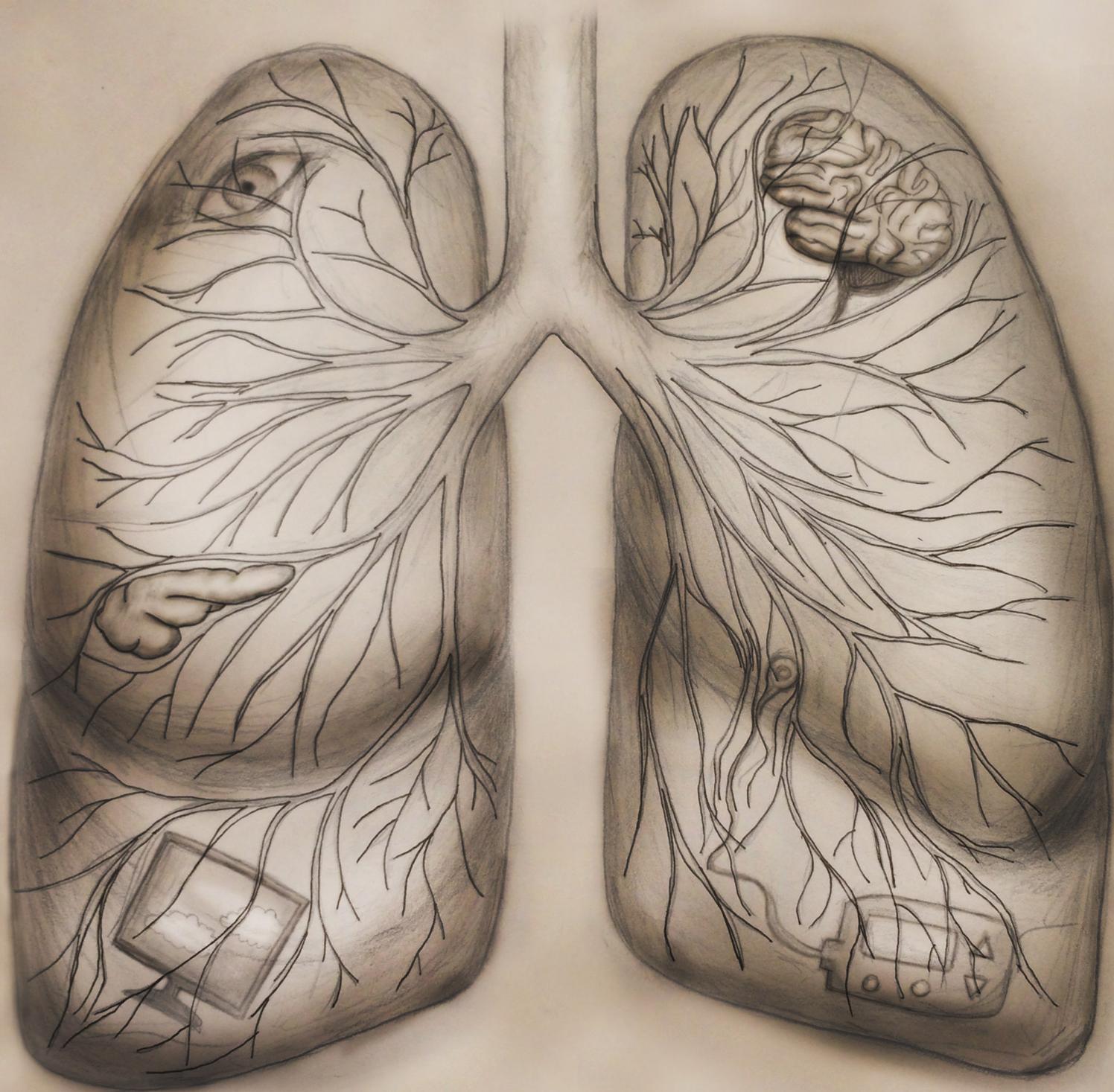


Sackler Journal of
MEDICINE

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MISSION STATEMENT

What's emerging in medicine today? The Sackler Journal of Medicine – a forum where trends in medicine including translational research, the economics and policy of healthcare, and clinical experiences are explored, analyzed and discussed. SJM is a peer-reviewed journal for medical students to discuss and learn about the latest medical breakthroughs and the fundamentals of medicine.

We encourage student and physician collaboration to bring you literature reviews, case reports, original research, reflective pieces, and short commentaries on published papers. Take the opportunity to contribute your work, experiences and voice to the conversation.



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Email: editor@sacklerjom.org
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The Editorial Board would like to give a special thanks to Tami Lipkin-Zur and Adi Knaan for their support.

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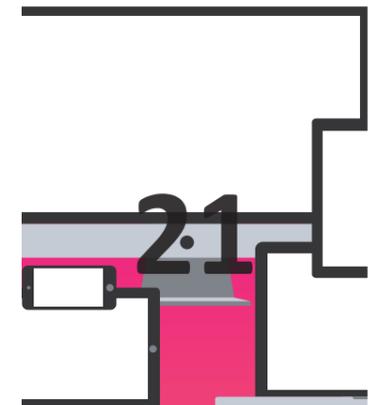
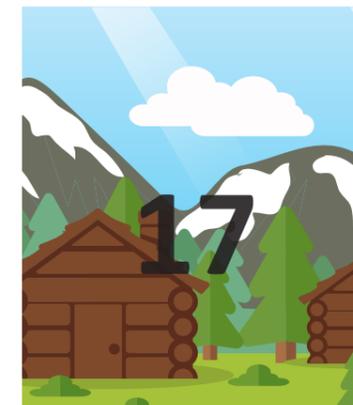
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Letter From the Editor

Brian Wolf

editor-in-chief

This issue marks an exciting time for the Sackler Journal of Medicine. We began in the spring of 2016 with the idea of a medical journal by and for medical students. Now, in 2017, with the publication of our second issue, we are continuing to develop the journal's voice in the ever-growing field of medicine. The goal for this journal is to publish pieces by medical students who are studying the foundation of medicine and are beginning to apply this breadth of knowledge outside the classroom. These students also happen to have particular interests in medicine that they want to share and discuss with their fellow students; this journal provides such a medium for discussion.

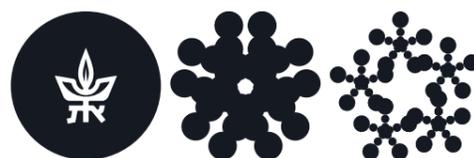
Our second issue brings together various topics from a piece by Joseph Mehrabi on Med App Jams to Alison Dallich, Elana Cohn and Alyssa Caplan's case report on different presentations of frontotemporal dementia to Eitan Fleischman's review on "big data" and its medical applications. As with our inaugural issue, the journal delivers a diverse collection of papers through commentaries on recent research and current events, reflection pieces, reviews and original research. Want to learn more global health? Zachary Mostel brings to you a reflection piece on his summer in India during which he volunteered with Unite for Sight to help deliver proper ophthalmologic healthcare in developing countries. Jeremy Grossman provides a powerful firsthand account of his diagnosis of type I diabetes, along with his experiences at Camp Conrad-Chinnock. Jason Hubsher's original research on the views of medical students on treating LGBT patients illuminates an interesting issue in the medical field that warrants further exploration. A review on inferior vena cava filters by Ezra Schrem is a must-read for students who want to better understand pulmonary embolisms and the treatments for this condition. Not to mention, David Ben Nun's excellent analysis on the use of the latest breakthroughs in cancer detection technology and their application for pancreatic cancer. Overall, these pieces provide a snapshot of what's happening in medicine today.

Last year, we saw the Sackler Journal of Medicine grow

from a relatively small organization to now being an established publication with over thirty students on staff and a large online presence through the website (www.sacklerjom.org). We are confident in our staff and are excited to see SJM grow even further in the future. If you are interested in joining or submitting a piece, email us at editor@sacklerjom.com.

We hope you enjoy the issue.

Brian Wolf



Letter From Dr. Allen

Aaron Allen M.D.

Faculty Adviser- SJM

Deputy Director

New York State Program

Sackler Faculty of Medicine

Tel Aviv University

Israel

I am often asked what is the most important quality in medical students. What is it that makes them exceptional? Is it their sharp intellect, their motivation to improve, or their dedication to patients and serving humanity? This question lies at the heart of what is medicine and what it means to be a physician.

In today's medical industrial complex, a physician can take many forms and roles. A physician can focus his or her time on drug development and research and never actually see a patient. A physician could also choose to be an educator or to be a healthcare administrator focusing on health care systems and economics. Perhaps the most common are those that choose to devote their entire existence to patient care. All of these are critical tasks for physicians in our society. As a medical school, how can we possibly prepare our students for all of these important yet vastly different roles?

The answer, I believe, lies in basics and simplicity. We educate students to be careGIVERS. It's just that simple. Of course, there are pages and pages of facts and skills to be learned, but that is the technical information for which a computer and a few questions banks would suffice. We have chosen to focus instead on the core values of learning to give. It would seem elementary, but this is a skill that can take a lifetime to master. How does a 20+-year-old highly educated and focused graduate student learn to put their ego aside and focus on the 5-year-old that needs their attention? This is the art of medicine. To see every patient as an opportunity to give is the motto that we strive for at Sackler.

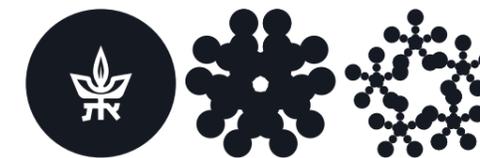
A student who learns to be a giver with patients will be an outstanding researcher who understands

not only to work in a team but understands the importance of writing and publishing their work to give to the medical community. The same is true for the health care administrator who looks to his task in managing the system in the best interest of the clients and patients rather than but not in spite of the bottom line.

It is with great pleasure that we are able to once again congratulate the student run staff of SJM on their second and very impressive issue. This amazing project of SJM exemplifies the spirit and attitude of giving so important to the Sackler experience. We, in the administration, are proud to have this as an important part of the Sackler family.

Wishing everyone a healthy and successful year of giving in medicine!

Dr. Aaron Allen



Letter to the Editor

Jeffrey H. Kern, MD

Clinical Associate Professor of Pediatrics

Weill Cornell Medical College

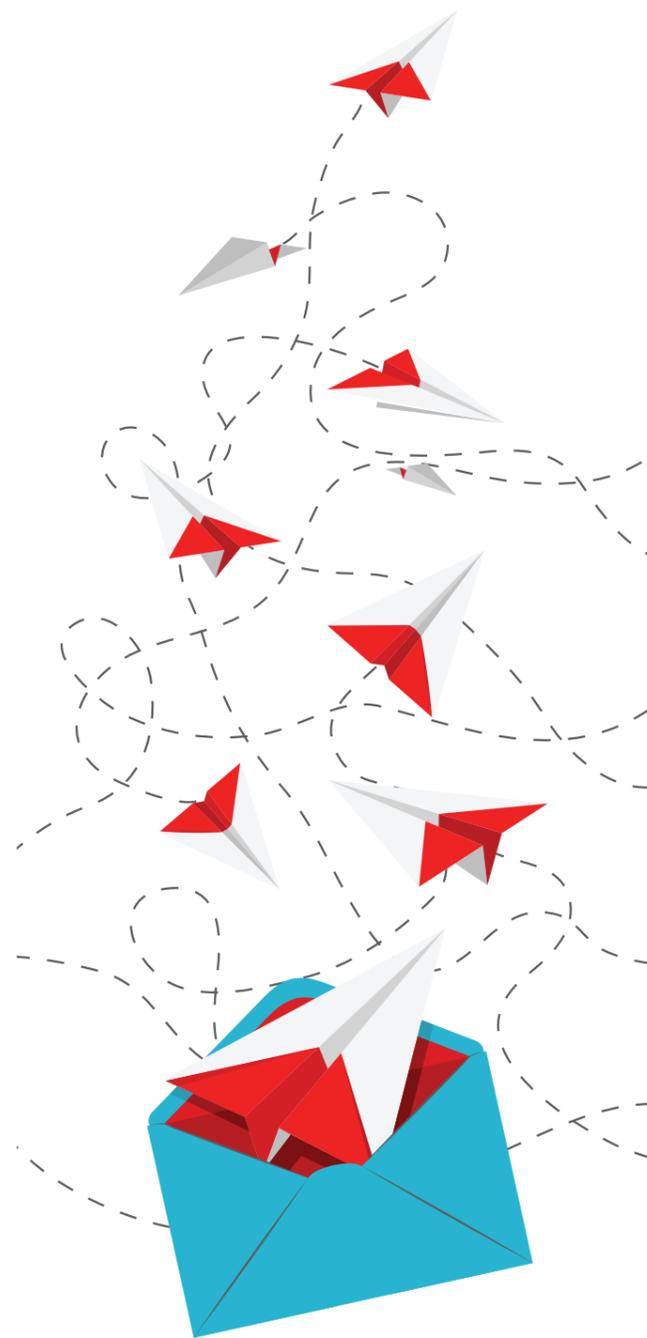
New York

Correspondence: Transition Care for Congenital Heart Disease

To the Editor:

It was with great interest that I read “Proposed Analysis of the Transition Process from Pediatric to Adult Care for Patients with Congenital Heart disease in Israel” (Burke and Beeber). As a pediatric cardiologist in practice for more than 20 years, I have many adolescent patients with congenital heart disease (CHD) who are nearing adulthood and the necessary transition of care. The authors correctly point out the transition and subsequent care during adulthood are exceedingly important. Historically, a major problem has been that pediatric cardiologists, while expert in management of CHD, are not experienced in managing the other medical conditions that arise during adulthood. Conversely, adult cardiologists, while very familiar with adult ailments, have little experience with CHD.

It is for that reason that the relatively new field of adult congenital heart disease has emerged, in which cardiologists trained to care for adults undergo additional special training (typically 2 years in the United States) in congenital heart disease. While this is important for all patients with CHD, it is most important for those individuals with more complex forms of CHD. This includes single ventricle lesions (including hypoplastic left heart syndrome and tricuspid atresia), pulmonary atresia, tetralogy of Fallot, transposition of the great vessels, and endocardial cushion defects, all of which can have significant sequela during adulthood. I applaud the authors for recognizing this problem and the need for further study in Israel.



Micah Belzberg:

Air Mail

SJM Commentary

Medical Students and Mental Health

Benjamin Grinzaid

Sackler School of Medicine, Tel Aviv

University, Tel Aviv

The quality of mental health among medical students worldwide is an issue that has existed for decades, but one that has not, as of yet, received sufficient resources, time, and practical consideration. A recently published meta-analysis of 195 studies in JAMA calculated the overall pooled prevalence, globally, of depression or similar indications of medical students was 27.2% (1). This clearly illustrates a concern among the mental health status of medical students. In conjunction with this meta-analysis, JAMA also published a systemic review by Wasson et al. who focused their research on reviewing 28 different implementations thought to improve the mental health of medical students (2). Such implementation included a pass/fail system and mental health and wellness programs, all of which revealed an improvement in the medical students' mental health status.

Given the growing need to solve issues involving mental health in the medical school setting, why has this subject not received the attention it clearly deserves and warrants? The accompanying editorial by Stuart J. Slavin, MD, MEd lists 5 reasons why this is the case (3). He first states that there is a belief that if a student cannot handle the stress and pressure and workload of medical school, then they should “seek another profession.” Dr. Slavin states that this leads to a flawed logic, which indicates that more hours and rigorous education must lead to better “educational outcomes” and that anything less than this is considered a lowering of the standards. Interestingly, curriculum changes at one medical school that implemented pass/fail grading system, less detail oriented study and more student involvement in volunteering and extracurricular showed less stress and anxiety and better overall quality of life among their students.

The second issue in medical school culture is the concern for physical illness over mental health. This is revealed in the lack of prevention of mental health related issues in a medical school setting. Thirdly, most of the resources, money, and medical research have been directed towards the curriculum and how



Karen Arane & Micah Belzberg:

No Comment

to make the actual medical material better rather than towards the Student Affairs offices. While this might result in better teaching methods and more efficient presentation of material, the quality of the mental health of the student can be overlooked. A fourth aspect of the atmosphere in medical schools that leads to decreased concern for mental health among students is that the medical school administration remains indifferent. Stuart states that the reason for this indifference could lie in the fear that addressing these issues could reflect badly on the particular medical school.

The fifth and final cultural finding in the medical school setting is the attempt by medical schools to implement mindfulness programs, self-care courses, and resilience programs without addressing the issue of the learning environment of the student and how this affects their mental health. Simply providing students with these generalized programs, while well-intended, takes the responsibility away from the medical school administration, as they are not necessarily addressing the true mental health needs of their students.

Dr. Slavin states that “student wellness must be everyone’s concern” and should not be limited to just the Dean of Students office. It is crucial that such mental health concerns are valued just as much

as board scores and residency matches and that the entire administration work together to create a culture in which the mental well-being of the student is the utmost priority.

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Medical Students and Back Pain

Edmond Adhoot

Sackler School of Medicine, Tel Aviv
University, Tel Aviv

Musculoskeletal (MSK) disorders are injuries that affect the body's muscles, bones, and joints. Lower back pain is one of the most predominant MSK disorders in working class Americans, especially in service workers, craftsmen, operatives, and laborers (1). This pain is defined as a non-traumatic MSK disorder affecting the low back, including lumbar disk problems and sciatica, and not caused by injuries, other diseases, or cervical spine problems (e.g., neck pain) (2). While the prevalence of lower back pain in working Americans is well known, little data has been collected on the prevalence of MSK disorders in medical students.

In a study quantifying the musculoskeletal ailments that 4th year medical students suffer in a medical school in Mainland China, information was obtained from 207 students using an updated Standardized Nordic Questionnaire, a questionnaire that allows for comparison of neck, shoulder, lower back and general complaints amongst a sample (3). Approximately one-third of subjects reported that they suffered from an ongoing MSK disorder, the most common region affected being the lower back (40.1%), followed by neck pain (33.8%) and shoulder pain (21.7%). The study concluded that time spent doing deskwork or on the computer is likely a contributing factor to the high prevalence of MSK disorders in this medical student population (3). With the high prevalence of back, neck,

and shoulder pain in medical students, it is important for this population to be informed regarding exercises that may mitigate such disorders. A systematic review concluded that there is a positive therapeutic effect of yoga in individuals who suffer from chronic spinal pain (4). The authors of this review highlight how certain yoga positions correct vertebral curvatures and strengthen the thoracic, abdominal, and respiratory muscles needed to maintain a proper posture. Yoga, therefore, can be an effective preventative measure and treatment for medical students who may be predisposed to back and neck pain (4). In fact, one of the authors of this review teaches UK medical students about the benefits of yoga. In light of these findings, it is important for medical students to be aware of their bodies while studying and engage in physical activities that deter the onset of MSK disorders.

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Mental Health and the 21st Century Cures Act

Benjamin Grinzaid

Sackler School of Medicine, Tel Aviv
University, Tel Aviv

The awareness and treatment of mental health in the United States has made great strides recently, as evident by the approval of the 21st Century Cures Act by the House of Representatives and by the Senate and approval by President Obama. According to Dr. T. Scott Stroup, a psychiatry professor at Columbia University College of Physicians and Surgeons in New York, there is finally in place a bill that is based on evidence and research rather than opinion or ideology. The bill provides access to treatment for individuals with psychosis, requiring 10% of states' mental health

budget be directed toward this issue. In addition, the bill states that a \$5 million grant will be dedicated to community-based mental health, enabling individuals access to a 24-hour on-call professional service team. Another section of the bill requires the United States Attorney General to make mental health programs accessible to patients with severe mental illness or drug addiction. Many of these patients receive large jail sentences for minor crimes, and this program would give these people the support they need rather than keeping them behind bars with no access to mental health care. The bill also aims to clarify when physicians can share information with family members of a patient who cannot provide proper information because of his/her disability.

In the past, the United States has lacked severely in funding and programming for pertinent mental health issues. According to Dr. Maria Oquendo, the president of the American Psychiatric Association, this bill "marks the passage of the first mental health reform bill in more than 50 years and is long overdue." From how mental illness is handled in the criminal justice system to the improvement of mental health services for children, the treatment and services provided for mental illness will continue to grow and improve from the approval of this legislation. Additionally, the strong support for this bill strengthens the need for physicians to learn more about and, if needed, utilize the resources that are currently and will become available for their patients. Lastly, the mental health programs outlined by the bill are crucial to the health and wellbeing of the citizens of the U.S.

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The Death of Animals in Medical School

Zack Cohen

Sackler School of Medicine, Tel Aviv
University, Tel Aviv

The authors take note of the rapid decline in the use of live animals in medical schools. In 1987 over 90% of schools used live animals as part of their curricula. This number plummeted to 32% of U.S. medical schools in 2001. Today, there are no U.S.-based medical programs that make use of live animals. Many older medical graduates that employed this practice during

their studies are strong proponents for the invaluable experience that comes with handling a live subject. They argue that no simulation can replicate the atmosphere or elicit the same requirements for swift decision-making and teamwork that are used when handling a live animal. On the other hand, animal rights groups, who have fought for such changes in the curricula for several decades, are rejoicing in the results. The authors note that all physicians will eventually have to hold a life in their hands, and with the abolishment of live animal experiments, many trainees' first experience will be with a human. Additionally, given the fact that most patients demand the most experienced physicians, trainees are left to practice their skills on less fortunate individuals, including uninsured, undocumented, and other marginalized groups. Thus, the question remains as to whose body will be the first to be practiced on by newly-trained physicians, and whether simulation technologies are adequate in refining these doctors' skills.

Reference

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Genetic Testing and Alzheimer's Disease

David Ben-Nun

Sackler School of Medicine, Tel Aviv
University, Tel Aviv

A new study published by the Dementia Research Centre at University College London's Institute of Neurology has concluded that the age of onset and clinical features of autosomal dominant familial Alzheimer's disease (ADAD) may be influenced the position of the mutation that causes the disorder and the specific causative gene responsible. This conclusion reinforces the importance of considering genetic testing in younger patients who present with dementia and additional neurological features to ensure proper diagnosis and treatment.

Familial Alzheimer's disease is clinically similar to the sporadic form of the disease in that both are associated with progressive impairment of episodic memory, though the heritable form of the disease typically presents with a younger age of onset. Despite ADAD affecting less than 1% of all Alzheimer's patients, the disease has long been considered a useful model to study to shed light on the disorder in general.

To further explore the relationship between the genotype and phenotype of ADAD patients, the Dementia Research Centre reviewed medical histories of approximately 213 patients in the UK and Ireland who were shown to be carriers of two mutations that led to the disease over a 28-year period. The two specific genetic mutations examined were mutations in the gene presenilin 1 (PSEN1) and mutations in a gene responsible for producing amyloid precursor protein (APP).

The results indicate that age of onset is significantly later for individuals who are carriers of APP mutations (50.4 years) than for those with PSEN1 mutations (43.6 years). Moreover, researchers learned that the age of onset in patients with PSEN1 mutations was influenced by the position of the mutation in the gene. The study also shows that the type of symptoms that presented were different between the two mutation carriers. Carriers of mutations in PSEN1 tend to present with atypical cognitive symptoms and other neurological features such as spastic paraparesis, rigidity, and ataxia in addition to the typical Alzheimer symptoms.

The study's findings suggest that it is important to consider ADAD as an option in differential diagnoses of patients with early onset dementia and other neurological features. Moreover, the authors suggest that these findings serve to highlight the importance of investigating atypical genotypes of non-familial Alzheimer's to better understand the complex mechanisms that lead to the disease.

Reference

Ryan NS, et al. Clinical phenotype and genetic associations in autosomal dominant familial Alzheimer's disease: a case series. *The Lancet Neurology* 2016;15(13):1326 – 1335.

Gamma Oscillations: Possible Treatment for Alzheimer's Disease?

David Ben Nun

Sackler School of Medicine, Tel Aviv University, Tel Aviv

In a recent research paper published by the Massachusetts Institute of Technology, and featured on the popular NPR podcast "RadioLab," neuroscientists have shown that subjecting mice suffering from pathology similar to Alzheimer's disease to oscillating light may reduce the buildup of amyloid plaques that lead to neurodegeneration. The study focuses on gamma oscillations, a pattern of electrical

activity between excitatory and inhibitory neurons observed in a healthy brain, and how inducing these oscillations can actually reduce the levels of amyloid plaque buildup in diseased mice engineered to mimic Alzheimer's disease in humans.

The study confirmed that mice that showed an increase in the concentration of amyloid in the brain also showed deficits in the gamma oscillation patterns observed. This conclusion strengthens previous research, which has shown that gamma oscillations are abnormal in humans suffering from Alzheimer's disease. When the MIT team induced the gamma oscillations in mice where the pattern was deficient, they found that the exposure decreased the amount of two different isoforms of amyloid plaques ($A\beta$ 1–40 and $A\beta$ 1–42) by 53.22% and 44.62% respectively. In other words, by simply shining a light at the right frequency on specific brain cells, these scientists were able to remove approximately half of the amyloid plaque in these mice.

Furthermore, by performing genome-wide sequencing on the brain tissue of the mice after 1 hour of exposure to 40 Hz oscillations, the MIT researchers found that 35% of the upregulated genes in the tissue were related to the function of the brain's microglia cells. The genes affected tended to be related to macrophage-stimulating factors and other elements involved in the phagocytosis activities of these neuron-assisting cells. The scientists concluded that the amyloid plaque was reduced due to the enhancement of activity of the brain's microglia, which become more effective at ridding the brain of the harmful plaques as a result of the "restoration" of gamma oscillations.

These results could mean that a similar method could be engineered to treat humans suffering from Alzheimer's disease. With that in mind, the scientists showed that they could replicate the results attained in amyloid plaque removal by simply placing diseased mice in an environment with a light flickering at 40Hz, instead of the much more invasive procedure of shining a light at specific neurons in the brain. However, the researchers remain cautious about replicating the results in humans and emphasize that further study is required to determine whether a similar treatment will be therapeutic for humans.

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Learning How to Learn

Zachary Mostel

Sackler School of Medicine, Tel Aviv University, Tel Aviv

A middle-aged Sikh man, dressed in full Punjabi, turban and scraggly beard sat at my right en route to Delhi. It is no secret that a trip to India is filled with pearls of wisdom. For me, though, the take-home lesson began on the plane ride there. We chatted and laughed between the inflight Bollywood films. "Sikh means 'student,'" he said. "Every state of India you will visit will have different teachings and many different colors. We are all students." When I told him that I am a medical student, he joyously exclaimed, "Then you are a Sikh!" It had been only a few hours into my flight and I had already been welcomed into a new faith about which I knew little.

This man was just one of the many characters I would meet along my summer journey. His warmth was immediately evident, introducing me to the tenets of his faith and even extending a generous invitation to show me his home state, but his greatest lesson was that we are all students. In order to navigate the terrain that is India, I made use of many teachers, namely backpackers, doctors, volunteers and locals. All of them had invaluable insight and useful guidance to offer along the way.

Early in the academic year, I had decided that the best use of my first summer of medical school would be to volunteer abroad in an underserved area. Over the last few years, my enthusiasm for global health has grown tremendously, and I wanted to be an active contributor to the wellbeing of a community in need of greater access to healthcare. A friend from school, also involved with the Global Health Club, suggested a few

summer programs to me, and I decided that Unite for Sight (UFS) would be the best choice. From the looks of it, the program offered comprehensive public health training, cultural immersion and learning opportunities for medical students. It was an easy decision.

Over 18 million residents of India are blind, of which 9.5 million are cataract-related and 3 million are refractive error-related (1). In particular, in India, cataract-related blindness disproportionately affects the poor and the treatment of this condition has important secondary societal benefits (2). When evaluating the benefits of corrective cataract surgery in the Indian state of Tamil Nadu, benefits included an increase from 44% to 77% of patients engaging in income-generating activities and a significantly higher monthly household income one year after cataract surgery (3). Optimizing patient flow and efficiency, manufacturing of supplies domestically, and using a specialized workforce and standardized protocols have been helpful in providing an efficient model for delivering high quality and low-cost cataract surgery (4).

UFS is a non-for-profit organization that strives to eliminate patient barriers to proper eye care in developing countries. They help reduce typical patient impediments to quality healthcare by funding surgeries (volunteer fundraising pays for their operations), bringing eye-care directly to rural villages, providing transportation to the hospital for surgery and educating communities about blindness prevention and ocular health.



Elana Cohn: *windows*

My month as a volunteer with UFS in Chennai, India, was an incredibly satisfying learning experience. I was sent to local villages to pitch “eye camps” as part of an outreach effort for the underserved. At these camps, we gave visual acuity examinations, took patient histories, screened for cataracts, distributed prescription eyeglasses, and compiled global health research data for the ophthalmologists working with UFS. Dr. Senthil, the local ophthalmologist with whom I collaborated, took much of his own time to show me the steps involved in cataract surgery and even provided a goat’s eye to perform my own surgery! There was no shortage of endemic medical lessons throughout my stint. Some of the cases that casually strolled into our eye camps included leprosy, elephantiasis, wound infections and a range of parasites. The volunteering provided round-the-clock opportunities to learn the “tricks of the trade” of ophthalmology, Hindu cultural practices and how to effectively and altruistically dispense care in the realm of global health service.

Traveling abroad usually means a language barrier, and rural India may be the pinnacle of such struggles. Many of the villagers have no education and have little access to the larger society. Additionally, a month of working in small villages meant I needed to learn enough of the local dialect to dispense proper eye care. I soon found that trying to get someone to understand you is stressful, but when he or she finally does it is extremely satisfying. Some of the Tamil phrases I picked up include: “po-tih parun guh” (try them on), “teh ree-yir-dah?” (can you see clearly?) and “purchenna illai” (you’re welcome). Even with my broken Tamil, the villagers were overjoyed and entertained by my attempts to converse.

In addition to my role as volunteer, I also had the privilege to serve as a research fellow and design a global health study in collaboration with Pranav Eye Hospital in Chennai, Unite for Sight and Sackler School of Public Health. The optometrists at the camps referred potential pre-operative cataract patients to participate in my study and even served as translators. We assessed pre-operative cataract patients for preliminary understanding of prescribed ocular drug regimen. UFS and the partner hospital are investigating risk factors for poor comprehension and absorption of instructions for eye-drop use. It took a great deal of time, effort and sweat (summer in Chennai was sweltering) to see the study to completion, but the end result made it a worthwhile endeavor. Just to hear a heartfelt “naandri” (“thank you”) at the end of a patient survey was enough to show me how much the villagers appreciated the

work we were doing. Simple acts like fitting them for glasses or screening for cataract surgery elicited ear-to-ear smiles. These small gestures were life changing for them.

Vision can mean the difference between unemployment and the ability to earn a livelihood. One patient told me his narrative as he awaited his cataract surgery. He had been a security guard with declining vision. His employer informed him that he would have to be let go, but could return if his vision improved. The man emphasized that this operation impacts his ability to provide for his family. For the many Indians who cannot afford cataract surgery, the complimentary services of Pranav Eye Hospital are life-changing. This first-person description of how a cataract surgery, which is sponsored by volunteer fundraising, can be the difference between steady income and unemployment in Chennai. I will never forget this man’s personal account of how UFS and the ophthalmologists at Pranav Eye Hospital change lives for the better on a daily basis.

When he saw me writing in my journal at the end of our flight, the Sikh asked if it was poetry. I explained my newfound interest in journaling, to which he enthusiastically said, “Always put down your thoughts, you want them for later.” There is wisdom in the seemingly mundane encounters of everyday life. Unexpected pearls, unrealized at the moment of incidence to be profound insight, can only be gained from upon a second glance. I am sure there have been life-saving medical epiphanies that have been credited to good note taking. Returning to these thoughts today brings me back to the details and emotional response to said encounter. Every person, be it friend, stranger or patient, has those unshakeable lessons to share, so have a pen handy and an open mind.

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The Therapeutic Value Of A Diabetes Youth Summer Camp

Jeremy Grossman

Sackler School of Medicine, Tel Aviv University, Tel Aviv

In late 2004, emergency room doctors disclosed to me that I was bordering on falling into a coma with a blood sugar reading of 1100 mg/dl. I was led to the hospital with the symptoms of polyuria (the production of large quantities of urine) and polydipsia (the urge to drink) appearing shortly after my 12th birthday. Before that life changing day fell upon me, the constant and looming urge to leave class and other activities in order to relieve these symptoms made it increasingly arduous to keep up with my academics. I had lost 15 pounds in the course of just 2 weeks, dropping to a mere 85 pounds. After running a number of both physical and hematological exams, my physicians diagnosed me with Type I (Juvenile) Diabetes. I had been suffering from diabetic ketoacidosis. There, it was explained to me that my pancreas was shutting down. A combination of environmental and genetic factors had triggered T-lymphocytes in my immune system to attack the beta cells of the pancreas. The lymphocytes had identified this group of cells, which synthesize and secrete insulin, as foreign invaders that required immediate removal from my body. Over the course of the next 3 days, I was told that for the rest of my life I would require self-injections of both long- and fast-acting insulin, to make up for the loss of these insulin-producing cells, in addition to multiple daily fingerstick blood tests. The next few days in the hospital became the beginning of a new way of life. This fearsome realization of a profoundly altered lifestyle was emotionally devastating and enervating. This, of course, is not the end of the story.

In the weeks and months following my discharge, I found the burden of my condition to be nearly unbearable in spite of the assistance I received from my immediate family and friends. My days consisted of pricking my fingertips until scar tissue and callouses enveloped them, counting carbohydrates in what seemed like an endless course in mathematics and injecting myself with insulin in any area of adipose tissue I could sequester on my, at the time, very thin adolescent body. As a result of this or perhaps in combination with the routine mental changes that occur at this phase of



Micah Belzberg: Summer

Key Point: Studies on Diabetes and Camps

A recent three-year study of US diabetes camps showed a 10% increase in campers’ feeling of confidence in their ability to manage their diabetes, with the greatest increase (16% increase) among the newly diagnosed.

Additionally, a meta-analysis that reviewed 31 studies published from 1973–2010 of camps in 6 different countries, which included data pertaining to a total of 1,782 child summer camp attendees, demonstrated a small yet statistically significant improvement in self-perception following attendance at a camp for children with a chronic health condition such as diabetes. A statistically significant effect was also found for those reports examining extended follow-up on the summer camp attendees.

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development, my grades in school began to decline sharply. Surprisingly, the factor that contributed most to this mentally exasperating period was not the inception of these new and profound requirements for managing diabetes, but was instead a lack of emotional support. This perceived lack of support arose not from a deprivation of medical resources, but rather from the absence of a platform through which to connect with other diabetics. Only they could comprehend the complex and arduous life that the diabetic and his or her family lead in managing this chronic disease. Support from empathic, knowledgeable and similarly afflicted group members can help with feeling less isolated but also more hopeful for a positive future while coping with the condition. By chance, my family was introduced to an individual who frequented such a supportive venue as a type 1 diabetic. Upon further inspection, we learned of a summer camp for diabetic children in the mountains of Big Bear, California and promptly registered for the upcoming session with the hope that it may help fill the void of the present.

The first time I stepped foot onto the campgrounds of Camp Conrad-Chinnock, I was astonished at what I saw. Surrounding me were hundreds of diabetic children from the ages of 5-17 years who appeared equally ebullient to their disease-free cohorts. They were occupied with playing basketball, shooting rifles, bows and arrows, completing arts and crafts, swimming, hiking and rock-climbing. Most extraordinary was their apparent freedom from anxiety, which was a luxury I had not known could exist with my circumstances. The most inspiring aspect of this diabetes camp was the chance to meet adult diabetics who held esteemed roles in society: college students, firefighters, nurses, psychologists, engineers, etc. Hearing the stories, as a young teenager, of what these individuals had accomplished despite their medical conditions gave me the confidence to pursue my own path in medicine. Had I never attended this summer venue, my goals may have been quite different. Additionally, I must stress that my visits to the camp every year were vital in sustaining my confidence in living as normal a life as I could given my condition. Indeed, it has also played an immeasurable role in my development as an aspiring physician, opening a window on the emotions and tribulations that patients encounter in dealing with chronic conditions.

Camp Conrad-Chinnock, established in 1957, was founded by an endocrinologist who well understood

the need to treat the psychological symptoms associated with the diabetic condition. However, he was not the first. Dr. Leonard F.C. Wendt, M.D., founded the first diabetes camp in Michigan in 1925, which led to the establishment of hundreds of similar camps that now serve nearly 20,000 children every summer worldwide. Stressing the potential benefit that such organizations can have on the lives of so many with chronic conditions is urgent. With the prevalence of diabetes rising from approximately 333 million persons in 2005 to approximately 435 million persons in 2015, an increase of 30.6%, establishing standardized criteria are needed to assist these patients in dealing with the psychological impact that diabetes has thrust upon them (1). Additionally, as of 2012, about half of all adults living in the U.S.—roughly 117 million people—have one or more chronic health conditions, according to a CDC report released in 2013 (2). Further studies on the value of this suggest that a system of intervention and care would almost certainly demonstrate its profound potential benefits for the chronically afflicted, as it did for me. “Group therapy” or a “shared cathartic outlet” could and should become a standard protocol whenever possible, in the care of all such patients, and might very well be of value for certain clinically diagnosed mental conditions.

Largely from personal experience living with diabetes and through my own observations of diabetic children and adults over the past 10 years, supplementary treatment should be provided to newly diagnosed type 1 diabetics in addition to the current regimen. A form of peer group therapy, all of whom have been given a type 1 diabetes diagnosis, could provide some relief to the psychological manifestations that the management of the disease brings with it. Furthermore, I hope that one day this form of therapy can be applied to a number of other chronic illnesses.

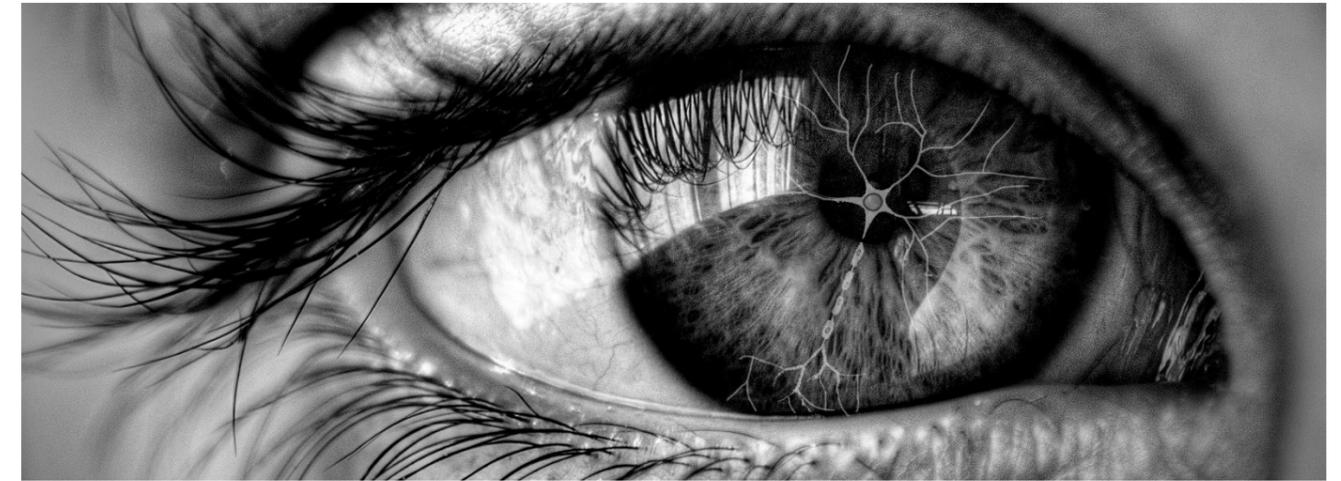
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The Lens

Joshua Hillman

Sackler School of Medicine, Tel Aviv University, Tel Aviv



Karen Arane: *i-nervate*

If you asked me what a lens is, I would not know how to answer. What type of lens are you asking about? The lens of an old pair of binoculars, the one on your iPhone camera, or of a magnifying glass you used to play detective with when you were little? As a medical student, when I think about the lens I am struck most by the anatomical lens. With her biconcavity, she plays gate keeper to images, exerting her presence as the primary processor of light. She is the first to decide how to refract the incoming image, soon to be delivered as pure sensory afferent signals through the optic nerve en route to the occipital cortex.

When I remove my white coat, my concept of a lens changes with it. The idea of a lens morphs into an abstract entity—a vantage point through which I view the world. A collective consciousness of the people I've encountered, places I've seen, and times I've contemplated what it is that I think and why I think it. For me, mentors have always played an integral role in helping me chisel away at shaping that consciousness. One such mentor, Dr. Norman Adler, passed away earlier in the year and I'd like to share a few thoughts about how he has helped me as a medical student.

Dr. Adler was my professor at Yeshiva University under whom I studied Psychobiology and Neuropsychology, and my faculty advisor for a group of students who were interested in learning about Neuroscience. We created our own *Neuroscience Society* not too dissimilar from the students in *Dead Poets Society*, rallying around Adler like the students of Welton Academy rallied around John Keating. Adler reveled in our reveling by helping us host events and inviting his colleagues to give intimate lectures to interested students and faculty. Scientists, doctors, and religious thinkers such as Dr. Donald Pfaff, Dr. Sam Sacher, Dr. Jonathan Berger and Rabbi Dr. Abraham Twersky were just a few of the invitees. As a neuroscientist, Dr. Adler was interested in exposing us to a wide breadth of science from neuro-economics, psychology of religion and cognitive neuroscience. Adler recognized that each student had their own calling and that we each had to find our own way based on what we found captivating, so he invited a broad range of speakers. This was one of his greatest attributes as my mentor—he was never trying to make clones of himself, rather he sought to help each individual to evolve.

As a student, listening to him describe how he felt about neuroscience powerfully impacted my personal approach to my studies. Adler would poignantly describe neuroscience as the most unique of the sciences, not to say that it was superior, but that it was different. It was not like cell biology which looks at the nature of different cell types throughout the body, or like microbiology which looks at the bacteria, viruses, fungi and parasites that share in inhabiting the earth with us. Nor was it like biochemistry which looks at the enzymes and molecules responsible for mechanisms of metabolism and cell function that give rise to greater structure. Neuroscience was unique because it was *interdisciplinary*. A culmination of blood vessels and brain tissue responsible for innervating every aspect of the body, every organ, every fiber, the stomach, the heart, sympathetic and parasympathetic, somatic and autonomic, nicotinic and muscarinic. The brain is responsible for balance and memory and hormonal regulation, and temperature and sleep. It is an all encompassing organ and field of pursuit. In Adler's realm, to be a neuroscientist was not to know the brain, but to know all aspects of the brain—the embryology, physiology, histology, biochemistry, epidemiology, pathology, pharmacology, organic and inorganic chemistry, physics, and calculus. Looking back on the first time he articulated that thought to me, I now envision the scene in Margaret Edson's *Wit*, when Dr. E.M. Ashford, great scholar of John Donne's holy sonnets criticizes a young Olivia Bearing for failing to use the Gardner Edition of the text—"This is metaphysical poetry, not the modern novel. The standards of scholarship and critical reading... which one would apply to any other text are simply insufficient. ***The effort must be total for the results to be meaningful.***" Witnessing the level of excellence and academic scholarship he held himself to allowed us as students to set our own lofty goals and ambitions, again shaping our own outlook on just how much we could expect of ourselves to know and accomplish.

While Adler taught me a lot academically, the most valuable thing I learned from him was to ask better questions and think outside the box. One of my favorite examples was the time our homework assignment was to go outside and count how many windows there were on a certain building on campus. When we came to class with our answers the next day, everyone was certain in their count, and no two peoples' counts were the same. Adler loved these types of exercises because

they cleverly demonstrated two things: 1) people look at the world differently, and 2) if you don't define your terms (what is a window), then you can't begin having a conversation.

Adler always reminded me of Antoine de Saint-Exupéry's little prince—perpetually curious and continuously striving. This was the ultimate blessing in a mentor because everything anyone said had substance. There is a famous saying in the Talmud that says, "Despise no man and deem nothing impossible for there is no man who does not have his time and no thing that does not have its place." Adler was the master of this, respecting everyone's opinions and learning something from everyone.

While Adler held himself to high standards and took academic scholarship very seriously, he also carried himself with a sense of congeniality. In my final class with Adler in my junior year of college, Adler assigned me another assignment that seemed to have nothing to do with the class he was teaching. I was to prepare John Keats' piece *Ode on a Grecian Urn*. In class that day he went line by line through the poem, dissecting its sentences and phrases and words and letters and punctuation. Only later did it occur to me that this poem had everything to do with neuroscience because it had everything to do with the outlook on life Adler was trying to convey to us—that everything is interconnected. The humanities, he sought to demonstrate, was not individual pursuits of philosophy, art, science, music and history but again a collective understanding at the crossroads of them all. I'll never forget how he found himself on the verge of joyful tears as he recited the final lines:

When old age shall this generation waste,

Though shalt remain, in midst of other woe

Than ours, a friend to man, to whom thou say'st,

"Beauty is truth, truth beauty,—that is all

Ye know on earth, and all ye need to know."

An Undergraduate Reflection of Participating in the Autism and Med App Jams at UC Irvine

Joseph N Mehrabi

Sackler School of Medicine, Tel Aviv University, Tel Aviv

Abstract

App Jams are increasing in popularity as a way to stimulate innovation and creativity in the practice of app development directed at solving a particular problem. They are two-week long competitions where teams of about 5-6 students must collaborate to develop a practical, relevant, and competitive software application pertaining to the theme of the competition. The following discussion focuses on my participation in two App Jam competitions from the perspective of an aspiring medical student at UC Irvine. Both competitions were medically themed; Autism App Jam was a competition that directed teams to develop apps for patients with Autism, and Med App Jam focused more on apps for the general practice of medicine. I am going to reflect on my experiences with the App Jams and make a case for why it is important for similar events to be held at other medical programs around the globe.

What is an App Jam?

An app jam is similar to what is known as a hackathon, where participants compete for a set period of time in teams to develop an app or solve a problem. A hackathon is an intense competition that presents teams with a single, designated problem and gives them the opportunity to write code or develop software to solve such a problem in the span of a weekend or 2-3 days [1]. Awards are given to teams that either finish the fastest or finish with the best software.

App jams are two-week long competitions where teams are encouraged to think creatively and to develop software applications relating to a theme [2,3]. Each team develops their own application

which varies from team to team based on the problem that they wish to solve related to the theme. In the UC Irvine Med App Jam that is held annually in the Fall, teams are formulated from students at the UC Irvine School of Medicine and the Donald Bren School of Computer Science to collaborate and develop mobile health applications for use by clinicians and patients. Medical students are traditionally designated to help formulate ideas for the computer science students to implement. The UC Irvine Autism App Jam, which was last held in 2015, recruited any student regardless of area of study for the development of a mobile applications directed toward helping patients with autism. The UC Irvine Med App Jam was a more organized event that had the most lasting impression, and it will be the focus of my reflection.

Why did I participate?

I had always been interested in studying and practicing medicine, yet I took on a major in computer science to learn something quite practical and different and separate myself from other applicants. It was not until late in my second year of undergrad that I began to think that I should combine the two disciplines and try to develop technology for medicine. Aside from working in a radiology research lab, the Autism and Med App Jams at UC Irvine were the conduits to do just that. They presented to me the opportunity to explore and apply my skills in software engineering in the context of medicine, however I was not great at writing code or developing software, so naturally I was apprehensive about participating. Nevertheless, I decided to challenge myself.

In the Spring, I participated in Autism App Jam. It was a rewarding experience to work with others to develop a tangible product as part of Autism App Jam; we developed a simple tap-the-moving-dots game for

Android, called DotDotDot, that would help autistic patients develop their hand-eye coordination. This first competition helped me find my niche in the software engineering process, applying my project management skills and design prowess even though I could barely code. I helped craft the app idea, design wireframe mockups (drafts of the user interface), compose the promotional video, assemble the poster, and keep our project on track to finish on time; I was the project manager. I embraced that role and wanted to bring that role to fruition in the Med App Jam.

The Med App Jam

The competition began with a sign-up process right before the opening ceremony, and I was assigned to a team with two 2nd-year medical students and three

computer science students, one of which named himself the head developer because he was the most experienced. We were pitted against 14 other teams to develop the best mobile iOS application with the theme of improving communication between the doctor and the patient. After about a day and half, the medical students came up with the idea of using the iPhone's internal sensors to measure and quantify hand tremors for patients with Parkinson's Disease. The app that we used as a model for similar function was the LiftPulse app on iPhone. For reference, the company and software was purchased by Google in 2015.

I tasked myself with the same responsibilities as those of the Autism App Jam: drawing mockups for the user interface, writing the obligatory daily



Figure 1: The SWOT analysis that depicts the strengths, weaknesses, opportunities, and threats of developing a product (our app) in the context of entering a business market. This was one major component of the Business Case Analysis.

blog, assembling the poster, writing the business case analysis, the SWOT analysis (shown in Figure 1), and requirements specification, and assigning deadlines for certain parts of the project. The business case analysis was my main task which involved an introduction to the app including its functions, the problems it solves, and how it can impact the market. I communicated with every single member of our team all throughout the competition to make sure the project was on track to finish. I worked with our head developer to help him understand how hand tremors would impact the movement of the phone's gyroscope and accelerometer and how that movement should be visualized. The other two developers were assigned the task of implementing a medication reminder component to the project, which the medical students felt was necessary for patients with neurodegenerative diseases such as Parkinson's Disease. I had even reached out to neurologists with one of the medical students to determine if a mobile application like this would be useful; we received overwhelmingly positive feedback. The medical students were quite busy with their studies, but they checked in every few days to witness the manifestation of their idea.

Over the course of the project, I found myself taking on another kind of role. I understood a little bit about Parkinson's Disease and neurodegenerative disorders from my own research and personal experience in the hospital, and I was familiar with the process and demands of software engineering for an app jam. I

found myself to be a communicative liaison between the computer science students and the medical students because I understood both fields and needed to bridge the knowledge and communication gap between the medical and computer science students. Each area of study has its own jargon and method of understanding that must be effectively communicated. From the perspective of a computer scientist, the medical students had relatively unrealistic expectations for the implementation of the software in two-weeks, and the computer scientists, namely the head developer because he was working on the main functionality of the app, had a difficult time comprehending how we wanted the data of hand tremors visualized. I assisted by communicating the necessary software engineering steps to the medical students and explaining to the head developer Parkinson's Disease and essential hand tremors in non-medical, layman's terms and how they could be measured.

The algorithm for the tremor quantification was optimized 3-4 times, adjusting the accuracy of the tremor detection and increasing the number of axes in which the device movements were recorded. The data presentation originally displayed bar graph depicting the change in amplitude with respect to frequency (Figure 2). Two days before the closing ceremony, the medical students later suggested to display the data as a line graph conveying the change in relative amplitude over time, which we deemed

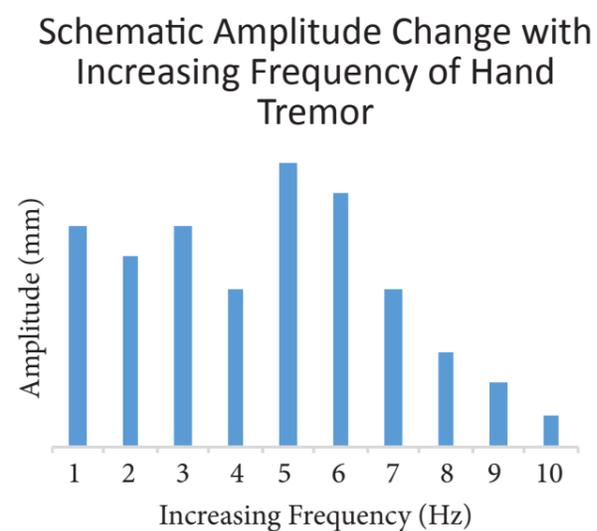


Figure 2: An example of the original depiction of the device tremor data on a bar graph conveying amplitude with respect to frequency.

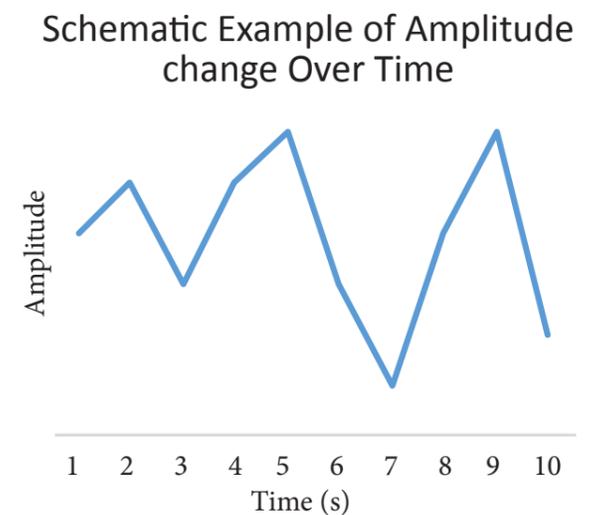


Figure 3: An example of the updated depiction of the tremor data on a line graph conveying the change in amplitude with respect to time. This was deemed a more intuitive representation of the data.

more intuitive for the judges (Figure 3). I completed the poster the morning of the closing ceremony, the developers combined their different components into one app later that day. The medical students took on the responsibility of editing the demonstration video for the app, which we later called Panda, and uploaded it to YouTube that day as well [4]. Everything was finished very close to the deadline, which I noticed was the nature of this kind of competition.

At the closing ceremony, we presented and demonstrated the app to the judges, medical professionals, and other competitors. It was an remarkable feeling to witness our idea become a tangible and usable product. We received praise from the judges, clinicians, and professors from the medical school, making a strenuous two-week effort quite valuable. In the end, our app, Panda, was awarded the Most Innovative Application of the competition, and one of the most rewarding two-weeks of my undergraduate education was swiftly over.

Personal Reflection

Both competitions, the Autism and Med App Jams, were somewhat similar. Figure 4 compares the two competitions. The Med App Jam was a much more in-depth competition that demanded more from the participants: a poster, video, business case analysis, and daily blog updates. A working application, video, and poster were all that was needed for presentation at the Autism App Jam. Nevertheless, both were two-week competitions that involved working in teams to develop mobile applications. In both competitions, I took on the role of project manager to make up for my poor coding skills.

Participating in App Jams was a unique and priceless experience. It added value to my education in software engineering and exposed my skills in project management, writing, and communication. I also gained a much better perspective on the use of technology in a medical setting. Both competitions led to development of two fully functional applications that I could add to my portfolio. DotDotDot did not win any awards at the Autism App Jam, yet Panda was awarded the prize for the most innovative mobile application in the Med App Jam. Both competitions, whether they resulted in an award were difficult yet fulfilling because I applied my developing software engineering skills in a way other than coding to create

tangible apps that could potentially make a difference in the field of medicine.

There were at least three things that I learned from participating in the App Jams. (1) There is a role for everyone. I was not a good coder, and I hardly participated in the coding at all, yet I made myself useful by tackling all the side projects such as the writing the app documentation, composing the poster, helping to film the video, designing the user interface, and facilitating communication between the entities of the team. Of course, a good team requires competent coders, and medical students are necessary for coming up with medically relevant ideas for the project, but I was a good example of someone who was an expert at neither yet I was crucial for the project. (2) An App Jam is a powerful tool to facilitate innovation and interprofessional collaboration. The most lauded accomplishments are achieved when professionals of different disciplines collaborate. The App Jam Model exposed students of different backgrounds to the utility of their skills in other academic disciplines, which emulates the working world. (3) The creativity of each team will be tested, which leads to a richer competition. Fifteen teams competed in each competition, which bred thirty different apps all trying to solve different problems in the field of medicine and autism rehabilitation. In the span of two-weeks per competition, one could say the field of medical technology had been greatly advanced.

The App Jams at UC Irvine provided students with the opportunity to enhance their education and skillset as well as forge a path for potential business ventures, clinical research studies, and career development. My team and I had become more familiar with the app creation process and how difficult, yet rewarding it might be. Adding software projects to a student's portfolio is critical to the advancement of a career in software engineering, and it potentially separates medical students from the crowd when they attempt to apply to specialty training programs after medical school. In my case, my participation helped me develop my skills in software engineering to make progress in the field of medicine and ultimately reinforced my career choice.

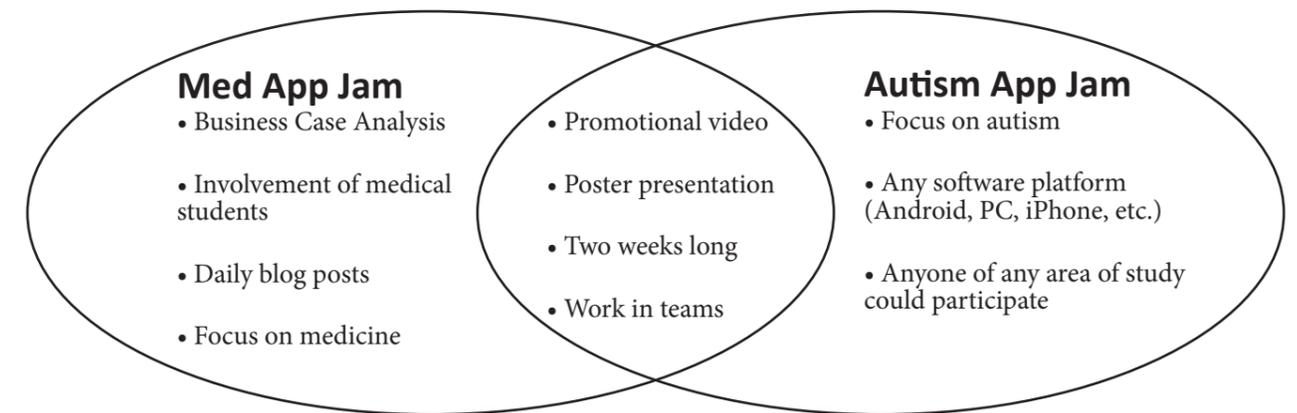


Figure 4: A comparison and contrast of both Med and Autism App Jams. Both had similarities but enough differences to keep both competitions interesting.

Moving Forward

As an aspiring medical student, I did my best to embrace the practical knowledge I was earning by studying the basics of Autism and Parkinson's Disease. Because of my interest in attending medical school, learning medicine was one of my top priorities with the participation in the competitions. I tried to spend plenty of time with the medical students on my Med App Jam team and speak with esteemed neurologists at the project symposium and award ceremony of the Autism App Jam. I wanted to learn more about medical school and the practice of medicine, namely the involvement of technology in medicine. I constantly asked how could the practice of medicine be improved by technology, and what can I do to help it.

Now as a medical student, I approach my studies with the same question. I think each medical professional should be asking that question, which is one reason I encourage the establishment of Med App Jams at all institutions of medical education around the world. I would embrace the opportunity to participate in another App Jam, but this time I would like to contribute to the other side of the competition, facilitating ideas for innovation in the space of medical technology and even organizing the competition itself at my institution. At UC Irvine, it spurred computer science students like me to apply their knowledge and make something tangible that could impact the world, and medical students were able to tap into their creativity and expand their impact of their knowledge of medicine beyond the hospital and potentially

into the palms of patients around the world. It is not understatement to say that an App Jam catalyzes innovation.

Technology is becoming more ubiquitous in health care settings, and it will become a requirement for medical professionals to have a solid understanding of the language of technology in order to optimize the care for their patients. Medical schools are tasked with adding this to their curriculum in one way or another, and the establishment of a Med App Jam could be a great start to addressing this issue.

Useful Links

<http://www.medappjam.com/wp-content/uploads/2016/11/MedAppJam2016InformationalPacketRevised-1.pdf>

<http://www.medappjam.com/press/>

<http://2015.autismappjam.com/>

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“You’re Fat and Hairy,” A Case Series on Frontotemporal Dementia

Alyssa Caplan, Elana Cohn, Alison Dallich

Sackler School of Medicine, Tel Aviv University, Tel Aviv

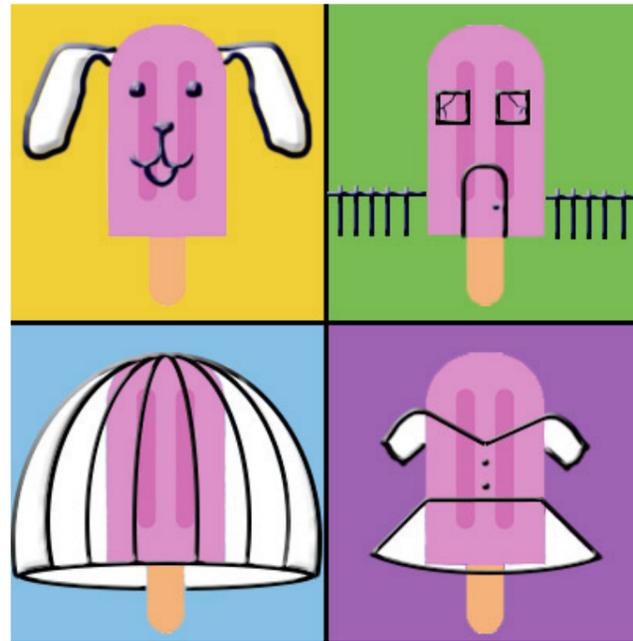
Introduction

Frontotemporal dementias (FTD) are a group of neurodegenerative diseases defined by progressive changes in personality and social behavior and, in some variants, a decline in speech, marked by visible atrophy of the frontal and/or temporal lobes on MRI. FTD is one of the more common causes of early-onset dementia, with a similar incidence to Alzheimer’s in adults ages 45-64. The average age of symptom onset is in the late fifties, and it is rarely diagnosed before 40 or after 75 years of age (1). FTD syndromes share the following core diagnostic features characterized by the Neary Criteria: insidious onset and gradual progression, early decline in social interpersonal conduct, early impairment in regulation of personal conduct, early emotional blunting and early loss of insight (2).

FTD can be classified into three classic forms: behavioral variant, semantic variant, and progressive non-fluent aphasia. This article aims to further elucidate the three classic presentations of FTD through a series of case studies. These subjects were seen at the University of California San Francisco, Memory and Aging Center, given a clinical diagnosis of FTD and enrolled in a large research study. As part of this study, they underwent a neurological exam with a neurologist and a neuropsychological assessment with a trained neuropsychologist. MRI images were acquired on a 1.5-T Siemens Magnetom VISION system.

Case Study 1: Behavioral Variant FTD

Mr. X, a previously healthy, right-handed 66-year-old man, presents to the clinic due to progressive changes in behavior and personality. At baseline, he is described by his wife as “reliable, quiet, dignified and intelligent.” His family first became concerned



Karen Arane: *Fat & Hairy*

when he began to develop an uncharacteristic ease for speaking to strangers, often initiating conversations and providing unsolicited advice. Shortly after, he began making inappropriate comments in public, loudly calling people “fat” or “hairy.” His inappropriate comments were exacerbated in structured and ritualized situations, such as telling a TSA agent that he would “shoot them” while going through security at the airport. From a quiet baseline, he had become loud and impulsive. He was also noted to have a severe decline in empathy, no longer showing any concern for what his wife was saying. Mr. X’s diet changed dramatically, including eating large quantities of sweets and adding syrup to all desserts. On neurological testing he was noted by the examiner to be impulsive, apathetic, stimulus bound, and distractible. He required frequent prompting throughout. His MRI showed severe atrophy (R>L) of

the frontal and temporal lobes, including ventral and dorsal regions of the pre-frontal cortex, confirming his diagnosis and explaining his significant behavioral and personality changes (Figure 1).

The most common form of FTD is the behavioral variant (bvFTD). Patients with bvFTD show a significant and persistent change in their personality and behavior from their pre-disease state (3). They may become socially uninhibited and apathetic and may be unaware of their changed behavior and the distress it may be causing their family members (4). They also may develop hyperorality (consuming excessive amounts of food too quickly) as well as compulsive behaviors that cause a very rigid personality state (5). A meta-analysis of imaging studies found that frontomedian networks, which mediate impulse and behavioral control, are most affected in bvFTD along with the right anterior insula and medial thalamus, which regulate emotional awareness (6).

Key Point: Frontotemporal Dementia and Pharmacology

Antidepressants or selective serotonin reuptake inhibitors (SSRIs) may help control the loss of inhibitions, overeating and compulsive behaviors seen in some people. The mechanism by which these medications (i.e., fluoxetine, sertraline, escitalopram, and citalopram) work is by preventing serotonin (5-HT) reuptake and usually take 4-8 weeks to have an effect with possible side effects of GI distress and sexual dysfunction.

Reference:

Lee SE, Miller BL Frontotemporal dementia: Treatment. UpToDate 2017. Retrieved from <https://www.uptodate.com/contents/frontotemporal-dementia-treatment>.

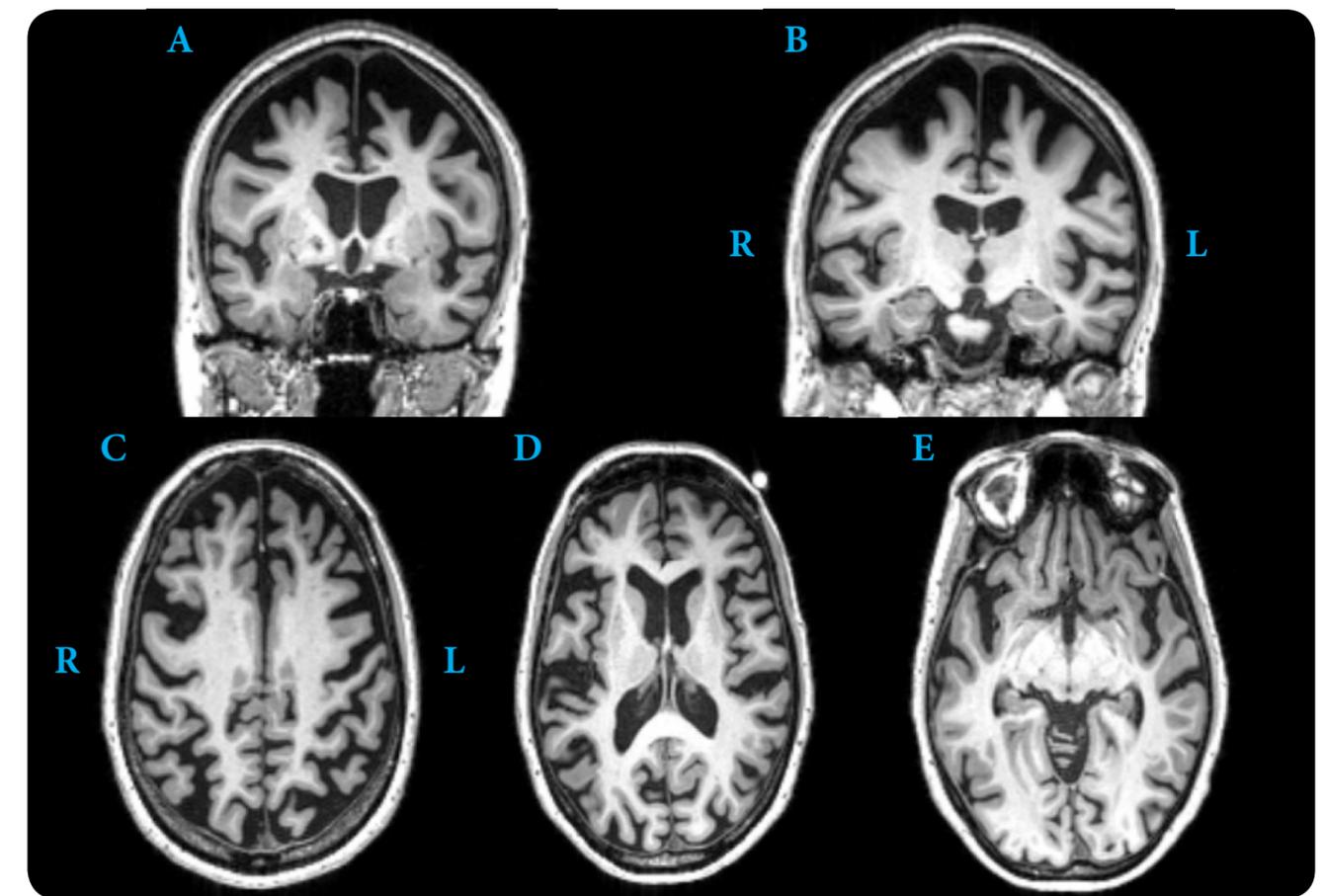


Figure 1: Case 1 brain MRI of Mr. X showing atrophy in the coronal plane (A, B) and axial plane (C, D, E)

Case Study 2: Semantic Variant

Mrs. Y is a 69-year-old, right-handed former teacher who presents to the clinic due to changes in language and behavior. At baseline, Mrs. Y was described as “intense” and “demanding.” Currently, Mrs. Y exhibits severe difficulties with language with some inappropriate behavior. Her language has declined severely. She uses the term “icepops” as a substitute for many words. When she speaks, she says only a few phrases that are not always appropriate to the situation. She can still comprehend some commands, but even when told simple things like “go to desk,” she will not know what a desk is. On cognitive testing she scored 0/15 on the Boston Naming Test, a test where participants are shown pictures of items and asked to name them. Her husband describes that she will want to grab strangers’ hands and kiss them. She is also described as acting “childlike” and will frequently tap her foot impatiently. Her MRI shows significant atrophy in the bilateral temporal lobes with anterior and lateral portions more affected than medial portions, and left

greater than right, which helps to explain her language manifestations. There is also mild medial ventral frontal and parietal atrophy seen (Figure 2).

Semantic variant FTD differs from bvFTD in that its core features are not based in behavioral changes but in language loss, specifically impaired single word comprehension while maintaining fluency. Early on, word-finding difficulty is limited to low frequency items, words and objects they don’t use regularly (7). As the disease progresses, the difficulty assigning meaning to words becomes more pervasive, and they lose both the ability to recall everyday words as well as the concept behind the word. In patients where the right temporal lobe is more affected, remembering faces of friends and familiar people is more troublesome (1). Similar to bvFTD, these patients have significant difficulty understanding the emotions of others and lose empathy early on in their disease (8). MRI reveals bilateral atrophy of the anterior temporal lobes responsive for semantic processing, with the left more affected than the right, as the left

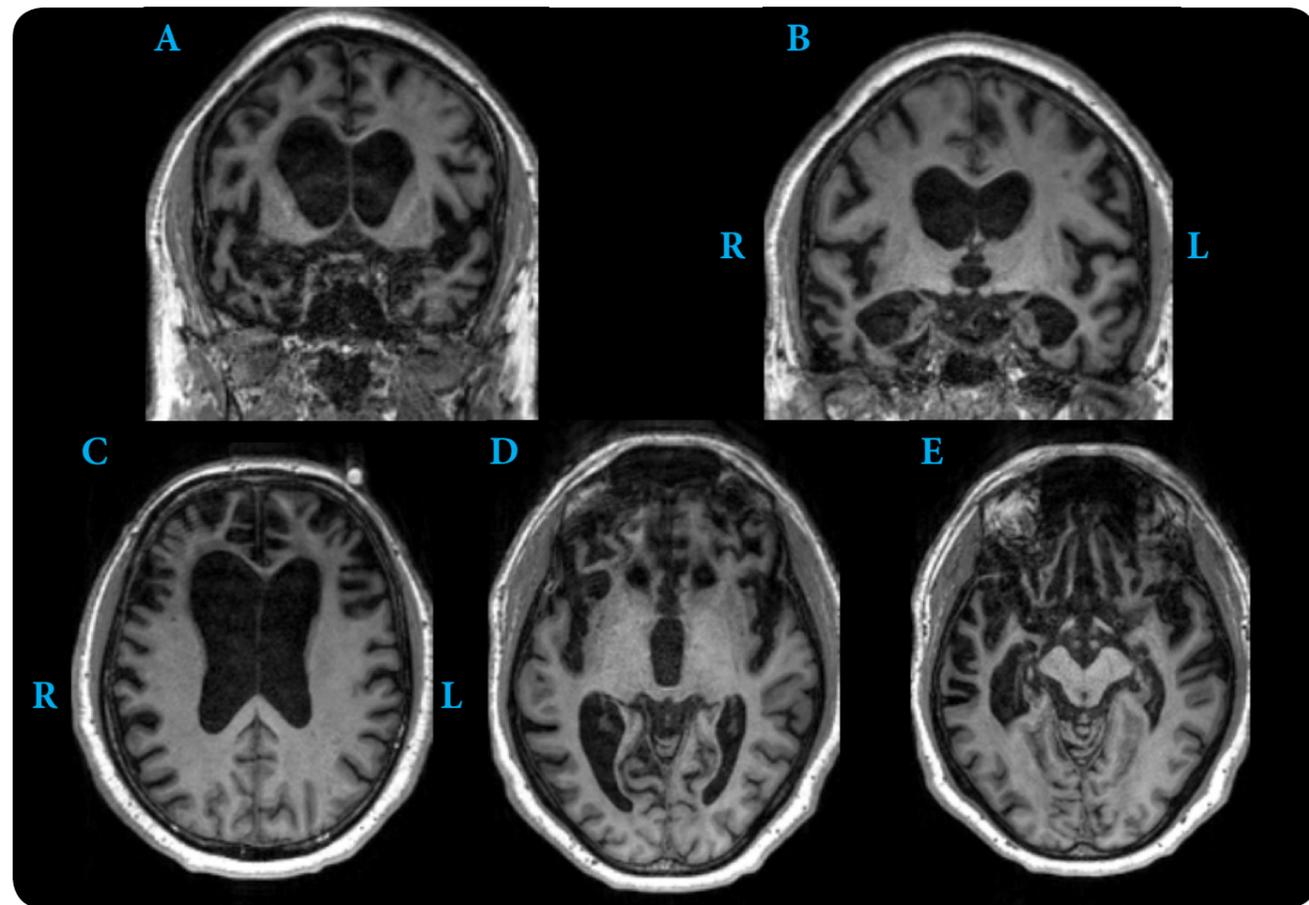


Figure 2: Case 2 brain MRI of Mrs. Y showing atrophy in the coronal plane (A, B) and axial plane (C, D, E.)

cortex is more greatly involved with language than the right. The atrophy spreads to the posterior temporal and/or inferior frontal lobes as the disease progresses, which is significant due to its integral role in language comprehension (9).

Case Study 3: Progressive Non-Fluent Aphasia

Mrs. Z is a 72-year-old woman who presents to the clinic because of concerns related to progressive language issues. She first noticed language changes four years earlier when she began to have difficulty pronouncing words and getting words out, although her family did not notice these changes. A year later, her family began to notice language changes including problems with word finding and pronunciation. Currently, Mrs. Z’s speech is slow and intensely effortful. She is deliberate in pronouncing each syllable, often breaking up words into component syllables. She has many distortions in her speech such as “wroot” for “wrote.” Her speech is agrammatic, dropping pronouns and verbs at times.

She also has some difficulty understanding people, especially when they speak in longer sentences. Other than language issues, she and her husband note no additional changes. She is still good at organizing and planning, shops for all of the groceries and takes care of her home, and volunteers a few days a week. On cognitive testing, she named 15/15 items correctly on the Boston Naming Test. Her MRI showed prominent posterior and dorsal atrophy with widened left sylvian fissure, bilateral supplemental motor area (SMA) atrophy, and anterior thinning of the corpus callosum (Figure 3). The left sylvian fissure contains the major areas for language comprehension, recall, and articulation, which helps to interpret her clinical presentation.

The distinguishing feature of the final variant, progressive non-fluent aphasia, is articulatory difficulty with effortful, halting speech, and numerous linguistic errors (10). In contrast to the semantic variant, these patients typically retain their single word comprehension but have difficulty understanding long

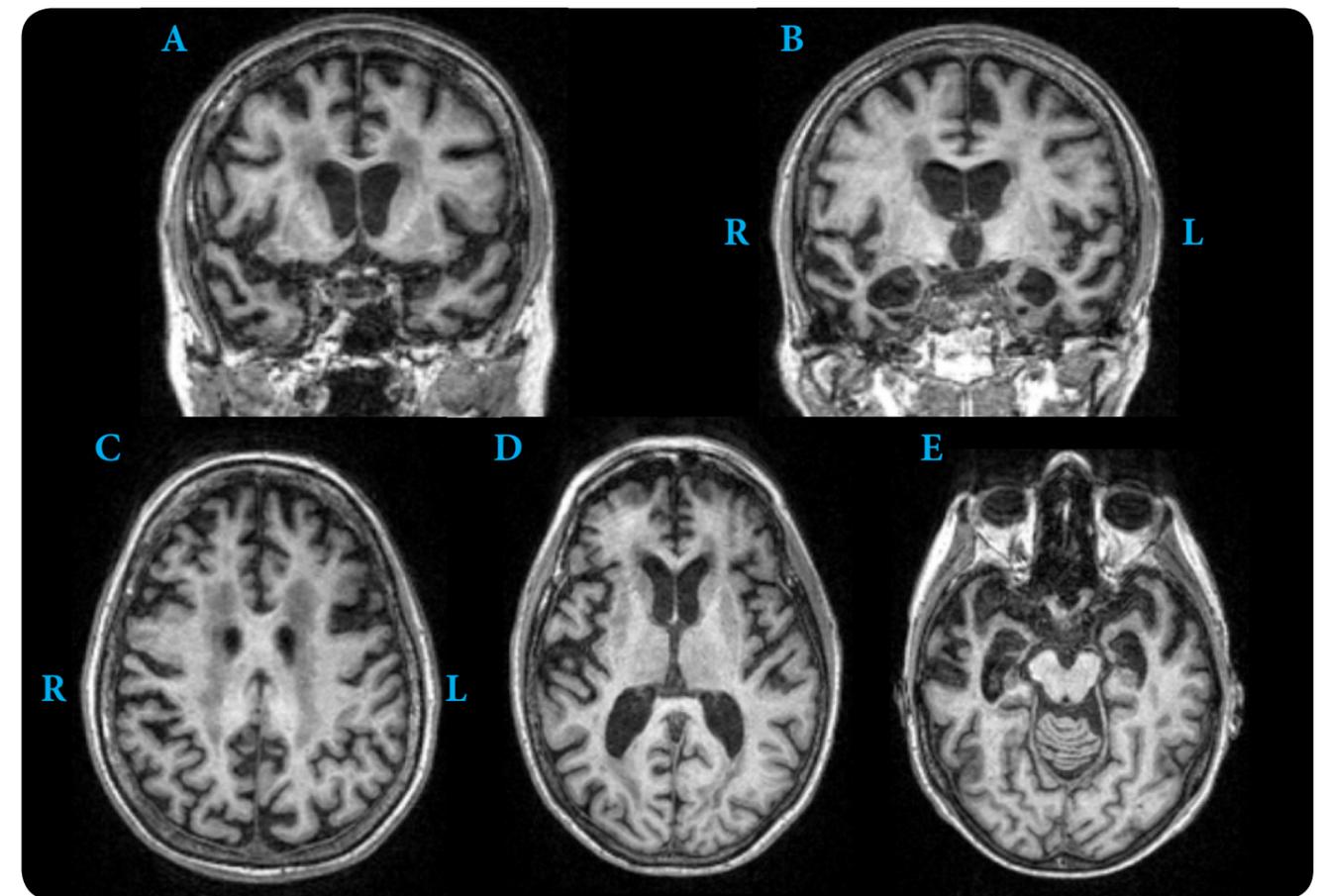


Figure 3: Case 3 brain MRI of Mrs. Z showing atrophy in the coronal plane (A, B) and axial plane (C, D, E.)

sentences, particularly those with complex sentence structure (11). In the non-fluent variant, deficits may be restricted to language function for several years before progressing to a more widespread dementia (12). An imaging-supported diagnosis will include atrophy of the left posterior frontal-insular region on MRI, specifically responsible for language articulation (8).

It is important to keep FTD on the differential diagnosis when examining patients with behavioral or language changes as they are often mistaken for psychiatric conditions or other forms of dementia. As with other types of dementia, over time each variant of FTD progresses to affect overlapping areas of the brain and eventually progresses to an inability to communicate and independently complete activities of daily living.

Current Research in FTD

Current research in the field of dementia is investigating the genetics of these diseases as well as the molecular pathology and various biomarkers, so as to hopefully develop targeted treatments. For example, a clinical trial at the University of California San Francisco is using a histone deacetylase inhibitor to treat FTD patients with a specific gene mutation (13).

Symptom management is the main goal of most clinical trials. A phase two clinical trial actively recruiting bvFTD patients is looking at the effects of intranasal oxytocin on neural activity and emotion, hoping to target the loss of emotion and empathy (14). A 2015 case study presents a bvFTD patient showing reduced negative behavior symptoms and an improvement in motor symptoms and activities of daily living following four months of treatment with methylene blue (15). A phase two study not yet recruiting would test low-dose lithium, used to treat symptoms of bipolar disorder, to decrease behavioral symptoms, while potentially inhibiting a protein involved with FTD (16). While there is currently no definitive treatment for FTD, there are many promising and exciting therapies in development and in various clinical trial stages.

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Inferior Vena Cava Filter Thrombosis and Retrieval: A Literature Review of IVC Filter Implications and Their Removal

Ezra Schrem

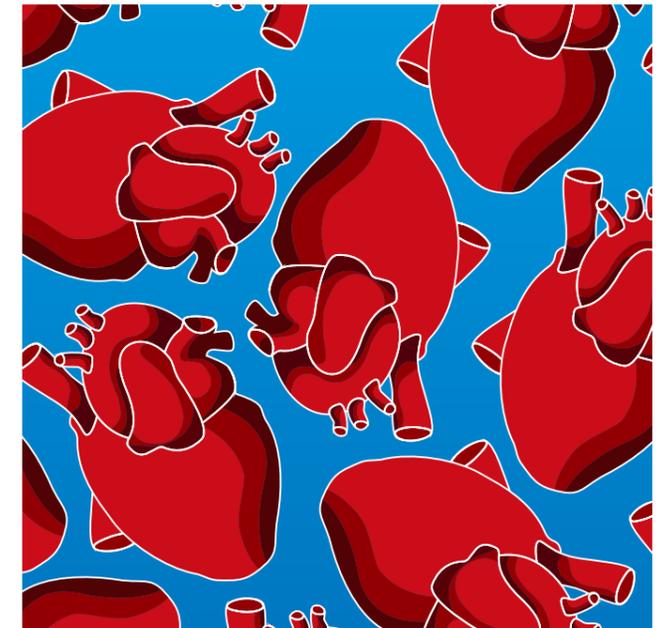
Sackler School of Medicine, Tel Aviv University, Tel Aviv

Abstract

Inferior vena cava filters are used in healthcare settings today in patients to prevent the migration of blood clots from the lower extremities, or elsewhere in the body, to the pulmonary arteries. This is to prevent a type of venous thromboembolism (VTE) known as a pulmonary embolism (PE) from forming. PE can be life threatening if not treated correctly. Although the IVC filters help prevent PE, the filters themselves can induce thrombosis and may result in occlusion of the IVC. The IVC filters can also cause other complications such as deep venous thrombosis (DVT) of the lower extremity and promote unnecessary long-term anticoagulation (AC) therapy. Therefore, IVC filters should be retrieved as soon as the indications to have one in place are no longer applicable to the patient, and the patient is no longer at high risk of developing PE. Retrieval must also be done in a timely manner; the longer an IVC filter is in place, the more difficult it is to remove. This paper aims to provide a review of prior research that deals with the thrombosis of IVC filters, its possible treatment, filter removal, and the importance of follow-ups.

Introduction

Inferior vena cava (IVC) filters are small devices placed into the IVC just below the junction of the IVC and the lowest renal vein (1). They serve to prevent the migration of a blood clot from the lower extremities, or elsewhere in the body, to the pulmonary arteries, which is where they can lodge and cause a type of venous thromboembolism (VTE) known as a pulmonary embolism (PE). The filters are generally not used as the first line of treatment in



Micah Belzberg: *Hearts*

preventing a PE from occurring, but rather are used in patients that are susceptible to complications arising from the use of anticoagulants, or blood thinners, such as gastrointestinal bleeding; anticoagulants are generally the first line of treatment (2). The IVC filters themselves, however, can cause thrombotic activity. Therefore, their retrieval is suggested. Many patients, however, fail to have their IVC filters removed due to the lack of appropriate follow up with their healthcare providers. Developing simple plans to help monitor IVC filters, patients can significantly assist in morbidity and mortality reduction. This signifies the opportunity for crucial improvements in clinical care that can lead to more effective and efficient prevention, diagnosis, and treatment of IVC filter thrombosis, which can ultimately help improve the quality of healthcare today.

Key Point: What is a Catheter-Directed Thrombolysis?

This procedure involves the threading of a wire into the site of the clot, and direct delivery of thrombolytic drugs. This procedure requires lower doses of drugs than systemic therapy, and thus reduces overall risk of bleeding.

Reference: Sista AK, Kearon C. Catheter-Directed Thrombolysis for Pulmonary Embolism: Where Do We Stand? *JACC Cardiovascular Interventions*. 2015; 8(10).

Key Point: What is a Coronary Angioplasty?

Coronary angioplasty, also known as percutaneous coronary intervention, is used to maintain the patency of blood vessels with severe atherosclerosis. It involves the insertion of a balloon into the vessel of interest with subsequent widening of the artery. Often, a wire stent is placed to prevent future narrowing.

Reference: Mayo Clinic Staff. Coronary Angioplasty and Stents. Mayo Clinic. 2017. Retrieved from <http://www.mayoclinic.org/tests-procedures/coronary-angioplasty/home/ovc-20241582>.

Predisposing Factors of IVC Filter Thrombosis, and Management

The physical design of the filter can directly correlate with the risk of developing a thrombotic event of the filter (3). It has been shown that the greater the number of perforations in the filter, the higher the likelihood of the pathological condition (4). IVC filter thrombosis is not exclusively related to filter design, but also to patient underlying conditions including comorbidity, anticoagulant intolerance, and malignancy. Therefore, there is a dilemma due to the fact that contraindication to anticoagulants is among the most common reasons for filter placement in the first place, but this condition itself can create a predisposition to IVC filter thrombosis. In regards to management of the thrombosed IVC filter, the main lines of treatment are the use of catheter directed thrombolysis and adjunctive balloon angioplasty. There is little published data on endovascular treatment methods; however, these methods are technically feasible with great success.

Event Rates in IVC Filter Patients

It has thoroughly been found that patients with IVC filters installed are more likely to develop a lower extremity DVT and IVC thrombosis (5). The PREPIC study was conducted to analyze the effects of permanent IVC filters and VTE. In this study, there were two experimental groups: one with patients on anticoagulants (AC) and permanent IVCF and another with patients on AC without the filters. The study shows how in increased-risk patients with

proximal DVT, the initial benefit of PE prevention through IVCF is counterbalanced by the excess of DVT and IVCF thrombosis. In other words, although PE rates decreased in patients with IVCF in this study, DVT rates increased in patients of this same study group, and therefore mortality rates remained nearly the same between the patients with the filters and without the filters (21.6% vs 20.1%). These results are derived from patients that had a filter in place for 2 years. The study also demonstrated how the lower number of PE in the filter group is similar to the higher number of IVC thrombosis of the same group of patients. Additionally, it also clearly demonstrates how patients that had the filters in place for a longer period of time had higher rates of IVC filter thrombosis (9% for patients with the filters in for 2 years, and 16% for patients with the filters for 8 years) (6). Therefore, once patients are no longer considered high risk for developing PE, the IVC filters should be retrieved to prevent its thrombosis. Permanent filters should certainly not be used, in order that retrieval will be more successful. On a side note, it is worth mentioning that the data presented in the study described above only includes patients on AC therapy with and without permanent filters that are symptomatic for VTE. The study fails to include data on patients who were asymptomatic for any type of venous thrombotic activity.

Complications of IVC Filter Thrombosis

IVC filter thrombosis can give way to serious health complications (7). IVC filter thrombosis can range from small local clots to thrombi that could extend into the lower extremities and even completely occlude the IVC in its most severe form. The filter thrombosis can harm lower extremity venous return, which may lead to slowdown or complete stoppage of venous blood flow or static ulcers. The cause of IVC filter thrombosis may be due to emboli entrapment within the filter or in situ thrombosis because of device intrinsic thrombogenicity. In addition, the prevalence of retrievable filter thrombosis has been shown in a study to range from 0.6% to 8%, with an average of 2.8% (8). This rate of thrombosis is significantly lower than that of permanent filters. This study was a review of many other studies that have been previously conducted, and aggregated its results.

Importance of IVC Filter Removal

It is very important to remove an IVCF that is no longer necessary, as an IVCF can lead to many complications including a deep venous thrombosis (DVT) of the lower extremity, caval thrombosis, and unnecessary life-long anticoagulation (AC) therapy (9). The combined duration of treatment for a DVT/

Key Point: Pulmonary Embolism

A pulmonary embolism or PE refers to an obstruction in a pulmonary artery by a substance that has traveled from elsewhere in the body. As a result, there is a decrease in lung perfusion, leading to a decrease in blood oxygen saturation, which results in less oxygen available for the body to consume. Treatment initially involves anticoagulant therapy with heparin administration in a hospital setting followed by warfarin.

Reference: Thompson BT, Kabrhel C. Overview of acute pulmonary embolism in adults. *UpToDate* 2017. Retrieved from <https://www.uptodate.com/contents/overview-of-acute-pulmonary-embolism-in-adults>.

PE should be about 3-6 months with a combination of both AC and filter treatment modalities. After this time frame, the associated complications of the IVC filters outweigh its benefits and therefore the filters should be retrieved. Therefore, it is of great importance to follow up with an IVCF patient to ensure that a filter that is no longer critical to the patient can be removed early to prevent potential harmful effects such as IVC filter thrombosis. Filter retrieval rates need to be improved; through simply implementing a better system of monitoring IVCF patients, the medical community can prevent these patients from becoming lost to follow up.

IVC Filter Retrieval Rates

Although IVC thrombosis rates in retrievable IVC filters are quite low, retrieval (removal) is still highly recommended as its prognosis has devastating potential, and the longer the filters are in place, the more likely they are to cause thrombosis. Furthermore, other conditions such as filter-induced DVT can also warrant filter removal. Yet, according to the American Association for the Surgery of Trauma (AAST), only 22% of retrievable filters were removed in patients nationwide in 2007. Another study claimed that the international retrieval rate is 34% (8). These retrieval rates are simply not sufficient as the US Food and Drug Administration (FDA) generally recommends that all patients with temporary IVC filters installed have them removed within 25-54 days following insertion (10). The IVC filter removal procedure has a relatively high success rate, but the removal rate still remains quite low due to the lack of appropriate patient follow up.

A Canadian study monitored all IVC filter procedures at a healthcare institution in Toronto between January 2001 and July 2013 and found that IVC filter thrombosis is the most common complication, accounting for 61.4% of all long term IVC filter related complications (11). In addition, the study demonstrated that the retrieval rate of retrievable IVC filters was 41.6%, and the average time from insertion to removal was 76.4 days, which is longer than the recommended guidelines set forth by the FDA. This low retrieval rate may be due to the lack of appropriate patient follow up, as is evidenced by the fact that in this study only 16.3% of patients with documented filter insertions had been given discharge instructions

for filter retrieval or follow up. Methodic follow up is needed to help limit the development of IVC filter related complications.

Methodologies for Increasing Follow-Up and Retrieval

A comprehensive method designed to increase IVCF retrievals has been devised by a number of researchers (9). This method essentially consists of three components which include education, tracking, and having a dedicated person oversee the process. It is imperative that IVC filter patients, their families and friends, and healthcare providers are thoroughly informed of the implications of the filters and are able to determine when having a filter inserted is no longer necessary. It is essential that a patient understands the importance of IVCF retrieval when it is no longer required and realizes the importance of following up with their appropriate physician. Tracking refers to a system used to accurately keep tabs and records on those patients with filters in place. This could be done through the use of giving patients a wrist band or placing reminders in medical records. Other creative ways of tracking IVCF patients may also be of benefit. For example, it has been suggested that healthcare professionals place reminders on the reverse side of their business cards which tells the patient with a retrievable filter to call the office. Additionally, a study conducted at Parkland Medical Center in Dallas, Texas, followed trauma patients and non-trauma patients with IVC filters and found that trauma patients had much higher rates of IVCF retrieval compared to the non-trauma patients (55% vs 19%) (12). Here, the trauma patients were tracked and the non-trauma patients were not, suggesting the importance of follow up. A healthcare professional devoted to overseeing the whole process of IVC filter placement up until the time of its retrieval would also prove to be beneficial. Having dedicated staff can certainly help retrieval rates.

Another study was conducted to demonstrate the importance of following up and its effects on the rates of IVC filter retrieval (13). In this experiment, filter placements were studied over a 15-month period in a group of 33 patients. The study monitored the group twice: once before the implementation of a management strategy for IVC filter follow up and once after the strategy. Through the implementation of a formal plan for follow up, the number of filters

with no attempted retrieval and no consultation about retrieval decreased from 27% to 9%. Temporary IVC filters should not become unintentionally permanent because of patients overlooking the importance of a follow up.

Conclusion

IVC filters are given to patients as a prophylactic measure to help reduce the risk of life threatening pulmonary embolism formation. The filters, however, can induce thrombosis of both themselves and the surrounding area of the inferior vena cava. Therefore, once a patient is no longer considered at high risk for PE development, the filters should be promptly removed to prevent further harm to the patient. Many patients, unfortunately, fail to get their IVC filters removed solely because of the lack of appropriate follow up from their healthcare providers. Devising simple plans to help monitor IVC filter patients can go a long way in morbidity and mortality reduction and help save lives. In addition, despite prior research such as that presented, there is still a large knowledge gap in our understanding of IVC filter thrombosis pathogenesis, management, and IVC filter retrieval. This represents an opportunity for significant improvements in clinical care that can lead to more effective and efficient prevention, diagnosis, and treatment of IVC filter thrombosis, which can ultimately help improve the quality of healthcare today.

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Key Point: Precision Oncology and Genomic Data Commons (GDC):

In oncology field, various organizations, including the National Cancer Institute, have developed an information system called the NCI GDC to collect raw genomic data as well as diagnostic, histologic, and clinical outcome data from NCI-funded projects such as the Cancer Genome Atlas (TCGA) and the Therapeutically Applicable Research to Generate Effective Treatments (TARGET) program. One of the goals is that the GDC could recognize patients with rare molecular subtypes of cancer who could be contacted for potential participation in clinical trials appropriate for their cancer.

Reference: Grossman RL, Heath AP, Ferretti V, et al. Toward a Shared Vision for Cancer Genomic Data. *N Engl J Med* 2016; 375:1109-1112.

Social

Social data is the newest form of big data being incorporated into the healthcare field. It harnesses data from large web-based applications and personal user devices to gather medical trends and data (11). Data is congregated from online applications such as Google Trends, Twitter, and Facebook, as well as wearable devices such as fitness trackers, step counters and other self-reporting devices and sensors.

Similar to “omics data”, social data is subject to complications of data pollution and size. It has been estimated that 2.5 quintillion bytes of social data are created each day (11). It is a lower quality data because it is unstructured and the data producers are not vetted data analysts. Tweets, Facebook posts, and chatrooms express opinion but aren't necessarily factually accurate. Compared to data collected by researchers in individual studies and questionnaires, social big data may be viewed as unscientific and unreliable. Additionally, the data isn't inherently medically related and must be combed through and parsed to find relevant medical data.

Despite its drawbacks, social data represents the most attainable source of data in medicine. It is not restricted by healthcare privacy parameters like EMR and “omics” data, and, as the largest data of the three subcategories, is utilized in machine learning algorithms (11). Machine-learning algorithms find data cluster correlations and devise hypotheses. With larger data sets, machine algorithms generate more hypotheses and have higher confidence than with smaller data sets. Social data isn't inherently healthcare oriented, but it can be used to detect and identify medical trends. In 2004 early social data indexed from Chinese press reports predicted the acute respiratory syndrome epidemic (12). While the algorithm was unrefined, it showed that social data may potentially inform the medical world.

Applications of Big Data

Big data has the ability to improve quality of care, healthcare access, more efficiently distributing finite medical services while reducing costs in an overly expensive field. Big data achieves this by augmenting current prescreening protocols, reducing readmissions, optimizing spending, and reducing fraud. The emphasis on preventive medicine and the subsequent redistribution of other services results in improved patient satisfaction and increased patient access to medical services (3). We will discuss archetypal examples of big data implementations at different stages of a patient's time course and finish the discussion with the economic implications of big data integration into healthcare practice.

Patient prescreening can exceed its current utilization boundaries through incorporation of big data trend analysis and modeling. Using social data, a physician could analyze current medical web searches, stratifying for location, population, and age group, to begin forming an idea of possible questions or problems related to an incoming patient. A careful analysis of social data products led researchers to determine a correlation between a silicosis outbreak and the public's silicosis related searches and social media (12). They proposed using Google Trends, among other social media outlets, to aid physicians in proactively approaching patients during physical exams and meetings with questions or concerns they might have, thus improving quality and accuracy of

care. Familiarity with population clusters' concerns and risk factors will allow physicians to more quickly and accurately address a patient's concerns.

“Omic” data in combination with patient prescreening can also be used to increase accuracy and speed of patient diagnosis. Columbia University Medical Center utilizes big data advanced analytics to diagnose brain aneurysm injuries faster than current protocols allow (5). Utilizing physiological data linked to a patient's brain injuries allows physicians to diagnose serious brain complications 48 hours faster than previous diagnoses. This allows physicians to avoid serious complications and death in many of their aneurysm patients. Blue Shield of California is developing an integrated big data system collaboration between doctors, hospitals, and healthcare plans which delivers evidence-based diagnostic recommendations to physicians, improving diagnostic precision (1). The evidence based diagnostic recommendations are built from “omic” and healthcare big data sets analyzed for trends in diagnoses which can be applied to new patients. With this analysis information in hand, Blue Shield doctors will be able to more accurately and efficiently diagnose and treat patients in a shorter period of time, resulting in shorter hospital stays.

Eliminating monetary inefficiencies also contributes to optimized patient care. Earlier release, faster diagnoses, and elimination of service redundancies allow for an optimized redistribution of finite medical resources. In 2012, the Minnesota Department of Health conducted a study to analyze the state's hospital admissions, readmissions, and emergency room visits to determine if there were any “preventable events” (14). They utilized existing claims data in combination with big data analytics to determine that 1.3 million patient encounters costing approximately \$2 billion qualified as “preventable” hospital visits. Approximately two-thirds of the hospital visits may have been preventable if patients had been treated via primary care, been given more medical and hospital information, and/or if there had been better coordination between physicians, social services, and the patients' families. Beyond reducing costs, reduction of readmissions and hospital stays leads to a direct reduction in postoperative complications and comorbidities (15).

Eliminating fraud in the reimbursement system is an integral part of reducing healthcare costs. The National

Health Care Anti-Fraud Associated estimates that 3% of healthcare spending is lost to healthcare fraud (16). These numbers constitute a massive hemorrhaging of healthcare funds, increasing costs and lowering reimbursement pools. The Centers for Medicare and Medicaid Services (CMS), representing the largest healthcare provider in the United States, has over the past five years implemented big data fraud prevention services (FPS) to combat fraud, waste, and abuse (17). The big data FPS predictive algorithms have already saved the US government over \$1 billion and represent a return on investment of \$11.60 per federal tax dollar invested in the big data asset.

Challenges

Currently big data's main challenge is the lack of a user friendly architectural framework (9). All the promise and potential discussed above is hindered by lack of accessibility for the lay physician, nurse, or hospital administrator. Current programs require a deep understanding of machine learning and computer sciences. In the future, developers need to create large, accessible databanks that both retain patient data security while simultaneously creating an intuitive and standardized program that contains a full suite of analytical capabilities.

Another major challenge is working with strict privacy restrictions on medical data. HIPAA regulations include mainly “omic” and health data, although recently social data has been questioned as well (11, 18). HIPAA regulations currently make it difficult for hospitals to share data with each other. Hospitals need to focus on the transmission and sharing of de-identified data with other healthcare providers. Without shared data, smaller healthcare networks will have a harder time developing the care improving, cost saving big data tools. The US Government has realized big data's current restrictions, and have begun implementing programs like the NIH Big Data to Knowledge Program (BD2K) to support big data sharing and ease of access (11).

Conclusions

Big data represents a significantly impactful technology in the world of medicine. This article discussed the background of big data, several relevant applications, challenges, and opportunities for future use. Although in its infancy, big data has the capabilities to change

the healthcare arena through increased efficiency and decreased costs. If analysts are correct, big data represents a \$300 billion a year infusion of funds into the healthcare system. Implementing big data translates into direct healthcare solutions for various populations by reallocating limited medical services and improving healthcare outcomes for all.

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Circulating Tumor Cells in Pancreatic Cancer

David Ben Nun

Sackler School of Medicine, Tel Aviv University, Tel Aviv

Introduction

Pancreatic cancer has a very dismal prognosis with a 5-year survival rate of approximately 5% and a high rate of recurrence following attempted curative resection surgery (1). The vast majority of pancreatic cancers are adenocarcinomas of the ductal epithelium, and they represent the fourth most common cause of death in the US (2). Moreover, this trend shows no sign of abating. Pancreatic cancer is projected to be the second most common cause of death by 2030 (3).

The poor prognosis in cases of pancreatic cancer is associated with three key factors: delayed diagnosis, anatomic location and aggressive biology (4). Resection surgery remains the only curative option for patients diagnosed with pancreatic cancer. However, only 16% of patients typically present with Stage I pancreatic cancer in which the tumor growth is confined to the pancreas only (5). As a result, the overwhelming majority of patients present with tumors that have spread beyond the pancreas in which surgical resection is typically not an effective option.

Due to the anatomical location of the pancreas, performing a biopsy in order to offer a concrete diagnosis of pancreatic cancer is a challenge. In the past, biopsies have been obtained by aspiration of pancreatic or duodenal fluid via Endoscopic Retrograde Cholangiopancreatography (ERCP), mechanical exfoliation of pancreatic cells via brushing techniques as well as Endoscopic Ultrasonography via Fine Needle Aspiration (EUS-FNA) of the lesion (6). Of these, EUS-FNA has been shown to have a high sensitivity, specificity and diagnostic accuracy with minimal complications (7). As a result, this modality has emerged as the most useful when diagnosing pancreatic cancer. However, EUS-FNA can be expensive, inconvenient and is ultimately an invasive procedure that does carry some risk to the patient.



Micah Belzberg: *Pancreas*

In the cases of pancreatic cancer when the disease is found early enough to allow for curative resection surgery, the aggressive nature of the cancer makes it such that more than 80% of the patients who successfully undergo the procedure will experience distant cancer recurrences (3). This is an indication that metastasis, which usually occurs in the liver and peritoneum, has already taken place at the time of surgery and should serve to emphasize the aggressive nature of the primary tumor.

In this context of late diagnoses, complex and invasive biopsy procedures and high probability of recurrence, circulating tumor cells (CTCs) may provide an efficient solution to allow for a less invasive, more detectable and more easily monitored indicator of the progression of the disease. CTCs can appear early in the disease’s progression, which could aid in early detection and thus increase the number of patients that are candidates for curative tumor resection surgery (8). Additionally, the liquid biopsies performed to collect CTCs in the peripheral blood are far more practical for diagnosis and monitoring of pancreatic cancer in particular due to the anatomic position of the organ

in the body (9). Beyond the limitations of the typical methods of tissue acquisition referenced above, clinical staging based on cross-sectional imaging such as CT and MRI may not be sensitive enough to detect small-volume metastatic disease in the case of pancreatic cancer (3). Circulating tumor cells may thus be able to provide information about distant recurrences that typical imaging methods may render quite difficult. Many studies have shown that the presence of CTCs in peripheral blood can be a strong indicator of the likelihood of metastasis to occur (8). For example, in a recent examination of nine cohort studies that included 268 CTC-positive pancreatic cancer patients and 355 CTC-negative pancreatic cancer patients, the results showed that patients in the CTC-positive group showed significantly worse progression-free survival rates and overall survival rates with hazard ratios of 1.89 and 1.23 respectively (10). Moreover, beyond testing for the mere presence of CTCs in peripheral blood, additional studies have shown that the risk of metastasis formation is proportional to the amount of tumor cells in the blood (9). As such, CTCs could serve as a powerful indicator for the likelihood of a patient diagnosed with pancreatic cancer to suffer a recurrence and could then help clinicians tailor the therapeutic regimen accordingly.

Obstacles

Current methodologies of detection of pancreatic cancer CTCs are not adequate enough to allow CTCs to serve as an efficient indicator. The most well-known CTC platform, and the only one currently approved for use in the US by the Food and Drug Administration called CellSearch, identifies CTCs via the epithelial cell adhesion molecule (EpCAM), a glycoprotein on the cell surface (11). The platform parses through cells in the blood and allows for the counting of CTCs via immunomagnetic separation using EpCAM-specific antibodies conjugated to magnetic particles. However, current rates of detection via the platform for pancreatic adenocarcinomas are quite low. Gao et al. claim the platform is only able to attain an 11% detection rate of CTCs in peripheral blood in the case of localized advanced pancreatic cancer and 19% for metastatic pancreatic cancer (12). These low detection numbers may result from a number of factors including the localization of CTCs in the portal vein, a decrease in blood flow in malignant pancreatic tumors when compared with normal pancreatic tissue

and the epithelial-to-mesenchyme transition (EMT), which decreases expression of the epithelial markers on CTCs that are essential for their identification.

Additional obstacles remain in the path of using CTCs as a better diagnostic and monitoring tool for pancreatic cancer. Firstly, there remains robust debate about the proper protocol to collect and identify CTCs in general and in the case of pancreatic cancer in particular. Many studies have stipulated that due to the fact that some CTCs may lose their epithelial characteristics because of the epithelia-to-mesenchyme transition (EMT) that occurs to the CTCs, the current practice of using anti-EpCAM antibodies to identify CTCs may not lead to precise results (13). Some studies have shown that coupling the collection of circulating free DNA (cfDNA) known to have been shed by the primary tumor alongside or instead of CTCs in peripheral blood may provide a more accurate set of biomarkers for managing patients with pancreatic cancer (14). It seems fair to say that in the case of pancreatic cancer, the current methodologies available for identifying CTCs may not be sensitive enough to collect, analyze and diagnose the status of the progression based on CTCs alone.

Secondly, a recent study showed that CTCs released from cancers of the pancreas were more likely to be found and were found in higher numbers in portal blood vis-à-vis peripheral blood (15). This finding may necessitate the somewhat less convenient practice of gathering blood from the portal vein when attempting to collect CTCs for diagnosis or monitoring of tumorigenesis in pancreatic cancer patients, thereby nullifying the potential advantage of using peripheral blood.

Lastly, when compared to other forms of cancer such as colorectal cancer, studies have shown that the frequency of CTC detection in peripheral blood was very low in pancreatic cancer. This may be due to the fact that pancreatic tumors tend to be poorly vascularized and the disease is more localized with metastasis likely in the liver or in the peritoneum (12). Moreover, as mentioned above, CTCs from pancreatic cancer seem to be localized in the portal vein and this may indicate that peripheral blood will not yield enough CTCs for material observations of the cancer progression to be made using currently existing protocols.

Current Research and Future Directions

Researchers continue to attempt to identify the optimal proportion of CTCs per unit of blood in order to develop a protocol for establishing the meaning of CTC levels in peripheral blood in the case of pancreatic cancer. Researchers Bidard et al. and Khoja et al. have used a detection cutoff point of 1 or more CTCs per 7.5 mL of blood to indicate a poorer prognosis when compared to patients without detectable CTCs (10,16-17). On the other hand, Maestro et al., have claimed that 2 or more CTCs per 7.5 mL could show a positive prognostic marker for patients with solid tumors (10,18).

Moreover, it appears that researchers continue to search for additional complementary biomarkers to CTCs also found in peripheral blood that could provide more specific and detailed information about the progression of cancer. In Earl et al.'s study on CTCs in pancreatic cancer, for example, researchers demonstrated that patients who tested positive for either CTCs in peripheral blood or KRAS mutations in circulating free DNA (cfDNA) in plasma had a significantly poorer survival rate. The researchers in this case tested pancreatic cancer patients for the specific presence of KRAS mutations, the most common genetic alteration in cancerous pancreatic tumors found in approximately 90% of tumors (14). They concluded that "the concentration of cfDNA may act as a surrogate marker of disease stage." However, they simultaneously qualified their conclusions by stating that more rigorous analysis of pancreatic cancer samples during the disease's progression and examination of larger patient cohorts would be necessary in order to explore the viability of CTC and cfDNA as prognostic and predictive biomarkers. Similarly, in He et al.'s overview of cancer biomarkers, the researchers provide evidence that the increased presence of specific free circulating micro RNAs (miRNA) in whole blood may indicate poorer prognosis for pancreatic cancer patients (19-20). Specific miRNA strands labeled miR-200a-3p and miR-200b-3p are posited to serve as an indicator of detection of previously undiagnosed cancerous tumors of the pancreas and another, miR-196a-5p, is posited to predict poorer survival for previously diagnosed pancreatic cancer patients (19,21-22). As researchers continue to parse through the cells and nucleic acids sloughed off by cancerous tumors in the

blood, perhaps the most effective prognoses will be produced by using a combination of CTC, cfDNA and miRNA analysis together.

Given the nascent nature of CTC research in general and with regards to pancreatic cancer specifically, many studies on the matter make clear that more research with larger cohorts is necessary to further substantiate the strength of the claims that CTCs may help detect the disease, monitor its progression, track its response to curative surgery and ultimately improve patient prognoses. Additionally, it increasingly appears that diagnostic and prognostic accuracy may be boosted by complementing CTC analysis with information gleaned from circulating nucleic acids shed from cancerous tumors present in peripheral blood. Combining these methodologies may yield earlier diagnoses using less invasive methods and thus hopefully lead to higher overall survival rates and less recurrences for pancreatic cancer patients.

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Examining the Views of Medical Students on Treating Patients with Various Sexual Orientations and Genders

Jason Hubsher

Sackler School of Medicine, Tel Aviv University, Tel Aviv

Abstract

The physician-patient relationship is essential for providing quality and efficient care to the patient. Lesbian, gay, bisexual, and transgender people have specific medical needs, conceivably due to the high rates of discrimination that these communities face. This paper focuses on medical students at the Sackler School of Medicine in the American/ New York Program and their outlooks on treating LGBT patients. This study was designed using an anonymous online survey and was open to medical students in all four years of the program. Overall findings show that the students have positive personal feelings towards LGBT patients, but are apprehensive in treating these patients because of a lack of knowledge of how to approach LGBT topics. These views are not due to a personal bias towards LGBT people, but are due to a lack of education that would train physicians on how to approach LGBT patients and topics in medicine.

Introduction

Throughout history, LGBT people have been marginalized in many sectors of life. In medicine, specifically, LGBT patients were not seen as mentally healthy until recent years. Homosexuality was classified as a mental disorder until 1973 when it was removed from the second edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM) (1). This recent stigmatization of non-heterosexual people still plays a role in today's society and continually needs to be addressed. Discrimination of LGBT people is very prominent in the daily life of these individuals; homosexual and bisexual individuals



David Musheyev: *Rainbow Caduceus*

were far more prone to reporting discrimination in their lifetime and in general day-to-day experience (2). Specifically, gay men were much more likely to report discrimination in health care settings and in public areas, citing being threatened with harm and name calling (3). All of these forms of discrimination affect the individual receiving the negative criticism and can have disastrous outcomes.

Studies have shown a correlation between homosexuality, various mental disorders, and suicide attempts. In recent years, sexual orientation has emerged as an enormous risk factor for adolescent suicide (4). Results of meta-analyses reveal that, over the lifetime of gay and bisexual men, they are at least four times as likely as heterosexual men to attempt suicide. It was also found that it is 1.5 times more

likely for non-heterosexual people to suffer from depression, anxiety, alcohol and substance abuse (5). In a study regarding high school students, the students who identified as gay, lesbian or bisexual were three times more likely to have attempted suicide than their peers (6). The stigma placed on these individuals may predispose them to discrimination, mental disorders, substance abuse, and an increase in suicide attempts. This makes the access to quality healthcare even more important for this community.

While lesbian, gay, and bisexual are sexual orientations, transgender is an umbrella term for people with various gender identities. Gender identity is a complex topic and represents an individual's internal awareness of being masculine, feminine, or androgynous. It is not a binary concept and can include stages of masculinity to femininity and maleness to femaleness, including identifying as neither male nor female (7). Transgender people can also have different sexual orientations, not depending on an individual's gender. Similarly to lesbian, gay, and bisexual people, findings suggest that transgender people experience widespread discrimination in health care, employment, and housing (8). Subsequently high rates of substance abuse, anxiety, and depression are witnessed in transgender individuals with the prevalence of attempted suicide at 32%, according to the results of a population-based study in San Francisco (9-10). Lesbian, gay, bisexual, and transgender are very subject to discrimination, mental disorders, and suicide attempts with varying degrees.

In medicine, LGBT patients have many obstacles to obtaining quality health care. Patients that identify as LGBT delay or even avoid medical treatment because of a fear of encountering prejudice while in a health care setting. Some seek treatment and are even turned away because of their gender identity or sexuality. Many receive subpar treatment from medical practitioners who may be discriminatory, uncomfortable, or lack sufficient knowledge towards LGBT patients (11). Patients may not even disclose their sexual orientation or gender identity to health care providers because of a fear of being stigmatized, homophobic reactions, or confidentiality concerns. Past negative experiences in health care settings can also play a role in the amount of personal information volunteered. They may end up withholding important

information that is essential for quality treatment, and this compromises the health care being given (12). This makes the role of a health care provider extremely important for not only being able to give quality healthcare to LGBT patients, but for being non-judgmental, empathetic, and welcoming. In order to put LGBT patients at ease and allow them to divulge important information regarding their health, a warm and accepting environment is critical. With the increased incidence of mental disorders in LGBT patients, their access to healthcare is very important in general so that these issues can be positively dealt with.

This study was designed to evaluate the mindsets of medical students in the American Program at the Sackler School of Medicine, in Tel Aviv, Israel, towards treating LGBT patients. The future of medicine and patient care relies on current medical students and how they will treat their future patients. This study is aimed to 1) evaluate personal opinions of medical students on treating LGBT patients related to non-LGBT patients, 2) determine what subgroup of LGBT patients medical students felt most uncomfortable dealing with, and 3) their perceived challenges treating LGBT patients.

Materials and Methods

An anonymous survey was created using SurveyMonkey, which provides free, and customizable surveys, as well as data analysis. The survey was open to all students in the medical school and consisted of ten questions, ranging from multiple choice to ranking scenarios to open-ended responses. The survey was anonymous in order to allow students to share their true feelings without any judgment or coercion. One question involving ranking LGBT subgroups in the order of how comfortable students would feel treating these patients was purposely left without a no preference option and without the inability to give two groups the same ranking. This was done to most effectively determine which subgroup of LGBT patients medical students feel the least comfortable treating. In total 83 students participated in the study, with 22.89% being MS1 (first year medical student), 48.19% MS2, 15.66% MS3, 10.82% MS4, and 2.41% recent graduates.

Results

When asked about preference of their patient's gender, an overwhelming amount of students, 86.75%, said that they have no preference of the gender of their patient. Whether male or female, students thought that the gender of their patient would not play a role in the quality of the care they could give to the patient.

When asked about preference of their patient's sexual orientation, 87.95% had no preference about the sexual orientation of their patient.

Participants were then asked to rank in order what they would most likely do when feeling uncomfortable with a specific patient. Refer the patient to another doctor, avoid eye contact, and shorten interaction with the patient were the options. 51.25% of students would first refer the patient to another doctor first. Approximately 42% of students would shorten their interaction with the patient, and only 9.76% would mostly likely avoid eye contact.

Sackler students overwhelmingly think that there is significant discrimination in medicine today. About 54% of students think that there is discrimination when it comes to both certain genders and sexual orientations.

When asked if they think it is more difficult to discuss sexual behavior with homosexuals than with heterosexual patients, about 61% said there was no difference and 35% said it was more difficult.

Students were given eight options of heterosexual and LGBT subgroups, which included heterosexual male, heterosexual female, homosexual male, homosexual female, bisexual male, bisexual female, transgender male (born female), and transgender female (born male). They were asked to rank in order the patient-group that they would feel most comfortable treating to the group of patients that they would feel least comfortable treating. Heterosexual patients were the group of people the medical students felt most comfortable treating by far. 96.66% felt the most comfortable treating a heterosexual patient, with 53.42% preferring a heterosexual male patient and 43.24% preferring a heterosexual female patient. Comfortableness with both homosexual and bisexual patients of both genders was very similar to each other. These four groups of patients fell with a huge majority

between the 3rd to 6th rankings, with all groups having over 75% of their rankings between 3rd and 6th. By a large majority, students felt least comfortable treating transgender patients. Transgender males and females were both over 88% likely to be placed in one of the last two ranking spots. Transgender females, individuals that were born male but identify as female, were mostly likely to be in the last ranking spot. 54.67% of students placed transgender females as the group of people that would be least comfortable treating.

Participants were lastly asked to explain what the most challenging aspect would be when treating a heterosexual patient, a homosexual patient, and a transgender patient.

For treating a heterosexual patient, the most frequently given answers were that there were no concerns, addressing the patient's clinical presentation, and STDs. For homosexual patients the most common concern was making sure the student-physician was not disrespectful to the patient and that the patient was comfortable, followed by STD/HIV concerns. One student said that they would be concerned with a homosexual patient's "comfort level with me as a heterosexual physician" and in "addressing sexual risk factors without coming across as passing judgment on their lifestyle choices." The concerns with dealing with transgender patients largely have to do with using the correct pronoun, not understanding the patient's situation, and being unaware of transgender issues in medicine. One student exclaimed that they were worried of "offending the patient by calling them by the wrong gender," and another has concerns of not being "sensitive enough to their situation, and needing the time to understand their situation." "Being unclear about the medicine" and a "lack of knowledge" when dealing with transgender patients were other challenges facing students.

Discussion

By a large majority, the medical students surveyed had no preference in the gender or sexual orientation of their patient. They did, however, acknowledge that there is discrimination in medicine when it comes to both gender and sexual orientation. Most of the students have no apprehensions when discussing sexual behavior to homosexual patients compared to heterosexual patients. This signifies the fundamentally

Key Point: Communication strategies for patient interviews

- Active listening: minimizing external distractions (ringing phones, creating a quiet, private space for the interview) and internal distractions (thoughts unrelated to the current patient, refraining from judging the patient)
- Empathy: affirmative statements and body language to indicate you understand the experiences of the patient. Make reflective statements that restate and reaffirm the patient's feelings.
- Nonverbal communication: tone of language, facial expressions, posture, gestures, and eye contact are all key in expressing understanding and building a rapport with the patient. Certain components may need to be modified to accommodate individual and cultural differences.

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non-judgmental attitude towards LGBT patients in these students. Data from these questions point to the fact that these medical students do not have a personal bias towards LGBT patients whatsoever. The point that these students had no preference about these criteria in their patients may indicate that there will be less discrimination in the future when these open-minded students start practicing medicine.

In ranking how comfortable the students would be treating patients, transgender patients made the students most uncomfortable, specifically transgender females. However, when asked about the challenges in treating these patients, the students did not have personal bias towards these patients at all. However, based on the responses, the uncomfortable nature of the patient-physician interaction would not be due to the negative attitudes towards transgender people. The students, in fact, seem to accept the choices of transgender people. Instead, the factor that makes this

interaction-possibility uncomfortable for the students is their lack of experience with transgender people in general. They are nervous to offend a transgender patient with their choice of words because they are not familiar with how to approach the situation. As a result of being niche topic in medicine and still somewhat taboo in society, transgender issues in medicine are often overlooked.

The LGBT issues in medicine, such as the mental disorders and high disposition to suicide, can be dealt with in and out of a healthcare setting. The degree of protection under the law for LGBT people has a correlation with the amount of discrimination, mental disorders, and suicide attempts in a given LGBT population. In the United States, the degree of protection under the law varies according to each state in regards to LGBT rights. Some of these social policies are marriage equality, prohibiting employer discrimination based on sexual orientation, and including sexual orientation as a protected category in federal hate crimes legislation. LGBT individuals living in states with policies that offer protections under the law have a significantly lower association between LGBT status and psychiatric disorders. Moreover, LGBT individuals living in states without legal protections have a stronger relation between sexual orientation and psychiatric comorbidity (13). All of these neglected policies are a type of institutional discrimination and must be improved upon to promote the well-being and status of LGBT persons. With an increased perceived acceptance of society, by LGBT persons, the rates of mental disorder and suicide attempts will decrease.

In the healthcare setting, there are many ways to improve the experience of LGBT patients and the effectiveness of their access to healthcare. Two of the main issues that LGBT patients face in medicine today are the reluctance by some LGBT patients to disclose sexual or gender identity when receiving medical care, and healthcare providers not being competent in dealing with LGBT issues as part of the medical care (12). To promote optimal care to sexual and gender minority patients, there must be clinical environments that advocate for open communication, and which allows for LGBT individuals to feel comfortable in discussing matters of their sexual identify and any other issues they may be having (14).

The most important aspect to creating a welcoming setting is having healthcare providers that are trained to professionally deal with these issues. These patients should be approached in a non-judgmental, gender-appropriate way. During the training of physicians and medical professionals, there should be an implemented program to address underlying issues surrounding LGBT issues in medicine. Physicians need to be prepared to treat LGBT patients and their specific needs. These specific aspects of medicine and the physical exam should be taught in the medical school curriculum, both in a clinic setting and in the classroom.

A survey of American medical students on ways to improve clinical knowledge showed that the students would like to have clinical exposure to LGBT patient groups at their schools (15). Students also suggested that their comfort with LGBT patients is strengthened when the students are exposed to LGBT culture outside of a teaching environment. In order to improve their comfort and readiness when dealing with LGBT patients, students want opportunities for clinical interactions with patients from this community and to learn how to bring classroom knowledge into clinical practice (15). This could mean that medical schools need to encourage students to have non-formal interactions with the LGBT population. Ways to bring medical students around the LGBT community to understand their daily life should be further researched.

At Case Western Reserve University School of Medicine, medical students benefited from courses that teach LGBT general knowledge and health issues (16). After a mandatory course consisting of a student-delivered presentation, a patient panel, and a small-group session, medical students were more confident in dealing with LGBT health issues and had an increase in their knowledge of LGBT topics. This course did not consist of a physical exam workshop, however, so this would be a great next step to incorporate into the LGBT healthcare curriculum. About one third of medical schools have zero hours of mandatory clinical teaching of LGBT health topics, and only about 14% of schools offer a clinical site dedicated towards teaching about the LGBT community (17). Improvements to the current curriculums of medical schools can offer ways for students to be exposed to more diverse patient groups.

Learning from LGBT patients themselves may be the most beneficial way for medical students to increase their healthcare knowledge of these patients. There should be outreach from medical schools into these communities in order to provide medical students opportunities to interact with these patients. Incorporating mandatory classes dealing with LGBT topics in healthcare should be implemented at medical schools. There should also be a comprehensive physical exam and history-taking workshop designed with LGBT patients in mind. Other possible integrations into the curriculum include clinical experience at specifically LGBT centers and opportunities to hear the experiences of LGBT people in a group or individual setting. Interactions with LGBT persons, who are willing to discuss their positive and negative interactions with physicians, is a essential way for medical students to understand what these patients want and expect from a healthcare professional. With the implementation of medical school programing that caters to LGBT issues in medicine, medical students will be more prepared to treat LGBT patients and will feel more comfortable doing so. The education of medical students is essential to improving the quality of care given to LGBT patients both in the present and future.

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