terminal decision at the outset, like, for example, buying a car or a house. Finding the set of questions on which you will eventually channel your energies and passions toward is often a heuristic, iterative process: do not sweat the details before you start the journey. Finding the right set of questions is an anxiety-provoking decision process to face for a young trainee or a faculty, who rightly views the vast expanse of questions and methods as daunting. That expanse is daunting no matter what career stage you find yourself at. Standing at the ocean’s edge looking out to sea, the horizon does not change over the years, it is just one’s appreciation of what might lie beyond it.

In my conception, a mentor is more than someone who guides and advises you. Intellectual capital is exchanged. At the outset, the flow is from mentor to mentee. There are undoubtedly exceptions, but the lion’s share of those starting off need some concrete place to start their scholarly inquiries. I know that I certainly did. My interest was in the general area of brain injury, but had I been left to my own devices, I would have most certainly foundered on the academic reef.

My first infusion of intellectual capital was my initial research project under the mentorship of Richard S. Matteo, M.D. (Professor, Department of Anesthesiology, College of Physicians and Surgeons, Columbia University, New York, New York), which dealt with muscle relaxant pharmacology.
in neurosurgical patients. To say that this topic seemed alien and unnatural at the time is a gross understatement. However, what I could not have known was that the experience bootstrapped me sufficiently to take the next steps toward studying brain injury, the object of my real interest.

Perhaps in the end, we all must “bootstrap” ourselves. The mentor provides the intellectual and logistical locus in which to do that and protects that locus. In this way, the mentor acts as an enzyme, not a reagent. I have been fortunate to have been associated over the years with a number of masterful “enzymes.”

Further, in addition to this more passive aspect of locus protection, a mentor needs an active component: to clear the path. It is not so much to provide thrust, rather it is to remove obstacles, of which there are many and of all kinds. In my case, for example, Bennett M. Stein, M.D. (Professor and Chair, Department of Neurologic Surgery, College of Physicians and Surgeons, Columbia University, New York, New York) took me under his wing and prevented me from being eaten by the academic wild—some of them in my own department—thus allowing me to progress forward with our research efforts.

Mentorship has a long history, and this has been extensively discussed in other venues. Since the beginning of recorded history and undoubtedly before that, very few outstanding contributors in the arts or sciences arise in a vacuum. Even the great Isaac Newton, not generally known for humility, said, “If I have seen further than other men, it is because I stood on the shoulders of giants.”

Even if you do not know there is one lurking, they are there. Even the best of the best have mentors. If you shake the “family tree” of a successful artist or a scientist, good mentors will fall out. Leonardo da Vinci was an apprentice with Andrea del Verrocchio. Who? Few but the art historians among us recognize that name. Even those great contributors, whose contributions we might otherwise have thought to have been spontaneous aberrations (“black swans”), are probably embedded in a matrix of good mentorship. For example, John Coltrane did not spring from the brow of Zeus spewing out melodic and harmonic ideas that would forever reshape jazz. He spent a formative period under the wing of Miles Davis.

I wonder if we have lost something by abandoning the concept of apprenticeship. Modern sensibilities have tended to shed off these aspects of mentorship. Too often, modern mentorship is diluted by arm’s length arrangements, checklists and policy statements, and a presumption of independence. There is common concern that those who are inadequately distanced from mentors will not receive tenure, especially in basic science departments. Do not be overly concerned about working with a strong mentor. You are far better off with strength in training; breaking free can always be engineered.

**Independence and Productivity in Career Development**

Strong mentorship should allow the mentee to thoroughly develop all the necessary tool skills to eventually strike out on his or her own. “Achieve escape velocity” is one metaphor, but I would say it is not the best. I mentioned “obstacle clearing” as a prime function of mentorship, rather than provision of “thrust.” Here is perhaps a better concept: neoteny.

This idea is borrowed from the field of developmental biology. Neoteny is when physiologic (or somatic) development of an organism is slowed or delayed. Some make the case that there was a major evolutionary advantage in human development to remain in a protected state allowing maturation of key systems. This is in contradistinction to, for example, baby sharks, which come into the world already well equipped to maintain the species’ position at the top of the food chain.

Consider the graphs in figure 1. In figure 1A, the timeline on the x-axis runs from when a young faculty starts out after training and progresses toward some point at which he or she will be considered for having “established him/herself.” This corresponds to the vertical dotted line. This timeline would correspond, for example, to promotion from assistant to associate professor, perhaps including the granting of tenure. The candidate needs to attain some measure of achievement, as denoted by the X on the dotted line.

There are two powerful concepts here: “independence” and productivity. It is commonly—and intuitively—thought that development of these two traits is colinear. This can be a mistake. Independence is a powerful motivating force and a necessary eventual goal. It can, however, be like a narcotic and interfere with acquiring key skills and intellectual development. It is not uncommon for a junior faculty to assert the desire for more independence far too early.

There is also enabling at work here: our academic culture further compounds the problem with the very title “Assistant Professor” itself. Our Ph.D. colleagues in basic science departments usually do not earn that title until they have finished extended postdoctoral fellowships and are truly independent, more like the baby sharks referred earlier. In our specialty, and in many clinical disciplines that I referred to earlier, the title of Assistant Professor is given after completion of clinical training only, or on the basis of having earned a combined M.D.-Ph.D.

If independence is too early, productivity can lag behind, as depicted in figure 1B. When candidates are called to the bar for assessment, their project may be insufficiently productive. Of course many systems admittedly have a “prepromotion” formal assessment, but that is not very reassuring. There is something that is probably even more important than actual failure to be promoted or to achieve tenure: a frustrated young faculty may simply decide that it is not worth it to stay on the arduous track of scholarship. There are many distractions, both on and off the field.

But productivity is also a powerful medicine. What needs to happen in my view is shown in the set of curves shown in figure 1C. One should closely support the trainee to maximize productivity without undue preoccupation with “independence,” and then in the period shortly before assessment,
Many of us recognize this in more familiar terms such as “write the mentee’s first grant” or the like. To be sure, there is a wide range of skills and sophistication present when a trainee is ready to write his or her K-grant. We should err on the side of helping too much. Dick Matteo would tell me, “We’re here to help you, whether you like it or not.”

Tenure committees do not really care about how one arrives at productivity and independence, as long as it is present at the dotted line. It is the attainment of both that counts, not the trajectory.

In terms of strategic planning for bootstrapping the scholarly research output of our specialty, we have an urgent need to better exploit the National Institutes of Health (NIH) K-award system and expand our use of the T32 training grant program. And at a more root level, we must ingrain research training and scholarship into our residencies and fellowships to achieve parity with other clinical specialties in terms of NIH funding. Several notable departments, our own included, have started innovative residency tracks to foster the intellectual spirit and fan the creative flames in our resident trainees.

Teams and Networks

The concept of “teams and networks” is another key aspect of modern academic success. Going outside of your specialty to get answers and form questions naturally leads in this direction. Too often a sort of specialty-based “tribalism” conspires to impede that. Mentors have to champion breaking down such walls, trying to obtain a sort of intellectual comity in an interdisciplinary community. Comity is a legal concept; it refers to respect for other branches. For example, it is the courtesy one jurisdiction gives by enforcing the laws of another jurisdiction. Comity is granted out of respect, deference, or friendship, rather than as an obligation.

No matter how brilliant your insights or how sharp your skills are, in the modern scientific world, being trapped in a silo is not conducive to success. The “one man, one lab” notion is a model with great historical precedent; one might argue that the NIH R01 funding model was largely based on it. However, it is now an anachronism—it should be in one of those dioramas in the Museum of Natural History as an extinct species. The concept dies hard, perhaps especially for Americans. We have this sort of lone-cowboy-riding-off-in-the-sunset image, like Shane. But it is a last-century approach. You can be both “independent” and “networked.” Networking leads to team building. My best advice to the junior investigator is: either build a team or be part of one.

A special case of “team building” is having a network of professional friends, an enriching and invaluable part of academic life, and one of the true benefits of being an academic. It is very easy to find people whom you like and like to be with, in a group of people who are passionate about the same things as you. Beware of manipulative relationships.

Fig. 1. Neoteny. (A) The timeline on the x-axis runs from when a young faculty starts out after training and progresses toward some point at which he or she will be considered for having “established him/herself.” This corresponds to the vertical dotted line. The timeline would correspond, for example, to promotion from assistant to associate professor, perhaps including the granting of tenure. The candidate needs to attain some measure of achievement, as denoted by the x on the dotted line. (B) If independence is too early, productivity may lag behind. When candidates are assessed, their project may be insufficiently productive. (C) Ideally, we should closely support a candidate to maximize productivity without undue preoccupation with “independence” and then in the period shortly before assessment, ramp up and give a “burst” of independence. See text for further explanation.
North Atlantic Treaty Organization, his critics said, “You’ve abandoned your friends,” to which he replied in his inimitable fashion, “France has no friends; France has interests.” Friends chosen as pure academic interests will only disappoint in the long run. One of the best ways to make professional friends is the relative intimacy of subspecialty societies. Subspecialization is an invaluable career development forum. For example, in my case I am indebted to our neuroanesthesia society, the Society of Neurosurgical Anesthesia & Critical Care.

Boundaries and How We Fit into the Intellectual Cosmos

A whole research program can spring from a single case, at least the ideas and problems that are suggested by it. I would argue that our whole research effort sprang from a single patient study that ended up becoming a modest case report.⁶ Carrying through the ideas embodied in that case report was made possible by the right mentorship. Our large cerebrovascular research program at the University of California, San Francisco, expanded well outside of not only the “operating room,” but also beyond the confines of traditional perioperative medicine.

We have a multidisciplinary vascular biology and genomics-based National Institute of Neurologic Disorders and Stroke program project grant, entitled “Integrative Study of Brain Vascular Malformations.” Our efforts are now not only multidisciplinary but also multicenter. Our research group, the Center for Cerebrovascular Research, has embarked on a large clinical project called the “Brain Vascular Malformation” Consortium (U54 NS065705).† The NIH has established 19 Rare Disease Clinical Research Consortia, spanning every organ system and specialty, and we are one of them.

In terms of pure clinical research, my former teammates at Columbia went on to develop the clinical side of the research project and obtain NIH funding for a large international trial with 90 centers worldwide that is currently studying treatment outcomes.‡ This trial, called A Randomized Trial of Unruptured Brain Arteriovenous Malformations, questions conventional wisdom about treating asymptomatic cerebrovascular disease. It is a highly controversial trial, but it is almost always good to question conventional wisdom. Although I have played a relatively minor part in this randomized controlled trial effort, I would like to think that the larger view of what was possible with programmatic arteriovenous malformation research—flowing from that original case report—was an integral part of setting the stage.

Recounting these personal details leads to another deep point: all of this activity was made possible by starting with a basic “anesthesia” or “intraoperative” question and then following the scientific questions for the disease of interest as they arose (fig. 2). The questions—and the answers to them—did not respect the largely synthetic boundaries imposed by nineteenth and early twentieth century categorization of medical specialties. This is hypothesized to be a payoff from working with teams and networks, and mentors from a wide range of intellectual domains.

Basic scientists figured this out a long time ago. Many new frontiers in biomedicine lie at the boundaries of established departmental or specialty divisions. A look at any large institution’s roster of academic divisions yields a growing number of “centers,” “programs,” and “institutes,” reflecting the ever-increasing interdependency of branches in biomedical knowledge.§ The conjugate names, like Physiology and Cellular Biophysics, Anatomy and Cell Biology, Biochemistry and Biophysics, and Cellular and Molecular Pharmacology, bring home the message that the interesting stuff may well be in the cracks between big stones.

Thomas S. Kuhn (1922–1996), author of The Structure of Scientific Revolutions,⁷ was one to argue for this cross-specialization as an important aspect of scientific progress, by fostering paradigm shifts. Not only are the interesting things sometimes hidden at the fringes of established domains, but there is also a perspectival component to looking at a problem from the outside in. Kuhn cites the example of John

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Dalton (1766–1844), who most of us learned was one of the fathers of modern chemistry. He famously undertook the investigations that eventually led to his chemical atomic theory, for which he is remembered by the eponymous unit of atomic weight.

Kuhn wrote, “But until the very last stages of those investigations, Dalton was neither a chemist nor interested in chemistry. Instead, he was a meteorologist investigating the, for him, physical problems of the absorption of gases by water and of water by the atmosphere. Partly because his training was in a different specialty and partly because of his own work in that specialty, he approached these problems with a paradigm different from that of contemporary chemists.” Training in a discipline is of course necessary: what we see depends both on what we look at and also on what our previous experience has taught us to see. Otherwise, in the absence of such training, “there can only be, in William James’s phrase, 'a bloomin' buzzin' confusion.'” So there is potential strength in having a unique lens through which we view the world, allowing us to generate questions and answers to problems that confront us in the clinic. But therein lays the potential rub: intellectual handcuffs.

Just because you are an anesthesiologist does not necessarily mean you have to study anesthetics—you need to "think outside the bag." Undue focus on "anesthetics" or techniques, rather than diseases and outcomes, is a major blind spot that, in my opinion, threatens our specialty. Anesthesiology is running a series of editorials on "long-term consequences of anesthesia." This series is a welcome breath of fresh air and is right on the money. But it does not go far enough.

Those of us in Anesthesiology can take a fresh look at many perioperative problems and their underlying diseases that can bring patients to surgical intervention in the first place. The perioperative experience can serve as the unifying, central focus for a wider range of biomedical questions. Any number of questions that are rooted in perioperative concerns may be extended to encompass the entire disease or care process.

This is a way to conceptualize the study of a disease or a problem (fig. 3). It is sort of a Copernican shift from looking at the perioperative experience as some distant rock circling other specialties, but rather the central focus of an entire range of experiences that all pass through the perioperative period.

Our training as anesthesiologists provides a set of skills and perspectives that can ably serve as a sort of "academic enzyme" that musters activity from a wide range of intellectual domains over an equally as broad spectrum of a disease. In particular, our close one-on-one relationship with patients allows high-quality and high-temporal resolution clinical phenotyping, which is a unique aspect of our clinical practice. This positions us well for the "personalized healthcare" revolution.

What then should aspiring clinician scientists choose to interest themselves in? As a general precept, you should strive to study systems and not things. Not that things are unimportant, but they lose biologic and then translational significance if they become ends in themselves. If you want to study Beethoven’s symphonies or John Coltrane’s saxophone solos, you do not study the instruments, at least not primarily. Violinology or saxophonology are self-limited. Rather, you should strive to get to the system that ties the notes and rhythms together to result in the final product. There is nothing wrong with studying basic cellular level signaling, or growth factors or inflammatory cytokines, but make sure they fit into a disease model.

**How the Specialty Performs in Academic Success**

Why does anesthesiology fare so poorly in NIH funding, for example? There is no a priori reason why anesthesiology should differ from any other medical specialty in terms of research output. Undoubtedly, this is a complex question that needs more than these few pages to consider.

J. G. Reves, M.D. (Dean, College of Medicine and Vice-President for Medical Affairs, Medical University of South Carolina, Charleston, South Carolina) in the 2005 Rovenstein lecture presented disturbing data. An analysis of NIH dollars awarded per faculty member showed that our specialty is abysmally low compared with others. Debra A. Schwinn, M.D. (Professor of Anesthesiology and Pain Medicine, University of Washington, Seattle, Washington) and Jeffrey R. Balser, M.D., Ph.D. (Dean, School of Medicine, Vanderbilt University, Nashville, Tennessee) also critically examined various aspects of NIH funding to Anesthesiology. They concluded that we are at risk of losing our status as a respected academic discipline within the broader biomedical community and made a "passionate call for decisive action." Many erudite commentaries were published in response to their plea, so somebody is listening. But are there enough?
I offer a simple example that makes a comparative point using a more recent dataset. In Table 1, I show the top 10 departments in the United States in NIH funding for two specialties in 2008: Anesthesiology and Neurosurgery. Cursory inspection shows that perhaps the Neurosurgery top end is a little higher, but the range is roughly similar and the same departments more or less populate the lists. What should be shocking is that there are roughly 10 times as many anesthesiologists in the United States as there are neurosurgeons!

As another index of our scientific performance as a specialty, there is a recently published examination of what specialties are chosen by M.D.-Ph.D. graduates. Figure 4 shows the Relative Risk for M.D.-Ph.D. graduates choosing one of several specialties (taken from a much longer list) compared with all other American medical school seniors. The higher the Relative Risk, the more likely the M.D.-Ph.D. student will enter that specialty. Not only do we do poorly, but also the Relative Risk is actually less than 1; that is, our specialty has a “protective effect” against being chosen by M.D.-Ph.D. graduates. Another dark day in a forest of nights for our specialty’s standing, relative to its peers.

What explains our poor showing? The easy answers are often sound bytes, like “too many service responsibilities,” necessitating a redistribution of (potential) academicians and resources to provide clinical coverage. As Ronald D. Miller, M.D. (Professor, Department of Anesthesia and Perioperative Care, University of San Francisco, San Francisco, California) and William L. Lanier, M.D. (Professor of Anesthesiology, Mayo Clinic, Rochester, Minnesota) wrote in an editorial a few years ago, the effect of this course this is too simplistic, but it makes the point.

In my opinion, however, the roots of the problem run much deeper. One hypothesis is that we need to be looking at what causes and treats diseases of the patients we care for, like our counterparts in other specialties. Figure 5 is a graph based on several simple searches of PubMed for the journals listed in the figure. The number of hits containing the keywords [etiology or pathogenesis] and [journal name] was divided by the total number of hits by searching [journal name]. This fraction is shown as a percentage on the x-axis. I rather arbitrarily picked these journals roughly corresponding to those in Figure 4. Not only are we not a very high percentage, but we are also below the mean for all PubMed citations. Of course this is too simplistic, but it makes the point.

Some may say, well, first of all, etiology or pathogenesis is not anesthesia research, and that we have to “focus” on what we do. However, for our scholarly inquiry, I think this is part of the problem: focus is a good tactic but not a good strategy.

We should not limit our horizons. First, we can certainly investigate the wisdom and efficacy of any procedure we are involved with. Those in the readership providing clinical care appreciate that, with respect to patient outcomes from their

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<th>Table 1. Ranking of NIH Funding to U.S. Medical Schools in 2008*</th>
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<td><strong>Neurosurgery</strong></td>
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<td>University of California, San Francisco $12,705,339</td>
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<td>University of Pittsburgh $6,254,822</td>
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<td>Yale University $5,580,804</td>
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<td>University of Washington $3,808,255</td>
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<td>University of California, Los Angeles $3,421,509</td>
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<td>Penn State University $3,460,805</td>
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* From the National Institutes of Health (NIH) Research Portfolio Online Reporting Tool (RePORT) (http://report.nih.gov/award/trends/BrowseOrgs.cfm?NameBegins=A&InstFilter=MS). The total awarded to each Medical School is the sum of (a) the School of Medicine and (b) the overall medical component.
Disease process, there is no shortage of safety and efficacy questions out there in the cases that flow in high volumes through our operating rooms. But that is just the tip of the iceberg. The etiology, pathogenesis, and natural history of any disease of any patient group we care for is open for scholarly inquiry; there are no inherent boundaries.

**Definitional Challenge**

There is a definitional problem that compounds—and perhaps undergirds—the issue of proper focus on appropriate questions. The scientific activity of anesthesiologists should not be dictated by our “name,” or *necessarily* defined by our current clinical activities. The philosopher, Karl Popper (1902–1994), once said that good definitions in science are to properly read from right to left, and not from left to right. To paraphrase his example, take the following sentence:

“Ischemic stroke is a syndrome of focal brain injury from inadequate perfusion.”

This statement is the neuroscientist’s answer to the question, “What should we call a syndrome of focal brain injury from inadequate perfusion?” It is *not* an answer to the question, “What is ischemic stroke?” The term used here, “ischemic stroke,” is just a handle, a shorthand sort of substitute for the long description to the right of “is.” There is no information about neuroscience contained in “ischemic stroke,” our shorthand term.

In a similar sense, “anesthesiology” is another handle, admittedly for a much more complicated description. However, it is just that: a *description* and not a *prescription*. The creative activity of anesthesiologists defines what we are. If those activities change, so does what lies to the right of the “is” term. Our term, “anesthesiology,” should not dictate what we are supposed to be. Do not read the definition from left to right. Otherwise, we are risking being trapped in the present by mistaking the map for the territory.

We need to widen our horizons on the questions we ask. Ideally, the current state of the specialty should be a result of the questions we ask—not the cause. Any question that impacts perioperative patients and perioperative care is open.

**Conclusions**

“We need to widen our horizons on the questions we ask. Ideally, the current state of the specialty should be a result of the questions we ask—not the cause. Any question that impacts perioperative patients and perioperative care is open.

**References**


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Fig. 5. Is anesthesiology deficient in seeking out questions related to etiology or pathogenesis for the diseases of our patients? Percentage of hits for journals with the key words “etiology” or “pathogenesis.” The fraction was calculated as (journal) and (etiology or pathogenesis), divided by (journal), multiplied by 100. For all citations, “all” was used instead of journal name.
10. Reves JG: We are what we make: Transforming research in anesthesiology: The 45th Rovenstine Lecture. Anesthesiology 2007; 106:826–35

ANESTHESIOLOGY REFLECTIONS

Churchill Acupuncture Needles

In A Treatise on Acupuncturation (1821), James Morss Churchill describes how he conducted acupuncture with thick-gauged British sewing needles (above), the ivory finger holds of which he “pressed gently, whilst a rotary motion is given . . . by the finger and thumb.” When asked how his acupuncture worked, the English surgeon preferred “preserving a profound silence.” Years later, a grateful 3rd Earl of Egremont would reward Churchill’s acupuncture prowess (in relieving the Earl’s rheumatism and sciatica) with both fame and fortune. The latter the Earl bestowed in pounds sterling; the former, as long-term publicity afforded by dubbing the Earl’s most prized racehorse “Acupuncture.” (Copyright © the American Society of Anesthesiologists, Inc. This image appears in color in the Anesthesiology Reflections online collection available at www.anesthesiology.org.)

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