H&P

The Stanford Medical Student Journal

Volume 13, Number 1 Autumn 2008

100 Years: A Century of Medicine

Contents

H&P
The Stanford Medical Student Journal

H&P, the Stanford Medical Student Journal, is published by students of the Stanford University School of Medicine. All articles are written by students. *H&P* is not an official publication of the Stanford University School of Medicine or its faculty. Expressed written opinions are solely those of the authors and do not necessarily represent those of Stanford University or the School of Medicine.

H&P is published quarterly. Submissions are accepted on CD or by email.

Please submit inquiries to Sean Sachdev (sean.sachdev@gmail.com). Correspondence may be addressed to OSA, Stanford University School of Medicine, Stanford, CA 94305.

Front/Rear Artwork:
Courtesy Lane Library

Editors' Note

This year we celebrate 100 years of medicine at Stanford. In 1908, Cooper Medical College officially became part of Stanford University, and thus began the tradition of excellent clinical training and groundbreaking biomedical research that we are fortunate to be part of today.

In this issue of *H&P*, Ron Alfa, SMS II, peruses the Lane Library archives, and invites you to imagine a day in the life of a Stanford medical student in 1908. Anatomy, clinical training, studying into the small hours of the night. Sound familiar? Sean Sachdev, SMS II, takes us through an awe-inspiring timeline of the many biomedical discoveries and breakthroughs that have occurred under the auspices of Stanford Medicine. Mike Sundberg, SMS II, reflects on the evolving vision of Stanford Medical School, in terms of medical training, research and patient care, from Elias Samuel Cooper to our own Dean Pizzo. These forays into the past serve as a humbling reminder that, even as students, we are part of the long and rich story of Stanford Medicine. The front and back covers give us glimpses of what medical education was like at Stanford nearly a century ago, with a portion of the official photo of the class of 1929 as the front and a part of Elias Samuel Cooper's introductory anatomy lecture as the back.

Rounding out this issue is an ethics piece by Jocelyn Grunwell, SMS IV, who asks us to consider key questions concerning the ethical framework in which to consider neuroregenerative medicine. James Colbert, SMS IV, presents us with the case of an infant with weakness and guides us through the work-up to the diagnosis.

Complementing these pieces in the Humanities section, Blake Charlton interviews Abraham Verghese, Professor of Medicine, Senior Associate Chair for the Program in the Theory and Practice of Medicine, and author of both fiction and non-fiction. They discuss the medical narrative, the importance of writing, and technology in medicine. Recent graduate Dona Tversky, SMS Class of 2008 and now a first-year psychiatry resident, shares a powerful photo-essay on health and aging based on her conversations with four patients, who graciously agreed to have their stories re-told on our pages. We also proudly showcase the 11-Sentence Medical Mystery, a competition that took place for 10 weeks this past spring to create suspense and intrigue based on one sentence, releasing the creative energies in all of us who participated and read the story each week.

Last, but not least, Sean Sachdev relays his conversation with Dr. Robert Negrin, an expert in bone marrow transplantation and a true triple threat, who shares both inspiring thoughts and grounding advice to medical students.

Our student journal, *H&P*, has a past of its own. We wish it dated as far back as 1908—what a window into the interests and concerns of students that would yield. The journal began 13 volumes ago, in 1995, as the *Stanford Medical Student Clinical Journal*, with the goal of providing a forum for student expression, artwork, and reflection on the art of medicine. The journal was renamed *H&P*, as described below, in 2006. It has been a pleasure to be part of the journal's staff, and to continue to be inspired by our fellow students' contributions with each issue. As we begin clinical rotations, we are pleased to leave *H&P* in the very capable hands of Sean Sachdev and Mike Sundberg. We look forward to the recording of another year of Stanford Medicine in words and pictures, and hope that Stanford medical students of 2108 might get to know us through these pages one day.

Chantal Forfota
Malavika Prabhu
Senior Editors, *H&P*

The title H&P reflects the importance of the basic history and physical examination in clinical medicine in every corner of the world. It also represents Hygeia and Panacea, two daughters of Asclepius. In Greek mythology, Hygeia is the goddess of welfare and the prevention of sickness, while Panacea is the goddess of healing and cures. We believe that these figures represent the two facets of our medical education—to treat and cure illnesses while promoting the welfare of our patients by preventing disease. The title H&P also reflects our interest in the metaphors of medicine. What an illness means to a patient may be as important as the diagnosis itself, and a practitioner of the art of medicine attends to each of these meanings.

Infant Hypotonia: A Four-Month-Old Boy with Weakness and Poor Feeding

James Colbert, SMS IV

CL is a previously healthy four-month-old boy who was brought to a pediatric urgent care center for decreased energy, inability to feed, and a weak cry. His parents note that his illness began 10 days previously with rhinorrhea and nonproductive cough and has progressively worsened since then. He has not had fevers, sweats, or chills. A nurse practitioner at the urgent care clinic diagnosed CL with otitis media and sent him home with a prescription for amoxicillin.

Acute otitis media, an infection of the middle ear, is the most common diagnosis in the outpatient pediatric setting. The main symptoms of AOM are ear pain, hearing loss, and vertigo. It often affects children with upper respiratory symptoms such as rhinorrhea or sinus congestion, as obstruction of the Eustachian tube leads to negative pressure and accumulation of middle ear secretions. Clinical complications include tympanic membrane rupture, mastoiditis, and, very rarely, meningitis or CNS abscess formation. AOM is predominantly a bacterial infection; however, two-thirds of infections involve a mixture of bacteria and viruses.[1] The three most common pathogens responsible for AOM are *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*. Approximately 30% of all antibiotics given to children in the United States are for the treatment of otitis media.[2] Amoxicillin is generally the treatment of choice for patients under the age of two. For patients over the age of two with AOM accompanied by fever less than 39 degrees Celsius and mild ear pain, the American Academy of Pediatrics 2004 guidelines offer the option of watchful waiting rather than antibiotic treatment.

The patient was born at term following a normal pregnancy with no complications. The mother is 27 years old and this was her second pregnancy and second delivery. Until this recent illness, CL had been healthy and developmentally normal. He received his regular two-month vaccinations. He has no known allergies. The patient lives with his parents and two-and-a-half year old brother in a small town in the Central Valley of California. The mother works as a waitress at Olive Garden and the father works as a plumber at construction sites. There is no recent travel history, although the father did serve as a Marine in Afghanistan and Iraq six years ago. He has not had any known sick contacts.

The "classic" disease associated with the Central Valley of California is coccidioidomycosis, a systemic disease caused by inhalation of the spores of the dimorphic fungus *Coccidioides imitis*. In most patients the respiratory infection is self-limited, but the fungus may spread hematogenously and present as a disseminated disease involving the skin, bones, joints, lymph nodes, and other organs. The Central Valley is a predominantly agricultural environment, thus one should always consider fertilizer, pesticide, and organophosphate poisoning in any patient from this region. Also, the region is dry and arid, thus patients from the Central Valley are also at increased risk of inhalation of spores and soil bacteria such as *Clostridium spp.*

One day after initiating a course of amoxicillin, CL did not have any improvement in his symptoms and he was brought to his primary pediatrician for further evaluation. During the visit the pediatrician noted markedly decreased tone and decreased motor activity. CL was no longer taking milk from his mother's breast, was producing little urine, and was constipated with infrequent, hard stools. He was admitted to a local hospital for IV fluid hydration and further evaluation.

At this point the differential diagnosis of a hypotonic infant is quite broad. The initial evaluation of the child should be to evaluate for a serious bacterial infection. SBI is among the most common reasons for hospital admission of neonates and infants in the United States. Infectious disease processes to be considered in an infant presenting with decreased tone and activity in the setting of recently diagnosed otitis media include sepsis, meningitis, (meningo)encephalitis, urinary tract infection, and pneumonia. The likely bacterial pathogens in the neonate include Group B Streptococcus, *E. coli*, *S. aureus*, and Listeria. Children older than 1-2 months are less likely to be infected with Listeria, but "late-onset GBS" can cause disease in infants of this age group. A full work-up for serious bacterial infection includes empiric antibiotic therapy; blood and urine cultures; cerebrospinal fluid cytology and culture if the patient is under a month of age, appears neurologically impaired, or has meningeal signs; and, sometimes, a chest X-ray and chemistry panel depending on patient presentation.

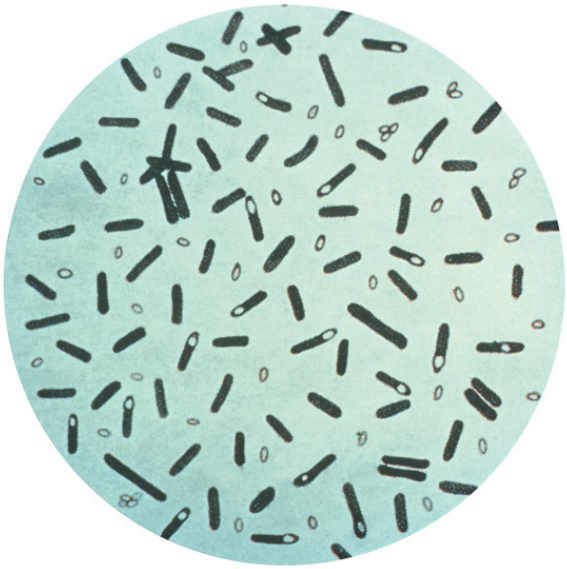
At the hospital, blood, urine, and CSF were obtained. CL was switched from amoxicillin to a broad spectrum antibiotic regimen of ampicillin and cefotaxime. The patient

had a normal CBC, chemistry panel, urinalysis, and CSF profile; blood, urine, and CSF cultures did not show any growth of microorganisms. Additional metabolic studies including lactate and ammonia were within normal limits. Chest X-ray showed clear lungs with no signs of infiltrate. Head computed tomography was obtained, which did not show any abnormalities. The patient also received a cardiac echo, which showed normal cardiac function. He had episodic desaturations requiring supplemental oxygen for respiratory distress. As the patient had persistent weakness with intermittent desaturations and his workup was thus far negative, the patient was transferred by ambulance to a tertiary care pediatric hospital for further evaluation.

The results of these studies suggest that sepsis and meningitis are unlikely to be the cause of the patient's illness. However, the differential diagnosis for hypotonia is still broad and includes anterior horn cell disorders such as spinal muscular atrophy or other myelopathies, muscular dystrophies such as Duchenne's or Becker's, neuromuscular junction disorders such as infant botulism, disorders of glycogen metabolism, carnitine or mitochondrial disorders, congenital myopathies such as nemaline or central core disease. Also on the differential should be toxic ingestion of prescription drugs, drugs of abuse, fertilizers or pesticides, as well as heavy metal or other environmental toxicity.

Upon arrival at the tertiary care pediatric hospital, the patient appeared lethargic with markedly decreased tone, minimal spontaneous movement, a weak cry, and bilateral eyelid ptosis. He did respond to stimulus with opening of the eyelids and movement of the arms. On physical exam, he had a temperature of 36.2 degrees Celsius, pulse of 138, respiratory rate in the 30s, blood pressure of 90/55, and oxygen saturation of 96% on room air (all normal vital signs for a 4-month-old infant). His height was at the fifth percentile and his weight was at the 25th percentile for his age. His anterior fontanelle was flat. He had sluggishly reactive pupils, an erythematous right tympanic membrane, and a clear oropharynx with intact gag reflex. He had no cervical or other lymphadenopathy. He was breathing comfortably with no retractions, grunting, or flaring of his nostrils. Auscultation of the heart revealed a regular rate and rhythm for a four-month-old infant with no murmurs or extra heart sounds and 2+ peripheral pulses. There was some mild mottling of his extremities. Cranial and deep tendon reflexes were intact, but the patient had significantly decreased muscle tone with marked head lag.

Given the clinical picture of a four-month-old infant from the Central Valley with acute onset hypotonia, muscle weakness, poor feeding, and constipation, one should be concerned about infant botulism. Diagnosis can be confirmed by obtaining a stool sample and sending it for detection of *C. botulinum* toxin and spores. However, as the stool analysis takes multiple days and the clinical course of botulism is progressive muscle weakness, it is important to treat empirically with botulinum immune globulin if a physician has a high clinical suspicion of botulism. The clinician should also proceed with investigations into metabolic and congenital sources of hypotonia, which would involve testing for abnormal metabolites in the plasma and urine.



Clostridium botulinum stained with gentian violet
Source: CDC Public Health Image Library

Since the patient was constipated, a saline enema was performed in order to obtain a stool sample for *C. botulinum* toxin analysis. The California Department of Health was notified, and measures were initiated to obtain botulism immune globulin. Twelve hours after arrival at the tertiary care children's hospital, CL had an acute desaturation into the 50s, became bradycardic, and a code blue was called. Multiple attempts were made to intubate the patient but each time the endotracheal tube was inserted, the patient's oxygen saturation dropped. Bedside bronchoscopy was performed and the patient was noted to have a copious amount of thick secretions within the airways of the lungs. These secretions were removed by suction and irrigation. Endotracheal intubation was then achieved successfully and the patient was transferred to the pediatric intensive care unit where he remained for the next 10 days. He received one dose of botulism immune globulin the day he was admitted to the ICU. While in the ICU he was initially given IV fluids; a feeding tube was then inserted and he was able to tolerate tube feeds of his mother's breast milk. After seven days of intubation the patient was weaned to nasal canula, and upon transfer to the floor, he was breathing well on room air. At discharge on hospital day 15, the

patient had regained much of his strength; however, he still had persistent weakness, with head lag and diminished deep tendon reflexes. He was playful and interactive, and was able to feed from his mother's breast. Since discharge the patient has been healthy without evidence of any lingering deficit from his disease. Final pathology results from the patient's stool sample revealed the presence of *C. botulinum* toxin.

Commentary

Clostridium botulinum is a gram-positive spore forming bacteria that produces a potent neurotoxin blocking presynaptic cholinergic transmission. Botulism infection in humans can be classified into five syndromes: 1) foodborne botulism, the ingestion of food contaminated by botulinum toxin; 2) wound botulism, an infection of a wound which leads to production of the neurotoxin within the wound; 3) adult enteric infectious botulism, the ingestion of *C. botulinum* spores leading to colonization of the GI tract and production of neurotoxin; 4) inhalational botulism, the spread of aerosolized botulinum toxin as a biological weapon; and, 5) infant botulism, the ingestion of *C. botulinum* spores by an infant. Of these five entities, infant botulism is by far the most common in the U.S., accounting for 62 percent of all cases.[3]

The classic initial presentation of infant botulism is a child with poor feeding and constipation who then gradually develops hypotonia and generalized muscle weakness. The toxin affects neuromuscular junctions of both skeletal and smooth muscle; however, the central nervous system is not affected. Muscles innervated by cranial nerves are generally involved early on in the disease followed by progressive weakness of the trunk, extremities, and diaphragm. Involvement of the diaphragm can lead to respiratory failure and death; thus, intubation and monitoring in the intensive-care setting are frequently required.

While epidemiologic studies have shown honey to be a reservoir for *C. botulinum* spores, the majority of cases of infant botulism in the United States result from ingestion of environmental dust containing bacterial spores rather than from the ingestion of honey.[4] Thus, the disease seems to occur most frequently in areas where there is heavy agricultural cultivation or construction. *C. botulinum* spores are actually quite commonly found in soil and can be routinely isolated from the surfaces of fruits and vegetables.[5] According to the Centers for Disease Control and Prevention, in 2006 there were 106 cases of infant botulism in the United States.[3] Of those cases, 46 occurred in California. For unknown reasons the infant intestine appears to be more susceptible to germination of botulinum spores than the adult intestine.

Adult botulism has traditionally been treated with equine antitoxin. However, this drug cannot be given to children because of serious risk of side effects such as serum sickness and anaphylaxis.[6] Because of its low incidence, infant botulism is classified as an "orphan disease" and no pharmaceutical company has invested in the creation of a drug that would serve 100 children each year. In response to this need, BabyBIG® (botulism immune globulin) was developed in 1989 by the California Department of Public Health in conjunction with the Food and Drug Administration. The immune globulin preparation includes preformed antibodies to botulism toxins A and B, and it works by neutralizing all circulating toxins for a period of six months after administration. The cost of a single dose intravenous preparation of BabyBIG® is $45,000. However, a randomized clinical trial found that administration of botulism immune globulin reduced mean hospital stay from 5.7 to 2.6 weeks, reduced mechanical ventilation time by 2.6 weeks, and reduced total hospitalization costs by $88,600. The same study also showed that early administration of botulism immune globulin reduced total intensive care stay and decreased feeding tube requirement.[7] Because of the efficacy of this treatment, if the clinical suspicion of botulism is sufficiently high, BIG should be given even when stool studies are still pending.

In summary, infant botulism is a rare clinical entity that classically presents in children less than 12 months of age as hypotonia, poor feeding, weak cry, and constipation. The majority of infants with botulism can expect a full recovery with no long-term muscular or neurological deficits. However, infants who experience diaphragmatic paralysis and respiratory distress may suffer from hypoxic cerebral damage. Thus, even though infant botulism is rarely seen in clinical practice, one should be familiar with its presentation, as prompt recognition can lead to early administration of immune globulin and a more optimal clinical outcome.

References

1. Ruohola, A, Meurman, O, Nikkari, S, et al. Microbiology of acute otitis media in children with tympanostomy tubes: prevalences of bacteria and viruses. Clin Infect Dis 2006; 43:1417.
2. Nyquist AC; Gonzales R; Steiner JF; Sande MA. Antibiotic prescribing for children with colds, upper respiratory tract infections, and bronchitis. JAMA 1998 Mar 18;279(11):875-7.
3. http://www.cdc.gov/nationalsurveillance/PDFs/Botulism_CSTE_2006_website.pdf
4. Hauschild, A. H. W., Hilsheimer, R., Weiss, K. F., et al.: Clostridium botulinum in honey, syrups and dry infant cereals. J. Food Protect. 51:892-894, 1988.
5. Dowell VR Jr Botulism and tetanus: selected epidemiologic and microbiologic aspects. Rev Infect Dis 1984 Mar-Apr;6 Suppl 1:S202-7.
6. Black RE, Gunn RA. Hypersensitivity reactions associated with botulinal antitoxin. Am J Med 1980;69:567-570
7. Arnon, SS, Schechter, R, Maslanka, SE, et al. Human botulism immune globulin for the treatment of infant botulism. N Engl J Med 2006; 354:462.

Advancing Neuroregenerative Medicine: A Call for Expanded Collaboration Between Neuroscientists and Ethicists

Jocelyn Grunwell, SMS IV, Katrina Karkazis, and Judy Illes

Introduction

Scientists hope that the replacement or repair of damaged cells in the central nervous system (CNS) using stem cells will be an important tool to restore impaired function and slow deterioration in deeply debilitating CNS diseases such as Parkinson's Disease, Alzheimer's Disease, and multiple sclerosis.[1] Although scientists and others are hopeful about the possibilities of neuroregenerative medicine (NRM) for the treatment of neurodegenerative diseases, a host of ethical questions about NRM research and its clinical applications still need to be answered. We sought to identify key concerns of scientists working in NRM with the goal of developing a preliminary framework outlining ethical and social issues of using of stem cells in NRM. To achieve our objective we conducted in-depth interviews with ten senior scientists in the United States working in the field of NRM.

Ethical discussions about stem cell research largely have been limited to the morality and acceptability of the use of human embryonic stem cells (hESCs).[2-5] Governments in many jurisdictions have addressed whether and how hESCs should be used and whether this research will be supported by public funding [3] Scientific articles on stem cells implanted into the CNS, if they address ethical concerns at all, have focused primarily on the scarcity of source material and the safety of controlling stem cell differentiaton.[8] In this commentary, we move beyond these concerns to discuss three major themes that scientists hoping to move toward NRM therapies will face: 1) the novel ethical concerns raised by research on the brain; 2) the ethics of the translation of basic research findings into human applications; and 3) the social-scientific interface.

Neuroexceptionalism

Neuroexceptionalism is the idea that neuroscientific research and its translation pose unique ethical challenges that require a heightened level of scrutiny compared to other types of biomedical research because the human brain is central to self-identity, consciousness, and what many think of as an individual's essence, and also because it is critical to morally relevant capacities such as rational thought and decision making.[6, 7] As a consequence, we would do well as a society to consider the unique ethical issues raised by neuroexceptionalism before scientific advances in NRM are translated from the lab to the clinic.[7]

Scientists we interviewed recognized the uniqueness of the brain and expressed concern that because the frontal cortex and limbic areas are critical for executive decision making and emotions, any intervention may fundamentally change oneself.[8] Interviewees were torn between the utility and unknown consequences of experiments that could potentially lead to a deeper understanding of how humans learn, remember, and perceive feelings, since so little is known about how interventions that utilize regenerated tissue might affect these processes. Although it is not always clear how neurological information and interventions are different from other medical information and interventions, the perception that it is different means that neuroexceptionalism is a crucial concept that needs to be incorporated into experimental and therapeutic discussions between scientists and the public.

Animal-human chimeras

A critical obstacle to realizing the promise of NRM research is that there is no adequate model system to understand how neu-

Ricky Tong

ral progenitor cells will proliferate, differentiate, integrate, and function in the immature and adult human brain. Because of these technical hurdles, the FDA will likely require preclinical trials on animals with human neural progenitor cells implanted into their brains. Scientists are working toward creating human neural-grafted chimeras to produce a research model to study human brain development and disease, to accelerate the screening process for therapeutic drugs, and to have a source of stem cells for xenotransplantation.[9-11] Placing human neural progenitor cells into animal brains is controversial in the United States and elsewhere, and societal concerns over this issue have prompted legislators in the US to propose a bill criminalizing the practice.[12, 13] Still, scientists have carried out chimeric neural-grafting experiments. Redmond and colleagues, for example, implanted neural stem cells into the brains of monkeys with the hope they would supply dopamine and help people with Parkinson's disease.[14, 15] Others have conducted or proposed similar experiments.[10, 16]

Scientists and ethicists recognize that chimeras must have enough biological similarity to humans to be scientifically useful. Human neural-grafting in animal brains, however, raises the concern that chimeras will develop brains capable of human-like cognitive or mental characteristics. Indeed, the bulk of ethical writing on this issue has centered chiefly on whether scientists would "confer humanity" on these animals.[16] Commentators have raised various arguments against human neural-grafting including that it violates moral taboo, degrades species integrity, and unsettles socially defined categories and order.[17-19] Scientists and ethicists must therefore strike a balance between creating a useful model versus conferring "personhood" on the chimera, which makes it likely these issues will need to be examined on a case-by-case basis.

Several have urged caution about such experiments, outlining important factors to consider: the proportion of human progenitor to host animal cells, the timing of introduction of neural progenitor cells into the embryonic versus the adult animal, the degree of relatedness of graft species to humans, the recipient animal's brain size, the specific sites into which neural progenitor cells integrate, and the brain pathology being investigated.[20] Others are concerned primarily with the source of human stem cells, animal welfare, the propriety of such uses of human brain tissue, and the risk to public support of science.[21] Even if there is ethical and scientific resolution of the aforementioned concerns, the public perception that the brain is the seat of consciousness and self-identity may make this research very controversial and hence this may be an instance where the concept of neuroexceptionalism is apt.

These ethical concerns are embodied to varying degrees in current policies on stem cell research from the International Society for Stem Cell Research (ISSCR),[22] National Academy of Sciences (NAS) and the California Institute of Regenerative Medicine (CIRM). ISSCR, for example, recognizes the need for special consideration for human neural-grafted chimeras, and while this international body does not legislate or enforce policy, its goal is to reach consensus to facilitate international collaboration. NAS and CIRM guidelines prohibit the transfer of hESCs into non-human primate blastocysts and the transfer of any species ESCs into human blastocysts. In addition, the breeding of any animals into which hESCs have been transferred at any time is barred. There is no way to gauge, however, the extent to which ISSCR and NAS guidelines are being followed by research institutions and scientists. CIRM, however, has an enforcement mechanism incorporated into their mandate in that funding of the research is tied to approval of the research plan by stem cell research oversight committees (SCROs).[23] ISSCR, NAS, and CIRM are consistent in their ethical concerns about human neural-grafting. CIRM differs in that it addresses the ethical issues by mandating that researchers answer specific scientific issues listed in the regulations in order to be funded.

Scientists we interviewed believe that a human neural-grafted animal would not result in human qualities such as language, cognition, and emotion. Rather than addressing society's most pressing concern of conferring human qualities on a neural-grafted mouse,[15, 24] scientists were more concerned with the experimental problems of rejection, transfer of viral infections, and different physiological environments. Scientists acknowledged that there is difficulty in predicting and assessing the outcome of human neural-grafting experiments, but scientific progress is not always made in predictable and logical steps. Interviewees believed that the scientific hurdles will not result in a chimera with human qualities, yet ethics demands that scientists consider this possibility in addition to the other ethical considerations outlined above. The implantation of human neurons into animals thus requires careful deliberation and consideration that in many instances will require an analysis specific to the experiment at hand.[20]

Aaron Wang

Therapeutic misconception and informed consent

Ethicists have long recognized that research participants all too often fail to understand that research studies in which they enroll will not have a therapeutic benefit—a misunderstanding known as the therapeutic misconception.[25] Several scientists we interviewed felt that any novel therapy could raise patients' false hopes of a cure. The therapeutic misconception may be especially problematic in NRM because many patients with neurodegenerative diseases and families of patients with cognitive dysfunction have exhausted their traditional treatment options and may be desperate for a cure.[26]

This is illustrated in an example cited by a scientist discussing the implantation of human fetal brain tissue into patients with Parkinson's disease. In these surgeries, implanted human fetal brain tissue led to the gross repair of bradykinesia, however, mild to moderately severe dyskinesias (abnormal involuntary movements and postures) increased postoperatively.[27] Patients must understand the potential benefits, risks, and unknown consequences of the intervention to make sure that the hope and hype surrounding NRM does not overshadow realistic expectations.

Volition, the act of making a conscious choice or decision, is of critical concern regarding informed consent in NRM because often what one is trying to correct in the brain is what makes the person least able to evaluate risks and benefits. Both the NIH and the National Bioethics Advisory Commission (NBAC) have policies regarding research related to individuals with impaired or limited decision making capacity such as people with dementias and psychiatric illnesses.[28-32] These protections include the assignment of surrogate decision makers, procedures for assessing intellectual capacity, and periodic reevaluation of cognitive capacity.[28] In addition, the research subject's autonomy is respected by requiring assent to participation, if able, and the participant is always permitted to withdraw at any time during the course of the study. Nevertheless, there are ethical concerns not only about these groups being exploited as research subjects but also their ability to consent to participation in medical research.

The NIH has declared that it is imperative that children not be categorically excluded as research subjects—and indeed has mandated and provided incentives for the inclusion of children [33, 34]—in part to avoid them becoming "therapeutic orphans" denied access to research and its benefits.[35] The first FDA-approved Phase I (safety assessment) trial transplanting human fetal neural stem cells into children with Batten's disease began in late 2006 at the Doernbecher Children's Hospital in Portland, Oregon sponsored by StemCells, Inc. (Palo Alto, CA).[36] Batten's disease, a lysosomal storage disorder leading to neuron loss, is a fatal pediatric disorder in which children suffer from seizures and progressive loss of motor skills, sight and mental capacity. Using Batten's disease as a case study, Martin and Robert concluded that the therapeutic misconception coupled with the hype surrounding the promise of stem cell research as a panacea equates to the inability to attain proper informed consent.[37] Although interviewees agree that developing therapies for children should not be neglected, they acknowledged that there is not yet consensus about how to assess tolerable risk for this vulnerable population.

Enhancement versus therapy

There have been intense debates over the last few decades over the propriety of using medicine not simply to treat illness and disability, but to improve, enhance or modify human capacities and characteristics. These issues emerged perhaps most directly with genetic technology, but in recent years have centered as well on psychotropic drugs and surgical interventions to affect areas of memory, attention, and mood.[38-45] The issue of enhancement is not unique to NRM research per se, but because the brain is central to our identity, enhancement of mental capacity raises larger issues than enhancement of physical beauty, for example, because CNS intervention could fundamentally change the core of our being.

These ethical debates surrounding interventions for enhancement have generally weighed medical goals against societal goals. Medical goals concern the curing of illness, the easing of suffering, and the improvement of quality of life for patients. As NRM progresses, more effective medical technologies will not only be available to treat illness but will help patients beyond therapeutic use to enhancement. The thorny issue of what counts as "normal" function must be resolved. Societal goals concern the distribution of resources and the possibility that unequal access to NRM treatments and enhancements will create unfair advantages for some and disenfranchisement of others. Scientists we interviewed felt that future NRM technologies will allow increasingly sophisticated manipulations of the brain but allowed that every positive enhancement may risk an unpleasant side-

Alexander Cardenas

effect. For example, one researcher expressed concern that enhancement of memory could block the fading of traumatic and painful events. The use of NRM in enhancements raises two additional concerns; first, people may feel pressure to seek enhancement treatments to keep pace with others in society; and second, the cost of the procedures would again limit access for the disadvantaged.

Many participants saw the issue of enhancement of cognitive and emotional brain function, as opposed to the treatment of frank pathology, as analogous to the role of cosmetic surgery in the enhancement of physical beauty. Scientists did not see enhancement as part of the physician's role and felt that we should not be trying to decrease intellectual diversity. The problem is that the boundary between treatment and enhancement is not discrete. Interviewees felt that society will have to distinguish what constitutes enhancement because all interventions are improvements of a sort and determining when an intervention is a treatment and when it is an enhancement is an interpretational question subject to societal values.[46] Interviewees felt that this was not a concern of NRM bench scientists, but that it will be important for clinicians.

Policy

There has been a debate about whether the rules and regulations governing hESC research should be centralized at the international, federal, state, or institutional level to achieve the goal of advancing NRM as rapidly as possible.[47, 48] ISSCR was designed to facilitate international hESC collaboration.[22] NAS developed hESC guidelines, but the US federal government suspended funding for the creation of new hESC lines in 2001. In response, California voters passed Proposition 71 which allocated $3 billion for hESC research over 10 years and created CIRM. At the institutional level, IRBs function to oversee human subjects research. The worry with state and institutional policy development is that there will not be uniform regulations and standards to facilitate collaboration. However, CIRM regulations follow from the ISSCR and NAS guidelines on hESC research, and now serve as a model for other states to develop their own policies. Interviewees agreed that in the absence of a federal funding and enforcement structure that CIRM is a solution that allows NRM research with hESCs to progress. Most believed that the CIRM scientist-citizen oversight committee (SCRO) facilitated productive ethical debates. One scientist remarked that the lack of federal support could lead to emigration of scientists to places where hESC research is supported. This is not an unfounded concern as such "brain-drains" have occurred.[49, 50] This is analogous to medical tourism where patients seek off-shore treatments not provided in the US or provided at significantly lower cost than in the US.[51, 52]

Conclusion

These interviews represent the first attempt to define the ethical implications of NRM research and applications. This study defines a preliminary framework for further discussion between neuroscientists and neuroethicists. These are only some of the ethical issues and in fact most are not unique to NRM. But given neuroexceptionalism and controversy surrounding hESC research, they will be important. We have focused on the scientific perception of ethics in NRM. In order to establish an effective partnership, however, ethicists must also gain a basic understanding of the science of NRM. This partnership will facilitate translating basic discoveries into cures carefully attuned to the ethical, social, and legal implications of the science.

References

1. Greenwood, H.L. et al. Regenerative medicine and the developing world. PLoS Med 3, e381 (2006).
2. Bobrow, J.C. The ethics and politics of stem cell research. Trans Am Ophthalmol Soc 103, 138-41; discussion 141-2 (2005).
3. Greely, H.T. Moving human embryonic stem cells from legislature to lab: remaining legal and ethical questions. PLoS Med 3, e143 (2006).
4. Kiatpongsan, S. & Pruksananonda, K. International trends in bioethics for embryonic stem cell research. J Med Assoc Thai 89, 1542-4 (2006).
5. McHugh, P.R. Zygote and "clonote"--the ethical use of embryonic stem cells. N Engl J Med 351, 209-11 (2004).
6. Farah, M.J. Neuroethics: the practical and the philosophical. Trends Cogn Sci 9, 34-40 (2005).
7. Hyman, S.E. Introduction: the brain's special status. Cerebrum 6, 9-12 (2004).
8. Leshner, A.I. Ethical issues in taking neuroscience research from bench to bedside. Cerebrum 6, 66-72 (2004).
9. Brüstle, O. et al. Chimeric brains generated by intraventricular transplantation of fetal human brain cells into embryonic rats. Nat Biotechnol 16, 1040-4 (1998).
10. Muotri, A.R., Nakashima, K., Toni, N., Sandler, V.M. & Gage, F.H. Development of functional human embryonic stem cell-derived neurons in mouse brain. Proc Natl Acad Sci U S A 102, 18644-8 (2005).
11. Robert, J.S. The science and ethics of making part-human animals in stem cell biology. FASEB J 20, 838-45 (2006).
12. (2005).
13. http://www.hinxtongroup.org/.
14. Redmond, D.E., Jr. Cellular replacement therapy for Parkinson's disease--where we are today? Neuroscientist 8, 457-88 (2002).
15. Shreeve, J. The other stem-cell debate: to test the potential curative powers of human embryonic stem cells, biologists want to inject them into lab animals. Creating such chimeras makes perfect sense, to a point: a sheep with a human liver? O.K. A mouse brain made up of human cells? Maybe. But a chimp that sobs? N Y Times Mag, 42-7 (2005).
16. Greely, H.T. Defining chimeras...and chimeric concerns. Am J Bioeth 3, 17-20 (2003).
17. Embryonic, fetal and post-natal animal-human mixtures: an ethical discussion. Hum Reprod Genet Ethics 12, 35-60 (2006).
18. Karpowicz, P., Cohen, C.B. & van der Kooy, D. Developing human-nonhuman chimeras in human stem cell research: ethical issues and boundaries. Kennedy Inst Ethics J 15, 107-34 (2005).
19. Robert, J.S. & Baylis, F. Crossing species boundaries.

Mike Sundberg

Am J Bioeth 3, 1-13 (2003).
20. Greene, M. et al. Ethics: Moral issues of human-non-human primate neural grafting. Science 309, 385-6 (2005).
21. Greely, H.T., Cho, M.K., Hogle, L.F. & Satz, D.M. Thinking about the human neuron mouse. Am J Bioeth 7, 27-40 (2007).
22. http://www.isscr.org/guidelines/index.htm.
23. http://www.cirm.ca.gov/meetings/pdf/2005/08/083005_item_7a.pdf.
24. Wade, N. Chimeras on the horizon, but don't expect centaurs. NY Times (Print), F1, F8 (2005).
25. Appelbaum, P.S., Roth, L.H., Lidz, C.W., Benson, P. & Winslade, W. False hopes and best data: consent to research and the therapeutic misconception. Hastings Cent Rep 17, 20-4 (1987).
26. Henderson, G. et al. Clinical trials and medical care: defining the therapeutic misconception. PLoS Med 4, e324 (2007).
27. Hagell, P. et al. Dyskinesias following neural transplantation in Parkinson's disease. Nat Neurosci 5, 627-8 (2002).
28. Cahill, M. & Wichman, A. Research involving persons with cognitive impairments: results of a survey of Alzheimer disease research centers in the United States. Alzheimer Dis Assoc Disord 14, 20-7 (2000).
29. Cook-Deegan, R.M. Protecting the vulnerable in brain research. Cerebrum 2, 73-91 (2000).
30. http://bioethics.gov/reports/past_commissions/nbac_mental2.pdf.
31. http://bioethics.gov/topics/children.html.
32. http://grants.nih.gov/grants/policy/questionablecapacity.htm.
33. http://grants.nih.giv/grants/funding/children/pol_children_qa.htm.
34. Magnus, D. Playing it safe. Am J Bioeth 7, 1-2 (2007).
35. Blumer, J.L. Introduction. Pediatrics 104, 582 (1999).
36. http://www.stemcellsinc.com/clinicaltrials/clinicaltrials.html.
37. Martin, R.A. & Robert, J.S. Is risky pediatric research without prospect of direct benefit ever justified? Am J Bioeth 7, 12-5 (2007).
38. Bioethics, P.s.C.o. (ed.) Beyond therapy: Biotechnology and the pursuit of happiness (Dana Press, New York, 2003).
39. Butcher, J. Cognitive enhancement raises ethical concerns. Academics urge pre-emptive debate on neurotechnologies. Lancet 362, 132-3 (2003).
40. Chan, S. & Harris, J. Cognitive regeneration or enhancement: the ethical issues. Regen Med 1, 361-366 (2006).
41. Farah, M.J. et al. Neurocognitive enhancement: what can we do and what should we do? Nat Rev Neurosci 5, 421-5 (2004).
42. Glover, J. What Sort of People Should There Be? Genetic Engineering, Brain Control, and Their Impact on Our Future World (Penguin Books, New York, 1984).
43. http://www.ucl.ac.uk/~ucbtdag/bioethics/project.html.
44. Parens, E. (ed.) Enhancing Human Traits: Ethical and Social Implications (Georgetown University Press, 1998).
45. Penttila, N. The Neuroethics of Ehnhancement: How Smart Are Smart Drugs? Cerebrum (2007).
46. Juengst, E.T., Binstock, R.H., Mehlman, M., Post, S.G. & Whitehouse, P. Biogerontology, "anti-aging medicine," and the challenges of human enhancement. Hastings Cent Rep 33, 21-30 (2003).
47. Baylis, F. & Robert, J.S. Human embryonic stem cell research: an argument for national research review. Account Res 13, 207-24 (2006).
48. Magnus, D. Stem cell research: the California experience. Hastings Cent Rep 36, 26-8 (2006).
49. Owen-Smith, J. & McCormick, J. An international gap in human ES cell research. Nat Biotechnol 24, 391-2 (2006).
50. Russo, E. Follow the money--the politics of embryonic stem cell research. PLoS Biol 3, e234 (2005).
51. Kurlantzick, J. in The New York Times (2007).
52. Woodman, J. Patients Beyond Borders: Everybody's Guide to Affordable, World-Class Medical Tourism (Healthy Travel Media, Chapel Hill, 2007).
53. Barinaga, M. Asilomar revisited: lessons for today? Science 287, 1584-5 (2000).
54. Capron, A.M. & Schapiro, R. Remember Asilomar? Reexamining science's ethical and social responsibility. Perspect Biol Med 44, 162-9 (2001).
55. Hindmarsh, R. & Gottweis, H. Recombinant regulation: the Asilomar legacy 30 years on. Sci Cult (Lond) 14, 299-307 (2005).
56. Singer, M. What did the Asilomar exercise accomplish, what did it leave undone? Perspect Biol Med 44, 186-91 (2001).
57. Kimmelman, J., Baylis, F. & Glass, K.C. Stem cell trials: lessons from gene transfer research. Hastings Cent Rep 36, 23-6 (2006).

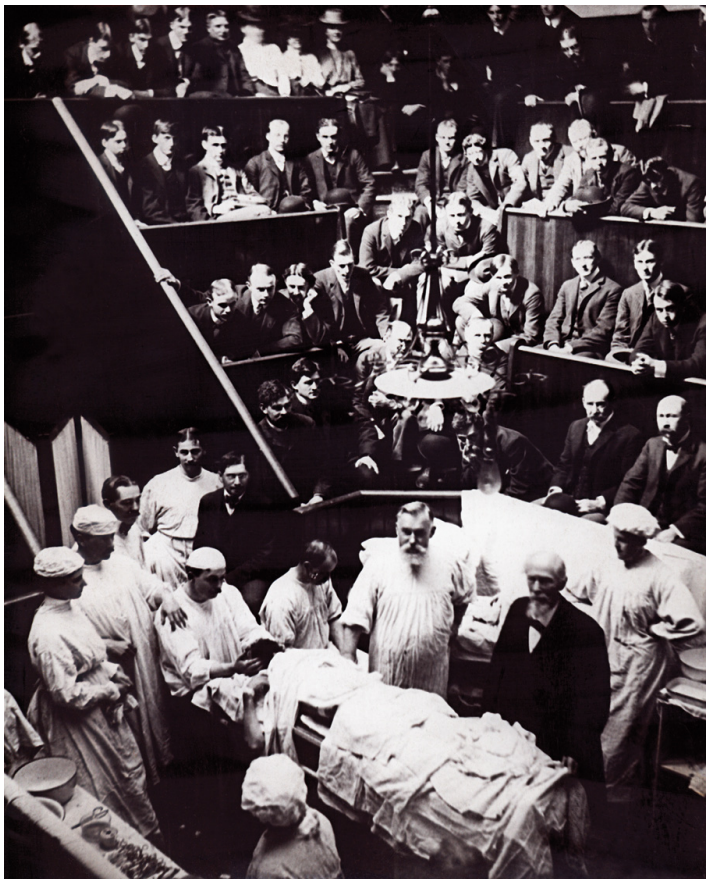
Medical Training in 1908: A Century's Worth of Change?

Ron Alfa, SMS II

The lives of medical students in 2008 : courses and clinics, high-speed lectures in libraries… learn study cram stop breathe play-for-a-minute and get-back-for-the-next-exam. The fast-paced choose-your-own-superlative rally towards the indefinitely impending ideal of medical perfection seems so often to be a construct of an infinitely expanding medico-scientific knowledgebase. But how would the script of your favorite medical student sitcom read a century ago? Unfortunately, smschat1908 does not actually exist, but perhaps we can take a short run through the archives.

Stanford Medical School was officially born in 1908 from the consolidation of Stanford University with Cooper Medical College in San Francisco. Cooper Medical College (1883-1912) itself followed from the revitalization of the Medical College of the Pacific by surgeon Levi Cooper Lane. While most medical schools were proprietary at the time—that is, anyone who could afford tuition could receive a medical degree—Cooper was among the few associated with a university. In 1908 this meant simply that Cooper medical students were taught by university-associated instructors while the school remained entirely dependent upon student tuition for financial support. The modern conception of the university-based medical school resulted from a report by Abraham Flexner of the Carnegie Foundation in 1910. Flexner surveyed all the medical schools in the nation and established a set of minimum criteria (largely derived from the German model of research schools) that a school needed to satisfy in order to receive a Carnegie Foundation endowment. As a result, proprietary schools were effectively eliminated. Given the changes that followed the Flexner report, we can best locate records on the life of a typical 1908 medical student in sources dating around the turn of the century but not later than 1910.

The incoming classes at Cooper Medical College in the first decade of the twentieth century comprised 10-30 members, mostly male, with 2-4 female students typically representing about 10% of the cohort. Though George Blumer, class of 1891, notes: "There was perhaps some slight feeling against the presence of women on the part of some of the male students…", female students do not appear to have been limited academically or in terms of the medical education they received. In fact, a letter to the Dean from the female members of one graduating class comments on their "courteous" and "considerate" treatment over the years, reaffirming, "We have never been made to feel in the slightest degree that we were not most welcome to each and every privilege of the college." While there were certainly admission requirements,



Dr. Czerny performing a gastroenterostomy in 1901
Lane Library

the incoming students were diverse. In his journal, Walter Alvarez, class of 1905, remarks on the class of 1901: "One man I am sure was insane; one was a funny old ex-carpenter; a few were good-for-nothing young toughs…. My impression of the first year at Cooper College was that the students prided themselves on being rowdy. We used to have free-for-all fights if the professor was late." Nonetheless, by 1908, most entering students held a college degree and some prior clinical experience with an experienced physician. The MCAT was decades away but laboratory-based physics, chemistry, and physiology increasingly became important requirements for admission in the post-Flexner era.

The first two years' curriculum was comprised mostly of lectures and some clinical experience. Blumer recalls it as "surprising that more students did not develop ['weavers bottom']…" Lectures began at 8 a.m. in the lecture theater and covered physiology, toxicology, histology, and materia medica among other subjects. Notably absent was a course in pathology. Mary Bennett Ritter, class of 1886, recalls: "Few incidents stand out during those years except hard work. There should have been thirty hours in the day in which to accomplish all the work laid out by the various professors,

to say nothing of the hospital work and clinics." Anatomy began after lunch and, according to Blumer, "Partly on that account and partly as a result of the dryness of the presentation, students were apt to drop to sleep."

Perhaps the opinions of medical students regarding class requirements seldom change; a petition submitted to the Dean by the class of 1892 asked that the class be excused from attending any additional lectures not prescribed in the original schedule of lectures. The reason for their request: "We are already crowded with work and the occasional hour that we would gain thereby could be profitably used by the great majority of the students in work on their theses, in studying lectures and reading for clinics." Similar petitions were not a rare occurrence. In fact, the class of 1883 found itself in a precarious situation after submitting a statement proclaiming one instructor's complete inability to make lectures "either interesting or instructive."

Following the second year, students spent mornings in the clinic and most of their afternoons and evenings studying. Alvarez's diary from 1904 is particularly instructive in illustrating the typical day. Monday through Saturday, Alvarez followed a relatively strict schedule of clinics in the morning, studying in the afternoon, followed by a break to the gym, and then continued studying until eleven at night. Despite the occasional evening break to practice the mandolin, Alvarez seldom spent the evening away from his reading of William Osler and others. Students studied extensively for clinical sessions, probably because attending physicians could quiz them at any time. On one noteworthy occasion, friends of Alvarez "were quizzed pretty steadily for an hour." Clinical students had Sunday off. A typical Sunday entry from Alvarez's journal included such descriptions as: "Got up early and studied all morning" and "went to Berkeley in the afternoon." On one especially eventful weekend Alvarez wrote: "…beat Cleland out on the fastball game—Horray!!!" Alvarez's 1904 and 1905 entries were roughly identical except for the addition of "worked on senior thesis" to Saturdays & Sundays in Spring 1905.

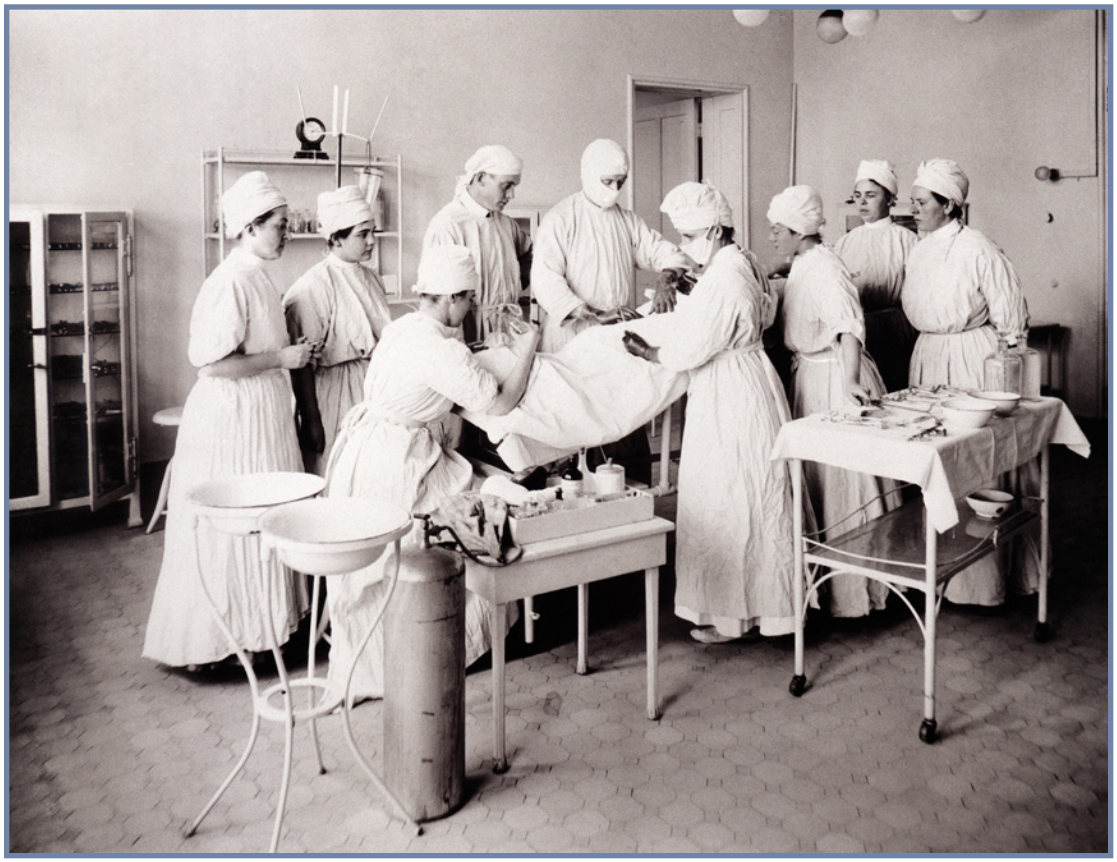
What then can be said of medical school one hundred years in the past; what is it that locates our existence in 2008 and not 1908? Strip away the CWP's and SMSlists, the iPhones and gchats, and we're simply left with the same story, different century. Fellow SMSers, when you wake up and think how strangely similar your day seems to the previous day, or when you feel less than inspired by the routine of class, lab, study, and sleep or just overwhelmed by the sheer magnitude of studying required to be a competent physician, remember that your complaints are no less than 100 years old. While medicine has evolved a great deal in the past century, the dedication required to hold the title of physician has changed very little.

(1) *Weaver's bottom: Inflammation of the bursa that separates the gluteus maximus muscle of the buttocks from the underlying bony prominence of the bone that we sit on, the ischial tuberosity. Weaver's bottom is a form of bursitis that is usually caused by prolonged sitting on hard surfaces that press against the bones of the bottom or mid-buttocks. In proper medical parlance, Weaver's bottom is called ischial bursitis.*

Andreas Rauschecker

The Evolution of Stanford Hospital: A Photoessay

Anatomy students dissecting a cadaver at Cooper Medical School, circa 1897.



Nursing students and physicians taking part in a teaching scenario at Lane Hospital, circa 1900.

Sir MacEwan demonstrating MacEwan's triangle to Dr. Lane.

Shadsworth O. Beasley (Cooper Medical College, 1897) with fellow officers occupying captured German quarters in Bois de Nonsard, France.

President Wallace Sterling (left) and the mayor of Palo Alto (right). Stanford became the sole owner of the Palo Alto-Stanford Medical Center (now the Stanford Hospital and School of Medicine) in 1968.

Cooper Medical College was built by funding from Dr. Levi Cooper Lane at the corner of Webster and Sacramento Streets in San Francisco, CA. This photo was taken in 1882

Lane Hospital, also built by funds from Levi Cooper Lane ($160,000), was dedicated in 1895. It was located at the corner of Clay and Webster Streets in San Francisco, CA.

Stanford Hospital, located on Clay street next to Lane Hospital in San Francisco, opened in 1917. Originally, the hospital maintained 45 private rooms and 125 beds within its wards. However, in the year after it opened, the hospital was expanded to add 26 more rooms.

Construction for the Stanford School of Nursing was completed in 1922. The original Lane School of Nursing was established in 1895 with the establishment of Lane Hospital.

Completed in 1959, the Palo Alto-Stanford Medical Center originally contained 440 beds. It was designed with three hospital and four medical school buildings.

The new Palo Alto Hosptial (1931-58), constructed on the Stanford Campus. This hospital was closed in 1959, and after renovations, was reopened as the current Hoover Pavilion.

Did you know?

Interesting Facts about the History of Stanford Medicine

Sean Sachdev, SMS II

The School of Medicine was originally the first medical school in the western United States

Stanford's medical school was previously Cooper Medical College (until 1908), before which it was the Medical Department of the University of the Pacific. When Dr. Elias Samuel Cooper first created the institution at the University of the Pacific, it was the first medical school founded west of Iowa. In fact its founding predated, by several years, the establishment of Toland Medical College, which would eventually become University of California-San Francisco School of Medicine.

Starting with humble beginnings in 1858, the school had only 13 students and five faculty physicians, with Dr. Cooper at the helm as professor and surgeon. In 1870, the school became Cooper Medical College and finally, in 1908, several years into medicine's scientific revolution, the school became the Medical Department of Stanford University. In 1958, the school moved from San Francisco to Palo Alto.

Four faculty members have won Nobel prizes while at Stanford

1. Dr. Arthur Kornberg won the Nobel Prize in Medicine (1958) for discovering DNA polymerase.
2. Dr. Paul Berg won the Nobel Prize in Chemistry (1980) for being the first person to create recombinant DNA.
3. Dr. Roger Kornberg won the Nobel Prize in Chemistry (2006) for discovering the molecular basis of transcription/RNA Polymerase.
4. Dr. Andrew Fire won the Nobel Prize in Medicine (2006) for discovering RNAi.

Stanford physicians conducted the first adult heart transplant in the United States in 1968 and the first successful combined heart/lung transplant in the world in 1981

Professor Norman Shumway, cardiothoracic surgeon at Stanford, played a pivotal role in both watershed procedures. Universally recognized as one of the most eminent clinicians of the past century, Shumway is often cited as the "father of heart transplantation." In addition to directly teaching some of the most renowned leaders in the field, including the current president of Johns Hopkins University, his methods of heart transplantation have been adopted worldwide.

1964 Demonstration of electrical stimulation of auditory nerve in deaf patients, leading to cochlear implants
1964 First successful clinical application of laser photocoagulation to treat detached retina
1965 Development of technique for extracting anti-hemophilic globulin, the blood fraction needed to prevent bleeding in hemophiliacs
1967 First synthesis of biologically active DNA in test tube
1968 First adult human heart transplant in the United States
1968 Discovery that insulin resistance is the principal physiologic characteristic of mild type-II diabetes and obesity
1971 Discovery of RNA priming of DNA synthesis
1972 First construction of a recombinant DNA molecule containing DNA from two different species
1973 First expression of a foreign gene implanted in bacteria by recombinant DNA methods
1974 Isolation of the genome of a virus that causes hepatitis B and a common form of liver cancer
1975 Discovery of link between exercise and increased "good" (HDL) cholesterol levels
1979 Discovery of dynorphin, a brain chemical 200 times more powerful than morphine
1980 First creation of human hybridoma cell line
1981 First successful human combined heart/lung transplant in the world (fourth attempted worldwide)
1981 First report of successful use of monoclonal antibodies to treat cancer
1984 Isolation of a gene coding for part of the T-cell receptor, a key to the immune system's function
1989 Discovery of the "homing receptor," which guides white blood cells into the peripheral lymph nodes
1990 Discovery of "off-switch" for genetic reproduction in bacteria
1992 Development of a genetically engineered vaccine to enhance patients' immunological response against B-cell lymphoma
1992 Discovered the gene underlying a group of diseases called the demyelinating peripheral neuropathies in which the protective covering on nerves breaks down and the nerves are unable to function properly
1993 Discovery of a protein that appears to be a root cause of type-I diabetes; prevention of the disease in mouse experiments
1994 Development of the new diagnostics for rapid bedside screening of hemolysis in jaundiced newborns
1995 Development of the microarray technology that allows researchers to see at once which genes of the thousands present in a cell are switched "on"
1995 First optical imaging of infection in vivo
1996 Discovery that the p53 protein works as a tumor-suppressor
1996 Discovery that mutations in a single gene are responsible for the most common form of skin cancer
1997 Completion of a multicenter trial showing that standard chemotherapy for most children with early-stage non-Hodgkin's lymphoma can be safely reduced
1997 First optical imaging of gene expression in vivo
1999 Discovery of a genetic mutation that causes narcolepsy
1999 First experimental demonstration that limiting children's television use prevents excess weight gain
1999 First clinical trial of bupropion and nicotine replacement for smoking cessation in adolescents
2000 Solution of the structure of the RNA polymerase protein
2000 Discovery of hereditary arthritis gene
2001 Identification of a novel gene family involved in asthma
2002 First use of RNAi to switch off genes in mice
2002 First use of gene expression profiling to predict cancer outcomes
2002 Discovery that training exercises can physically change the way the brain is wired
2003 Discovery that Wnt genes, first discovered as critical genes in cancer, are also critical regulators of stem cell development

Other Stanford Medicine breakthroughs in a timeline format (source: http://med.stanford.edu/centennial/milestones.html)

The Stanford Med Experience: Where We've Been and Where We're Headed

Mike Sundberg, SMS II

If your family attic is anything like mine, it's the one 20-foot-by-30-foot space that holds more of who you are—albeit in a materialistic sense—than any other room in the house. Attics are the archive of our lives; they hold our first bikes, our failed science fair projects, even our college papers from English 101 that show we actually knew how to write before science got the better of us. Every big achievement in life, every lingering mistake that's been made—much of what's important for our reflection—eventually makes its way into the attic in some tangible form. For me, it's the one room in the entire house that remains a consistent reminder of where I've come from and where I'm headed. Haunting at times, yes, but attics also give us the space we need to place what we already know about ourselves aside and move into the future.

It seems entirely suitable, then, that Stanford Med should trace its beginnings to a cold, cramped, San Francisco attic. It's true: the Medical Department of the University of the Pacific, one of the Stanford School of Medicine's predecessor schools, held its first classes on the top floor of Elias Samuel Cooper's medical infirmary at Mission and Third Streets in 1859. It would be another 100 years before these classes would be permanently relocated to a university hospital setting on the Stanford campus. Much change, both structurally and academically, was necessary to bring the medical school to its current geographic and ideological position. So, just as with our personal attics, perhaps in looking back at Stanford Med's history we'll be able to catch a glimpse of where the medical school is going in the future.

The Vision of Elias Samuel Cooper

With the founding of his curriculum in the mid 1800s, it's unlikely that Elias Samuel Cooper could have predicted his once entirely clinically-oriented medical school would eventually rise to prominence as one of the world leaders in biomedical research. The size and splendor of buildings such as the Center for Clinical Sciences Research, or the up-and-coming Li Ka Shing Center for Learning and Knowledge, were beyond the scope of his architectural plans. But what Cooper did have was a vision for a leading medical education center west of the Mississippi. In the development of Cooper Medical College of the Pacific, E.S. Cooper and his nephew, Levi Cooper Lane, were able to establish the groundwork of the scientific education that remains a part of Stanford's academic framework to this day.

Dr. Barkan teaching class in ophthalmology circa 1872
Lane Library

It was Lane who, prior to his death in 1902, came to the conclusion that medical education was necessary within the academic setting of a university. Under his direction, Stanford received the property of Cooper Medical College as both a gift and a means to see that the dream of a West Coast medical school would live on after the deaths of Cooper and Lane. And so, as medical education was beginning to become a responsibility of universities across the nation, Stanford joined the ranks of the major academic medical centers.

Cooper Medical School had moved from the attic and into the ivory tower, and in so doing had achieved the dream of its founders.

A Research-Intensive Academic Medical Center

It wasn't until the 1950s, when Stanford University School of Medicine under Dean Robert H. Alway made a commitment to basic science and clinical research, that the school truly found its niche among other notable medical centers throughout the country. Despite Dean Alway's lack of research experience, he was dedicated to the scholarly pursuit of the basic sciences. He appointed top scientists, such as Nobel Prize winners Arthur Kornberg and Joshua Lederberg, to head many of the school's departments. Research funding tripled during these years. With the constant need for more attic space to hold the burst in biomedical knowledge, construction has rarely slowed since the opening of the current medical school in 1959: the Fairchild and Beckman buildings were erected in the third quarter of the past century, CCSR unveiled in 2000, and the Clark Center dedicated a mere five years ago.

In reality, the current construction of the Li Ka Shing Center for Learning and Knowledge is only one of a progression of movements made by the medical school in its attempt to keep up with the progress and pace of medical developments that it has itself helped to shape over the past century. However, as with the buildings before it, the center is a physical projection of how knowledge about medicine is to be stored and put into practice at Stanford. Though medical research continues to be at the forefront of this school's objectives, the center will also house a variety of disciplines that harmonize with medicine and serve to look at health problems from new perspectives. As Dean Philip Pizzo has said, a goal of Stanford Medicine in the future is to continue to engage science, politics, and religion in order to regain the trust of the public in medicine.

The Emergence of a Collaborative Atmosphere

Integration of disciplines, an idea promoted as far back as the Stanford curriculum restructuring of the 1950s, seems to be ever more the wave that Stanford Med will ride into the future of medicine. As a case-in-point: the Stanford Institutes of Medicine were originally created in an attempt to bring together academic resources from across the university (and the world) in order to advance our current models of disease and human health. The Institute of Regenerative Medicine for example, designed to look into the power of stem cell therapy, must also have a means of addressing the economic, ethical and societal consequences of performing stem cell research. Likewise, an understanding of how to design an appropriate collaborative effort comes from both innovation and drawing on past experience and knowledge.

Often, these collaborative efforts remain between the School of Medicine and other Stanford schools and departments. However, working with other institutions (even the University of California-San Francisco School of Medicine, originally designed by E.S. Cooper's greatest physician-rival, Dr. Hugh Huger Toland) for the purposes of education and academic progress are now considered a norm. Medical students often move through dual institutions, receiving their education at Stanford and conducting their research through faculty mentors at another academic center. Had it not been for the advocacy of early Stanford medical department faculty who felt that the juxtaposition of arts, sciences, and society were the best means of developing future physicians, our medical curriculum may have looked a bit less colorful today.

Revisiting the Attic

Much of what we take for granted today in our medical experience has come from hard lessons learned, stored away, and re-examined in the academic attics of our predecessors over the past one-and-a-half centuries. Elias Samuel Cooper himself firmly believed in the ability of leaders in medicine to instigate and calculate necessary change: "While some men are reared amidst circumstances calculated to develop them, others are compelled to wait until the time arrives in which they can place themselves in the midst of circumstances calculated to call forth their energies..."

Let us then, as the current students of Stanford's medical school, remember that we are engaged in an ongoing, vibrant, and constantly changing field; one that may, on the surface, look very different tomorrow than it does today. Yet, as we look back—as we revisit the attic of medical lore and knowledge—we can see that the direction we're headed is ever toward improvement.

Joanna Wrede

Abraham Verghese: Understanding the World of our Patients at the Bedside & on the Page

Blake Charlton, SMS II

Source: Stanford Faculty Research Profile

When first encountering Dr. Abraham Verghese—professor of medicine and chair for the theory and practice of medicine—one is most likely to focus on his unique medical background: political strife interrupted his initial training in Ethiopia and spurred him to become first an orderly in New Jersey and then a medical student in India. After earning his degree from Madras University, Verghese returned to the U.S. to practice infectious disease in East Tennessee just as the HIV/AIDS epidemic spread into the country's rural areas. The resulting experience inspired him to describe America's plague years in his first book, *My Own Country*, which was a finalist in the 1994 National Book Critic's Circle Awards and won wide popular acclaim. His second book, *The Tennis Partner*, was hailed by the Boston Globe as "indelible and haunting, an elegy to a friendship found, and an ode to a good friend lost." His scholarly work and shorter articles have appeared in *The New England Journal of Medicine, The Wall Street Journal, New Yorker, Texas Monthly, and The New York Times Magazine*. His first novel, *Cutting for Stone*, is scheduled for publication in 2009.

Remarkable as a background spanning medicine, literature, and three continents is, it does not convey the true sense of purpose one detects when talking to Dr. Verghese about clinical practice. His descriptions of the changing patient-physician relationship and the vanishing art of the physical exam illustrate that he is a clinician first, an author second. Recently, I sat down with Dr. Verghese to discuss the importance of literature and technology to our profession.

What would you say is the value of studying literature to the medical profession?

I've spent the last five years teaching literature and humanities to medical students. And the goal has been to help students maintain their imagination for the suffering of people. The great danger of medical education, because we are so disease-oriented, is to see the diabetic foot in bed three and lose site of the whole. I think literature has two functions: one is that it allows medical students and physicians to continue to imagine the whole world, the complete world of their patient; second, it is an important way to keep hold of oneself. There are a lot of threats to being a physician—your selfhood, your patienthood, all these things are very crucially threatened and affected.

And how do you see the 'medical narrative', in which physicians retell their own and their patients' stories, fitting in to the importance of literature to medicine?

We have become much more conscious of the medical narrative and physicians writing, but there was a lot of that kind of writing before—it just didn't necessarily call itself that. I think we almost make too much of physicians being writers. For example, I don't put a degree behind my name on any of my books because it shouldn't be relevant. If the book has relevance, what does it matter if I have an MD or an MA or a Bachelor of Divinity or a Doctorate of Jurisprudence? When we use our status as physicians to justify our writing, then I wonder what we are really writing about. There has been a great emphasis—there should be and there always has been—on the words on the page and what [they are] doing for you. Do they work? But over the years, the emphasis has shifted too much onto who is writing and what their credentials are. And that's not irrelevant, but the ultimate gold standard should be the words on the page.

So, other than an emphasis on credentials, have you noticed other changes in medical narratives?

What has become much more evident is consciously writing about the craft of medicine for the public. I think that's very typical of what Jerry Groopman does and what [Atul] Gawande does, and they both do it very well. I think Oliver Sacks is the master of that genre. But I think as more colorful and diverse people come to medicine, we'll see more writers of all sorts. I would hate to see them all fall into this narrow cone that's called "physician-writing."

Let's change topic slightly and talk about the how we encounter our patient's stories. One concern repeated to me by physicians who write is the fear that technology might be threatening the medical narrative in the clinic. Specifically the computerized history—with pull-down menus and cut-and-paste comments¬—raises suspicions. Do you feel that technology endangers how we hear our patients' stories?

Again, I know there's a whole sort of industry around 'the medical narrative'—breaking it down, deconstructing it. And that doesn't interest me at all. It keeps people busy, but does it change the way I think about medicine? No. And the threat of technology in terms of the history—the real threat is that the precious patient-physician interaction can't take place very well when the physician has got his back half-turned to the patient so he can enter data. Recently, my son saw a pediatrician, not at Stanford but in Texas. And you know how critical it is to bond with the child with all the tips and tricks we are taught as students. Well, this pediatrician had his back to my wife and our son as he worked on the computer. And maybe that's what his system requires, but I thought, "We're never going to come back here." I just don't see how he could form a bond with the child. That's the threat, not the computerized medical record per se. *In fact I think the computerized records have saved many lives by reducing medical errors and increasing access to vital information.*

So would you say that technology has been an overall boon to clinicians?

I don't want to sound like a Luddite because I'm not. I think we have great technology. But it should have made us a lot better at the bedside. Sir William Osler was a phenomenal physician. How much more phenomenal would he have been if he had had ultrasounds, angiograms, and all the things that allow us to instantly see what's going on? You could argue, "What does it matter? Times have changed; we don't need to do what Osler did." But I think patients recognize our drift away from the bedside. They see it as inattentiveness; they're not privy to the conference rooms where we have these wonderful conversations and discuss their images in detail. All they know is the physician came by for three minutes when they have been there for twenty-four hours. We can focus so much on technology that a patient in a bed can become an icon for the real patient in the computer; whereas, a good physical exam really conveys our attentiveness to the patient. My best medical education came when I was an orderly and saw what happens in the twenty-three hours and fifty-five minutes when the physician is not there. And so much of that is missed now—not that doctors can be there all that time, but we can certainly be respectful that the patient has to be there all those hours. And we can be more conscious that patients are unaware of everything we learn about them and how busy we are with their concerns.

Do you think new technology or new applications of the technology might remove this danger of displacing the patient-doctor relationship?

I think we can do more with technology in ways that we might not think the technology is for. For example, in El Paso, I had a patient with an amoebic liver abscess. He was very sick, so we were delighted to make the diagnosis. We started him on treatment and things were getting better, but he wasn't looking any better. There was no medical reason for this, and there was also a language barrier, as my Spanish was not that good. So, finally, I went down and got the CT scans and showed him "el absceso en su higado" and how it was shrinking. And it made all the difference; he was a much better patient the next day. That represents the kind of technology information transfer that we don't make.

I wonder if we can shift gears now and talk briefly about your forthcoming novel, *Cutting for Stone***. Could you sketch the outlines of the story for us?**

It is very much an epic medical story, beginning in Africa and ending here in America. It has in it all my love of medicine and to some extent the underbelly of medicine, which we all encounter. There are characters who are saved by becoming physicians, and characters for whom giving their life to medicine was, in a way, their biggest mistake. The story really affirms to me what I love most about medicine, which is that medicine is life. If you go to it hoping to flee the rest of the world, as many of us do, it doesn't always work. At some point you have to pay the piper. So it is sort of an old-fashioned novel in that sense.

What would you say are your aspirations for this book? Is there a particular area you hope to explore or particular readers you hope to reach?

My first goal, of course, is a good story well told, which is no small feat. For the second goal, I want the book to do for the reader perhaps what certain books did for me, which was to make me feel that medicine was a worthwhile and romantic pursuit that involves a lot of sacrifice but which affords a special insight into life. It involves the idea that in treating patients' pain, you can heal your own. And I don't know if we convey that idea very well today. I don't know how people come to medicine anymore. I wonder if it's from "Scrubs" or "Gray's Anatomy" or the Discovery Channel. And maybe that's how it should be, but I like the notion of falling in love with medicine. And that's what I've tried to write about: loving the mystery of it, the danger of it, the grief of it. I don't know if I've succeeded, but that's what I'd like to convey.

My Health, My Self: Images and Words of Older Adults

Dona Tversky, SMS '08

While people 65 or older represent just 12% of the population, they are estimated to receive nearly a third of all medical services and more than half of all physician time. Plus, about 80% of seniors currently face at least one chronic health condition, 50% face two, and several million find themselves without the ability to perform even basic daily activities such as eating, bathing, or shopping. The situation presents an obvious concern. As the number of elders continues to grow, will future medical professionals be prepared to handle the change in the patient population? Will they see aging only through lenses of physiology and pathology – as a declining process – or will they also incorporate the psychological, personal, and emotional changes that accompany it into a more complete understanding of how their older patients think and feel? In order to highlight the importance of the latter, Dona Tversky presents us with thoughts by seniors reflecting upon their own health, bodies, and sense of identity. Their candid portraits and insightful words illustrate the importance of more closely understanding the changes brought about by aging.

Dona Tversky

I have arthritis, and I don't think about it. I get up and go with the arthritis. I get up in the morning and go take me a hot shower, I love taking my shower. I wash myself real good, soap myself, and let that water run on me, clean myself up, and put my clean clothes on every day. Every morning, I get up like I've got a job.
Willie Marie Brown
Hammond, Louisiana
16 January 1926

Dona Tversky

I will tell you a story. I was waiting for somebody on 59th street, between 5th and 6th in New York. And I was leaning against a wall and a very striking elderly person with white hair was there also waiting. And he started to say, "you see this beautiful woman…you see this beautiful gorgeous lady…" I said "gorgeous, yes." He said "Twenty years ago there was no such thing as a young lady like this walking by without looking at me. I was alive! And now I can sit here for 3 hours and not one young woman will look at me." He said "Do you know how bad it makes me feel?"

For you in America to become part of social activities you have to be a part of the social group in a certain age. Otherwise you are just a passerby. There is nobody who stops even to ask you how you are doing.

Rafael Ben Natan
24 January 1932
Berlin, Germany

Dona Tversky

We were in China this last summer for a month—in the villages in southwestern China. I think the people there age a lot more quickly than we do because it was a hard life. I was in an elevator one day in the hotel, and there were these two men. And they were saying in Chinese, "I wonder how old she is." They're not used to seeing people with white hair. They're not used to seeing older people out in the open, and here was one in a hotel elevator. So finally they couldn't stand it—they asked me, and I told them, and they nearly flipped. And they said: "You have your teeth." I didn't tell them that some of them weren't real.
R.W.
April 1914
Victoria, Canada

Dona Tversky

I miss driving the car. When I was 90 years old, I took the car. They had said, "you mustn't go in to town – Palo Alto." And I disobeyed, and I went. And do you know how Long's– in the back there is that door, and they move by themselves. And I just fell like this. So I broke my elbow there.

Getting older, it's boring, it's like a prison. You live on memories. I try to remember always the good things and don't remember the bad things, but sometimes they come, you know.

Raimonda Bartolini
19 May 1912
Florence, Italy

An 11-Sentence Medical Mystery: The Case of Drs. Spanish Trueblood and Anna Della Riddle

Compiled by Dona Tversky

Introduction

Beginning last January, the Arts, Humanities and Medicine Program of the Stanford Center for Biomedical Ethics sponsored what would become the first 11-Sentence Medical Mystery created by the Stanford Medical Community. The mystery, which features contributions of affiliates to SUSM, was designed as a competition in which potential authors submitted additional sentences each week; winners were chosen by a panel of judges. The thrilling story of Drs. Spanish Trueblood and Anna Della Riddle is a tribute to the creative literary genius that can be found throughout the medical school. So catchy was the short story that we at *H&P* have reprinted it below for our readers, along with credits to each author. Enjoy!

Yi-Ren Chen

The Final Work

Nothing in his months of planning—the selection of which carrier for which drug, the choice of who and how and when—had prepared him for this much screaming. While he was not unfamiliar with the muffled cries of the very ill, he was not prepared for the hundreds of patients queuing for the Emergency Room, and the incessant screaming of the cerebrally affected... it closely paralleled his personal vision of Hell. Yes, it had to be hell, he thought, since his eyes then locked upon her: Dr. Anna Della Riddle—flame-red hair, steel gaze, and supposedly dead for the past five years. He couldn't help but nod to the mysteries of the gods, for who but Anna would be most prepared to help him solve his current dilemma—her skills in neurosciences were renowned and her now-questionable death was thought to have been due to exposure to the very affliction he sought to cure. Anna, his ex-wife and favorite collaborator until the day she demanded to be first author, held a loaded syringe in one hand and an issue of *Cell* in the other.

The horrifying scene sent him into an uncontrollable screaming fit, and while on the verge of a nervous breakdown, he realized that he had succumbed to the very same mental malignancy that afflicted the myriad of patients overflowing the ER. As his knees crumbled, first toward one another and then to the floor, he noticed Anna's crimson heels moving his way—her every step a clap of thunder between his ears—as she swiftly positioned the syringe above his trembling thighs and took aim. "Hold still, Span," she intoned with what a casual listener might mistake for concern; with herculean effort Dr. Spanish Trueblood wrested enough control of his system from the rapacious madness hurricaning his mind to croak, "Don't... inject.... the... counteragent... doesn't... work.... It... it...."

The sardonic fire in her green eyes smoldered through the tortured fabric of his mind as she crouched tensely above him, like a panther over its prey, the close intensity of her body heat overwhelming even his high fever, and hissed, "It what? I know we've always been at odds since you stole the Nobel from me, Span, but the cure is in my blood, my bones, in my very soul, and you could say there is madness in my method....now take it!"

"Hippocratic harlot!" came his guttural shriek of terror and fury—then lightning struck his groin as his inexplicably non-dead ex, product of an enigmatic Italian inventor and a wildly unpredictable MD/PhD from Dublin, jabbed the thirteen-gauge needle into his upper thigh, parking its tip in his femoral artery; his mind displayed the pain in his visual field, multicolored sparkles like tiny cartoon animals, marching in spirals and tracing frenetic patterns, and as the fire of the flawed cure flooded across his blood-brain barrier, a moment of crystalline lucidity and a vision of a red dress left him with a shocking yet simple realization.

He was dead and his multicolored lunacy yielded to an eternity in darkness before he lurched back to life, where the first person he saw was Anna, tucking her copy of Cell between his teeth, then walking out of his life forever, adding: "The prototype you covertly injected into me five years ago induces brief cardiopulmonary arrest, until traces of cardiac troponin engage as the cofactor to complete the vaccine and it kick starts the heart, but I'm surprised it worked on you, since it requires a heart and you definitely don't have one."

Contributing Writers

Sentence 1: Joshua Spanogle, author of "Isolation Ward" and "Flawless", former Stanford Medical student and dermatology resident at Mayo Clinic.

Sentence 2: Ann Marie Kimball, MD, MPH, FACPM, Director of the Asia Pacific Economic Cooperation Emerging Infections Network and Stanford alum (BS Biology and Humanities 1972).

Sentence 3: Karen Walsh, wife of Jim Berbee, SMS III.

Sentence 4: Christine Kurihara, manager of special projects at the Biodesign Program.

Sentence 5: Eran Bendavid, MD, fellow in infectious diseases and health policy.

Sentence 6: Aaron Wang, medical student and PhD candidate.

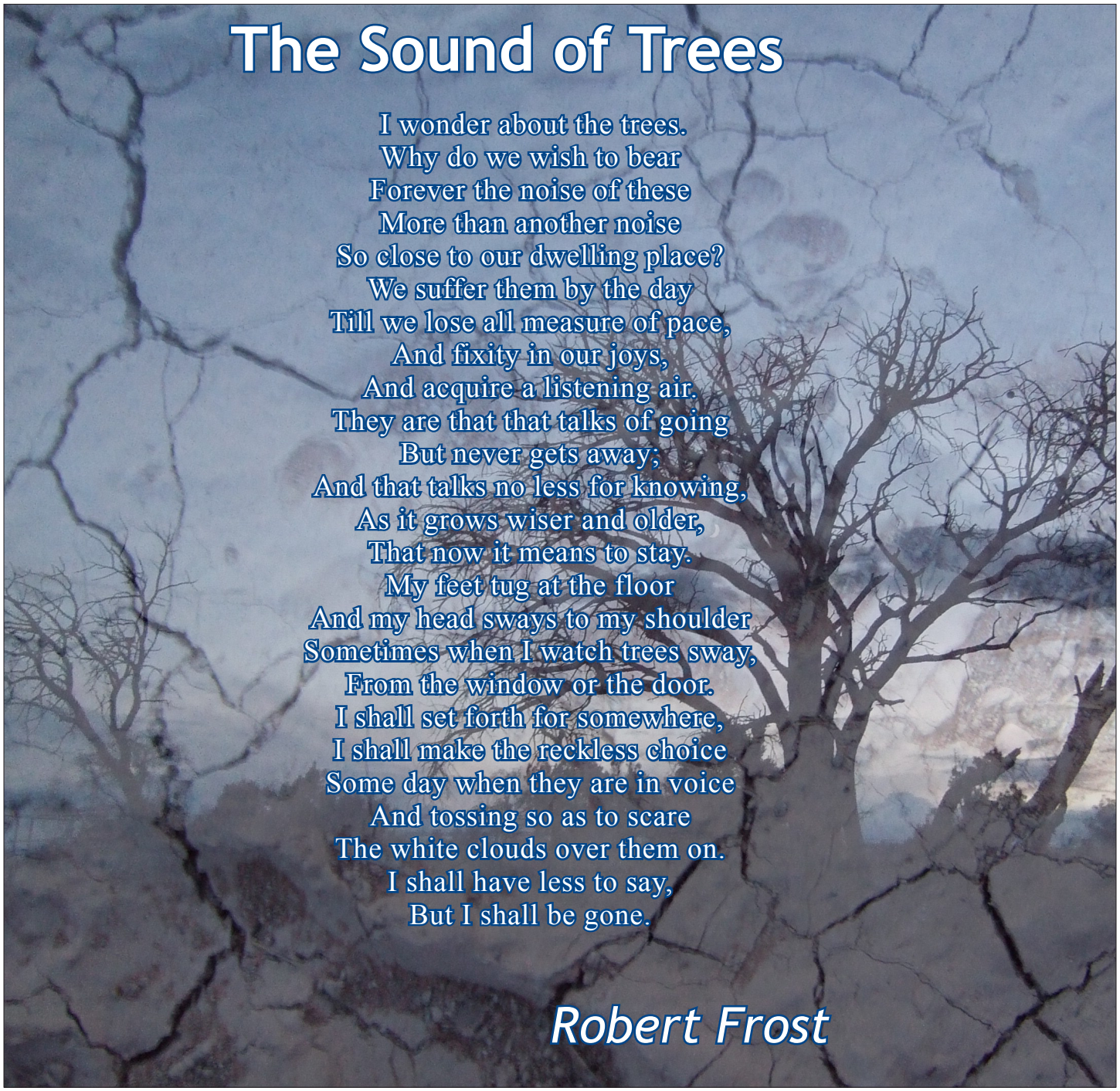
Sentence 7: Sahar Rooholamini, SMS Class of 2008

Sentence 8: Jacqueline Welch, SMSV+, and Clay Welch.

Sentence 9: Emma Bakes, SMS III.

Sentence 10: Clay Welch and Jacqueline Welch, SMS V+.

Sentence 11: Emma Bakes, SMS IV.



Alexander Cardenas

Leader in Medicine: Dr. Robert Negrin

Sean Sachdev, SMS II

Dr. Robert Negrin, Professor of Medicine, is the Medical Director of the Clinical Bone Marrow Transplant Laboratory and Division Chief of the Bone Marrow Transplant Division. As a world renowned scientist, he is currently leading research to elucidate molecular mechanisms that might reduce or slow graft vs. host disease and improve a graft vs. tumor response. He is also investigating new techniques of bioluminescence that might provide an insight into the complex biological processes that occur amongst tumor cells and effector cells of the immune system. Previously the President of the American Society of Blood and Marrow Transplantation, in 2004 he was named a Doris Duke Distinguished Clinical Scientist, an award that provides $1.5 million dollars of research funding to a physician-scientist who shows unusual promise in translating advances in science to next-generation patient care.

Interviewer's note:
I interviewed Dr. Robert Negrin in his office on July 2nd, 2008. Surrounded by busy laboratories, the home of the hematology department isn't located in the hospital, but rather in the Center for Clinical Sciences Research building (where a lot of the exciting lab work of the field takes place).

I first met Dr. Negrin before I even interviewed him, when he came into our first-year class last August. In his lecture, he presented the science behind hematopoietic stem cell transplantation along with the stories of a few of his patients. His quick, confident answers to some tough hypothetical questions (including one of mine) showed the level of his experience and scientific aptitude—considering all possibilities at all times. Moreover his calm demeanor seemed to instill a sense of ease and relaxation among his patients, who, facing an audience of nearly 100, glanced at him with a look of respect and trust.

I remember myself, a freshly-minted first-year, taking all this in with admiration. Here was a physician who was an expert in his scientific field, but at the same time a comforting and skilled clinician—able to elicit positivity in his patients. It made such an impression on me that I vividly remember his lecture to this day.

Source: Stanford Faculty Research Profile

My interview with Dr. Negrin confirmed my initial impression. It revealed those very qualities that I had first seen: here was a true-to-the-bones scientist who was also a wonderful clinician. I only spent a half hour with him, but, even then, his excitement for science and dedication to his patients was contagious.

The interview follows:

How long have you been practicing medicine since after your training?

I finished my fellowship in 1990… so 18 years.

If you think back to your earlier years of school and training, what led you to specialize in Hematology?

I realized that I really enjoyed working with very sick patients. Now, of course, it is important to care for patients on every level including telling the less-sick ones to smoke less, exercise more, and eat healthy. However, I think one of the keys to success in life is learning more about yourself, and I discovered that I enjoyed focusing on few really sick patients rather than spreading my focus out on many (perhaps not-so-ill) patients.

I also discovered that Hematology is a field on the cutting edge. With easy access to patient tissue, it is possible to do advanced forms of testing and apply exciting, groundbreaking cellular therapies to help a patient get better. Moreover, all this occurs in a team concept that I have really come to love.

I should also mention that I made all these conclusions with the help of great mentors who guided me every step along my path.

Why did you go into academics?
I wanted to be around smart and talented people. I wanted to teach and to be taught and I wanted to be involved in both basic and clinical science camps, and Stanford is probably one of the best places on this planet to be at for something like this.

In your opinion, what are the most difficult or challenging aspects of your career as a scientist and a clinician?
I think one of the most challenging aspects of a career like mine is striving to have a research program that moves. In order to do this you have to pick your questions carefully and collaborate thoughtfully. I can't stress enough how important it is to find valuable collaborators that can really augment the level and significance of your research.

Operationally, you must strive for a program that is fundable and cutting edge. You must attempt to pick questions that are closely related to your clinical work. This way unearthed lab concepts are applied to the clinic, which in turn gives you more questions to investigate. The science and medicine feed off each other.

In the clinic, it is tough when patients die or don't improve as much as we'd like. However as you go along and gain experience, you start to realize you're doing the best you can—which makes the decisions a bit easier. In my opinion, one of the most important things to remember is being open with the patient. Although it can seem tough talking to patients with difficult cases, I think patients fear the unknown more than they fear death and it is important to form good, open, and upfront relationships from the beginning.

What are the most rewarding aspects?
The ability to make a real impact on a patient's life. We're reminded of this every year during our annual patient reunion in July. This is when many of our former patients come back to visit us, affording us a fortunate opportunity to hear their wonderful stories and what they've been doing with their time.

As for the research side, there are few feelings like the rush you get when you see a significant result of a successful experiment. It is exhilarating to be on a leading edge of a concept you know can feed into and help shape other fields over time.

I also enjoy mentoring students. It is great watching young people mature and succeed.

Who or what influence in your life has had the most significant impact on you?
Definitely my mentors. Great mentors over the years have guided me every step of the way. Students should realize how important it is and how valuable it can be to connect with faculty members for their help and guidance. This is what we are here for, and it's not just a one-way street either. Faculty members learn from students too and are usually happy to interact with and work with them

When all is said and done at the end of day, what motivates you?
This is a great question—one I urge all of my students to think about. I have personally thought a lot about this over the years and I think what motivates me is the intellectual challenge of addressing a question important to me but also one that has a potential to make a significant impact on others.

For example, I am a great believer of basic science, but basic science in its purest form is not exciting to me, personally. I left a doctoral program before beginning medical school because I wanted to find a different, more specific, and more applicable question to work towards answering, which I am happy to say I have found.

What are your interests outside your career?
Family; in fact I just took a call from my daughter minutes ago. I make it a priority to spend a substantial amount of time with the close ones that I love.

Basketball; I try to play as much of it as I can. In fact, if I was good enough, the only other career I might have wanted to pursue would be one in pro basketball. I also love being outside as much as I can, interacting closely with nature.

There is so much to do and learn I could be here 24/7 if I wanted. But I think it's important to maintain a balance between your career and other important things in your life and I try my best to do that.

Do you have any advice for medical students?
Other than what I've said already, I would say: find something that excites you. Here you are at Stanford, surrounded by people who are allowed to be here because they're on the cutting edge, working on almost every question you could imagine.

Look around you and find out what motivates you. Then surround yourself with the people who can help you in your interest. Working hard, in my opinion, is the easy part. Finding out what can really shake and excite you deep down inside? That's the hard part.

Also, maintain a balance. Slow down and enjoy the process of where you're at. I see students these days rushing about, eager to finish school and "make it." Do I think I have "made it?" Really, there is nowhere "to get." A career in medicine, in my opinion, is a process. It is a process when you're a student and it's a different process when you're in my spot. The key is to enjoy the process.

Gentlemen

My colleagues and myself
have decided not to deliver any form
introductories to the present course
lectures; but as there are some po
I wish to discuss which cannot
opportunely introduced into the
regular course of daily instructio
I have concluded to embrace
in a first differing somewhat fro
those which are to follow.

One object, or the principle o
in this lecture is to impress upo
your minds an important truth,
that is this. you should study ecl
ticism thro[illegible] Study it in
collecting [illegible] your regular
pupilage, and study it especially
in reference to your future adaptat

H&P
The Stanford Medical Student Journal
Volume 13, Number 1, Autumn 2008