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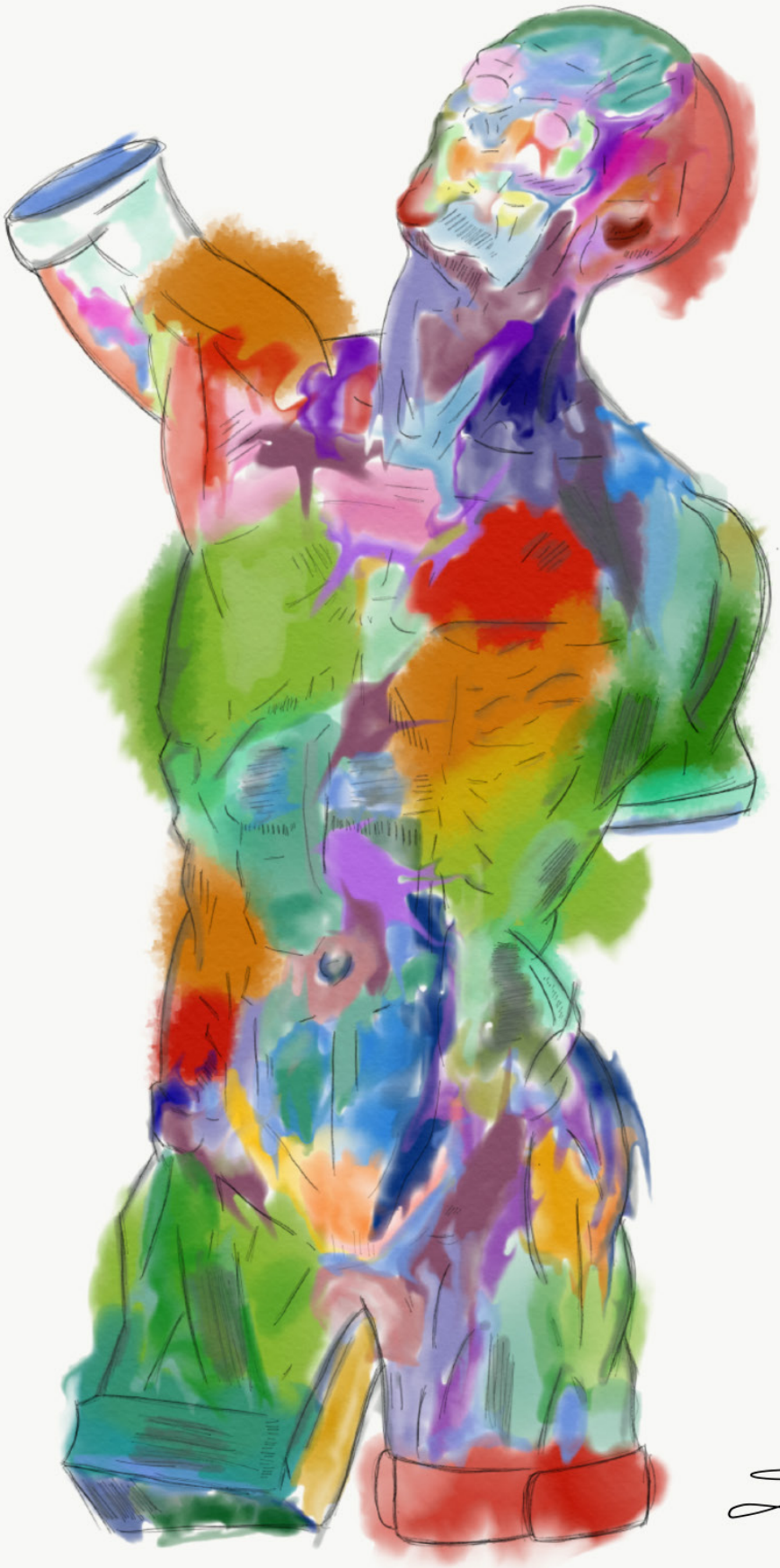

MISSION STATEMENT

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.

SUBMISSIONS INFORMATION

Submissions from students, faculty, and individuals are welcomed. For more information please visit the "Submissions" page on the Sackler Journal of Medicine website at sacklerjom.org

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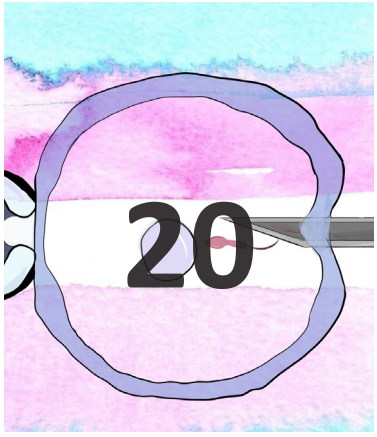
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Letter From the Editors

Madhu Govindaswamy and Amanda Katz
Editors-In-Chief

This issue marks an exciting time for the Sackler of Journal of Medicine. Three years ago, Brian Wolf conceived and published its inaugural issue in 2016 as a medical journal by and for medical students. Now, in 2019, the Sackler Journal of Medicine has evolved into an integral piece of the Sackler School of Medicine culture. Students have grown this issue like never before, and we are incredibly excited to announce that, for the first time since its creation, the Sackler Journal of Medicine will be published biannually. Such an accomplishment would not be possible without the unwavering support of our journal staff, student submissions, mentors and faculty advisors alike. The journal has always been predicated on providing a medium for discussion among and for medical students; we are proud to continue showcasing student research that applies the foundations of medicine beyond the classroom.

Our fourth volume is tasked with casting a wider net, reaching a broader audience, and diversifying its contents more than ever. We have achieved this through featuring commentaries on current events, reflection pieces, reviews and original research. Ranging from Emmy Hamilton's recognition of the unique obstacles facing transgender infertility treatment, to Melissa Bendayan's insight into the unique factors that threaten health care in elderly populations, this issue undoubtedly pushes boundaries of traditional medicine. Anika Paradkar, Liad Maslaton and Kyle Miller, Isaiah Grossman and David Shimunov offer interesting glimpses into the inquisitve field of medicine with unique case reports, while Erica Cohenmehr reveals the unfortunate reality of nosocomial infections and white coat contamination. Ilana Lefkovitz explores the potential of Blockchain technology to extend into the healthcare field, and Jordan Halevy sheds light on innovations to come for the International Classification of Disease codes. Indeed, volume 4 is dedicated to exploring the medical field from all angles, and continuing to provide a forum for medical student expression.

Over the past three years, we have seen the journal grow immensely. With over 20 journal staff, an online presence (www.sacklerjom.org) and a new biannual publication, we are both excited for and confident in the future and breadth of the Sackler Journal of Medicine.

If you are interested in joining or submitting a piece, email us at **editor@sacklerjom.org**

We hope you enjoy this issue.

Madhu Govindaswamy and Amanda Katz

Letter From Dr. Allen

Aaron Allen M.D.
Faculty Advisor- SJM
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Dear Sackler Journal of Medicine Readers,

"Statistics is the plural of anecdotes"- Van House

This pithy quote is one that I have loved for many years. So much of what we do in research is based on statistics. Is the p-value significant? This question alone can determine the approval of new drugs, the financial success or ruin of large and small companies, the academic advancement of doctors, and of course, impact the lives of patients everywhere. When we read or see new studies presented, we are drawn to the statistics and results; how often do we think of the anecdotes or the patients and caregivers that lie behind these findings?

Recently, I had a long-term follow-up patient come into my clinic and ask me if I still needed him to fill out the quality of life questionnaire he was accustomed to filling in as a patient on a pivotal phase III trial for his prostate cancer. I told him that fortunately, the study was completed and reported as being positive; the data on his follow-up was no longer needed. The next question he asked threw me for a loop. He asked me: "so I am not your patient anymore? Can I still come to see you even though the study is over?" "Of course you can still come for follow-up, your care has nothing to do with the study results," I responded.

Several hours after our visit had ended, I thought about his question and realized that the trial he was enrolled in had almost 2000 men with prostate cancer. Each participant has a family, a medical history, and a relationship with their physician. How often do we, as busy physicians, think and consider the anecdotes of the trials that we read about and base our practice on? Maybe, not as much as we should… The more I thought about my patient and his question, the more I started thinking about all the patients I had enrolled in this study. I wondered aloud how everyone was doing.

As the faculty advisor for SJM, I am pleased and thrilled at the level of scholarship and professionalism that goes into every issue and certainly, the one you are now reading. The editors- Madhu Govindaswamy and Amanda Katz, authors, and reviewers deserve tremendous credit for their efforts and successes.

As you read SJM- or any other journal, I implore each of you to remember the anecdotes that lie behind the data. Each anecdote has a family that experiences hardships, trial and struggle to make up one small data point. Perhaps if we personalize the data in our lives, we can make ourselves more motivated to read, conduct, publish and truly appreciate our research.

Happy Reading!

Aaron Allen M.D.

1st Place Award: Valentine's Day

Anisha Vasireddi
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I felt my pulse quicken when I heard my phone ring while on-call. Pacing back and forth along the lengthy, beige-walled corridor, I picked up the phone with my sweaty palms.

"Pediatric heart, 2:00 p.m. pickup time. See you soon, Jasmine," Dr. Stevenson said on the phone.

I wiped my hands against my blue, soft, pillowcase-like scrubs. Filtering out all the mumbling voices in the office, I gathered all required document sheets. I changed out of my knit shoes into my sturdier sneakers, the ones stained from dried blood. I threw my phone charger, ID, down jacket, and post-it notes in my backpack and scurried off to the supply room.

Pressure bags? Check. Clamp, two-spike tubing, snares? Check. Syringes, needles, blood tubes? Check.

"This is my thirty-something procurement. I doubt it can be that different from all the rest," I said to Michael, my fellow preservationist.

"Yeah, hopefully we get back at a decent time to rest. I've really been hit hard with all these runs, I could use a break," he replied.

I watched him pack the deep cooler with our preservation solutions and saline. I then helped cover it all with buckets of ice. I glanced at my watch— 1:55 p.m. I removed my slippery gloves and repeatedly pushed the elevator button. We outpaced the others in the hospital lobby, maneuvered our cooler and bags through the stubborn revolving doors, and hopped into the emergency organ transport vehicle with a single minute to spare. Michael and I climbed over to the back of the car to make space for Dr. Stevenson and surgical resident Dr. Lee.

"You know the deal by now. Lights and sirens, my man. Let's go!" Dr. Stevenson said to Rico, our driver. "They are waiting for us in Ohio," Stevenson said in his firm, low-pitched voice. "The other teams have already arrived."

We reached the NY Hasbrouck private airport, where the pilots who would fly our team to Ohio greeted us. I felt my face getting hot as I boarded the Learjet 60, with no bathroom and barely any legroom. I realized months ago that flying private wasn't as glamorous as it seemed. I shut the cold, tiny window shades, as well as my eyes, in hopes of relieving the knot in my stomach from the bumpy ride. A few hours later, I woke up to the loud knocking noise of the landing gears being deployed. I rubbed my eyelids to help move around the contact lenses glued to my pupils.

"All right team, prepare for landing," the pilot announced.

De-boarding the aircraft, I felt a shiver from the strong winds blowing against my ankles. Upon arrival, an ambulance was waiting for us on the tarmac.

En-route to the hospital, our driver mentioned a deadly high school shooting that hit the headlines just prior to our landing. "Well, on a brighter note, shout-out to you guys for doing such a good deed tonight," he said.

I clenched my fists, trying hard not to search the details of the horrific incident on my phone. I took a deep breath, while trying to clear the distraction from my head and remain as calm as possible. I jerked forward as the vehicle came to an abrupt stop, my ears ringing a little from the siren. A tall security guard at Westerville Children's Hospital greeted us and gave us instructions on how to find Operating Room 7, where the procurement was taking place.

"Right, left, right. Pass the sunflower-patterned walls, take a left, walk through the automatic doors," I recited in my head. "Hopefully we find our way back to the ER ambulance bay."

Dr. Stevenson and Dr. Lee were rather quiet, other than some chatter about their cases that week. They must have had a gruesome day in surgery before we headed out to Ohio. We donned the hospital's green paper scrubs on top of our own, and we quickly threw on bouffants and masks before entering the sterile

area of the operating rooms.

"Hello! My name is Jasm--," I said and then was interrupted.

"Oh, hello. Sorry, I, uh, I can't talk right now. Please give me a few moments," the organ procurement coordinator said in a shaky voice, wiping the sweat off his forehead.

I went to find Michael who was gathering spare ice and supplies for our perfusion. "Heads up, give the co-ordinator some space for now," I whispered to him. Suddenly, a wailing sound echoed through the long, empty corridor. I glanced over my shoulder and saw a large family standing a few meters behind the entrance to the operating suites. As Michael and I began to make our way back to OR 7, I heard squeaking of wheels against a mopped, glossy floor. There she was. The brain-dead donor was rolled in by a group of nurses and staff, wrapped in a fleece, honeydew-green blanket, attached to IV fluids, oxygen, and tubes. I chewed on my lower lip and felt my cheeks get warmer under my foggy mask. She was barely the length of my forearm.

"Sorry for how I responded earlier," the coordinator stuttered. "My name is Jim. This is my first time witnessing such a young donor - just under two months old."

I unclenched my fists and replied, "No need to apologize. This is just the start to an emotional evening." Still startled by the sight of the baby donor, I reached into my back pocket with shaky hands to pull out the paperwork. "My name is Jasmine. Here is a list of the members of our NY Heart Team, as well as all the preservation solutions we will be using. I understand it will be tough to draw more than just a few tubes of blood from such a tiny donor for our cross-match. Whatever you can give us would be great," I said.

Dr. Stevenson and Dr. Lee shuffled to the shiny scrub sink. They peeled open the orange chlorhexidine soap brush and turned on the water. They began scrubbing their nails, and proceeded with circular motions down the forearm to the elbow. They gently rinsed off all the lather. With the smell of antiseptic wafting towards me, I tightened my mask and entered the OR behind the surgeons who walked in with their hands above their elbows. A scrub nurse handed them clean blue towels, tied their sterile gowns, and handed them their surgical gloves. Meanwhile, I slowly raised the baby's head, which barely fit in the palm of my hands, to place a miniature shoulder roll for better access to the chest.

"Is everyone ready for a time-out?" the coordinator asked. "Donor blood type: B. Reason for death: found blue in playpen. Today we gather here to appreciate the life of this newly born girl, as well as her family's choice to gift her organs. May we please take a moment of silence." He blew his nose with one of the surgical towels and said: "An incision can now be made."

5:27 pm. The first cut was made. As soon as the cauterizer was in use, I caught a whiff of the burning flesh. I furrowed my brows at the sight of the miniscule sternal retractor that was used to open up the baby's chest so softly. I turned over to Michael and said: "Have you ever seen something like this before?"

He wiped his upper left cheek and said: "N-n-ever."

Fifteen minutes passed, the abdomen was fully open. The kidneys were shiny and red-brown in color, and I had never seen such a pure pink donor pancreas before.

6:01 pm. "Jasmine, call our implanting surgeon and notify him we are accepting the heart," Dr. Stevenson mumbled under his mask.

"Of course," I responded. "Michael, call the pilots and ambulance driver. Give them our estimated time of arrival."

"Give heparin. Thirty-thousand units," Dr. Lee said to the anesthesiologist standing in the back corner of the OR behind the blue drape.

6:48 pm. Aortic cross-clamp. Within seconds, the OR became a zoo. Struggling to put the nitrile gloves over my sweaty hands, I quickly ran to our cooler. I placed our preservation solutions in pressure bags, and then hung them on the rusty, silver IV pole.

Dr. Stevenson handed over the tubing to me. Making sure I didn't touch his sterile glove, I carefully grabbed the tubing with still hands and attached the ports to the bags. "Flush," he yelled.

I was seconds away from delivering the freezing cold solution that would gush through my tubing to the surgeon's end to preserve the metabolic activity of this baby girl's heart until it reached our recipient. I slowly released my tubing clamp.

"Lower on pressure," Dr. Lee said.

As I deflated the bags, I softly shook them to gauge how much solution was remaining to perfuse. "Four-hundred millilitres left to give," I called out. A few minutes later. "About to close," I said, as I proceeded to secure my tubing clamp.

"7:14 pm. Heart is out," the coordinator shouted.

"Michael, keep an eye on your watch. Ischemic time starts now," I said.

I scurried back to the cooler to dig a hollow hole within the ice for the organ to be buried in. Dr. Stevenson walked towards me with his bloody mask and orascoptic loupes. I felt a chill ripple up to my spine. He was carrying the tiny heart, swimming in layered bags, buffered by pools of saline. He kneeled down and placed it in the deep space I made.

"Any abnormalities, diseases to the organ?" the coordinator asked.

"No," Dr. Stevenson replied.

"We are just going to have to take some photos of the packaged heart for documentation purposes," the coordinator explained.

Dr. Lee ripped off his surgical gown and turned to me. "Wow, that was the toughest dissection and explant I've performed. I almost nicked an artery," he whispered while rubbing his chin against his shoulder.

Donor chart? Check. Cross-match blood tubes, nodes, spleen? Check. I taped up our cooler, threw away my mask, bouffant, and paper scrubs. A friendly security guard escorted us back to the ambulance bay. The car ride was silent enough that I could hear my stomach making its hungry noises. Once we reached the Ohio Franklin County airport, I threw some Nutri Grain breakfast bars in my backpack before boarding the jet.

My eyes began to flicker uncontrollably, so I rubbed them, hoping to ease the twitching. Soon after take-off, I raised the window shades and looked at the starry sky. My eyelids slowly closed and I started to breathe deeply as the corners of my mouth slid slightly upwards. This was not just any other procurement. I spent Valentine's Day with a team who would soon deliver a gift for a child: a new heart. February fourteenth, twenty-eighteen; a broken heart can be fixed.

Acknowledgements

I would like to thank Dr. Catherine Wang, who has been an unbelievably supportive mentor, for giving me the opportunity to be a Research Assistant in the Division of Cardiothoracic Surgery at Columbia University Medical Center, as well as a preservationist on the heart and lung procurement team. I would also like to thank the Cardiothoracic Surgery residents from Columbia, who were the explanting surgeons I travelled with on procurements, for sharing their medical experiences and knowledge with me and always offering such insightful advice. Lastly, I would like to acknowledge all the hard-working fellow preservationists I worked with, both those who trained me and those who I was able to train. I would not be half the aspiring physician I am today without this position. I know these experiences have equipped me to take on all the challenges that will be thrown my way in medical school and beyond, and I could not be more thankful.

Anticoagulation in Older Adults: A Gap in Care

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A large aspect of medicine and clinical decision-making is risk assessment – will the treatment we choose help the patient, or harm them? Are the side effects too much to bear? There are many tools and risk calculators available to help clinicians find the balance between potential benefits and risks. However, what happens when risk calculators are not universal? An important example of this inadequacy is the frail: a growing subset of elderly patients that are more at risk for medical complications than the general patient population.

Frailty is a geriatric syndrome that increases an individual's vulnerability to physiological stressors, such as acute or chronic disease and iatrogenic stressors (1). This syndrome arises from an imbalance in multiple physiological systems that lead to the decline in homeostasis, and represents the difference between chronological age and biological age (2). The frailty phenotype is characterized by low physical activity, weakness, exhaustion, slowness, and weight loss (3). This plays an important role in guiding clinical decisions for older adults, as predicting risk is more complex given their highly variable status. For instance, preoperative presence of frailty can indicate the patient's ability to withstand the stressor of surgery, and their postoperative risk of mortality and complications.

A salient example of a risk evaluation is bleeding risk assessment when deciding on anticoagulation. Atrial fibrillation (AF) is the most common, clinically significant cardiac arrhythmia; 10 million North Americans are estimated to be affected (4, 5). AF increases the risk for stroke by five-fold and is associated with increased morbidity and mortality (6). Both the incidence and prevalence of AF increases with advancing age (7). Furthermore, 70% of those with AF are 65 years or older (8). Treatment for AF includes anticoagulation to prevent thromboembolic complications and address the increased risk of stroke. Warfarin, a vitamin K antagonist, was the standard treatment for AF and the most commonly prescribed anticoagulant. However, warfarin prescription rates have decreased since the approval of the direct oral anticoagulants (DOACs; 9). Since 2010, four DOACs have been approved by the United States Food and Drug Administration: dabigatran (2010), rivaroxaban (2011), apixaban (2012), and edoxaban (2015). The new generation of anticoagulants are advantageous and preferred over warfarin due to their predictable anticoagulant effect, shorter half-life, and can be prescribed in fixed doses without routine coagulation monitoring (10). The literature shows that the DOACs are superior or equivalent to warfarin in preventing stroke or systemic embolism, with lower rates of hemorrhage (11, 12, 13).

Clinicians have to consider both the stroke risk and bleeding risk when deciding on anticoagulation therapy. One tool that is commonly used is the CHA2DS2-VASc score, which assesses the stroke risk of a patient with AF (14). Estimating the risk of stroke is based on the following factors: congestive heart failure, hypertension, diabetes mellitus, and sex (1 point each), age ≥75 years old and stroke/transient ischemic attack/thromboembolism (2 points each), history of vascular disease, age 65 to 74 years old, and female sex (1 point each), for a total of 9 points. A higher score corresponds to a greater stroke risk and having a score of 2 or greater is an indication for anticoagulation.

Advanced age is a major risk factor for DOAC-related bleeding adverse events (15). The bleeding risk for older adults receiving DOACs is estimated to be 1.5% per year for major bleeding and 3.5% per year for non-major bleeding (16, 17). Oral anticoagulants are the most common cause of drug-related hospital visits in older adults, accounting for 18% of such visits (18, 19). The risk of bleeding is especially concerning for DOACs since antidotes are only now being developed and are not widely available for reversal in patients presenting with life-threatening bleeds.

Due to the known increase in bleeding in frail older adults, some clinicians are reticent to prescribing these medications. Physicians are uncertain about balancing the risk of stroke and the risk of bleeding in the elderly, leading to underuse of anticoagulation (20). In a study of family medicine residents, regardless of training level, the residents preferred warfarin to DOACs due to a fear of adverse bleeding events, highlighting the knowledge gap in this area (21). Moreover, dose reductions are often prescribed "off-label" for frail older patients due to the perceived risk

Lior Fusman: *anticoagulation*

of bleeding complications. In the Unites States, almost 1 in 8 patients received the wrong DOAC dose, with those who received an off-label dose more likely to be older (22). A recent Canadian registry found that 1 in 5 patients received an inappropriate DOAC dose (23). The patients who were dosed inappropriately were more likely to be older and of lower weight. Maes et al. found that half of the population above the age of 75 did not receive any anticoagulation, despite there being a clear indication warranting such therapy (24). Nursing home residents classified as frail were associated with low frequency of DOAC use despite high stroke risk, with fewer than 50% of residents receiving DOACs (25). Lefebvre et al. found that non-frail patients were 3.5 times more likely to receive anticoagulation therapy compared to patients who were severely frail, independent of age and bleeding risk (26). Despite the increased bleeding risk, older adults have higher stroke risks than the general population and would benefit the most from stroke risk reduction (27, 28).

There are no specified geriatric dosing adjustments for older adults. To limit the risk of bleeding associated with DOACs, dose reduction is recommended for apixaban-treated patients with two of the following three criteria: ≥80 years of age, low body weight (<60 kg), or high serum creatinine (≥133 mmol/L; ≥1.5 mg/dL; 29). Dose reduction is recommended for rivaroxaban-treated patients with a creatinine clearance of 30-50 ml/min, while age and body weight are not specifically considered (30). Furthermore, there are no specific dosing recommendations for frail patients (31). In practice, DOACs are frequently prescribed at a lower-than-recommended dose, such that 15% of low dose DOAC prescriptions do not meet the approved criteria for dose reduction (32). Off-label dosing is associated with worse clinical outcomes, including a higher rate of cardiovascular hospitalization, systemic embolism, major bleeding, and death (22).

Despite the prevalence of AF in older adults, less than 25% of the participants in the landmark DOAC trials were above age 80 (33). Many studies conducted on DOACs since their approval have included older participants, including a comprehensive meta-analysis of over 25,000 patients age 75 and above from Sardar et al. which confirmed the non-inferiority of DOACs compared to warfarin in this population (34). However, the authors of this meta-analysis cautioned that this did not truly reflect the "real word" elderly population, since elderly trial patients had fewer comorbidities, superior cognitive and physical functioning, and lower frailty. The absence of frailty is important, as using chronological age is not sufficient surrogate measure marker for biological age. Relying on clinician judgment alone has been shown to often overestimate bleeding risk and underestimate thromboembolic risk, especially in older adults (35). A reason for this may be that physicians are more concerned by the prospect of a harm, causing a hemorrhage from prescribing an anticoagulant, than the opportunity for benefit, of preventing more strokes (36).

There is a need for a frailty assessment in this context to better assess risk for older adults and help frame clinical decision making in an objective manner. The gap in knowledge regarding DOAC dosing in older adults has been well articulated in the literature (33, 37-40). A recent review of frailty in AF highlighted a treatment paradox in which higher risk frail patients were less likely to receive treatment for AF (41). The authors found that while frail patients had an increased prevalence of AF compared to age-matched non-frail patients, frail AF patients had lower use of oral anticoagulation, despite having a higher risk of fatal and nonfatal stroke and systemic embolism.

In summary, frail patients are more vulnerable to physiological stressors, and are therefore more susceptible to adverse events and medical complications. The risk of bleeding complications, which are strongly associated with mortality and adverse effects, is heightened in older adults. Incorporating frailty into clinical decision-making could help refine bleeding complication risk predictions for older adults and allow clinicians to tailor therapy accordingly. The "one size fits all" concept of dosing is gradually being replaced by strategies aimed at delivering "personalized medicine" to patients. The shift to individualized dosing has the potential

to improve drug efficacy, minimize adverse events, and optimize patient care. As the world's population ages and the number of older adults is projected to increase dramatically over the next two decades (42) it will become increasingly important to know how to properly optimize the dose for these patients to avert the adverse side effects.

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Key Points: Fraility and Anticoagulation Therapy

- Anticoagulants are commonly used forpatients with atrial fibrillation (AF). AF affects approximately 10 million North Americans. Roughly 70% of patients with AF are older than 65.
- Frailty is a geriatric syndrome that increases an individual's vulnerability to physiological stressors, such as acute or chronic disease and iatrogenic stressors.
- Warfarin is the most commonly used anticoagulant, but the new generation of anticoagulants (DOACs) is advantageous over warfarin due to their predictable anticoagulant effect, shorter half-life, and ability to be prescribed in fixed doses without routine coagulation monitoring.
- Advanced age is a major risk factor for DOAC-related bleeding adverse events. Not enough research has been done on the frail population.

Medical Application of Blockchain Technology

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Bitcoin is not the first digital currency. In fact, many digital currencies began surfacing in the 1990's. What makes Bitcoin revolutionary and why it has gained so much momentum over the last several years is the fact that it is encrypted and decentralized. The idea behind Bitcoin, as explained by its inventor, Satoshi Nakamoto, was to create "an electronic payment system based on cryptographic proof instead of trust, allowing any two willing parties to transact directly with each other without the need of a trusted third party," such as a bank (1). This system or ledger on which Bitcoin is built is referred to as a blockchain, a powerful technology with potential applications reaching far beyond Bitcoin, extending into such areas as medicine and healthcare.

Before exploring some of the potential uses of blockchain within the healthcare space, it would perhaps be helpful to provide a general sense of how a blockchain works.

The blockchain can be thought of as a database shared between all computers within a network, in which each computer contains a copy of the database. Anything could potentially be recorded in such a database—from cash and financial transactions to food inventories and medical records.

The process proceeds as follows: when one person wants to trade with another, the details of the proposed transaction are verified by any one of the computers in the network. Once verified, the record is stored in the blockchain as a timestamped, encrypted block. This block is assigned a unique identification number or hash, and the block additionally includes the hash of the prior block (2). Thus, all the blocks are linked together.

In addition to being encrypted, the blockchain is immutable (3). Whenever a change is made to a piece of information within a block, the block itself cannot be modified. A new block must be added to the chain to reflect the updated information. These various operational components of the blockchain all help to ensure a safe, protected means of storing and editing data, that can be accessed and verified by computers within the network.

Madhumita Govindaswamy: *pills & bills*

There are many transformative ways this could be implemented in healthcare. A key application would be in the storage and maintenance of electronic medical records (EMR). In addition to providing a higher level of security, a decentralized EMR based on blockchain would solve the incompatibility issue between different EMRs used by separate health networks. Also, since each computer would have its own copy of the blockchain, data loss or alteration would be nearly impossible (3).

So far, there have been two nascent implementations of a blockchain-based EMR. The first is one by the Estonian government, which uses a blockchain platform for verifying patient identities3. The second is MedRec, a project between MIT Media Lab and Beth Israel Deaconess Medical Center. This specific implementation of blockchain aims to give patients more control over their privacy. It does not store patient data itself, but rather the authorizations given by patients to various healthcare entities as to who may access their health information. This facilitates easier sharing of patient data (4).

The Center for Disease Control and Prevention

(CDC) has also expressed interest in blockchain for use as a public health surveillance tool. For example, if someone from one state becomes infected with hepatitis A, the CDC and other nearby states would want to be notified. A blockchain-enabled system would be able to record and distribute this information quickly, thereby containing and preventing the spread of infection (5). In the case of a future pandemic, the potential utility of this becomes even more apparent.

Other use cases that have been proposed include supply chain management of pharmaceuticals and medical devices. Health insurance companies are also investigating ways to incorporate blockchain to enhance data exchange between providers and customers.

Despite its great potential, the development and implementation of blockchain within the healthcare field still faces major obstacles. This is partially due to lack of expertise and awareness among healthcare personnel and the general public about how the technology works. There are also technical limitations. Verifying information on the blockchain requires a lot of computational power, and data sets such as EMR's are exceedingly large (6). This raises other perplexing considerations. If there is no intermediary or central authority overseeing the blockchain, and very sophisticated machines are required to operate it, it is unclear which computers should be used and who would have the authorization to access the patients' data (5).

It might take years to sort out these questions. Fortunately, companies like IBM, Microsoft, and Accenture are forming special units devoted to blockchain, researching ways to construct and deploy the technology (4). Additionally, in 2019, capital investments in blockchain are predicted to reach 400 million dollars (7).

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Transgender Fertility Preservation

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In the age of fertility treatment and in vitro fertilization (IVF), the ability to have biological children is an exciting possibility for many. But what about women who were born biologically male, or men who were born biologically female? Transgender fertility- the ability for transgender men and women to bear biological children- is clearly an increasingly relevant and pressing issue.

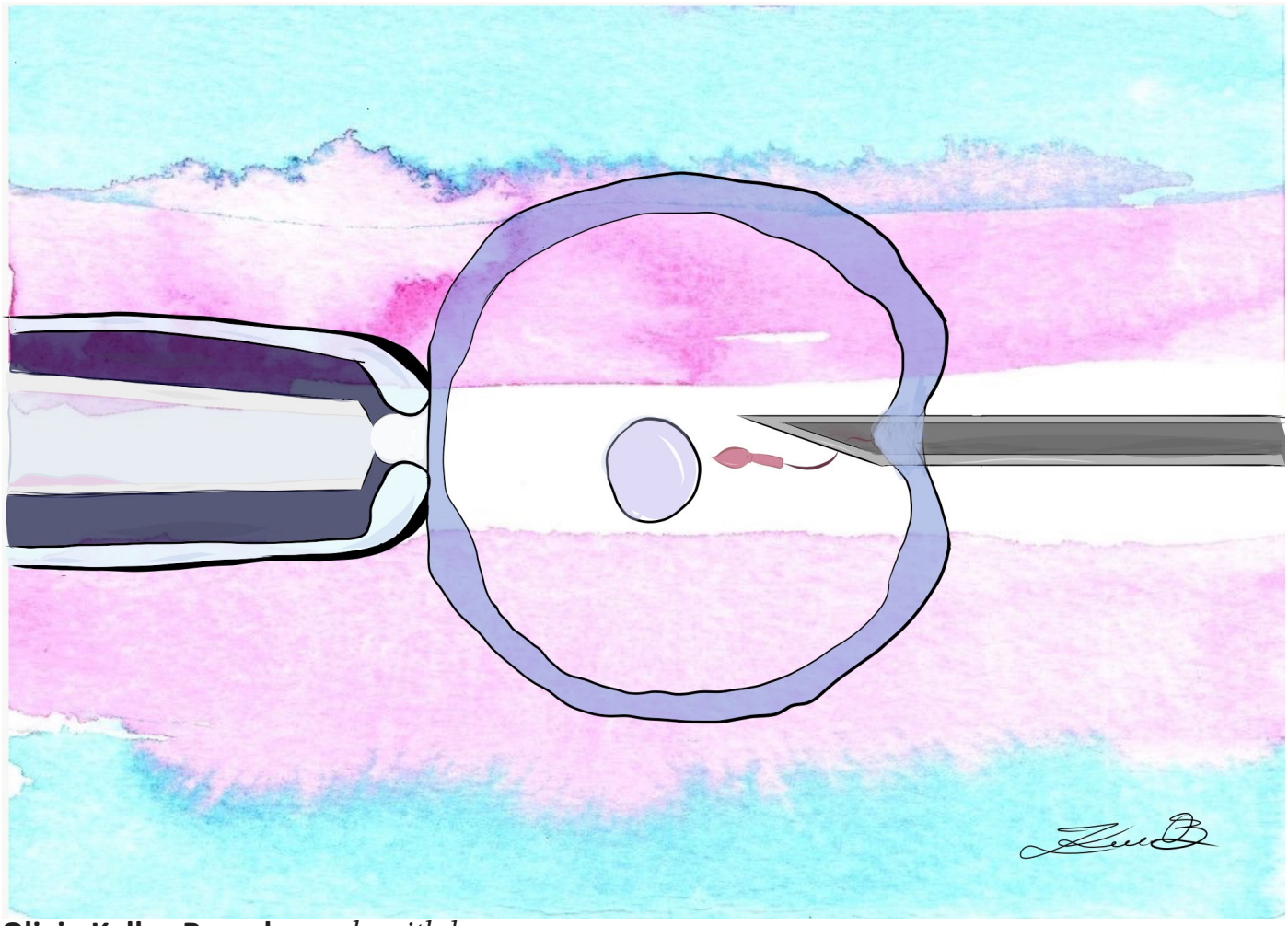
Over the past few decades, transgender individuals have become a more visible and accepted community in the mainstream United States society. This awareness has allowed for more and more individuals to live openly and undergo any relevant medical treatments that they feel are necessary. With hormone therapy, puberty blockers, and gonad and sex-change surgeries becoming more common, it is important to consider the long-term effects of these treatments on the ability to parent a biological child.

The implications for transgender men and women differ in relation to fertility. Hormone therapy is one common treatment that transgender individuals may choose to undergo. Before beginning hormone therapy, transgender women can quickly provide a sperm sample through ejaculation. A simple needle extraction can also be offered to patients for whom this process may be uncomfortable, or induce feelings of dysphoria: distress, anxiety and depression. Overall, sperm banking remains relatively easy, allowing for easy fertility preservation among trans women that costs in the range of a few thousand dollars (1, 2). It is imperative that transgender women are counseled about their fertility options before beginning hormone treatment. It is well known that feminizing hormone therapy (estrogen, testosterone blockers, and progesterone) decreases sperm count and quality, ultimately leading to irreversible infertility (1, 3, 4, 5, 6). In some cases, individuals taking hormones for only a few years may stop treatment and allow their testosterone levels to rise, regaining their ability to produce healthy sperm (4, 7). However, because there is no guarantee, it is important that individuals receive proper counseling before beginning hormone therapy.

Transgender men face a more difficult and expensive process. Their fertility can be preserved through the freezing of eggs or embryos. The process of egg removal requires several weeks of hormone injections and an egg-removal outpatient surgery. Ovarian tissue banking offers a quicker process but requires more invasive surgery (2). Both of these methods require individuals to delay the start of hormone therapy for a few weeks or months, which may be unappealing. The cost can also be prohibitive, ranging from $10,000-$20,000. However, unlike trans women, testosterone therapy used by trans men is not currently known to lead to sterilization. This presents the possibility for trans men to stop therapy at a later point, either to undergo egg retrieval, or to be inseminated by their partner or donor sperm, and carry their own child in their own uterus (1, 6).

Further challenges arise when working with transgender youth. Unlike adults who have mature gametes that can be harvested before beginning hormone therapy, transgender youth may not be biologically ready. Human gametes only mature in vivo when that person reaches puberty. For many transgender youths, puberty, a process that can last several years, is an incredibly uncomfortable and dysphoric experience. Doctors can suppress puberty and the accompanying development of secondary sex characteristics, such as the growth of sexual organs, in young transgender patients using medication before starting them on hormone therapy around the age of sixteen (1). The downside of this process in relation to fertility is that the individual never undergoes puberty for their natal sex, preventing the maturation of any gametes and making future biological children impossible. This issue exists for both transgender men and women.

The lack of mature gametes available for sperm banking or egg cryofreezing creates a problem for individuals who choose this treatment. Two directions of research exist, which may eventually overcome this obstacle. In 2016 in China, Quan Zhou and colleagues managed to create viable gametes in vitro using mouse embryonic stem cells (8). This research is promising, but limited by serious ethical and biological limitations, especially concerning transfer into humans. At present, the relevance of this technique to the transgender community is minimal. A more promising approach comes from E.B. Prasath and colleagues in Singapore (9). In 2014, these researchers published the first case study of in vitro maturation (IVM) of an egg, which resulted in a healthy pregnancy and live birth. The subject was a young ovarian cancer patient whose immature follicles were extracted and matured in a dish, before being inseminated by partner sperm.



Olivia Keller-Baruch: *made with love*

Though used to prevent infertility in a cancer patient, this research has broader implications for the transgender community, and could represent a promising and novel opportunity for transgender males who have not undergone traditional puberty to parent biological children in the long term.

There are additional mental health considerations when counseling transgender youth. A study by researchers published in the Journal of Adolescent Health surveyed transgender youth in the United States, ages 9-18 years (average age of 15 years), to learn about their experience with fertility counseling and transitioning (10). Of note, 92.3% of the participants had a history of, or were currently dealing with, a diagnosed psychiatric illness such as major depressive disorder or generalized anxiety disorder. The authors of this paper remarked that this vulnerable population may not be able to make informed decisions about their health care, or have the long-term perspective required for making decisions regarding fertility preservation. Of the seventy-three subjects in the study, seventy-two had received fertility counseling, but only two opted to attempt gamete saving procedures. Another study found that out of a group of 105 transgender adolescents, only thirteen received formal fertility preservation counseling, and only five completed gamete preservations (four sperm cryopreservation, one oocyte cryopreservation; 11).

This is not to say that transgender youth should be forced to save their gametes. The cost-benefit of delaying hormone treatment vs. living through puberty for a gender the person does not identify with is a serious consideration and should be dealt with on a case-by-case basis. However, a separate study of adult trans men found that the majority desired to have children, and 37.5% wished fertility options had been available to them when they were transitioning, suggesting that counseling methods must improve to specifically address this population group (12).

Recent studies suggest that not only do transsexual individuals wish to have biological children, but that new medical technology can help them achieve this goal (1, 2, 9, 12). Given the current resources available, as well as new breakthroughs just around the corner, it is imperative that transgender individuals are educated

about their options. Past research has shown that access to information regarding fertility preservation for transgender individuals remains challenging6. In order to provide equitable and just care to all patients, physicians in the fields of fertility, counseling, pediatrics and primary care must close this information gap by educating themselves about the many options available to preserve transgender patients' fertility before it is too late. Medical professionals must understand that fertility preservation is an expanding issue, and that for transgender individuals, the ability to have biological children is no longer a question of if, but a question of how.

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Key Points: Adolescent Transgender Patient Infertility

- Fertility preservation for transgender individuals is relevant for physicians treating this growing population
- As hormonal and surgical options for transgender individuals increase, so too must fertility counseling and fertility preservation treatments
- While promising research suggests that innovative treatments for fertility preservations are possible, this remains an under-examined field
- Physicians treating transgender youth must incorporate fertility counseling and be educated on possible preservation treatments, in order to best enable patients to make informed decisions

White Coats

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Hospital-acquired, or nosocomial, infections pose a serious yet avoidable problem to patient care in hospitals across the world. The World Health Organization estimates that approximately 15% of all hospitalized patients suffer from nosocomial infections. Patients who become infected require longer hospital stays, health care costs, morbidity and mortality. While any patient can acquire a healthcare-associated infection, those at risk include those in intensive care units, burn units, neonates, and those undergoing organ transplant (1). A 2009 study reported that the proportion of infected patients in the ICU may even reach 51% (2). A common vehicle for pathogens is hospital apparel, which may be contaminated with microbes that cause nosocomial infection. This paper investigates white coat contamination and laundering habits, which has important implications for patient safety.

Studies have found that over 50% of white coats samples may be contaminated with bacteria. In one such study, researchers administered a semi-structured questionnaire and collected swabs from the lower edge of the front of white coats of medical students in India. They found that 63.54% of white coats were contaminated (3). Similarly, researchers swabbed the collars, pockets, sides, and lapels of the white coats of 100 medical students in a tertiary care hospital (4). They found 74.3% of male and 62.8% of female medical students' white coats were contaminated (4). The isolates found may cause meningitis, pneumonia, and sepsis, and were found to be resistant to penicillin, erythromycin, and clindamycin (4). Hospital-acquired infections increase odds of mortality and median length of stay, with one study reporting 1.5- to 1.9-fold higher odds of mortality in patients with nosocomial infections, and 2-fold higher median length of stay (5). Patients infected in intensive care units face a two-fold mortality rate compared to non-infected patients (2).

These studies beg the question of why white coat contamination occurs in a place where cleanliness and antimicrobial considerations are of utmost value. A group of researchers determined the fabric blend of cotton and polyester used for making white coats could harbor bacteria for 10 to 98 days (6). Another important factor contributing to contamination is laundering and wearing habits of white coats. While health care workers know their coats may be contaminated, they wear them off hospital premises (7). Laundering habits also play an important role: in the same study, participants reported washing scrubs every 1.7 days, but white coats only every 12.4 days ($P < .001$). Only 50% of these clinicians reported washing their coats with warm water; low-temperature domestic laundry is not effective in decontaminating white coats (8). Another evaluation of laundering habits of 149 grand round attendees found 17% of grand round attendees had not washed their white coat in more than 28 days and 64% had not washed in more than one week (9).

Widespread white coat contamination and improper laundering habits hold important implications for the future of hospital wards. Bacteria is ominously ubiquitous on white coats, and antibiotic-resistant strains pose a dangerous risk. Being informed on white coat contamination and the risks of nosocomial infections is critical in improving patient safety.

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Direct Primary Care: An Alternative to Traditional Fee-For-Service Models

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The current conception of healthcare in America is beset by critics on all sides of the debate. Between private insurance companies and public programs like Medicare and Medicaid, the American system is an amalgamation of multiple models governed by various laws over the past century. Direct primary care (DPC) is an organizational sea change that sidesteps our bloated administrative system and passes the benefits on to physicians and patients alike. It is compatible within the current legislative framework and has already made an impact across the country. Before delving into the details of DPC, this paper will delineate the scope of America's healthcare problem so that this burgeoning industry can be understood in the proper context.

When it comes to healthcare in the U.S., no expense is spared. Health spending as a share of GDP has risen from 5% in 1960 to nearly 18% in 2016 (1). That growth is not reflective of trends seen in other developed countries within the Organization for Economic Cooperation and Development (OECD), where the average spending is a little under 11% of GDP (2). Medicare and Medicaid comprise a significant amount of that, with total government spending clocking in at $1.5 trillion for 2016 (or 24% of all government expenditures; 3). Unless major structural changes are imposed on these government programs, they threaten to swallow a majority of the government's resources. The Medicare Board of Trustees projects a $33.2 trillion deficit in the program over the next 75 years, and it will continue to balloon as more people draw from the system and fewer contribute (4). At its inception, there were 5.5 workers to every Medicare beneficiary. Today, that number has dropped to 4, and it is projected to decline to nearly 2.5 around 2030 as more baby boomers begin to qualify for the program (4).

On the provider end, physicians are increasingly skeptical of reimbursement rates and refusing to even accept more of these patients into their practices. Despite 96% of physicians continuing to accept more patients, 31% of those will not take on board more Medicaid patients (compared to 17 and 18% rejecting new Medicare and privately insured patients, respectively). Low pay is frequently cited as the reason for this discrepancy (5).

It may seem paradoxical that Medicare and Medicaid can simultaneously overwhelm government expenditures yet consistently underpay practices to the point that treating these patients necessarily incurs a loss for doctors. The administrative apparatus itself offers a compelling explanation for this gap; it's no secret that this institution has experienced an explosion of growth. For every 1 physician, there are 10 workers with absolutely no connection to direct patient care (they are purely handling health administrative tasks; 6). Practices are struggling to keep up with compliance of regulations and the tortuous process of filing insurance claims. Even with the addition of this ancillary staff, physicians still find their time exceedingly monopolized by work separate from patient care. Nearly 17% of a doctor's week is spent attending to administrative tasks. Moreover, career satisfaction was found to be negatively correlated with time spent like this away from patient care (7).

Given the myriad challenges and political infeasibility to these problems, DPC serves as an innovative alternative to the current system. A simple way to qualify as a DPC is by meeting three criteria: charging a periodic fee, not billing a third party on a fee-for-service basis, and the per visit fee must not exceed the monthly equivalent of the periodic fee (8). The final criterion is in place to delineate primary care from what would be an urgent care situation. At its core, DPC bucks the trend of traditional practices by cutting out insurance companies from primary practice. The doctor contracts directly with their patients, and many of the benefits are realized expressly because barriers are removed between these two parties.

An earlier prototype of DPC, concierge medicine,

is much more well known. Started in the 1990s, concierge practices pioneered the subscription-based model to primary care delivery. While the average patient would pay $200 a month, concierge medicine earned a reputation for catering specifically to wealthier clients and could be seen charging up to $30,000 a month for their services (9). Doctors, however, recognized the model's potential and began adapting similar methods to democratize the system. Since then, there are now 795 DPC practices in 48 states and Washington, D.C. (8). Most of these are "pure" DPC practices while others are "hybrid" and still retain some form of a traditional system within the practice. To realize the full benefits of DPC, proponents advocate cutting the cord completely to eliminate the overhead that comes with managing patients in the traditional fee-for-service system, but there can be drawbacks to switching wholesale to DPC immediately. New practices may struggle to attract enough patients at the beginning to sustain themselves, and the problem can be compounded by legal and regulatory hurdles (9).

It is difficult to understate how cumbersome the traditional system is. Shedding light on its pitfalls will help put in to context how astronomical savings under DPC can be. The Direct Primary Care Coalition estimates that 40% of all primary care revenue is devoted to claims processing and profit for insurance companies (10). Most doctors surveyed believe that their profession is in decline; some of the "very important" reasons given by a solid majority of these physicians include too much regulation and paperwork, loss of clinical autonomy, and erosion of the physician-patient relationship (11). Eliminating this overhead by adopting the DPC model unleashes the potential for numerous improvements. One study assessed the literature on DPC practices and found that they charged an average of $77.38 per month as part of their model (12). Practices are able to charge 10% of the total healthcare dollar as opposed to half that seen in traditional practices, yet considerable savings are also passed along to the patient. The Medical Group Management Association found that the average traditional practice managed a patient panel of 2,251, with an annual revenue of $276 per patient. DPCs charging just $60 a month receive $720 per patient, meaning they can operate with the same level of revenue on a panel size 2.6 times smaller than other practices (9). Once the suffocating volume problem is lifted off physicians' backs, a virtuous cycle of quality patient care emerges. Qliance, a DPC network serving almost 3,000 patients, is easily able to schedule appointments lasting 30-60 minutes (13). Greater opportunities for patient interaction are superimposed on this by allowing the physician to be more intimately involved in patient care. Providers now have the time to take on tasks that were previously shunted to ancillary staff, like performing their own phlebotomy, giving injections, and returning and making patient phone calls regarding lab results (14). This is how patient satisfaction and perceptions of quality are able to stay high within this model. When doctors, not other personnel, are intimately involved in all steps of a patient's care, those patients will rate their experience more positively. Qliance, for example, maintains a 99% renewal rate on top of a patient base growing 5-20% a month (13).

Staying involved with patients also has the effect of avoiding unnecessary emergency room visits and better management of care before diseases progress to a level requiring hospitalization. By capturing patients in ambulatory care-sensitive conditions like those requiring casting, splinting, or treatment for asthma, pneumonia, and others, Qliance patients have netted 35% fewer hospitalizations, 65% fewer emergency department visits, and 82% fewer surgeries compared to similar populations (15). Much of this can be attributed to the freedom and time afforded to doctors to effectively treat their patients. The standard healthcare model fails far too many patients with chronic conditions, and the issue is compounded by half of chronic patients leaving their appointments without understanding what the physician told them (16). The traditional system is fraught with issues like this, and they are frequently not the fault of physicians or patients. As doctors expand volume to stay afloat, there simply is not enough time with each patient to convey everything that needs to be said.

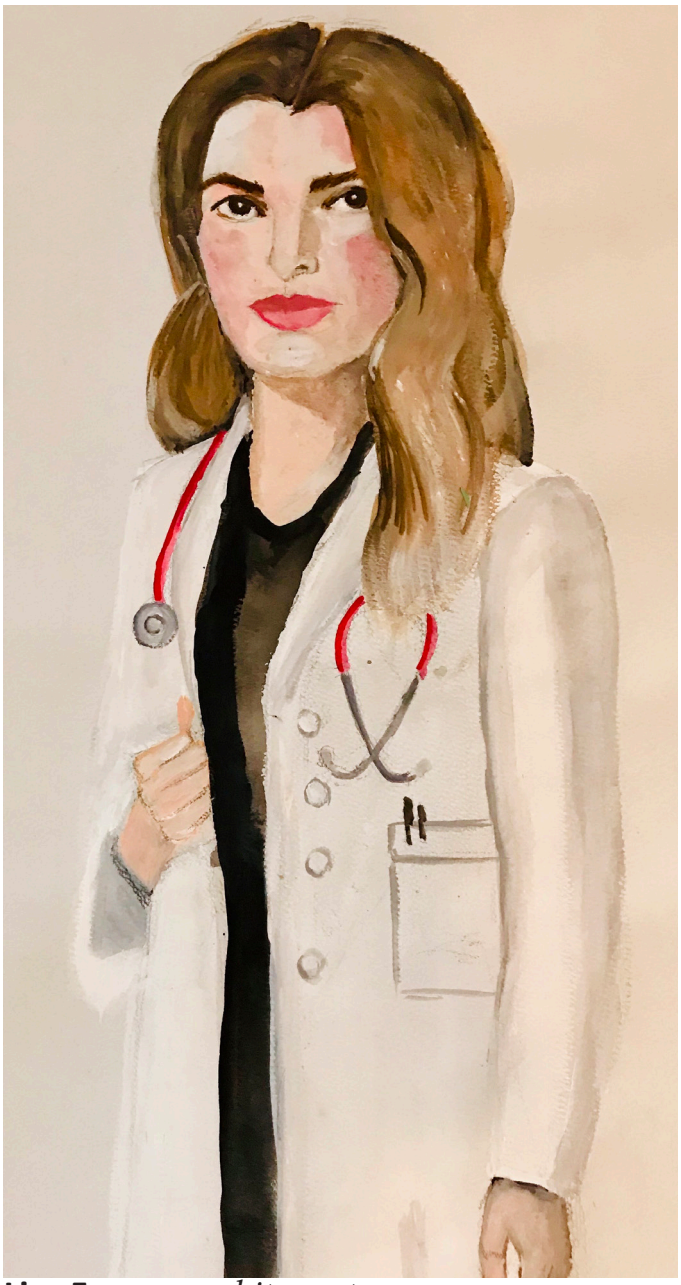
Intervening at these earlier stages is precisely what is needed to take the strain off America's hospital system. MD-VIP, another DPC group, was also able to significantly reduce hospital visits. It is estimated that the decreases in preventable hospital visits from this single network saved $119.4 million in one year alone (15). Primary care physicians are capable of integrating care beyond what is currently practiced, and the emergence of DPC networks has unlocked that potential. Within the traditional system, time cannot be blocked off in the average provider's day to accommodate these patient cases, let alone coordinating patient care with other facilities. Access

Healthcare employs a scheduling model that enables comprehensive care like this for all within its patient panel. 8 to 10 patients are scheduled for a day, and the remaining time is left open for same day call-in or walk-in patients (14). This can be done precisely because physicians are not worried about meeting revenue targets to stay in business. What's more, Access healthcare can charge a flat $150 rate for house call visits and actually has the freedom and time to perform this for home-bound patients (14). All of these factors promote quality physician-patient interaction, and the end result is better care with less need to hand off patients to emergency departments. At its core, improvement in care can be attributed to doctors being able to directly negotiate with their patients. The concept is applied elsewhere so that doctors can further empower their patient panel.

Providers are able to negotiate directly with suppliers like labs and imaging facilities, and this creates savings in the same vein as DPCs eliminating third party payers. Access Healthcare is able to directly pay labs for their services, circumventing the need to work with the ICD coding system mandated within traditional payment models. The practice is able to offer payment in full because there is no concern for claims being rejected due to disputes over improper coding. This alone results in discounts being 50-90% off the list price for lab items (14).

Medication is another expense that DPCs are working to streamline where possible. 35 states currently permit in-house pharmacies, and these DPC practices are capable of providing generic medication at low prices or even at cost. AtlasMD is a prominent DPC that has integrated medicine dispensation, and patients reap the benefits. To cite one example, the practice is able to prescribe Zoloft for depression, direct the patient to their pharmacy to immediately fill the prescription, and refills are made at just $1.50 per month (9).

Traditional insurance still plays a vital role in certain aspects of the healthcare system, and DPC patients are not encouraged to confine health spending to only a membership at their local DPC. "Wraparound" insurance is frequently encouraged to complement the care received at one's family physician. These plans are high deductible, low premium catastrophic insurance that are designed to take care of those suffering a serious health issue that could incur tremendous costs. DPCs are increasing in popularity because their



Lior Fusman: *white coat*

prices are still competitive after accounting for this additional expense. In the case of Qliance, combining the annual membership cost with that of a wraparound plan is still 37% less expensive than purchasing a more typical low deductible, high premium plan seen with the average consumer (13).

Given the intractability of America's situation politically, a search for immediate healthcare solutions is inevitably disheartening. DPC has a proven track record of success, and it is expected to expand in the coming years to cover more and more patients. There are and will continue to be growing pains in this new industry, but this paper has highlighted

unprecedented metrics already being achieved by DPCs across the country. To summarize, the DPC model brings affordable care to patients from lab fees to routine doctor visits. Physicians are able to enjoy manageable patient panel sizes and dedicate more time to each patient, thereby capturing those who would otherwise end up in our congested emergency departments.

It is clear that an alternative model is necessary to supplant the fee-for-service system that stifles both physicians and patients, and DPC may very well be the leader in that movement.

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Key Points: Evolution to Direct Primary Care

•In health insurance, premiums are a fixed amount that must be paid periodically (typically monthly) to have access to that insurance plan. Deductibles list an amount that one must pay for a service. Beyond that value, the insurance company will cover the difference (except for a flat rate or percentage you will still need to contribute)

•The International Classification of Diseases (ICD) is the coding system used to classify every possible health event. Coding is necessary for physicians so that they may be reimbursed by insurance companies for the services they provide. The latest edition, ICD-10, has ballooned to 87,000 codes. For example, Y93.D: V91.07XD is "Burn due to water-skis on fire, subsequent encounter."

Home Cooking: A Simple Way to Reduce Risk of Type 2 Diabetes Mellitus

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With obesity on the rise in the United States, it is no surprise that the prevalence of associated metabolic disorders such as type 2 diabetes mellitus (T2DM) is also increasing. Type 2 diabetes mellitus presents with a decreased ability to utilize sugars in one's body, due to insulin resistance, and is highly associated with obesity. According to a 2017 statistical report released by the Center for Disease Control (CDC), more than 100 million adults in America are currently living with diabetes or prediabetes (1). Furthermore, diabetes was the seventh leading cause of death in the United States in 2015. However, what makes diabetes even more insidious is the alarming lack of awareness that Americans have regarding their disease status. CDC Director Brenda Fitzgerald, M.D. states that "more than a third of U.S. adults have prediabetes, and the majority, don't know it" (1).

Thankfully, diabetes can be managed through proper exercise, diet, and medications if needed; lifestyle changes can drastically alter and improve the prognosis of the disease for the better. In a recently published review titled Prevent Type 2 Diabetes with Home Cooking: Current Evidence and Future Potential from the October 2018 copy of Current Diabetes Reports (Volume 18, Issue 10), researchers drew upon various publications across multiple medical journals in order to highlight the inextricable link between proper dietary intake and prevention of T2DM (2). Specifically, the article discussed the use of home cooking as a means for healthy nutritional intake, thereby reducing one's risk for developing T2DM.

Some may wonder what exactly is "home cooking". According to Mills et al., home cooking is defined as "the action required for preparing hot or cold foods at home, including combining, mixing and often heating ingredients" (3). Thus, contrary to what the term suggests, simply preparing cereal with milk or heating a microwaveable meal at home does not constitute "home cooking." Rather, home cooking should be seen as a method of self-care, a conscious effort of fueling the body with nutrients and "[creating] meaning, purpose, and connection" in life through food.

Madhumita Govindaswamy: *cooking therapy*

Researchers in the United Kingdom evaluated a population-based cohort consisting of individuals between the ages of 29 to 64 and found that those who consumed home cooked meals more frequently (>5 times per week vs. <3 times per week) had a greater chance of having a BMI and body fat percentage that fell within the normal range. These individuals also consumed 62.3 g more fruit and 97.8 g more vegetables per day, on average (2).

The relationship between home cooking and nutritional intake was investigated further in a cross-sectional study from the National Health and Nutrition Examination Survey (NHANES). Data from NHANES showed that individuals who cooked dinner at home more often consumed less calories, less fat, and less sugar compared to their counterparts who did not cook at home as frequently (2).

New findings from the Harvard T.H. Chan School of Public Health report that people who ate more meals prepared at home were less likely to develop T2DM, while those who dined out more frequently increased their risk of developing T2DM. Over the course of 26 years (1986 – 2012), 58,051 women and 41,676 men and their dietary habits were followed. Researchers concluded that people who ate 11 to 14 homemade meals per week had decreased their chances of developing T2DM by 14% compared to people who ate 6 or less homemade meals per week (2).

The results from this study was covered in the media, not only due to the sheer magnitude of the study, which involved a large cohort of individuals over a significant period of time, but because it provides the average individual with a simple and effective method to decrease their risk for T2DM. As diabetes continues to become a global health crisis, more research that looks into the relationship between home cooking, diet, and health is being conducted. Not surprisingly, more and more evidence supports the notion that home cooking is associated with decreased risk of developing T2DM and other cardio-metabolic disorders, in addition to improved overall health.

Key Points: Homecooking Decreases Risk of T2DM

- Homemade meals require active preparation such as by combining, mixing and heating of hot or cold food at home and it does not include heating microwave dinners or having cold cereal.
- People who ate 11 to 14 homemade meals per week had a 14% lower chance of developing T2DM than those who ate 6 or fewer homemade meals per week.
- People who consumed homemade meals >5 times per had a greater chance of having a BMI and body fat percentage that fell within the normal range.

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The Global Refugee Crisis: Health, Policies and Practices

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Refugee protection: then and now

As Erika Feller, Director of the Department of International Protection, United Nations High Commissioner for Refugees (UNHCR), eloquently states: "refugees have existed as long as history, but an awareness of the international community to provide protection to refugees [is far more recent]" (1). The end of the first World War and the Paris Peace Conference catalyzed the establishment of the League of Nations (LN) in 1920 and the appointment of Dr. Fridtjof Nansen as the first High Commissioner for refugees in 1921 (1). The LN's primary intention was to resettle Russian refugees, which later extended to Armenian, Assyrian, and Turkish refugees in the late 1920's (1). This represented a fundamental shift from the preceding years on a global scale: for the first time, refugees were formally recognized in the global arena as individuals in need of protection and resettlement. Following the Second World War, the International Refugee Organization (IRO) was established in 1947 as a temporary measure to address the needs of refugees in Europe (1). However, by 1950, the breadth of the European refugee crisis required a much greater, multilateral approach than purely focusing on resettlement. Indeed, the refugee crisis required refugee registration, status determination, repatriation, resettlement, and protection in a concerted effort on an international scale. Thus, in 1949, the United Nations General Assembly formally replaced the IRO with the UNHCR, tasked with "providing international protection for refugees and [seeking] permanent solutions to their problems" by collaborating with and assisting governments in refugee resettlement (1). In 1951, with a budget equivalent to just $289,000 and 33 staff, the UNHCR began its work in the global refugee protection scheme, beginning with the resettlement of millions of individuals fleeing European Communism and Nazi Germany (1).

Yet again, the world faced another paradigm shift in refugee protection following the conception of the 1951 Convention and Protocol Relating to the Status of Refugees (Hereafter "1951 Convention"; 1). Grounded in human rights principles such as the right to seek asylum, the 1951 Convention is the first and only enduring, universal refugee protection instrument (1). Above all, the 1951 Convention established guidelines for refugee protection, established the "non-refoulement" principle, and created a global definition of a refugee, applying to any person who:

Owing to a well-founded fear of being persecuted for reasons of race, religion, nationality, membership of a particular social group, or political opinion is outside the country of his nationality, and is unable to or, owing to such fear, is unwilling to avail himself of the protection of that country (2).

While the 1970's was a decade that fostered international solidarity in resettling refugees and asylum seekers (AS), the 1980's and 1990's stood in stark opposition. Fearful for the threat that refugees may impose on political, economic, and social structures, many governments started closing their borders and retrenching upon their 1951 Convention obligations (1). A paradigm shift in refugee protection is noted yet again: restrictive policies and resurgent xenophobia were provoked by a growing concern about the cost- in all definitions of the term- of resettling refugees.

Recently, conflict and political unrest in the Middle East and Africa have redefined refugee and AS migration patterns (3). Current research suggests that the refugee and AS migratory period involves three main stages: premigration, migration, and postmigration (4). During these periods, refugees and AS are confronted with three sets of transitions: reconstruction of social networks, migration from one socioeconomic structure to another, and migration from one cultural system to another (4). Each migratory phase and transition is associated with serious physical and mental health risks.

In 2015, UNHCR Global Trends reported that the three major countries of refugee resettlement, offering legal and physical protection and access to civil and social rights, were the United States of America, Canada, and Australia (5). Interestingly, in the face of the exponential growth of the global refugee crisis, high-income countries have instead enacted harsher, more violent, and more restrictive migration policies (3). These measures shift the emphasis of protecting the refugee to protection from the refugee, overriding the principle of humanitarianism with fear of the other and a need for control.

By the end of 2016, the UNHCR proclaimed that the world is witnessing the highest levels of displacement ever recorded (6). With the well-known health risks of the migratory experience and global refugee and AS numbers as high as 22 million and 3 million respectively, a consorted global effort is as pressing as ever (6).

A note on global health

The World Health Organization (WHO) defines health as a state of "complete physical, mental and social well-being and not merely the absence of disease of infirmity" (7). Health is also a fundamental component of attaining peace and security, dependent on individual, state, and international cooperation (7). The definition of global health goes one step further by acknowledging that the spread of disease is not bound by social or geographical barriers, thus emphasizing the role of globalization and increased global connectedness in attaining health (8). Global health explores the links between health, human rights, economics, political discourse and equity. To quote Benatar and Upshur (2011), global health is thus "about health in a world characterized by spectacular medical advances and amazing economic growth but also by aggravation of wide disparities in health and well-being by powerful social forces" (8; p.14).

With numbers of refugees and AS reaching never-before-seen heights, and an increasing awareness of the unique health and mental health concerns and barriers that this group faces, refugee and AS health is an ever-important area in the global healthcare arena. But in the face of the growing refugee crisis, the prevalence of restrictive refugee policies begs the question: are countries enacting refugee policies to ensure the wellbeing of this vulnerable population, or are they doing so with the intention of merely upholding international law?

Intersection of migrant status and health outcomes

Health status is largely influenced by social determinants of health: access to healthcare services, language and literacy, housing, education, employment, and absence of racism, xenophobia, and discrimination (9). Interestingly, these determinants are in fact barriers to refugees and AS in both Canada and Australia, as many struggle to access language services, lack familiarity with new health services and systems, and perceive discrimination fostered by a migration policy based largely on deterrence. Of particular interest, Australia's policy of indefinite and arbitrary detention has been noted to contribute to detrimental physical and mental health outcomes for detainees. The health consequences of mandatory detention are well-documented and vast: self-harm, suicidal ideation, Major Depressive Disorder (MDD) and Post-Traumatic Stress Disorder (PTSD) represent just four of the numerous negative mental health outcomes of the policy (10). In a 2013 report of 12,000 AS in community detention, over 2300 disclosures of torture and trauma, and over 30% of adults suffering from MDD, anxiety, and stress was noted (9).

The health implications of mandatory detention for children are especially concerning and highly documented. In 2004 and 2014, The Australian Human Rights Commission (AHRC) published national inquiries into the treatment of children in immigration detention entitled, "The Forgotten Children". Between 2013 and 2014, the AHRC reported over 230 of documented assaults involving children, and 128 incidents of self-harm in children (9). Yet, in spite of the well-known health implications of held detention for children, as of June 2016, 49 children remained in offshore detention centers, while nearly 300 resided in community detention (11).

The implications of Canada's refugee determination policies and practices on refugee and AS health are less well known; recent changes and revisions to Canada's refugee policy in 2012 have resulted in confusion about who holds health insurance, leading to poor differentiation of migrant groups in research findings (12). Research suggests that socioeconomic factors are more important in determining health for

migrants than non-migrants; therefore, policy changes may disproportionately affect health access and outcomes of refugees (13). Moreover, policy changes that affect health service availability for refugees may disrupt social support systems, threatening refugee health even more (13). This is demonstrated by Evans et al (2014) identifying that while the proportion of refugee admissions to the emergency room significantly decreased following the 2012 policy changes, admission rates for refugee children doubled significantly compared to six months before the changes. Compounded by the fact that refugees are twice as likely to encounter difficulties in accessing healthcare, these findings suggest that refugee policy changes are an additional barrier when accessing healthcare (14).

Olivia Keller-Baruch: *Save one, Save the world*

Globalization and the sovereign state

Globalization, the "increased connectedness and interdependence of peoples and countries" has resulted in the opening of international borders to the flow of goods and services, finance, ideas and people, and has marked the latter portion of the 1900s (15, 16). With the rise of contemporary globalization came the mobilization of refugees and AS; enhanced transnational networks lowered the cost and difficulty of transnational migration (15). However, this era of contemporary globalization also introduced a threat to border control, security, national identity, and state sovereignty (17).

Joppke (1997) defines state sovereignty as "the assertion of final authority within a given territory" (p.292). Indeed, the idea of a national identity is predicated on the assumption that there is a clear division between the "self that is part of the nation, and the external which belongs to another nation" (18, p.253). The blurring of national-foreigner distinction offers a reason for why migration is interpreted as a distortion of national security and identity and therefore, an assault on state sovereignty. In this sense, the UNHCR's 1951 Convention challenged the notion of national identity and state sovereignty, causing a conundrum that is commonly referred to as the Liberal Paradox: economic competition in the global arena pushes borders open to trade and migration, while security and political concerns pulls borders closed (15). In an attempt to defend national identity in the era of globalization, states may implement restrictive refugee and asylum policies, excluding migrants through visa requirements, safe country rules, interceptions at sea, or inadvertently targeting certain migrant groups (17). This gives states the power to neutralize international obligations without violating them, and protect their borders without closing them.

One way to preserve national identity and sovereignty through policy is by creating an "othering" refugee discourse, marking refugees as different from the "self" part of the nation (19). In differentiating state nationals from refugees and AS, the "othering" discourse secures and clarifies national identity by effectively creating a distinction between "us" and "them" (19). Therefore, othering not only strengthens national identity, but also associates refugees and AS with threatening national security, and intruding on state sovereignty. By this logic, the "othering" discourse frames refugees and AS as illegal, and can contribute to a paradigm shift that focuses less on protection of the refugee, and more on protection from the refugee instead.

Conclusion

Paul Flowers (2001) states, "the social construction of boundaries of 'self' and 'other' and their relationship to boundaries of 'safety' and 'danger' are particularly relevant to understand notions of health and disease" (20, p.51). In the wake of over 25 million refugees and AS seeking protection worldwide, compounded by restrictive and deterrent refugee policies, policy reform is more important now that it has ever been. The "othering" discourse, seeking to differentiate

state nationals from foreign nationals in the era of globalization, has painted refugees and AS as both illegitimate and threats to national security and social services, which therein threatens their access to healthcare and jeopardizes their health outcomes. The significance of the global refugee and AS crisis is more prevalent than ever before, and cannot be understated. Indeed, although the 1951 Convention is approaching its 70th anniversary, the human rights principles on which it is grounded cannot be weakened by age.

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Key Points: Globalization, Global Health, Refugee

- The United Nations defines "refugee" as any individual who is fleeing their country of origin due to fear of religious, racial, national, social or political persecution
- The world has recently experienced the greatest refugee crisis, with global refugee and asylum seeker numbers as high as 22 million and 3 million respectively
- Instead of opening borders, high-income resettlement countries have enacted harsh migration policies predicated on avoidance and deterrence that negatively impact health opportunities, health seeking behavior, and health outcomes of refugees and asylum seekers alike

A Unique Case of *Salmonella Paratyphi* Leading to Myocarditis

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Abstract

A 19-year-old male presented to the ED with fever, rash, and chest pain. History included recent travel to India, MSM (men-who-have-sex-with-men) with unprotected intercourse, and never receiving childhood or travel vaccinations. The patient had an ECG, which was normal, was put in an airborne infection isolation room, had blood cultures drawn, was started on broad-spectrum antibiotics, and had an echocardiogram performed. His WBC count was within normal limits, while his troponin levels were elevated to 100 µg/L, and LDH elevated to 924 U/L. On the fourth day of admission, blood cultures were positive for *Salmonella paratyphi* leading to clinically suspected myocarditis. The patient was monitored until his vitals returned to normal, and was discharged on outpatient antibiotic treatment.

Background

Many Israelis travel in their early twenties to areas endemic to many pathogens that are not present in the Western world. This case was unique in its combination of several high risk factors of non-vaccination, MSM, and recent travel. Furthermore, it is unique in its presentation, as *Salmonella paratyphi* is a rare cause of myocarditis.

Case Presentation

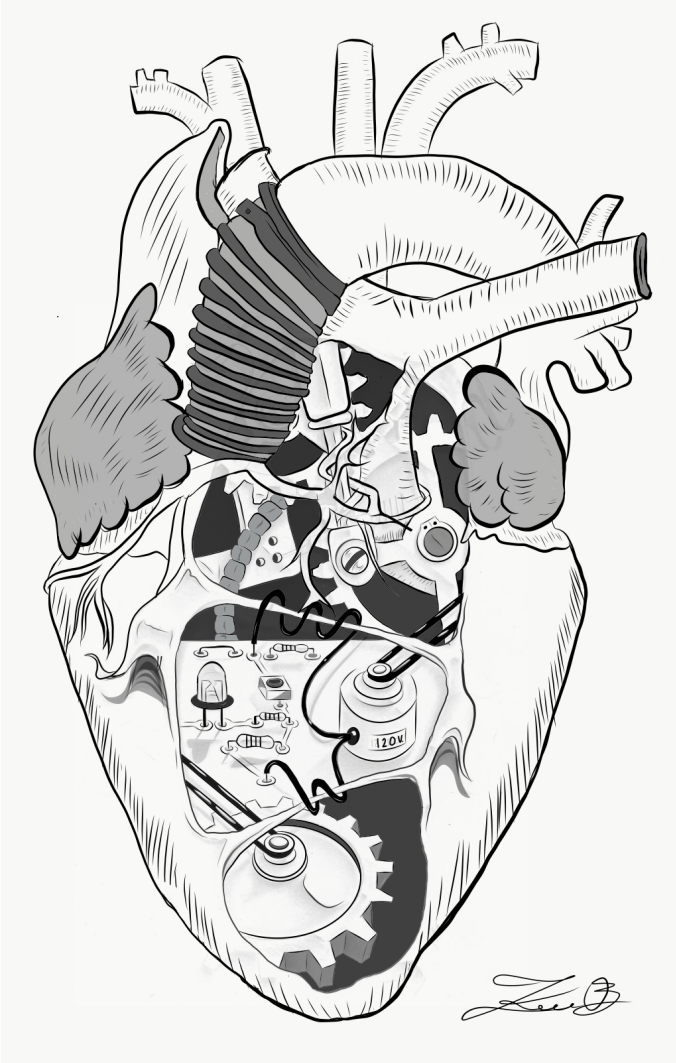
A 19-year-old male patient presented to the ED with complaints of one week of fever and one day of chest pain. Sixteen days prior to admission, the patient returned from a two-week trip to India with his family. On the sixth day of his trip, he experienced one day of diarrhea, which he described as watery, large in volume, and non-bloody. He had nausea, but no vomiting. He felt fine for the rest of his trip and upon his return to Israel. During his trip he ate chicken, fish, masala dosa at restaurants and got a tattoo. While in India, he did not come into contact with animals, had no known insect bites, and denied use of drugs or sexual contact. A week prior to admission, the patient started experiencing headaches, fever, shivering without teeth involvement, loss of appetite, and night sweats. The headache was described as bilateral, and mainly in the paranasal, parietal, and occipital areas, without auras or photophobia. No medications were taken for his pain or fever. The fever, shivering, and headache continued for a full week up to his admission. One day prior to admission, the patient complained of a pressured chest pain that localized to his sternum and left side. The pain decreased when the patient leaned forward, was undulating every 30 minutes, non-pleuritic, non-radiating, and not related to exertion.

On admission to the ward, the patient had a fever of 39°C, a headache, chest pain, and a newly discovered rash on his chest. The rash was well circumscribed, erythematous, blanching, non-pruritic, and covered his entire chest down to his epigastrium. His vitals were: heart rate 102 bpm regular, blood pressure 121/67 mmHg, oxygen saturation 100% on room air.

Upon further questioning several important risk factors came to light. First, he never received childhood vaccinations or travel vaccinations. Second, he had an episode of unprotected anal sexual intercourse with a man, six months earlier. He was never tested for sexually transmitted infections, including HIV. These risk factors, combined with his recent travel to India, significantly broadened the differential.

A focused physical exam was performed:

The patient was alert and oriented, appeared unwell. Skin had color. Lung exam was normal. Cardiac exam was normal with no murmurs or extra heart sounds. No friction rub. Abdomen was soft, with normal bowel sounds. Tenderness was present in the LUQ



Olivia Keller-Baruch: *Heart of tin*

upon palpation with deep inspiration. Liver span estimated to 10 cm along mid-clavicular line. Spleen was not appreciated. No Koplik spots on buccal mucosa. No conjunctivitis. No evidence of DVT. No nuchal rigidity.

Investigation

After the physical exam, an electrocardiogram and chest radiograph were ordered and found to be normal. Blood analysis revealed WBC of 7.34×109/L, Neutrophils 3.3, and Hb of 15.1 g/dL. His troponin was elevated to 100 µg/l, LDH 924 U/L, and CRP 5.1 mg/L.

The differential diagnosis for fever and rash in an unvaccinated patient included:

Viral: Measles– the patient is unvaccinated, recent outbreak in Israel. However, no Koplik spots, no coryza, no conjunctivitis, not maculopapular. Rubella, EBV, CMV, HIV, Zika, Japanese Encephalitis, Calicivirus.

Bacterial: *Salmonella Typhi/Paratyphi*– the patient was not vaccinated, known to cause abdominal pain, fever, usually presents with rose-colored macular rash.

Differential diagnosis for chest pain: Myocarditis– chest pain along with infection, elevated troponin. Myopericarditis– chest pain that is relieved by leaning forward. But no typical ECG changes for pericarditis. Variant Angina– pressured chest pain, elevated troponin, can have normal ECG. No known risk factors. Pneumonia– fever, can cause sharp chest pain. Patient did not have a cough, chest pain was described as substernal pressure. PE– patient had good saturation, no evidence of DVT.

Further studies were ordered:

Triple blood cultures; NAAT blood and/or urine testing or antibody tests for Viral causes; HIV Ag/Ab test; Echocardiogram to assess for pericardial effusion. He was prescribed broad-spectrum antibiotics, Ceftriaxone and Azithromycin.

On the third day of admission:

The patient appeared to be improving. His temperature is now 36.5°C. The blood culture grew a gram-negative organism. His echocardiogram was normal with no effusion and no regional wall motion abnormality. The rash disappeared and he no longer had chest pain. PCR test results came back negative for acute EBV, CMV, and negative for HIV. The patient still has abdominal tenderness.

On the fourth day of admission:

On appearance, the patient experienced further improvement and is in good spirits. His abdominal tenderness had lessened. The blood culture was shown to grow *Salmonella paratyphi*.

On the seventh day of admission:

The patient continued improving and was released with home IV antibiotic therapy.

Discussion

Salmonella paratyphi is a motile gram-negative bacterium that causes enteric fever, similar to that caused by *Salmonella typhi*. It has fecal oral transmission, with a higher likelihood of transmission outside of the home, such as travellers eating at street vendors (1). In a study of travellers from developed countries who were infected with *paratyphi*, 34% visited India (2).

Salmonella paratyphi can survive the acidic gastric juices of the stomach, invade the small intestine through the epithelium to lymphoid tissue, and disseminate through lymphatic or hematogenous channels. Enteric fever onset typically begins 5 to 21 days after ingestion, which fits the timeline of our patient. The fever is described with bacteremia responsible for associated chills, without teeth chattering, which is what our patient describes. Concurrently abdominal pain frequently begins and typical salmon coloured "rose" macules break out. Our patient described abdominal pain, however the rash on presentation was not the typical macular rash associated with Enteric Fever. Other typical symptoms include hepatosplenomegaly, intestinal bleeding, and perforation. Although our patient had pain in the left upper quadrant, an enlarged liver and spleen was not appreciated upon palpation or percussion. He also denied bloody stools (1).

The typhoid vaccine has not shown to be effective in preventing infection with *Salmonella paratyphi*, although the oral Ty21a has shown inconclusive results (3).

Myocarditis is an inflammation of the heart myocardium, due to a wide variety of instigating factors. Some non-infectious causes include allergens, toxins, heavy metals, and radiation, while infectious cause include: Coxsackie A and B, adenovirus, parvovirus B19, HIV, *Staphylococcus aureus*, *Streptococcus pyogenes*, and *Borrelia burgdorferi*. *Salmonella paratyphi* is considered a rare cause of myocarditis, with only 1 – 5% of infections leading to cardiovascular complications (4). The diagnosis of clinically suspected myocarditis was made based on criteria from European Society of Cardiology 2013 position statement requiring at least one clinical presentation and one diagnostic criteria. Our patient presented with acute chest pain and elevated troponin, meeting these criteria. A definitive diagnosis could not be made as the patient did not undergo biopsy or MRI testing, due to his improving condition (5). A diagnosis of myopericarditis was considered. Pericarditis is the inflammation of the pericardium due to infectious, and non-infectious causes. Furthermore, inflammation can spread from adjacent myocardium. This patient experienced relief of pain by leaning forward, a classic physical finding for pericarditis. However, this sign alone does not satisfy the criteria for pericarditis, which requires at least two out of four criteria: typical chest pain, pericardial friction rub, suggestive ECG changes (diffuse ST elevations), and new or worsening pericardial effusion (6). The patient had normal auscultation findings, a normal ECG, and no pericardial effusion on echocardiography. Myocarditis is a serious complication of infection, which can result in global dysfunction and dilation of the four chambers of the heart. The family's initial reluctance to seek medical attention, waiting for a week with a high fever, put the patient at extreme risk. This allowed the bacteremia to spread to his heart, and could result in long-term complications, such as congestive heart failure.

Although significant, the risk factors that this patient had, did not affect his infection or prognosis. There is no proven vaccine for *Salmonella paratyphi*. Therefore, this patient's lack of vaccination did not change the likelihood or timeline of him being infected with *Salmonella Paratyphi*. Although the patient has a history of unprotected anal intercourse with MSM, this did not directly affect his risk of being infected with *Salmonella Paratyphi*. The most significant risk factor in this case was travel to an endemic area.

Unvaccinated patients are at increased risk for several life-threatening diseases both in childhood and adulthood. Measles virus can cause encephalitis, mumps can cause orchitis and sterility, *Streptococcal Pneumoniae* can cause pneumonia and meningitis, *Haemophilus Influenza* can similarly cause pneumonia, meningitis, and epiglottitis, Hepatitis A and Hepatitis B virus can cause hepatitis and liver failure, Human Papillomavirus can cause genital warts and lead to cervical, penile, or anal cancer. Vaccinations have significantly reduced the incidence of these illnesses, provide herd immunity to those not able to be vaccinate, and ease the burden of antibiotic use.

Men who have sex with men, MSM, are at increased risk for HIV and other STIs. MSM represent the largest proportion of those newly infected with HIV, representing 70% of new cases in 2014. The recommended screening is once a year for asymptomatic patients, and more frequently for those engaged in high risk behaviour. The spread of HIV and STIs can be stopped by using barrier contraception, while other options such as PREP are shown to minimize risk of infection of HIV only.

Therefore, it is highly recommended to get vaccinated with childhood and travel vaccines, use protection during sexual intercourse, and undergo frequent screening for HIV and STIs for those at increased risk.

Conclusion

A patient that presents with several high risk factors must be investigated thoroughly, with weight given to each risk factor. Precautions such as isolation, ancillary tests such as STI testing, and a detailed patient history including travel and sexual history, should be taken. We presented here a unique complication of a serious infection in a patient with several high risk factors. This patient, who presented with fever, rash, and chest pain, had recent travel to India, where he ate local food and contracted *Salmonella paratyphi*. The untreated infection worsened in its second and third week, eventually spreading to his myocardium. Upon initiation of antibiotic treatment, the fever lowered, the rash resolved, and chest pain diminished. Another example of modern medicine extending the life of a young man.

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Key Points: *Salmonella Parathyphi* Associated with Travel and Pericarditis

- Recent travel should be included in any clinical investigation. For example 34% of Salmonella paratyphi cases came from patients with recent travel to India.
- It is important to remind patients at routine visits that they should book an appointment if they have plans for travel to makes sure they have the appropriate travel vaccinations and receive counselling.
- Signs of pericarditis include chest pain, pericardial friction rub, suggestive ECG changes (diffuse ST elevations), and new or worsening pericardial effusion. Clinical diagnosis requires 2 of the 4 criteria.

Dizziness in the Elderly Patient

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Abstract

The patient presented in this case came to the emergency department with sudden onset of dizziness, a common presentation with a wide differential diagnosis in medicine. Neoplasm, trauma, neurologic, and drug-induced are a few of the many etiologies of this particular symptom. This case highlights the importance of taking a thorough history and exploring the patient's past medical history, as well as his social habits, in order to narrow the diagnosis and provide the appropriate treatment. Our case explores transient ischemic attacks, and distinguishes them from cerebrovascular accidents and other illnesses that could present similarly.

Case Presentation

A 68-year-old single male presented to the emergency room after a day of dizziness and unsteadiness while entering his car on the way to the gym. As he was entering, he "felt as though he was drunk," despite not having consumed any alcohol. He went back into his house to rest and slept for five hours; during this time, the symptoms resolved. As he rose from his bed, he again felt dizzy and weak, resulting in emesis. At this point, no change in positioning helped with his symptoms and he went to the local clinic. Following evaluation, he was sent to the emergency room and admitted into the internal medicine department. During the early hours of his hospitalization, he developed a headache upon waking from sleep as well as double vision, more prominent in his left eye. We evaluated him for other concerning neurologic abnormalities – speech and visual disturbances, motor weakness, or sensory abnormalities – all of which were negative. We also checked for other nonspecific yet concerning symptoms – fever, nausea, and sweating – which were negative as well.

Based on this patient's presenting symptoms – dizziness, weakness, headache, and double vision – a neurologic etiology is the most concerning at the moment. Although all patients should undergo a complete physical examination upon admission, our patient should especially undergo a full neurological exam. This exam includes testing for: cranial nerve function, sensation of the body and extremities, motor function, muscle strength, reflexes, and cerebellar function (repetitive motion, proprioception, gait stability, and coordination). If a neurological cause is the source of our patient's symptoms, a thorough neurological exam can localize the insult. The patient underwent a complete neurological evaluation, and everything was normal aside from a wider stance while walking.

Thus far, our clinical suspicion still pushes us towards a neurological cause. However, we want to take a deeper look into our patient's history, to see if there are any risk factors that would support our current suspicion or contradict it. Our patient has had hyperlipidemia and hypertension for 25 years; they are managed with Lipitor (atorvastatin) and Vector (valsartan), respectively. He is mostly compliant with this medication regimen. He was involved in an accident at work two and a half years ago, resulting in a leg injury. He opted for natural recovery rather than screw placement surgery. The patient was also involved in a car accident with head trauma that required 36 staples in his head; however, he could not recall when this accident occurred. Our patient's hypertension and hyperlipidemia put him at higher risk for a transient ischemic attack (TIA), which helps narrow down our diagnosis. Additionally, our patient had a 185 pack year smoking history and 30 year history of drinking half a bottle of vodka a day. Although he quit smoking 20 years ago and drinking 6 months ago, these habits put him at a significantly higher risk for TIA as well.

Differential Diagnoses

A TIA describes a brief moment of neurologic dysfunction, during which time there is a loss of blood flow in the brain without tissue death. Within this

category, vertebrobasilar artery insufficiency seems to fit the clinical picture the best. It is a brief loss of blood flow in the posterior circulation of the brain. The vertebrobasilar arteries supply the upper spinal cord, brainstem, cerebellum, and posterior part of the brain. This localizes the TIA to a specific artery that characterizes the presenting symptoms.

Patients typically experience symptoms affecting the visual fields of both eyes. Our patient described double vision in his left eye, which would also be consistent with the partial occlusion of vessels for both eyes. Additionally, cortical ischemic attacks are typically brief in duration and occur in older individuals, and the patient has a history of hyperlipidemia and significant smoking history, which contributes to atherosclerosis and stenosis of the vertebral arteries. Finally, CT angiography showed significant stenosis of both vertebral arteries, confirming the diagnosis. However, the quality of the visual disturbance contradicts this diagnosis. Typically, the visual symptoms include fogging or graying of vision, with flashing lights or other indications that mimic a migraine (which the patient did not describe). Additionally, the TIA was followed by headaches in the hospital, which is atypical for this kind of ischemic attack; these negatives are not sufficient to rule out TIA of the vertebrobasilar arteries. Finally, this diagnosis does not explain the macrocytosis (large blood cells) seen in laboratory tests. This could be explained by the history of alcohol consumption and unrelated to the present illness.

Also on the differential is vestibular neuritis (vestibular neuronitis, labyrinthitis), an inner ear disorder that affects the vestibulocochlear nerve (cranial nerve VIII). Our patient presented with sudden onset vertigo, vomiting (although only one episode), and gait instability – pathology of this cranial nerve can cause this presentation. He also had positive serology for EBV IgG, indicating a past infection, and this infection has been found to be associated with vestibular neuritis as a precipitating factor. However, brain imaging shows vertebral artery stenosis, and vestibular neuritis is typically ruled out based on imaging. Finally, and most importantly, there was no evidence of hearing loss, which rules out labyrinthitis.

Although less likely, included on the differential is Wernicke Encephalopathy (WE). Our patient presented with gait ataxia and ocular disturbances. The classic triad for WE is encephalopathy, oculomotor dysfunction, and gait ataxia, but studies have shown that this triad is only present in about a third of patients (1), and patients will usually only have one or two of the symptoms in the triad. The patient presented with nystagmus and dizziness without hearing loss, common findings in WE, with the latter contributing to gait ataxia. Cardiovascular changes were apparent on EKG (tachycardia), however beriberi (thiamine deficiency) is a common manifestation of WE, causing high output heart failure, which was not shown to be present. The most significant support of this diagnosis was the patient's history of alcohol abuse. However, the patient does not present with encephalopathy, a symptom that defines the illness. Generally, patients with a strong history of alcohol abuse, as present in our patient, do in fact present with the classic triad, but our patient does not present with marked encephalopathy (2).

Conclusion

After exploring our top three potential diagnoses, vertebrobasilar artery insufficiency seems the most likely diagnosis. Imaging clearly showed stenosis of the vertebral artery, which is sufficient evidence to rule out the other two possible etiologies. Fortunately, our patient's symptoms were transient and did not progress into a cerebrovascular accident with any permanent loss of function. Treatment will entail managing the stenosis such that there are no future TIAs or ischemic infarctions of the brain as a result of dissolution of thrombus causing the occlusion.

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Fever of Unknown Origin With Suspicion of Rickettsial Infection

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Abstract

We report a case of Fever of Unknown Origin in a 36-year-old man admitted to the hospital with a one-week history of fever, weakness, chills and myalgias. Infectious etiology was suspected, however the diagnosis remained inconclusive after thorough investigation. The patient developed a rash on his chest on the third day after admission, which disappeared after 24 hours. Upon initial presentation, the patient was immediately started on doxycycline to no effect after 8 days of hospitalization. Despite this, he began to clinically improve after two weeks of hospitalization. We suspect rickettsial infection based on the presentation and the patient's occupation exposing him to fleas. However, because it highly unusual to see no clinical improvement after 8 days of doxycycline treatment, further discussion is warranted.

Background

The modified criteria for Fever of Unknown Origin (FUO), originally set forth by Petersdorf and Beeson in 1961, includes the following: a temperature of 38.3 Celsius on at least two occasions; an illness duration of at least three weeks; failure to reach a diagnosis despite thorough history-taking and physical exam; and unrevealing obligatory evaluations (1).

The majority of cases can be classified due to infectious, malignant or autoimmune disease (2). More than 50% of FUO cases remain undiagnosed. Diagnostic approach should include a thorough history taking with the following information: animal exposure, travel history, immunosuppression, drug and toxin history, and localizing symptoms. A minimum routine evaluation should include inflammatory markers, LDH, creatinine, three routine blood cultures, tuberculin skin test, HIV immunoassay, antinuclear antibodies, rheumatoid factor, serum protein electrophoresis, and whole-body imaging (3).

Case presentation

A 36-year-old male veterinarian presented to the emergency department secondary to a history of fever, weakness, and chills. He described waking up with weakness and chills on the first day without fever. Taking two pills of paracetamol temporarily alleviated these symptoms. The following day, the symptoms returned and were similarly alleviated by medication. On the third day, the patient woke up with a new aching pain and fever, in addition to the previously mentioned symptoms. At home, his fever was 38 Celsius. He took ibuprofen PO 400mg, which alleviated the pain. One day later, the patient's fever rose to 39 Celsius and he presented to the emergency department. On his third day of admission, doctors noticed a maculopapular rash on the abdomen and back that disappeared within 24 hours. After the rash disappeared, the patient noticed muscle pain localized to his legs and abdominal bloating.

His wife reported a few days of diarrhea one week prior to his symptoms. Patient has significant exposure to dogs, cats and a horse in the last month, with reports of scratches and contact with fleas. He also travelled recently to northern Israel, where he went swimming in the Jordan River. Patient denies any diarrhea, constipation, changes in urine frequency, dysuria, or swelling. He has no history of pork consumption and no relevant past medical history.

Investigations

Blood investigations were unremarkable apart from normocytic normochromic anemia and lymphocytopenia. Chemistry was remarkable for elevated liver enzymes with a hepatic pattern, decreased synthetic function, and elevated lactate dehydrogenase. Inflammatory markers were elevated,

Olivia Keller-Baruch: *health*

and hypocalcemia and hypouricemia were also noted.

Autoimmune screens, including antinuclear antibody (ANA) and rheumatoid factor were negative. Imaging studies such as abdominal ultrasound indicated a slightly enlarged spleen, without gallbladder obstruction. Chest X-ray and ECG were unremarkable. During admission, total body CT was performed to investigate for malignancy, but no new findings were seen.

Infectious etiologies such as hepatitis A, B and C were ruled out by antibody testing. Serological and PCR testing for *Coxiella burnetii* (Q-Fever), *Bartonella henslae*, *Brucella*, *Leptospirosis*, HIV, Cytomegalovirus, Ebstein-Barr virus and Parvovirus were negative. Serology for the working diagnosis of Rickettsia also came back negative one week after admission.

During hospitalization, the patient was given antipyretics and started on doxycycline promptly to cover possible rickettsial infection. Little improvement was seen after eight days of hospitalization following recommended guidelines for rickettsial treatment.

Differential diagnosis

The etiology of FUO can be categorized as secondary to infectious, inflammatory, malignant or miscellaneous causes including endocrine abnormalities (4). Through thorough investigation, we narrowed our focus to an infectious etiology. Zoonotic diseases were brought to the forefront of our differential because the patient works with animals. Certain diseases such as Rocky Mountain spotted fever (RMSF) and *Salmonella typhi* were ruled out, as they are not endemic to Israel. However, other causes of spotted fever, such as Mediterranean spotted fever (MSF) and Israeli spotted fever (ISF) can be found in Israel.

Given the clinical picture of prolonged fever, elevated liver enzymes, and history of animal contact, Q-fever was the most likely diagnosis. However, the high mortality rates of MSF and ISF warranted immediate treatment with doxycycline after blood cultures were drawn. Brucellosis was considered as it is also common in Israel, can be transmitted by horses and ticks, and presents with fever and maculopapular rash. *Bartonella* also presents with persistent febrile illness and approximately five percent of cases have truncal maculopapular rash (5).

Although rare, Murine typhus was considered as it typically presents with febrile illness, myalgias, truncal maculopapular rash that spares the palms and soles, and occasionally hepatic dysfunction. Furthermore, the patient reports contact with fleas (6). All of the previously mentioned infections can be treated with doxycycline.

Treatment

The patient was started on doxycycline with continued investigation for rickettsial infections and continued on this treatment after provisional diagnosis with Q-Fever. The patient's fever was treated with multiple doses of methimazole throughout hospitalization.

Outcome and follow-up

After eight days of hospitalization with doxycycline treatment, patient reported no improvement of symptoms and was still febrile. We would typically expect to see some clinical improvement with appropriate antibiotic treatment in this timeframe. The patient's fever only began to improve approximately one week after completing the doxycycline treatment regimen. The patient was discharged with instructions to return if symptoms recurred.

Discussion

After reviewing the patient's course during his hospitalization, we narrowed our differential diagnosis

to suspected rickettsial etiology. Veterinary medicine is associated with high risk for zoonotic diseases, with some reports indicating that zoonoses account for up to 10% of all occupational disease complaints (7). Murine typhus is a widespread, typically flea-borne infection caused by *Rickettsia typhi,* an obligatory gram-negative bacteria. Rats typically act as reservoirs, after which infected fleas transmit the bacteria to humans by inoculation of flea feces during the bite. In Israel, 403 cases were reported between 1991-2001, of which 57% occurred between the months of August and November (8).

MSF, caused by *Rickettsia conorri* infection, should not be missed in patients with a history of possible tick exposure, fever, and rash in Israel, as it has a high mortality rate. MSF has a typically abrupt onset, and initially presents with fever and headache. Rash may appear a few days after inoculation. Unlike RMSF, patients may have an eschar at the site of tick bite. In ISF, caused by infection with *Rickettsia Conorri israelensis*, eschar was observed in only 4% of patients in a study conducted in 2008.8 In one study, the mortality rate of ISF was reported at 29%, and as such patients with suspected disease should be treated immediately with doxycycline (9).

It was important to rule out *Leptospirosis* in our work-up of this patient, as there was a recent outbreak in Israel during the summer of 2018. The State of Israel's Ministry of Health reported 253 suspected cases of *Leptospirosis*, of which 32 were tested positive. The patient has multiple risk factors, including swimming in a fresh body of water and working with dogs, which are the vectors of this infection. Nonetheless, the patient was treated appropriately with doxycycline, and diagnostic evaluation was negative for *Leptospirosis*.

The patient's tests for rickettsia and other zoonotic diseases came back negative. Ultimately, the patient had a presentation of FUO that remained undiagnosed, and we can only speculate the causal pathogen.

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Key Points: Fever of Unknown Origin

- A 36-year-old man presents with elevated liver enzymes, and did not respond to 8 days doxycycline treatment under hospitalization
- Zoonotic disease suspicion, but tests for rickettsial infection and other zoonotic diseases were negative.
- Suspected diseases caused by the rickettsial infection included Mediterranean spotted fever and Israeli spotted fever and Murine typhus, which was reported 403 times in Israel between 1991-2001.

Lung Cancer Presenting with Seizures

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Introduction

Irving is a 39-year-old male born in the Ukraine and immigrated to Israel in 1999. He currently lives in Petach Tikvah and works with microprocessors as his occupation. He is not married and has no kids.

Presenting Illness

Irving presented to the ER a few hours after experiencing a new-onset generalized seizure. The seizure occurred around 7:30am on October 21st. Moments proceeding the event, he recalled seeing a "rainbow" as he describes it, in both eyes. He also became aware that he started talking nonsensically to his friend who witnessed the event. There was no associated diaphoresis, palpitations, or lightheadedness. His next memory is waking up in a hospital bed.

During the event he had jerking movements and foamy discharge from his mouth but without tongue biting. He suffered a second episode on the way to the emergency room. He denied any recent head trauma, fever, prolonged fasting, and has no family history of seizure disorders.

He has a history of a vertebral fracture in L4 after suffering a fall in 2009 and was treated with 6 months of wearing a back brace and percocet for chronic pain. He now also complains of new back pain radiating posteriorly down his right thigh and leg for the past 3 months.

The patient has a history of alcohol abuse, drinking approximately half a liter of vodka per day. His last drink was around 8pm the night before. He has a 25-pack year history. He does not use illicit drugs.

He noted a 7kg weight loss and loss of appetite over the previous 3 months, and complained of occasional constipation but no abdominal pain. He denied headaches, cough, hemoptysis, and any difficultly breathing. He has no recent history of travel or pets. He has no known allergies.

His past medical history is negative for head injury, abnormal early neurologic development or intellectual disability, stroke, intracranial infection, immunosuppression, cancer, SLE, APLA, or disorders of porphyrin metabolism.

Irving reports his mother died at 49 from abdominal cancer. His father is alive and is 76 years old. Not much is known about his medical history other than that he suffers from chronic back pain and has hypertension.

Physical exam shows a thin male who appears alert, oriented to person, place, and to situation. Patient's hygiene is poor. BP is 142/102, HR is 101 and RR is 16 per minute. Temperature is 36.9 degrees Celsius, taken orally. Patient is 178 cm tall and weighs 57 kg BMI is 18. O2 Saturation is 100% in ambient air. Pupils are equal, reactive to accommodation. Sclera are normal. Conjunctiva are normal. Sinuses are nontender to palpation. Patient's dentition is subpar. Oral mucosa is normal with no tongue lacerations.

Cardiopulmonary exam was unremarkable. Abdomen is soft, non distended and non tender. There are normal bowel sounds are present in all 4 quadrants. Dullness to percussion is noted in the right upper and lower quadrants. Inspection of extremities reveals no cyanosis, no calf tenderness and no edema. Clubbing was noted on the patient's fingernails. Patient notes that his nails have always been like that. There was no lymphadenopathy.

Investigations

Laboratory work up revealed the following:

CBC: WBC 13.5 , RBC 5.7, Hb 16.7, Hct% 54.1, Plt 400, MCV 104.7 , MCHC 30.9, RDW 12.9 NEUTabs. 8.1, LYMPHabs 4.1, EOSINab 0.4

Chemistry: Na+ 140 , K+ 3.9 , urea 6, Cr 1.09, glucose 164, Ca+2 10.4 , uric acid 9.2,

Hematological: INR 0.97, PT 11.3, PTT(sec) 37.4, fibrinogen 524

Blood gases: pH 7.34, pCO2 44.3, pO2 47.7, HCO3 23.5, lactate 19

Liver function tests: total protein 8.4 , albumin 4.3, bilirubin 0.72, ALP 234, AST 64, ALT 36, GGT 368, LDH 758,CPK 85, CRP 3.114

Immune serology: negative for Hep C ab, Heb B Ag, and HIV Ag/Ab combo.

Other markers: Cancer markers, CA19-9 120.1, Alpha fetoprotein 1.6, CYFRA 21-2 (ng/ml) 26.3

Urinalysis was unremarkable. Toxicology showed alcohol was <10 mg/dl

Given his smoking history he was given a chest X-ray. Chest X-ray revealed a small opacification near the heart border on the right lower and right upper lung fields with some cavitation in the upper right lung field. He subsequently underwent a chest/abdominal CT.

CT revealed the following:

1) A spiculated nodule was found in the right upper lobe of the lung as well as scattered smaller nodules in the lung that may represent metastasis.

2) Liver was revealed to be very fatty and texture is uneven. Due to this morphology of the liver, presence of an abnormal mass was not able to be determined.

3) A condensation was seen in the transverse colon, which may represent an abnormal mass or may simply be peristaltic movement.

4) T6 fracture was seen probably not new (known fracture in L4 from CT in 2009)

5) New infiltrate of L5 vertebra, possible metastasis.

Fearing additional metastasis to the brain that may have caused his seizure, an MRI was conducted. Brain MRI revealed 7 intra-axial discrete ring-enhancing lesions with surrounding edema found in the frontal and occipital lobes. The largest lesion was 23 millimeters.

He also underwent transbronchial biopsy that revealed "poorly differentiated carcinoma of unknown origin".

In the hospital he was treated with:

Dexamethosone 10mg x1 daily
Thiamine 100mg x3 daily
Dipyrone 1000mg x4 daily
Oxycodone 4mg x4 daily
Pregabalin 75mg x1 daily
Fentanyl x1 patch every 3 days
Levetiracetam 500mg

Discussion

Metabolic and/or Alcoholic withdrawal seizure

Metabolic/electrolyte abnormalities should be ruled out before exploring other possibilities of seizure. This patient had normal sodium, potassium, calcium. However it is warranted to have also checked his magnesium levels.

Alcoholic withdrawal seizure should be considered and ruled out, given the patient's strong history of alcohol abuse as well as the onset of the seizure in the morning. Morning seizure is common in alcoholic withdrawal, as hours have passed since the last drink. High blood pressure and tachycardia further support this diagnosis.

The presenting focal nature of the seizure (rainbow lights, broken speech), which later secondarily generalized, lends more support to a structural lesion in the brain. The patient also lacked fever, diaphoresis, and tremors which are other features of alcoholic withdrawal seizures. Lastly, the timing of less than 12 hours, rather than 36-48 hours, while still possible, make alcoholic withdrawal seizures less likely.

Metastasis to brain

Brain CT/MRI showing multiple ring enhancing lesions and space occupying lesions from metastasis would explain the seizure. Additionally seeing an aura as well as production of broken speech preceding the seizure fits with imaging findings of lesions in the occipital lobe and frontal lobe (Broca's area). The challenge is to find the site of primary cancer.

Lung: The patient has a 25 pack/year smoking history; imaging showing a spiculated mass in the right upper lobe and scattered nodules in all lung fields; a highly elevated CYFRA21-2 (a sensitive and specific

tumor marker of NSCLC; 1), as well as the lung cancer predilection to metastasize to the brain points towards the lungs as being the primary site. Physical exam finding of clubbing also supports cancer from pulmonary origin.

However, the patient's young age, mild smoking history of <40pack/yr, lack of pulmonary symptoms (coughing, hemoptysis, recurrent pneumonia, dyspnea) as well as a non specific pathology report of his transbronchial biopsy (see section on work up) warrants further investigation to rule out other possible primary sources.

Colon: A possible mass of the transverse colon seen on CT, a history of occasional constipation and a possible history of his mother having colon cancer, a slightly elevated CA19-9 (120.1 normal<37; 2), as well as the colon being a known source of brain metastasis, makes the colon a possible primary source.

However, the patient's young age, lack of change in stools and normal RBC count make colon cancer less likely (but still possible). Additionally, the constipation can be explained by possible transient hypercalcemia due to bone metastasis or paraneoplastic syndromes. The elevated CA19-9 can be explained by a number of different processes in the abdominal area (i.e. inflammation, metastasis to the abdominal organs etc.). Finally, the image of the transverse colon in CT could have been simply peristaltic movement.

Other primary sources of metastasis: Renal cell carcinoma (no mass on abdominal exam or CT, normal urine analysis, no flank pain). Melanoma (no moles), Liver (extremely rare brain metastasis and if it does usually presents with brain hemorrhage)

A PET-CT should be conducted to better localize the site of primary mass.

Cerebral toxoplasmosis: Can present with seizures and multiple ring enhancing lesions. However, the patient has no pets (cats). More importantly, cerebral toxoplasmosis is most common in advanced HIV (CD4 <100). This patient's HIV testing was negative and he has no fever suggesting infection.

Glioblastoma: Can present with seizure. However imaging would most likely reveal a single lesion rather than multiple ring enhancing lesions, and mass effect is typically associated with glioblastoma that was not seen in this patient's imaging (a midline shift). Metastasis to the brain (especially in someone with a smoking history with lesions found on chest CT) is much more common than primary brain cancers.

Neurocysticercosis: may present with new onset seizure. The patient's poor hygiene makes its transmission (fecal-oral) more likely. However Taenia solum is not known to be endemic to Israel and imaging would reveal cysts at various stages of development including enhancing and hypodense lesions and even calcified granulomas. Invasive lesions to the lunar spine (L5) suggest a more metastatic processes rather than an infectious one.

Ultimately, the patient was diagnosed with brain metastasis from primary lung cancer.

Conclusion

In an adult patient with a history of tobacco use presenting with a seizure for the first time, metastatic lung cancer must be suspected. Lung cancer is the most common malignancy to spread to the brain and most often manifests in multiple lesions. These lesions may cause a mass effect from growth and edema.

Up to 30% of patient's with primary lung cancer present with brain disease before presenting with pulmonary symptoms. Symptoms include, headaches, seizures, focal neurological deficits, and cognitive changes.

MRI w/contrast typically shows multiple well-circumscribed lesions at the gray and white matter junction (the location of vessels). As these lesions frequently cause vasogenic edema, glucocorticoids are often prescribed to reduce swelling and relieve symptoms.

The primary site must be identified, either with chest x-ray or CT, and biopsied for definitive diagnosis.

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"I Felt a Funeral:" The Fragmentary Figures of the Postmodern Disease State

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"Everyone who is born holds dual citizenship, in the kingdom of the well and in the kingdom of the sick"

-Susan Sontag, Illness as Metaphor (1978)

Diagnosis does. When a forensic psychiatrist testifies in court, it legalizes. When someone tells a friend that they are dying, it socializes. Diagnosis brings physiology into language and law, and, in so doing it becomes a structuring element of personal, political, and social life. Below, I raise two examples of the wide-ranging effects of diagnosis. One is a famous case, the other is a personal anecdote. This leads me to discuss the ethics of diagnosis as contained in a foundational document on medical ethics, The Charter of Medical Professionalism. I then discuss three alternate paradigms of illness and responsibility, one from antiquity, and two more from poetry. My goal is to give doctors a reason to reflect on the wider consequences and responsibilities that come with making diagnoses, but also impress on them how these responsibilities have and continue to evolve.

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In 2017, several women accused a prominent Hollywood film executive of sexual misconduct. Dozens made allegations of behavior that ranged from crude to criminal. The scandal became a spectacle that sparked a movement: complaints piled up and destroyed the careers of powerful men in Hollywood and elsewhere.

The media coverage quickly cemented public opinion. The allegations circulated across the globe and inscribed the image of a monster into minds around the world. Harvey Weinstein's reputation was irreparably damaged as prosecutors in New York and California launched criminal inquiries.

Weinstein responded with a short public statement that acknowledged some unspecified "mistakes." His statement expressed remorse for the injured and stated a desire to change his behavior. He did not deny the allegations. Instead, Weinstein countered them with the claim that he is "sick," and in "an effort to conquer [his] inner demons," he checked himself into a rehabilitation clinic.

The kind of statement he made is not uncommon in the courts of law and of public opinion. In his short statement he makes a medical claim ("I am sick"), which precedes a supernatural reference ("my inner demons") in forming a legal defense in a court of public opinion. Evaluations of the statement's truth-value from a medico-ethical or even legal perspective is less compelling than considering the work that the statement carries out, successfully or not, intended or not, within the world.

The "sick" individual occupies a position of privilege in society (1). The universality of illness makes it a powerful reference point to launch appeals for mercy. Accordingly, invoking illness has become a tactic used to mitigate various forms of liability. As the Weinstein statement shows, the appeal often takes the form of a rhetorical sleight-of-hand in which the accused calls to the mind of the jury the helplessness they experienced in their own encounters with disease. In doing so, the accused hopes for rebirth as a victim. For Mr. Weinstein, it suggests, in thrall as he claims to his so-called "inner demons," that he cannot be held responsible for actions that he undertook but could not prevent.

Public sentiment is so strong on issues of behavior, illness, and culpability that they appear formally within jurisprudence. The Weinstein statement is an example of a strategy that has become more common in the courts of law and public opinion, as acceptance of mental illness has become widespread.

Just as mental illness complicates our ability to draw clear distinctions between persons and diseases, a recent encounter I had with a patient reminded me how fraught it is to draw basic distinctions even with

diseases of the body. The patient was a 75-year-old man with a several-year history of cancer that metastasized. In contrast to Mr. Weinstein, this man's medical status was unequivocal. It was poignant to hear him declare that he was in fact "not sick at all" even though he acknowledged that he "had a disease." The declaration is especially provocative regarding cancer whose pathogenesis begins when natural and normal physiological processes spin out of control. How can physicians reconcile this contradiction? How can someone be perfectly healthy while having a terminal disease?

The patient mentioned he had been pain-free for years. The special treatment he received from friends, family, and members of his community disturbed him more than his cancer. His account reminded me that disease is both intensely personal and at the same time social. The categories diagnoses place us in entitle us to privileges while diving our self-conception apart from how others perceive and treat us.

Weinstein wants to claim a diagnosis. A surplus of diagnoses burdens my patient. Their twin assertions bear witness to the disparity between clinical standards and patient experiences. Accordingly, their perspectives ask physicians to reflect on who is sick and who should receive compassionate care. For those found to possess an illness, found to be sick, they ask us to consider where the lines lie between people and diseases, if indeed they exist at all. These issues confront doctors even before they can begin to diagnose and to treat. They ask us to consider how treating a pathology may conflict with treating a person, a subject which raises ethical concerns and shapes treatment approaches.

The Charter on Medical Professionalism offers guidance that both clarifies and complicates these issues. Its foundational principles include the primacy of patient welfare and the principle of patient autonomy. The first instructs physicians to dedicate themselves to "serve the interests of the patient," free from the influence of, "market forces, societal pressures, and administrative exigencies" (2). The Charter then reminds physicians that these interests are never simple: "the center of patient care is not in the physician's office or the hospital. It is where people live their lives, in the home and the workplace. There, patients make the daily choices that determine their health." Conventional wisdom suggests that patients want a diagnosis and treatment above all. By removing the clinical encounter from the clinic and placing it in the home, the Charter proposes a view of patient desire that is less obvious than it may seem.

The Charter then directs physicians to imagine the patient's experience at home while encouraging physicians to leave their ego in the clinic. Thus, the Charter's second fundamental principle, of autonomy, reminds physicians that "patients' decisions about their care must be paramount," and to "view [themselves] as advisors, often one of many, to an autonomous patient." Physicians ought to inform the patient about their disease, the treatment options, and their consequences, without swaying the patient in one direction or another. Earlier approaches to patient care, on the other hand, placed the doctor and the disease at the center of the clinical encounter.

The modern paradigm, however, places the world of the patient in the center. It proposes that the doctor imagine concentric circles encompassing his family and society. The doctor becomes a marginal figure in this theater, a role that emphasizes empathy and humility.

Conceptions of the western medical encounter have traversed a long history to arrive at this point. Their earliest formulations took shape around 400 B.C. and offered a more integrated view of the individual's encounter with disease. People were thought to consist of "four humors," fluidic substances whose imbalances corresponded to disease states (3). Hippocrates reconciled each of the four—blood, black bile, yellow bile, and phlegm—to psychological states known as the four temperaments—the sanguine, choleric, melancholic, and phlegmatic. This was among the first formal attempts in western history to bring mental states under medical models. Notably, this early conception grounds diseases of the mind entirely within material processes of the body.

The Hippocratic Oath contains few and passing references to patients. Instead, the physician sits front and center. The oath-taker promises: "I will follow that system of regimen which, according to my ability and judgement, I consider for the benefit of my patients, and abstain from whatever is deleterious and mischievous" (4). Here, the course of action to undertake is whatever the doctor decides. Physicians are morally bound in the oath, but specific appeals to

empathy or to conceptions of patient interest do not appear. Even the abstentions themselves fall under the physician's discretion. Thus, in stark contrast to the Charter, the physician's agency is central to the Oath.

The entanglement of physical and mental disease posed problems for representations of patient agency in classical Greece. Once disease has disrupted physiology, it has also inevitably disturbed the patient's psychology. In this sense, disease has always compromised patient agency, which does not appear as a legitimate concern for physicians in the Oath and elsewhere.

Conceptions of disease that appear in the early Renaissance hearken back to these classical depictions while also anticipating more modern views. Poetry of the late medieval period in Europe was preoccupied with themes of love sickness, a concept that blurs distinctions between mental and physical disease. In Chaucer's 14th century poem, Troilus and Criseyde, love is seen as a powerful force that attaches itself to and disturbs the soul.

"as love deprived him of sleep, and made his food his foe, and as his sorrow began to multiply, so that to whoever might keep a watch, it showed in his hue, eve and morrow, therefore the name he began to borrow of another sickness, lest, of him, men learned that the hot fire of love him burned." (70; 5)

The first encounter presents love as external to the lover. This force disturbs two of Troilus' fundamental and involuntary physical processes including hunger and sleep. Notably, love does not sustain the parallel structure established in the preceding lines and 'multiply his sorrow' as it 'deprives him of sleep' and 'makes food his foe.' Rather, the line reads: "his [own] sorrow began to multiply." However, the ownership over his emotions that he possesses erodes in the next line where it becomes unclear whether 'his sorrow' or love itself manifests in facial discoloration. The 'it' here equally and ambiguously refers to either object, as if love itself has now colonized his physical structure, a depiction backed up in the physical metaphor that appears in stanza's final line ("of him, men learned that the hot fire of love him burned.")

Subsequently, love brings the protagonist into its captivity:

Madhumita Govindaswamy: *oath*

he said: 'O fool, you are now in the snare, who formerly mocked at love's pain: now you are caught, now gnaw at your own chain. (73)

Here we find Troilus ensnared by love, dehumanized, and presented as an animal on a leash. His only agency is to gnaw at his chain. Notably the chain is considered 'his own,' and not 'love's.' An external hand does not hold the chain, rather, the disease or the chain, which holds him, he also holds.

By the nineteenth century, western conceptions of mental illness had further complicated notions of self and agency. Ideas about 'unconscious' mental processes that could only be examined through symptomatic behaviors began to appear and were popularized by Freud. The notion of the unconscious describes an agency that both is, and is not, a part of the self. It is not part of the self insofar as we have no direct knowledge of or control over it, and yet it is a part of the self insofar as it influences or determines a wide range of our choices, ideas, and behaviors.

During this time, many literary examples examine themes of mental illness through a lens of futility and self-consciousness. Take, for instance, Emily Dickinson's 1862 lyric, I Felt a Funeral in My Brain, which describes an encounter with mental illness. With the title and opening line, we find the speaker only able to express a part of the self ('in my brain') indirectly, through metaphor. The speaker describes her experience of mental illness as if her brain is the setting of a funeral scene. In the poem a group of mourners enter her brain, sit and experience a service, and then leave bearing a casket. As they walk across her mind, their heavy footsteps begin to disrupt her mental and metaphysical processes:

and then I heard them lift a Box
And creak across my Soul
With those same Boots of Lead, again,
Then Space—began to toll, (6) (9-12)

The speaker 'hears' and 'feels' the so-called mourners, but she does not see them, she cannot directly describe them, and nor can she interact with them. They are figures of the speaker's experience, but she does not seem to create them. Instead they appear to bear upon her; she is a bystander to whatever is unfolding within her.

The poem reaches its conclusion as the speaker describes, whether by the efforts of the mourners or not, a break and a descent:

And then a Plank in Reason, broke,
And I dropped down, and down –
And hit a World, at every plunge,
And Finished knowing—then – (17-20)

The 'I' of the speaker reappears most prominently in these closing lines. Deprived of reason, the 'I' plummets from world-to-world, each lacking solid ground. Notably, the speaker of the poem is also the subject of the poem. The poem presents the speaker's rational and calm account of her very loss of reason. What is striking is how the self-awareness of the speaker. It presents a view of mental illness as an experience that overtakes one's agency while leaving awareness and understanding intact. In effect, the mentally ill patient is rendered a bystander unto himself or herself.

It has been a century-and-a-half since Dickinson's poem has seen an explosion in the amount and accessibility of medical knowledge. This has both positive and negative consequences. Physicians have never been more equipped to understand, diagnose, and treat disease. At the same time, patients are more apt than ever to research their illness online and either self-diagnose or inaccurately assess treatment plans. In either case, the expansion and democratization of access to medical knowledge has made patients more self-conscious of their diseases. Yet, this has not led to more satisfactory treatment outcomes or even improvement in psychological experiences of disease. In this sense, the patient in Dickinson's poem offers a figure of the modern patient. Patients today experience disease as a fragmentation of self. In fact, their enhanced understanding of disease processes often presents a painful irony when physiology works in discordance with desire. The universal charter for medical practice nowadays offers several worthwhile commitments, to competence, to honesty, and to confidentiality. I would add one more, namely a renewed 'commitment to patient experience' in the information age. This commitment would remind and encourage doctors to acknowledge and appreciate the disparity between the patient's twin identities, the self that is sick, and the self that is not, and to be mindful of both in the practice of medicine.

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Olivia Keller-Baruch: *Better Half*

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