
gene
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please
Elaine
Katz

GENE EDIT ME, PLEASE

Elaine Miriam Katz

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A Creative Memoir-Based Thesis

LPP

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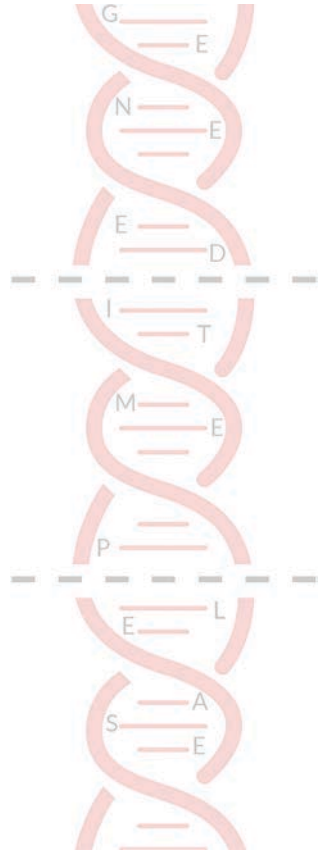
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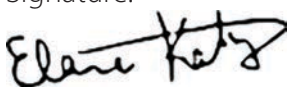
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In submitting this thesis to the Department of Organismic & Evolutionary Biology in partial fulfillment of the requirements for the degree with honors of Bachelor of Arts, I affirm my awareness of the standards of the Harvard College Honor Code.

Name: Elaine Katz

Signature:



Dedication

To Kate Vieni for teaching my sixteen-year-old feet how to walk and to Dr. Marin Jerome for reinstating my faith in my body at age 26. Without Kate as a teenager and Dr. Jerome as an adult, my legs would have succumbed to immobility well before they could carry me into the narrative I am proud to call my own.

To Rebecca Alexander for bearing the burden of illness with me and for demonstrating that disease can pave the way for an uncertain but exceptional life. Without Rebecca, my thesis would have been laced with defeat, rather than with triumph. It is precisely because of our bond that I am no longer a prisoner of my own history and that I have the audacity to move forward with purpose.

To Dr. Andrew Berry and Dr. Elena Kramer for their continuous support, time, and commitment to my academic career and to my personal circumstances. They are the reason that I was granted the opportunity to tell my story as my senior thesis through the lens of science, psychology, and creative nonfiction.

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Endorsements

An extraordinary tale extraordinarily well told. This story of Elly Katz's struggle with genetic disease (and, all too often, with the medical establishment) is simultaneously inspiring, tragic, and informative. The book's two strands—memoir and science—are masterfully interwoven: The scientific complexities brilliantly unpacked as an integral, organic part of Katz's story. Written with verve and wry humor, the book engenders in equal part tears and smiles, sometimes both on the same page, but it remains throughout upliftingly positive. It succeeds superbly in personalizing its message—that rare diseases are too frequently overlooked by doctors—and will have a far-reaching impact.

Andrew Berry

Lecturer on Organismic and Evolutionary Biology

Assistant Head Tutor of Integrative Biology at Harvard.

I have advised over a dozen senior theses in my career at Harvard but this is easily the one of which I am the most proud, both of the student's accomplishment and the work itself. Elly poured her heart and soul into this work and it shines through on every page. It is a unique work that synthesizes personal memoir, human genetics, molecular medicine, and biohacking, all seen through the lens of her life. The work blends two distinct perspectives. First, there is a comprehensive coverage of relevant

scientific literature that helps us put the author's genetic diagnosis in scientific context and, second, what I would call the "biohacking" component provides deep insight into how patients with rare diseases have to be their own best advocates and literally experiment on themselves. The perspective on modern medicine is particularly compelling and should be read by anyone who actually has the power to address these issues.

Elena Kramer

Professor of Organismic and Evolutionary Biology at Harvard

Director of Graduate Programs in the Natural Sciences

This is a story of exceptional resilience, on physical, mental, and spiritual levels.

If you want to understand what it's like to live as a gifted young woman with a rare and debilitating genetic disease, then this is the book for you.

Beautifully written, Katz interweaves the science of her rare disease with descriptions of daily life as a Harvard undergraduate and the many challenges she faces.

Her resourcefulness is remarkable—in overcoming roadblocks to her academic career and in creating cherished interludes of "regular" social life that other college students take for granted. Throughout, she is a detailed observer of her life, showing vulnerability and humor.

("It's a good day since I only had to relocate my shoulder joint and not my hip joint too.")

Her disease is all-consuming, yet she forges strong connections with friends, professors, lab mates, and clinicians with abundant support from family and mentors.

This extraordinary book is perfect for anyone with a rare disease, for their loved ones, friends, doctors, and nurses, and for all those advocating for more research on rare diseases.

Maryellen Ruvolo

Research Professor of Human Evolutionary Biology

Harvard University

Foreword

Metta Scan by Elly Katz

Feet—those motivated and unstoppable soles forever forging onwards—good morning to you. May you be peaceful. May you be happy. May you be liberated from the shackles of pain. May you forever remain undaunted by life. May you trail forward, despite the tide that seems to pull you back to the darkness from whence you came. May you carry my spirit through the earth.

Legs—those muscular pillars of support that somehow bear the gravitational brunt of all that lies upstream—hello from your inattentive, distracted inhabitant.

May you be free from spasms. May you courageously move me into experience. May you delight at the momentum life affords. May you forever gaze ahead at that which is always unknown.

May you never give up, give in, nor succumb to defeat. May you continue to staunchly rebuild me as life demands. May you be content.

Pelvis—that parabolic bowl that steers the ship of my being—I will never forget you.

May you refine the art of alignment. May you find tranquility in equilibrium. May you smile contagiously and grant me the pleasure of singing at life. May you savor the movement of the moment. May nothing preclude you from directing me into phenomena.

Ribs—that accordion encircling me into myself—I acknowledge you silently at each inhale. May you expand and contract with ease. May you learn that you are independent from shoulder blades and pelvis—that you can move autonomously. May you have the audacity to respire throughout the day and night. May you permit me to breathe into you as I please. May you find solace in the overlooked and infinitely interesting task of gas exchange.

Neck—general headquarters of my peripheral nervous system—I wish we were less acquainted with each other, that you occupied less of my time to sustain yourself and carry my cranium.

May you become stronger each day. May you become the resilient highway of my nervous system and demand less attention. May you carry my most prized possession, this thing I call self—that tangle of neurons above—with ease. May you be happy. May your pain dissolve into the atmosphere. May you be free from persistent distress.

Cerebrum—that essence I call self—I am awed by you, by your constant adaptability to the shifting conditions of the body, by your capacity to change and render me someone different in each moment.

May you continue to shape me into myself. May you continue to refine your ability to be present, to land upon each moment gently. May you take me everywhere. May you lead me into whoever I am meant to be.

Comprehensive being—that totality that forever outshines and baffles the sum of its parts. Thank you for today. For being here. For enabling me to complete this sentence, to type this poem. Thank you for every moment you give.

Artist's statement

When I arrived at Harvard seven years ago, I presumed that I, despite my lengthy medical history, would fit the mold of an average student. However, as my body presented one roadblock after another to my completing Harvard on my own terms,—joint dislocations, gastrointestinal dysmotility, a spontaneous cerebrospinal fluid leak, cervical instability, temporomandibular joint dysfunction—it became clear that my physiology was uniquely mercurial. As a freshman, I was finally diagnosed with Ehlers-Danlos syndrome (EDS), a debilitating and incurable disorder that renders connective tissue throughout the body friable.

As a science student at Harvard researching polyglutamine and musculoskeletal diseases, I futilely tried to outrun EDS' hold on me, to carve out a realm of experience outside of its domain. I soon learned, against my will, that I could no longer retreat from the systemic symptoms that defined my life; instead, I went on the offensive and transformed my physically circumscribed world into a research laboratory designed to fight EDS.

For most, the defining feature of 2020 was, of course, the COVID-19 pandemic. In my case, however, that year is synonymous with the inability to talk, walk, sit, or do anything. Now, as my recovery progresses with the help of regenerative medicine and I gradually develop musculoskeletal strength, I am finally confronting my disease head-on through this thesis. While I am not currently well enough to return to laboratory work, crafting the following

research-backed account of my illness has transformed me from someone who can only suffer its symptoms into someone who can actively combat them.

Gene Edit Me, Please is my attempt to embed EDS and, by extension, my personal narrative in the language of science. In this effort, I leverage my educational and research background to ground my disease in disciplines including but not limited to psychology, molecular biology, genetics, epigenetics, neuroscience, and evolutionary biology. While scientific explanations are scattered throughout the text, the manuscript begins with an in-depth scientific introduction (Chapter 2) that serves as a framework to understand the nature of my condition and concludes with a detailed discussion of potential EDS causes and therapies (Chapters 23–24). In the intervening chapters, I explore the development of my EDS, starting with my early childhood when I began to experience symptoms that culminated in my diagnosis two decades later. The innocent memories I depict (Chapters 3–4) function as a reference point for the narrative that follows. In addition to exploring EDS through the lens of scientific mechanism, *Gene Edit Me, Please* is about Western medicine's inability to deal with rare "zebra" diseases, how the isolation imposed by EDS's many assaults (beginning during my teenage years) shaped me into who I am becoming, and about my relationships with others and with science itself. At its core, my thesis has become a narrative of adversity and triumph, of getting knocked down and clawing my way back up. I am immensely grateful to have the opportunity to look my disease in the eye—to unpack its scientific underpinnings and, consequently, to make sense of my life. Thank you for taking the time to read my work.

Disclaimer: *What follows is a work of creative nonfiction. I have tried, to the best of my ability, to recreate events, people, and conversations based on my memories of them. Although all the episodes portrayed are true, in some cases, I have altered names of individuals, identifying features and/or institutions to maintain anonymity. All ascribed quotations are my recollections of conversations, not direct quotations. In my recreation of these discussions, I tried to do justice to the essence of what was conveyed, not to reconstruct them verbatim.*

A note to the reader:

This book was written as Elly's college dissertation in the field of Evolutionary Biology, but, as was her way, Elly brought her full and creative intelligence to the material. The result is a deeply personal memoir that tells the story of learning to live with a genetic disease, and that, with the exception of two chapters, will engage and inspire all readers. The two science-heavy chapters are Chapters 2 and 23. For the uninitiated, they might be daunting. For those who choose to do so, those chapters can be lightly-read or skipped altogether, without losing the thread of the narrative.

Only I can tell myself the next sentence of my story.
I craft adventures out of walks and dance down Cambridge streets utterly and innocently credulous of Sia's words: "I am unstoppable."
I am buoyed by my bounce back, by my spirit's dogged capacity to resuscitate after ricocheting off the unforgiving walls of existence.
And, yet, I feel defiled by experience, robbed of something I once called joy.
In making meaning, I am forced to literally redesign the dictionary, to redefine happiness, wellness, and so much more.
The world resonates with perspective.
Walks can be journeys, moving can be wellness, disease can set the stage for an unexpected, unscripted, yet magnificent life.
My world echoes with the hum of something I call bliss, which I will define and redefine ad infinitum forever undaunted.

1
The peril of spontaneity

I am okay with being out of place, with arms out of sockets that rest on bed pillows, with knee caps that pop in and out as they try to figure out where they belong in this universe, with nerve pain that glides like a practiced figure skater down the midline of my arm, with bruises canvasing my thighs, with life in pieces, with fragments.

For what are we if not broken?

Drip. Drop. Drip. The inaudible and ceaseless internal leak continues. The rupture within and the gap between me and my world widens. Seated in my introductory genetics course, I observe my professor point to the evolutionary diagram in a corner of the classroom. I adjust the glasses on my nose, thinking doing so would somehow rally my internal reservoir of concentration. I remove them from my face and place them on the table before me. Fruitless in my effort to focus, I stand up with my legs encircling an exercise ball, which had recently replaced my classroom chair.

The professor draws a curlicue emerging from a string of DNA on the chalkboard to elucidate the defunct genetic byproducts of a particular chromosomal rearrangement. But the mutation

extended beyond his drawing. Little did I know, it had taken hold of me. My brain struggles to interpret his illustration, to envision the sequence of the two-dimensional genetic code after its contents are shuffled. I feel heavy and lethargic all over as though my cerebrum had been replaced with a bowling ball. The dizzying sense of my own weight encourages me to resume my position on the inflated seat. Notwithstanding my confusion, something within me experiences a kinship with the genetic anomaly being expounded upon; I feel scrambled, my insides garbled like the adenine and cytosine nucleotides on the board.

After a summer research internship at Harvard, I can only classify as a mental high, during which my mind felt unstoppable, I was floored, only two weeks later, by my brain's own waning computational power. I felt like I was running on some basal level, as though I was walking through mud and endeavoring to see clearly through a thick and impenetrable fog. A switch within dimmed and, by the conclusion of the first week of the term, was flipped off, rendering me lost en route to class buildings I had frequented for the past three years and unable to hold my head upright against the unforgiving tug of gravity.

My characteristic 10pm bedtime trended asymptotically toward 8pm, but my widened sleep window did not help; I awoke enervated and bleary-eyed. Presuming that I, even in the face of the multitude of energy-enhancing supplements I consume daily, had succumbed to the fatigue often associated with my disease, I began ingesting potentially record-breaking quantities of almond butter, avocados, and collagen protein. In doing so and forgoing my usual half-hour of aerobic exercise on an elliptical machine,

I was confident that the exceedingly positive value of my calories in versus out equation would synergize with the extra hours of rest to yield a more stable and energized version of myself. But I was wrong and misread the signs my body was sending.

I cannot recall the last time, at least in the previous half decade, that I have been at such an impasse. My disease has armed me with an arsenal of tricks that probably strike any able-bodied person as preposterous. I can rapidly relocate my shoulders, knee caps, fingers, ankles, hips, and ribs, all of which test their boundaries of stability and dislocate at the slightest provocation. I dare anyone to beat my time of popping a rib or shoulder back into place. I have the jigsaw puzzle of my body down to a science; I know its cryptic physics and how to unify its parts. I have relocated my arm into its socket as many times as my mother has kissed my cheek. As though out of a science fiction film, hives erupt like landmines across my legs and abdomen. My gastrointestinal cavity expands with the force of a helium balloon. I vomit until I am hollowed out and spend nights on my bathroom floor listening to audiobooks about people wrapped neatly into narrative confines, characters who suffer but achieve some climactic sense of wholeness in the story's denouement.

Occasionally, I awake on my right side, evidence that I jostled my right shoulder and hip in the night, which is sufficient grounds for my daily right shoulder and hip dislocations. I may slip on or take off my undershirt in too much haste and dislodge my shoulders. I may step off a curb gawkily and torque my ankle or knee cap out of socket. I may perch myself on a hard surface, and, in five minutes, my hip will emanate from its girdle, sending nerve pain ricocheting down the outer lining of my leg. I may consume

a histamine-releasing food, like honey or banana, and witness my skin become engulfed by orange-sized red patches.

This new setback at the outset of senior year, however, did not fit that causal mold. I propelled myself, fueled by sheer willpower, from my off-campus apartment to class and back again. After four days of a full course load, I began to consider the option that I was dying.

Weakness and fatigue crept into every part of me; I moved down Concord Avenue maladroitly like the animated Gumby. My proprioceptors—responsible for telling me where I was in space—went on strike, and I ambled this way and that, weaving myself through an invisible loom that stretched across the streets. I was utterly unsure of what to do with the alarming heft of my head when I sat and resorted to creating my own type of dance, a pattern of sitting and standing, to get through my classes. Upon arriving home, I sprawled myself on the floor for hours praying to something in Einstein's "out yonder" that this unbearable and so unclassical Elly sentiment would pass. But it did not. I tried to put in words how I felt during my near-hourly phone calls with my mother.

"My scalp feels like it's being yanked backward. I feel like someone slipped me a hefty dose of roofies."

We laugh because I have never been a mile within a situation in which date rape drugs, or even dates, are present. Because, at age twenty-four, my body acts more like a prison than a vehicle for experience. Although I have been at Harvard College, the home of finals clubs, and exclusive social organizations, for just over three years, I have never found my way into anything

resembling a party or a date. I have yet to be kissed. My journey, against my will, diverges from that of most because of my connective tissue that hardly connects. Our laughter holds so much pain and mutual understanding.

"Mom, I can't think. The lights are off inside my brain. I am not sure where I'm heading or why I'm heading there. This headache is nonstop. A reprieve only comes when I lay down."

Typically, after someone concludes a thought, there is a pause on both ends for the speaker to gulp some air and the listener to process what has been uttered. Even over the phone, across wires and distances, my mother knows my thoughts before I speak them. She does not require a quiet interlude. There is something telepathic about the bond we share.

"El, I'm leaving work and coming to you. Stay put."

Within four hours, my mother was at my door and shepherding me into a car bound for the emergency room at Beth Israel Deaconess. This was certainly not our first trip to the ER. I have spent probably as much time in hospital corridors clutching my mother's palm as I have in Harvard College classrooms. In fact, it was only four months ago that we found ourselves in the very same hallway as electrolyte-rich fluid migrated down narrow plastic tubing into my veins. Back then, at the end of April, a headache that only let up upon lying down and a sense of cerebral heft, which seemed to accrue as the day wore on, left me incapable of holding my own head up. By evening, my fists had to become a prop on which I rested my chin so I could scan articles on *NOTCH2NL*, a human-specific gene, in preparation for a paper I was ironically writing on the genetic architecture of the human brain.

During this initial stint in the ER, doctors interpreted my cradling of my scalp with my hands, an effort to lure it upward against the sensation of quadrupled gravitational force, as simple dehydration. "Doctors are trained to think horses, not zebras, when they hear hoof beats," my mother would tell me later. But this approach of seeing the majority and forgetting those on the margins does exactly that; it overlooks zebras like me with ease. If doctors are blind to medical zebras, or rarities, who is responsible for sighting them? After a night's worth of Ringer's lactate solution doused my venous network, the attending doctor proudly noted that "I was a dead flower that he had sprang back to life." That might have been the case, but he could not predict that the life he (or the fluid) had bestowed came with an expiration date of about four months.

As my wheelchair rolled through the ER doors in late August for the second time, I felt smothered by fear. I wondered if I would ever again find a way to trust my body after its latest betrayal or if the panic I felt would become a part of who I was for the long term. My mother played up her doctor status the way she always does in these circumstances. She whipped out her Weill Cornell Medical College badge as though it were a weapon and told the attending at the check-in desk that I needed hydration immediately. My mother is, rather rightfully, protective of me, even more so in ERs than in bustling New York City crosswalks.

Patients with my zebra disease have been painfully misunderstood by doctors who, more often than not, are incapable of appreciating the fragility of my condition. Operating under the false premise that my connective tissue is in tip-top shape, physicians jam my shoulders into place with undue force that causes

refractory dislocations and nerve impingement. In addition to her certified doctor decal, my mother is compulsive about her lipstick, which she applies with the diligence of an A+ schoolgirl. I have learned to diagnose my mother's sanity, or lack thereof, by decoding the frequency with which she outlines her mouth with Lancôme. Regularly spaced applications every ten or so minutes indicate that she is even-keeled, but, as the lipstick-free intervals shrink to five minutes and trend toward five seconds, I know that the robust mantle of my mother's emotional stability has begun to fragment, that she will soon lose it and her Lancôme will run dry.

ER doctors strictly follow my mother's orders to the letter. One glance at the red and white plastic pronouncement of her medical credentials and they abide. A female nurse strung one bag, and then six more, of clear liquid onto a pole and drove a small needle into my arm. She proceeded to take my temperature, harness a blood pressure cuff around my bicep, and measure my oxygen saturation using a device I can only describe as a finger hugger. The ER was packed, and I was stationed on a stretcher. My mother sat beside my head and witnessed the electrolytes oozing into me. All suffering demands a witness. My mother is just that and so much more.

Between my diagnosis three years prior and my visit to the ER in August, I became my own experiment. Because my disease lacks a course of treatment or anything close to a therapeutic blueprint, I subjected myself to elimination diets, ultimately landing upon a cyclical ketogenic diet, and prescribed myself supplement cocktails consisting of ingredients including aloe vera, bovine bone marrow, lamb liver, and vitamin C. I spend roughly

15 minutes each morning extracting the closest approximation to a cure for my disease from the insides of fifty-four bottles.

When my head pain developed in April, I substituted gastrointestinal-aggravating Aleve with CBD and arnica pellets, the latter of which I had been ingesting strictly on the hour. As I lay on the stretcher grasping my mother's hand, the hour struck, and the time for ten more of my arnica tablets arrived. My mother surreptitiously placed the cylindrical dispenser in my hand as her eyes darted from one nurse to another. When our eyes met, uncontrollable and unbridled laughter ran out of me and my mother faster than the electrolytes ran into me. Once we began, there was no stopping us. That's what my mother and I excel at: Finding pearls of joy and togetherness in the darkness of illness. If you can find laughter in the ER, you can do almost anything. Beneath the transparent bedsheets, I rotated the movable circle at the tip ten times as ten pellets fell synchronously into my palm. That is the closest I come to rebellion: Furtively taking my own medication in the hospital.

While the liquid resuscitated me to an extent, it was not as magical an elixir as it had been in April. The morning after my overnight hospital stay, I had enough vigor to attend a meeting with my genetics professor, but, by 3 p.m. that day, I felt like roadkill again. My father decided to come to Cambridge for the weekend and aid my mother in my return trip home to New York City on Sunday.

If my mother is my medical middleman who alarms ER doctors into submission, my father is the highway to my innocence. My Dad has this transfixing way of making me erupt into laughter

until I hurt all over and forget the initial source of my pain. He will do anything to set my smile dancing. He brings me back to a carefree part of myself that I thought I had shed when illness initially set in at age ten.

The air pressure in the main cabin was unbearable and sent the nerves in my skull ablaze.

I spent the ride clenching my jaw and cradling my boulder of a head in my palms to ease the gravitational burden. Back in my bedroom at home, I was terrified to close my eyes, frightened that if I did, I might never open them again. The pain in my scalp was so acute, so intense, that I could not even process the reality that I was forced to take a leave from Harvard, yet again, that my senior year had been so rudely interrupted, and, most of all, that I was at the mercy of my failing body.

Against my will, I had become an expert at fleeing from my reality. I have been derailed from mainstream academics by my own biology so many times that my disappointment is my most frequently used emotion. Despite the fact that I possess approximately twenty thousand functioning genes, I own several that will forever hold me back. The ground beneath me seems to shift each time I trust it to remain stable. I have learned the harsh reality that dreaming only begets distress.

After a visit to Cornell's ER and a brain MRI, during which my head was stuffed into something like an immobile fencing helmet, it was apparent that I had a spontaneous cerebrospinal fluid leak. The word "spontaneous" hit me like a sharp knife. The fact that my protracted comatose-like state had brought me within reach of death's door and that my brain was somehow leaking and in

desperate need of a plumber did not seem as terrifying as the fact that it occurred without cause. The word had, like the leaking lining of my cerebrum, acquired a sort of weight that could not be subdued by grunting, bearing, and teeth-clenching.

The attending physician was completely calm about the whole affair, as though he were ordering pasta and wine at a restaurant. He reasoned that my dural ectasia—the stretchiness of the tissue that coats my spinal cord, a common symptom in the grab bag of my condition—was to blame. There was no means of avoiding recurrence. The abhorrent word "spontaneous" had come to encompass so many moments that I was supposed to define for myself. The notion of an internal leak was far from novel; my joints readily dislocate, leaving my skin lacerated and oozing with blood. Rivulets of red and bruises in purpling hues decorate my exterior. I often liken myself to a Jackson Pollack painting on the wrong type of canvas. On top of all that, my innards are not leak-free. My gut wall leaks, or so I have been told, and microbial byproducts have benefited from my intestinal pores, viewing them as wormholes to the rest of me.

But, despite my unsettling familiarity with the whole scenario, the brain was a new and frightening context for a rift to take root. My weariness had its upside. I felt so incredibly doped up that expressing fear was impossible. I was emotionally numb. Plus, I think my parents exuded the entire package of trepidation and panic on my behalf. My mother quit her lipstick habit without looking back. My father left his workplace and sat beside us in the pitch-black ER room.

After I was escorted to a procedure room, an incompetent team of residents rotated my arm this way and that, puncturing it about nine times before blood emerged. To plug my leak, an anesthesiologist planned to inject the collected blood from my arm into my lower spine. Oddly enough, I have had more success when doctors remove blood, bone, or cells from one location in my body and put it into another than when they make me into an archaic cyborg by fusing my being with something exogenous, like metallic rods or screws. It is troubling to consider the potential that the cure for my disease rests within me, just in the wrong place.

"Not to worry, Elly. I administer epidurals to pregnant women all day. This will go off without a hitch."

I wanted to ask the doctor where my baby was but stopped short. The residents continued to stab my arm, which bore the greenish-purple marks of their attack, as they belittled my purportedly collapsing veins. Upon rising from the operating table, my head felt like something I could hold above my shoulders again. My eyes opened with ease for the first time in months. My universe was restored, at least in part. The nerve pain in my scalp remained and was even exacerbated by the re-equilibration of my cerebrospinal fluid. That is how the tides usually turn for me. In healing one ailment, I agitate another. My path is more often one of concentric circles rather than lines.

Dr. Robbins, the neurologist, almost effortlessly labeled the residual neuropathy as occipital neuralgia, another rare diagnosis. The nerves whose axons feed the occipital aspects of the skull and bifurcate to provide sensation throughout the scalp were

jammed in my cervical spine. My sole solace came when I delivered manual traction to myself and lifted my head upward from the base of my ears, thereby relieving the entrapped nerves positioned cozily between my vertebrae. Despite the white coat and medical license that often segregate physician and patient into the categories of powerful and powerless, respectively, Dr. Robbins had no intention of placing himself and me into these preordained boxes. He sat in his office chair without regard for the messages pinging and buzzing for his attention. His socks made me smile, even in the face of the eddying nerve pain that wreaked havoc on my skull, not only because they took up a larger than expected amount of territory between shoe and pant leg but because they were covered with what appeared to be a child's scribbles.

Rather than aiming to make a show of his own intelligence, as many doctors do before my mother, Dr. Robbins listened to me tell my own story instead of reading the massive collage of doctors' transcripts that disfigured the file folder with my name on it. He pierced the base of my scalp with a mixture of lidocaine and steroids and vowed, with the dedication of a parent, that this too would pass.

2
A cruel genetic dance

I am leashed, tethered to something far more unforgiving than a human hand, tied irrevocably to mutated genes and malformed proteins that lace my bloodstream, a virus I may never expel.

My story begins well before I do. I owe more to my conception, or even to its prelude, than anyone should. It was an insidious yet gradual beginning with an end product of me that no one could foretell, a single pellucid vaporous wisp riding through the night that serves as a cautionary sign of a fire gathering on the horizon.

Genetics is a game of Russian roulette in which the odds are typically stacked in your favor, which means that there exists a small but real probability that you may find yourself sporting a losing hand. In preparation for mitosis, the process of conservative cell division, genetic material is replicated and sister chromatids, tethered together at a region of constriction called the centromere, segregate before each strand serves as its own template for the next genetic generation. Notwithstanding the proofreading capacity of enzymes, including DNA polymerase, replicating three billion base pairs is a statistically daunting feat. Given the magnitude of the human genome, it is astounding that the majority of us comply, for the most part, with normative conceptions of a healthy human being.

The Predominant Symptom-Based, 'Whack-a-mole' Approach to Healthcare: Anatomy is reduced to a map of delineated and independent territories to be diagnosed and treated by uncoordinated specialists
'I am a single interconnected entity. Do not break me down into my subcomponents and offer me a barrage of diagnoses. Instead, sum my systemic symptoms rationally so I can make comprehensive sense to myself.'
Symptomology: exhaustion, fatigue, disorientation
Diagnosis: dehydration
Therapy: intravenous fluids
Symptomology: shoulder instability & reduced range of motion
Diagnosis: Ehlers-Danlos syndrome
Therapy: No established course of treatment
Symptomology: distension, abdominal pain, nausea, hives, dermatographia
Diagnosis: mast cell activation syndrome
Therapy: antihistamines

The numbers tell me that, probabilistically speaking, my father is to blame for at least a part of this nasty affair stamped on my genome. Whereas maternal meiosis, the mechanism of reductive cell division that gives rise to gametes, is frozen in time when Mom is born and resumes at puberty, paternal meiosis is continuous, rendering Dad's genes potential targets for statistically more copying mistakes. To prove that I hold no grievances against my father, with the exception of my paternally inherited stunted right thumb and bunions, I must bring some science to bolster my claim. Augustine Kong and colleagues (2012) examined the complete genetic sequences of 78 parent-offspring trios and deduced that a child inherits roughly 15 single nucleotide substitutions from his or her mother, independent of maternal age, and about 70 of these mutations from a father at age 40, my dad's age at my conception (Kong et al. 2012). The one asset of my mutations is that they arm me with a free pass to forever fault dad, and my father takes my censure in stride.

My genome could have been flawless, if not for two overwhelming and unforgiving blemishes in my code. A mutation in the *BRCA1* gene, a breast cancer risk factor preponderant in Ashkenazi Jews, was dealt to almost everyone in my immediate family. I dodged that bullet but was hit, perhaps more penetratingly, by two others, one on chromosome six and another on chromosome 19.

Located on chromosome six, *TNXB* encodes the extracellular matrix (ECM) protein tenascin-X, which regulates the production and organization of collagen, a key structural element that comprises the connective tissue throughout the body (Mao et al. 2002).

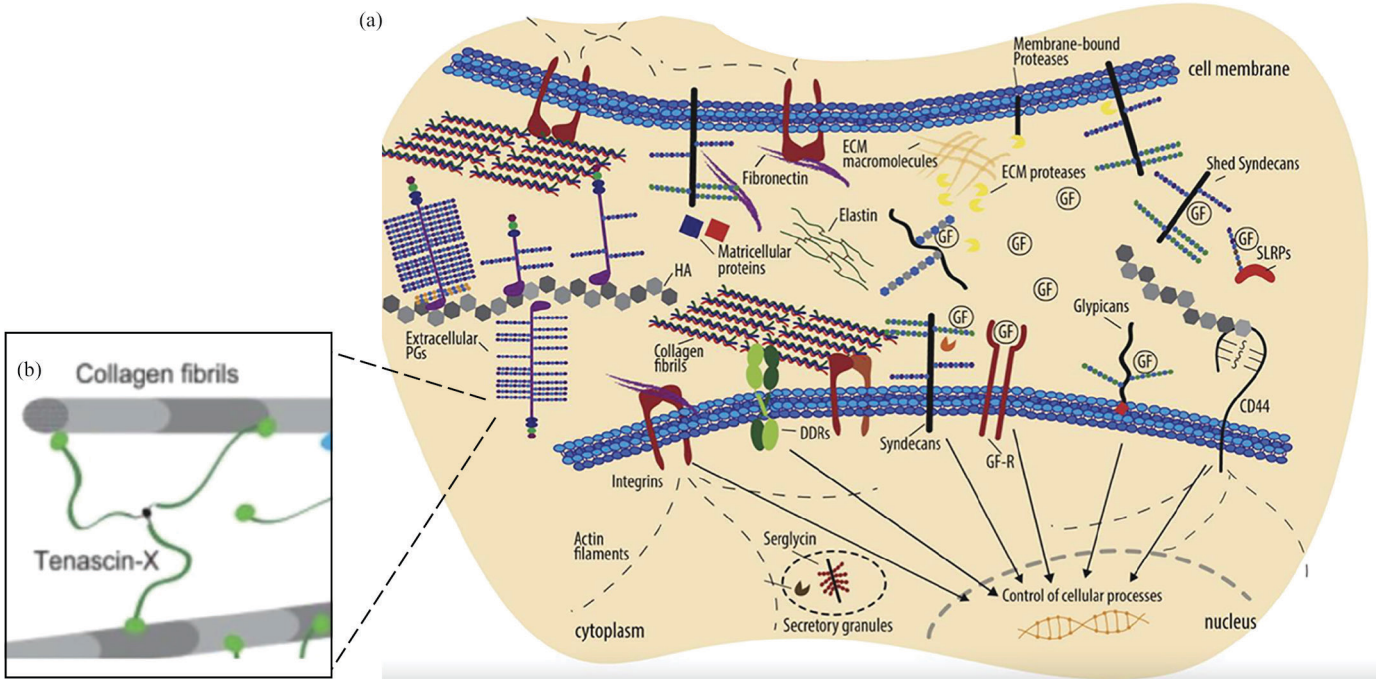


Figure 2.1: *Continued*

Figure 2.1: *Graphical schematic of the Extracellular Matrix (ECM).* (a) The ECM is a complex three-dimensional network composed of collagens, elastin, fibronectin (FN), laminins, glycoproteins, proteoglycans (PGs), glycosaminoglycans (GAGs), hyaluronan (HA), and matricellular proteins. Cells interact with aspects of the ECM by binding to integrins, PGs, syndecans, glypicans, the HA receptor CD44, and discoidin domain receptors (DDRs). Growth factors (GFs) are secreted subsequent to ECM breakdown and bind to growth factor receptors (GF-R), which leads to activation of signaling cascades. Enzymes involved in ECM degradation include matrix metalloproteases (MMPs), a disintegrin and metalloproteases (ADAMs), a disintegrin and metalloproteases with thrombospondin motifs (ADAMTSs), cathepsins, and plasminogen activators, and GAG-degrading enzymes, such as heparanases and hyaluronidases. Proteoglycan serglycin within the cell interacts with proteases and other molecules and is released into the ECM in the presence of inflammation and tissue reorganization. Adapted from "Extracellular Matrix Structure," by Theocharis et al., 2016, *Advanced Drug Delivery Reviews*, *97*(1), 6. (b) Tenascin-X regulates the distance between and organization of collagen fibrils. Adapted from "Tenascin-X: Beyond the Architectural Function," by Valcourt et al., 2015, *Cell Adhesion & Migration*, *9*(1–2), 158.

The ECM is a three-dimensional scaffold that is highly dependent on collagen, among other proteins, enzymes, and minerals, and is essential for cytokine and growth factor-mediated cell-to-cell communication, embryonic maturation, and tissue repair. While the ECM is composed of roughly 300 macromolecules, its chief constituents are protein compounds called proteoglycans and adhesive glycoproteins, including tenascin-X and laminins, hyaluronic acid, and fibrous proteins, such as collagens and elastin. Given its central role in regulating connective tissues, it is not surprising that genes integral to ECM structure and regeneration are implicated in connective tissue and musculoskeletal diseases, from Ehlers-Danlos syndrome (EDS) to osteogenesis imperfecta (Yue 2014; Theocharis et al. 2016; Chiarelli et al. 2019).

In their publication, Nicola Chiarelli, Marco Ritelli, Nicoletta Zoppi, and Marina Colombi (2019) examined the transcriptional profile of cells derived from hypermobile EDS (hEDS) patients (Chiarelli et al. 2019). They demonstrated that relative to healthy cells, hEDS cells differentially express genes responsible for pain reactions, inflammation, and cell-to-ECM interactions—cadherins, protocadherins, and desmosomes requisite for tissue development and configuration. These gene regulatory modulations cause hEDS cells to adopt proinflammatory myoblast (muscle cell precursor) phenotypes. In addition to acting as scaffolds, ECM-associated proteins mediate gene regulatory networks, such as, but not limited to the wingless and int-1 (Wnt) pathway that governs cell and stem cell homeostasis and the nuclear factor kappa-light-chain-enhancer of activated B cells (NF-kB) pathway that modulates inflammation and is critical for cell survival. The unique transcriptional aberrations observed in hEDS cells cause

the cells' phenotype to shift from connective tissue cells called fibroblasts to pseudo-myofibroblasts.

Unlike the former, the latter cell type induces the remodeling of cell-to-ECM connections, boosts cell contractility, and enhances alpha smooth muscle actin (α-SMA)-stress fiber production, all of which foster chronic inflammation that may be at the root of EDS pain, gastrointestinal distress, and other EDS symptoms.

Tenascin-X, in particular, promotes ECM development during wound healing and is thought to be integral to the configuration and laxity of elastic fibers that underpin connective tissue stability and flexibility. Jau Ren Mao and his collaborators (2002) demonstrated that tenascin-X regulates skin cells' secretion of collagen by generating mice in which both copies of *TNXB* were deleted (Mao et al. 2002). As these mice matured, the researchers observed the distinctive EDS phenotype of hyperextensible skin and hypermobile joints. In the setting of humans, a complete lack of functional tenascin-X (inherited as an autosomal recessive condition) would definitively diagnose a person as having *TNXB*-based EDS, which is currently referred to as classical-like EDS. In my case, however, the medical verdict is not yet as clear-cut.

While my error in *TNXB* appears to be more benign than a complete gene deletion, the consequences may be the same. One of my copies of *TNXB* contains a small but critical, spelling and proofreading oversight, or a missense mutation, in the 17th exon of the gene. Instead of an adenine nucleotide, I possess a thymine, which causes an amino acid change from a negatively charged aspartic acid to an uncharged valine in the resultant protein. Due to their differential polarity, researchers

hypothesize that this shift in amino acid influences protein structure, thereby potentially rendering my valine-containing copy defective. Despite its recessive mode of inheritance, *TNXB* is a haploinsufficient gene—two normal copies are required for wild type function. Manon C. Zweers and colleagues (2003) demonstrated that *TNXB* haploinsufficiency causes the EDS phenotype in 64 percent of females and in zero males harboring the same genetic anomaly (Zweers et al. 2003). The influence of sex on EDS pathophysiology, as reinforced by studies examined below, likely emerges during puberty and stems from the differential hormonal milieus in males and females. However, the mechanistic underpinnings responsible for this phenomenon are currently poorly understood.

In short, a single nucleotide change in *TNXB* alone may prime my ligaments and tendons to be lax, leaving my bones loosely connected to each other and to my muscles. Consider a plan to build a house that accounts for purchasing all the materials without any intention of assembling them into anything coherently resembling a home. What's the point of the entire ordeal? Why expend precious cellular currency transcribing and translating collagen into its proteinaceous form without providing it with a purpose for being? That is exactly how my cells feel about collagen: Like repositories of expensive provisions without a construction crew.

However, as researchers at the Broad Institute, the University of South Carolina, and Italian and Israeli universities continue to delve into my genetic blueprint, it seems as though my *TNXB* defect is merely one of possibly several puzzle pieces in my story. In early 2021, an examination of my genes revealed a

loss-of-function mutation in a critical kallikrein (*KLK*) gene (the specifics of which I am unable to disclose due to ongoing and currently unpublished research) residing in a cluster of 15 closely related genes on chromosome 19 that encode proteases, or protein-degrading enzymes, that operate on specific tissues throughout the body.

KLKs serve as biomarkers of cancer and other skin diseases, are involved in inflammatory processes and wound healing, dismantle components of the ECM, and can even prevent collagen synthesis and expedite its breakdown (Nauroy & Nyström 2019; Sotiropoulou & Pampalakis 2010). As these enzymes are regulated and expressed as proteins in synchrony with each other, the KLKs likely constitute a regulatory cascade in which a given KLK has a domino effect on another. As such, one aberrant *KLK* may have widespread systemic implications for the 15-piece enzymatic chain reaction. Might my mutated *KLK* and *TNXB* loci collaborate to modify my ECM and collagen to render my specific EDS phenotype? Although the connection between these two mutations has yet to be studied, it is conceivable that the combined dysfunction of these genes may be a case in which one mutation plus another mutation spells synergistic disaster.

Old photographs from December 15, 1994, my birthday, whisper small details that fit into each other, creating a comprehensive enough image of my Simchat Bat, the Jewish ceremony that welcomes a female into the world. I am draped in a white silken onesie patterned with translucent lace and miniature cream roses about my perimeter. My head is hidden beneath a canopy of white fabric as are my feet. An air of purity hangs about

me, which is probably a byproduct of all the white, a front-and-center metaphor of my newness. But something else new also lurks with far less grace and innocence than the white frock in which I rest. Several genetic errors are sown into the seams of my code. I had been hacked, the core of my being forever compromised, and I, in my white drapery, did not even know it.

In retrospect, it strikes me as rather disquieting that I cleaved to genetics, rather than to any other scientific subarea, prior to coming to terms with the fact that my fate had been sealed within my gene mutations. EDS comes in fourteen general flavors, at least, that is the consensus for the time being, each of which is malignant in its own way. The classification of the disease fittingly seems to mirror its phenotype in its dynamic flexibility; once there were six subtypes, then nine, and now, the EDS Society has rounded out the figure to fourteen (Malfait et al. 2020). The entire venture of placing patients into smaller and more specific gene pools seems rather silly to me. I am already rare enough. I would rather not be more alone than I already am. It is hard for me to pin myself down hard and fast into a single division at this moment. I either have hypermobile EDS, a polygenic condition in which several mutations contribute to systemic hypermobility, or a form known as classical-like EDS that is circumscribed more by my tenascin-X deficiency than by the popping in and out of my joints, my susceptibility to fractures, the collection of bruises on my legs, my faulty clotting system, my wayward gastrointestinal tract, and, of course, the spontaneous leaking of my cerebrospinal fluid. This as-of-now unclassifiable version of me has a ring of poetic romance. I am in limbo, in some liminal space between here and there. I am so convoluted that not even science or the taxonomic jargon of modern

medicine can define me. Part of me likes that idea. Only I can tell myself who I am.

Hippocrates (400 B.C.E.) allegedly documented the first cases of EDS (though the disease had yet to be named) among Nomads and Scythians, who exhibited joint laxity and extensive scarring. The latter may have resulted from cauterization treatment, which may have been implemented to reduce joint hypermobility (Littre 1840). While scattered anecdotal reports, such as that of Niccolò Paganini, the renowned violin "Virtuoso in Excelsis," highlight symptomology consistent with the EDS phenotype, the aim of exhaustively describing the disease was not realized until the late 19th century (McKusick 1972). At the 1892 Moscow Venereology and Dermatology Society meeting, Dr. Tschernogobow discussed two patients with EDS-associated features, including "fragility and hyperelasticity of the skin", "a failure to hold sutures", [and] "hypermobility and luxation of joints" (Tschernogobow 1891). In 1901, the Danish dermatologist Edvard Ehlers published a case study involving a patient with hypermobile joints, stretchy skin, bruising, and a history of subluxations. Seven years later, Henri-Alexandre Danlos, a French physician, assessed another patient with skin lesions that he believed were rooted in vascular and inflammatory etiologies (Beighton 1970). In an attempt to classify the condition in 1936, Dr. Frederick Parkes-Weber named it Ehlers-Danlos syndrome (Parapia & Jackson 2008).

Based on pedigree analysis, a study posited that the condition followed an autosomal dominant mode of transmission. However, the first unearthed molecular cause of EDS was autosomal recessive in nature. Another study discovered this recessive variant in

the gene coding for lysyl hydroxylase, an enzyme that attaches a hydroxyl group to collagen lysines, a reaction essential for ECM development and remodeling (Beighton et al. 1998; Scietti et al. 2018). Classification of EDS dates to the 1960s, and Peter Beighton (1998) (after whom the current EDS clinical scoring method is named) refined six subclasses of EDS proposed by an international connective tissue cohort a decade earlier (Parapia & Jackson 2008).

Although its prevalence is contested and continually revised in the scientific literature, EDS affects a minimum of 1 in 5,000. As hEDS is thought to comprise up to 90 percent of EDS cases, its frequency in the general population is, likewise, at least approximately 1 in 5,000. Epidemiological data suggest that hEDS is the most common genetically transmitted connective tissue disease that afflicts roughly two million in the United Kingdom, 10 million in the United States, 17 million in Europe, and 255 million internationally (Steinmann et al. 2002; Mulvey et al. 2013).

Although Dr. Johnson and Dr. Falls' conclusion regarding its dominant mode of inheritance is supported by ongoing pedigree analysis, hEDS transmission (unlike other forms of EDS) is far from that of a clear-cut Mendelian disorder. On top of its poorly elucidated and likely heterogeneous polygenic background (to be elaborated on in Chapter 23), hEDS exhibits sex bias, variable expressivity, and non-penetrance. Twin studies strongly indicate that joint hypermobility (JH), a defining feature of hEDS, has a genetic basis; among 483 pairs of female monozygotic twins, the concordance rate of JH was 60 percent, whereas 472 pairs of dizygotic female twins demonstrated a concordance rate of JH of 36 percent (Hakim et al. 2004). It is challenging, however, to pinpoint the genetic and biological mechanisms underpinning

Type	Mode of inheritance	Defect	Examples of clinical presentations
Classical (EDS I and II)	AD	Abnormal type V collagen	Skin laxity, scars (Fig 4), joint hypermobility, easy bruising, muscle hypotonia, hernias.
Hypermobility (EDS III)	AD	Unknown	Skin laxity (Fig 1), velvet skin, joint hypermobility, recurrent joint dislocations.
Vascular (EDS IV)	AD	Abnormal type III collagen	Arterial rupture, easy bruising (Fig 5), hypermobility of small joints, varicose veins.
Kyphoscoliosis (EDS VI)	AR	Deficiency of LH	Joint laxity, muscle hypotonia in infants, scoliosis from birth, sclera fragility.
Arthroclasia (part of EDS VII)	AD	Deficiency of chains in type I collagen	Joint hypermobility (Figs 2 and 3) and dislocations, skin laxity, easy bruising, muscle hypotonia, kyphoscoliosis.
Dermatosparaxis (was included in EDS VII)	AR	Deficiency of enzyme in type I collagen	Sagging redundant skin, soft, dough skin texture, easy bruising, hernias, premature rupture of fetal membranes.

AD, autosomal dominant; AR, autosomal recessive; LH, lysyl hydroxylase.

Figure 2.2: *Beighton's 1998 classification of Ehlers-Danlos syndrome (EDS).* In the 1960s, experts began to classify EDS into subcategories. Beighton revised EDS classification according to six major subtypes in 1998.

Adapted from "Ehlers-Danlos Syndrome—A Historical Review," by Parapia, L. A., & Jackson, C., 2008, *British Journal of Haematology*, *141*(1), 33.

the constellation of the hEDS phenotype, which itself differs from one patient to the next.

Like most chronic pain conditions, hEDS, as described below in Joanne Demmler and associates' longitudinal study, primarily impacts females during puberty. In a study of 143 males and 275 females reliant on Beighton scoring, a clinical proxy for joint laxity, demonstrated a compelling association between developmental stages, sex, and hypermobility in which females undergoing and following puberty were disproportionately affected relative to males proceeding through parallel maturation stages (Tinkle et al. 2017).

While hEDS, especially in females, often rears its head during adolescence, its heterogeneous manifestation and its overlapping symptoms with chronic fatigue syndrome, irritable bowel syndrome, temporomandibular joint dysfunction, sleep disorders, depression, and anxiety often render the condition undiagnosed or misdiagnosed until later, if at any point, in adulthood.

Often concealed behind alternate diagnoses, hEDS manifests uniquely in each patient on account of its variable expressivity, pleiotropy, sex bias, individualized genetic origins, and interplay with other environmental factors (to be addressed in Chapter 23). The plastic phenotype associated with hEDS spans the spectrum from highly functional celebrities, including Sia and Lena Dunham, to wheelchair-bound incapacitated individuals subsisting on disability benefits. In short, while EDS is itself a medical zebra, its wide-ranging phenotypic variability means that EDS patients frequently fail to conform to any "normative" expectations of an EDS zebra. In addition to confounding and

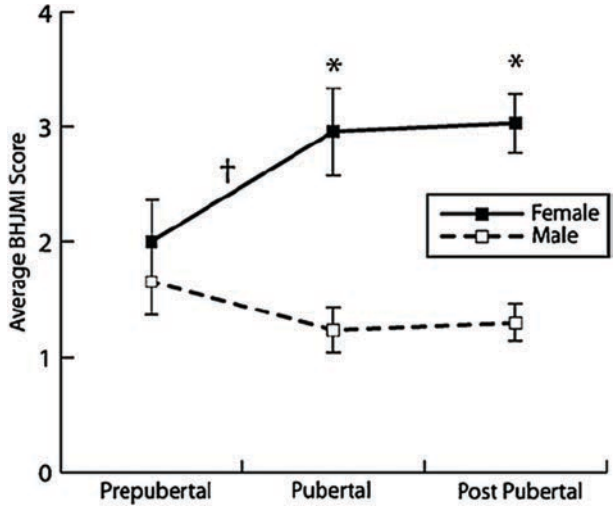


Figure 2.3: *Association between sex, hypermobility, and puberty:* Correlation between sex, maturation status, and Beighton score (BHJMI), a proxy of joint hypermobility, in a population of 143 males and 275 females. While BHJMI increased in females during puberty, scores decreased in males over the same developmental period.

Adapted from "Hypermobile Ehlers-Danlos Syndrome (a.k.a. Ehlers-Danlos syndrome Type III and Ehlers-Danlos Syndrome Hypermobility Type): Clinical Description and Natural History," by Tinkle et al., 2017, *American Journal of Medical Genetics. Part C, Seminars in Medical Genetics*, *175*(1), 51.

stalling the diagnostic process, this heterogeneous clinical presentation contributes to a sense of isolation; each hEDS case is essentially its own disease, even though Western medicine calls each instance by the same name. As a patient, it is only natural to experience anxiety secondary to the uncertain course that lies ahead—there is no prognostic roadmap for hEDS patients. Because the hEDS phenotype does not fit any comprehensive mold, each patient's series of ebbs and flows belongs solely to them. While marginal cases (mentioned above) certainly exist,

my story (and that of other females I have encountered) involving fluctuating severity falls within a sliding intermediate range.

Lara Bloom, President and CEO of The Ehlers-Danlos Society, Suzanne Gauron, Goldman Sachs managing director and Lime Connect board member, and Cortney Gensemer, who is earning her Ph.D. in EDS research, are examples, like myself, of mid-range phenotypes. Each of them copes with routine dislocations, among other daily obstacles. My relationships with each one of these empowered but challenged females ignite a hope that I too will ultimately be able to manage EDS's vicissitudes and a career. All three women have not only become their own medical advocates but have each pursued EDS-related work—in the forms of international outreach, promoting disabled people in the workforce, or science; far from permitting their disease to define them, these females continue to channel their experience as de facto experts in a condition that is too often misdiagnosed and neglected by the medical system.

Founded on the acute care model, the Western medical establishment was not designed to manage chronic conditions. Instead, it relies on pathological and physiological metrics to define what, on average, constitutes binary "normal" versus "diseased" states and to unearth mechanisms and treatments for short-term ailments. In the setting of chronic disease, this translates into a disease-based "Whack-a-mole" approach whereby patients become a repository of one-size-fits-all diagnoses and therapies that do not treat the foundational systemic physiological issue, but rather mitigate symptoms as they arise. The tendency to reduce chronic disease patients to a specific manifestation or diagnosis is generally an outgrowth of a "silo-based" outlook on

medicine that arms clinicians with increasingly specialized skill-sets instead of with mastery to probe human biology holistically (Institute of Medicine 2001; Rothman & Wagner 2003).

Furthermore, the acute care paradigm, while incredibly effective at targeting infections, fails to address many modulators of chronic illness, including diet, physical activity, and psychosocial factors. Western medicine falls short of recognizing EDS when its symptoms initially surface and of collaborating with the patient following diagnosis to handle and prevent setbacks (Leveille et al. 1998; Lorig et al. 1999). As an EDS patient at the mercy of Western medicine for over two decades, I have learned firsthand that chronically ill patients require chronic coordinated medical attention that encompasses the multiplex matrix of lifestyle and biological aspects of disease. Rather than collecting unactionable labels and diagnoses, patients would benefit from dynamic partnerships with their care providers. With the aim of optimizing quality of life, both parties should aggregate personalized data—by way of health-tracking technologies, omics platforms (e.g., proteomics, genomics, metabolomics, transcriptomics, and epigenomics) and biophysiological assessments—that is analyzed by machine learning. In doing so, the patient adopts the role of an invested agent, not a passive subject, who accumulates real-time health metrics that collectively comprise a closed-loop mechanism for habit recalibration.

As my blood continues to be analyzed via different genetic screens, including whole-genome and exome sequencing, scientists are discovering novel EDS-associated genes and I am becoming convinced that multiple genetic errors contribute to

my EDS. My mutations are like a hydra; as researchers discover one coding flaw, another seems to emerge from its hiding place among my chromosomes. Due to the scientifically reconfirmed links between EDS and a disordered ECM, I am convinced that my mutated *TNXB* and *KLK* genes (in addition, perhaps, to yet undiscovered EDS-related mutations), both of which impair ECM architecture, contribute to my EDS. In their paper, Nicola Chiarelli (2016) and her coworkers disclosed that cells extracted from hypermobile EDS patients exhibit disorganized ECM proteins, including collagen (Chiarelli et al. 2016). To identify candidate genes responsible for this finding, the authors investigated the differences in gene expression between EDS patients' skin tissue and control subjects' skin tissue and isolated 208 genes of interest. As research gradually accumulates, it is solidifying from conjecture to fact that ECM disorder and EDS are intimately related. It appears to be far from coincidental that both of my currently established mutations disrupt ECM integrity. Thus, notwithstanding the reported association between classical-like EDS and a reduction in tenascin-X levels, the genetic etiology of my EDS seems to lean more toward the multigene hypermobile variety than toward the monogenic *TNXB* type.

On top of all the boxing in and labeling that account for genotypic and phenotypic manifestations of the disease, once you get sorted into one of these dystopian Hogwarts houses, that is really it. You get a label and that is all; there is no means of erasure, no cure, just a life sentence, assuming that, like me, you are not afflicted with a form of the disease that threatens your vascular system. EDS does not possess the sexy research appeal of cancer or Alzheimer's, and there is a paucity of funds invested in finding a cure. Perhaps, if the

condition's name had not morphed from ED to EDS, people would be more willing to donate to funding efforts under the misconception that their finances were aiding males' sex drives.

EDS is a genetic black box and science only offers, at best, tenuous connections between associated genetic defects and its spectral clinical presentation. Often, the disease emerges from a rather quiescent state during puberty, and common opinion attributes the development of EDS symptoms to the hormonal hailstorm that hits. The latter may explain Joanne Demmler (2019) and her collaborators' findings based on medical records from 1990 through 2017 of roughly 6,000 hypermobile EDS patients that 70 percent of the patients were female while only 30 percent were male (Demmler et al. 2019). Furthermore, while males tended to be diagnosed between ages five and nine, females, as per the researchers, were commonly diagnosed with EDS patients between the ages of 15 and 19, at the earliest (Gensemer et al. 2021). Such findings are secondary to the hormonal fluctuations during a 28-day menstrual cycle between estrogens, which stabilize collagen, and progestogens, which loosen collagen. In males, however, androgens, such as testosterone, are the only predominant sex hormones and do not influence collagen and EDS symptoms (Heraty 2014). If anything, testosterone aids in building muscle and may thus assist with muscle strength surrounding loose joints, which may be the reason behind the earlier age of diagnosis in males as testosterone levels climb during puberty. Additionally, hormones may mediate the epigenome, the deposition and removal of methyl and acetyl groups on genomic regions, and thereby modify gene expression to ramp up disease pathology. Even in the absence of a plethora of

scientific validation, I buy into the hormonal hypothesis because it fits into my own narrative arc.

That is all to say that on the morning of December 15, 1994, my genes did not feel askew in my cells, and I appeared and felt as content and healthy as any other child.

3
Innocence unencumbered

As a child, I expected the times to carry me, to swaddle me like a comforting tide that carries but does not overcome, to drift me toward the shores of where I should be. A current that carried me from present to future, blurring the boundaries between what is and what will be.

My father was anchored in Memphis soil like a firm oak. I can picture him walking down Memphis streets as a young boy in white knickers, impeccably polished black Sabbath shoes, and a white polo shirt. His hair is lightly salted with product and combed so a part falls just above his ear, a bit off-center on purpose, of course. Years later, he would even take his Scotch neat.

Notwithstanding its insular, retrograde, and religiously polarized stink, Memphis was a sort of paradise for my innocent self. Utterly unaware of who I was or wanted to become at the young age of three, I giddily flaunted that reality and never dressed simply as Elly. My wardrobe contained far more costumes than T-shirts. I would have slept in *The Wizard of Oz*'s Dorothy garb, ruby slippers, and all, if my mother had permitted. I often picnicked on a swatch of green beside the pool in our backyard. I splayed myself stomach-side down with my hand cradling my chin, a posture

that would haunt me two decades later, as I listened to the ontological musings of the mammoth stuffed black bear, who dined on my imaginary biscuits and tea without a fuss.

The figments of fancies, however, did not fill any social void. My three and four-year-old being did not want for people. I ambled beside my mother to the Memphis Jewish Community Center daily. My mother would kiss the faint lines spirographed across my small palm and gently fold my digits to safeguard the ellipsoid outline of red. "This kiss will keep you safe. This is your kissing hand. I am with you." Looking back, the four words "I am with you" were a vow, a sincere and permanent promise my mother would need to painfully fulfill in due time. Upon crossing the classroom threshold, my mother's embrace was rapidly substituted by that wonderfully delivered by Miss Jamie. She would wrap herself around me until I disappeared inside her and then hold me before her, her massive soft hands clutching my bony shoulders, and ask, "So Miss Elly, how are we doing today?"

Memphis took formality as seriously as lawyers view the law. Once one is born at Baptist Hospital, one implicitly accepts the stipulations of Southern hospitality as readily as one welcomes one's own existence. At age four, I was so assimilated into the system that I did not even wonder why I was never just plain Elly, but always Miss Elly. Why in the world did a four-year-old need to be greeted with such pomp and circumstance?

My school days during which I sat huddled between Cara and Caroline were often followed by ballet or gymnastics. We were something of a trio, me, Cara, and Caroline, with my untamable blond curls yanked into a bun overlaid with a pink crocheted

covering, Cara's dark ringlets spinning about her head, and Caroline's electric red hair. We ran on tiptoes in our pink tights, leotards, and ballet shoes.

The journey to gymnastics in the backseat of Tanya's Volvo made me realize the wonder inherent in the mother-daughter bond. I was always tucked so nicely into the one my mother and I share that I inevitably only perceived it from the inside, so unaware of its form, its contours from afar. But seat-belted beside my mother, I watched a parallel dyad in action as Tanya and her daughter, my dearest friend at the time, Polly, weighed the virtues of a new barrette Polly was fashioning.

On Sundays, Mom would loop me into the car seat and halt at Polly's front gate. With our mothers lounging by the pool and sipping on iced tea, Polly and I invaded the cooler in the small cabin adjacent to the main house and began guzzling cans of Sprite and Coke. It was not the sugary content that we were after but the colorful cans in which the beverages were stored. We adjusted the dial on the radio beside the pool until both of us started to move; each of us clutched a Sprite can in one hand and a Coke in the other as we pranced across each other's shadows with our own impromptu choreography. The cans seemed so requisite, back then, to our inane dancing, which always ended in peals of laughter that bounced contagiously from us to our mothers and back again.

My lack of dancing skills did not only emerge when I was in Polly's company but was also laid bare before my brothers on several occasions. My parents used to claim in jest that they were blessed with two families and one marriage, as Avery and Jason,

my two brothers, are ten and eight years my seniors, respectively. I am essentially a single child of three fathers and one mother. Avery, my mother, and I, for the most part, seem to harbor three shards of the same soul. Each of us came into this world as a poet, a quester uncertain of what is to be quested.

Ave's lanky six feet and two inches, coated in peaches and cream, is topped off by a head of dark hair. He is handsome, my brother, but not so startlingly beautiful that he is a cause for people to pause. There is something so sincere, so irrefutably honest, about his look, the way his brown eyes take you into their orbit and demand nothing of you but to let him in.

Jason, like my father, is not as straightforward. His expression does not say quite as much, or, if it does, you must know its language before you can decode its creases. Jason is striking; his physique is toned in all the right places, and the black curls on his head just know what to do. We all need a Jason, that sibling who knows exactly what to say to set your frame vibrating in a frenzy of full-bodied laughter and plots adventure without displaying it in the lines of his face and the darting of his eyes.

"El, apply one. Look how awesome they look." Jason spun about and crouched, his body dripping wetness all over the pool deck. His figure emerged from our backyard pool, and he was elated and in disbelief that the plaster on his bony bicep had persisted in the still-chlorinated water, even though the box explicitly noted the waterproof nature of the tattoo bandages.

He was not concealing a scrape or a cut. He patted the enrapturing whorl of rainbow as though it were an army medallion he had earned by the skin of his teeth, rather than an ornament

he had taken from a cardboard box and pressed against himself. That summer of 1998 was one of multicolored plasters applied to unblemished skin.

"Ja, I want one too," I intoned in a small voice.

I did not need to plead with him in any sort of manner. Within an instant, my shoulder was padded with a badge of fiery reds and yellows that, at the time, I innocently and fallaciously assumed would protect me from life's cruel incendiary path.

With my father directing his family's mortgage company and my mother working as a radiologist at the University of Tennessee, I usually found my small self under the tender watch of my nanny, Flora. Although I did not require protection of any variety amidst my slice of childhood suburban perfection, Flora continues to occupy the form of an angel in my mind. I would nuzzle my way into crannies of her expansive black arms, finding some solace when I cozied myself up to her being as she spoon-fed me rolled oats and we watched Mr. Rogers transport small trains across tracks.

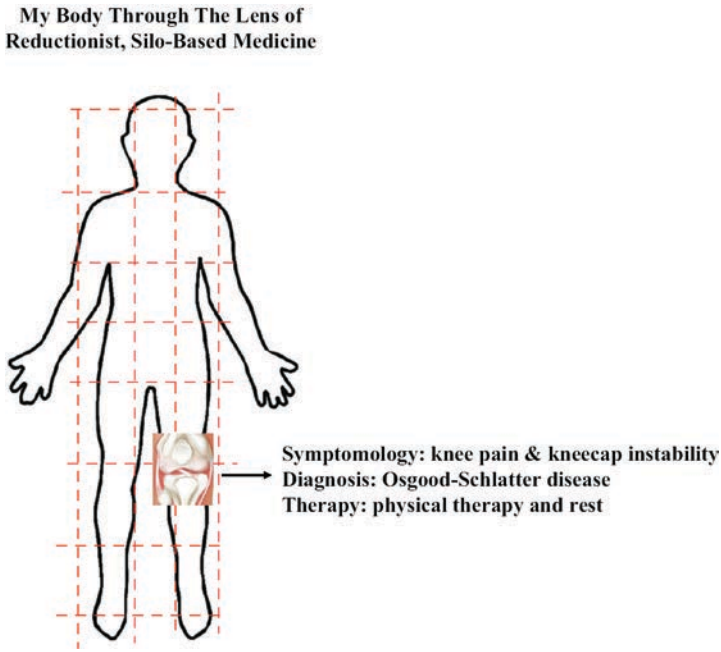
When a lump in my mother's breast was labeled cancerous, Flora filled the vacuum left in my mother's absence. As a four-year-old, the only oddity of which I took note was that my mother's frequent hugging halted. Flora's arms wrapped themselves about me, imprinting me with a permanent sense that I was loved.

It is challenging for a four-year-old to grasp the inevitability of death, and, in retrospect, I am not quite certain to what, if any, extent my mother's illness fazed me. I just knew that there was somehow less of her to spare, but I am not sure if I made more of it in my own head than I did upon noticing the carton of milk

in the fridge weighed less than would suffice to douse a bowl of Fruit Loops. The first time I think I actually processed her absence was when she reappeared, adorned in a dark green blouse that hung flaccidly about her chest to mask the scars she had to carry after her bilateral mastectomy a week earlier. She smiled my way in her usual manner. Seeing her at my ballet recital was like walking into the interior of a dream, a sentiment I would hold on to for dear life.

4
An early aversion to sitting solo

But bliss does not always confront us that easily. Sometimes, we must search for it, reveal it to ourselves. It may require us to stumble, to skin our knees.



My upturned eyes scanned the rooftop playground bounded by black metallic crosshatching that appeared to almost touch the sky from the corner of 85th and Park Avenue.

"That's it, El, your new backyard. You will see how wonderful it'll be." My father's statement sounded raspy. I ogled his dark eyes gloss over with loss, like chocolate truffles liquefying in the sun.

"But, Dad, where's the grass? Where are the trees? Where's the pool?" Evidently, the notion of geography was too oversized for my juvenile neurons. My interrogations rang with incredulity. My father took my small hand in his large one and gave it a gentle squeeze, a clandestine embrace.

My family relocated to the epicenter of the Upper East Side, to which my father was lured by Ramaz, a Jewish day school whose academic caliber far outstripped that of the Memphis Hebrew Academy. Although initially jolted into disoriented bewilderment by the lack of green, the dense crowds, and the interruptions of my own reveries among the incessant beeping of horns and the senseless segments of conversation, I, like any child in my circumstances, would quickly found my way and readily fall, without mournful regret, into a dazzling new pattern of being.

On the opposite end of Ramaz's kindergarten classroom, a paradox of milky skin and dark hair knelt on a wooden chair. Her eyes were fixed on a miniature chessboard. As she concurrently played the role of herself and her opponent, Ruby failed to recognize the firmness of my stare. Soon after, we became best friends.

We ambled through sweltering summer weekends at Ruby's Westhampton home, gulping peach Snapple between rounds of tennis or lolling about on inflatables in her pool. We drunkenly meandered across Beach Lane, two six-year-olds erupting into convulsive peals of laughter.

"One, two, three, let's go El." "You sure?"

"Yes, let's do it."

We shut our eyes, threaded our elbows into each other, and commenced running at full steam. Our bodies collided into helpless pedestrians, who were either aggravated by our act or deemed it frivolously endearing. With only four senses to guide us, it was a tough call.

Something about relinquishing sight and running into reality had a daring irresistibility to it.

In the second grade, our rabblerousing morphed into something for which I had to pay dividends. I was biologically at odds with the concept of sitting in my own classroom chair; I was decidedly unclear as to why I was ordered to place my bottom on a solitary slab of metal when it was so much more comfortable, and less isolating, to simply drape myself over Ruby's lap.

"Elly, return to your own seat, right now." The teacher's directives were shrill, like a siren.

I plodded reluctantly across the classroom until I reached my assigned chair. Little did I, or anyone else for that matter, know that my disinclination to station myself at a table was hardwired within the seams of my genetic code. My poor proprioception—my ineptitude to generate an internal map of my body in space and to internalize where I ended and someone else began—was rearing its head. In hindsight, I wonder if my game of musical chairs should have been more judiciously unpacked, and if it may have served as a faint flicker of a warning of what was yet to come.

During recess, Ruby and I often ran fearlessly about the fenced-in yard at the top of the school building. Afterward, we languished on the monkey bars, more often hanging by our knees than by our arms. I effortlessly perused the clouds in the sky as I dangled there or made my way back and forth across the blue metallic bars. My classmates applauded me for my agile trips, the endless to-and-fro as I thrust my being forward. I did not deserve any sort of credit or laudatory comments. My apparent talent likely had nothing to do with effort and resolve on my part and was, instead, an outgrowth of my limber tissues, my internal loose connections.

I should have come packaged with an accident-prone warning, a flashy yellow sticker on my head as I issued forth from my mother's womb.

My third-grade experience mainly featured Dana, whose lean angular face always appeared bunched about her eyes and prepared for laughter. From the back, with her hair the same golden shade as my own, strangers mistook us for fraternal twins.

I often spent the night on a mattress on Dana's bedroom floor. She slept on the top bunk of her bed. Dana's younger sister, Kira, lay on the bottom bunk and put up rather well with our shenanigans.

"Blastoff time! Prepare for my landing!"

"The mattress is all ready, El. You can fly." I dove, feet first, downward, cruising the air between Dana's upper bunk and the mattress on which I had slept the night prior.

Notwithstanding my blatant propensity for movement of any sort, however ludicrous, a worthy novel could often calm the

nerves in my lower half sufficiently to slow me down for hours, or even days.

"I'm fairly certain that I will clobber you this time." I flashed Dana my book and specified the slender stack of pages I had yet to turn, scanning over their frayed tips with my finger. We refrained from discussing current page numbers, for fear of disclosing too much information and spoiling our contest.

We raced each other through the *Babysitter's Club*, *A Series of Unfortunate Events*, and *Harry Potter*, which took up much of third and fourth grade. My monkey bar time was exchanged for recesses spent in unobtrusive corners of the rooftop playground, the soles of my shoes pressing up against those of Dana, as we sped through sentences with anticipation.

In the middle of fourth grade, when Dana began walking clumsily, she joined me on the sidelines of gym class. Shrouded in sweaty jerseys, my other classmates were commanded by our gym instructor to run within the fading white track marks on the gym floor. What a regal joy it was to reside on my throne of folded gym mats and observe my peers run indecorously. My viewership began earlier that year, when, much like Dana's situation, my knee caps were a source of pain and refused to remain in their respective patellar sockets. While each of our orthopedists diagnosed us with the same condition, Osgood-Schlatter disease—an inflammation of the shin bones—a pathology appallingly more egregious and systemic, unbeknownst to me or to medical providers, was pulsating through me.

"At least neither of us has to sit on this mountain of mats alone," Dana commented in her glass half-full cheeriness.

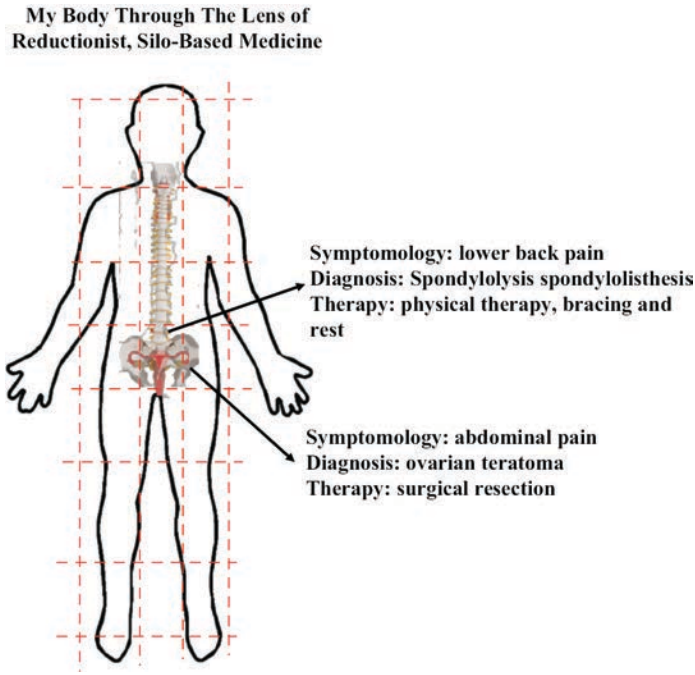
"That's true." I squeezed her hand.

Looking back, I recognize how fortunate I was to welcome a friend into my world of fractured health. The tides of illness would soon rise again, sweeping me into them in solitude.

5
Too much torque and torsion

My rainbows and dreams have shattered like fragile glass panes against the pain, the grueling, incessant blanket of darkness in which I dwell.

I have thrown God off his pedestal; I am alone with myself in the night of life.



Perspiration drizzled down my lower back, and the moist asphalt spattered about the bridges of my white tennis shoes. My hair was on the brink of coming undone from the grasp of its elastic holder. I was enveloped in Sutton East Tennis Club's colossal white bubble, and the only light making its way in the direction of my retinas was glaringly synthetic. I sported a wide-brimmed white cap that felt indispensable to the ensemble I was going for.

I prepared myself for my private lessons with Adam with the gusto that my Ramaz cohort would soon ready themselves for Bat Mitzvahs. With his stout five-foot stature and his muscles bulging at all possible angles, Adam's form appeared like a squat mountain range. The degree to which I comported myself like a tennis professional, in my white skirt and faded pink polo, seemed to sensibly correlate with the extent to which I played like one. My inner calculus was, of course, plainly flawed.

"Hey, Adam, how is my stance?" I primed myself to slice a crisp forehand and rotated my chest leftward while fine-tuning the pivot of my sullied shoes.

"Tilt your concentration upward, Elly. Look directly in front of you. Let your feet do what they know how to do without forcing them into place." Adam's words rebounded off the inflated walls and echoed before they reached my ears. With the thrust of auditory double vision, his syllables hit me once and then again.

"Like this?" I questioned in desperation. My breath felt thick, and my heart thumped in exhaustion.

"Ready to roll, Elly." He served the ball, shuttling it my way. The ball darted to my left; I braced myself for my forehand without administering my feet a visual check. I trusted my posture,

anchored my ribs leftward, and levered my arm to its maximal span as my racket confronted the ball, dead on.

The following Sunday, as summer rallied to a sweltering end, I pedaled my way in my parents' wake along the outer ring of Central Park. The pink and white streamers fringed about my handlebars wilted in the blistering heat. I had outgrown my infantile bike wheels, whose diameter was more apt for someone half my size. I strained my legs to keep pace and ramped up the number of rotations per second to the maximum frequency I could muster.

"Prepare for the downhill, Elaine," my Dad hollered. Unlike my mother, or anyone else for that matter, my father gets a kick out of calling me by my full name; I imagine him tasting its succulent memory of his departed mother as it rolls off his tongue. My legal name continues to pierce my eardrums with immense ceremony and provokes me to mull over superlatively folded napkins and silver-encrusted china plates. The title "Elaine" offers little, if any, room to accommodate an unruly constitution and chaotic curls. I prefer the more succinct "Elly."

The wind caught me by delightful surprise on the downward slope, and I beamed so expansively. Back then, I measured happiness by the downhills on bike paths, which took me by ideal surprise. Every concrete peak had its decline. Things were simple until they weren't.

The next morning, the alarm sounded at 7 a.m., blaring with insistency. My existence as a real person was beginning. Crossing the threshold from lower to middle school is like coming into being, relinquishing childhood nightgowns and making your

way from imaginings to reality. The world comes into focus before your eyes. Curves impose themselves about your waist. You glimpse your own metamorphosis. Jolted awake by these revelations, I struggled with the process of selecting a polo shirt suitable for the momentous day that lay ahead. To my astonishment, the color of my shirt had little to no bearing on the day's unraveling, which I would later identify as my own.

Gym class followed homeroom, and I was intent on making an opportune arrival. I feared the five-floor gap between homeroom and the gymnasium may pose a threat to my timely agenda. I bolted down the stairs, gym shoes in hand. In an effort to beat the clock, I alternated my sprinting with spurts of jumping. Swiftly, without any presentiment, a faint cracking noise sounded like a faraway glass shattering on a tile floor. The ominous clatter of wreckage, however, was all too near, sending dizzying throbbing pain down my spine and wooziness to my head. My lumbar spine was breaking. I blacked out. When I came to on the third-floor stairwell, the school nurse and my mother were pitched over me at their hips.

"El, don't fret. We will get all of this sorted out. We are headed to the very best pediatric orthopedist at Hospital for Special Surgery. I promise you will recover soon and be back at school." My mother's words rang with a partial truth. I would resume my education without a pause, at least for the time being. But returning to my pre-injured sense of naive levity was an entirely different pill to swallow. My mother balled her chunky knit sweater into a mock pillow that she positioned beneath my head, which reclined on her lap in the backseat of the cab. She did not utter much after her vow. The silence between our shared disquiet and the rest of

civilization seemed to stretch us into our own galaxy, a cosmos we would occupy as a pair for a lifetime.

At this point, I am confident that I could win a gold medal for the number of magnetic resonance imaging (MRI) scans I have endured. MRI machines rely on the body's effectively infinite supply of hydrogen atoms, which align in the direction of the MRI's magnetic field to generate images. I no longer mind the headache-inducing dissonance of electric saws slicing metal but meditate through it, instructing myself to "breathe in trust and to breathe out dread."

Dr. Gordon studied the Rorschach of my MRI like I stare at a piece of modern art, paint slanting here and dripping there. If you glance hard enough and twist your face beyond recognition into bewilderment, you can find meaning, fashion an attractively coherent bow onto God's work. But at the end of the day, your interpretation is primarily conjecture. No one really fully understands modern art or human biology. My mother fastened her eyes on the screen that engrossed Dr. Gordon. The radiologist in her emerged from her maternal shell and then retreated back into it again when my glance met hers. The dynamic dance between doctor and mother was certainly tricky to navigate, even then.

"So, Dr. Gordon, what's the verdict?" My mother's voice sounded gravelly, like she was contending with a virus.

"Dr. Katz, it's a clear case of spondylosis and a grade one spondylolisthesis."

"Huh?" I interjected quizzically. My mouth ached at the thought of pronouncing those terms. They sounded like a tripping hazard for one's tongue.

The doctor's eyes ping-ponged from my mother, whose expression was contorted with suppressed tears, to me and back again a few times to intuit an apt timing for his response.

"Elly, basically things are a bit out of place in your lower back. Spondylosis means that you have a stress fracture in the bridges between your lumbar spine facet joints, and spondylolisthesis means that your vertebral bones have slightly slipped out of alignment.

Typically, the former precedes the latter."

I wanted to be irate at my off-kilter and shattered status, but I was not sure how to go about this. I was uncertain as to the object of my anger or if my wrath was merely a mask for a penetrating fear. My feelings were not as clear-cut as my diagnosis, as categorical as the fracture in my lumbar spine. Dr. Gordon omitted, or failed to recognize, that my diagnosis was commonplace among hypermobile Olympic gymnasts, especially those with EDS. He overlooked the possibility that my lax connective tissue and low bone density, two hallmarks of EDS, contributed to my diagnosis. Years later, to his and to my own astonishment, I would glide my own displaced vertebrae into alignment on a daily basis.

My mother and I descended in the elevator in silence until we reached the hospital basement. A gentle man with a metal prosthetic for a leg jotted down my metrics as he wrapped different parts of my torso with a measuring tape, tightening his thumb and forefinger about numbers that told him where I began and ended.

"In two weeks, I will have this done. You will have to return to be sure the fit is correct. I will be in touch with you, Dr. Katz."

The plastic brace had a nice sheen to it, but that was its only redeeming feature. Its cumbersome whiteness mounted me from pelvis to collarbone, and three thick Velcro straps seat-belted me into its nauseating tautness.

My new fortification was, understatedly, not in favor among the parade of fifth graders of my sex, most of whom were decidedly fixated on the latest fashionable zip-ups. My thick slab of armor was, unequivocally, not in vogue. It proved quite challenging, if not totally impossible, to fully conceal the brace under any outfit.

"Knock, knock. Now, who's home today?"

"Quit it. I'm in enough pain without your jeering." I held my tears at bay. I sensed warm breath behind me and heard the soft whisper of an inhale.

"Yeah, Kimberly. Just leave her alone."

"Thanks, Luna. You can head to class now. I will be alright."

Each time Kimberly's spiteful face approached mine and her fist clambered against my new appendage, my patience thinned incrementally. I wobbled toward my locker without the intention of disposing of or retrieving books. I poked my head into its depths, permitting the tears to run soundlessly until my eyes dried and the liquid grief had run its course.

Three afternoons per week, I taxied from Ramaz middle school to Hospital for Special Surgery for physical therapy, an experience that I took to with unexpected fondness. My Mom departed her office at Weill Cornell at a quarter to four in the afternoon and threw open a taxi door so I could climb aboard.

Kendel was often poised in a squat with her arms outstretched when I leapt through the elevator doors and into her. I never considered that I would take a liking to someone who twisted my limbs to fit the angle specified on her protractor and demanded twenty leg lifts. She was well versed in how to push my buttons, and I complied without hesitation with her commands.

The physical therapy center at the hospital was the one place my body flowed synchronously with that of another human being. It was the one location that I was at liberty to separate myself from the clumsy brace, to reexperience the lightness of being, of skin, bones, and soul unencumbered by plastic walls. My boundaries were down. Music poured through the overhead speaker, leaving me feeling unbroken and stable for the time being.

When the brace ultimately came off after what felt like an eternity and a half, I was elated. My whole body was bathed in this newfound sense of freedom. I could move at my own whim. To my dismay, only three months later, my recent zest for moving through life with alacrity got the best of me, or at the very least, of my forehead.

"El, go pack up. There is a ton to place into the suitcase before we leave."

"Alright, mom. Don't worry, I can throw…I mean fold everything I need into place quickly."

We were bound for Florida as a family in two hours, and in the tumultuous terrain of my closet, in which more clothing was haphazardly strewn about the floor than located on shelves or hangers, I would be fortunate if I could pinpoint any of the attire my mother listed in a timely fashion. But none of that mattered after my forehead collided

so fiercely with the corner feeding into the hallway beside my bedroom. A fragment of plaster detached from the wall and wafted gracefully to the wooden floor. My landing was not as gentle as that of the segment of wall, and my body struck the ground with an alarming crash. My frontal bone cracked, and blood began to spill effusively onto the floor. The quantity of blood that poured out of me should have been another indicator that something, other than the gash on my forehead, was awry. EDS is associated with increased bleeding due to the faulty connective tissue surrounding my blood vessels. It is also related to another dominant genetic bleeding disorder, known as von Willebrand disease (VWD), that would, years later, be identified in my genetic data file. VWD results from a loss-of-function mutation in the von Willebrand Factor (VWF) located on chromosome 12 responsible for helping platelets bind to damaged blood vessels to form a stable clot. Due to my EDS, compounded by my VWF deficiency, I bleed profusely following an injury.

My mother stuffed a towel against my forehead in an ineffectual effort to halt the oozing of red. She struggled to hold me down in the ambulance's rear.

"We must staple the bones together and stitch the layers of skin into place." "Just help my daughter. Do whatever you must."

My mother's might as a physician toppled, as it would on many fateful occasions to come, in the setting of my undoing. Her credentials as a doctor gave way to her steadfast and unwavering role as my mother.

"The four sons are not to be taken literally. Each one represents a character asset or hamartia that each of us, at this very

table, possesses within." Isaac, one of our nineteen guests at our Passover table, was all too seriously contemplative. By age eleven, I was accustomed to the inevitability that my stomach's growls would linger from the moment the Passover Seder commenced until dinner was served four hours later.

My famished and irked face shot a glance across the table at Jason. My laid-back brother essentially had no interest in erudition. His skills were not illuminated in any classroom but brilliantly shone in social circumstances. Jason was a wiz at navigating the cliques that populate middle and high school. He was magnetic, and his peers could not resist the attraction of his field.

Before I could count to five, Jason's lips danced silently, mouthing the words to the most inordinately inappropriate song that popped into his head. My brother runs on music the way that most living creatures run on oxygen. It is his fuel, his raison d'être.

"I'm bringing sexy back…yeah…take it to the bridge." His smile sent me into a tizzy of unrelenting laughter. My brother followed in my lead, and his body shook. The light from the crystalline chandelier suspended above the Passover table refracted off the whites of my brother's eyes, which emitted phosphorescence in all directions. My father's voice broke through our brother-sister bond.

"Elaine and Jason, leave the table right now. Do not return until you are ready to get your acts together and start behaving like the children I raised you to be."

A decade later, as I sauntered through Harvard Yard after a linear algebra exam the week before Passover, my father phoned me.

"So, El, what's the plan for Passover this year?"

"Um, I was thinking of just going with my usual itinerary of re-listening to Feynman's *The Pleasure of Finding Things Out* and laying on ice packs arrayed in a humanesque shape. You know, to recover from this week's series of unfortunate dislocations. I'm fairly certain that after 23 trips to and from Egypt, I know its topology rather well. I don't really feel the urge to return. I may as well remain on the right side of freedom for one year, don't you think?" My Dad chortled uncontrollably. "Sounds like a wise plan, Elaine. I get it. I do."

What my Dad deciphered was something unsaid, something nuzzled between my words and the pauses between them, something too colossal, too amorphous for any vernacular. Our jocular dialogue had very little to do with Passover or Egypt and everything to do with our personal Egypt, the bondage I, and, by extension, my family, had endured throughout the past ten years. Our fates as captives could not be overturned by leaving any country; our serfdom was a life sentence, a cruel fate sealed within my genetic code.

I'm not sure where I stand vis-à-vis God. My mother is unambiguously devout; she passes Sabbath mornings hunched over our kitchen table rummaging through her collection of sermons on the weekly Torah portion. When she prays in the front entryway of our apartment, she does not simply mime the words, but her entire being revs up for the ordeal. She sways this way and that to the hushed music of the Psalms inside her head. Seesawing between illness and health is a recipe for a periodic back and forth with God, but, soon enough, the tango becomes a waltz

and, eventually, dissipates. Witness to my family's interminable support of me and to my body's resilience, I typically erect my altar at the feet of mankind, rather than at those of the divine. I would be lost to classify myself into a system, be it theistic, agnostic, or atheistic for too long because I consider myself far too dynamically unstable for that sort of labeling. My sense of equilibrium is borne through a momentary snaking into and out of those boxes. More often than not, I find myself in the spaces between them rather than within their confined parameters.

On the heels of Passover, the year I was in fifth grade, I awoke on my left side with my forearm and hand submerged beneath the yellow of my pillowcase. The total absence of sensation below my elbow was the first thing I felt that April morning as I gradually slid my arm from the underside of my pillow. My elbow was indisputably no longer connected, other than by my tearing flesh, to my upper arm, and this disjointed part of my being was turning a lifeless purple and blue. I unleashed a full-bodied scream, and my parents raced down the corridor linking our bedrooms.

"Elaine Katz, may we ask you a few private questions?"

"Sure," I responded with uncertainty as to what fishing expedition the emergency room resident was on. I was bookended by my parents on a white gurney. My limp arm dangled on my mother's lap, like an extinct portion of myself I could no longer carry.

"I mean, without your parents. I want to ask you a few questions alone. Is that OK with you, Elaine?"

"Um…I guess." Nerve pain ricocheted from my elbow to my fingers. I did not really have the patience, nor the stomach, for an inquisition into the details of my personal life. My father placed

a kiss on the blond hair that veiled my right cheek, clasped my mother's shuddering hand in his own, and my parents departed the hospital room.

"So, Elaine, I need to get to the bottom of this accident. Have your parents ever hurt you?"

"No, of course not. They love me and would do anything to help me." "Are you sure? No one in your family has ever laid a hand on you?"

"I have never been hurt by anyone. The only hands that have touched me have done so out of love, like to give me a hug," I blurted out. I stared at this stranger with confused disgust and began to weep, a bellowing cry that resounded with fury. Meanwhile, my parents were subjected to their own inquest concerning our domestic life and the potential incidence of violence therein.

The resident's accusations and gall to suppose that my affectionate parents could even conceive of striking me maddened me more than my bruised and distorted arm. The majority of physicians with whom I have crossed paths mistakenly equate medicine with science, imposing the laws of cause and effect, of action and reaction, on human biology. Despite their aim of cracking a diagnostic code to deliver an efficacious course of treatment, they often grope at a logic that is specious, at best, and fail to scratch the surface of the pathology that resides far below.

These general critiques of the Western medical system particularly hold water in the setting of EDS. Patients with my disease, more often than not, become victims of a medical system that fails to understand them because its practitioners myopically

seek to address symptoms, like my dislocated elbow, through the lens of causality. I am but the sum of dislocated shoulders, broken backs, ovarian tumors, bruises on fragile skin, an autonomic nervous system whose wires are crossed and fraying at the edges, a gut overpowered by histamine-releasing cells in overdrive, and a heart that occasionally fails to keep its pace. But that is not the whole of me. Do not break into my composite symptoms. Put me together.

Relocate my parts into something coherent. Whisper me the story of my defective genes; educate me about these antagonists in my narrative so I can discover who I am and what my life can be.

Until the summer that joined fifth and sixth grade, illness was overtly physical. I was well aware that pangs of sorrow could encompass the excruciating quality of pain, but I assumed that the latter always elicited the former, rather than the reverse. My injuries necessarily took a toll on my emotional well-being. With each physical setback, I did my fair share of moping and malingering. Yet, my mental health was like a rubber band that snapped back into place each time I recovered my physical wholeness.

"Mom, get the fuck out of the shower!" My shrill command was probably in earshot of pedestrians two floors south.

I perched myself on the blue and pink pansies that patterned the chair and adjoining ottoman in my parents' bedroom. My middle half was firmly tucked into my knees, and I quavered motionless to the rhythm of the churning pain rooted in my belly. However maladroit in the context of my ordeal, the F-bomb did exactly what I needed it to do. The sound of water droplets striking the

ground abruptly ceased. The bathroom door opened, permitting steam into the room, and my mother emerged. Her expression was something between horror and perplexity.

"El, what's going on?"

"Mom, something is really not right." My mother only had to take one look at me, even without her glasses, to see into my pain. "We are going to the emergency room. I got you, babe."

The ultrasound probe was icy cold as it traced my lower abdomen, which was caked with a gelatinous goop. With no knowledge of radiographic imaging, even I could perceive the misshapen soccer ball rolling about in the black-and-white cinema of my insides.

"Hey, Elaine, can you see that?" The technologist placed her finger on the monitor before her. Her smile felt indecorously broad for this situation.

"Dr. Katz, do you see that? That orb, right under my index finger. It's a whopping 10 cm."

I clasped my abdomen as pain ascended, contorting my entire being into the shape of a human snail shell.

"What you just felt, Elaine, is called torsion. The tumor on your ovary is rotating, cutting off blood supply to it and triggering your pain."

I thought of my ovary gasping for air and being strangled by this foreign entity that had more in common with science fiction than with human biology. The mass, as the pathology later reported, was composed of cerebral tissue, teeth, and filamentous hairs.

The surgeon continued his slicing, extracting, and sewing for two hours, endeavoring to preserve the function of my right ovary. My period, which had only started two months earlier, would no longer be a monthly event. The flow of blood through me that I once resented had ceased. Even then, at thirteen, I felt its absence seeding a hole in me, a vacuum that would expand with time.

In the aftermath, my veteran status as a survivor of life was writ large on my abdomen, which was tattooed with three thick red lines zipped shut with invisible laces. In an odd way, I felt homesick for the mass that was wreaking havoc inside me. I wanted to wrest back the stolen segment of my right ovary. I missed the even feel of my skin about my belly button. But, more than anything physical, I hankered for the once endless wad of innocence that nested itself in the back pocket of my jeans, that luminous flicker in the night sky that told me I would be alright.

6
A graduating class of one

It is far too taxing to find the light in all of this; the darkness is changing me, morphing my innocence into wretched experience, hardening my softness, freezing over my warm inner core. The frost is casing over and extinguishing the fire. I am in eternal winter inside.

Despite the half-baked fear of living that burrowed its way into me in the operating room, I managed to retrieve the Nike cap from the top shelf in my closet along with my flawless forehand. In the summer preceding seventh grade, I participated in a tennis sleepaway camp in upstate New York. Resolute in my desire to resume playing competitively under Sutton East Tennis Club's bubble, I scampered across every square inch of the camp's court for seven hours each day as a mechanical arm sent balls whooshing at an industrial clip. On the hour, I performed the assuaging ritual of slipping my hand underneath my soggy shirt, canvassing the bony protrusions of my lower back. Although rubbing my palm against my slick spine carried slim to no diagnostic power, there was something consoling about memorizing the feel of my intact backside and checking myself at regular intervals.

A week into the camp, en route to a night's worth of laser tag at a nearby pier, I felt myself come undone. The bony junction

that bridged the fracture in my lumbar spine shattered. I braced myself for the impact and wrapped my arms as far as they would stretch across my torso, thinking that I could somehow double as my own seatbelt. My screams rushed through the ajar windows of the school bus and into eventide as it fell in reds and yellows onto the horizon, which exploded into dark technicolor.

I first caught sight of my father through the space between my knees. He was chugging the last of the coffee he had purchased at the roadside Dunkin' Donuts as midnight and the need for caffeine struck. When he found me resting prone on the backseat of the school bus, my father's gaze penetrated right through me with the focus of an X-ray beam.

"I know, Elly, it's your back," he said in a soft, weary voice that led me to wonder if his remark was a statement of fact or a hypothesis in the works.

"Dad," I blubbered as I grabbed hold of his bushy firm wrist. "I got you, my sweet girl. I got you."

My MRI scan told the same two-word tongue-twisting story it had two years prior.

Refractory spondylolysis and spondylolisthesis. The heavy-duty white brace resurfaced from the underside of winter gear covering the floor of my parents' coat closet. My mother placed it beside me on the bedsheets, a nightmare revisited.

The second time my back fractured, it broke me in a completely new way in a location that no radiographic imaging could detect. At fourteen, I mourned the loss of my plucky self and the laughter that rattled me to my core with delightful abandon. The curtain

of my childhood seemed to have shut without my permission. I gathered the bright red and pink polo shirts onto a shelf in my armoire and draped myself in blacks that hung lifelessly about my brace, swallowing me whole. I searched for a piece of my reality that I could trust, something I could cling to with a chiseled scar on my forehead, half a right ovary, and a snapped spine. In the liminal space between questing and discovery, I became the woman I continue to become, a poet who rifles through words she chews over and regurgitates, spinning letters into visible thoughts I can read outside of my own head. I took hold of the reins of my mind, bending sentences to my own will, and exerting control over my schoolwork.

"What time did you want me to drop you off at the party?" I looked at my mother in disbelief. I shoveled spoonfuls of cinnamon puffs moist with milk into my mouth without looking up at her.

"El, you need to let me know so I can notify my office manager." I continued chomping at full steam until I set my spoon into the excess cinnamon-infused milk and confronted her stare.

"Mom, I think I'm going to sit this one out. My sleepover party years are long gone. I would much rather spend my evening doing practice physics problems to prep for the exam." My mother scrutinized my face as though it were a bomb on the brink of explosion. She was studying me sorrowfully. In her eyes, I saw my own sadness.

"It has just…you know…been so long since you had some fun with your friends. You used to get such a thrill out of Ruby's slumber parties. I want you to feel that again." My mother reached

toward my side of the table, caressing the peaks and valleys of my knuckles.

"Mom, please. I really do not want to go this year."

I could no longer stomach Ruby and Dana's escapades. I took refuge in the pages of Charles Dickens's *Hard Times* and *A Tale of Two Cities*; I found it far easier to identify with Thomas Gradgrind's utilitarian worldview averse to fantastical pursuits and with Doctor Manette's incarceration in the Bastille during the French Revolution than with my own contemporaries.

My insurrection against God began that year. Each morning and afternoon, before assuming my designated position in Ramaz's auditorium, I removed a prayer book from the shelf, as per the hectoring monitor who made her rounds up and down the aisles to chide students who sat empty-handed. Once the prayers commenced and the high-pitched voices coursed through the gymnasium, I remained motionless, only parting my lips to bite the jagged edges of my fingernails. The inside of my prayer book did not see the light of day. The rabbinic words of repentance and gratitude tasted rancid in my mouth and passed right through me like light through glass. Instead, I distracted myself by silently reciting Newton's laws or algebra equations. I fumbled through assignment pages, which I hid between the backside of the prayer book and my skirt. I turned my attention to my penmanship run amok across margins and binder holes.

The days pressed onwards, and I retreated ever deeper into my academic shell. I grew fond of the whip of goosebumps that tickled the hairs on my arm erect each time my teacher delivered my exams signed with near-perfect grades. In addition to my pride

in my scholastic success, I found solace in the mathematical equations themselves. Things either added up or they did not. Math was impregnated with a grace that escaped real life. I much preferred the world as it existed in theory beside an integral sign or penned within the beauty of a matrix.

I found myself, more often than not, laying stomach side down on my bedspread, the blond ends of my hair softly dancing across the pages of a precalculus textbook that would only be pertinent to my coursework three odd years later. I saw parts of my body in the angles of triangles, in the relationships between sine, cosine, and tangent. I imagined my knee or elbow contorting into each of the angles depicted on the textbook pages. I fell asleep with my face so bound up in the pages that one could probably not tell where I stopped and the math began.

By the near completion of eighth grade, I was liberated from my plastic white restraints, yet again. The high-stakes stress of Ramaz high school entrance exams, on which I earned perfect marks, was supposedly followed by a graduation ceremony. The week prior to commencement, I moseyed across the kitchen, making my way to the cereal. I wiped the lingering sleep from the corners of my eyes and collided with water-soaked tiles on the floor.

As I glided, my left foot darted behind the rest of me in a meek effort to break my fall and twisted itself out of its socket at my ankle. A preview that should have been a dead giveaway of my EDS reared its head in my dislocated extremity. My bruised foot ached as it slid in and out of place upon bearing the brunt of my being.

"Tell Elly not to concern herself in the least with today's ceremony. All I want is for her to recover. She will have her own graduation in

the aftermath." Through the crack in my bedroom door, I discerned my headmaster's voice booming through the speakerphone.

"Thank you. I will tell Elly you called." My mother returned our home phone to its cradle and entered my room.

"El, the rabbi phoned. He adores you. He said your graduation will happen too, on your body's schedule."

I took in a dizzying amount of air and let out an audible exhale. At fourteen, I abhorred being on my own solitary timetable and feeling out of sync with my peers. Soon enough, however, I would realize that I would live the rest of my life on my own calendar. EDS is not the kind of disease that waits for you to catch up with your world.

On the next Monday, I cloaked myself in my navy cap and gown and walked the five blocks between my apartment and the Ramaz School to Rabbi Lookstein's office. Everything about the rabbi is modest—his overflowing devotion toward his congregation and his firm enunciation of the Ne'ila service that marks the close of Yom Kippur. He is slight in dimensions, and even the goatee anchored to his chin is miniature. He does not impose himself, even physically, on his universe.

"Elaine Miriam, you have arrived." The power in the rabbi's voice coursed through me, sending a chill up and down my jaw.

"Yes, Rabbi. I am finally ready to graduate. Better late than never." I smiled a real smile that smacked me into the present moment. I can walk, I felt my body tell me. The rabbi strode the perimeter of his mahogany desk and brought himself before me. I held myself steady in his embrace, not wanting to part from him.

The summer that followed, my family and I voyaged to Rome to take in the mythic vista of Romulus and Remus and a portion or twenty of gelato. With the elasticity of a hair tie, something in my spirit rebounded, invigorating, if only in part, the sense of wonder that the brace wrested from my grasp.

After gawking at Michelangelo's frescoes in the Sistine Chapel for the better part of twenty minutes, Avery and I were ready for a gelato break. As I walked, my brother's hip collided with my ribs. The throng was dense, the foot traffic unending. I liked Avery's hip so close to my body. Its insistent clicking in and out of its socket, a rhythm we share that is a hallmark of EDS, told me I was safe. While hypermobile EDS only manifests itself in a maximum of 30 percent of males carrying genetic variants associated with the disease, Avery, unlike Jason, displays a portion of my phenotype. He can stretch the hyperextensible skin on his cheeks until his face transforms into a rubber sheet, his shoulders glide in and out of their grooves, and his hips protest each time he runs. I know he carries at least some of my genetic burden, but he does so with far more grace than I could ever muster on account of his sex.

The following morning, my family made its way to the Coliseum. My sandals were clearly not primed for the barrage of cavities and depressions of Roman side streets. My father's stern grip prevented my being from tipping this way and that across the patchy road. The panorama of beige stony detritus, vestiges of arches that gave way to adversarial fire or to the tides of time, appeared like graveyards in disarray in which the pride and purchase of man, not man himself, rested into eternity above ground.

As we neared the ancient gladiatorial hub, I experienced something unquestionably occurring in the present tense. I took mental leave of the historic remains and felt my body lurch, feet first, onto the cobblestone. Searing pain festered in the place of my again broken spine. My personal Rome had toppled, and the excruciating dust refused to settle in its wake.

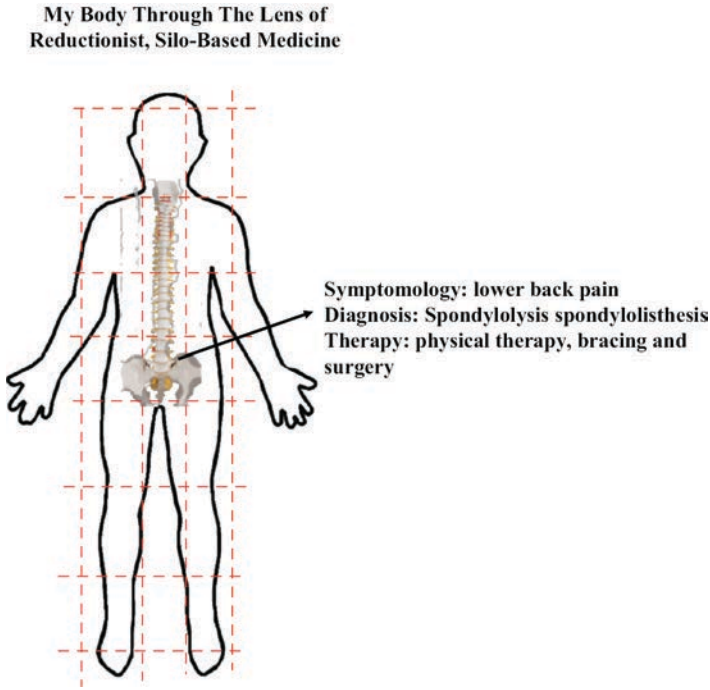
7
A fruitless runaway

I have all of my wits together but nothing to do with them, weapons without ammunition. I exist in the barest of ways, like the chair across the room.

It feels as if my cells were met with liquid nitrogen and froze, jolted into persistent stagnation, as though my electrons fell off the orbits of my atoms and my very fire, my electricity, was cut.

The program of my being is bugged.

My spine no longer binds the pivotal axis of my being.



I heaved myself, clad in my infamous white shell, up the mountainous steps of the school bus. As I broached the final step, Doug, a student entering into his senior year, rose from the front row and came down the aisle toward me.

"Hey, brace girl. There are no freshmen allowed up front. Take the back row." Red rushed into my cheeks, and I touched my front, trying to identify the source of my newfangled epithet. The limp blue of my blouse was caught in the Velcro strap, revealing my back brace that I was trying so hard to conceal.

"Would you mind, you know, um, making an exception to the rule and permit me to sit up front? The bumps hurt my back, which you now know is injured." Doug's face creased itself into a tight growl and his blue eyes glowered.

"What did you say, brace girl?" His whole being shook with laughter. I felt perspiration pool underneath my arms and tears gush into my eyes. I did not let them fall.

"I'll head to the back." The wheels of my backpack scurried down the aisle.

In the aftermath of my out-of-sequence graduation and slew of middle school setbacks, I coerced my parents, against my father's rational pushback, to succumb to my plea to run away from Ramaz. I did not find fault with my former school, but the establishment had become inextricably intertwined with my experience in its halls, with the clamor of fists against my brace and with the stealthy burgeoning of a tumor on my ovary. I craved a clean slate. Little did I appreciate back then that beginning anew was independent of my physical location. No gulf could segregate me from my hardship.

Oddly enough, with no thanks to the bus ride debacle, I managed to navigate the social fabric of Carmel High School, where I commenced ninth grade, with ease. My capacity for forging friendships hit a personal climax, and, after just two weeks, I settled into a sweet spot at the intersection of three social groups. The brace did not impede my zigzagging between these circles, but, in fact, seemed to fade into the backdrop of things. That October, I lodged in an inn in New Jersey during Carmel's Freshman Retreat.

When Sabbath eventually became Saturday night, we were instructed to ready ourselves for the Hora. As "Hava Nagila" rained through the auditorium and my feet scurried to the beat, I felt the bony gap in my lumbar spine widen. Even ensconced in my plastic brace, I was vulnerable. Back then, I failed to realize that my current broken status did not equip me with a free pass that safeguarded me from further decomposition. There were, and would always be, smaller segments into which I could fragment. In the coming years, I would unwillingly discover the minimum whole sliver of self I could occupy and still, at least to some extent, be me.

My schooldays came to a screeching standstill, and my entire existence seemed to decelerate. I languished between my parents' bedsheets and peered into the pages of *Jane Eyre*, thinking that I could read my way into the fiction, into a sphere in which spines remained intact. As my parents' bedroom, in contrast to my own, contained a television, my mother supposed that I would be maximally distracted from my pain if she installed me on her mattress. A year of my life elapsed while I bided time mainly in an unflinchingly supine position.

Walking and sitting elicited piercing pain across my lower back that coursed down the backsides of my legs. I loathed the myelin that sheathed my axons and facilitated the rapid transmission of agony throughout the lower half of my 15-year-old frame. Only years later, as an undergraduate at Harvard, would I come to admire the phospholipids that encase my neurons and view pain from the luxuriously impersonal vantage point of conduction velocities and neuroscience problem sets. Even with my scientific calculator in hand, however, I knew that sensation did not boil down to capacitance and ionic flux. The memory of my suffering became a part of me, as real and steadfast as a limb. Pain was not a perception that you could simply acknowledge and back away from, especially when it took root in your own body. My penetrating anguish demanded to be felt.

Acute and chronic pain go hand in hand with EDS, especially with the hypermobile variety I suspect I possess. While research has only identified a partial mechanism for this pain, Dr. Fransiska Malfait (2017) and her collaborators hypothesize that multiple mechanisms, including nociceptive pain stemming from injured ligaments and tendons, compromised proprioception, and neuropathic pain, are all at work in the context of EDS (Syx et al. 2017). Nociceptive pain often emerges before the other two contributing factors and is acute and localized, such as in the case of my lower back. However, as I would personally learn over time, EDS pain typically becomes chronic secondary to muscle weakness and altered proprioception. In turn, the nervous system undergoes a wind-up process, and the somatosensory system becomes trained to remain highly reactive, causing central sensitization to set in (Rombaut et al. 2015).

Yasuhiko Kawasaki (2008) and his colleagues demonstrated a link between the extracellular matrix (ECM) and acute and chronic pain following an injury; the researchers observed a marked increase in matrix metalloproteinase (MPP), an enzyme that degrades proteins like collagen and tenascin-X, integral to ECM functionality (Kawasaki et al. 2008). This upregulation of MPP induces microglial activation, thereby turning on proinflammatory cascades throughout the body that our brains interpret as pain. Furthermore, Maral Tajerian and David Clark (2015) found that the ECM is critical for central and peripheral nervous system plasticity and connectivity, both of which are integral to the body's capacity to modulate and to adapt to pain signals (Tajerian & Clark 2015). Thus, scientists, including Dr. Nicol C. Voermans (2009), speculate that the dysfunctional ECM present in EDS patients (on account of mutations in its composite proteins) results in a malformed peripheral nervous system in which neurons are friable and less plastic in response to sensory input relative to those of healthy subjects (Voermans et al. 2009).

Using scientific literature published between 2011 and 2015, Dr. Fransiska Malfait (2017) and her associates assembled a mechanistic theory that ties together the altered ECM and pain perception in EDS (Syx et al. 2017). They reason that abnormal ECM proteins in EDS patients serve as damage-associated molecular patterns (DAMPs) that set off danger alerts, which are, in turn, acknowledged by the pattern recognition receptors (PRRs) of the immune system and sensory neurons. This domino effect leads to continuous activation of sensory nociceptors and causes EDS-related chronic pain.

Notwithstanding these emerging mechanisms, pain amounts to more than misfiring neurons and aberrant ECM-associated proteins. It not only heightens your somatosensory system but also alters your psyche, breeding fear, depression, and a sense of loss of control and innocence. We are biologically and evolutionarily wired to flee from pain, to find a refuge from discomfort. But when the brutal pangs are rooted in you, where are you supposed to find asylum? Oftentimes, to avoid any pain-triggering movement, it is our instinct to learn to live in stillness, an inclination that may proffer temporary respite but, in the long run, only begets muscle wasting and permits our bodies to forget how to move at all.

"Mom, I have to go but—" My words broke into a wail that scaled in pitch and volume. "El, I'll take you. We can do it, and I promise the pain will subside shortly after." My mother did not require me to explicate what I needed. She knew me too well to rely on words. There were no boundaries between us. She slid, effortlessly, into my skin, owning my instincts as her own.

Illness has its own language composed of vacant looks, clasped palms, listless tears, and muted static nights. After 24 years of EDS, my mother and I are fluent in the syntax and semantics of grimaces and feeble smiles. One may consider it incongruous that each of us wrests meaning from existence by putting pen to paper. To the contrary, we only value the slurry of syllables because we continually experience the limits of their holding power, their gaucheness in containing the bond, and thus the pain, we share.

The toilet in the adjacent bathroom is exactly 22 steps away from my father's bedside table. Even now, each time that even

figure crops up in the context of a math problem, I mechanically bite my tongue between my top and bottom rows of teeth to distract my brain from the emotional pain by inducing an immediately pressing physical one. My mother girdled my ribs from behind, motioning me softly forward across the creaking floorboards. Our conjoined presence tarried every two paces or so as I inhaled a mouthful of discomfort and exuded a hissing exhale. After undressing me, my mother lingered on the other side of the ajar bathroom door, affording me a semblance of privacy for which I would never ask, not in these circumstances at least. My mother's stationary feet awaited my scream. The act of squatting so that my bottom confronted the porcelain toilet seat was so excruciating that I repetitively drove my fingernails into my thigh.

When she was not whispering Toni Morrison's *Sula* or *Beloved* into my ear, my mother recounted episodes in her patients' lives. She recounted the striking 30-year-old mother of six whose husband's caress unearthed a devious mass of tissue after it had hitched a ride on her lymph nodes and metastasized to her organs. I observed evening rush through the bedroom window and rebound off the crystalline chandelier to manufacture a fleeting geometrical collage on the ceiling. Meanwhile, my mother's voice quavered over another patient who was finally impregnated, after four rounds of in vitro fertilization, with both twins and a tumor. Her life was pitted against those of her unborn children. I wondered how much suffering the world could stomach before it imploded. Mathematicians should devise some sort of algorithm capable of predicting not only the physiological carrying capacity but the emotional holding capacity of mankind.

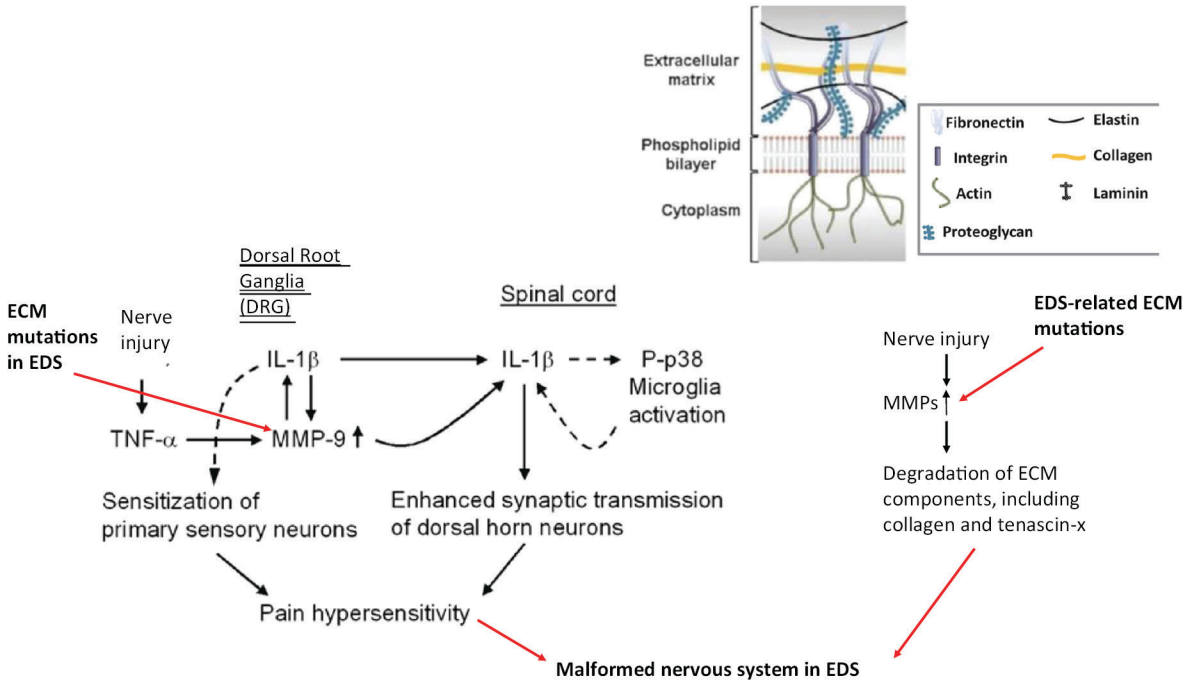


Figure 7.1: *Continued*

Figure 7.1: *The Link Between Ehlers-Danlos Syndrome (EDS) Pathophysiology and Extracellular Matrix (ECM) Integrity.* After nerve injury, matrix metalloprotease 9 (MMP-9) levels increase, which promotes interleukin-1β (IL-1β) cleavage in the dorsal root ganglia (DRG) and spinal cord. Dashed arrows denote previously confirmed mechanisms. Positive feedback between IL-1β and phospho-p38 (P-p38) increases IL-1β, thereby exacerbating pain. The red arrows illustrate Voermans and collaborators' (2009) and Syx and associates' (2017) hypotheses that upregulation of MMPs in EDS compromises ECM integrity, increases pain signaling, and induces maladaptive nervous system changes.

Note. Graphic of the ECM and its components (right) is reprinted from "The Role of the Extracellular Matrix in Chronic Pain Following Injury," by Tajerian, M., & Clark, D., 2015, *Pain*, *156*(3), 367.

Adapted from "Distinct Roles of Matrix Metalloproteases in the Early- and Late-Phase Development of Neuropathic Pain," by Kawasaki et al., 2008, *Nature Medicine*, *14*(3), 333.

In addition to the members of my family, Sarah, my tutor, furnished free rein to come and go as she pleased. Sarah settled beside me in my parents' bed. The red of her Vespa helmet glistened in the lamplight by her feet. She wielded a geometry text above our heads and pointed to a polygon and then to a formula contained within a box beside it.

"To determine the number of degrees in the polygon, you subtract two from the number of sides and then multiply that result by 180. That make sense?" I could see through the slit in my eyelids that she peered my way. Then, I suddenly sank into a deep slumber. The hefty doses of opioids and Ketamine the doctors prescribed may have, at best, scratched the surface of my searing back pain, but they also knocked me out cold.

Only later would my mother inform me of the reality that my complexion had turned sheet white and my blood pressure plummeted startlingly from the medication and the cruel games it played with my autonomic nervous system, sending my postural orthostatic tachycardia syndrome (POTS), a blood circulation disorder that is often comorbid with EDS, into a tailspin. Only later would my mother communicate Sarah's fear. Almost as much as I did, Sarah yearned for the return of my excitement, my keenness to partake in the lessons she conducted, and my tendency to try words, like "echelon," on for size between my lips.

The crisp November breeze flowed in plumes through the open windows and rattled the chandelier. My mother was stalwart about feeding my lungs fresh air, however adulterated with automobile exhaust and cigarette fumes featured on Park Avenue below. When it was just the two of us and words felt too clumsy

inside of my mother's mouth to be spoken impromptu or relayed from the pages of a novel, we permitted the silence to wash over us, or, more aptly, to smother us. Often, however, in conjunction with autumn, segments of life in medias res gushed through the windowpane. The mainstays of human interaction agonizingly jolted my eardrums. "What would you like for dinner?" "Mom, I'll have pasta." "How was school today?" "Mom, I'm fine, school was…you know…alright." "What did Mary think of the birthday gift you gave her?" "Mary liked the gift." Trivial snapshots of lives being lived. I detested these anonymous pedestrians for existing within earshot, for asking questions that I could not. I craved trite dialogue with my mother. I longed for insignificant steps that I could walk through painlessly without the need to lull myself forth by counting down from twenty-two. I beseeched my mother's God, with every fiber of my being, for our world to resonate with less meaning.

After devouring Charles Dickens's and the Brontës' fiction, Miss Havisham's matrimonial fiasco no longer cut the mustard. I desired to peruse pages of misery into which I could sink my teeth, the kind experienced by real humans. I resorted to Elie Wiesel's *Night* laden with the austerity of the crematoria and starving flesh. I neglected words for two days as depression set in like a peach pit in my trachea. I overheard my mother choke on her tears as she spoke to my father on the phone, reporting her struggle to locate her daughter under the blanketing trio of immobility, pain, and unreachable silence. My sojourn into Auschwitz came to an end, if only for my mother's sake. In its stead, I turned to something as invisible and intangible, but as real, as the pain that ransacked my backside, theoretical physics.

I studied the paths of positrons and electrons laid out by Richard Feynman into the past and future, tracing my fingers over their convergence and divergence. Feynman diagrams were the one place in my universe where physics met fiction with an alluring appeal; the possible trajectories of the subatomic particles therein were only potentialities. One could not pinpoint the location of a boson in the future, at least not with certitude. Like the bones in my lumbar spine, there was nothing fixed about the lines, each with its own momentum, energy, and spin, interposed between particles and antiparticles. The infinitely many quantum-mechanically feasible paths huddled together beside the path integral, bespoke of nothing definite and shunned certainty. I preferred the company of bolded lines, sine waves, blunted arrows, Greek letters, and the imprecision of chance that lurked in their graphical unity to that of any creature who perceived the world in black and white and existed, so unaware that the extremes could mix into uncountable shades of gray. In the setting of Feynman diagrams, the opioids were an asset and launched me, full force, into a quantum mechanical stupor in which the subatomic loomed large.

As my wheelchair came to a halt inside Hospital for Special Surgery, I clenched all of the skeletal muscles I could contract. My back pain referred its way here and there, checking out every cubic inch of my being. Perched on the footrests of the wheelchair, my feet were restless in the air-conditioned room, indefatigable in their effort to keep me warm. Dr. Manning, the pain specialist, inched toward me, his white coat slathered with authority.

The physician released a syringe harboring a murky fluid from his pocket. My veins were poised for the task at hand and bulged forth from the inner crease of my elbow as the faceless and mute nurse practitioner, whose existence I could only infer from her pitter-patter behind my wheelchair, secured a blue elastic about my bicep. Suddenly, my mother's lilt ruptured the silence.

"More? You are really giving her more Ketamine?"

"Don't you want me to quell the pain? The last ten boluses really tided her over for hours at a time. I want to help her get more comfortable."

"But is it safe to administer this many doses in such a short window?" my mother asked, incredulous of Dr. Manning's guidance. I heard his polished shoes clatter backwards as though he sought to flee the examination room. Before he could rotate the doorknob, my mother added, "I know you care, Dr. Manning. I know you are trying your very best to help us." I heard my mother's eyes overflow with tears.

"Dr. Katz, I know. And the bonus of Ketamine is that she will really have no memory of this horrible pain she must endure."

"That is a benefit. This shit she has to deal with—" My mother's voice broke as did she. "I mean, she should never ever have to relive any of it, even in her own head." The doctor sliced the needle into my vein, shuttling in the analgesic.

When the searing ache in my lower back abated, my mother hoisted me by the armpits out of the wheelchair. She guided my dependent faltering strides toward the backseat of a taxi as I held steadfastly to her arm. Once she positioned me on the

unforgiving pleather, I planted my palms on the cushion beside my hips and edged my bottom upward, retaliating against the onslaught of gravity and the nefarious toll it took as the cab navigated potholes and bumps. My bleary cries rang through the yellow interior of the taxi.

The next day we traveled to Columbia Presbyterian Hospital to meet with a surgeon. My mother fingered the knuckles on one of my hands, a tactile I love you.

Dr. Higgins and his fleet of medical students clattered into the room. My mother was slumped on a stool with her lips pursed and her blonde hair wandering in all possible directions in the aftershock of her morning swim. On the nearby table, I was in full fetal position. Dr. Higgins maneuvered his electronic mouse to different locations on the screen before him, charting buried treasure on the cartography of my spine. He looked my way, and his suave face broke into a sincere clean-shaven grin. A massive brown suitcase stood in the corner behind him.

"How are we doing today, Elaine?" The doctor sounded all too jovial for the occasion and spoke in a cadence that veered on patronizing. My mother eyed him scornfully and replied on my behalf.

"Dr. Higgins, we are doing horribly. This pain has persisted long enough."

"I would agree, Dr. Katz. Your daughter's series of refractory fractures and bracing, in conjunction with her MRI findings, make her an excellent candidate for surgery. In my opinion, Elly needs

a fusion from L5 to S1 in order for her pain to go away." I remained inanimate on the table.

"How soon can we do it?" My mother probed, breathy with urgency. Dr. Higgins swiveled his eyes toward his suitcase.

"Well, I'm supposed to board a flight to Istanbul for a medical conference this evening.

But, if Elly were my daughter, I would want her to be operated on as soon as possible." He loitered in his contemplations for a moment, wrapping his mind around a plan as it crystallized. Dr. Higgins went on, "I want to do this surgery. I will postpone my departure."

Dr. Higgins elucidated that at age 15, I did not quite qualify as a child or as an adult but existed in the murky limbo of adolescence. If he approached my case as a decidedly pediatric one, he would recycle autologous bone dust generated by high-powered drills and burrs that would serve as local autograft. If, on the other hand, he treated me as an adult, he would excise a bony fraction of my iliac crest for this purpose, thereby engendering a superlatively stable bony fusion at the cost of a protracted rehabilitation. My mother's directives to cater to me like a child so I would recover expeditiously seemed sound. However, reason and EDS do not meld well; my disease does not succumb to logic but is armed with a consciousness of its own that is inaccessible to understanding.

The inside of Dr. Higgins' operating room was a hardware haven that struck me as the ideal place to stock up on building tools. Hammers, nails, saws, drills, and blades of all sizes were affixed to

the white walls. Masked men in mint green gloves began poking and prodding my veins and jabbing needles deep inside me. It was rather horrifying to consider how it would feel to lumbar about this planet with metallic rods and screws fortifying my backside. I deliberated the likelihood that I would feel somehow weightier on my own two feet after being cranked open and fused with titanium.

"Now, Elly, count out loud in descending order from ten."

Following my surgery, in the prison of my parents' bedroom, Avery's visitations were a kind of departure into a space I equated with liberty. As soon as he crossed the threshold, my brother dove into the vortex of my pain, abdicating his qualms about his performance at the hedge fund for an hour or four. He slithered his towering six feet and counting beside me on the bed; his expansive dark eyes met mine as he stirred, reading my expressions to extrapolate if I stomached his most recent micromovement. He released the top button of his pinstripe shirt and gave me a feeble smile, exposing the rather extensive chasm between his two front teeth, a biological heirloom from my maternal grandfather. Avery always came armed with a shopper and an agenda.

His hand disappeared in the white tote and remerged connected to a rectangular black box, home to the delectable chambers of rice surrounding clumps of salmon nested beside avocado. My brother unfurled a terry cloth towel atop the table of my chest and proceeded to bisect the pieces and drizzle them in soy sauce. As he slid the Japanese cargo between my lips, he assumed his role as a talk show host.

"Today's numbers are as follows…" He unearthed a penny from the pocket of his dress pants and rotated away from me and toward my father's bedside table. A piercing grating filled the room with a persistence that only wavered intermittently when Avery's hand brushed away the silvery remains, luring the digits on the card into visibility.

"We have a five, a twenty, an eight." His breathing hastened in the excitement with which he sought to saturate the moment. His melodrama gained footing, and he turned about-face to determine if I quaffed it down as brilliantly as he had. I disclosed my one dimple.

In all of the rubbish we accumulated from scratch lottery tickets, Avery and I never quite broke even, running our luck bone dry after we succeeded in cobbling together a measly two dollars over the course of three weeks. The charade was a carbon metaphor of what had become of mine, and, by extension, my brother's, fortune. The astrological dial of the universe was pitted against us. We were short on reason, deprived of justifications and causality, and only had each other and the scattered debris of lotto cards in spades. Precisely because we had nothing left to lose, we gambled more away, hoping that we could marshal the world to spin in our favor by squandering dollars and accumulating a backlog of black detritus under our fingernails.

"Avery, can you make me a promise?" My brother clicked the remote, pausing Leonardo DiCaprio's avaricious trek through a decimated region of Sierra Leone. The soil was streaked with the atrocities of war, the redness percolating into its crannies. The remainder of *Blood Diamond* would have to wait.

"Anything, El."

"What the South Africans put up with—warmongers' merciless corruption and gluttonous aims of power and the bottom line…" I trailed off into my thoughts.

"I know. It's egregious. And the crazy thing is it's not just a movie, El. The Sierra Leone Civil War broke out for real in 1991." My brother's bachelor's degree in history from Columbia University clearly had an upside; he could detect fiction from fact, thereby embellishing the cinematic experience. He clasped my meek hand between his warm oversized palms.

"Make me a promise that you will tell my future husband that he, in no set of circumstances, should purchase me a diamond ring. I need to wear a stone on my finger that does not bring the hardship of Africa to mind." He looked at me, his face contorted with repressed laughter.

"How about a sapphire?" We shook on it, slowly motioning our hand sandwich through the air.

As I lay beside my brother, I maintained a tarnished yet unbroken sense of an ending. I saw through the prism of the hapless present into a painless future in which I could fit into whatever normal-shaped whole normal people occupy. I envisioned my future fiancé gliding a band about my bony finger and whisper something about forever. Far from the vista of my 15-year-old imagination, my twenty-four-year-old reality skulked, waiting to snag me by the arm sleeve when I least expected. I am more acquainted with my dislocated left lower rib jutting its way forward, with the lifeless dead weight of my right shoulder lying beside me on the mattress bearing testimony to the perils of vivid

dreams, with my oatmeal-colored vomit, and with the backslide of my right hip gliding out of socket from perching on a wooden surface than any person should be with any anatomical part, or, really, with anything. I do not have the luxury of a boyfriend, or even of a pet dog. Now that I deliberate the matter, I probably would not trust me with fish, or even with a plant, particularly if you are keen on its survival. I do not mean to come across as hyperbolic or histrionic. I am simply stating the facts. EDS is not merely a diagnosis or even a disease. It is a life. My wayward body parts are more than enough of an occupation. Little did I know, as I held onto my brother, that he might be the only middle-aged dapper man in my life for the long-term.

Through no fault of his own, Jason, in contrast to Avery, was conspicuously missing in action while he worked on the set of Ellen DeGeneres in California. There existed no SparkNotes edition of my pain that he could read to come up to speed. It is an impossibly unreasonable plea, at least from my perspective, to truly recapitulate illness in all of its horror in any stroke of the tongue. Disease crawls into you in nuanced expressions. Updating a sibling on your hardship swallowing food or tending to nature's calls is a far cry from filling him in on a first date or a summer at camp. I certainly did not strive to reexperience my anguish, in any way, shape, or form, let alone flaccidly couch it in sentences that would never do it justice.

The vehement vitriol that gathered in me, like hairs in a drain that eventually occlude the passage of water, had nothing to do with Jason. I could not blame my brother for living his life while mine was on hold. I was fed up with reality and desperately needed someone for my finger to point at as the object of my

resentment. Jason, without any reasonable cause, became that entity, a role that concretized in my own head far too intensely. My brother warranted neither the anger nor my radio silence that he has endured gracefully over the years.

Assuming the position of a chronically ill person in any context, let alone in the setting of a healthy family, is no easy feat. I often feel like a penurious child peering through the glass of a well-stocked candy store, glimpsing all of the spectacular delights that are out of reach. My father saunters through the corridor in his bike shorts and loafers awash in perspiration and adrenaline. My brothers glide in their socked feet about the kitchen, shoveling cereal into their mouths after a run in Central Park. My mother puts a towel to her forehead, stopping the rivulet of sweat that breaks free after a training session in our basement gym. I want to scream, to release myself from the fetters of EDS, to move disembodied, outside of myself, in accordance with my will. Permit me to commandeer my own life, if only for a day or a moment. I will never ride a bike, nor jog, nor lift anything heavier than a water bottle above my own head. Aside from walking, it is an arduous undertaking for me to conjure up a single activity in which I can partake alongside other humans without dislodging various parts of myself. It is only fitting, or perhaps some shard of a blessing, that I favor solitude.

Two months after my surgery, it was clinically evident that the fusion of my lumbar spine did not take. A follow-up scan depicted that the bony gulf had only widened, and a revision surgery was in order. In early November, my mother sat beside my wheelchair in an examination room at Maimonides Hospital. It was all too rehearsed; even

the silence tasted stale and acrid in my mouth. It seemed I was making my rounds to all of New York's finest hospitals.

Dr. Jean Pierre Farcy was something of a varnished relic out of a French gallery. Even his binary name stood on ceremony. He was an elegant titan. He swaggered into the room, his open white coat flowing behind him, wearing unmistakably orange pants.

"Mademoiselle Katz, describe what you feel in your back."

"I feel a sharp pain right here." I fingered my lower back, demonstrating the location to which I referred.

"What happens if you twist yourself about or bend down?" He looked his way into me, trying to feel what I felt, to dissect what it was like at that very moment to be me.

"The pain travels and shoots down my legs." "Ah…I see. Now, give me some time."

My mother cracked open *The Fabulous Fibonacci Numbers* and proceeded to read aloud for the better part of an hour. Through a sliver in the agape door, I could make out Dr. Farcy seated at a desk in what I deduced was his private headquarters. He toyed with an object that appeared to be an action figure. Once he adjusted his grip, however, and rotated the object that manifestly enraptured his full attention, I recognized that the reflective beige entity studded with protrusions was indisputably a part of human anatomy. It was a three-dimensional prototype of the lumbar spine.

Dr. Farcy dressed for my revision fusion the next morning in early May like he was attending an engagement party, or even a casual wedding ceremony. Before he put on surgical scrubs, he

wore a blaring red sport coat, a lavender silk scarf fastened just so about his neck, and, of course, red pants. Plainly put, he seemed handsomely well-equipped to take on the fissure in my lower back. As the anesthetic dripped into me, my head went empty of everything save for the prospect of the overdue sense of wholeness that awaited me in the recovery room.

8
A cyborg no longer

Experience will teach you the beauty of black, just you wait. Its severe permanence, its capacity to clasp all the suffering of humanity as though it were an infinite palm.

I look to black to release me from myself, to abandon my image, to sink into certainty, into a vagueness I can trust. I look to black as a mirror of my insides, a reflection of feelings I have buried beneath beginnings that swoon me into misanthropic memories.

"El, I'm sorry but you cannot return to Carmel High School. Dr. Farcy explicitly informed me and Dad that riding there and back in a vehicle could undermine the fusion. School buses are strictly off limits for a year, at a minimum. He is confident that you will be able to ambulate on your own soon, but we need to avoid any jostling of your back." From within my wheelchair, I eyed my mother's profile as she spoke into the pan simmering with pancakes.

"But where will I go to school?" Shards of June light scattered the kitchen as my mother wedged blueberries into the browning batter.

"I spoke to Rabbi Lookstein. He is willing to let you skip ninth grade and slot into the tenth grade at Ramaz." My mother launched the pancakes onto a plate and moved toward me, her eyes filled with desperation and a lack of a proper night's sleep. She was wholly

aware that the prospect of circumventing the freshman curriculum would never sit right with me.

"Mom, then I would miss biology labs. I deserve to do high school from the beginning." My mother flashed me a grin.

"El, I was just going to tell you that Dad and I spoke, and we actually don't think Ramaz is the best idea right now. The dual curriculum and long school day from 8 a.m. to 5 p.m. does not really seem appropriate for you in light of the physical therapy you are going to need.

We want you to enroll in a single curriculum and non-denominational school. We will let you begin ninth grade anew." I shot my Mom a glance and nodded.

It was naïvely comical that my parents expected to secure a place for me in September, a mere two months away, at a New York City prep school. Mothers typically phone school administrations to reserve a coat peg in a kindergarten classroom before their child's lungs are completely formed in utero. Somehow, The Billard Grammar Academy managed to make room for one more inside of its purple doors.

It strikes me as anachronistic that the potter's wheel, a hand-me-down from the Ubaid period, should serve as the centerpiece in a twenty-first century classroom located in the heart of the Upper East Side. I slumped forward on the barstool in ceramics class with my elbows planted on the table before me. Hunks of clay thudded onto desks with reckless abandon. I darted my eyes about the room, aiming to surmise today's project. Margery, the girl to my left, whispered "we are making self-portraits of our faces" into my ear.

I removed my navy plastic frames from my face and stroked my way from forehead to chin, feeling my contours so I could do them justice. Words are my preferred medium. Patience may be a virtue, but back then it was certainly not among my assets. Only a year later would this absent character trait hypnotize my gaze in a staring contest. I have yet to blink.

"Elly, is that your face?" Sonia's maligning sneer appeared behind me, and her massive green eyes leapt over my shoulder to view my clay appearance. She pursed her lips to refrain from laughing.

"What about it?" I peered downward, utterly unaware of the joke at hand.

"I mean, just look at it. It's not obvious?" I rotated on my stool, so my eyes met Sonia's. I had to tilt my gaze upward. She was something of a blonde beanstalk.

"I am not quite sure what you are hinting at." She broke into fits of malevolent laughter.

"You are not quite sure? Well, why don't you fix your eyes on *that*?" She gestured toward the nose that protruded from the table. I rotated my neck in slow motion, scanning from her face to my deplorable sculpture and back again. I waited for her derision to proceed.

"Are you blind? That nose is, without a sliver of a doubt, of Jewish descent. It bulges here and there just like yours does." She continued, full steam ahead. My heart skipped a beat, and I could feel the color drain from my face. I made my way to the restroom, where I remained until the bell chimed.

I was, by that juncture in my academic career, rather accustomed to assuming the mantle of the outsider in the classroom.

However, defamation due to my religion was not simply the other side of the coin of fists pitched against my back brace. While both instances rendered me an anathema for reasons beyond my personal control, Sonia's words sliced into me with an unfamiliar vengeance.

For the first 15 minutes of the school day, my classmates and I passed time in homeroom. In the classroom, a wheel of blondes and brunettes gathered on the carpet. A lump settled and expanded in my throat as I ogled them. I was not envious of their unimpeachable exteriors nor the ease with which the school's uniform unveiled their chiseled hips. As their silly chatter continued and my stare persisted, I felt my eyes begin to fill. I craved to understand what it meant to belong, to be a spoke on the Billard wheel. I passed this quarter of an hour in a discreet corner of the classroom conversing soundlessly with the pages of *Madame Bovary* as I turned them.

As one of the impious students at Ramaz, it was ironic if nothing else to find myself cast as the token Jew at Billard. It is wild how contextual creed can be. I had not turned over a new leaf with God or anything, but my peers approached my unquestionably Jewish surname and my academic past as though God and I were on speaking terms. In fact, the one instance during my entire freshman year that I came within reach of popularity was at lunchtime during the Passover holiday. The indiscernible Jews in my class surfaced from the cupboard of assimilation with their matzah in hand as though it were a spontaneous clandestine handshake we shared. Welcome to my tribe. My peers acknowledged me by name for the first time. Their Judaism came out in spurts and was merely an outfit they could don and doff as

they pleased. My religion was more constitutive, like an unregulated promoter that leads to the continual transcription of its respective target genes. I had to localize a corresponding repressor protein, to turn off the interminable mass production of my Jewishness.

Lunchtime was typically followed by math, the class I depended upon for the staunch logic of geometrical proofs. I admired congruent angles, parallel lines, the ease with which the similarity theorems integrated the Euclidian world into coherence almost as much as I venerated Mrs. Edmond. The slender weed of her being formed a perfect perpendicular angle with the earth. She was math incarnate.

"Good morning, Elly." She halted my gait in the hallway. "Good morning, Mrs. Edmond."

"Elly, I know you love math. Do you have a favorite number?" I gave her a perplexed glance, trying to probe how serious of an answer she was looking for.

"I'm not sure. I mean, I've never really given it much thought." As I spoke, it dawned on me that it was only rational, given all the hours of math homework I completed over the years, for me to take a liking to an entity on the number line.

"Well, maybe contemplate it for a bit before you fall asleep tonight. My husband and I love the number four." She was supremely serious about this digit. I could see the lines on her face crinkle into blunted edges of admiration.

"Will do, Mrs. Edmond. I will report back to you tomorrow." I felt happiness wedge its way into my expression and the corners

of my mouth inch upward. I esteemed that vigorous woman and the unconditional love she exuded toward the number four. Only later, when my joints began to give way with undue facility, would I come to recognize the safety imbued in such an affection. Numbers did not ask much of me or require me to be vulnerable. They offered me a protected romance suffused with consistency. Till death do us part.

The brunt of my freshman workload revolved around my imminent class trip to London. Each student in my class was assigned a piece from the National Gallery's trove with the aim of serving as the class's docent. I acquainted myself with Luca Giordano's *Perseus Fighting Phineus and his Companions*, an oil painting finalized circa 1670 that depicts Perseus, the son of Zeus, flaunting Medusa's wide-mouthed cranium before Phineus and his devotees, whose flesh consolidates into stone at the mere sight of the monster's head. In the upper right corner, a maroon Broadway curtain lingers, an allusion to the fictitious nature of the scene. If only displaying an anatomical component was actually sufficient to freeze your enemies and your pain into oblivion. My EDS readily equips me with an unattached limb. If only I could infuse it with some of the Medusa's clout and, thereby, transform my curse into an asset. If only life were as romantic as Greek mythology. As I commanded my peers' concentration at the National Gallery, I focused my gaze on Mrs. Edmond's smile, a calculation I could trust.

That summer, I was selected to partake in an intercollegiate biotechnology camp. We inserted circular stretches of DNA containing green fluorescent protein into bacteria and isolated genetic material from our cheek cells.

"All OK, Elly?" Sasha queried in a soft and faintly audible voice.

"Yes. I just…I mean, I'm having trouble with my thumb. It keeps dislocating each time I press down to the second stop on the pipette." Silence. I could not blame her. Honestly, I am not sure how I would have responded to my remark either if the tables were turned. Hesitantly, she elevated her pointed chin and met my gaze.

"Don't worry." Sasha used a sharp implement to prod the surplus clear liquid from her Petri dish into a miniature glass chamber. She jabbed a cork into the exposed pore, laced a string through a metallic disk affixed to the stopper, and handed it to me.

"Here you go. You can pretend it's your DNA in there. No one has to know." I slipped the necklace over my head and put my arms around her. I would wear Sasha's genetic material for a month until the cord ruptured.

Aside from the malaise of adolescence, my health, or lack thereof, did not really rob me of much during freshman year. At the outset of tenth grade, Dr. Farcy sanctioned my return to gym class. Mrs. Tilly instructed us to pose in a side plank on the hardwood floor. I rotated onto my side, anchored my forearm beneath my ribs, and pushed myself skyward. Abruptly, the ivory tower of rods and screws that promised to hold me together came loose. My body gave way under me, and I thudded onto the floor.

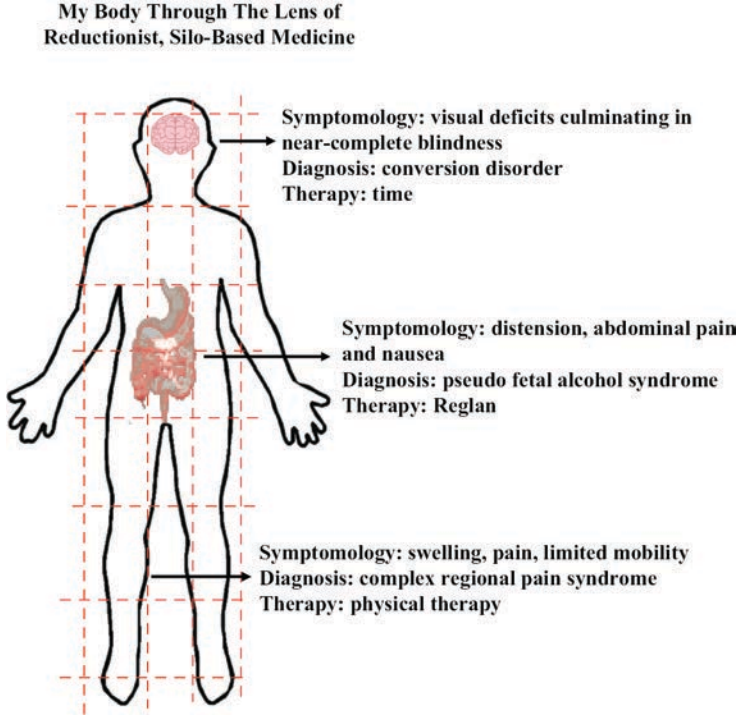
I let out a howling scream that I could not withhold. The pieces of my undoing fit together, as do many things, in hindsight. My EDS means that some part of me, however unconscious, is fervently opposed to stability and permanence. I wear my mortality,

my fragility, on my proverbial shirtsleeve. My connective tissue is incapable of connecting, be it muscle to bone or bone to screw. The next day, tenth grade came to a rapid close, and the dislodged metal was excised from my spine. My story, however, does not halt in a neat bow right there. EDS would not authorize such a clean conclusion to sorrow. At age sixteen, I would have to marshal an obscene quantity of grit to teach my feet the art of walking.

9
Becomingiatrogenic collateral damage

I look to black to find myself, to lose myself in a way, to retrieve the inner belongings I abandoned with haste, with neglect.

I look to black for honesty, for integrity, for solace in something constant in the jumble of variables. I look to black to abandon my sight so I can regain it.



The hardware removal surgery appeared to go swimmingly, at least initially. However, a fresh and unforeseen pain lurked that would break me more than any back fracture. A sensory neuron that traveled from my pelvis to my left leg entangled itself around one of Dr. Farcy's screws. To excise the titanium components from my lumbar spine, the surgeon was forced to lacerate this errant neuron to liberate the metal. In turn, my left leg forgot that it belonged to me and parted from me like an unsympathetic classmate in the schoolyard.

In retrospect, my mother would have done things differently on my behalf. She would have protested against my initial fusion and the opioids that dripped into me. She would have, had she the dimmest intimation of my EDS. Only then, she would have realized that opioids can exacerbate, or even cause, central sensitization and lead to hyperalgesia in EDS patients. Only then, she would have pursued any alternative to surgery, which poses life-threatening risks of bleeding and neural damage, as it did in my case, in the setting of EDS. But we were driving blind in the dead of night and would be for another six years.

As my father draped me over his arms and hauled me from the backseat of the taxi, I was mildly aware of the pain that was taking root in my dangling left foot. The wooden floorboards creaked beneath my father's and my own combined weight until my father crossed the threshold of his bedroom and gently positioned me on his bed. I mourned the loss of my titanium reinforcement. Something about being sealed over with hardware imparted me with a false sense of shelter. While my body languished on the bedsheets, my foot called my attention as pins and needles gave way to the severe zinging of revved-up

neurons that fired of their own accord, innervating my limb with electricity. I belted a hollowing cry. Beneath my being, sweat pooled from every pore on my backside. My autonomic nervous system was not built to handle this blistering agony. I heard my father's feet retreat from the bedroom into the corridor. His pace quickened as he tried to back away from the crossfire of my pain. Despite his efforts, my father would always be collateral damage to my faltering body. He would not have it any other way.

My mother approached my bedside and cocooned her arm on the pillow; the crook in her elbow met the top of my skull. My scream persisted. My mother's arm did not flinch. The night passed, stealing its way into us. Unbeknownst to us, the darkness was here to stay.

By five o'clock the next morning, my red sock had found its way to my parents' floor beside the bed. My body was slanted on the mattress, so my naked left foot and calf were surrounded by atmosphere alone. What started as a faint trickle of unwelcome feeling had morphed overnight into unrelenting agony that careened about the axons of my left leg. My extremity felt as though it had walked its way into a furnace. The severed sensory neuron unleashed pandemonium within and duplicitously persuaded my brain that the softest touch was a blowtorch. My wires were horribly crossed. My nervous system was in sensitized overdrive. Despite my current passion for neuroscience, I never longed to be that acquainted with my own synapses.

"Mom, get your hand off me now!" My mother fingered my unsupported calf. My brain mistook her affection for a conflagration. If the language of pain is cast in feeble glances and sympathetic

caresses, we were profoundly at a loss for its words. I could no longer interpret my mother's love. She recoiled at my cry.

Over the course of that week, my left leg decided to call it quits on the anatomical front and became a repulsive work of modern art. Eddies of red, blue, and purple bloomed on my foot and calf. It is daunting, if not impossible, to put proper words to pain, to coat it holistically in sentences, irrespective of how far they run on. No reservoir of words, no matter how recondite or chockfull of syllables, could hold it all. It is distressing to consider that my stab at my story will never do justice to the feelings behind it, the agony that shook me to my core with its rawness until the feeling transgressed a certain threshold and I became numb. It is hard to pin down the hoarseness of my vocal cords that gave way after a night of endless screaming. The pain rattled through my whole being but refused to settle itself into understanding. Perhaps that is rather fitting. There is nothing legible about pain. Your only choice is to become a victim. You are at a stalemate with your world.

It is far easier to ascribe words to that which you can see—the hopeless anxiety that inserts itself in dark circles and wrinkles on your mother's face, the salt and pepper stubble on your father's usually clean-shaven chin. I witnessed my parents skulk about the apartment in absolute silence as they mourned the life they had assumed was my birthright rather than my privilege.

The most strenuous aspect of my day involved transferring myself between my wheelchair and the bed. Rightfully, my parents did not possess adequate trust in my overtaxed ligaments and off-duty proprioceptors to permit me to maneuver myself on my own. But

I resolutely insisted that I could independently transport myself across the two-foot gulf without a ready supply of additional arms at my disposal. I clamped my teeth around my tongue, and pressed downward on the armrests of the chair, lunging myself upright onto my right foot, on which I hobbled until I reached the bed. Four years later, this one-legged routine would pay me a harrowing visit to exact its recompense. It seemed I could not get away with much, not in my body at least. My right hip has become something of a nefarious professional when it comes to lurching itself out of socket. My hip's gawky shuffle into and out of joint was one of the preliminary dark clouds on my horizon, a tipping point that sprang my EDS into disquieting technicolor.

I passed the majority of my time engrossed in my laptop as Richard Feynman pranced across my monitor in his black-and-white glory stringing electromagnetism and quantum mechanics into sense on his Caltech blackboard. I was taken by his dignified derivation of Maxwell's equations and by his application of Gauss's law and the Hamiltonian matrix.

Feynman was more than an ambulant calculator familiar with the loopholes in Newton's universe. He was an excellent pickpocket, an infamous code cracker, and a charming jokester. I desperately wanted to find a wormhole from my present bedridden state in 2011 to Feynman's 1962 classroom.

After a day at his office, my father tarried at the bedpost and shot me a grin that was so spatially demanding that it caused the slits of his eyes to narrow. It was a gesture that required requiting. I felt my mouth crease into a beam as my father puckered his lips against my temple.

"Hey girl. You game for some Gilmore Girls?" I fumbled for the bottle of Lyrica, the nerve medication prescribed by my surgeon, and fished out my fifth daily dose of 300 mg.

"El, turn it on. Let's have fun." My Dad had the power to channel the excruciating sensations that leapt about the room like shadows on the ceiling into full-bodied levity. In his hilarious presence, reality felt like something I could hold in one fist or an inoffensive powder I could dissolve into a glass of water and drink down.

"There goes Lorelei again." My father chuckled and gave my blanketed thigh a pat.

Lorelei Gilmore was a pixelized impressionist version of herself. The scene depicted crumbled into pieces my brain refused to assemble into lucidity. I rotated my neck toward my father, whose manifestation half an hour prior was crystal clear. His face was a jumble of hazy bronze. I grasped my palm toward the trace of stubble on his cheek, feeling my way into him.

"Dad," I released a cry that became a scream. "Dad, I can't see the television or you clearly." My voice quavered, and my father's footsteps made for the hallway with haste.

"Kar, come in here. Now!" My mother ran from whatever she was doing in her office. "Mom, I can't see!" I was hysterical at this point as the veracity that my eyes were not functioning as they should sank in. I wondered how much left of me I had to lose, how many parts of me would become obsolete without my consent.

Throughout the next two weeks, my one-legged shuffle took a turn for the worse. It was plenty taxing to hop my way from the

bed to the bathroom and back with clear vision. Doctors reasoned that I presented with a classic case of Lyrica toxicity, which is associated with a muddled visual field. Bumping into walls and corners became my new normal. Bruises blossomed on knees and elbows. My world went from blurry to black. I was stuck in eternal night. I left Feynman's lectures for Handel's concerti grossi and Ravel's boleros, the latter of which swelled at their inception and dénouement with the thrust of my fury. I sifted my way through the orchestral components, trying to tease their euphonious tangle apart like a math problem to which I was given the result and was tasked with working my way backward to divulge the question.

"I just can't bear to see her like that, moving with nothing but her hands to guide her. The sight pains me on a visceral level. How did we walk into this nightmare?" My father's stability was devolving.

"I know, Joel. It's impossible to watch. I can only imagine how difficult it is for you, given your mother's struggle." My paternal grandmother, Elaine, lost her sight to diabetes. My father's weeping rang with the apprehension that I would share, or, more aptly, lack, more in common with his mother than a benign name.

The dark curtain that stood between me and my world was more abstruse in origin than a simple Lyrica overdose. My vision was not granular, nor indistinct, but had gone extinct like *Tyrannosaurus rex* of the Cretaceous. In its stead, blackness washed over my vista. My thoughts moved through me in slow motion. I lamented the deficiency of visual cues, the sun-soaked petals of a dandelion that triggered my hippocampal cells to fire profusely and

unleash a torrent of childhood memories. To resolve my visual impediment, my parents enlisted the guidance of Dr. Rucker, a neuro-ophthalmologist. My parents sat beside me in her office, and I nudged one of their trembling hands into each of my own.

"Hello, Elly. Do you mind if I bring you into another room to play some computer games for me?" The prospect that I was supposed to engage in computer games at a doctor's office seemed mildly offbeat. But it was tough to turn down this gentle doctor's request.

"Sure." A nurse entered the room and offered me an arm to assist me to the game room, to which I hobbled on my right leg. Had I not been me, but an outsider to my story who ambled by in the hallway, I would have probably gotten a kick out of the look I sported. My left pant leg was bunched up to the crest of my knee and my unadorned limb hung like a baited fish from a pole. But my appearance was nowhere near as amusing from the front seat I occupied. With the nurse as my human crutch, I made my way to the computer area, where I remained for two hours pouncing on the spacebar each time I viewed a glint of light on the monitor. Subsequently, Dr. Rucker conducted an extensive examination to detect any deficits in my visual field.

"Elly, the good news is that your tests look pretty normal. Your retinal imaging is perfect. Based on the light testing you performed on the computer, however, you are visually impaired at the moment. But that should pass soon." Dr. Rucker placed a consoling hand on my thigh.

"Is it from the Lyrica?" I questioned, the scientist in me inching her way forth.

"I think what you are experiencing, Elly, is in part due to the medication. However, all your visual loss cannot really be explained by that alone. What you are going through is real and the label I am going to put onto it does not detract from that, not in the slightest. You hear me, Elly?" I shook my head before she went on. "Elly, what you are suffering from mainly is called a conversion disorder. In plain English, that means that your brain is taking all the pain signals that your leg is communicating and all the emotional burden that naturally accompanies a drawn-out period of suffering and telling you that you cannot see, even though there is nothing anatomically or functionally wrong with your eyes. That may seem crazy, but Elly, with all you have endured, it makes sense. You feel like your world rejected you, so your brain decided to reject the world." Dr. Rucker's touch lingered on my leg as she spoke.

Initially subsumed under hysteria in Hippocrates' gynecological treatises (5th and 4th centuries BCE), conversion disorder (CD) received its current and less pejorative nomenclature in the hands of Sigmund Freud (1856–1939). In keeping with his psychodynamic theory that linked unconscious conflicts and involuntary physical ailments, Freud coined the term CD to reflect cases in which sublimated psychological states are converted into pseudoneurological symptoms (The Marshall Protocol Knowledge Base 2012; Owens & Dein 2006; Scott & Anson 2009). In addition to blindness, CD manifests in the forms of paralysis, speaking difficulties, and swallowing challenges. The disorder disproportionately affects young females with a history of trauma, like me. While the incidence of CD varies with demographic factors, roughly 20 to 25 percent of hospitalized inpatients possess a subset of CD

symptoms and approximately five percent of these patients are diagnosed with the disorder (Engl 1970; Feinstein 2011).

Since Freud's contribution, clinicians and scientists continue to investigate the disorder's neurological and psychosocial correlates. Despite the predominance of single case studies, almost exclusive enrollment of young females with a range of sensory deficits, and divergent experimental approaches, emergent research associates CD with functional brain changes. Using functional magnetic resonance imaging (fMRI), Omar Ghaffar (2006) and associates exposed CD patients with unilateral sensory loss to sensory stimuli (Ghaffar et al. 2006). In contrast to the sensate side of the body, which elicited contralateral somatosensory activity upon stimulus application, the numb side of the body failed to recruit this brain domain in the presence of the same trigger. In the latter case, patients' fMRIs demonstrated activation of the orbitofrontal (OFC) and anterior cingulate (ACC) regions, critical limbic networks involved in modulating emotion and affect. Although the mechanism responsible for Ghaffar and colleagues' observations remains controversial, these results, which have been replicated in other studies, suggest the CD patients' limbic hyperactivity inhibits sensory and motor activation (Marshall et al. 1997; Vuilleumier et al. 2001; Ali et al. 2015).

The reality that my subconscious was retaliating against my hardship made some sense to my sixteen-year-old self. But, had I been informed of my EDS, reason would have more fully reared its head. Able-bodied individuals, and even medical professionals, presume that the absence of pathological findings rules out the presence of pathology. This circular logic holds for the majority of

people, but not for EDS patients. Our MRIs and X-rays often reveal no marked aberrations, but we tear at the seams and our connective tissues' inordinate amount of give fosters joint and gastrointestinal pain. We stumble into doctors' offices with dislocated arms and knee caps and obtain nothing short of a condescending glance and a diagnosis of insanity or a conversion disorder. Notwithstanding our determination, we cannot help but fall prey to white-coated acumen. We begin to wonder if we are irrational or even downright delusional. But our tenuous internal connections are not solely in our heads. They are genuine, programmed into mutated genes, such as *TNXB* and *KLK*. Had Dr. Rucker known of the typographical blunders in my genetic code, she would have recognized that the fragility of the tissue and the abnormal ECM surrounding my neurons may potentially have been to blame, that there was more to my story than the conversion of my sorrow into darkness. But I cannot fault this considerate physician for not seeing through me into my modified genome. Even 20/20 vision was not capable of that type of sight.

Without Lyrica in my system, my vision gradually returned to the extent that I could decipher vocabulary terms and math problems etched in sizable black print on oversized notepads or whiteboards. My foot continued to take on a life of its own, and its purpling bluish tone occupied increasing dimensions as time elapsed. The whole of my attention was not drawn into its gravitational field so long as hands, socks, blankets, nor any other entity dared not touch my discolored flesh. Sarah resumed her position beside me in my parents' bed, filling me in on the nuances of tenth grade algebra and trigonometry. She jotted life-sized equations onto the whiteboard and requested that

I apply the quadratic formula to solve for X or plot the complex and real aspects of a sum. I found solace in the fact that the imaginary elements of mathematics could be assigned a place in a quadrant or along an axis. Even the chaos of the complex sphere could be set right in Euler's formula or in the letter i. All quantifiable entities are granted their rightful residence in mathematical terms. If only the invisible nature of EDS were enunciated in mathematics. Then, we would surely be seen from the start.

My parents appointed another tutor, Kim, to draw out the scientist in me. Well informed of my fascination with Stephen Hawking, Kim advised me to enter the experimental contest spearheaded jointly by YouTube, NASA, and Stephen Hawking.

"So, Elly, let's plan to craft an experiment together. The gist of the project must revolve around the conditions in outer space and how they differ from those on earth. You ultimately must record a video in which you propose an experiment and hypothetical results." Kim reached for the whiteboard on the table beside her and positioned it directly in front of me.

"Kim, I'm just not sufficiently familiar with the conditions in space to design an experiment. I can hardly make do on Earth, let alone on another planet. Although, the prospect of wandering about without any gravity to weigh me down is quite tantalizing." She grinned, and her eyes flashed as an idea came into focus.

"Elly, that's it! Let's think of a project that relies on the divergent gravitation conditions in outer space." I reflected on the biology education I received at Billard. The word gravitropism hit the bullseye in my mind.

"Kim, doesn't plant development, both the plant's physical layout and its hormonal responsivity, depend on gravity? I remember something about microgravity and auxin trafficking but can't quite unpack it." I watched Kim's proud smile unfold.

"Yes. The central plant hormone auxin is influenced by microgravity. What if we look at something related to floral development and the disparate microgravity environments in space and on earth?" I felt the excitement build in Kim's being as she spoke.

"What if we look at the aromatic ramifications of the different microgravity environments fields and the implications for commercial products, like perfumes?" Kim raised her palm, and I returned her high five.

As it happens, no part of the body is immune to EDS. Every aspect of human biology, from organs to joint capsules, is lined with connective tissue, which, of course, is my weakest link. While I tapered my post-surgical opioids and Lyrica, I developed abdominal distension. Notwithstanding the fact that I was unable to take down food, I vomited around the clock. I glimpsed a precursor to a bad dream that would emerge in its full nefarious grandeur three years later when my mother and I would inhabit the sterile halls of Mayo Clinic.

"I see this clinical presentation in fetuses born to drug addicts. I am under the impression that Elaine's peristalsis is paralyzed at the moment," the callous gastrointestinal expert reported. The doctor handed a prescription for Reglan, a motility agent, to my mother, which she filled at our neighborhood pharmacy after we returned home.

"Mom, get in here now!" I strained my vocal cords to gather my mother's attention. She and Avery ran into my parents' bedroom,

where I was seated on the edge of the bed as my foot dangled and my eyes fixed themselves on my convulsing hands splayed on my thighs.

"My hands! They won't stop shak-." My jaw broke into a paroxysm and juddered, without my permission, from side to side. My arms broke into an unruly dance. But there was no music to be heard. My body was seizing. My muscles were contracting without upstream approval. The rapid motion of my jaw impeded the passage of words. In all the medical travails my body has endured, I have never been as overcome by fear as I was in that very moment. My mother plied me with Valium and my parkinsonian crisis came to an end.

"Joel, I do not know how to care for our daughter. This is out of control. I do not know how to do what's in Elly's best interest anymore." I heard sobs break free from my mother that evening as she spoke to my father over the phone.

"I want to admit her to the hospital. I mean, I don't want to, but we need the oversight.

She needs more than I can offer." My mother sniffled as she came into her bedroom and told me that the task of mothering me was too much to bear right now, that she would resume her position as soon as she knew she could stomach it. She would not leave my side during our three-day stint at Mount Sinai Hospital but was allayed that I was under the supervision of a team of doctors for the time being. She would retreat to the sidelines, if only temporarily, and play the role of my mother rather than that of my doctor who just happened to give birth to me.

After my release from the hospital, my abdominal distention persisted, my visual impairment lingered, and my foot and calf circumference mushroomed. To be honest, I am not quite sure what was accomplished during my time as an inpatient. In any case, the day following our return to the apartment, Kim appeared at our doorstep with provisions in hand. We crafted an experimental script in large block letters on what could have been the world's largest notepad. I donned a jean shirt that buttoned up the front and positioned myself at the desk in our library, intentionally concealing my distorted abdomen and lower extremity. My mother wielded the camera and Kim raised one enormous cue card at a time. The resulting two-minute video required three hours to record as we were constantly interrupted by my vomiting.

By the conclusion of December, the prescriptions had finally leeched their way out of my system. My eyes resumed the responsibility of seeing, and my stomach reverted to its discreet and unobtrusive proportions. My leg, however, did not kowtow to any span of time. Conversely, it burgeoned by the day into something that shared more in common with a purple duffle bag than with a human limb. Furthermore, the pain that sprinted along my neurons was more than just an emergent property but became a disease unto itself. The world was a threat to my leg, which maliciously informed my pain fibers each time a gust of wind or a human hand came into its path. My father drove, with my mother and my screams seat-belted behind him, to Children's Hospital of Philadelphia, where we would convene with the chronic pain guru, Dr. Sherry.

"Hello, Elly. I see you are struggling with some horrific pain." Dr. Sherry studied me, taking in my crutches leaning against the wall beside me, and then my posture on the chair. My weight was shifted onto my right hip and sneaker.

"Yes, Dr. Sherry. I have never experienced pain like this before. I cannot touch my leg with anything, even my own mattress or water from the shower, without shrieking in terrible anguish." He figured me out within five minutes of meeting me.

"Elly, I know what's wrong with you. You're going to need patience and fortitude to set yourself right again. It is going to be a battle." I nodded and trusted his prophetic words. My mother flushed the tears from beneath her eyelids.

"What you have going on is known as Complex Regional Pain Syndrome, or CRPS. This amplified pain condition comes in two flavors. The first, which is known as CRPS type 1, is due to nerve impingement or injury. That is what you have as a result of the complication during your hardware removal surgery. The second form, known as CRPS type 2, does not have a known etiology but is spontaneous and typically manifests itself in more than one limb. You are not being dramatic. You are not going insane. I know it may feel like that. But your pain is about as real as pain gets." I clenched my jaw and pressed my tongue against the roof of my mouth. "The cure for you is going to be painful. You must work to win your leg back. You need aggressive inpatient physical therapy. Otherwise, your leg will never really be yours again." I tried to push his words down into someplace I could digest them. I choked on the phrase inpatient physical therapy, which necessarily implied a temporary separation from my one constant, my mother.

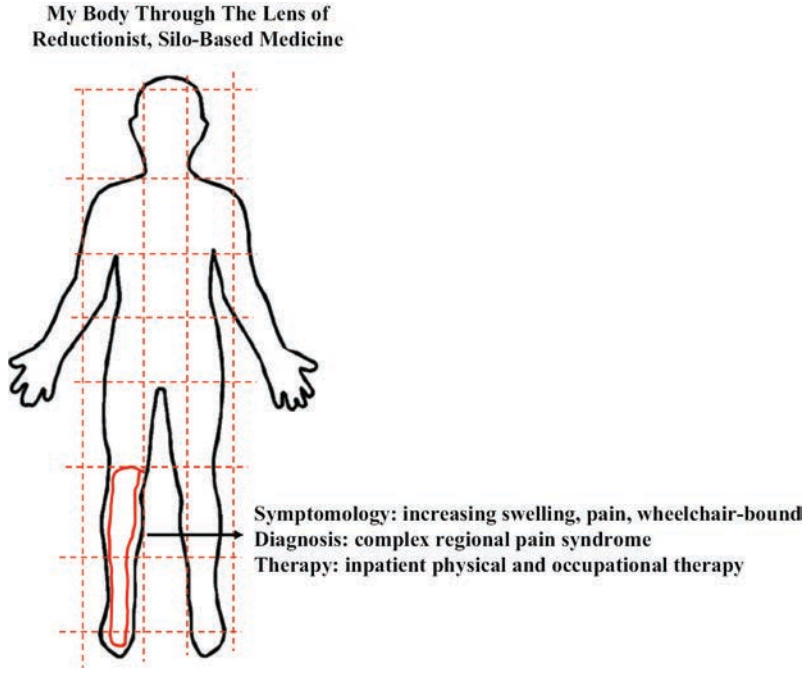
"Dr. Sherry, can you secure Elly a place in your amplified pain program and allow her to begin her stay as soon as possible?" I could feel the desperation in my mother's quavering tone.

"Dr. Katz, I'm afraid my program's waitlist extends through the next three months. I can, however, obtain an immediate place for Elly at Children's Specialized Hospital in New Brunswick, New Jersey. I trained Kate, the therapist there who runs the CRPS program." Once again, my EDS suggested itself, but eyes refused to acknowledge its existence. Due to the ease with which EDS patients' nerves stretch and the fragility of their connective tissue, research suggests a robust correlation between EDS and CRPS, the latter of which frequently follows surgical interventions, as it did in my case.

10
Walking myself through fire and out of pain

Spasm. Muscles that demand to live, that quiver to astound themselves into existence. Quadriceps belt my upper thighs in a most intimate embrace, a micro-siege.

My being revolts and riots against a furlough of stagnation.



In the acute aftermath of tissue injury, such as my spinal surgery, the central (CNS) and peripheral nervous systems (PNS) adapt to play regenerative roles; in the long term, however, alterations in nociceptive networks can lead to chronic pain (Syx et al. 2017). In addition to changes in neural circuits and immune cell activity, the extracellular matrix ECM–neuron interactions shift as pain transforms from acute to chronic (Tajerian & Clark 2015). Pain is associated with spinal neuron plasticity, which involves modifications in the length and branching patterns of dendritic neurons that relay nociception and, in turn, trigger chronic pain.

The ECM is central to CNS remodeling and connectivity due to the crosstalk between neurons and their respective ECM microenvironments. As my ECM, on account of my EDS, is dysregulated from birth, I am vulnerable to chronic pain conditions, which are known to induce and to be due to ECM anomalies. The ECM is central to the progression of these syndromes because the CNS serves as the control center of the body's immune system (Syx et al. 2017). The trauma and atrophy developing in my left leg discharged ECM-derived damage-associated molecular patterns (DAMPs) recognizable by dendritic cells, which are typically maintained in a state of immune tolerance by nearby lymph nodes. However, my autonomic dysfunction, a comorbidity of my EDS, unleashed proinflammatory immune cascades that released cytokines and resulted in further injury that culminated in my CRPS diagnosis. In short, my EDS-related ECM mutations and my dysautonomia rendered me vulnerable to chronic pain conditions.

Even now, almost a decade later, it is difficult to say exactly what such knowledge of the roots of my strife would have

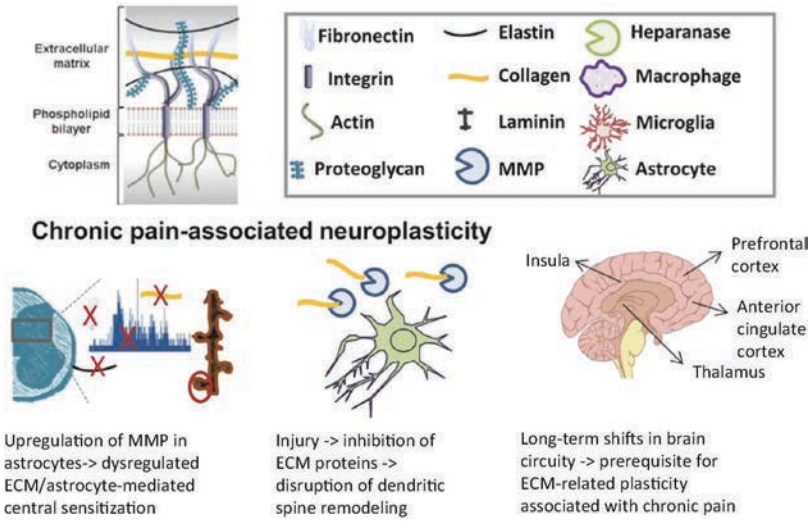


Figure 10.1: *Extracellular matrix (ECM) involvement in chronic pain.* Tissue injury leads to defects in ECM function (red 'x's in leftmost panel), which, in turn, interferes with normal dendritic spine remodeling (red circle in leftmost panel). Collagen degrading matrix metalloproteases (MPPs) are upregulated in astrocytes, a process that ultimately culminates in central sensitization due to dysregulated interactions between the ECM and surrounding astrocytes (central panel). Long-term changes in brain circuits (labeled in rightmost panel) are essential to ECM-associated chronic pain plasticity.

Adapted from "The Role of the Extracellular Matrix in Chronic Pain Following Injury," by Tajerian, M., & Clark, D., 2015, *Pain*, *156*(3), 367.

accomplished or if my EDS diagnosis would have simply filled another line in doctors' charts. Currently, eight years later, my EDS label essentially functions like a catch-all, an excuse or explanation for any setbacks devoid of actionable power.

As my father wheeled me through the automatic entrance of Children's Specialized Hospital, a lump gathered in my throat. The

prospect of surviving on my own with nothing but physical therapy and my own devices to occupy my time seemed daunting. What frightened me the most was indisputably bidding farewell to my parents, especially to my mother, who bore the mantle of pain with me. My father situated himself on an isolated bench in the center of the lobby. As we sat silently with our gazes fixed directly in front of us, a woman with slick brown hair pranced toward us.

"Well, you must be Elly. What do you like to do in your free time? Do you enjoy any particular board or card games?" Her sweeping smile resumed its position. I reached my right arm behind me and felt for my father's hand, for a familiar touch. This employee of Robert Wood Johnson's Child Life department seemed far too thrilled about my impending hospital stay. I gave her a solemn look in a futile attempt to shrink her grin.

"Elly's dad, do you mind if I wheel her up to her room?" My father squatted on the other side of my chair and gave my cheek a peck.

"Sure. Elly, I will get your stuff from the car and meet you upstairs. That's alright, darling?" I shook my head. It was impossible to respond to my father's tender question in any other way.

"Alright, doll face. I'll see you in a few." The glass doors swiveled in my father's wake, and he faded out of sight into the hospital's parking lot.

My parents stepped into the room and relieved the Child Life professional of whatever role she fulfilled by simply existing next to my chair. Before this woman left, she instructed my parents to place all my valuables in a bedside locker. I honestly was not sure if I was in a prison or a hospital. My mother arranged

stacks of folded shirts and shorts on the shelves opposite my bed as though she were moving me into a college dorm or a new apartment. A slender, worn face, which I would later learn belonged to the hospital's psychologist, presented itself after an arm slung back the curtain, the last flimsy vestige of my privacy, and instructed, "Katz family, please make your way into the orientation room." My mother took the reins of my wheelchair for the final time as we made our way to orient ourselves to whatever lay before us.

The psychologist's expression gawped at me from a seat in the corner of the chamber.

Beside her, the three additional members of my team idled on a divan. Eight eyes followed me as I was wheeled into the room. My parents positioned themselves on the empty sofa across from the teeming party of three and locked my chair into place. My Mom slid a tentative hand beneath the armrest, then retreated it and replaced it to see if I wanted to take hold of something steadfast. I gripped her for dear life.

"Welcome to Children's Specialized Hospital's Pain Program. I'm Kate, your physical therapist, the lady to my right is Violet, your occupational therapist, and beside her is Dr. Meade, the physician who will supervise your progress. To my left is Devon, the program's resident psychologist, who will help you manage the emotional element of the journey that lies before you. It is going to be a difficult two months." Kate took a deep breath, and her bouldering blue eyes meandered from my exposed limb to my face and back until they settled somewhere midway and seemed to pierce right through me, to sum me up in a single

stare. Kate possessed an intimidating beauty. Her glossy blond hair was pulled into a firm ponytail, and her athletic build even found a means of making scrubs appear in vogue. Her chin was harshly angular, and everything about her had a purpose, a designated role in the organization she imposed on her world. I would quickly learn to dread Kate's footsteps as she approached my bedside before our morning physical therapy sessions. But this fear would gradually erode, leaving nothing but reverence, and even adoration, in its stead. Without this brilliant blond drill sergeant to guide me, I may never have had the courage to walk through my pain. Kate is the reason I am complete enough to tell my story.

"My oh my, I cannot wait to get my hands on that foot." Violet's voice crackled with malevolence.

"Elly, I know you must be scared, but we are all here to help you. This is going to end well, and I am here to support you throughout." Devon scooted her chair toward me as she spoke. My mother broke in with her readymade list of questions in hand.

"When will we be able to see our daughter? Will Elly be allowed to take Aleve or Tylenol for her pain? How often is she permitted to call us?" My mother dashed through her barrage of concerns as though she tried to fit them into a single breath. She shot me an empty look. My mother seemed to be mourning for something irretrievably lost. Little did I know at the time that she was lamenting for me, for my forsaken limb, and for the innocence I once had stockpiled somewhere deep within.

"We don't permit any medications. We don't want to mask any of Elly's pain. We want her to feel it and to move through it. You can

see her on weekends only. She can phone you whenever she is not in therapy." The mustached doctor leapt awake to smother the silence. My mother and father exchanged glances riddled with a mixture of grief and distress. My father seemed to have aged by a decade during the half-hour that transpired since our entrance into the room. The lines on his face somehow hit me as more permanent and penetrating.

Humans are generally not preprogrammed for farewells, but this parting from my parents was crueler than any other. I remember my mother's soft warmth against my front and my father's scratchy cheek as he bestowed a closing kiss upon my forehead. The loneliness settled, a pit in my stomach I would never fill. The notion that they were abandoning me in a hospital because my pain had become too intense for them to manage on my behalf, that they were throwing in the metaphorical towel and moving on from my hardship without me, caused rage to simmer inside me. I was uncertain of the road that lay ahead and speculated how broken I would have to become before I could be made right again.

Within a week, I found a rather stable footing in the pediatric ward. Unexpectedly, I located an Elly-shaped space among the band of misfits on my floor scattered with teenagers battling sarcoma, cerebral palsy, gunshot wounds, pulmonary hypoplasia, and muscular dystrophy. Ironically, I felt more at home with these patients than I did in my luxurious apartment with my salubrious family.

When I wheeled myself into Katherine's room, she was in her usual contorted position in her bed. Due to her cerebral palsy,

Katherine, like I, was all too accustomed to a body that did not function at her mind's beck and call. Her combed hairs eddied above her head like brown spaghetti on the pillow. Her hand lingered in a perpetual fist. A devoted mother sat motionless in a chair by Katherine's bedside.

"Elly, my dear. So wonderful to see you." She gave Katherine's leg a tap, pulling her out of her musings. Katherine's eyes shifted in their effort to orient her in time and space.

"Katherine, I'm so glad you are awake. So, tonight, the gang and I were thinking of doing something that we do not really think you will enjoy." My oblique humor was in desperate need of a hook. She looked at me vacantly.

"So, since I know how much you hate Wheel of Fortune, I thought I would advise you to remain in your room tonight when the rest of us watch it in the common area." Katherine's teeth emerged front and center and a smile took form. It was an untainted expression bursting with an innocence she did not know was hers to lose. In a strange way, for a few milliseconds, I was envious of her illness and her brain that could not keep pace with the travails her body endured. I craved to turn down the volume or slow down the rate of my own thoughts. She erupted into a frenzy of laughter that spread contagiously to me and then to her mother like an idyllic virus.

"Come on, Elly, you know that's my favorite show. We watch reruns of it every night together." Katherine stuttered as spittle dripped downward from her lower lip.

"Alright, alright. I'll come by soon to pick you up." Katherine brimmed with happiness and peered toward her mother, who

caught my eyes as I backed out of the room facing Katherine's bedpost. She mimed the words "you are an angel."

My evenings were neatly scripted and did not require much of my body, which was spent after a full day of therapy. I passed the hours from six to nine with other adolescents who took life by the minute and did not dare glare into their respective unknown futures. Katherine, Brad, and I merged into something whole on the sofa in the teen lounge. Our broken pieces came together in a way that made a modicum of sense, which was more than sufficient to carry us through the night. Brad removed the black beanie from his bald head. His cancer could not defeat him in our company. Our laughter left us so numb and exhausted that Brad did not have enough left in him to unleash an angry yelp or cry when the light poured through the window at just the right angle to capture his hairless reflection on the television screen. Between Brad's chemo-induced emaciation, Katherine's lopsided shuffle behind her walker, and my wheelchair bedecked with the ready cannon of my limb, we complemented each other's incompleteness and scratched every possible surface of personal loss. But, by some token of prosperity, as Wheel of Fortune materialized on the screen before us, we found a few reasons to fantasize, if only for an hour or two, that we were only teenagers who happened to be viewing television and nothing more. Incongruously, I have never before or since felt as unalone as I did in that lounge seated beside a gang of indefatigable sufferers I never deemed I would befriend.

"Knock, knock. I hope someone is up and ready for a swim in there." It was a quarter after 7 a.m. on the dot. I slid myself off the bed, onto my functional leg, and into the wheelchair. Kate took

hold of my chair, which she drove to the pool in the basement of the hospital. She maneuvered me toward a white plastic bench suspended above the clear blue water.

"Elly, this is probably going to hurt, but I need you to stay submerged in the water for five minutes. You cannot come out before then." Her enormous blue eyes and her sober expression seemed to chastise me.

"Why is it going to hurt?" I attempted to prepare my mind for the torrent of fallacious pain signals my body was imminently going to deliver.

"You know this, El. Your pain fibers are hypersensitized. The only way we are going to desensitize them is to provide your nervous system with a slurry of information. We need to retrain it to feel things as they are, rather than as signals warranting a pain response." Kate fixed my chair in place as she spoke and refrained from eye contact. She hoisted me upward, placed me onto the harsh white plastic, and heaved me into the water.

I bellowed a deafening scream as my left foot sliced through the pool. Exacting sensation cut through everything else like a refined knife. My limb was ablaze. Nerve pain demands to be felt. It resounds and consumes your whole being. Your five senses funnel into one: Malignant touch.

Pool time was characteristically followed by three hours of physical therapy. Kate and Violet rummaged through a black wardrobe adjacent to the elevated mat on which I rested as my flaccid leg drooped below. The duo approached me, their respective arms filled with roughly twenty rubber objects scattered with spikes, textured surfaces, and grime.

"What are all those sharp objects for?" I discerned the answer before the question.

"Elly, do you think you can stay still while Kate tests these toys against your left leg? We want to determine if you can distinguish the different surfaces so we can understand your tactile deficiencies." Violet gave me a timid smile.

"I can try my bes-ow! Kate, pleeease stop now!" Kate revolved a spongy sphere about my left calf. Viscous droplets of sweat mobilized on my lower back and saturated my underpants. I bit into my tongue as though it were an apple and rammed my uncut fingernails into my right thigh. Blood dribbled onto the floor and my wounds seeped with red that would not quit.

After the lunch hour, during which I could not bring myself to eat, Violet roamed into my room.

"Elly, I believe in you. We are going to do this, one day at a time, together." She exhibited a full-toothed, uncompromising beam and steered my chair to the accessible bathroom down the hall. The granite floor accommodated two bathtubs. She left me sitting in my chair listening to the clatter of water against water. Violet returned with a colossal ice bucket, which she emptied into one of the tubs.

"Elly, this is how our therapy is going to work. I am going to give you two crutches so you can hop onto this bench, which you are going to sit on." Violet craned the wooden seat into the air with all of her might and situated it beside one of the tubs. "Once you place your left foot into the hot water tub, I'm going to start the timer," she continued. "When two minutes have elapsed, I will maneuver the bench to face the ice-cold tub and we will repeat

the process." I nodded reticently in her direction. It proved impossible to say no to the only people whose sole job was to help you help yourself. I pogoed on three legs to the tub, plunged my left foot into its shallow depths, and let out a shrill cry.

"Can we swing her loose?" My father locked eyes with the charge nurse. "Yes, you can sign Elaine out for three hours."

On Friday evenings, my parents kidnapped me. I felt like human contraband as they wheeled me across the ward's threshold. We took a taxi to what could have been the one and only Starbucks in New Brunswick. My father wheeled my chair into the table and situated himself beside me. My mother sat on my other side and began dealing the SET cards into organized rows on the table's surface. As we played, I slapped the table and gathered the entire deck into my possession in three card increments.

Save for the pounding of flesh against wood, I did not emit a peep in my parents' company. As soon as they released me from the hospital, I was overcome by muteness. I knew that if I let words erupt without a filter, I would never cease. My tears would come to no end. The pain I endured in therapy would be too real to bear. I could not christen my agony in any vernacular. I did not want my parents to feel the excruciating throbbing that I had no choice but to feel.

As soon as we arrived at my parents' hotel room, I propelled myself onto the bed as my mother combed her hair. A wistful look crept onto my face. It may seem crazy, but I was painfully resentful of my own mother.

"El, I love you. Tell me how therapy is going. I care so much." She gave me one of her weak smiles, which could not scratch the surface of the heavy silence that stood between us. I did not know where or how to begin, so I did not begin at all. I looked at her without giving anything away. I just stared at her immaculately made-up face and golden hair like I was observing a Renoir, not my mother.

"Elly, talk to me. I miss you." I did not know what she was after. My mother placed a doting palm on my forearm, and I flinched.

"Elly, what's going on? Why won't you talk to me and dad? We miss your voice." I felt a tear make its way down my chin. I felt so wrong, so broken. I did not even know how to string a response together into sense, to tell them that life had become too heavy, something I could no longer carry.

During my second week as an inpatient, I rejected food. The trauma of pain buries itself into your palate. There were no mirrors in the hospital in which I could have sighted the minimal amount of flesh I did not have to lose. My anorexia had nothing to do with weight. It was about making my exterior match how I felt, like something frayed and secondhand, a skeletal version of the girl I used to be. So, I pared myself down to skin and bones, to the essentials that I could not abandon by forsaking lunch and dinner. No amount of food could have made me whole.

"Alright, El, say goodbye to the wheelchair. The crutches are going to be your only mobility aids now." Kate's voice roused me awake. I looked at her unreadable face, trying to decrypt if the slightest bit of her firm body was being flippant. I should have known by then that Kate was not disposed to jest.

"You really think I'm ready for that?" I fanned sleep out of the corners of my eyes.

As I bounded into the hospital gym on my metallic legs, I felt Kate's touch against my elbow. It was not quite affectionate, but I inferred that she was proud of the literal and metaphorical strides I was making.

"You're going to take your first steps today, El. Don't worry, you will not have to carry your whole self nor fret over sustaining your balance."

"Ugh?" I quizzed.

"El, see this?" Kate pointed to a purple vest chained to a rope that hung from the ceiling. "I'm going to harness you into this device. It's a gravity machine that offsets your weight by whatever amount I enter. I'm going to start with forcing you to carry twenty-five of your ninety-nine pounds. Sounds like a plan? I'm going to find us a good song." I gaped my eyes as far open as my lids permitted, trying to take in as much as I could. The purple equipment appeared potent enough to blast me into outer space. As I steadied myself on my right foot, Kate belted me into this bulky ensemble and clipped me into the contraption connected to metallic tracks on the ceiling. She amplified the volume on her mobile, and Dave Grohl belted, "Learning to walk again. I believe I've waited long enough. Where do I begin?" Hesitantly, I placed my left foot before my right one and plodded about the parabolic track. I was doing it, this unassuming neglected act. I was walking.

In the week leading up to my homecoming, the vivacious Child Life specialist and Kate walked with me to the nearby grocery

store. As we plodded through the hospital lobby and onto the street, an elderly woman approached Kate and raised her palm in front of her mouth before she vociferously inquired, "does that girl have Down syndrome?" My gait was, without a doubt, as rickety as ever, but the idea that someone could pin such a label on me in a single look was unconscionable. Because my disease is often only granted recognition in the second or third decades of life, I would currently require more than three sets of hands to count off the number of diagnoses that have been wrongly attributed to me over the years. Only now do I realize that no medical verdict or jargon will ever sum me up. I am more than my unstable joints, more than the physical and emotional distress that accompanies a dislocation, and more than my EDS will ever encompass. No doctor or stranger could persuade me otherwise.

"Mom, the sadness of my hardship is still tugging at me. It's inexplicable. My foot works again, but something inside me is still unsure that it actually does. This voice in my head is telling me to stop moving. To stop living. To just give up when I have just won a battle. I can't figure it out. I feel so broken still, but I'm whole, at least on the outside." My mother and I sat in the backseat of my father's car as he drove to our New York City apartment.

"El, don't force it. Things will feel right again. You just need to take things in measured pieces. You have been through a lot of suffering. No one expects you to bounce back. It would scare me more if you did not feel any of these feelings." My mother's fingers traced my spine, my internal pillar. Her touch told me I would again emerge, more comprehensively than ever before.

"I think I should talk to someone about all of this. Someone who is on the outside of it and is more removed from everything than you and Dad are. I want to speak to someone who can just listen without causing me to worry about inflicting verbal pain." My mother conferred a red outline of a kiss onto my cheek.

"You are so wise, my dear. I did some research on the off-chance you wanted that and found a delightful psychologist for you. I think you will take to her."

As I made my way down the hallway to Dr. Stein's quarters, the psychologist rotated her chair and revealed a sympathetic smile. Once we entered the small space, I squatted onto the sofa and she occupied the armchair facing me. She advanced toward a glass cabinet against the wall and snatched something from its interior.

"I know you have experienced a ton of pain, enough for several lifetimes. I want to help you overcome it and to live with the parts of it you cannot overcome." Her voice had a spineless soothing texture. She glanced at me without penetrating too deeply into my dark parts that I was not yet ready to bring into the light.

"Cup your hands and close your eyes." I obliged, and a small morsel landed in my palms. "Can I open them now?" I asked in my politest of voices.

"Yes. Of course you can." I bowed my head to discover two broken fragments of shell. "What are these broken pieces for?"

"These ocean shards are something for you to identify with. You are not the only person nor object that has ever been fractured. Each time you feel alone, just look at them. They are beautiful,

despite their cleft, as are you." She returned to her position and looked at me. I had never felt that seen.

That March evening, I settled into my designated post at the kitchen table, and the caged parakeets in the corner of the room saluted me with their chirps. To my right, my father's head was hunched as he loaded as much hamburger as the size of his mouth permitted. Opposite him, my mother brought a forkful of salmon to her lips. My right upper thigh began to vibrate, and I extracted my phone from my pocket.

"You will never believe it, but I am somehow one of the semifinalists of that NASA space competition that I entered with Kim." An unfamiliar satisfaction with being Elly crept along my exterior. I shivered despite the fact that the thermostat read eighty degrees Fahrenheit.

"Wow, El. That's awesome!" My father articulated between bites. "Elly, that's fantastic!" My mother chimed.

"I think I just had an epiphany. I want to be a scientist." I felt a flash ripple through me. It was the counterpoint to the incendiary pain that devoured my limb. It was ecstasy.

Most people commence high school once at a single institution. I am, undeniably, not most people. I would inaugurate my high school education three times at three separate establishments. It seemed, however, that if I intended to graduate anytime in this decade, I must overlook the tenth grade. Resuming my outsider status at Billard did not hit me as an exhilarating prospect. Rabbi Lookstein, as my mother told me, was more than willing to permit me to enroll in the junior class at Ramaz.

"El, what do you think of studying for an SAT Subject Test? You have two months until the exam is administered, and I think it would shed light on your academic focus even in the aftermath of your setbacks that caused you to miss tenth grade." My father propped himself up on his forearm and paused the television.

"Dad, two months is hardly enough time to master a subject area," I announced, clearly not as confident in my scholarly faculties as my father.

"Give yourself more credit than that. If you set your mind to it, you can do it. I know it." He cracked a smile and rifled through my rumpled hair like I was five rather than seventeen.

"Fine. Chemistry it is."

The following morning, I introduced myself to ionic charges and the periodic table, which I speedily committed to memory. I balanced the net charge on either side of equations, apportioning two potassium ions here and three calcium ions there. Chemistry had a glorious symmetry when it took place outside my body. The scientist in me was taking the front seat, a place she would occupy until she could not.

11
My inner Jew rises

You stumble slowly into the person you are becoming, a walking being on two legs, a simple spine spanning your stature, a mind that can hold reality and shape it into verse, into complex equations, into brushstrokes and song that show your rendition of this world how to scintillate within.

You require no further possessions, no additional provisions for contentment.

Your feet are walking. Your reflection glistens across the tops of your toes; the creases in their knuckles narrate your fear of walking, of resuming existence, your trepidation about failure, about catastrophe over which you can exert no control no matter your intelligence, about free-falling into stillness, into a catatonic counterfeit of yourself.

"Get away from me! Leave me alone!" My paddle beat against the muddy waves. Liquid waded into my canoe and drenched my gym shorts.

"You will never outrun me. I am you! You can't escape me. I am the voice inside your head." I propelled myself forward with more muscle than my gaunt arms had to offer. I could no longer make out the guide's trite commentary on Lenox's colonial roots. I could no longer perceive my mother's flighty golden wisps bend in the

breeze. I was blind and deaf to everything, save for the deafening voice inside my head.

"I will get you. You can count on it." I clasped the oar with everything I had in me and paddled rabidly for two miles until my canoe was flush against a sand dune. I edged my sodden bottom onto the parched earth, but the voice persisted, "You will always be something irreparably fractured, something no one wants. You may as well just die and get the whole show of your life over with. If you do not, you will only cause yourself and other people pain." I shook like a frantically paddling dog that forgot which direction was home. No amount of frantic motion, however, would relieve me of myself. While self-destruction was a far-fetched hyperbolic response to this murmur that resounded with past pain, in retrospect, this uninvited internal guest was brutally prophetic. Existence would entail living with adversity, with pain that would slash through me and my family again and again. EDS tests your limits and pushes buttons you never knew you had with a brutal tenacity. But, if you let it, the disease can, ironically, put your pieces into something not quite whole but, nonetheless, sacred.

My mother's swollen knuckles caressed the back of my neck. Following her mastectomy, my mother's implants composed of silicone, a gel capable of migrating through its intact covering, began to leak and to ransack her immune system. Three years later, we would both be diagnosed with connective tissue diseases. Whereas my condition is secondary to deficient and lax collagen fibers, my mother's illness, ironically, is due to excess fibrotic collagen. The scientific literature remains controversial as to whether silicone breast implants (SBIs) can cause scleroderma,

an autoimmune connective tissue disease that leads to systemic fibrosis. Rubio Rivas (2017) and collaborators' meta-analysis of four case-control studies revealed an odds ratio of 1.68 with a statistically significant p-value, which indicates that silicone implants have the potential to increase the risk of developing scleroderma (Rubio-Rivas et al. 2017). SBIs are known to trigger an autoimmune reaction that disrupts the innate and adaptive immune systems, provoking a cascade in which macrophages entrap silicone particles and activate the inflammasome complex, thereby generating proinflammatory molecules and causing an imbalance in immune system T cells, all of which contribute to the scleroderma phenotype. But, back then, my mother's scleroderma and my EDS were under wraps.

"El, are you alright? You sound out of breath, and you are really sweaty." My mother dabbed at the trickle down the midline of my forehead. If we had been apprised of my dysautonomia, or the dysregulation of my autonomic nervous system, perhaps my mother would not have spent all those years asking me if I was alright.

I broke into a high-pitched sob that felt like it was coming from outside of my body. My mother took hold of my trembling being as though I were a radiographic film she sought to steady into some sort of clarity.

"I am here, babe. I got you." I cowered into something slight and manageable against my mother's chest. If only I could dwell there slick against her warm skin.

On the final night during our stay at the Canyon Ranch resort in Massachusetts, I observed my mother as she fell into a deep

slumber. I traced the tender arc of my fingertip about the roadmap of my mother's face, the peaks and valleys that I wanted to have at my ready disposal for a comparison when I reached my mother's stage in life. I hoped to mirror her to the wrinkle.

When we returned to New York the next day, I made for Dr. Stein's downtown office. I had memorized the layout of her workplace as though it were a mathematical theorem. Moving about the walls became a walking meditation.

"Elly, I'm ready." Dr. Stein peeked her head out of her door. I situated myself in my customary position on the leftmost side of the couch. Dr. Stein brushed her hair back into a ponytail, rendering her blue eyes somehow more central to her being.

"So, Elly, can we discuss your return to Ramaz tomorrow? How are you feeling about the transition?" I cocked my head downward and investigated my brand-new black Converse.

"I guess I'm rather on the nervous side. I will be a totally unfamiliar type of outsider starting tomorrow, and I just don't really know what to expect." She gave me a befuddled look as though I were a convoluted crossword clue.

"Can you elaborate on that?" I intuited that I had to spell it out for her in plainer English. "Alright. At Carmel and Billard I was the invalid, at Billard I was the only legitimate Jew, and at Ramaz, I'm going to be a social loner for the reason that I'm slotting into a different class. My original peers at Ramaz will be in the twelfth grade this year because I "redid" my freshman year. So, you see, I have to prepare to become a totally different species of outcast tomorrow." I motioned air quotations as I articulated the

word redid. I either sought to be dramatic or sardonic. Dr. Stein folded her face into a considerate smile and approached the whiteboard plastered onto the wall beside me. She unearthed a black marker from her pants pocket and commenced her work of art.

"Elly, do you know what this is?"

"It's a bell curve representative of a normal distribution." My early knowledge of statistics finally had a practical application.

"Yes, that's right. These vertical lines I am drawing denote deviations from the mean." Dr. Stein ticked the marker downward three times so that the curve on the board was divvied up into five subdivisions. She reached over the couch cushion behind me to place a dab of ink at the nearly horizontal tail of the arc.

"See that small dot?" Dr. Stein queried with an outstretched finger in the black orb's direction.

"Yes, I do. It's not really on the distribution curve. It's like half on and half off." "That's intentional. The dot is you, Elly, on almost every normal distribution that comes to mind. You are at the tail end of average. You have been the sickest among the well, the traditional Jewess among the secularists, and will be the eldest among your peers. The labels change in each case, but one thing stays the same. That is you. You are the most brilliant and most resilient patient I have. You do not belong on any normal distribution." I felt my eyes well with something between grief and pride. In hindsight, Dr. Stein's words were a subtle warning, like a far-off road sign impossible to decode at midnight. There is no shame or misery in living under the parabolic canopy of the mean. EDS thrusts you into the margins, into the liminal space

between far from average and not plottable. I will always be one standard deviation too far from the rest of my world. Find me a path, and I will gladly walk, hobble, or wheel toward the mean.

The following morning, I rolled my Jansport eleven blocks south on Park Avenue until I came upon the Ramaz Upper School. Unlike Billard's prescribed uniform, Ramaz mandated a lenient dress code involving a knee-length skirt and a modest top of our choosing. After regaining the 15 pounds I lost as an inpatient, I was neither skeletal nor plump and neither beautiful nor unattractive.

Prayers commenced at 8 a.m. pronto, and I located an unoccupied seat in the auditorium. I felt my way to a random page in the Hebrew book and sank into the background silence without even bidding God hello.

That year, physics was something of a godsend. I was not head over heels for Newton or Faraday, *per se*, but took an almost immediate liking to my teacher, Mr. Klotz. He was a small, middle-aged man with a head of tarnished silvery hair who often wore a necktie decorated with abstruse mathematical formulas. On several occasions, I encountered him outside of Ramaz's entryway as he dismounted his bicycle. We rode in the elevator to his fifth-floor office discussing kinetic friction or Richard Feynman's brilliant sense of humor. It was challenging to look away from Mr. Klotz's disarming smile that saw into me with a gentle understanding. Some implicit bond existed between us that seemed to have been there long before we came into each other's contact, like a sixth sense of mutual understanding. Just as it is impossible for me to segregate myself from my EDS, it is challenging for me

to determine where my passion for kinematics and electromagnetic fields began and where my veneration for Mr. Klotz ended.

The forty-five minutes allocated to lunch quickly became my favorite portion of the day.

I was not keen on fending for myself among the cliques encircling cafeteria tables and contentedly forsook the rubber hot dogs and stale bread for the stillness of the library. I came armed with the only bible in which I trusted, my boulder of a physics text. I hunkered down in a crisscross pose in the dim corner behind the bookshelves. As I worked through problems on simple harmonic motion and centripetal force, I felt myself dissolve into the calculations I was penning. The Elly show inside my head went quiet. My past drifted to someplace it could not puncture me. I was thoroughly immersed, body and soul, in quantifiable certainties.

Charlotte, who perched on the stool beside me in physics class, had artificially stick-straight blond hair. As Mr. Klotz dismissed our class one day after returning our graded exam papers, Charlotte's limber legs inched toward me.

"Elly, how did you do on the exam?" I resented this sort of question, but, at this point in the term, I expected it. Charlotte had no personal investment in my erudition but instead enlisted my grade as an unhealthy litmus test of her own success. I downturned the corner of my paper marked with a red ninety-four.

"I did fine, thanks." I responded in as composed a voice as I could manage. She turned her anxious face to meet mine.

"Elly, I feel like I've hit rock bottom. I'm never going to get into the college of my dreams if my physics grades continue to falter."

Behind her, Mr. Klotz examined an electrical field diagram in the teacher's edition of our textbook. He slanted his gaze for an adequate fraction of a minute and gave me a sympathetic smile, which I served back to him.

As I moseyed down the hallway to my locker, I deliberated what rock bottom actually looked like. I soon realized that I was rather acquainted with it. I bowed my head to scan my Converse. Yep, both legs function. I became giddy with an inner glee. Rock bottom was far away from me at the moment.

The subsequent week, my peers and I delivered oral presentations in Spanish class on reputable artists. I selected Frida Kahlo because I saw my own reflection in the greens, reds, and blues of her self-portraits. At face value, Kahlo and I shared rather little, if anything, in common. The raven of her unibrow and her hazelnut skin seemed to belong to a different species than did my fair complexion flossed with veins at the temple. Despite our distinct appearances, we mourned a mutual loss that inevitably accompanies teenage trauma and spinal fractures. We both bore the mental blowback involved in being a broken and hollowed out version of the person you once were and longed to be. We were each released from plaster braces after our respective bones healed, but we each felt an internal fissure widen. We both knew that we would never again be whole. We broke from the inside out. Some parts of us cannot recohere. Some parts of us cannot be braced.

I gestured toward Kahlo's "The Broken Column" on the projector located behind Mr. Pluebla's desk. In this self-portrait, Kahlo is belted into a white leather corset consisting of three straps that give way to her nude breasts. She is cracked down her central

axis like something made of primeval stone rather than of flesh and bone, and an iron column exists in the place of her spine. Metallic nails protrude from her arms, chest, and abdomen. Aside from a faint trickle of tears, Kahlo's expression is aloof and unaffected as though it were riveted by a film outside of the purview of the canvas rather than attached to her stricken body. She portrays herself as a cyborg at the mercy of an unbridgeable rupture. She is vulnerable but transcendent. The sight of the penetrating steel tacks took me back in time to my own fingernails burrowing bleeding arcs into my right thigh. In Kahlo's brokenness, I could feel my own.

"Las uñas de metal en su pecho representan su dolor," I specified as I pointed to the nails scattered about Kahlo's chest. I felt my own chest tighten, my airway constrict, and a lightness rush to my head. I scurried out of the classroom mid-presentation to the restroom, where I vomited until I was numb and vacuous. I nudged my being up against the stall door and perched there with my knees nuzzled into my chest like a child who sighted a ghost underneath her bed. Warm tears rippled down my face. No part of me sought to revisit my past in my present. Tenses ought to remain in their respective bins.

Illness gives you a unique kind of sight you never wanted. The language of suffering seems to write itself in fine print all over your world. You do not want to read it, but, yet, you cannot help backpedaling into memories you thought you could leave behind. In English class that year, we focused on *The Great Gatsby* and the recurrent motifs therein that are germane to time. Mrs. Henry was a slight blond woman with a dispassionate expression.

"Everyone, please turn to page eighty-seven in your books. Lia, will you read the passage aloud that begins with 'Gatsby, his hands still in his pockets' please?" A delicate brunette slumped down in her chair and nodded meekly.

"*Gatsby, his hands still in his pockets, was reclining against the mantelpiece in a strained counterfeit of perfect ease, even of boredom. His head leaned back so far that it rested against the face of a defunct mantelpiece clock, and from this position his distraught eyes stared down at Daisy, who was sitting, frightened but graceful, on the edge of a stiff chair.*" Lia's voice was small and fragile.

"So, what do we think of Gatsby's counterfeit comportment juxtaposed with the defunct clock behind him? How can we make sense of Fitzgerald's depiction of Gatsby's reunification with Daisy?" Mrs. Henry's questions were clearly directed to the class, but her head did not waver from its downturned position toward the novel on her desk. I darted my hand upward. Just as Kahlo's pain resonated with my own, Gatsby's unrealistic desire to find a pause button he could press to sort out his past and bring a revised edition into his future hit me in a place I knew well. EDS transforms you into a version of Gatsby you never wanted to become. I want to glue my parts together but am at a loss as to where to begin. Mrs. Henry turned a finger in my direction.

"Gatsby is stuck in his past, not in his present. He is the reason the dial on the wall, which is emblematic of that of his larger universe, has come to a halt. But he will forever be a sham of the person he was when he first met Daisy. He cannot return to his past self, despite his efforts to do so. He is unrealistic, and his reality is passing him by without him."

"Don't forget," Mrs. Henry broke in before the bell rang, "about your personal essays due next week. They need not be polished and perfected to the standards of a college admissions committee. Just put yourselves on paper so you can see how it feels before you actually need to apply to schools." She offered me a parting wink as I stood erect and paced to the door.

That evening passed with me clicking away at my computer until two thirty in the morning. I finished composing a piece about Katherine and the unforeseen friendship I forged with her at Children's Specialized Hospital. Memories shot through me, and I came undone.

As I rode down Park Avenue, I sketched the circuit presented in the textbook with a crude finger and calculated its capacitance. Rain thumped against the taxi windows, and I rested an ear against the glass to feel its percussion. I let rainwater seep into my jean jacket as I walked from the curb to Dr. Stein's office building.

"Elly, how are you?" Dr. Stein gave me a curious smile that genuinely wanted to know what I held in me.

"I guess I'm OK. I just—" I felt myself collapse into a human ball on the couch. I grabbed the pillow beside me and shoved it between my knees and my chest.

"What's going on, Elly? Talk to me. That's why you're here." I paused and looked at her. "I just assumed I didn't recall all of the pain and suffering that went on during my hospital stay. But last night I sat down to write a mock college essay. As soon as I sat down to write, it was like I could enter my old skin and walk around in it again. The experience just felt so real. Too real. As ludicrous as it

sounds, I think I'm scared of the memories I have. I thought I'd lost them, but I really was just too nervous to rehash them in my own mind. I hate that I'm embarrassed about my own life. I mean, it's my story, and I want to own it. I just don't know how to do that without hurting myself in the process." Dr. Stein offered me a plaintive nod, and her blue eyes became fuller as though they had wrested some of my sadness into them.

With the exception of that personal essay, the beauty of Ramaz was that it kept me preoccupied with Talmudic commentary and electrodynamics to the extent that I literally ran out of excess mental space. During that year, I convened with Sarah on a biweekly basis to ramp up for the SAT. I respected problems that could be resolved by simply shading in the right bubble with a number two pencil. If only EDS came packaged in the form of a standardized exam. In that case, I could crush it so hard that it would never have a chance to break me. I passed each Sunday from eight to noon taking a practice exam, a routine I unabashedly enjoyed.

The week after the SATs, I was stooped over my physics textbook in preparation for the final exam when I heard a shriek come from another room. All the cries that transpired in my apartment, until that moment, came from someplace inside me. I bounced off my mattress and into the hallway. I rushed into the living room to find my mother lying on a couch with her legs elevated against the wall. Her feet were swollen into shapes that were more fitting for an elephant than a human.

"El, it's my heart." My mother's voice dissipated into something she could not retrieve.

In the morning, my father chaperoned my mother to the cardiologist, who informed my mother that her heart valve was obstructed. She required urgent valve replacement surgery. My mother's inexhaustible dedication to my well-being throughout the years solidified into a paradigm for empathy that I felt motivated to emulate and to reciprocate. Almost instinctively, I became a conduit between my mother and the world; I relayed her needs and medical status to my immediate family, purchased her favorite foods from nearby cafes, and updated her friends on her progress. While she convalesced, I walked the ten blocks home from Ramaz daily during lunch period and recess daily to read poetry aloud to her, our roles of patient and caretaker temporarily reversed.

12
Up close and personal with cell membrane trafficking

I have become a sounding board of my surroundings,

taking in the syrup of experience, letting it soak, unfiltered and raw in my bones, letting myself let go of my shortcomings.

My parts may not adhere, but I am veering toward completion.

"Hey, Elly, the FPLC is available now. Pop on your winter coat and get started when you are ready." Rich detached his stare from the monitor on his desk and gave me an affable smile.

"You got it, Rich. I'll be in there in two."

"Is this the Falcon tube that contains the proteinaceous mixture you would like me to analyze?" I fingered a plastic tube located on a rack. Rich replied with an assenting nod. I tugged a pair of purple gloves onto my hands and cavorted to the cold room maintained at a staggering two degrees Celsius. I was in my element. I coded in the program I wanted to run on the fast protein liquid chromatography (FPLC) machine and took a frigid front row seat before the display monitor.

As a member of Rockefeller University's Summer Science Research cohort in 2013, I was assigned to The Blobel Laboratory spearheaded by Dr. Günter Blobel, the recipient of the 1999 Nobel Prize for his discovery of inherent tags that dictate protein transport and cellular localization. He coined the term nuclear pore complex, or the set of proteins that facilitate bidirectional cross-talk between the nucleus and the cytosol. Under the mentorship of Rich, I was tasked with determining how the two outermost layers of this complex interact to facilitate the expansion and contraction of this communication tunnel.

Dr. Blobel was a German colossus. His astonishing stature struck me as that of a man on stilts. He was a bowtie aficionado whose stern Germanic tone did not detract from his compassion for his underlings and the imported chocolate caramels in ready supply on his desk.

He was the kind of rare breed that you sought to reproduce in yourself, particularly if you took pride in purifying proteins and figuring out macromolecular interactions.

"Good morning, Rich. I hope you had a pleasant night. I know it's already ten past eight, and I told you I would be here a full ten minutes ago. I'm sorry. The traffic was just rather intense this morning." His face parted into its characteristic beam.

"Elly, really, it's no biggie at all. Also, you were the one who insisted on your eight o'clock start time, not me. Relax a little. You still have several weeks left of your program and can afford to slow down a bit and breathe every so often." His face lit up as he looked at me, and his smile stretched into a fuller expression. I flashed him

a full-toothed smile and ambled toward the centrifuge to extract the canisters of freshly precipitated protein.

I parted from the rancid laboratory flasks around noon each day in sync with Angie, a visiting research assistant, and we strolled to the research building's roof. A sort of tacit pact rested between us to take our lunch in this cloistered park ornamented with a wooden table and two benches.

"Elly, how's your project going?" Angie spun her neck down and to the right to catch hold of me. She was at least a generous two feet taller than me.

"It's going rather well, actually. I finished purifying both of Rich's Nup93 constructs and am going to begin the binding affinity experiments this afternoon." Angie tenderly knocked the back of my forearm with her elbow. If I threw around the Nup lingo, the shorthand for the nucleoporin proteins that comprise the nuclear pore complex, at anyone outside of the lab, they would probably look askance. Fortunately, Angie was rather well-versed in the dynamic constituents of the complex.

"That's great, Elly. Rich is a fantastic mentor, don't you think?" She parted the glass door that opened onto the outdoor roof.

"Yes, he is amazing. I'm just scared that he is setting my mentor bar rather high from the get-go. After him, I'm just going to expect that all of the future postdocs with whom I will work will be sunny and encouraging." Angie sat down beside me and started to work on her cheese sandwich.

On Wednesday evenings, I cut out of the lab prematurely at a quarter to five and meandered uptown toward the Ronald

McDonald House. I put on my headphones. As I passed Rockefeller's wrought iron gates, I sifted through the lab papers in my backpack until I came upon my iPhone. It struck me as rather unseemly to invite Miley Cyrus to strain past my eardrums and into my auditory cortex in such a dignified citadel of science as Rockefeller. I fingered my way to the album I fancied but dared not press play. Cyrus' belly shirt and her come-hither expression on the screen did not, upon first impression, synergize well with the gel electrophoresis and protein assays underway a mere ten paces north.

While I walked further away from the labs, I turned up the volume of "Robot" just as Cyrus belted "Stop trying to live my life for me. I need to breathe. I'm not your robot." At the time, I could not quite pinpoint precisely what about those lyrics or their resolute delivery prompted me to feel like Cyrus was speaking directly to me. I selected the song with the foreknowledge that it would accompany the lachrymose effect it always did. Something in me sought to bring pent-up and uncooked feeling forth. Even I realized I was abysmally pathetic as I walked down the pavement and wept to Miley Cyrus. Now, roughly six years later, I understand my response. On a subconscious level, the lyrics forged a kind of prefigured framework through which I could whisper to a part of myself I did not know was broken or was even breakable. The words formed a sort of personal echo. My EDS was my "robot" that would apportion me scant breathing space in the years to come.

Annie's small pale brown face was pressed up against the glass entrance to the House as I strolled up. She was twelve, but her age had little, if any, bearing on her four-foot-tall exterior.

She was withered and hollow, like an empty beverage bottle flattened by taxi tires. Three rows of her ribs protruded from her yellow tee-shirt that read "life is good," which stung me with a brutal irony. I swallowed hard, forcing back any hint of sadness. Her blue jeans were on the cusp of falling down over her knobby legs. Everything about Annie was miniature. Her brown eyes glistened in the eventide that reflected off the glass. As she fixated on my quickening gait, the edges of her mouth tugged upward.

"Hey, Elly!" She yelped as she looped her arms around my middle. I felt like a magician who simply had to show up for a weekly pizza date for the illusion to take its full effect.

"Hey, Annie! It's so wonderful to see you." My eyes wandered to the chemotherapy portal devastating her inner arm, and she mechanically jerked her rolled shirtsleeve downward to conceal the harsh tubing. The Ronald McDonald House had a rather romantic and cheerful feel to it. Colors popped out at you from chairs, tables, and wallpaper. The place was a haven, or it could have been if it had not been a refuge for children with cancer.

"Pizza time?" Annie asked as she fought the thwarted zipper on her coat. I bent to meet her gaze and coaxed her jacket shut. I curled her delicate palm into my hand, and we made for the neighborhood pizzeria.

Annie sank in her chair, making herself appear smaller than she already was, and brought a slice of pizza oozing with mozzarella to her lips. She looked starving and nauseated at the same time in the aftermath of her chemotherapy infusion. It is difficult to know where to begin with Annie, so I waited for her to lead me to the topics that she deemed worthy of our discussion.

She skimmed my expression like a tourist in desperate need of directions.

"I had a hard chat with Mom last night." Annie changed into something sober. Her mother was a mystery to me. Five years prior, she traveled from California with a newborn and Annie to New York for Annie's sarcoma treatment. I was uncertain as to the whereabouts of Annie's father.

"Do you want to tell me about it?" I asked, not wanting to overstep. Annie curved her back and neck so her chin was seated on the table.

"Yeah. I want to ask you a few things." I steadied my jaw on my fists and offered her my devout attention.

"So, last night, Mom told me that I was on my last round of chemotherapy. The doctors told her that they can't do much for me after this. Mom told me that I might die in a few months if some miracle doesn't happen." Annie rolled her hazelnut eyes as she uttered the word miracle as though she were a child who had long since come to terms with the fictitious nature of the tooth fairy but, nonetheless, continued to speak of the mirage. In reality, she was merely a preteen who was precociously aware of her own mortality. She wiped a nostril with the back of her hand and continued, "But, Mom says I'm kinda lucky. She said growing all the way up is no easy feat, cancer or no cancer." Annie swiveled her tongue about the edges of her lips to guide some runaway tomato sauce to its proper destination.

"How do you feel about all of that?" She let out an exasperated breath in reaction to my question.

"Elly, my Mom and I are hostages of the medical system. She was only spelling out the truth before it becomes our reality. But there are a few things I guess I want to know about before I'm out of time." She summoned the tepid pizza to her mouth and let the silence sit between us, like an uninvited guest. I began biting my nails coquettishly and then realized that in our game of vocal tag, Annie had tagged me. I was it, and it was my turn to speak.

"What do you want to know? I would love to help you in any way I can," I rejoined, wholly unaware of the debriefing that lay ahead. I was hardly the person who I would turn to for questions relevant to normal experiences. Her brown eyes darted into me.

"Well, I guess I want to know what it feels like to kiss a boy." Annie could not afford to tiptoe around the brunt of what she wanted to know, especially in my presence. Our friendship dated back four years, and I delightedly assumed the role of the outsider she blabbered to about R-rated films. I repaid her piercing stare with my own self-effacing one. I felt the lines on my face crinkle in discomfiture. I became unnaturally conscious of my heart rate, which felt like it was exceeding some biological limit.

"To be honest, Annie, I do not really have experience in that area." I let out a sheepish laugh, trying to cut through my mortification with feigned levity.

"Really? You are eighteen and have never even kissed a guy?" Annie sat poised in disbelief.

"Really. I'm eighteen and I've yet to exchange saliva with any other human. It's not really an opportunity I seek out on a regular basis. What would you like me to do, walk up to an arbitrary man on the sidewalk and ask him if he would like to swap some bodily

fluids?" Annie raised herself on her knees on the seat cushion so that our eyes came up to the same latitude.

She reached across the table and took hold of my wrist. We eyed each other and began to laugh unreservedly. Three weeks later, Annie died.

After Annie's passing, I pledged to myself that I would test the limits of my comfort zone and engage in experiences, like a first kiss, that Annie would never have. Thus far, my promise is unfulfilled. I am a tenaciously ritualistic woman. Not in the religious sense, of course, but in the way in which I take in life in manageable and computable bite-sized servings. Like my father, I possess a laser focus that annihilates people and objects beyond the periphery of my attention.

The rationale behind my preoccupation with school was twofold. On the one hand, my commitment to my studies layered a nebulous smokescreen over Violet's mandated ice baths and Kate's ruthless expressions. Concurrently, my academic edge thrust me into a cryptic future over which my pristine 4.0 GPA would hold sway. I stowed my vow on Annie's behalf in a holding place in the rear of my cerebrum and let it rot there into ashes that no longer groveled for average experiences I would never call my own. EDS chomps on and swallows normal situations right out of you.

As a senior at Ramaz, the mantle of the outsider weighed on me less than it had during my junior year. It still surfaced in full force at lunchtime as I hunted for a solitary table at which to consume my peanut butter and jelly sandwich or in the hallway lined with lockers as my contemporaries quibbled about the proper attire

for the birthday bash to which I was not invited. In the classroom, however, I assumed the role of a fierce insider. My peers, not I, skirted the margins, and an auspicious about-face ensued. Mr. North, my honors English teacher, wore oversized round bifocals and suspenders. He maneuvered between the rows of students with *Sons and Lovers* in hand until the bell chimed and class commenced. In the intervening silence, I was guilty of the charge of book murder. I penciled downhill in a shorthand code. Lawrence's pages became a flip book of my own rambling exegesis.

"Please turn to the final page. I would like to conclude our discussion of the text with an analysis of the final passage." Mr. North perused the classroom as if to gain his own footing.

"*But no, he would not give in. Turning sharply, he walked toward the city's gold phosphorescence. His fists were shut, his mouth set fast. He would not take that direction, to the darkness, to follow her.*" Mr. North formed an exaggerated fist and clenched his jaw in his cinematic rendering of the line "*His fists were shut, his mouth set fast.*" He pursed his lips as he finished and greeted the silence that filled the room until he cut in, "So class, how can we interpret Lawrence's finale?"

A helpless heaviness hung about the stale air. I turned my head in both directions from my front row seat to discover only two out of twenty-five books were open. I let a thought simmer in my mind until it was charred. I felt my arm inch upward of its own accord. My intellect outran my body by a mile or two, an occurrence that would soon become commonplace. In two years' time, I would gather that my body would never come up to speed and would lag behind my cerebral cortex for the remainder of my life.

"I construed that excerpt as Paul's psychic maturation and overdue separation from his departed mother. He chooses the industrial and artificial phosphorescence over the darkness of the suicidal tendencies he confronted following his mother's death. He is finally ready to move on, to accept a life of his own making, but he comprehends that such a path will be fraught.

Hence, his body tenses up at the thought of the path before him." The words tumbled out of me like a wave. As I finished, Lia's arm to my left bolted upward.

"Paul seems rather immature to me. His mourning for his mother is maudlin and occupies far too much of the novel. The portion you read, Mr. North, should have come about a hundred pages earlier." Her voice was feeble but assertive. Lia looked at me with something I translated as belligerence. She had visibly not confronted any real hardship of her own. Irretrievable loss involved more than she could gauge through her privileged lens. Countenancing suffering was an expandable process that took sufficient time to effect internal permanent changes you then had to acknowledge as part of yourself. It was not the kind of ordeal that you could delineate in your timetable to occur precisely between four and five in the evening like a math problem set. Life does not abide by that type of bookkeeping.

I employed myself in the myopia of academics and practiced an abstinence from liquor, parties, and the opposite sex with the unflinching piety of a Mormon. Life had jostled me by my left leg and had instructed me that when push came to shove, I could only rely on my mind as my guide. I could lose hold of my vision, my gastrointestinal tract, my menses, and my legs, but my brain

would remain my stronghold, at least until my cerebrospinal fluid leak. I was sharp, rapt, perspicacious, and mildly superhuman. No physics problem nor math question could stare me down for long. Due to the scheduling overlap between advanced placement chemistry and physics, Mr. Klotz consented to meet with me on an individualized basis to enable me to take both classes. In addition to integrating velocity functions and calculating ionic flux on the blackboard, Mr. Klotz became a person to whom I could turn in times of personal need. I often promenaded into his office under the guise of a physics question that served as a mental band-aid I readily tore off to let what festered beneath breathe. I felt a supreme level of comfort with this modest and brilliant disciple of Lagrange and Newton.

"I think I'm taken by physics because I know what life looks like without momentum.

I'm rather familiar with inertia, deceleration, and jerks. I've been broken by the founding principles of physics. But now, I'm the one in the driver's seat with the calculator in hand who can put things in order." Mr. Klotz's eyes began to liquefy in sympathy or empathy. It was difficult to untangle the two. I was providing him with a context for the following poem I emailed to him the night prior:

> *I walk myself into morning, into November wind that batters cheeks to blush, into the taste of over-brewed, burnt coffee, and into the shards of sunlight strewn upon winter. I have mastered this sacrificial act of abandoning what could have been and pacing towards what could be, this two-year-old rite of passage, this privilege of navigating according to my internal will, of halting occasionally to witness my tracks. My*

> *feet are learning. I walk myself into my best thoughts, into unique solutions to differential equations, and into cross products between vectors. I walk myself into memory, into a whirlwind of firsts, into an unparalleled friendship with my physics professor, into clamping down on pedals and handlebars, and into learning that I can fall. I walk myself into evening, into a future that once painfully escaped my anemic grip, into territory that once outlawed my gate, and into knowledge of the universe I never dreamed I could attain.*

"Elly, you are remarkable. You have clearly been through a lot. But you are wise and strong. I'm impressed by your writing. You're amazing, and I mean that, and I'm sure you know I mean it." His statement was packed with a sincerity that I accepted as genuine. Mr. Klotz was not given to trite discourse.

My parents' suburban pedigrees did not really set the stage for any expectations with regards to my college prospects. Instead, I was the one calling the shots as to where I would apply. In an effort to determine my worth, I placed every ounce of my confidence in the Ivy League. I may seem like an insecure carbon copy of a multitude of other white female students on the Upper East Side, except for the fact that I was not. I had a biting past that only dawned on me in a one-off nightmare and, despite my entreaties, continues to shape who I become.

The give and take between illness and the patient is almost impossible to perceive as it occurs, like the muffled hum of a sonata in a windstorm, but is blatant in remembrance. At age ten, I could effortlessly detect the fine exacted by illness, my confinement in plastic and my limited mobility. But I failed to notice

the recompense of illness, the perspective I never asked for that became mine for the long-term.

I clattered away on my MacBook at the kitchen table as I attempted to sum myself up in seven hundred and fifty words. The front door to the apartment sounded. My father's leather work shoes crunched against the wooden floor toward the kitchen. Beneath his navy suit, my father's pale blue pinstripe shirt was undone at the collar and the color was drained from his stubbled cheeks. He placed his leather briefcase on the limestone counter at the kitchen's threshold and occupied the chair facing me.

"Hello, girlfriend. Fill me in on your day." My father's hazy eyes studied me.

"It was not too shabby. I think my physics exam went rather well, and I finally polished off my English essay. I'm just feeling uncomfortably lukewarm about all of this college stuff." I felt the grinding mechanism of my jaw kick into full gear. My father's smile became a straight horizontal. He squinted, but I was certain he could take all of me in.

"Why would you think that? You are applying to 15 schools, and I know that more than a few of them will want you. Just because Mom and I didn't go to the upper crust of colleges, does not mean that you do not possess incredible merit in your own right. The focus on legacy may not be in our favor when it comes to schools beyond the league of Hopkins and Barnard. I know that. But you, Elly, are something magnificent." My father's smile surfaced, and his dark hair became tinged with a dignified silver as partial night poured through the window.

Bare feet rattled in the corridor, and my mother looked at us from the kitchen entryway.

As she entered, the front door squealed shut with a subtlety that I attributed to Jason, who had clearly mastered the art of the Joel Katz door closure with far more flair than anyone other than the maestro himself. The rusted hinges on the wine cabinet moaned as Jason returned the pass to our basement gym to its designated place.

"Hey Ja!" My brother neared the table, and a reflective trail of sweat followed in his wake. In the sheen of perspiration, Jason looked like a walking advertisement. His crew neck clung to his chest, and his black curly hair shone in the faint moonlight.

"Hey, El Bel," Jason replied in a breathy voice. No part of me was militant against my brother's brawn or the athletic mixture of body odor and adrenaline that he exuded. Back then, no part of me considered the fact that I owned fifty percent of his genes but was downright incapable of building myself in his image. No part of me knew that I harbored stop signs in my genetic code that would prevent me from moving in ways I would soon lament.

"You staying for dinner finally? I've not seen you much since you moved into your new apartment." My brother's eyes wavered from mine, to my mother's, and, ultimately, to my father's.

"I'm not sure if Mom made enough food for me. But it's OK. I've got plenty of food at home," he ventured, not wanting to intrude on a dinner prepared for three.

"Of course we have enough," my mother persuaded.

Jason pulled a chair up beside my father. My eyes darted between my parents. My mother caught my distressed stare.

"El, what's up? Are you not feeling well?" We locked eyes, and my mother saw further into me than my look let on.

"It's the application process that's getting to you, isn't it?" she stated as though my face were a verdict she read with ease. From across the table, Jason shot me a smile that was so insistent it caused his eyes to curl into inverted parabolas.

"You got this, El," Jason added in attempt to inflate a confidence with which he could not personally identify. School and my brother were never on the best of terms. Jason did not have to balance equations to feel a chemistry with his world. He did not need to measure the kinetic energy he mustered on the treadmill.

"El, repeat after me. I can walk. I can see. I can beat CRPS. I can do anything," my mother intoned. She looked at me with a blend of triumph and defeat.

"I can walk. I can see. I can beat CRPS. I can do anything," I repeated. My father angled his gaze so it met my mother's, and his eyes were overcome with a sadness of my past pain.

Two months later, I huddled over my laptop by my bedside as if I were in a lavish bomb shelter and my parents were the enemy troops. It was half past five on Tuesday evening, and six windows were staggered on the screen. I dashed my cursor between the refresh symbol on each of the browsers and heaved several breaths. I compulsively refreshed each window, and my mother's bare feet told me they were on the other side of my bedroom door.

"I can walk. I can see. I can beat CRPS. I can do anything," I murmured. No college could validate or expunge those four truths from the person I was. A "Congratulations" message appeared on my Penn, Stanford, Columbia, Hopkins, and Yale profiles. I was waitlisted at Harvard. I felt myself sigh in relief, and a giddiness washed over me that I assumed I had left behind me on the Ramaz Lower School playground with Ruby. I leapt to my feet and bounded for my door, which I flung open with abandon. "I'm a bulldog through and through!" I shouted into my mother's apprehensive expression. Harvard was my preferred contender, but Yale was undeniably a close second.

"El, I'm so thrilled for you." My mother trembled gleefully. She tacked a kiss to my cheek and reached for the landline on my bedside counter to dial in my father.

"Your God works in mysterious ways, mom." My mother's blue eyes glassed over with an ironic ecstasy.

"Yes, my love. He does." She enveloped me in her naked arms and held me still like something capable of crumbling that she yearned to keep whole. As I reposed my chin against the soft of my mother's shoulder, I let go of my cynicism and took hold of her piety for a few deep breaths.

"Elaine Katz! I am so very happy for you, my darling," my father's staticky voice thundered through the speakerphone.

"Thanks, Daddy! I love you," I hollered.

"Where's my favorite bulldog?" Avery's spirited voice echoed as his lumbering footsteps came to the threshold of my bedroom. He rushed into me and swooped me into the air.

"El, come check something out in the living room." Avery grabbed my hand and escorted me through the door. Two navy balloons, each a with a giant silver "Y" in the center, bobbed against the ceiling.

"Thanks, Ave!" I shrieked. I pressed my face up against my brother's soft stomach and wrapped my arms as far as they would go about his waist.

At the close of school the following Tuesday, my mother waved a hand in my direction through a rolled down taxi window. I boarded the passenger seat beside her, and we made for Bed Bath & Beyond to investigate the store's dorm room décor offerings.

"El, because we don't really know where you will be next year and whether or not you plan to take a gap year, let's just peruse without purchasing for now."

"That makes sense. Sounds like a plan." My mother's hand fell into its habitual place within my own.

We promenaded up and down the store aisles with a scanning device at our ready disposal. We parted the shop at eight o'clock with nothing but pleasant exhaustion and the world's most outrageous shopping list.

On the return trip to the apartment, my mobile vibrated in my jean jacket. As I retrieved it, a number beginning with 617 flashed on the screen. The call was from Massachusetts, which could only mean that it was from Harvard.

"Hello," I stuttered as though it were my first time relaying the greeting. The word got caught in my throat like water that went down the wrong pipe.

"Is this Elaine Katz?" A gruff masculine voice questioned. "Yes, it is," I established.

"Well then. Hello, Elaine. This is Ryan from Harvard's admissions office. I am pleased to offer you a place in the incoming freshman class. You have been selected from the waitlist." My lips parted but no words came out.

"Elaine, are you still there?"

"Yes, I am. Thank you for calling to let me know," I articulated in a subdued tone. I hung up. Exhilaration crept into my stomach and lurched its way into my larynx. A shrill scream rang through the taxi, which came to a rapid halt.

"Are you alright?" the driver enquired in a European accent.

"Yes. I have never been this alright. I just got into Harvard," I blurted. My mother exited the cab, but we had not yet reached our apartment.

"Come on, El. Dad and the boys are away on their golf jaunt until tomorrow. You and I deserve to celebrate." I walked in step with my mother for two blocks under the quiet dark lid of sky. We were fluent in the mute back and forth of pain. But this quality of silence had an unfamiliar bounce to it as though the night had become a sort of trampoline that would not let us fall or skin our knees. It was the kind of silence to which I skipped, rather than walked, until we approached my preferred sushi purveyor in all of New York.

Atlantic Grill was unexpectedly congested for nine o'clock at night. As we sipped on tap water, my mother gave me a look of gravity and admiration.

"Bel, you know how much I love you, right?" My mother choked on the beginnings of her tears.

"Mom, I don't really think I can know. It's like attempting to come into contact with infinity. I think that type of mathematics is on reserve for science fiction." She broke into a laugh that was incomplete. Tears streamed down my mother's cheeks, and she fanned them backwards with the stroke of her index finger. We gazed at each other like strangers until our food arrived. Our unbreakable bond would prove itself to be the only constant in my life. I could not look to Yale, or even to Harvard, to tell me who I was or upon what I could depend. To answer those questions, I now realize that I only had to glance into my mother's dedicated eyes. I would soon appreciate firsthand that chronic illness demands a witness, and that person sat directly across the table clutching my palm.

13
Oxford commas and upset stomachs

I am in motion, in flux, a derivative, a delta sign. You will not pin me down or box me in.

The taxi sped until it came to a shuddering halt at the bend of Cowley Road. A sequence of duplexes leaned against each other, framing the arterial boulevard. Each façade consisted of a uniform width of roughly ten paces across and shackles of blinding neon hues.

Drunk from our aircraft catnap, my mother and I stumbled in black tracksuits toward a blaring turquoise rental and banged on the door. It croaked open on hinges, and a petite nineteen-year-old woman came into view. Her face was composed of a wan elongated ellipse with deeply set enormous brown eyes.

"Hey. You must be Elly. I'm Alice, your flatmate." The girl drew out a scrawny hand from her blue jeans.

"Yes, I am. It's lovely to meet you. This is my mother, Karin." I gestured toward my mother as I mentioned her name as if I were referring to her at an amplified concert or in a throng of Elly doppelgängers. My mother was undeniably *my* mother.

"Brilliant. Why don't you both come in. It's rather humid out there. Welcome to September in England. It's either raining or fuming hot." Alice directed us into the apartment.

"This is the kitchen. The landlord restocks the fridge every Tuesday with ham, beef, and chicken. Otherwise, we are responsible for procuring our own food." Alice slid into a bright red plastic seat at the circular table situated in the center of the tiled floor. My mother's expression turned into a distressed sheet-white as Alice rounded off the list of unkosher slaughtered organisms on exhibition in the fridge. An upturned hardcover book rested on the table, and Alice's arm made for it and then retreated when she caught my gaze.

"I don't think I spoke much about myself. Sorry, I'm rather unfamiliar with welcoming newcomers into the flat. I'm from Germany and study the poetry of Larkin, Auden, and Eliot at Oxford. I'm a keep-to-myself kind of girl, and I prefer to lodge in a flat instead of at one of the colleges." My mother's arm swept itself beneath my curls and hung over the pole of my neck. Alice's wistful and distracted eyes made for the hardcover on the table.

"I'm studying abroad as an Oxford tutorial student for the year. I'm attending Harvard University afterward. While here, I am planning to pursue Shakespeare and philosophy. I am a huge fan of Eliot's work, especially of *The Waste Land*. What are you reading?" I signaled a finger at the book that absorbed Alice's focus.

"It's a Larkin anthology of essays and poems. I'm composing an essay on Auden's influence on Larkin's style as it pertains to Larkin's capacity to imbue commonplace observations with poetic panache and to locate meaning in the midst of meaningless circumstances."

I walked my mother to the entryway and gave her a tight squeeze. She placed a damp kiss on my cheek, and I looked steadily into her overflowing eyes.

"El, I love you. We are one. Remember that," my mother whispered.

"We are unbreakable, mom. I know that by now." I felt a pit start to emerge in my throat, and I swallowed hard.

While three quarters of my Ramaz class boarded a plane to a religious seminary in Israel for a gap year, I elected to strengthen a distinct personal component that had little, if anything, to do with God. I put Harvard on hold for a year while I busied myself with humanities *in situ* in their universal bastion. Once at Harvard, I was determined to pad my academic course load with math and science. The opportunity to expose myself to the other side of the intellectual tracks at Oxford proved impossible to resist.

I settled into my navy cubical chamber and decided to withdraw into its dark interior for the remainder of the evening. Hunched over *In Search of Schrödinger's Cat,* I was finally overcome by sleep. I was, in a literal sense, prepackaged for the theoretical world. Intangible neutrinos and the wave-particle duality of light appealed to me more than did observable Newtonian physics.

So, too, my tissues would soon notify me that I was designed for a different planet, perhaps even for a different cosmos.

In the morning, I wandered across the uneven cobblestone streets to my philosophy course. Upon my arrival, two of the desks were already populated.

"Good morning. I'm Phillip, your philosophy tutor for the term. Take a seat. Your other term mate is Michael." A blonde in his mid-thirties tapped on the desk to his left.

Michael's skin was a starched white, an inhuman shade that was only exaggerated by his flaming red hair. His deep green eyes shone and probed me from head to toe.

"Alright. Michael and Elly, the time is as good as any to meditate on René Descartes' 'First Meditation.' Elly, would you read the first passage?" I nodded my head fervently.

"*Some years ago I was struck by how many false things I had believed, and by how doubtful was the structure of beliefs that I had based on them. I realized that if I wanted to establish anything in the sciences that was stable and likely to last, I needed—just once in my life—to demolish everything completely and start again from the foundations… So today I have set all my worries aside and arranged for myself a clear stretch of free time. I am here quite alone, and at last I will devote myself, sincerely and without holding back, to demolishing my opinions*." As I halted, Michael broke in without hesitation.

"What's the point of Descartes' undertaking? In a summer course at MIT, we examined this text. Descartes does not really seem to accomplish much. He ends right where he started, that is, not knowing what he can trust. He knocks everything down that he can't trust, but even the subjects in which he initially has confidence, like math, become slippery to him." Michael's sentences toppled into each other as though he were running out of time to get them out until I responded.

"Phillip, to me it seems like an incredibly tall order. I mean, Descartes thinks he can reach a resolution about the heart of knowledge in

a few hours. That strikes me as impractical." A year later, I would, against my will, grapple with Descartes' imperative dilemma. Under the mallet of EDS, the ground beneath my feet and the limbs I took for granted would slide away into questions rather than givens. Like Descartes, I too would challenge my senses and my own anatomy. My own logic would come tumbling down.

My Shakespeare course took the format of a private tutorial with an elderly American woman. Slight rectangular spectacles dwelled at the tip of her nose. She saw the world by looking down at it with condescension.

"Welcome, Elly. I'm Dianne. Have you reviewed *Macbeth* for today's lesson?" She reached a fleshy arm behind her and removed her copy of the play from the bag hanging on the back of her chair.

"Yes, I have. I'm slightly lost on the premise of Macbeth's bloodshed. Based on the prophecy of the three witches, he proceeds to murder the current King and others who stymie his efforts. Shakespeare paints Macbeth as someone who is swept away by self-seeking ambition until he goes mad, but it seems like Macbeth is doomed to insanity from the start. After all, who actually listens to witches?"

"You are missing the point, Elly. The witches are purely figurative. In fact, the entire play is a metaphor for the boundless capacity of the human psyche. You are reading too much into the text. Step back from it a bit." She spoke in a measured blasé tone. Her assertion angered me. I mistook *Macbeth* for my own life and pondered if my existence constituted some celestial testing ground of the limits of human psychological endurance and resolve.

"So, the entire plot is simply metaphysics?" I challenged. "The storyline must also serve some type of end in itself, right?" Dianne raised an eyebrow.

After class, I ambled to Pret A Manger on Cornmarket Street, a pedestrian precinct scattered with eateries. After purchasing a bagel, I positioned myself at a solitary table and cracked open my book on quantum mechanics. I spied a flaxen girl I recognized from the abroad program's Facebook page. I clapped the book shut and made for the familiar stranger's table.

"Hey. I think we're in the same program, and I thought I would introduce myself. I'm Elly." The girl took a swig of water while her brown eyes studied me. She gathered her blonde hair and fingered it behind her ears.

"Yeah. I think I saw you on that page as well. I'm Maya, and I'm from California. Want to join me?" I took the vacant seat beside her as I unwrapped my lunch.

The next Saturday, Maya and I convened at the entrance to Magdalen College. The weather was nippy but balmy. As I approached Magdalen's English Gothic quadrangle replete with historic pointed arches, large windows, ornate tracery, and seamlessly trimmed flora, I suddenly felt unnervingly measly and mortal. My humanity became overwhelming to carry. Maya appeared, and the weight of things seemed to diminish as her footsteps drew nearer.

"Morning, Elly. Want to walk along the dirt footpath near the deer park?" Maya gave me a subdued smile.

"Sounds perfect." We started on the constricted dirt path that encircled a barbed wire fence enclosure swarming with deer. Maya shot me an incredulous glance that I reflected back to her. The scene was cinematic.

"Maya, what do you plan to do after your year abroad?" She hid her face beneath the veil of blonde and focused her gaze downward. I had evidently broached the wrong subject. We walked in silence, and the network of roots beneath our soles made a crunching noise as though we were inflicting pain on the arborizing nature.

"I'm sorry. It's just a hard question for me to answer. My life is not nearly as planned out as yours is. You have Harvard ahead of you. I just don't know what my future looks like." Maya rotated her head and combed her hair back so we could exchange glances. She looked so innocent, but her words echoed with a pain that I could not identify.

"Well, what do you want?" I prodded, moving further into the taboo topic. I looked away as I spoke, not wanting to impose on Maya's field of view. Three deer skipped about in a spirited loop. Part of me wanted to join them, to move myself with a modicum of their grace. But I would never prance with such poise. I would learn to live on high alert that movement of that sort would come at the cost of a patellar, ankle, or hip dislocation. I would soon be relegated to an observer of nature if I wanted to remain whole. Maya's voice sliced through my ruminations.

"I honestly don't know what I want. I've not really had the time to think about that or even to see myself as something independent from my mother's shadow." She swatted at the start of a tear with her fingers as if it were a disagreeable insect. I slanted my gaze toward her, and she dodged it.

"I'm sorry. I didn't mean to pry or to push something out of you that you don't want to discuss. It's none of my business if you don't want it to be. And, yes, it's true. I am Harvard-bound, but my life is not as tied over with a holiday bow as it may seem. I have been through a lot of my own hardship, and it still haunts me. I did not walk for months and had to rely on my Mom to put on my own underpants or to use the restroom at age seventeen. I even wanted to kill myself. I am intimate with pain. I only lay all of that out because I want you to know you can talk to me. I am not an Ivy League poster child. I sum up to much more than that." Maya gaped at me without blinking, and her eyes welled up. I did not know if her tears were on my behalf or on her own. She positioned her fingers on my far shoulder. Her delicate touch, even though my t-shirt and jacket, prompted me to sob. I also failed to discern the object of my own tears and whether they constituted a parting gesture to a pain past or a mournful welcome to what was yet to come. We stopped in our tracks, and Maya bound her slight arms around my neck.

"Thanks for sharing that. To be totally open, the reason why I've not dedicated much forethought to what I want from life is not because I don't care. I wouldn't be in Oxford if that were the case. It's because my Mom is a drug addict. My father died of an overdose before I was born, and I basically grew up taking care of my mother. I went from high school to a narcotics anonymous meeting with her every day, but she still abused drugs every night after I would fall asleep. I would find her limp and drugged body on the kitchen floor most mornings. Sometimes it felt like God gave me to my mother so I could keep her alive. She OD'ed on heroin two months ago, and that's when I decided to join the

abroad program." Maya looked at me with wide wet eyes. I did not really know how to respond to her flavor of sorrow.

"Yeah, I've been through the ringer. Mom even caused me to miss the SATs three times because I had to drive her to the emergency room. I finally took them pretty close to the wire and got admitted to Brown, but I don't want to go. How can you think about sitting in a classroom all day jamming a bunch of information into your brain when you know it's not going to fix you or the people you are supposed to care about?" Maya's voice became filled with indignant fervor, and I could detect that it was difficult for her to speak. The words became stuck in her throat like adhesive. In the distance, the deer were still dancing.

"Sometimes, learning is the only thing you can do. Sometimes, you can't fix anyone or even yourself. There is a beauty in knowledge, in figuring things out, and in solving problems that can be solved. It may seem silly given where you're coming from, but it's the only way to get beyond it, to make something of yourself that you can't even imagine right here and now." Maya's expression relaxed, and the creases on her face softened. She sheepishly nodded as though she consented with my response, or at least understood that I understood her. She gave me a naïve expression, but I knew that she was hardly immature. She had been a parent before she had even been a teenager. She drew my hand from my jacket pocket and held it. My message would articulate itself again and again as my disease took my life down an unexpected path. I would soon encounter the limits of my fragility. In the uncertain darkness of my illness, I would do what my fractured spine taught me to excel at. I would solve the problems intended to be solved.

At the outset of September, I emailed Elliott, a Ramaz alumnus who resided in London, and he invited me to his home in Hampstead Garden Suburb for the Jewish New Year. In light of my Jewless setup in Oxford, I accepted Elliott's offer.

Elliott transported me from the London station to his white-shingled triplex on Linden Lea Street. He was a gentle strapping man with a thin sheet of dark hair. As I secured the passenger door and Elliott cranked his car into gear, he flashed me a convivial smile that told me I was no imposition, and even that I was wanted in his home. When we arrived, a stunning woman stood on the other side of an open door. Melissa fashioned a black pencil skirt, a white lace blouse that billowed over her thin middle, and pointed black vertiginous heels. Beside Elliott's wife, Mia, Olivia, and Charlie, ages six, four, and two respectively, were arranged in descending height beginning at Melissa's waist. All three petite girls were in shipshape for the impending holiday.

"Elly, welcome! Now girls, bid Elly hello." As I stepped inside, Melissa reached her slender arms around my shoulders, and her daughters each offered me a timid wave.

The oval mahogany dining room table was arrayed with platters featuring chicken, steamed vegetables, brisket, and rice. As the seven of us filled our stomachs, I witnessed mainstream family life unfold before me. Elliott discussed his workday with Melissa. Mia chimed in and offered an unprompted recap of a book read aloud to her in school. Olivia, envious of Mia's limelight but at a loss for words, unleashed a wail that Charlie echoed. I was dumbfounded by this idyllically conventional family drama.

This was as near as I would get to any ordinary family. But as I assumed the velvet seat cushion between Melissa and Mia, I deluded myself and presumed that I would one day begin a family of my own. In about a year's time, however, my fanciful vision of my future would expire into a mere hallucination. I would begin to accept that I could no longer reach for a normative life. I would begin to wrap my head around the disconsolate reality that giving birth to a child could come at the expense of my own life. Even if I survived, my offspring would likely inherit my EDS. I would not know how to live if I bequeathed someone I adored unconditionally with the same life sentence sown into my genome. I am still mourning the little Ellys that will never be and the future I wrongfully concluded was indisputably mine. That is a loss that I expect will die with me. I am not sure how to go about burying something so life-size, and so life-defining. I did, however, contemplate during my healthier intervals, the potential of a surrogate and having the opportunity to be a mother even if EDS did not permit me to give birth to my own offspring.

That evening, after the girls, Elliott, and Melissa fell asleep and quietness came over my guest room, I released my MacBook from my overnight bag. This sacrilegious act seemed to carry far more weight under a religious roof than it did in the absolute irreverence of my Oxford flat. I arched over the keyboard for five hours as I composed an essay for my philosophy tutorial on Ludwig Wittgenstein's stance on mathematical proofs and their derivation. At a quarter after three in the morning, my draft was complete.

Sometime around 7 a.m., Charlie released a high-pitched whine, and I heard Melissa's subtle footsteps gallop upstairs to the nursery. After getting dressed, I tiptoed down the stairs in case

Mia and Olivia were still sleeping. Over breakfast, I scanned my assigned philosophy reading. Two hours later, Melissa notified me that she and the girls were ready to attend synagogue for the New Year service.

The sanctuary was packed to capacity with throngs of men in ceremonial white robes and women in stiletto heels and designer attire. I felt out of place as I stood mute beside Melissa, as if I were observing a foreign people with whom I did not personally identify. In addition to a twinge of homesickness, a biting repugnance to this God in whom I was inculcated to place my faith took hold of me. This ostensibly ubiquitous being had deserted me again and again through spinal surgeries, ovarian torsion, and a blindness of my own making. I neither longed to supplicate toward nor appease this almighty with scripted words. I craved to revisit Wittgenstein's text, to dissect veracity that could not abandon me through thick or thin. I detained the sealed leather book on my lap and fingered solutions to triple integrals I conjured on its covering.

One evening in October, as I underlined the text of *Hamlet* and penned my own interpretations in the margins, Alice sighed and examined me. Her long, dark hair was pinned at the back of her head, and she was seated on the kitchen chair with her lean legs folded into her chest.

"Everything alright, Alice?" I queried, wholly unversed in the language of her exhales. "It'll be fine. T.S. Eliot is just a bit over my head. I can't figure out the strained romance between the young man carbuncular and the typist. Why does Eliot paint their bond as one cloaked over with indifference? I'm sorry. I don't mean to

be a bother if you're in the middle of your own schoolwork." Alice gave me an imploring look.

"It's no bother. Trust me, Shakespeare can wait. These pages are not going anywhere." I grinned and swiped *The Waste Land* off the tabletop and raised the passage before my eyes to refresh my memory. I perused the scene to which Alice alluded.

Though I might be a scientist, dissecting and discussing Eliot excites me. His work, so densely packed with historical and literary references, seems to demand that the reader assume an active role to uncover the layers of nuance and meaning. For this reason, when I engage with Eliot's text, I feel as if I am embarking on a mental archaeological dig. I enjoy the endless excavating, probing, and connecting involved in understanding Eliot's allusions. Revisiting *The Waste Land* or *Four Quartets* is a study in persistence and patience, a lesson that life would require I learn over and again.

On November 1, I hobbled into bed at midnight after revising an essay on *Coriolanus* for the morning's Shakespeare lesson. An autumnal gust filtered through a slit in the window behind my pillow. As I dismounted my bed to retrieve a supplementary blanket from my closet, excruciating pain rippled through my abdomen. I collapsed onto the hardwood floor into a fetal position and clutched my stomach. Beads of sweat washed down my back. My pain rigs the thermostat of the outside world and kicks my dysautonomia into full force. My insides grumbled. The next thing I knew, I was bolting to the lavatory. I retched bile-streaked fluid onto the white tiles until I felt hollow and numb, save for a persistent throbbing on the left side of my stomach. I mustered a shallow breath and pain zinged up and down my chest as though

my nerves were playing a ruthless game of phone tag charged with an electricity reminiscent of my CRPS. My heart pulsated, and a woozy lightness settled over my cranium, a symptom set associated with EDS that I would soon identify as postural orthostatic tachycardia.

I caressed my fingertips beneath my clammy tank until I landed upon what felt like a shard of Dr. Stein's fractured shell. I bunched my undershirt in my fists and bowed my head. I released a thundering scream. For the first time, I was genuinely petrified of my own anatomy. My left lower rib was rotated and jutted out of me like a blade. Surrounding the dislocation, my skin was dyed a blackberry shade of red. I felt as though I had made my way, against my volition, into someone else's nightmare. I failed to grasp the harrowing truth that my body had outsmarted me, that it had triumphed in a way that no math problem could, that it could turn on me without warning and render me so defenseless.

Alice floated through the door with soundless footsteps and ran a damp cloth across my forehead. She gathered me, like a wounded animal, so my back hinged against a wall. Tears streamed out of me, and I raised my shirt. Without flinching or uttering a word, she layered a sympathetic palm over the gruesome site and rubbed it gently. My rib cracked back into its biologically appropriate position. Blood stained the lower half of my tank. I felt like something that forgot how to be whole. Alice strung an arm about my neck and craned me toward her until my head settled onto her shoulder. At three in the morning, I awoke to horrific abdominal pain. Alice's tender hand lingered

on my shoulder, and her arms caught me before I could collide with the tiles below.

After I came to, Alice supplied me with her mobile, and I plugged in my mother's number. I was winded, and a rancid taste dominated my palate. Alice witnessed me gag and unearthed a fresh bottle of Listerine from the base of the sink.

"Mom, I need you," I choked on my tears.

"El, what's going on? You're scaring me," my mother reacted. My four blubbering words had rendered my mother defeated. Her voice dropped in volume as she spoke, and her words sounded forced as though she wanted to check out of this scenario. But signing my insurance bills and leaving me to put my pieces back into a semblance of order was not my mother's modus operandi. My EDS was *our* disease, something we carried in the small space between our joined palms. Alice clutched at her phone and informed my mother of my predicament.

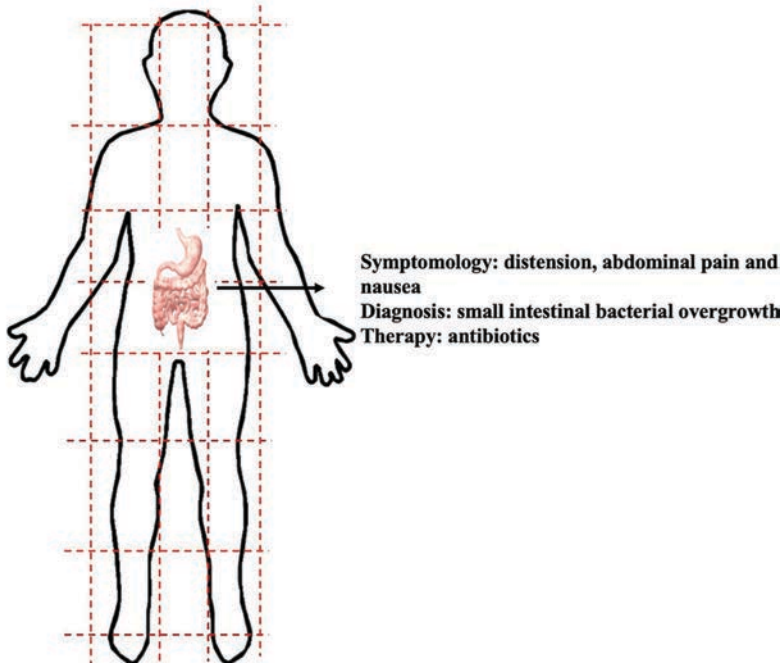
"Don't worry, Bel. I'm coming. I'll be there ASAP," my mother's voice bellowed. My Oxford coursework came to a cruel standstill that echoed my compulsory flight from Carmel and from Billard. I was exiled from my intellectual paradise, and my unglued being steered me down a volatile path that would commandeer the remainder of my life.

14
Scientist and specimen

Pain, only wholly felt in an ineffable glance, mocks language, our human attempt to veil the inexplicable in an overcoat of comprehension, or miscomprehension.

Moments of emotion loom like flies refusing the capture of human hands, fleeing into the night sky far above our conscious heads.

My Body Through The Lens of Reductionist, Silo- Based Medicine



I pressed my thighs into my chest and took hold of my shins. To my left, my mother assumed the physician's stool. For her classy standards, she was anything but put together. Her black skinny jeans displayed a splash of coffee creamer at the thigh, and her lilac cashmere top was torn at the elbow. The creases at the edges of her eyes seemed harsher and more furrowed into her than I had remembered.

She anchored an index finger and thumb at the skin between her eyebrows; her hand functioned as a visor to block out the tell of my agony. I lacerated my lower lip with my front teeth. My disheveled hair felt like the mane of a derelict wild horse. A masculine hand wrung back the curtain that stood between my pain and the rest of the universe.

"Hello, Elly. Tell me about what's going on with your stomach. From your chart and discussions with other experts in my field, I gather that you are in severe agony." The gastrointestinal expert smiled, revealing only his upper row of teeth.

"I'm in pretty horrific pain and can't stop vomiting for more than an hour or so. Also, my left lower rib is persistently dislocating, and I'm massively distended." I sprang off the examination table and onto my Converse as I straddled my arms around my stomach. Dr. Sacks was the ninth gastrointestinal authority my mother and I had gone to over the week since leaving Oxford. I was well aware that my words could not do justice to the outrageous visual on my biological display. I shimmied my black top toward the bottom of my breasts. The practiced physician gawped and pursed his lips in contemplation and incredulity. I was something out of science fiction. He stole a glance at my mother, who

evaded his eyes, and then returned to my exposed abdomen. My ribs were splayed a finger's width apart from each other. Blood was caked onto my left side from my rib's popping out of and into the socket during my vomiting episodes. My stomach ballooned out of me with the forcefulness of someone impregnated with twins and in her second trimester.

"Based on Elly's clinical presentation and intolerance to food, I am of the belief that she has small intestinal bacterial overgrowth, otherwise known as SIBO. This condition occurs when bacteria that typically colonize other parts of the gut grow in the small intestine. The hydrogen-methane breath test used to validate my assumption will make Elly queasy, and I am confident of my diagnosis without it. Elly's deleterious bacteria are proliferating in her intestines at an alarming rate. I am going to prescribe the antibiotics Augmentin and Xifaxan." Dr. Sacks issued his medical assessment as if he were lecturing during Grand Rounds or discussing me with a colleague in hospital corridors. I had evidently warded him off with my shocking exterior. He no longer spoke to me but around me as he focused on something riveting on his monitor.

"These antibiotics are each to be taken t.i.d. and should be started immediately." Dr. Sacks scribbled something down and hastily ripped at the perforations on his notepad. He slapped the prescriptions onto the countertop before he excused himself without a farewell or even a hurried wave.

The smug doctor simply threw antibiotics at my problem. His visit with me was a swift 15 minutes, the majority of which he passed with his eyes fixed on his computer screen. He was

somehow above palpating my stomach and methodically reaching a diagnosis. Trying an antibiotic regimen on for size is hardly a benign approach. Microorganisms outnumber human cells by a staggering ratio of ten to one. Sure, antibiotics wipe out bacterial populations. But in doing so, they also modify ninety percent of what it means to be a human. These drugs are not merely atomic bombs aimed at depositions of objectionable bacteria. They can indelibly amend our thought processes and demeanor for the worse due to the vagal nerve shaft linking the gut and the brain.

The gut–brain axis has been implicated in many diseases, including autism, depression, irritable bowel syndrome, and EDS by enabling peripheral disturbances in the enteric nervous system (ENS) to impair mitochondrial and glial cell function (Zhu et al. 2017; Ballard & Towarnicki 2020). The ENS, a subdivision of the autonomic nervous system, is responsible for gastrointestinal function; it is capable of detecting the physiological state of the gut and integrating the former information to initiate gut movement. It does so autonomously without the governance of the sympathetic or parasympathetic nervous systems and has thus been dubbed the second brain. A diverse community of enteric microbiota, with genetic repertoires that outnumber those of their host by a factor of 150, colonize this region immediately following birth and the bacterial population fluctuates throughout life in response to shifts in internal and external surroundings. Bidirectional crosstalk between the gut and the brain occurs via the vagal nerve, and bacteria are capable of modulating this "dialogue" by innervating sensory neurons in the ENS.

Despite my distended abdomen and the periodic vomiting, I was dogged when it came to how I would, or, more aptly, how I would not, fill my downtime between my medical appointments. When she was not escorting me to hospital buildings, my mother resumed her career in radiology. I refused to retreat into the Elly-shaped hole in my parents' bed that I occupied years prior. I emailed Dr. Fahey, the principal investigator of Weill Cornell's endocrine oncology laboratory, and explained my extenuating circumstances. Almost immediately, he replied to my message and proposed that I intern in his lab for the duration of the year. Brandon, a technician in the lab, requested that I conduct a statistical analysis of Dr. Fahey's surgical cases pertinent to the BRAF-V600E mutation, a substitution in the *BRAF* gene that interferes with the fidelity of an enzyme involved in cellular development. This missense mutation in exon 15 is commonly found in the setting of melanoma and colorectal cancer and promotes cancer cell proliferation and metastasis.

I peered into my MacBook with my knees tucked firmly underneath a relaxed blouse, which intentionally camouflaged my swollen stomach. I perused PubMed for the mutation of interest. As I scrolled through my browser, I bit my tongue to halt the vomit that was threatening to launch out of me with the force of a projectile. Brandon touched my shoulder, and I spun around in my chair. I eyed my mentor with an uneasy mixture of delight and nausea.

"You interested in following me to the operating room? Dr. Fahey requested that I head down there so he can hand me a pancreatic nodule he wants me to freeze for sectioning. I have an extra pair of scrubs that you can suit up in over your clothes. It's up to you. Just thought it might be a needed diversion from all of

your article reading." I responded with a coy headshake. Brandon handed me teal scrubs. We headed for the operating room in our matching attire.

"So, Elly, have you been into an O.R. before?" His blue eyes refracted the blinding light that scattered the vestibule from above. I felt my face crease into an exaggerated smile I could not suppress.

"Yes, I am an unfortunate expert in that arena. In my eighteen years, I've had three spinal operations and an ovarian tumor removed. I've bopped around to essentially every hospital in New York City. I've even gone so far as to venture to a borough or two. But that aside, I've never been on the non-patient side of an O.R. transaction." Brandon beamed and drew two pairs of purple nylon gloves from his pants pocket. He extended a set to me. I was euphoric. My heart skipped out of its measured beat as I came to terms with the sublime role reversal ensuing within. I was the scientist, not the anesthetized specimen. In reality, however, I was both. Unbeknownst to me, I was at the mercy of EDS and its paranormal manual. I scoured the literature pertinent to *BRAF* on chromosome seven, a single chromosome away from *TNXB*, a locus that silently demanded my resolve to establish who I was and set the limits that would soon fence me in. I was gloved and equipped to collect a tumor, but I failed to realize that a horde of unruly cells was multiplying without regulation on my left ovary. I could not have anticipated that the scientist in me would come to a stalemate against the specimen, and my tumor would be next in line for bagging and freezing.

In early December, my O.R. exploits with Brandon dissolved into wistful reveries. I existed in a perennially doubled-over state and

seized my stomach in my hands as though I could shield myself externally from the pain surging within. For an entire week, I lived in a single pair of tattered pajamas that were accruing an expired fragrance. My blond curls aggregated into dense knots at the base of my skull that I had to relegate to my mental backburner. Pain leeches its way into your life and transforms a mundane morning routine composed of a quick shower and hair brushing into a most formidable task. I could not muster enough grit to accomplish such a feat on a daily, or even on a weekly, basis. My geometry became severe. The dulled angles of my chin, elbows, hips, and knees grew harshly prominent from my dwindling food intake and my hourly vomiting regimen.

As I awoke one morning to sweat-soaked bedsheets, I felt an internal churning like a doorknob being turned in my left lower quadrant. The sensation resembled my ovarian torsion four years earlier. Pain is wired into the brain like a childhood lullaby. It does not permit you to forget its acuteness. It lodges quiescently in your pain fibers and upstream neurons like a latent virus until you experience its memory. Only then will your cells fire until they reel in your complete focus and make you question the ground on which you stand. Are you in the present or caught in a cruel reenactment of pain past? I braced myself and retched onto my carpet. The clock on my bedside counter flashed 7:46 a.m. My mother was not due to depart for her office for another fourteen minutes.

"Mom! I need you in my room," I squealed at the top of my vocal range. Gastric acid singed my throat, and my voice sounded gravelly. I maneuvered a fistful of hair to the backside of my head. I recoiled at my own touch. I felt like something used, like

something several notches below human, and like someone I could not recognize as the Elly who deciphered Shakespeare and Descartes. My mother's kitten heels clattered swiftly down the hallway to my bedroom.

"Babe, what's going on? This stomach issue of yours is really starting to scare me. I'm not going into work today. We need to get you some relief." My mother flicked off her heels and darted, barefoot, into my bathroom. I heard water run out of the faucet for a few brief seconds.

My mother returned to my side armed with a cold cloth that she wiped over my mouth. She knelt on the sullied floor and positioned her forearms beside my pillow.

"Love, we are going to Dr. Pound this morning. I'm going to reserve the soonest opening she has. You, or rather we, cannot endure this pain any longer." My mother laid a tender hand on my chest.

Dr. Pound was my primary care physician who failed to live up to her title. By some stroke of misfortune, she was the ringleader of my medical team throughout my second decade. As my mother and I entered Dr. Pound's office building that morning, we cruised through the waiting room bookshelves for an entertaining novel to read aloud until our appointment time.

Every title that crammed the extensive shelves began with the word anorexia or bulimia. Especially on the Upper East Side, many physicians presume that all teenage females are too vain to harbor any problems that fall beyond the purview of caloric restriction. I gathered myself into a chair and assembled into what had become my characteristic rocking posture. My mother sat beside me, bookless and speechless, until my name was called.

"Elly, I'm ready for you," Dr. Pound hollered. I craned forward at my hips and trolled to Dr. Pound's office with my mother.

"Now, let's see that tummy of yours," Dr. Pound exclaimed in condescension. As I raised my top, Dr. Pound placed a giant cold palm on my belly. She maneuvered to the cabinet beside the examination table and extracted an alcohol wipe that she delicately swept across the blood stain overlying my left lower rib.

"Elly, you are distended to a disconcerting extent." Dr. Pound shook her head from side to side as though I had committed a misdemeanor. Her reaction was a far cry from insight.

"What happened to your rib, Elly? Why are you bleeding?" She looked at me attentively. I felt sickness creep up my throat, and I jammed my tongue against the inside of my front teeth to occlude its passage.

"My rib has been coming out whenever I vomit. But I can snap it back into place rather easily." Dr. Pound searched my face in disbelief and pivoted in my mother's direction.

"Karin, Elly needs more help than her ten gastrointestinal doctors in New York are clearly offering. I suggest you take her to the mecca of all things medical, the Mayo Clinic." A black tear sprang loose from my mother's eye as her distress swirled with her deftly applied mascara. My eyes bounced from my mother to Dr. Pound.

Dr. Pound was witness to my unstable knees, my spinal fractures, and now to my dislocated rib but simply bestowed me with an impassive expression and an automatic grin. It was her task to put my pieces together into some coherent medical jargon, to take stock of my threadbare connective tissue, and to hazard me of the three capital letters, EDS, that would make and break who I was becoming. It was her duty to be my body's oracle, not

to be a visionless middlewoman who shuttled me and mother across Manhattan to specialists. EDS is readily disregarded by doctors who, like Dr. Pound, are incapable of spotting the rare zebras among the anorexics that dominate the Upper East Side. It was because of her oversight that I went undiagnosed until I was twenty. I am not sure who I would be today if Dr. Pound had presented me with a five- or ten-year headstart to live with the knowledge of my disease, to grow with it rather than under its anonymous shadow, to delineate my limitations before my dreams took root beyond them, and to defend myself from the emotional pain that would soon take hold of me as I mourned the future I thought I possessed. Doctors are human, but their white coats also equip them with an overdose of trust. I invested too much of myself in Dr. Pound's incompetent care and would pay the alarming cost of her lapse in judgment.

The following morning, my father scooped me up from broken slumber on my bathroom tiles. Without uttering a word, my father maneuvered my frail legs into fresh black sweats.

Flanked by my parents, I hobbled through our lobby and into the backseat of my father's car. The notion that I had stymied the gamut of New York City's medical system struck me as outrageous. The majority of people flock to Manhattan, not away from it, for health-care. As I would soon fathom, however, I was a dreadfully exotic breed of human who operated in accordance with an arcane rubric that extended beyond the constraints of commonplace logic.

Once I was curled up into my smallest dimensions on the leather seat, I shut out the dark ribbon of highway and oscillated in and out of consciousness.

"Kar—" my father began before his voice trailed off. I inferred that my mother suggestively presented my father with a mute cue, like an inert upright palm.

"For goodness sake, Joel, Elly is sleeping. Keep your voice down. I overheard her vomiting all night. She must be exhausted," my mother stated in a muffled cadence tinged with irascibility.

"I'm driving, Kar. It's obviously not an opportune time for me to check in on El in the rearview mirror. I really don't need your anger right now," my father whispered. He sounded livid, and I imagined exasperation knitting itself into the stubble on his cheeks.

"I get it, Joel. I'm just as overcome by this whole scenario and by the pain with which Elly has to contend. I feel like I'm reliving the harrowing experience of Children's Specialized Hospital, only now Elly's stomach is swollen instead of her left foot. But this time, Joel, I'm not leaving our precious girl alone." I sensed tears aggregate in my own eyes as my mother vented her analogy of the course that lay ahead.

"How long do you anticipate being there?" I cracked my eyelids open and beheld my mother's noncommittal shrug.

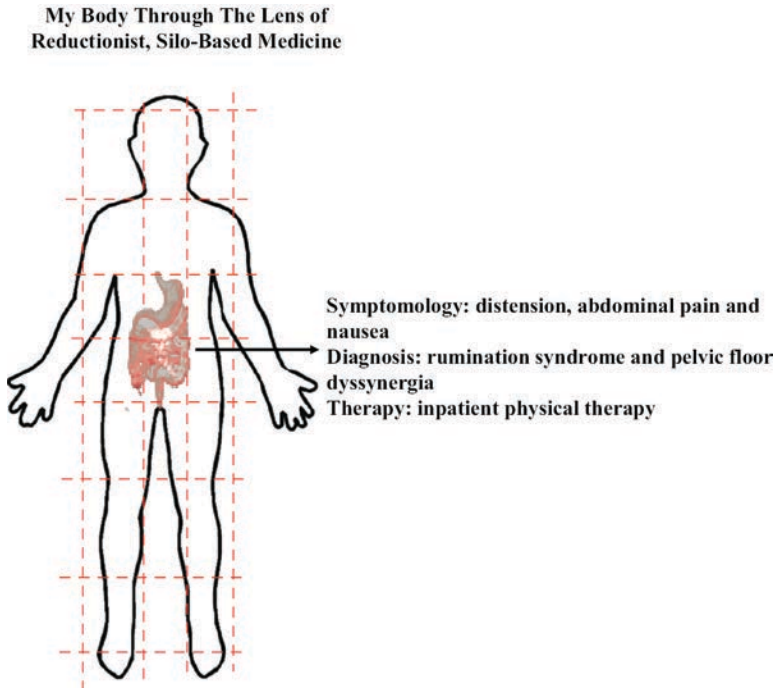
"Joel, that's not a question I can answer. You know that. I packed mine and Elly's suitcases with sufficient provisions for a month."

"Just get my Elaine better. I need that girl of ours back in her life." My father's voice cut in and out like a malfunctioning record player. He emitted an inconsolable weep that hit me as distressingly out of step with his Southern composure and gentility.

15
The monstrous maze of Mayo

I am done with shadows, with games that sustain unhealthy masquerades.

I want to be real, like this poem, to begin to be understood by eyes that easily misunderstand.



As we pulled into the lot at Mayo Clinic in Rochester, Minnesota, I let my eyes wash over what would soon become my distinctively retrograde neighborhood. It was chockfull of decomposing limestone, dingy taverns, fast food eateries, and rickety storefronts. My father hurled our luggage from the trunk onto a curb. As I descended from the car's backseat, an uneasy lightness seemed to blanket my brain. I felt blood drain from my cheeks and inundate my lower extremities. My heartbeat went into overdrive. Instead of initiating a cascade of endogenous opioids in response to my pain, my body revved up the faulty gears of my autonomic nervous system.

The Mayo Clinic was a mammoth complex with an aesthetic footprint of glass and stone dominating a roughly 210-acre campus. The central edifice was patterned along its stature with silver trimming and glass windows that forged a façade of vertical hills and valleys, like a stationary ocean wave.

After we drifted through the building's roundabout, a jolting pain rattled through me.

Instinctively, I folded myself over my enlarged abdomen. My father mournfully gathered me into his arms, and I offset my own weight into him. I felt too substantial for myself, like I was enshrouded in one of the leaden aprons X-ray technicians drape over you. My parents navigated to the motility wing, and my father sat in an enormous upholstered armchair while he held steadfast to my ailing body. The vast open space swarmed with wheelchairs, walkers, oxygen tanks, and wearied patients of all ages, shapes, and countries of origin. I experienced an unexpected kinship with this shadowy throng of wounded victims

and mused over their uniquely abominable circumstances that landed each of them into the present space.

A nurse escorted me and my parents into a modest office with pale yellow walls, an examination table, three armless chairs, and a workstation. Dr. Cane, the motility expert reaching the end of middle age, was seated on a stool. He exhibited a droll grin. A printed article entitled "Rumination Syndrome" lingered on the doctor's desktop. In a barely discernible font directly following the title, I could make out Dr. Cane's name.

"Elaine, I'm just reviewing your radiographic imaging and your charts from New York.

Can you explain your persistent vomiting to me?" He turned in my direction.

"I have been experiencing a stirring pain in my gut approximately on the hour for the last few weeks, and I typically throw up when the pain comes on. I've also been struggling to keep my food down." My mother situated an upturned hand onto my kneecap. I slid my fingers into the spaces between hers.

"Dr. Cane, Elly's pain is markedly increasing by the day. She was thriving in Oxford until this pain started. Then, when we brought her home to investigate the matter, she was well enough to participate in lab research, and currently, she can hardly get out of bed in the morning to shower and dress herself. In fact, nine mornings out of ten, she spends the night on the bathroom floor because of the constant vomiting. Her stomach is so distended that her skin has begun to tear, and her rib is dislocating often." My mother wrapped up her summary of the last four months

and freed her hand from my grip to manually sublimate the beginnings of a cry.

"Just take a look at Elly's stomach," my father chimed in. "Her stomach is usually flat as a board, but she has been living with this tummy for the last few months," he went on and lobbed a finger in the direction of my hunched over middle. "Elly, show the doctor." I assembled myself into something upright and inched my top up with the practiced flair of a circus animal.

"I know exactly what is going on with Elly. In my opinion, she has a typical case of Rumination Syndrome combined with pelvic floor dyssynergia. I have yet to see a case quite like this. Elly needs pelvic floor retraining. You will be here for three months." The doctor conceitedly patted the article before him as he issued his edict. Dr. Cane seemed rather pleased that he could wrap me into his scientific findings and use me as a pawn to substantiate an empirical theory in the works. His examination table was but an outmoded relic.

Dr. Cane, like Dr. Sacks, did not percuss a hand against my abdomen to estimate its give.

He did not rest the chilly metal of his stethoscope over my intestines to hear what they had to say. He spun a diagnosis out of thin air that was biased toward him rather than toward his patient. He perceived me as a statistical outlier, an intriguing bullet point that he would denote on the clinical plot featured in his article. He looked right over me and around me to come to the conclusion he probably homed in on before I even entered his private office. He unduly prescribed three months of grueling and dehumanizing pelvic floor training. This world-renowned

motility authority not only overlooked my EDS, but he did not spare a moment to see me outside of the Rumination Syndrome box in which he confined me. He swiped the last shard of my dignity in exchange for the publication of his manuscript and never looked back to offer his condolences. It is only because of my unfaltering mother that I would not take my own life at the close of the month when, because of Dr. Cane's calculated gaffe, I would feel like something disposable and hollow.

We departed the Motility Clinic that evening and strolled in silence to our rooms at the Marriott. When we arrived, my father knelt to deposit a film of kisses on my forehead. I observed his reluctant strides toward his car, which he drove back to New York that night to resume his work. My mother's polished face gave way to a crestfallen watercolor of gray eyeshadow and mascara. She bound her arms around my neck and brought me into her until my distended stomach confronted her middle. A parabola of space formed between our breasts, a subtle distance between patient and physician, a nuanced rift between daughter and mother, an indistinguishable kink in an otherwise unbreakable bond. My mother was unswervingly beside me, but she only experienced my pain by proxy through a once-removed lens.

The next morning, my mother and I ventured to Mayo Clinic's physical therapy department. We settled quietly into leather armchairs in the waiting area pending the pronouncement of my name. Illness hardly sets the stage for trivial small talk or for a dialogue involving normal mundane life from which it extricates you. Illness is recursive, authorizing you to exclusively speak of itself, to attach words, numbers, and facial expressions to your agony and to, thereby, endow it with a life of its own. In harping

on your malady, you allocate it more of yourself. Silence is your only viable option.

"Elaine Katz," a slender blonde in lime green scrubs broadcast. As I trailed the therapist to a private chamber, my leg muscles felt spasmodic and uncoordinated under my sweats.

"I'm Lucene, and will serve as your pelvic floor therapist for the next few weeks. We will begin with the basics and build up over the course of the program. This toilet in front of me," Lucene articulated as she gestured toward the beige plastic seat, "will be your practice toilet for the duration of our work. Now, get yourself changed into the hospital gown on the countertop." Lucene studied me out of her wide blue eyes. I undressed and hung the shapeless gown over my atrophied skeleton.

"Alright, Elaine. Let's have you take a seat on the toilet. You removed your underwear, correct?" I shook my head and tugged at the material covering my privates. I marshaled myself onto the plastic throne, absolutely uncertain of what was to follow. Lucene jostled through what looked like a plastic boxful of children's blocks and fished out a red pyramid. The hairs on my forearms stood vertically, and a foreboding fear came over me. I grew numb from all of the feeling.

"What's that for?" I audaciously probed.

"I am going to insert the tip of this block into your rectum. I need you to clench it for five seconds and then try to push it out of you. It will help you to learn how to operate your pelvic floor muscles." I inspected Lucene with skepticism and clenched my jaw.

"Are you serious? That sounds like a rather extreme measure." Lucene handed me a deadpan stare, brushed off my concerns, and jammed the block up me. I sensed its sharp apex scrape my insides. I felt violated. I felt raped by a ruthless fist and a child's toy. A surging cry escaped me as I heeded Lucene's directives.

I bolted into my mother's arms beside the reception station and she nuzzled my woeful face into her chest. I lingered against her, moistening her unkempt hair with my tears, conveying my distress through a wordless howl. We wandered in sweatpants and parkas, like nomads without a refuge, to a smoothie bar three miles north of Mayo Clinic. The quiet seemed to expand like a prechewed wad of gum to which we each took hold, testing the limits of its elasticity. My mother rummaged through her shoulder bag for *My Beloved World*, a memoir by Sonia Sotomayor, the first Hispanic Justice appointed to the Supreme Court. The book was assigned by Harvard to its entering freshman class as a tribute to the opportunities that can be borne out of hardship, out of coping with an alcoholic father and diabetes. As my mother curled back the cover and commenced reading, I saw a glint of my future peek out from the darkness of my present. She tasted Sotomayor's words in her own mouth and, in doing so, my mother intimated that I was still whole and that I would overcome Mayo with the Elly spring back I had refined over the years.

Our days were structured with pelvic floor rehabilitation for two hours in the morning and reading in the afternoon as we roamed Rochester's sidewalks. My swollen belly persisted. My weight dwindled by the day, and I became the sheared version of myself that shuffled through Children's Specialized Hospital.

There, I was all lines and austere corners. My womanhood vanished. My breasts retreated and my curves dissolved. Save for my pseudo-pregnancy, I reverted to something infantile. Just as I could not bring myself to frame my CRPS in any vernacular, I refused to brief my mother on the repugnant happenings that transpired in therapy. At age eighteen, or at any age for that matter, how do you go about broaching the topic of an outsider funneling blocks and water balloons up your rectum? How do you contain such remarkably mortifying pain using an unremarkable alphabet? How can you charge language to obtain such bottomless holding power?

One evening, I knelt on the bathroom floor and leveraged myself forward. I ping-ponged between puking and rinsing with Listerine until I felt faint. My head crashed against the lip of the bathtub. The next thing I knew, my mother was sprawled on the bathroom floor beside me. She cupped a hand over my cheek. I crooked my head to meet her eyes.

"Bel, your agony is really worrying me. Wow, babe, you're so pale. Let me get you in some clean clothes. I want to take you to see a hematologist this morning." I heard my mother pry open a dresser drawer. She motioned my limbs into fresh pants and situated me on the mattress before she readied herself for the day.

Before my therapy that morning, my mother guided me to the hematology subdivision of the Mayo complex. A nurse chaperoned us down a long corridor to an examination room. Within it, a small, frail woman enveloped in a doctor's coat was seated before a monitor. Dr. Glassner detached her gaze from the screen and darted her eyes from me to my mother as though she were

reading sequential lines in a novel. She drove her front teeth into her bottom lip. The hematologist seemed to be at a loss for words.

"Elaine, welcome. I have reviewed your labs and the imaging you had done in Manhattan. Firstly, your labs are concerning to me. You have a markedly reduced white cell count, severe anemia, and elevated C-reactive protein levels, which means you are experiencing systemic inflammation. In evaluating the MRI scan you had done in New York, I identified a tumor on your left ovary." I beheld Dr. Glassner as if she had pulled a rabbit out of an invisible hat. Her expression was empty, so I angled myself to meet my mother's stare. I watched the color drain from my mother's cheeks.

"Dr. Glassner, I knew about the tumor. Elly's gynecologist in New York did not make much of it. She reported that it was too small to cause any real harm at this point." My mother scrutinized me and mumbled "I'm sorry, El. I didn't want to alarm you" into my ear. An unfamiliar rage filled me as I came to terms with my mother's duplicity.

"What do my abnormal blood levels have to do with this tumor?" I inquired with a breathy eagerness.

"Well, Elaine, the confluence of these two events may be a sort of warning sign. Even if your tumor is small, I have seen teratomas that secrete chemicals that can easily throw off your labs. From your chart, it seems like the pelvic floor regimen you are currently in is not really touching your symptoms, is that right?" Dr. Glassner tossed a handful of her curls behind her head, and I nodded.

"I'm thinking then, Elly, that this tumor should probably come out of you. It's also pressing right onto your sigmoid colon in your lower left quadrant, which may be, in part, causing your

massive distension and vomiting. At the end of the day, all of this is up to both of you. Elly, can I bother you to get gowned so I can examine your abdomen?" The doctor tilted herself toward me. Her face was packed with genuine sympathy that seemed to come in short supply at Mayo Clinic. After I looped the formless gown over my shoulders, I cradled my mother's neck and whispered into her ear "I'm not mad at you, Mom. I understand you were only trying to protect me." Despite Dr. Glassner's addendum to my chart detailing the conceivable role of my tumor in my intestinal mayhem, Dr. Cane never entertained the potential that his premeditated diagnosis was incorrect. He did not even go so far as to follow up with my care.

In our session that morning, Lucene and I did not exchange words or facial expressions.

Our communication was stripped of anything human. It was mechanical, like a scene out of Eliot's *The Waste Land*. I surmised that in Lucene's mind, I had to become a composition of voiceless and emotionless moving parts for her to dispassionately introduce foreign objects into my rectum. I had no syllables left in me. Perhaps they drained from my system with my vomit. Perhaps my muteness was akin to another conversion disorder, another means for me to cut off the circulation between me and my reality.

My smoothie escapades came to an abrupt end that afternoon. In light of my throbbing stomach and my faintness, I was barely capable of navigating the two brief blocks between physical therapy and the Marriott. My mother's forearm became a human crutch. I blended into her like an appendage, like something

unqualified to operate on its own. My left leg buckled beneath my ninety pounds, and my mother's arms formed a safety net into which I let myself fall. She clasped me like a fetus, supporting the crooks of my neck and knees in the insides of her wrists just as she had eighteen years prior.

As I tucked myself between the bedsheets in the evening, I heard my mother through the ajar door between our bedrooms. I flipped through *The Brothers Karamazov* until her voice faded into the silence of the night. My attention flitted between Dostoyevsky and my mother.

"Joel, come say your goodbyes to Elly," my mother blubbered in agitation into her mobile.

"No, I mean it, Joel. I think Elly's on death's door. She is so haggard. She is disappearing. I need you here." I contemplated the possibility that my life would reach its end at Mayo Clinic, that Harvard would never materialize for me, and that I would come to a permanent halt. The notion of not being was too large to fit inside my cranium. I let go of it. This was not the end of Elly.

"I know how much you care. So does Elly. We both know you are working to support our family, not because you don't love Elly as much as I do. I know you wish you could be here with us. I love you." My mother flicked off the light on her bedside counter, and the pathway linking us overflowed with blackness. I listened to her beseech "God, please look after Elly. Do not let my daughter die."

At my mother's behest, we convened with a rheumatologist, Dr. Deluca, the following morning. As I limped and held fast to her arm, my mother rationalized that a systemic disease of some

sort may bring my medical past and present into cohesive clarity. Dr. Deluca's features had a soft, almost cherubic, quality. His nose had an unimposing elegance, and the cobalt of his eyes was rimmed by a thick ring of white.

"Good morning, Elaine. I have comprehensively reviewed your medical history and have a hunch of my own as to what may be going on. Do you mind if I test how your body moves?" The white of the doctor's teeth emerged as he smiled. I shook my head.

"Alright, can you touch your thumbs to the insides of your forearms?" I craned one thumb and then the other with my contralateral hand, and the digit on each hand struck my inner wrist.

"Can you lift your shirt so I can see your spinal scar?" I scaled my tank upward. A cold hand brushed against my lower back. "Just as I thought, Elaine. Your scar is papery and atrophic."

"Now, outstretch your arms with your palms facing upward." The doctor fumbled on his desk for his goniometer and quantified the hyperextension at my elbows. I felt like I was playing a rather boring version of Simon Says. I could not deduce if I was winning or losing. My mother gave me an apprehensive expression and swallowed hard.

"Lift your pants up above your knees, bend forward, and see if you can place your palms against the ground without bending at your knees." I fulfilled Dr. Deluca's order with ease. He shot a look at my mother that I could not quite identify. It seemed to be a clandestine doctors' exchange that was laced with disquieting assent.

"Elaine, the test I just conducted is called Beighton scoring. It is a clinical diagnostic test for Ehlers-Danlos syndrome, a connective

tissue disease that can cause joint and gastrointestinal complications. It does not inform me with regard to the form of the disease you have, which can only be determined using a genetics screen. But, in addition to your skin elasticity, your high palate, and the piezogenic papules on your heels—fat herniations through your fascia—the test does tell me that you have the condition. Your score is an eight out of nine." Dr. Deluca scratched at the outgrowth on his chin and bobbed his eyes from me to my mother.

I huddled my knees into my chest as though I was preparing for a missile to strike.

Unbeknownst to me, the bomb had already detonated. My mother remained motionless. That was my first encounter with the bizarre hyphenated surname that would flip my life inside out and make me who I would become. However, in that office, Dr. Deluca's judgment sat undigested by both me and my mother. The acuteness of my abdomen absorbed our joint focus. Our mental space was fully occupied and could hold no more. The tumor strangling my left ovary drowned out the faint grumbling emanating from my *TNXB* and *KLK* mutations. The phrase "gene edit me, please" cowered in the shadow of my ovarian torsion and queasiness. I let Ehlers and Danlos wash over and out of my head like shampoo beneath the shower.

"But what do we do about this massive distension? How can we fix Elly's motility?" My mother's rapid-fire of questions was hastily snuffed out.

"That tumor on Elly's left ovary needs to come out. I am in full concordance with Dr. Glassner on that front. The best person for that job is the surgeon in New York who removed Elly's first

tumor. I suggest you head home and have the operation as soon as possible. The pelvic floor physical therapy is not in Elly's best interest. In fact, I am of the opinion that she never needed it at all. Her connective tissues may compromise her pelvic floor function, but that tumor is the key factor at play here." Dr. Deluca packed my overstuffed medical file into his fists and exited the office. My mother gathered her arms around my bony figure and rested her head at the juncture of my neck and shoulder. Our game of medical musical chairs was drawing to a finale, if only for now. We would return to New York City to take more of me out of myself, to excise a chunk of my remaining ovary, and to break me more so that I could once again become whole.

At this point in my medical odyssey, after years of battling heterogeneous symptoms, a clear-cut diagnosis should have accompanied a sense of clarity and resolution. However, this novel and permanent label hit me like overheard bits of conversation in a foreign tongue; I heard the doctor's verdict but did not read anything into it. An outsider to my narrative may perceive my response as anticlimactic. How could I fail to find solace in the knowledge I had been seeking for roughly a decade? If EDS was the 'q' to my 'p'—the logic at the crux of my tragic and labyrinthine past, the variable I could not ignore nor name until this moment—why was I not elated to finally call it by its rightful name?

In the wake of the myriad diagnoses that doctors piled onto my symptoms, I had grown wary of the medical system's diagnostic power. Even more so, I had come to terms with the distinction between information and actionable knowledge—the dividing

lines between nouns and verbs; the *why* intrigued me far less than the *how*. I craved to know how to move forward into reality physically intact and with the minimum dose of suffering. Identifying with a new disease (notwithstanding the upside it provides in the setting of insurance agencies and medical providers) was far less satisfying than I had anticipated. Even now, I manage my EDS setbacks as they emerge as if each was its own ailment related only tangentially to the next. Even now, the ability to call my disease by its proper name does little, if anything, to advance my course of treatment. Outside of the context of medical forms and reimbursement, integrating my constellation of setbacks under the EDS umbrella arms me with no further ammunition against my disease. I have learned the hard way that understanding, especially in the setting of an intractable illness, can itself prove to be a dead end. If words are powerless to change or to motivate behavior, what is their purpose?

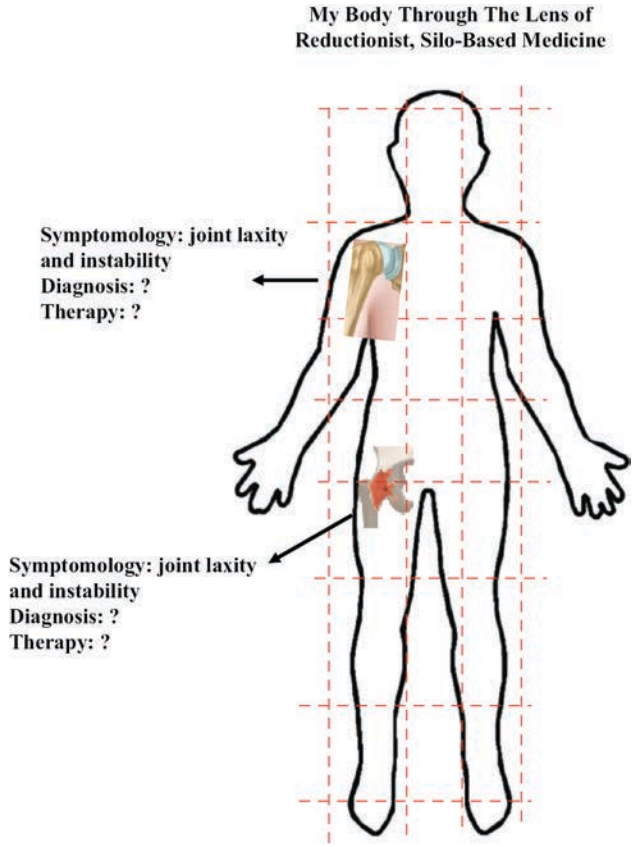
16
Revival in Harvard Yard

I have walked to the pinnacle of the brink of ending and turned around, reverted my soles to fashion a beginning. A start from nothingness, nada, squat.

Like a painter with the daintiest provisions who is forced to exchange canvas for cerebrum.

I had to bear a blackout without any bearing, to quest deeply, sharply within, to find the balance my body abandoned.

"To my Elaine Miriam, May God make you like Sarah, Rebecca, Rachel and Leah. May God bless you and protect you. May God's light shine upon you, and may God be gracious to you. May you feel God's Presence within you always, and may you find peace." My father's voice trembled as he finished, and his tears drizzled onto my hair. He unhurriedly detached a palm poised for the benediction from either side of my scalp. My father squatted so his lips were level with my left ear. "My girl, this is going to be your best chapter yet. You have just come back from the brink of death, but you have never been this alive. Welcome to your marvelous future. It is excited to have you back," my father murmured. I was only in the company of my parents, but my father never turned down the opportunity to deliver a secret. I wore a



high-necked mustard tee featuring a miniature pair of Converse and the slogan "not all who wander are lost." It seemed that my misadventures in New Brunswick and Rochester had incubated my inner existentialist, a persona that I, quite literally, wore on my shirt sleeve. My father surveyed my countenance. Our eyes appeared to partake in a conversation of their own. The memory of Mayo Clinic ambushed our present. I wilted into my father's arms, and he pressed me close.

I felt the sharp corners of my hipbones slice into my father's toned body. He let out a sigh. It had been less than three weeks

since my distention decompressed following the operation, and my weight had only increased by five pounds. Just as my left foot had to relearn how to walk, my intestines had to come back up to speed on unidirectional peristalsis.

Being alive hit me with topspin. A hard and fast breach seemed to form between my vomiting spells at Mayo and this very moment as my parents and I personalized my dorm room in Harvard's Massachusetts Hall. The dormitory's red brick inlaid with evenly spaced white windows oddly reminded me of myself. The building was a warrior. It persevered throughout the Continental militiamen's demolition of its doorknobs and varnish in 1776 and survived a crushing conflagration in 1924. My quarters were only marginally larger than they were in Oxford, but the space around me felt flawlessly fit to my size. My father commenced tidying my clothes on the shelves while my mother strung an impressionist rendering of the Viennese Bridge of Sighs above my oak desk.

"El, is this where you want it?" My mother released the edges of the frame from her grip. "Yeah, mom. It looks pretty even across the top. The thought of completing math problems with the view of an enclosed passage between The New Prison and the Doge's Palace is ironically satisfying. It will restrain me from panicking if I make a mistake. Thanks to the image, my train of thought will be as follows: At least a botched math problem won't land me in prison." My father chuckled, and I shot him an amused grin.

"El, I think we have been in our own penitentiary and have done more than our fair share of time." My mother embraced me as she combed through my curls. Where my father perceived humor,

my mother glimpsed an occasion for lament. I could shuffle through the gamut of paradoxical emotions if I stood between them for a sufficient amount of time.

"Mom, I was only being facetious," I informed her.

My mother extended her slender arms, and I enmeshed myself in her, burying my cheek in the silk of her shirt. A wooziness settled over my shoulders, and I felt a trickle of sweat glide between my shoulder blades. A cry escaped me that I could not contain. I kneaded my face raw with my hands, and my mother clasped me at arm's length by the shoulders.

"Bel of my life, what has come over you?" I squinted the residual tears out of my eyes and sniffed.

"I think the emotional ordeal of Mayo is suddenly hitting me hard. The contrast between here and there is just a lot to take in. It's amazing how far we have come, but I'm not sure what to do with the experience now that it's over." My mother dabbed at my final tear. My jaw shuddered. My mother's eyes moved around my face as though it were something foreign.

"El, why do you have to do anything with it? Just move forward with the strength I know you have. Let's part on a high note." My mother wore a half-smile, like she was unsure about the full-fledged expression. I threaded my fingers into my mother's hand.

"I can walk. I can see. I can beat CRPS. I can do anything," we shouted in unison and childishly leapt up and down. My father entered into our revelry. Our hugging bodies forged a pyramid.

Nicky was a gangly pale girl with blond curls who resided in the room beside my own. After my parents departed Massachusetts

Hall, I roved about the narrow passageway linking the fourteen freshman singles.

"Mom, can you just leave already? We're done with the move. Please, I'm asking you to go back to Connecticut." Nicky's imploring tone slid through the slit in her door.

"Alright, just promise me one thing, Nick. Don't let the freshman fifteen ruin your figure." Nicky's mother slammed the door theatrically behind her. I darted down the hall and collided with an alluring brunette in a gray tee that read Trinity across the chest.

"Oh my, I'm so sorry. I'm Elly. Are you also from New York?" The girl broke into a sophisticated laugh.

"Not to worry at all. It's a zoo in here. I'm Serena. Yes, I went to school at Trinity in the City." She offered me a benevolent smile.

"Want to grab something from the Annenberg dining hall? I was going to head over there for dinner soon." She studied me and then slanted her gaze toward the suitcase before her.

"Let me just pop this in my room and then we can head over." Serena vanished into her chamber, and I dawdled in the hallway. The rusty hinges on Nicky's entry sounded.

"Hey, I'm Elly. I live right next door. We're practically roommates." Nicky's tear-stricken face searched me as if in an effort to construe if I had overheard her mother's farewell words.

"Cool, I'm Nicky." Her blue eyes strayed across my face.

"Well, I just met Serena, who lives right down the hall from us. She's going to join me for dinner. Want to come with us?" Nicky beamed.

As we sojourned through Harvard Yard landscaped with manicured lawns and snaking footpaths that fed into a multitude of dormitories, I let the scent of freshly cut grass suffuse my nostrils and lobbed my head backward to take in the cover of sky. I felt lightness settle over me. Not the bleary kind that heralded my vomiting fits at Mayo, but a sense of shedding some of my past, of letting it go, like a balloon into the firmament, and of unleashing myself into my own becoming. The liberty of being my own agent and of being able to walk to destinations far more exciting than the toilet at the Marriott shot through me with what felt like the inverse of agony. I grabbed upward at nothing and furrowed my fingers into empty fistfuls of air, authorizing my past to trickle out of my fingertips. I was alive. For the first time, I was delighted by the world's sensory assault. The evening breeze tickled my cheeks. I began to laugh at nothing and everything. I lowered my gaze so it landed upon the two girls beside me. The reality of my existence sank in like a warm hug.

"I'm sorry. I don't usually walk around laughing without cause. I spent the last few months at Mayo Clinic and nearly died. I'm just realizing the miraculous fact that I'm here right now in Harvard Yard." Serena and Nicky's mouths dropped as they chewed on the facts of my life.

We mounted the small case of steps before the entrance to Annenberg Hall, an expansive space decorated with wooden trusses, walnut panels, a domed stenciled ceiling, and stained glass. It was impossible to refrain from gawking at this august hall. We surveyed the food stations and transported our trays to a vacant wooden table. Whereas mine and Serena's receptacles

were clogged with all of the options from plain cinnamon cereal flakes to lasagna, Nicky's only bore a plastic cup of water.

"You not hungry?" Serena quizzed.

"I don't really eat much. I'm trying to watch my weight." Serena gave me a perplexed look. I rejoined with a shoulder shrug.

"You are so skinny, Nicky," I cut in, pointing out the obvious.

"I'm just not hungry. I have not been for a while. It's like my body understands that I'm not going to give it food, so it eventually stopped asking for it." Nicky observed us eat, sipped her water for a moment, and then excused herself from the dining hall.

"That's a tad concerning," Serena commented between bites of lasagna. "Yes, I guess so," I replied, unsure of what she was looking for from me.

"What do you mean, you guess so? Eating disorders are pretty horrifying," she continued. "I just mean, I'm not really up for getting hung up on someone's anorexia. I'm not going to fix Nicky. I don't want to, and she is not our mess to clean up. I have been through enough of my own hardship that I'm just getting out of. I'm hardly ready to let myself loose into someone else's. If she can't step out of her own skin and realize how much she has, she is in some deep trouble." I eyed Serena. Part of me was furious with Nicky for getting mired in herself, for chalking up life to her dress size, and for not appreciating the health stored within her body. I felt as though she had affronted me personally by refusing to eat and dwindling into the frail state of the patient I once was. Part of me wanted to wake her up from her delusions but did not know where to begin. Alternatively, perhaps I did not know how to begin at all with

someone who had two functional legs, 20/20 vision, and operating intestines but was still locked inside of the prison of herself.

The next morning, I allocated surplus time to my wake-up routine and arrived at calculus class with twenty minutes to spare. A solitary girl slouched in a green chair. Renee's russet tumbling waves were restrained into a partial ponytail, and her brown eyes shimmered in the morning light that leaked through the window at the classroom's rear. She tossed me a tentative grin as I sat beside her.

"Hey, I'm Elly. I'm a freshman in Mass Hall. You like math?" Renee's beam expanded into a smile, and she rotated herself by ninety degrees so she could take me head-on.

"I'm Renee, and I'm a freshman in Lionel. I love math, but I want to be a doctor one day, not a mathematician." Her voice was mellow and understated. My cadence suddenly felt outrageously bold.

"Well, that's probably a sound call. I mean, math and man can be a recipe for catastrophe. Just look at Alan Turing and Kurt Gödel, who were nuts for math and literally went nuts themselves. It's a wise play to go the medical route. I also hope to have a career in the sciences." Renee released a modest giggle. Everything about her was unassuming and real. She lacked artifice.

"Elly, I'm not going into medicine to prevent myself from going insane." I let out a laugh, and Renee followed. We examined each other's expressions with an almost familial understanding.

"Then, what's your logic behind the doctor agenda? Between three spinal operations, two ovarian tumors, and a recent nightmarish stay at Mayo Clinic, I have come close to distrusting the system entirely. I am not sure if I will really ever trust a doctor

again after all that I've been through. Doctors have misdiagnosed, mistreated, and misunderstood me again and again." She stared at me as I spoke. Her eyes filled with tears. The syllables fell out of my mouth in an ironic harsh jest. Then I could not have appreciated the gravity of my words, which would arrest me in my tracks a few months later. I presumed that my medical mishaps exclusively lagged in my Rochester past. But the three capital letters, EDS, that my mother and I drowned out at Mayo would soon resurface and derail me again and again.

"My father was an orthopedic surgeon. He died a month ago from cancer. I'm only getting this personal because you were so open with me. My Dad was more than just a father. He was my best friend." Renee's eyes filled. I layered my fingers on her unoccupied hand. In that moment, I found solace in our touch receptors. Language felt bulky and awkward, so I let the silence enter our discourse as my touch seeped into Renee.

"I get it. No—I don't get it. I mean, I get it but not exactly. I can't possibly recreate the loss and sadness you feel in myself, but I know what that kind of weight feels like. I know hardship up close and personal, but I have two healthy parents so I cannot tell you that I feel your feelings exactly. I have felt hopeless, especially when I could not walk or see at age seventeen, and I just came back to my life from a tumor that my Mom thought was going to kill me. I am here for you, Renee, in my own way." She permitted tears to roll down her tan face. I bent at my hips and draped my arms around her chest. Right then, it dawned on me that illness did not only function to isolate you from your world but that it could also attach you to it. Our distinct hardships forged an unforeseen footpath into each other's lives.

A slight pale professor with ebony hair fastened into a twist entered the classroom. On the whiteboard, she sketched a coordinate plane, which she overlaid with red dots, lines, and parabolas. As the remaining eleven students drifted through the doorway and the clock struck nine, the teacher commenced her lesson.

"Welcome to calculus. My name is Professor Ziesner. Now, let's begin with a one-sided limit review problem. Given the graph on the board, find the limit of f(x) as x tends toward a, if a equals three." My classmates turned toward each other with raised eyebrows. I dashed an enthusiastic hand into the air.

"Based on the fact that the two one-sided limits are different, the limit does not exist." The instructor flashed me a pleased smile and nodded. Renee butted my bicep with her elbow. I spun my head to her and she mouthed "way to go, Elly." I felt unstoppable.

Later that afternoon, I spied Renee in the immense lecture hall surging with upward of four hundred undergraduates. I felt walled in by dense white noise. With my MacBook balanced on my knees, I busied myself with adding and deducting punctuation marks in a poem I composed before class. Instinctively, I huddled my thighs into my chest and pressed my shins against the desk before me. My Mayo Clinic posture had apparently not been excised along with my tumor. After I deleted all of the commas I had recklessly sprinkled throughout the free verse, I sealed my laptop and waved an arm at Renee. She shuffled through the human obstacle course and parked in the seat to my left.

"Wow. This place is a total madhouse. There should not be this many humans on the planet, let alone in a single lecture hall."

Renee observed my mouth as I spoke. She burst into laughter. Professor Lucien's miniature being occupied the black stage before us.

"Life Science students, today we will begin our exploration of DNA structures and Gibbs free energy. As usual, I will throw out a question based on the pre-lecture reading. Pretend a synthetic DNA base is manufactured that has the same size as adenine and can likewise pair with thymine. As shown on the projector, this unnatural base has a methyl group where adenine has an NH2 and is missing adenine's interior nitrogen." Professor Lucien shifted his eyes from his audience to the gigantic screen above his head as he articulated himself. He gesticulated about the diagram of the base pairs under discussion with a laser pointer. A radiant red dot skidded back and forth along the monitor. "Why might a pairing between this artificial base and thymine destabilize the double helix relative to an adenine-thymine pairing?"

I heard pencils hit paper and whispers in transit. My notebook lay bare before me, and I rolled my pencil between my thumb and middle finger. I often found that when it came to math or science, I was not inclined to write my way through my thoughts. They just emerged coherently like a preformed Word document if I focused diligently on the problem at hand. I raised an intrepid arm into the air.

"Creating a bond between the synthetic base and thymine demands that the hydrogen bonds between thymine and water be broken, which is energetically unfavorable. The new bond is less stable than is that between adenine and thymine in which the hydrogen bonds to water are replaced by those between

the bases." I felt concentric circles of eyes hound me. I craned my head downward until I came upon my Converse. "I can walk. I can see. I can beat CRPS. I can do anything," I intoned inside my head.

"Yes, that is right. What's your name?" Professor Lucien approached the edge of the stage. "I'm Elaine Katz." My name tasted excellent in my mouth like an unfamiliar vocabulary word I desired to repeat.

"Elly, how did you work up the pluck to speak in front of all these upperclassmen with the knowledge that you might flop?" Renee's murmur slid into my ear.

"Honestly, after all of the medical challenges I have overcome, nothing about a colossal roomful of strangers scares me. It's a perspective that I always have at my ready disposal, a parting gift from Mayo Clinic." Renee turned in her seat to study me. Her expression creased into a genuine grin.

After exhausting my Life Sciences problem sets in Widener Library, I pranced up the staircase leading to my dormitory and lobbed my knuckles against a door. Kushan drew the knob toward him and appeared with an expansive smile. As a volunteer with Harvard's Kidney Disease Screening and Awareness Program, Kushan preferred to liaise between physicians and underserved populations rather than pack in a few dozen curl bar reps at the campus gym. He was unimposing and gentle.

"Hey, ready to compare problem sets? I was just memorizing the first five amino acid structures on the handout. I'm actually really enjoying this course." Kushan's inflection had a mild tinge of his

Indian ancestry that you could only make out if you were looking for it.

"Yep. Let's do it. Just a heads up: My reaction mechanisms are no da Vincis. I can translate them from Elly scribble into chemistry if need be." We locked eyes, and Kushan emitted a reserved laugh. When a minute was up, he left my gaze and organized himself cross-legged on his teal rug. I lowered myself onto the floor, emulated his position directly opposite him, and reclined against his bedpost. Kushan spun the stapled pages before me so they were juxtaposed beside his own. He fingered through a response on his paper and then a corresponding answer on mine. I was the chemistry referee. I examined Kushan and waited for his face to surface from my downhill penmanship.

"We conflict on number seven. I think the right response is mechanism b, not mechanism a." His voice was edgeless as though it discomforted him that my response was incorrect. I unfurled my legs and scooted myself until I was pressed up against Kushan's hip. I hunched over our homework to determine if I concurred with him.

"I'm pretty sure mechanism a is more thermodynamically favorable. At a temperature that surpasses the activation barrier of both mechanisms, there is an excess of product A, which suggests that the equilibrium between both products favors product A." I sat erect as I justified myself, and Kushan gave me an admiring grin.

In early October, Serena and I ran into each other on Harvard's Science Center Plaza, and I decided to accompany her on her one block voyage to CVS. Rain loomed on the horizon. A mob of Chinese

tourists outfitted in waterproof ponchos congregated beside the so-called John Harvard statue that did not actually depict John Harvard. They took turns abrasively rubbing luck out of his mythically charmed foot. One of them approached me to ask where The Fly, a final club, was located. I stood there mute. Even as a senior at the College, I remained rather oblivious to normative Harvard pomp and rituals. I could not point out any final club's headquarters or direct you toward an alcoholic cocktail if my life depended on it. My Harvard is anchored in my intellect, not in sacrificing a few of my neurons in exchange for beer or pot. I observe the social scene that forms without me from a distance, almost anthropologically.

"I'll be fairly quick. I just need to fill a prescription upstairs," Serena reported as she swung her hair over her right shoulder.

"You don't have to rush at all. I'll wait up front," I responded as she bounded the stairs.

I gazed at the glass fridge containing a variety of beverages. I opened a glass cabinet and extracted an interesting-looking orange bottle of kombucha, a drink I had yet to sample. I purchased it and drank it down as I awaited Serena's return.

An hour later, I was stationed at my bedside desk and working my way through a triple integral. My abdomen began to distend, and I groaned as my stomach rammed against the lip of my table. My stomach churned painfully. I fled to my closet mirror and elevated my shirt. Math would have to wait. I felt my teeth chatter. My breathing grew so shallow until I could no longer hear it. Tears trickled out of me as I closed my eyes and jabbed at the soft interior of my thumb with a fingernail, attempting to deflect my attention

from one pain to another. The only reassuring thought that entered my mind was that this was not actually happening, that it was only a dreadful nightmare. But the image that reflected back was not a figment of my own making; it was all too material. I was pregnant, yet again, with my nonexistent twins. The skin coating my abdomen was pulled into a taut dome. My infamous left rib was fully dislodged, and my overstretched skin tore. I cringed at the touch of my own blood. I felt faint. I bolted to the restroom and puked until my vision was blurred and I was too weak to walk on my own.

At the time, I was uneducated about my inner workings. I could not make sense of the fact that in the absence of a tumor, my distension resurfaced. I was not aware that my symptoms belonged to one of EDS's cruel relatives that went by the mouthful of mast cell activation syndrome (MCAS). I had no method of predicting that a cluster of immune cells in my gastrointestinal tract, known as mast cells, discharged an overabundance of histamine. I was unaware that the kombucha, rich in this chemical, was sufficient to throw me over the edge. I did not phone my mother or debrief Renee on the catastrophe. I did not want to make it more real than it already was. So, I curled into a ball on my bedroom floor and cradled my projecting rib until it found its way back into place. My distension finally subsided as the week drew to an end, but my digestive system remained irritable for the duration of the term.

I was among the minority who counted down the days until midterm exam season without grieving them as they expired. When examinations commenced, a pleasant silence drenched Harvard Yard. Whereas the dense wad of quiet that rested between me

and my mother at Mayo Clinic felt impermeable to syllables we did not have, this was a hush that rang with morning bird calls and Renee's laughter in response to my banter. Renee and I christened ourselves the twin grandmothers; we dined at five and ascribed to a self-imposed bedtime of nine. Between our math lecture in the mornings and my Hebrew class in the afternoons, we assiduously took to our problem sets or essays across from each other in Widener's reading room. We slanted our eyes up from an Etgar Keret short story or differential equations to swap smiles and muffled giggles. In the setting of academic assessments, I was the active subject, in control of my performance. I was not the passive Elly doubled over in Dr. Cane's exam room or in Lucene's therapy office. No one could diagnose me with a disease of his liking or insert children's blocks up my rectum while I solved for X.

On a Tuesday morning in November, I awoke with my alarm at seven and unwrapped myself from my worn bedsheets. I was underdressed for the nippy breeze that seeped through the windows. I caped my blanket about my shoulders before solving surface integrals for twenty-odd minutes. I experienced an impromptu respect for the electrical currents coursing through my cerebral neurons. After reviewing my math papers, I outfitted myself in a gray tee adorned with a conspicuous crimson Harvard crest, a top on exclusive reserve for college exams. I siphoned whatever faith I could have placed in God into a garment branded with a bold Latin emblem that seemed to prime me for the problems Professor Ziesner had in store.

The two-hour exam period flew by with ample time for me to quadruple-check my answers. As the bell chimed, I vainly

motioned my ankles out of their curled position behind the two front legs of my chair. My knees and the insides of my calves were completely numb. I glanced down to the outside of my left knee and then to my right knee. My gray sweats were streaked with blood. I delicately stroked the oozing stains, and bones butted against my touch. I jammed my teeth into my lower lip. I intuitively pressed my palms against my displaced patellae until they snapped into their grooves. I warily cupped my knee caps. I held them stalwartly like disloyal childhood friends I could not trust.

An uneasy blend of remorse and shame choked the pride of my inner math geek. For some reason that still evades me, I perceived my coming apart as a function of my own doing. I rebuked myself for the hyperflexible posture I sustained for the two-hour exam. Since my EDS was not yet a solidified fact of my life, a net into which I could blatantly toss the whole of my undoing, I reasoned that I was somehow to blame for my dislocated knee caps. I returned to Mass Hall to wash my lacerated knees. As the soap stung my outer legs, I groaned inaudibly.

Yet again, I barred Renee and my mother from my injury. I provided them with a slew of excuses to make the insults to my body seem like normal mishaps. Two days later, I encountered Renee on campus when I was departing a meeting with the editor of *Prescriptions*, an undergraduate medical humanities journal. I hobbled toward her, thrusting my weight clumsily from one Converse to the other in excruciating pain.

"Hey, Elly, you alright? Why are you having trouble walking?" Renee's smile faded and her expression became vaguely parental.

"Yeah, I'm fine. I just tumbled pretty badly down the stairs in Mass Hall. I'll be good as new in a few days." I parsed through my final sentence in my mind and questioned whether I said it more for myself or for Renee. I felt my conviction waver as I uttered it.

"I hope so. How was your *Prescriptions* meeting?" Renee asked sadly.

"It was pretty good. It's nice to be able to frame all of my medical hardship in an academic context, to disinfect feelings from my past that haunt me and put them into something neat and editable like a poem. Four of my pieces will be published in this coming issue. I'm tempted to submit another one that I wrote at the start of the semester but am not sure if it's too personal or crosses some kind of boundary that would make me feel too exposed." A gust of winter filled my mouth as I spoke.

"Want to read it to me, and I'll let you know what I think?" Renee was no poet, but she was a master interpreter of my psyche and, by extension, appreciated my free verse. She peered at me through slits in her wind-swept hair. I retrieved my iPhone from the pocket of my jeans and browsed through my emails to myself to locate the one that contained the text.

"That would be amazing. Here goes nothing: *Whisked from excavations of consciousness, from nightmares that bore themselves into reality, from normal gone astray, from a soul that forgot how to hope, from a foot that forgot how to walk, I glide into the swing of things, into valleys of contentment and comprehension, into linear progression. I look for remnants of the dark, for the girl rendered inhuman by illness. I wonder if crumbs of this girl exist. I wonder where she has gone. I search for her searching, untrusting gaze, the*

one that caused her eyes to withdraw in fear. I recall her tattered, graying adolescent back braces, her violet scars twining skin. These are my heirlooms of my long-lost friend. I attempt to confine her in a past that I no longer possess. The details of her being escape me. But occasionally, she rears her head like unexpected splinters rising from a smooth wooden table. I feel her tread upon my soul, the opacity of her shadow resting upon my current self. She is my glint of dark in the light, my fragility cased within my invincibility. Unable to live with her or without her, she is my sketch, my rough outline of the person I am becoming." My eyes filled as I read my own words in the hindsight of my recent rib and patellae dislocations. They did not settle on my tongue with the sense of belonging they had when I wrote them. They felt wrong in my mouth, like rancid milk.

This alter ego I referenced was no longer a sketch or a nebulous outline. She was my everything. Her brokenness was mine for the keeping. I wiped at my tears with the chaffed back of my hand. Renee's eyes shone and she sniffled as she entwined an arm through the bend of my elbow.

"Elly, that was stunning. Submit it for sure." She unhooked her arm and embraced me tightly, pushing all of my broken parts into her, transforming them into something we could share.

The next month, I revisited the horrors of Mayo Clinic in a nightmare. The vision was tormenting. I tossed and turned in a frantic frenzy and fell against the hardwood floor five feet beneath my bedframe. I felt electricity ripple down the outside of my right leg. My coping mechanism from Children's Specialized Hospital returned like a knee-jerk reaction. I stabbed the fingernails of my left hand into my right thigh, reinstating the red half-moons that

had scarred over. I felt compelled to prove to myself that I could still feel, even if I had to inflict more harm in the process. My effort was pathetic. I lacked all feeling in my right limbs. My right shoulder was not under me but was winged behind me and out of reach. My pelvis was torqued, and I felt my right hip give way and glide out of its socket. I was frozen in my own trauma. I unloaded a resonant piercing scream. My nervous system was at an impasse. The space around me swirled into a nauseating blur. When I awoke several hours later at Mount Auburn Hospital, my joints had been relocated and my mother stood beside me.

"Bel, we're going to figure this one out. You are coming home and we will make all of this make sense. I think we need to take some time to investigate the EDS possibility that Dr. Glassner at Mayo Clinic mentioned." I studied her, too petrified to nod, to move any part of me. I pined over my temporary leave from Harvard and felt myself mouthing "really?" But putting Harvard on hold was the least of what lay before me. My world would change in permanent ways I could not foresee. My mutant genes could no longer be silenced.

17
In far too many continents simultaneously

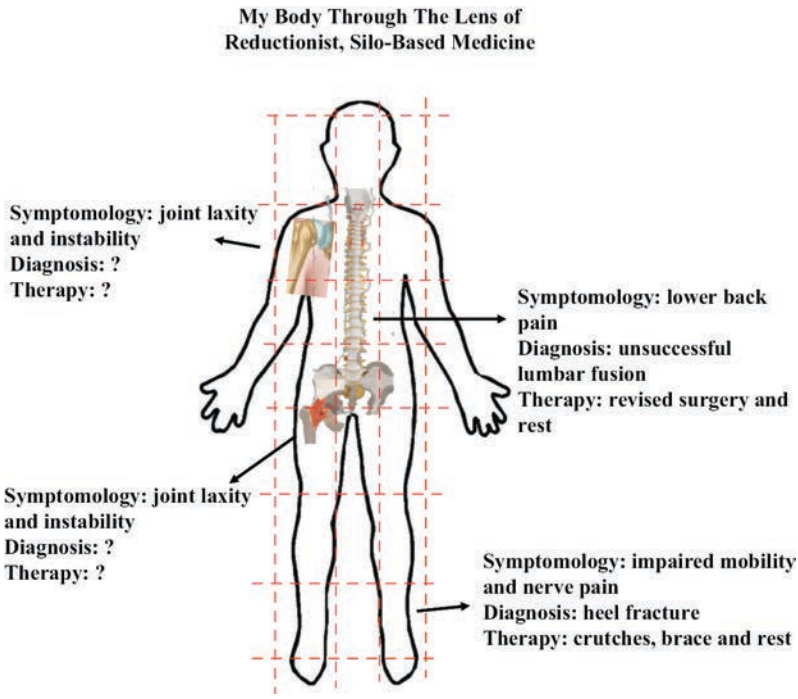
I feel a sudden kinship with the unseen particles eddying about me that exist

but remain unprocessed by optic nerves incapable of glimpsing the chaos of the microsphere. I know you are there, I want to say to swoons of oxygen and nitrogen.

My disease is the atmosphere—so raw, so real, so ignored. Here but not. Felt yet masked.

"Don't wish for it. Work for it. Your life is in your hands. Push yourself. Don't try to fit into anything you are not. No one remembers normal." In the dimly illuminated space, I listened to the cycling instructor as she competed with the outrageous decibel level pulsing through the studio. Her contours blurred into the blackness. I was panting. My temperature was elevated, but I was not ill. I never felt more alive.

I pedaled insistently to the surging rhythm. On the one hand, I wanted to lose myself in the dark box of winded bodies, to disremember my Harvard existence like a fleeting thought. If I forgot



Harvard, perhaps its forfeiture a month earlier would somehow take less of me with it. On the other hand, feeling the lactic acid and accumulate in my muscles was about resuscitating my control over my body. I was fighting for my autonomy.

Music thundered through the sound system, and I felt a jolting snap on the outside of my left heel. A searing ache shot up my calf. I pedaled onwards, transgressing some biological stress threshold. But blistering pain zinged up my leg again, reminding me of my CRPS. As a cycling neophyte, I was uncertain how to clip my shoes out of the bike. So, I perched on the saddle like something inert. On the surrounding stationary bicycles, my classmates continued to follow the instructor's directives. I eyed their moving parts with contempt.

Upon my return home from college, I walked with an overt limp. Despite its forced relocation into place at Mount Auburn Hospital, my right hip ached when it bore my weight. A gory bruise swelled on my right shoulder, which recurrently popped out of socket. Did my innocent fall from my campus bed trigger a biological cascade that rendered me vulnerable to recurrent dislocations?

I passed the first month in my parents' apartment in shock-induced silence. I was appalled by the fact that I had triumphed over the physical and mental tolls of Mayo Clinic, that I came into my own outside of illness at Harvard, and that I had to revisit my ground zero. The earth below me seemed to spin from on-center to off-kilter. I wanted to scream until my vocal cords ruptured. I felt a deep hatred for the anonymous pedestrians who scurried by my gawky shuffle without perceiving the legs beneath them, the bodies that enabled rather than withheld them from living.

I often sank into my parents' upholstered armchair in my frayed pajamas and mindlessly flipped through the channels on the flat screen. I was not hoping to come across anything in particular but took mild pride in the reality that the remote was something I could control. If only I could crawl into a reality show and become the seemingly normal person staring back at me on the screen.

When my gait stabilized and my orthopedist sanctioned physical activity, I threw my body into full gear. My immobility resounded with the memory of my back fractures and felt like a penitentiary from which I had to release myself all at once. As the music dissipated and fluorescence poured down from the ceiling, I raised

a hand and shrieked "help me, please." Bathed in artificial light, the cycling instructor neared me. In her clammy white tank, she squatted by my left pedal and then my right, extricating my rental shoes from the bike.

Reading the lines of agony on my face, she assisted me as I dismounted. A shooting pain zoomed up my left leg and along my outer foot.

"Can you call my mother? I don't think I can walk." I sat between two adjacent bikes and extended my left leg, seeking to distance my center of mass from its persistent throbbing. I pressed my palms into the floor behind me in an effort to feel grounded, and my right shoulder audibly clicked in protest. The instructor supplied me with her mobile.

"Mom, I can't walk. I'm sitting on the floor at the cycling studio. It's my left leg." Liquid trailed down my cheeks. I could not tell whether it was sweat or tears.

"I'm getting in a cab right after I finish this case dictation at the office. Don't move.""I'll sit with you," the instructor uttered. I folded my lips into the smallest shape I could muster and nodded my head. My mother sped into the studio breathlessly as though she had just raced up a flight of stairs. Her eyes took me in. She wrenched me up from the floor and onto my right foot.

"El, what happened?" My mother's voice quivered as she passed me a steady hand. "I really don't know. One minute I was cycling, and the next I felt a searing sensation creep along my left leg. Even when I'm not bearing weight on it, the sharp pain still persists. It feels like it travels up and down my calf." My mother's face swiftly transitioned from vacant to terrified. After I clasped my

hands about my mother's forearm, we headed to Hospital for Special Surgery. In the backseat of the taxi, my mother conveyed that she had secured an after-hours appointment with Dr. O'Neil, a foot specialist. When we pulled up to the hospital, my mother fetched a wheelchair from the security guard at the building's entrance.

She wheeled me through the antechamber, and we rode the elevator to Dr. O'Neil's floor.

She did not know how to keep me company or what to say. So, instead, she handed me my iPhone and earbuds. I fingered my way through Audible to Douglas Hofstadter's *Gödel, Escher, Bach: An Eternal Golden Braid*, a book that explores points of contact between abstruse mathematical concepts, art, and music. As Hofstadter discussed mathematical recursion, I felt my hollow breaths deepen. My mind busied itself with Hofstadter's logical tour de force, rather than with how wrong I felt in a wheelchair instead of on functional legs.

An X-ray technician maneuvered me to the hospital's imaging center, where my foot was blasted with a dose of radiation. We then made for an office, where a muscular physician with handsome blue eyes waited.

"Hello, Elaine. I am Dr. O'Neil. I am just pulling up your X-ray on my monitor. I would like to examine your foot." My bike shorts clung to my skin, my evaporating sweat acting as a sort of glue. I chucked my one-legged self onto the examination table and exposed my foot. Dr. O'Neil palpated a hand over my lateral heel.

"That hurts a lot," I shrieked.

"Elaine, even though I do not see a gross fracture on imaging, I think you have a calcaneal stress fracture."

"How is it possible that she developed a fracture from a non-weight-bearing activity like cycling?" My mother's tone was suspicious.

"Perhaps Elaine's weight was not evenly distributed across her foot and she pressed too forcefully into her heel on a down-stroke. Elaine needs a boot and crutches for a month or so to recover. She should bear minimal to no weight on her left foot." The doctor eyed my mother with confidence, rather than with speculation. Like Dr. Cane at Mayo Clinic, he was irrepressibly sure of himself and his credentials. A fracture was the only diagnosis in his differential. He did not even contemplate the rare chance that I had torn through a nerve responsible for relaying sensation to my outer foot, that I had a connective tissue disorder that rendered my nerve sheath friable, and that prescribing crutches and limited mobility would only provoke my EDS to become as manifest as my blue eyes and blond hair. He did not even consider for a moment that his treatment could set off an avalanche of catastrophes I have yet, six years later, to keep at bay.

The following morning, I crutched alongside my mother's measured gait to The Corner Bookstore. We were, yet again, looking for other people's words to put in our mouths.

After a single block, my underarms and right leg were exhausted from bearing the brunt of my being. I felt my mother's downcast eyes shift from me to the dense black boot bracing my left foot and ankle. As we wordlessly neared the bookshop, I focused on

natural sound effects—the whistling wind ruffle through dead leaves—until we approached a narrow entryway that prompted me to halt. A wave of children in school uniforms paraded through the doorpost, and a sign dangled that read Carousel of Languages.

"Mom, can we stop inside here?" My mother's glance was skeptical. I could sense she doubted what I could possibly desire from a children's language program. She held the door with her back, and I hopped inside. I let my eyes browse the compressed space stocked with red bookcases, circular blue rugs, and four classrooms filled with toddlers conversing in French and Mandarin in almost native accents.

"May I help you?" I hinged slightly to find a striking Italian woman. Her expression was mildly made up with suggestions of rouge and gloss.

"Yes, actually. May I possibly speak with the proprietor?" She examined me and then my mother, who shrugged.

"That would be me. I'm Patrizia. Come, take a seat in my office." Patrizia scanned me from top to bottom and hesitated while staring at my bandaged limb. Her face organized itself into lines of pity. Patrizia directed me to a red bench beside her white desk.

"I'm Elly, and I'm a Harvard student on leave. I'm fluent in Hebrew, adore children, and would be delighted to work for you while I am home. Lingering in my parents' apartment daily is getting to me, and I think I could really be of use here in any way you deem fit. I can provide you with my resume if you would like. I want to feel needed, not only needy, more than anything else." Her cheeks broadened into a grin.

"Elly, I think that could work. Want to start tomorrow, say around eight in the morning?" I sensed a heaviness dissolve in my throat and nodded. I would occupy the front desk, attend to incoming calls, and assist students with math and spelling homework as they awaited their language lessons.

On Friday evenings, Avery and Jason accompanied me and my parents for Sabbath dinner. I flashed them coy smiles as their suave, able-bodied frames ventured into the apartment. My brothers grew into attractive lanky creatures dressed in sport coats and bold neckties. I witnessed them from arm's length, trying to compute the unfathomable distance between their wellness and my illness in my head as though it were a complex derivative. They sandwiched my father at one end of the dining room table. I composed myself beside my mother with my leg outstretched onto the horizontal support anchored to the table's underside. I attempted to contort my face into a suitable expression as my family took shape before me like a foreign film without subtitles. I would have to make do with subtext.

"Dad, my investment is earning remarkable returns. The market may be bearish, but this stock is really defying expectations. You should get in on it." Avery's trim face expanded into a proud grin as he scored his meat.

"Ave, that's wonderful," my father said. I felt my mother's sympathetic hand creep along my lower back.

"I trained five new gym clients today. One of them called me a beast of steel," Jason brazenly let out, inserting himself into the

father-son dynamic. I observed him run a hand through his black curls. My mother took a long inhale and solemnly studied me. I obscured the center of my tear-soaked face with a cavernous tea mug.

My mother's eyes darted from my brothers to me. She seemed to be engaged in two parallel phone calls to different time zones. I knew she felt what I was feeling, that she longed for me to be on the other side of the chasm between me and my siblings. I knew she yearned to press resume on my life as much as I did. I braced myself and clenched as many muscles as I could muster. I felt like my whole being was under siege. I watched my brothers narrate their own lives while I served up only silence and pained effortful expressions. I sank myself as far as I could beneath the table without falling. I was afforded the same Jewish delicacies as every other member of my family and sat on the same nice chairs. At the time, these felt like immaterial facts.

Currently, six years later, between my compression garments that secure my joints, the kinesiology tape supporting entrapped ulnar nerves, the physioball under me that functions as the sole chair that does not dislocate my right hip, and my constricted diet secondary to mast cell activation syndrome, the space between me and the individuals who share an approximate half of my genome feels immeasurable. I now know that my illness is a life sentence, not a provisional furlough from reality. I ogle my brothers and their toned physiques, their girlfriends who become spouses, and, most poignantly, Avery's small daughter, Sami, who looks like my ancestor and my unborn child wrapped in a thick layer of innocence. I experience shameful rage as I take

stock of what I always wanted but will never have. I force the sincerest smile I can muster as I examine Sami, who, thankfully, is too young to detect the nuanced grief in the creases of my face and the moisture collecting in the blue of my eyes. The pain is almost physical.

I feel like something irrevocably wrong, like an off-putting dish at my parents' Sabbath meal, like something too vulnerable to be loved. I hate myself for hating my brothers' health, for despising them for constructing something of their own lives while I writhe in the agony of my dislocated limbs. I often take to my bedroom as Sabbath eve comes to a finish to enter into the narcotic stupor of solitude. I feel my shoulders relax. I let myself cry in short spurts before I submerge my face in my bed pillow and am overcome by sleep.

As I shuffled home from Carousel of Languages in the late afternoon, I surveyed night as it fell over the horizon. Across the street in her physician's coat, my mother waved her braceleted arms overhead. I leapt toward her, and a wooziness settled over me. A sharp throbbing nuzzled into my left lumbar spine and shot down the back of my left leg. I flung my back against a storefront and concentrated on my breathing. My mother scrambled toward me.

"Bel, you OK?"

"Mom, I feel intense nerve pain in my left lower back." I bit the inside of my cheek until I tasted blood.

"Do you think you can make it the three blocks home?" I despised the question as it slid from my mother's mouth. Her face glowed

in the descending streetlight, and I desperately wanted to regress into something infantile that could fit easily into her arms.

"I can try. Do you think it's from the prolonged use of crutches and the way I'm carrying myself? I feel like I'm coming apart. Mom, I'm scared." My mother mirrored my apprehensive expression.

"El, let's take a taxi home and get you off your feet." My mother reached a hand into the air on the corner of Madison Avenue.

The next morning, my mother informed her office that she would be excusing herself for the day and glided into the backseat of a cab beside me. When we arrived at Lenox Hill's radiology division, my mother gave my hand a resolved squeeze and loaded me into a wheelchair. After I was strapped onto the MRI table and shuttled into its bore, the familiar grating clamor commenced. I let myself fade into the discordant mechanistic noise. My mother's dialogue with a radiologist cut into my reverie.

"Elly's spinal fusion may be unstable. Her asymmetric posture may have jarred the bony union between her vertebrae. Or, her fusion may have been botched from the start and is only becoming manifest because of Elly's crutching," a masculine voice asserted.

"Are you sure?" My mother countered. Her words were hurried. I imagined her face contracting in alarm.

"It's my best guess based on Elly's images. I would have her rest and remain as still as possible," the male offered in a detached tone. My mother's heels drew close to the magnet. I felt her hand sweep a few blonde wayward hairs from my forehand.

"Babe, I'm here for you. You know that, right?" I surveyed my mother's affected grin plastered on top of her own sorrow. Mascara

tracked down the sides of her nose, and I rubbed it away with the soft inside of my index finger. I was not sure what to do with my face, so I just gazed back at her blankly and muttered, "Mom, that is the one sure thing in my life."

That night, my thoughts smothered sleep each time my eyes began to shut with fatigue. I reasoned that if I permitted my body to relax into slumber, I may toss or jolt myself in such a way that I would wake up in more pieces than I already was. The throbbing nerve endings in my left back and foot functioned as searing caffeine. The critical voice inside my head amplified, reiterating the phrase "you are irrevocably broken" until I was convinced it was an established fact.

I lifted my iPhone toward my face. The home screen displayed a quarter after two in the morning. In the backdrop, Renee and I were eyeing each other and laughing at something outside of the frame or at a private joke I could not recall. I felt loss leak into me. I flicked my way to Douglas Hofstadter's *I Am a Strange Loop* and entertained his notion that the self emerges from a feedback loop rooted in the brain. By this logic, I could think myself into who I wanted to be, despite my crumbling physical constitution.

Light tumbled through my bedroom windows, forming geometrical shapes on my floor. As Hofstadter's text concluded, I thumbed into my Harvard email to find the following message from my math professor:

> *First of all, you have my best wishes on your health. You occupied such a delightful presence in my classroom, and I know the other students will miss your brilliant solutions and comments.*

I wanted to send the in-class worksheets to you, in case you wanted to solve the problems in step with us. The worksheet we looked at today is attached to this email. I will send them for each class.

I dabbed at the attachment, and a document on directional derivatives popped up. Within half an hour, I solved the 15 included problems without scratch paper, a writing implement, or instruction on the relevant topic. I felt myself drift up and out of my pain and lapse into something quantifiable and solid. I remembered who I could be. I responded to the email with a concise thank you and returned to my inbox where a message from Patrizia hung in cyberspace. She mentioned that she was dismayed to hear of my bedridden state from my mother and provided me with a list of tasks I could accomplish from my mattress, which I took to with urgency.

At seven in the evening, Avery's hulking footsteps crunched toward my bedroom. He thrust a gleeful expression through the crack in my door while leaving the rest of him behind.

"Do you mind if I come in?" His voice was gentle, and I felt his eyes working their way around my body surrounded by ice packs and pillows.

"No, it's fine." My clipped syllables were tinged with aggression, but I could not refuse my brother. I did not know what would become of me if I rejected one of the few people who loved me unconditionally. He flung his loafers off at the door and shifted his weight onto the mattress beside me. A tense barrier of silence formed between us.

"I'm sorry I'm quiet. It's got absolutely nothing to do with you. I'm just feeling lost and like I've been robbed of everything I've

worked toward for almost two decades. I thought my travails were behind me, but I'm starting to realize that life, at least in my case, does not really work like that. Hardship is not really like money in a bank that you spend and run out of.

Sometimes, as petty as it sounds, I'm jealous of you and Jason for being well." Avery's hand located mine.

"El, you don't have to apologize to me ever. No matter how many times you try to push me away or lock me out, I'm not going anywhere. You know Jason wants to be here for you too, but he does not know how. He's scared to step on your toes, to say or do the wrong thing, so he maintains his distance. But that's not a reflection of a lack of love."

"I know that, yet sometimes I find myself wishing that he knew how to be here for me. In all honesty, I don't even know how to be around myself. I feel like I'm stuck inside a body that doesn't want me to live my life." Avery tightened his grip on my hand.

"El, I don't know how I would handle what you are going through." I revolved my head toward him. His face was streaming with tears.

"When you're fine, you expect that you can manage things, that you will somehow hold yourself together when adversity strikes. But that is not the case. It's almost impossible not to decompose into someone you despise. Please catch me before I become an abomination to myself." Avery emitted an exquisitely charming laugh that I wanted to record and play after he retreated from my bedroom. I felt a reluctant smile take shape on my face.

"You couldn't become an abomination if you tried. You are not going anywhere. I will never allow you to despise yourself. You can

count on that." Avery's calloused palm ran along my limp inner arm. He pulled away and swung his gangly legs over the edge of the bed.

For three weeks, I became a melancholic fixture in my bedroom. I inhabited threadbare pajamas on my mattress. The most micro of movements elicited agonizing signaling between my left back and my brain. I felt like something malfunctioning that I wanted to return to an electrical supply shop. I nurtured whatever shards of my dignity I had left in me by tending to math problems and Patrizia's instructions.

One evening, I fell into a sedative slumber. My mind wandered back into the freshly cut grass in Harvard Yard, to Renee beside me in math class, to the life that had vanished like air. At four in the morning, I was startled awake by an arresting ache. I was lying on my right side like a mangled bird of prey. Sudden pain filled my shoulder. Using my left hand, I brought my right arm under me and pressed myself forcefully into the mattress. My shoulder cracked back into its socket. My whole body trembled uncontrollably. My heart thumped furiously. I kept stroking my right arm with my left palm to confirm it was still a part of me. My dislocation from my life, or from anything remotely normal, felt complete.

A few long months later, I would understand why I was coming apart at my anatomical seams. I would come to realize that inertia was the imp of EDS. Due to my lax tendons and ligaments, maintaining the strength of my skeletal muscles is essential for me to remain in one piece. If these muscles atrophy, my bones readily slide in and out of their respective grooves. My right limbs, particularly my shoulder, began to glide out of socket daily; each

time, I felt as though I was coming undone anew. Even now, I have yet to acclimate to my regular dislocations.

Adjusting to this reality feels like succumbing to my worst nightmare, a complete absence of self-control. Because of my prescribed immobility, my EDS surfaced into something sizable and overbearing. I felt as though my stillness had flipped an internal binary switch that I, to this day, cannot turn off.

Renee phoned me in the afternoons, but I initially spurned her calls. I could not stomach the thought, let alone the reality, of her peppy voice taking me through her Harvard experience that should have been ours. But, more than with her commentary, I grappled with how to condense my paranormal situation into plain English, how to make myself legible to people with robust connective tissue and limbs that never failed them. By my thigh, my iPhone vibrated. I extended an arm toward it as an analogy came to mind.

"Hey," I answered meekly.

"Elly, I've missed you so much. It's so nice to finally hear your voice." Renee sounded wheezy. I assumed she was walking somewhere briskly.

"I'm sorry I fell off the face of the earth. I've just been through a lot, and I was nervous that talking to you would make me upset that I was not there next to you to view your expressions as I spoke." A pause emerged, and I wondered if Renee's phone ran out of battery or if she muffled her mobile to speak with someone she bumped into on campus. Rage sped along my jawline, and I felt my nostrils flare mildly.

"I'm so sorry you have to go through all of this. Your Mom texted me about your foot and back." Her voice winded down into a whisper. I could tell she did not know what to say next.

"That's really only the half of it. My right hip and shoulder keep dislocating out of their sockets at least once a day. I feel like I'm in too many continents simultaneously. I know that isn't impossible if you stand on the Silfra fissure in Iceland or on some special sites in Egypt or Russia, but I'm doing it right here in my own bedroom. All I have to do is roll over to land my hip in Australia and my shoulder in Denmark," I rejoined, tasting the levity cake over my tongue. Renee laughed for several seconds.

"So then, how many continents are we in now?" She quipped. I liked that I had become a plurality. For a moment, I felt fused to her and less alone.

"Well, before you called, I was in three. But now, I would settle on one and a half or so." I erupted into tremulous laughter that inflamed the ache in my lower back.

"You should win some sort of medal, or at least make the Guinness Book of World Records. I love you, Elly." I could almost feel her smile press against my ear on the other side of the line.

"Thanks for tolerating me," I ejected as the mirth dissolved.

"You are the most tolerable person I know. Thanks for tolerating what you are going through so I get to tolerate you." I felt the aesthetic echo of her words as they entered me like a cool waterfall.

"Bel, you off the phone?" My mother asked through my closed bedroom door. "Yep, just got off," I returned. My mother's bronzed

forehead was tense with wrinkles as though she had overdosed on thought. She lowered herself at my feet.

"I just got off with a terrific neuroradiologist at my office who looked at your scans. He does not think you have a calcaneal stress fracture. Based on the clinical picture and your images, he suspects a torn sural nerve on the outside of your left heel, which runs along the distribution of your pain. He also looked at your lumbar spine scans. El, he disagrees with the doctor at Lenox Hill. Your fusion is not impaired. Instead, you have a case of facet arthritis, which is treated by deadening the nerves that are causing your pain. He thinks it should be easy to get you out of pain. He got us in with a physiatrist this afternoon who's going to administer local steroids to the torn nerve in your foot and ablate the sensory nerve in your lower back.

Your misery should end soon, El. I lined up an ambulette to take us there." As I assimilated my mother's words, I was incensed. I was outraged at doctors for misinterpreting my body, for dictating that I overuse crutches, languish on my back for two months, and for letting me slip through the cracks of their massive egos. I felt defiled and aggrieved that I could be passively pushed around like barter in the human commodity market that passed itself off as Western medicine.

My mother shifted my wasted skeleton into a rental wheelchair at my bedside. The throbbing in my back climaxed and seemed to outgrow me; it felt like a serrated blade that punctured me from without rather than a sensation that emanated from within. My breath slowed until I was hardly breathing at all. I let out a falsetto chain of nonsense syllables. I felt like an exasperated infant trying

to do something effective with its mouth, to hopelessly channel sounds into words. Silently, my mother pushed me through the lobby toward a gurney.

As I mounted the coarse white sheets, I noted my mother's blotchy face and her spindly frame dressed in yesterday's clothes. Two paramedics hoisted each side of the gurney and hauled me into the ambulette's rear. My scream intensified as the vehicle skidded over potholes, clefts in the road, and speed bumps. My mother pressed her palms against the fronts of my shoulders in an effort to steady me. Her worn face looked into me, silently indicating how time would warp me, how experience would stencil its way into my forehead and around my eyes, and how my pain trickled into her through an emotive osmosis, a chemical reaction that catalyzed me into an enduring us.

When we arrived at Weill Cornell, the paramedics ushered us to the physiatry procedure unit. My mother rummaged through her shoulder sac and came up with a copy of Toni Morrison's *Sula*. She read to me in a placating voice that sounded like auditory silk. A manifestly devout Indian dressed in a snug turban approached my gurney. The lines of his face formed a sympathetic shy smile. "Hello, Elly. I'm Dr. Singh, and I'm determined to rid you of your pain. I hear you are a student at Harvard. What do you study?" I offered him a puzzled look. I was shocked that a medical professional wanted to sum me up holistically into a human being rather than into a grab bag of symptoms.

"I study biology. Currently, however, it feels like biology is studying me." I let my eyes drift across the ceiling overhead. I felt my

mother and Dr. Singh exchange glances that fell on my wounded body beneath the bedsheets.

"Well, we are going to get you back to your life, Elly. I'm really hopeful that these procedures will work, and biology will get off your case. You ready?" I nodded. Dr. Singh applied a green mask over his mouth, wheeled me into his procedure room, and locked my gurney into place.

"Elly, can you please roll directly from the stretcher onto the exam table beside you? I need you on your stomach." I winced and abided by his instructions. I heard a fluoroscopy device move through grooves on the ceiling and settle over my lumbar spine.

"Caudal tilt, please," Dr. Singh ordered. The table shifted, and I emitted a strident cry. "Elly, I know exactly what nerve branch I need to ablate. You will feel a pinch and then pressure as I inject anesthetic into the area. Then, I will hook you up to the current, which will generate sufficient heat to burn the nerve. You may feel a mild burning sensation as the current escalates over the course of three minutes. While this is happening, I'm going to inject a dose of steroids and lidocaine into your torn sural nerve." Dr. Singh's voice was reassuring and maternal.

Fifteen minutes and three needle sticks later, a female aide conveyed that I had done a fantastic job at lying down, which hardly seemed to warrant any sort of congratulations at age twenty. My grueling discomfort departed as though it had never been there to begin with, like a flawed penciled solution to a problem set that could be erased away and only leave the vaguest residue behind. The sensation was gone, but that did not mean that it had never existed, that I could somehow move forward without

being changed. Just as I mourned the removal of my titanium hardware, in a strange sense, I lamented my pain as it left me. I dreaded wellness as it entered me, knowing all too well that it was capricious and could take leave of me without my permission, or even a considerate forewarning.

At eight o'clock the next morning, my mother and father strode up to my bedside with a walker. My father's face glistened with aftershave. The lines on my mother's face told me that she had passed an undue quantity of time querying my medical history on Google to string me together into jargon and sentences that could make sense of my life.

"Bel, can you try to walk with me and Dad before we go to work?" I gave my mother a critical stare, and her face hardened.

"El, you're not in pain anymore, right?" My father's voice was raspy. My parents glanced at each other and then at me as though we were all meeting for the first time.

"No. I'm not in pain. I can try." My voice felt small and nervous. I steadily swung myself erect on the edge of my mattress and tucked my bare feet into the slippers beside my bed. My mother motioned the walker toward me, and I took a few dawdling steps in the direction of my doorframe. I could feel my parents' eyes gawping at my deliberate paces. In my slow motion, I felt more alive than I had in more than two months. As I neared my door, my right leg gave way under me, and my walker toppled into my wooden armoire. My father dashed behind me in time to break my fall. I squealed in my father's arms. The three of us watched my right leg rotate its way out of socket like a strangled fetus. My father discharged a gagging noise as though he was going to be

sick and rested my disjointed body onto the carpet. I nuzzled my right leg under me until it clicked into place.

"Dad, I don't think I can walk. Can you carry me back to bed?" My words were syncopated and abrupt. I choked on my tears. I felt defeated. I wanted to be a small insect right then, something my father could stomp on and bring about its demise. I wanted Dr. Singh to ablate every part of me until I could no longer feel or reflect on feelings I did not want to own.

"My Elly. I got you." My father sighed and gathered me into his strapping arms. My bones felt distressingly heavy as they collapsed into him.

My father pressed his mouth against my forehead. I listened to his retiring footsteps until they faded out of earshot. At the foot of my bed, my mother took a moment to mourn the loss I had just suffered. I glared at her mutely.

After an hour, a fetching twenty-something female entered my bedroom. Her bipedal youthful wellness seemed profoundly out of place as though we were cast in motion pictures of contrasting genres that were intended for totally different audiences.

"I'm Brooke. Your Mom let me in. I hope that's alright. I'm looking forward to helping you get stronger. I spoke with Dr. Singh at length on the phone, and he briefed me on which muscle groups he wants me to help you strengthen." I ogled Brooke as she spoke, and her words reached a deadlock someplace between my eardrums and my auditory cortex. They sounded more like a static buzzing to me than anything coherent. My attention was

consumed by her simple stance before me that felt like an out-of-budget luxury product.

"Can you stand up?" I studied her and felt my jaw clench in apprehension.

"I'm not sure. I tried to walk earlier with a walker to my door, and my hip fully dislocated." She shot me a curious expression.

"Let's begin with something on the safer side then. How about lifting your right leg slightly off the mattress for me?" I trembled as I thought about the prospect of doing anything remotely normal with my right leg. I tensed my abdominal muscles and craned my gawky limb upward. I felt my face contort into a strained grimace. An unnerving cracking sound was elicited from the small movement of my hip joint and my leg dropped flaccidly onto the mattress.

"I can't feel my leg at all," I whimpered. I screwed my eyes shut and sampled bile as it scorched my esophagus and soaked my bedsheets.

"I'm sorry. I'm so sorry." Tears spilled down my face. I hated myself and Brooke for witnessing my repulsive exposé. A chilly sweat drenched my being.

"It's OK, Elly. Try to take a few slow breaths. I'm going to reset your leg." Brooke mounted the bed and straddled my right leg, which she aligned and propelled back into me. I let out a grunt. I crammed my palms against the sides of my wet face as though I was going to be sick again. Brooke disappeared into my restroom and reemerged with a damp bath towel that she wiped affectionately over my chest. She wheeled my desk chair

beside my bed and sank into its pink cushion. Her expression was dumbfounded, but she managed a small smile. My mother's bare feet drew near, and Brooke fled into the corridor. I overheard their voices through the fine crack in the door.

"Elly seems quite unstable, too unstable for outpatient physical therapy." Brooke's voice was gentle.

"What does that mean? Elly needs to get stronger. What are her options?"

"I think an inpatient program may be best for Elly. She can't even use the restroom on her own really." I heard my mother release a long sigh.

"The only way Elly would ever tolerate that is if she went back to Children's Specialized Hospital under the care of Kate, a phenomenal physical therapist who succeeded in teaching Elly how to walk again before." I heard them withdraw from the small strip of hallway, the front door slam to a close, and my mother's bare feet pitter-pattered in the direction of my bedroom.

The prospect of returning to Children's Specialized Hospital, to the ward where I battered and starved myself, to learn how to walk, yet again, caused me to cringe. It sounded like a horrific act of regression. Harvard suddenly seemed like a mirage. I was aggrieved that my circumstances had the effect of redrafting my memories, of contracting delightful moments on Harvard Yard into dented and shrunken dimensions, into what felt like an origami version of my past.

18
My nightmares, revisited

Reluctantly, I learned that I must carry myself, that I must not be a bystander in my life but an active participant, directing the waters rather than yielding to the tides' whims.

Yet sometimes, the harsh current is far too overwhelming for human effort to matter. There are parts of me that I will never combat.

Sprawled on the backseat of my father's car, I was overcome by a deep sleep. As we pulled up to the hospital, my mother laid a warm hand on my abdomen and gently shook me awake. My parents did not exchange a word. My mother let herself out of the car and retrieved a wheelchair from the front of the institution. After my parents quietly unpacked my belongings into a private hospital room, they took turns supplying me with what felt like a week's worth of hugs. I remained motionless and did not wind my arms about their necks. I felt stoic and sterile, like someone undeserving of their love, like something caged and breakable.

The following morning, a scintillating orange seeped through the massive square windows. I fluttered my eyelids open and shut several times as if to fractionally orient myself to the three

months of inpatient therapy ahead of me. My right shoulder was lifeless against the bedsheets, and a stinging pain shot around my right chest. Almost automatically, I levered myself onto my right side and popped myself back together. Knuckles wrapped against my door, and Kate's distinct voice sounded. I was filled with a queasy mixture of deference and paralyzing fear.

"El, I knew you liked me, but I was pretty convinced that a one-time stint here was adequately traumatizing for you." Kate's beauty appeared untouched by the last four years. Her celestial blue eyes looked at me fondly, like something they knew well. I felt safe for the first time in months. I emitted a timid grin.

"It's hardly the kind of place you want to come to, even to visit someone else. But I think in your hands I can walk myself out of here soon and never look back." Kate's expression became stern.

"El, this is going to be hard work. I am going to get you moving in the pool every morning, and then we will do a few hours of land work in the afternoons. I am hoping to wean you from your wheelchair to a walker, and, ultimately, to your own two feet. I will get a nurse in here to get you dressed for the pool and wheel you down there." Mechanically, I dug my nails into my thigh under the white bedsheets. Tiny red splotches formed on the starched material. It felt as though I had never left New Brunswick four years earlier.

The next morning, a nurse swaddled me in my navy swimsuit as if I were too infantile to change myself. When I arrived at the pool, Kate was already waiting there, tending to a file of stapled pages on her lap.

"Ready, El?" Kate slid off her chair and came to kneel beside me.

"I'm not sure if I'm ready. I have not been in a pool since my CRPS. Just looking at the water and remembering what it felt like as my discolored foot painfully cut into it feels like a lot, like touching a raw gash. I don't know if I will ever be ready to be alright with everything that happened in this pool. But I'm motivated to get my life back."

"That makes sense, El. You went through a lot in this pool. But you also overcame a lot.

You took your own life back in this water. You can do it again." Kate gave me a look of sympathetic encouragement. She wheeled me to the plastic chair that would catapult me into the water. I broke through the surface and paddled my arms toward Kate like someone who was doggedly fighting for herself.

At six in the evening, I often maneuvered my chair to the crammed game room in the far corner of the ward. I knew all too well how hazardous my isolation could be. One night, a slight sallow child with smooth shoulder-length brown hair ambled into the game room. As nurses escorted her to the vacant seat beside me, I noticed a shaved patch of skin at the base of her skull that enclosed a raised purple scar. I offered her a wide smile, and she stared back plaintively.

"I'm Elly. Want to play Connect Four?" The small child's face brimmed with glee. "That's my favorite. I'm Maggie, and I'm only seven. I fell backwards while I was doing a backflip and almost died last month. I can't walk on my own now." As her youthful mouth moved, forming words that sounded obscene in it, I tried to restrain myself from feeling her grief. I served her a counterfeited smile.

"Then, that makes two of us. I can't walk on my own either." Her face uncoiled like a spring into something innocent and childlike.

"I like that. I like that because it makes me feel not alone." She eyed her lap and wound her fingers into each other.

"You make me feel less alone too. I have an idea. What if we have a Connect Four tournament every night?" She lifted her gaze, shook her head jubilantly, and doled out the game pieces.

Between meals and after my right limbs dislocated, my stomach grumbled painfully and occasionally distended until I retched up everything in it. It felt like a key was turning hard inside my intestines and opening them up wider and wider until my belly billowed out, my skin tore, and hives bloomed on my chest. I decided to keep a daily meticulous record of my meals and intervening symptoms in a gray spiral notebook. I noted things down like "*ate a yogurt at 8 A.M. and vomited an hour later*." I even penned how different consumables impacted me emotionally and mentally. For example, on September 24th, I scribbled the following in my usual downhill cursive: "*Experiment: Ate pizza at noon. Findings: Felt somewhat glum and unable to contemplate much around 1:30 P.M. Broke out into itchy red blotches at 1:56 P.M. Conclusion: Cut out pizza and its composite ingredients.*"

After a month, I appraised my strict ledger and devised a list of taboo foods, including gluten, dairy, pineapples, nightshade vegetables, bananas, soy, cinnamon, and artificial sweeteners. My body became a pseudo *in vivo* laboratory, and I approached myself scientifically like a science problem set. For the first time, I realized that food could do more than sustain, that it could be medicinal and heal. I sipped on chicken broth and lactose-free

smoothies and observed my skin scab over, my rashes vanish, and my abdominal swelling ebb. I was empirically treating a disease I could not yet call by name.

When I was not in therapy or performing food experiments on myself, I busied myself with *Darwin and Design*, an online course offered through MIT. The lectures revolved around Charles Darwin's *On the Origin of Species* and his notion therein that natural objects can demonstrate design without requiring intelligent agency. Late into the night, I hunched over texts by Darwin, Voltaire, and Alan Turing. I tried to determine what it meant to be a breathing object of happenstance in a world without a designer. Unlike during my previous stay at Children's Specialized Hospital, I felt a sudden drive to make something of myself rather than to disappear into emotional and physical disrepair.

Near the end of November, Kate startled me from behind a hardcover copy of *Alice in Wonderland*. She appeared uncharacteristically enthused to see me.

"Ready, my dear?"

"I guess so." I extended Kate a confused expression.

"El, today is the day. We're going to say so long to your wheelchair when we get to the gym." Her smile hit me like a boomerang. I beamed.

Kate wheeled me over to an elevated mat in the gymnasium's center. She rolled a walker toward me. A small pause formed like an opaque shape in the air between us. Kate fumbled in her side pocket for her mobile. She thumbed through the screen and adjusted the volume bar on the side of her phone. Sia's "Unstoppable" rang through Kate's speaker.

"Come on, El. Use the walker and walk." I looked down at my legs distrustfully. Kate laid an encouraging hand at the curve in my lower spine. I felt myself pitch forward at my hips and thrust my weight into the walker. I took a step and then about a hundred more. Meanwhile, Sia chanted "I'm unstoppable. I'm a Porsche with no brakes. I'm invincible. Yeah, I win every single game. I'm so powerful. I don't need batteries to play. I'm so confident, yeah, I'm unstoppable today." I quaked and began to cry, to rid myself of my fear and sorrow. Despite the reality that I was recurrently stopped, I was willing to try on Sia's words and pray for them to stick, if only for a short while.

Renee routinely texted me messages like "*I felt wrong without you in math class today*" or, at her most humorous, "*what's your body's continental drift look like today? Has your inner Pangea reconciled?*" When her name flashed on my mobile screen, I experienced a swift buckling at my knees and a flushed heat work its way up my spine and into my cheeks. Even if I was in bed at the time, I impulsively curled myself into a tight ball like a radioactive substance on the verge of ignition. Her texts accumulated into a lengthy monologue. When I considered Harvard, either directly or by way of Renee, I felt a devastating resentment toward what had become of me. I hated myself for packaging my tragedy into a comedic act, for demanding that I become legible to my able-bodied best friend, for not accepting her calls and sobbing into her ear. I detested my body for compelling me to learn how to walk at age twenty when I should have been progressing, learning about Eigenvalues and epigenetics and charting a future rather than lapsing into my past.

On the morning of November 15, my mother phoned. Rain percussed against the windowpanes, and the sky was a woolen gray. My lopsided shuffle had finally balanced out into an almost normal gait.

"Hello." My voice was scratchy from sleep.

"My Bel. I know you have Kate soon, but we need to chat." The phone felt hot against my ear, but the rest of me shivered as a draft drifted through the window. My mother's voice sounded tentative.

"Sure. Is everything OK?" We were silent for a while. I heard my mother breathe heavily.

"El, the hospital called me yesterday. They told me you are progressing very well with your therapies and that you can be discharged on the twenty-sixth of this month, which, as you may recall, is two days before Jason's wedding. Dad and I spoke about this, and we feel it is up to you whether you feel emotionally strong enough to be there and celebrate Ja."

"Mom, I wish I could be there just like I wish I didn't have to be here. I don't think I can withstand that degree of happiness right after all of my sadness. I don't mean to come off as selfish or inconsiderate. I'm trying to process my suffering. But I'm hardly there yet. I'm not ready to answer to anyone about how Harvard is or why I'm not there. I don't want to play the part of someone who is fragile and ill. I can't stomach looks of woeful remorse. I can't even answer to Renee, let alone to a mass of five hundred people." I wound my Converse laces into knots as I spoke in an effort to manually distract myself from the words that tumbled

out of me. I felt like a vile sister for my response and for the veracity of the feelings that roused it. If I could not put myself and my sorrow aside on the occasion of my brother's wedding, who was I? My mother began to cough. Whether she choked on my words or a beverage, I could not tell.

"Babe, you have been through a lot. I get it."

"I just—I feel like a terrible person. I'm scared that all of these setbacks are freezing me into someone callous and harsh. I hate myself for not being able to get beyond me for Jason. I don't know why you love me. I don't deserve it," I blubbered. I wiped hard at my face until it was rubbed raw.

"You are by no stretch terrible or unlovable. Be gentler to yourself. You've dealt with a lot. You need time to heal, that's all. You are not broken or unfeeling. You need to be patient with all of this. I will call the hospital to extend your stay until the day after the wedding. I will just tell everyone that you could not be released early for medical reasons. Don't worry about all of this. I didn't think it was right for you to come anyway. Jason will understand. I love you, Bel." I wanted to reach into my mobile for my mother's hand, to take hold of the only object that always made steady sense. The call flatlined. In that moment, I could not have forecasted that my suffering would become mundane, that I would learn to fall asleep with the expectation that I would arise in dislocated pieces, that pain would permanently cloud my perspective.

The morning after the wedding, my mother came into my room, and I hurled myself into her, winding my arms about her concave stomach and nestling my neck into the space between her breasts.

"El, we are going to stop at Columbia Hospital on the way home. Some of the blood you had drawn before Dr. Singh performed his procedure was sent to a geneticist there. She has some results that she wants to share with both of us in person." I nodded my head and firmly gripped her hand as we ventured into the world and out of the hospital.

As I followed my mother into Columbia, I felt caught inside the enormity of my thoughts, of what my genes would tell me and how that would mold who I could be. I noticed that I was biting rather insistently at a cuticle and had begun to bleed. I soothed myself by engaging in one of Dr. Stein's mindfulness exercises. I reached inside my coat pocket for the broken seashell, my portable vestige of Dr. Stein.

The geneticist's office was sparsely furnished with an exam table and two small plastic seats. Dr. Chan entered the room with a packet of pages in hand that were stapled at one corner.

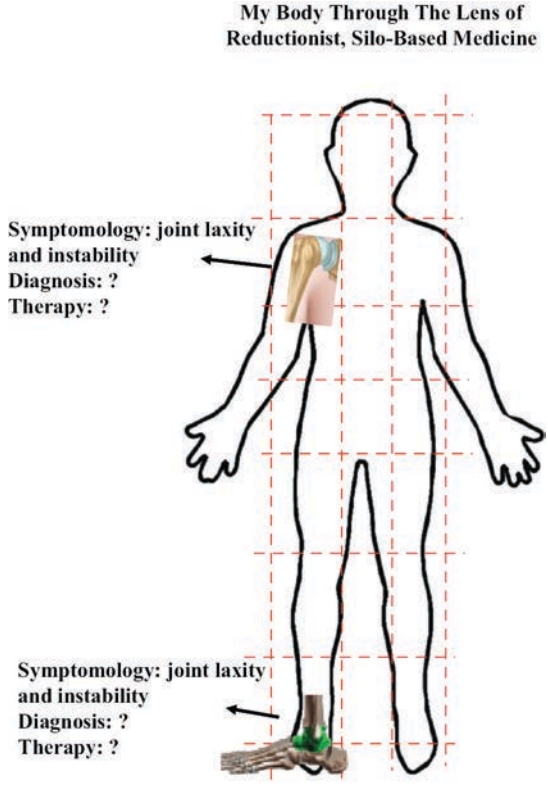
"Elly, it's nice to meet you. I've heard a lot about you from a few of your doctors and scanned over your eight of nine Beighton score in your chart from Mayo Clinic. Based on your exome sequencing, which tells me about all of your protein-coding genes, I can confirm your EDS diagnosis. You have a mutation in *TNXB*, a gene that produces a protein responsible for organizing collagen in your tissues, and abnormalities in other genes that may also be pathogenic. The dislocations that your mother told me about via email make sense in light of this. There is no cure for your disease." She extended the pages of my genetic evidence in my direction, but I did not take hold of them. Beside me, my mother reached for the document that had me and my mistakes written

all over it. I was wrong on a subcellular level. The doctor's ruling felt like frozen tap water against my teeth, and I began to chatter until I felt sick. My mother stroked the backside of my neck, but I flinched at her touch. Each of my cells felt like it was shaking into a panic attack of its own. Dr. Chan continued her conversation with my mother, but I could not make out what they were saying. Each of my approximately 37 trillion replicas of my exon seventeen on chromosome six, along with *KLK*, a gene not then known to be associated with EDS, shouted "gene edit me, please".

19
Harvard, take two

I look to my limbs and to my soul for guidance, for a sense of what to do and where to go. I prefer things in miniature, in small ingestible bites.

I am living in piecemeal and forging synaptic connections with my world, permanent touchpoints that strengthen with time.



The alarm clock bleeped ten to six in the morning. Faint shards of light radiated through the window. My private room in Harvard's Winthrop Inn, supplied with a self-contained refrigerator and an ergonomic desk chair, was on reserve for a physically impaired student like me.

I shot upright and scrammed toward my desk with the resolve of someone who could not afford to sacrifice another moment. I sat on the blue mesh chair and polished off the extra credit linear algebra problem. When I was manipulating numbers, my EDS seemed to retreat, to fold itself up into smaller and smaller dimensions until the three capital letters petered out completely. I drafted an essay for my music course on Wagner's *Die Walküre*, and I glanced at the time in the upper left-hand corner of my MacBook. It was a few minutes after eight. I rushed to ready myself for my nine o'clock math class.

I slipped off my pajamas and bandaged a green bath towel around my chest. I had yet to encounter my undergraduate neighbors, who, evidently, did not maintain my rigid grandmotherly 9:30 PM to 6:00 AM sleep schedule. I sustained a rather lax affiliation with Winthrop House and consumed all of my non-dairy and gluten-free meals at my desk in the sturdy company of homework assignments or novels. Perhaps I had sized up my peers and drawn hasty conclusions that they were somehow too vapid and conventional for me and my suffering.

In my flip-flops and towel, I walked to the hallway restroom. The lavatory stall was closed, and I observed a pair of pale ankles and blue furry slippers beneath the white door. I made for the vacant shower and precipitously felt my body deform under me

like modeling clay. The floor tiles were slick. My palms thudded against the floor, and my right leg was torqued in front of my pelvis. My right foot was upturned at a disturbingly acute angle and turning purple. My right shoulder clunked out of its socket like a cork expeditiously removed from a vintage bottle of wine. With my left fist, I dragged myself against a wall to relocate my arm.

The bolt of the bathroom stall squealed open, and a shriek bounced off the four walls and into the corridor. Quick footsteps moved around me. A student in a nightdress threw me an appalled look. She shoved a slender hand into her side pocket and took hold of her cell phone.

She was plainly too unnerved by my trauma to offer any sort of physical or emotional assistance and evaded my gaze. She was paralyzed by the mere sight of me and preoccupied herself with something on her iPhone screen. To reposition my right ankle in its socket, I pressed my left hand against the sole of my discolored foot. While it had only been three months since my diagnosis with EDS, I intuitively knew how to relocate parts of myself.

"Hello. I'm calling to report an emergency in the second-floor women's bathroom at 1201 Massachusetts Avenue. Two of a girl's limbs are detached from her body. Come soon." My classmate's voice was desperate. As my ankle locked into place, color and sensation flooded back into my limb. I gathered my towel about me and stood up. My shower would have to be postponed until tomorrow if I was keen on arriving in a timely manner to math class. I shifted my weight onto my left leg, and the repulsed stranger gave me a critical, appraising look.

"Where are you going? I called 911. Medics should probably check you out." Her tone was condescendingly parental.

"This is not a one-off fluke occurrence for me. I have a genetic disease. I never call 911 or go to the ER when things like this happen. If I did, I wouldn't have enough time in a day to live my life."

In January 2016, I resumed college with the insight that I was somehow girded by my EDS label. I would require a year to grasp how my diagnosis would shape my Harvard experience. As I walked from the Science Center to Widener Library, the greens, crimsons, and limestone in the Old Yard appeared dulled under the white blanket of snow. I chewed on the possibility that the manmade structures and the manicured nature had not simply faded by the passage of a year and by snowfall. I was the variable. My suffering had coursed through me like a decomposition reaction that yielded changed fragments incapable of reannealing. I felt a troubled absence of trust in medical experts and, more distressingly, in my own two feet and where they could take me.

I frequently stumbled upon Renee between courses, but I restrained myself at arm's length. She had outgrown solitude and moved through Harvard Yard with a posy of blonde girls. Renee messaged me invitations to a cappella concerts, but I either contrived an excuse or, occasionally, did not bother to reply at all. I felt an insuperable distance between me and what I perceived as normal. I felt queasy at the sound of other people's laughter. I drowned out the Harvard social scene with my diligent work ethic and the self-experimentation I initiated at Children's Specialized Hospital.

I continued to conscientiously journal my dietary intake and consequential symptoms, but found myself craving a therapeutic roadmap that Western medicine could not offer. The online EDS forums and blogs consisted of querulous remarks like "*Six of my limbs dislocated today, and I want to take my own life*" or gory images of distorted and discolored extremities with captions that read "*I'm breaking, and I have evidence to prove it*." In short, these sites communicated the hardship of individuals who had been wrecked by their own suffering. The emotional malaise I observed petrified me more than did any physical manifestation of my EDS. Scrolling through these webpages, I wept as I considered that my life could also amount to a heap of gruesome photos and capitulating remarks, if I let it. Reflecting from the distance of half a decade, the knowledge that each case of hEDS is effectively its own n-of-1 experiment soothes me. The disease's phenotypic and genetic heterogeneity renders the path before me unpaved. I will experience setbacks and interludes of relative wellness, but, not knowing when these periods will arrive nor how intense they will be means that hope is never completely out of reach.

One evening in February after I finalized a neuroscience problem set, I occupied seven hours on Google and PubMed, plugging in search terms, including "*TNXB* haploinsufficiency and EDS," "collagen regulation," and "boost collagen production nutritionally." I scanned the literature that provided an overview of collagen subtypes and the role of *TNXB* in the extracellular matrix (ECM). I was especially drawn to one article, entitled *Haploinsufficiency of TNXB Is Associated with Hypermobility Type of Ehlers-Danlos Syndrome*, in which Manon C. Zweers (2003)

and his colleagues investigated the inheritance of heterozygous *TNXB* coding mutations among 20 individuals within four families (Zweers et al. 2003). All of the family members exhibited an approximate 56 percent reduction in TNX serum levels with respect to healthy control participants. While nine of the 14 haploinsufficient females demonstrated a Beighton Score of two or more and the same hypermobile EDS phenotype as me, including joint hypermobility, chronic pain, and piezogenic papules, none of the six males heterozygous for a mutation in *TNXB* were symptomatic.

Based on their pedigree analysis, the authors concluded that *TNXB* haploinsufficiency is a dominant trait, which whole exome sequencing would reveal I inherited from my mother.

Perhaps my mother's cardiac scare and her Raynaud's disease, which temporarily restricts blood flow to her fingers and toes, are due to her possession of only one functional copy of *TNXB*. Perhaps her scleroderma is an ironic blessing that renders her EDS phenotype hidden. Or, perhaps, my other genetic defects currently being researched interact with my mutant *TNXB* through a process known as epistasis to yield my clinical presentation and astounding Beighton score of eight out of nine. Despite being a subject in two ongoing EDS trials, I am a scientist at my core and am inclined to hypothesize. Perhaps in the future, my genetic and phenotypic data point within the spectrum of hypermobile EDS will be fully understood and actionable. But until then, I embrace the opportunity to become my own experiment, to accept my EDS diagnosis but to simultaneously do everything, within reason, to live outside of the confines of illness.

Finally, at four that morning, I jogged my cursor over a link to Bulletproof, a scientifically based wellness and nutritional company. I scrolled through entries crafted by Dave Asprey, the biohacking guru and founder of Bulletproof. I perused Asprey's biography, in which he laid bare his affliction with chronic pain and fatigue secondary to toxic mold poisoning, arthritis, obesity, fibromyalgia, and even hypermobility. He abdicated high-power positions in the cloud computing sector and cybersecurity to hack his own biology, to wrest back control of his body from disease. After years of self-experimentation, Asprey devised the Bulletproof Diet in 2014, a modified ketogenic diet enriched in saturated fats, including avocados, coconut oil, nuts, and protein derived from sources such as pasture-raised and hormone-free animals. In one post, Asprey compared the human body to a distributed computational network system in which the source nodes consist of mitochondria, the body's subcellular energy generators. Asprey innovates avant-garde supplements that primarily enhance mitochondrial regeneration and function, thereby presenting the body with supplemental energy to heal itself and boost mental acuity.

I navigated through the retail items on the Bulletproof site and noticed that the majority of Asprey's merchandise consisted of collagen packaged as powders and protein bars. Tenascin-X is known to interact with collagen fibrils and regulate their deposition in the ECM; I reasoned that if I could not genetically edit myself, I would consume Bulletproof collagen daily with the faint flicker of hope that some of what I ingested would be integrated into my ECM. For the first time since my diagnosis, I felt a firm conviction that I could be my own advocate, that I possessed

ownership over my body rather than the inverse. If Asprey could expunge himself of multiple chronic diseases by adhering to his protocol, I could certainly manage one by following in his stead.

I reached for my mobile and fingered my way to Bulletproof Radio, Asprey's podcast. I listened attentively to his interviews with functional medicine physicians and laboratory researchers and took meticulous notes. I recorded remedies related to the gut-brain axis, strengthening connective tissue, and chronic pain, effectively commencing an auxiliary educational degree from the combined instruction of my bizarre body and Dave Asprey.

When rays flickered through my bedroom window the next morning, I squinted my eyes alert. I had, unwittingly, fallen asleep at my desk. My right hand was a ghostly white, and a throbbing voltage pulsed up and down the inside of my right arm like sensory lightning. I gripped my right hand with my left hand and dangled my dislocated arm in front of me as it resounded into its socket. I moved prudently to the freezer and located an ice pack. After I positioned it about my right bicep, I fastened yesterday's leggings over the frozen packet in a double knot.

I slid into my desk chair before my MacBook and opened Safari to the Bulletproof blog page, a message board through which Asprey's acolytes exchange opinions. I sifted through discussion threads concerning postural adjustments until I came upon Rolfing Structural Integration, a chronic pain treatment that reorganizes fascia, or the body's collagenous tissues that include the cells that comprise and stabilize the ECM. In response to a blogger's account of his back discomfort, an Asprey devotee alleged, "*Rolfing can elicit deep structural shifts. It can integrate your parts*

so you move more gracefully as one unit." With alacrity, I opened a fresh browser and keyed "Rolfing in Cambridge, MA" on Google.

The following afternoon, I meandered down Massachusetts Avenue with my eyes decisively planted like internal hawks on my knees. In lieu of adequate proprioception, patients with EDS commonly rely on visual feedback for joints to remain aligned. White earbuds jammed into my ears, seeping Nobel Laureate Eric Kandel's *In Search of Memory* into me. In this biography, Kandel traces his ascent from his Jewish upbringing in Nazi-occupied Vienna to his research on the biological basis of learning and memory. He attributes his passion for the science of mind to a fierce yearning to comprehend the neurobiological mechanisms at work in Nazi brains. I developed a quick fondness for Kandel's candor and, most of all, for his capacity to at once recollect his childhood strife and to transform an experience that could have broken him into his raison d'être.

I reached a narrow multifamily house. A slim woman with salient collarbones appeared at the entry.

"I'm assuming you're Elly. I'm Jazmine. Come on in." I trailed behind her up a flight of stairs. She guided me into a small office with scandent leafy stems that wrapped around the interior. In the center of the room, a massage table was poised on four wooden legs.

"So, what brings you to Rolfing? From your email, I understand that you have EDS, which I read up on yesterday. I have not worked with any clients with your disease, but I'm pretty sure I can help."

"I dislocate somewhere between one and three limbs per day, and I'm confident that my posture and gait habits have been derailed by my right hip and ankle dislocations. Because of my

EDS, my proprioceptors do not function as they should, and I feel unbalanced when I walk. I know how to pop myself back into place, but my pelvis often feels misaligned." As I spoke, I felt a pleasant detachment between myself and my explanation. I felt as if I were clarifying a scientific phenomenon that had nothing to do with me. Jazmine scrutinized me, revealing the hidden whites of her eyes.

"I am incredibly impressed with your management of all of this. I think we will work well together. You ready?" I tilted my eyes until they met Jazmine's and nodded.

"So, first, you need you to take off all of your clothes. You can leave on your undergarments, but that's all." I glanced around her face for some suggestion that she was being flippant but came up empty. Jazmine's expression was vacant, save for a diffident smile. I unzipped my coat and observed my garments as they fell on the floor. Jazmine's gaze fixated on me as my nakedness became complete.

"Can I see you take a walk beside the table?" I paced the short distance three times. "You can lie down now. Your pelvis appears to be rotated. Your right hip is significantly lower than your left one, which may be throwing off your gait and sacroiliac joints. I think this is partly consequent to your right-sided dislocations, to your winged rib cage, and to your lordosis. Can I try to stabilize you from your pelvis?" Jazmine's voice was soft. As I got into position on the table, her eyes swept across my face several times, construing my discomfort with my own nudity. I bit into my upper lip with my lower teeth to ground myself in pain that I could induce and bring to an end as I pleased. Jazmine's hand crept under my pelvis like a large insect.

Electricity wound into a knot in my left back.

"Your muscles are cramping around a nerve, which is why you feel some pain. I want to release them so I can equilibrate your hips. That's OK?" I jammed my teeth more intensely into my lip and shook my head. Jazmine wrenched her arm further under my back. She clasped my hip bones in her palms, pressing me together and fanning me apart like a respiring accordion. After a short while, she took a reprieve from the rocking motion and held me still by the hips. Her expression became studious as though all of her neurons were revved up in concentration.

"Alright, I think that should do it. Can I see you walk a bit?" Her face broke into a serene grin. I suddenly felt arrestingly safe, like my body could be a work in progress that Jazmine and I shared.

"Sure," I replied hesitantly. I inched myself incrementally upright. My eyes overflowed with liquid joy.

"You OK?" Jazmine's voice trembled with disquiet. I flashed her a full-toothed smile. "I'm way more than OK. I don't think I've ever felt this stable on my own two feet.

You've done more to help me than any doctor has in the last year. Can I see you every week?"

"Yes, you can. We are going to get you your body back." Her voice rang like a lullaby, something I would invoke again and again until the present day to set me right.

On Tuesday afternoons, I habitually attended Professor Lichtman's office hour. More frequently than not, I was the only undergraduate in the neuroscience professor's audience, and the designated

weekly hour elapsed while we discussed his lectures on action potentials and my medical past.

"I'm really enjoying your lectures. It may sound strange, but your lessons speak to me on a rather personal level. I've been through many medical setbacks and was recently diagnosed with Ehlers-Danlos syndrome, a congenital connective tissue disease. In addition to joint instability, I live with dysautonomia. I have also experienced CRPS in my left foot. My body has provided me with an all-too-extensive education with respect to how the human nervous system can go wrong. Your instruction is permitting me to come to terms with what happens when things actually function as they should. If only on an intellectual level, your course has enabled me to view the human nervous system through the lens of math and physics: As a well-regulated network." Professor Lichtman nodded his head and grinned compassionately. I felt a vague satisfaction in myself, EDS and all, as I hesitated for a quiet few seconds.

"I have a hypothetical question based on your lecture material. If you increase the number of voltage-gated calcium channels on the pre-synaptic terminal, quantal content would increase but quantal size would remain unchanged, right? Whereas, if you add botulinum toxin, the quantal content would decline and quantal size would also go unaltered, right? I just want to be certain that my understanding is correct." Professor Lichtman bowed his head in thought, and his charming smile resurfaced.

"Yes, Elly. You are correct. I think your understanding of the topic is more than comprehensive. I want to get something from my briefcase. One moment." He ducked over the arm of his chair.

Professor Lichtman reemerged with a sealed fist that he steadied on his desk. He uncurled his pale fingers and exposed a minuscule button that read "I climbed mount potential" in a fine typeface. He slid the metallic circle in my direction.

"I circulated these at the conclusion of class last week after I completed my lecture set on resting and action potentials. I noticed that you did not receive one. You more than deserve it for all of the effort and dedication you continue to put into this course." I unhooked the needle on the pin's underside and fastened it onto my sweater.

"Thank you. I love it. I think mount potential is the only mountain this body of mine is ever going to climb." Professor Lichtman produced a chuckle and studied me.

"Same time next week?" His question was rhetorical, but I was pleased to let it percuss against my eardrums like a gentle rain.

"Yes, of course. I will see you in lecture tomorrow." I withdrew from Professor Lichtman's office and skipped so exuberantly down the stairs that I nearly fell twice.

Before the neuroscience lecture, I scribbled notes in linear algebra class. In our small classroom arranged with two rectangular tables and eleven seats, Professor Belanger was well versed in the precise number of degrees she had to turn her head immediately after she tossed a question into the air like a verbal Frisbee I would catch over and again without dislocating any of my parts. She jotted a system of four linear equations onto the whiteboard and requested that we row-reduce the augmented matrix to arrive at the solution set. My hand cramped against my mechanical pencil. I pressed on, recording my way to the

reduced row-echelon form, etching my pencil so fervently into the page that it tore on several occasions. My classmates' chatter seemed to be silenced by the numbers and operations that I performed as I wound down the initial matrix into something splendidly simple. After a two-minute stretch, I unclenched my pencil, and it sounded against the table. I reentered the reality of the classroom. I blasted a hand mechanically into the air. Professor Belanger gestured for me to speak up.

"The augmented matrix represents the linear system $x1 = 1$, $x2 = -3$, $x3 = -4$, $x4 = 1$, which clearly obtains only one possible solution." My voice was swift as though my tongue were competing in some verbal marathon.

"That's exactly correct, Elly. Nice work."

My recurrent dislocations cemented into a sort of existential barrier between me and my peers. Their reveling in finals clubs and fraternity houses felt like the perfect converse to my evenings, which passed with bruised parts of me mounted on ice packs. Intermittently, I processed my peers' apparent sense of immortality as alarmingly at odds with my acute awareness of my own impermanence and brokenness. When this line of thinking cropped up, I felt an urge to write my way through it and into someone I no longer felt sorry for and even took a startling pride in being. Living with an invisible disease, an illness that only spasmodically came to my surface in the forms of braces or kinesiology tape, meant that my classmates probably often glossed over the fact that I was not built like them, that my body gave way under me multiple times a day. Ironically, I delighted in suiting myself up in neon violet shoulder and hip braces after

waking up out of socket. I felt a sense of honor when my peers eyed me with apologetic expressions creased with knowledge that I was somehow different. This almost physical pang to be seen motivated me to publish my poetry about EDS and its hold over me in *Prescriptions*. One evening, as I iced my knee, swollen from a recent patellar dislocation, I produced the following piece that was published under the title "The Hypermobile Zebra" in the mid-semester issue.

A stagnant, dynamic balance is the fulcrum on which my fragile world rests. My pieces are normally askew, off-kilter, and out of place.

The chaos of my body makes music: A crack here, a pop there.

My body defies anatomy, overlooks aged medical textbooks, and has a dialogue that rings true to this: Left knee cap to the rest of my joints, "So, I'm considering relocating but I want to keep it on 'the down low,' so don't say a word. I'm popping out now and trying out the real-estate on the inside of the leg."

All of a sudden, I am halted in my tracks.

But I can usually retaliate, counter the popping out with the popping in, put the world's most insane jigsaw puzzle back together.

Here's the upside: Every right and painless forward step counts and matters.

I am the conductor of my body's symphony, trying so hard to channel the allegro to a middle place, so I can put myself back together like cosine waves I can easily integrate.

20
Back to benchwork

Genomes off kilter due to untrustworthy polymerases and repair mechanisms that promise fidelity, but render disease. Slipping and expanding a repeat of three simple letters, CAG, nucleotides that promise to encode life, not to wrest it from one's grasp. We classify prokaryotes as the simplest of organisms, but then let them know they are worthy of assisting us. Armed to transcribe a remembered virus, these simple beings rely on innate gene-editing machinery. I use their evolutionary hack, exchange one base for another, and rectify nature's blunders while mutant genes inside my cells mime "gene edit us next."

That summer, as a Harvard-Amgen Scholar, I resumed scientific research at the Broad Institute's Liu Laboratory. Four years had expired since my exploits with Rich at Rockefeller University, and my admission to a prestigious biotechnology program felt like isolating a binary switch that might restore my inner scientist from the clutches of EDS. I was incontrovertibly invested in the minutiae of my project, but, simultaneously, I pursued a more sweeping and private agenda. Tacitly, I probed whether scientific research was something I had to discard, like a histamine-rich food, to maintain the basal level of dislocations that had become my new normal.

The Broad Institute is a monumental edifice of variegated gray marble and glass located in Cambridge's Kendal Square. As I approached the complex's entrance, I perceived an aesthetically disarming woman who smiled and extended a hand in my direction. Manda was a sublime mixture of brilliance and glamor.

"Are you Elly? I'm Manda, your mentor." I nodded. She pivoted in the direction of the staircase and mounted the two flights to the laboratory. Silently, I trailed behind her. After she flung the door on the second-floor landing ajar, Manda motioned me to a red couch. I occupied the seat across from her and retrieved a spiral notebook from my knapsack.

"So, Elly, I'm going to have you assist me with a project I'm working on involving polyglutamine diseases, including Huntington's disease and spinobulbar muscular atrophy. These diseases are consequent to expansions of the three-nucleotide sequence CAG, which encodes the amino acid glutamine. Proteins with expanded polyglutamine tracts aggregate in the cell and fail to function properly. I want to use base editing to effectively edit CAG to CAA, a nucleotide sequence that also encodes for glutamine. Inducing this silent mutation is thought to slow the repeat slippage process. To achieve this end, I need you to design and amplify guide RNAs that will provide the base editing machinery with site-specific information so that the cutting occurs at the location of interest. Does that make sense?" I enthusiastically shook my head as I scribbled down Manda's portrayal of my project on loose-leaf.

"I think you should begin with reading review articles concerning base-editing technology. When you feel you have a

solid grasp on that, try to design primers that are each twenty nucleotides in length and bind to the locations of interest. I will send you reference sequences via email. There's no rush with this. Science is really just troubleshooting. From your resume, I quickly deduced that you're a terrific student, but science in the lab is not as simple as penning reaction diagrams and stereochemistry. Don't be afraid to fail." Manda gave me a demure smile.

"Well, if that's really what science comes down to, I anticipate that I will get on rather swimmingly with it. As I indicated in my email, I live with a connective tissue disease that has habituated me rather well to failure. My life essentially boils down to nonstop troubleshooting. Perhaps, if I finish my summer project early, you can try gene-editing me. I promise not to hold you liable for any off-target effects." Manda released an amiable laugh and escorted me to a workstation.

I passed five hours scanning articles on polyglutamine diseases and gene-editing. As I read, I sketched awkward illustrations of uncoiled DNA segments and the requisite base-editing components. At noon, I copied the reference sequences from Manda's email into a fresh Word document and devised twenty guide RNAs by the day's end. As I departed my desk at ten past six, I was overcome with a callow faith that my EDS would not hinder my research into other people's diseases, that I would define science more than it would circumscribe me.

Later in the week, Manda invited me to accompany her at her lab bench while she centrifuged samples. She extended me a pair of nitrile gloves and a slimy translucent gel.

"These are my samples you should load into the wells. Before you pipette anything into the wells, you need to insert some of the loading dye into the sample tubes. You are familiar with running agarose gels, right?"

"Yes, that's right. I ran many gels at Rockefeller, and, more recently, in my biochemistry lab section at Harvard." We swapped hurried grins. I transported Manda's specimens to the gel-loading station at the opposite side of the lab. I prepared the samples and infused one blue-tinted mixture and then another into depressions in the solidified agar. As I ejected a third specimen from my pipette, a cracking noise emanated from my right thumb. My thumb throbbed for a minute or two before it was drained of all color and feeling. I sped to the restroom in the corridor beyond the lab. Once I barred myself in a stall, I gripped my right thumb between my left thumb and forefinger and jammed it into the socket as I held my tears at bay. I reviled the thought that this incident would cement my dire fear in my mind that my EDS and my scientific ambitions were at odds. I hastily returned to the lab and finished preparing and running the gel without contemplating the future or anything but the agarose and pipetted samples that lay before me.

For the remainder of the summer, I preoccupied myself primarily with computational tasks. When I occasionally dared to perform benchwork, my legs jittered and threatened to imminently buckle under me. I manipulated specimens and equipment with the tense stiffness of a geriatric resigned to the fact that my control over my body was winding down.

Following a visit with a gastrointestinal expert in July, who formally diagnosed me with mast cell activation syndrome, I persuaded

my parents to transfer my belongings from Winthrop House to an off-campus apartment. My rationale was twofold. First, I resented when my EDS aired itself in public, when my ankles dislocated in the company of other undergraduates, and when my peers responded to my disfigured limbs with derisive sympathy and evasive glances. I preferred to conceal my trauma like a secret and could only do so in the privacy of my own quarters. Second, on account of my intestinal distress I wanted the option to prepare my own food rather than eat in Harvard's dining hall. Dave Asprey's blog posts provided me with chicken, bone broth, and dairy-free smoothie recipes that I followed studiously. I had come to terms with the irreducible and unforeseeable complexity of my EDS.

While my mother unpacked my belongings into a rental studio on the seventh floor of 29 Concord Avenue, I systematically ordered my Bulletproof supplements and collagen protein powder on the kitchen shelves. When my duffels were emptied, my mother retrieved a cylinder of blue tissue paper from her jean pocket. She clasped a semitransparent wrapping between her palms as if it were a miniature infant and examined me.

"Bel, I get it if you are averse to this proposal, but would you consider letting me hang a mezuzah on your doorpost?" My mother's words sounded deliberate, like punctuation marks.

Within the mezuzah, the Hebrew Shema prayer inscribed by a reverent hand on parchment echoed something particular in my mother, a fragment of her character I did not possess. Just as she could not personally own my dislocated limbs, I could not directly identify with her religious fervor. I could only experience

it secondhand. The religious text rang hollow in me with the staleness of a poorly written novel I wanted to permanently slot onto my bookshelf or donate to charity. But my feeling for my mother exceeded my distaste for Jewish tradition. I felt my head nod robotically.

"I thought this would be more pleasant for you if I made the occasion something you could relate to, something almost scientific. I found a three-minute clip by Mayim Bialik, the Jewish neuroscientist who plays Amy on *The Big Bang Theory*," my mother continued in a convincing tone. She squatted on the wooden floor and scoured her purse for her iPhone. I surveyed her as she fingered her way to YouTube in an attempt to extend her religiosity over me. Mayim Bialik's voice dribbled out of my mother's speaker, describing a mezuzah as a physical reminder of the borders between her piety and the remainder of the world. Bialik articulated, "*Boundaries help me constantly redefine what works for me and what doesn't. I will devote my life to creating an existence that is defined by boundaries*." I felt tears swell into a lump in my throat as the video dissipated into thick silence. My EDS felt like a sufficiently watertight boundary between me and my reality that anonymously haunted my past, hampered me from experiencing Harvard on my own terms, rendered my right shoulder dislocated each morning, motivated me to forsake socializing to arrange myself on ice packs each evening, and ingrained a deep-seated internal suspicion of what was yet to come. The prospect of assuming my Judaism as an auxiliary boundary caused me to cringe. But I could not rebuff my mother. I let myself slip into her arms and displayed a deceitful smile that felt wrong beneath my faint tears and the feelings they bore. I inspected my mother as

she tacked the enclosed scroll to my doorpost as if she were a chemical reaction in the laboratory that required my full attention until it terminated.

In my junior year, I enrolled in a seminar that examined multifactorial disorders influenced by genes, the environment, and the interplay between these factors. At the classroom table, Dr. Ruvolo directed our weekly discussions with her head hunched over scientific articles annotated with interpretations penned in her blue ink. I perched on my mesh chair, a fixture that Harvard's Accessible Education Office maintained in all of my classrooms to stave off my hip dislocations. I flipped through this week's scientific literature on autism as the seminar began to take shape before me.

To my right, a student named Olivia braced herself as though she were rehearsing a thought before it glided out of her mouth. Seated beside Olivia, I could not have anticipated that she would renew my lease on friendship and edify me more than any other companion, with the exception of my mother.

"Oliver Sacks' "An Anthropologist on Mars" provides a fitting and complementary analog to this week's journal articles. He paints autism with a human face that extends beyond the symptomatic elements of the disease enunciated in the Nature article. At the start of his essay, Sacks touches upon the history of the disease, which is elaborated upon in my favorite neuroscience book called *NeuroTribes*. I thought I would recommend it to the class." I regarded Olivia as her words sprang into the atmosphere. Her voice was soft and unpretentious, and its contents and delivery impressed a crude mark somewhere deep inside me that

manifested as an uncharacteristic desire to reach beyond myself for company. In her, I perceived a flicker of my own appetite for science and literature. At the conclusion of the seminar, I introduced myself to Olivia. We decided that we would stroll around the Charles River during the coming week.

After my classmates' footsteps scattered, I dawdled behind Dr. Ruvolo down the tapered corridor to her office. I frequently convened with her for hours at a time that we crammed with dialogue surrounding the course readings, my final term paper, or my EDS. I let the door fall to a close behind me and installed myself opposite Dr. Ruvolo at the round table. I felt her considerate eyes search me as I fished out a sixty-page stack of typing paper bound by an oversized black plastic clip from my backpack.

"Thanks for making time for me, yet again. I wanted to discuss two things with you, if your schedule permits. The first is about Sacks' "An Anthropologist on Mars." The second is in relation to my final paper. I read Sacks' essay through twice, and, each time, Temple Grandin's words caused me to weep. Her words felt like they could have come from me, or at least sounded like things I would want to hear myself say about my EDS. Sacks describes autism as something larger than a disease, something that is akin to an overriding mode of being. Like Temple, I mainly keep to myself because of my disease and tend to observe the world around me from a distance as if through a telescope." I recovered Sacks' collection of essays from my bag, and cracked it open to a page flagged with a bright pink adhesive note.

"This quote by Temple, in particular, really resonates with me. She tells Sacks, '*If I could snap my fingers and be non-autistic, I would*

not—because then I wouldn't be me. Autism is part of who I am.' That is a sentiment I want to grow into about my EDS. It's difficult to feel that way all of the time, but Temple's words really struck some type of chord in me. I honestly don't think I would be at Harvard, let alone in this office right now reflecting on Temple's words, if I didn't have EDS. My disease is a daily struggle, but it has and continues to shape me for the better more than any other facet of my life. Right now, in your office, it almost feels like a blessing, something that landed me in the here and now." Dr. Ruvolo layered a delicate hand over my own.

"Elly, I knew this piece would speak to you, as things often do. You are just that kind of person."

"I know I'm several months early and forty pages over the limit for the final paper. But, as you know, I opt to get ahead of my schoolwork as much as possible with the foreknowledge that I will have days that my EDS does not permit me to get much done." I felt a wry smile crinkle onto my face.

"Of course, can we discuss your thesis?" Her voice lilted with attentiveness.

"That would be fantastic. I'm writing this paper in honor of my maternal grandfather, who recently died of Parkinson's. The gist of my thesis is that gastrointestinal disturbances in Parkinson's, which manifest over a decade before the motor deficits, should not be viewed as symptoms but as culprits in disease pathology. I investigate the role of the microbiome in the setting of Parkinson's and use scientific literature to demonstrate that microbial imbalances contribute to the hallmark motor deficits associated with Parkinson's disease."

"Elly, that sounds really wonderful. I am truly looking forward to reading your always brilliant words in full. As usual, you're well ahead of the game with respect to your work. I'm quite pleased with all of your progress and commitment to my course." We ascended from our seats in unison, and I motioned for the brass doorknob. Dr. Ruvolo wrapped her arms about me in a gentle embrace that I ardently requited.

The next day, I slumped in a plush lecture chair in a course on cultural evolution circa 3500 to 300 BCE. I felt myself squint to make out the Sumerian clay vessels projected onto the massive monitor at the classroom's fore. A hushed ringing shot through my ears like a dull bell sounding over and again. I rejected these feelings and brushed them off as though they were not mine. I deftly tiptoed to a vacant chair in the front row under the false premise that my sensations were a function of distance, that I could walk myself out of them by narrowing the gap between my eyes and the display. Hindsight is always incorrigibly 20/20. I had no means of determining, or even of conceiving, that I was leaking, that my cerebrospinal fluid sheathed in my faulty connective tissue was seeping out of my dura. The off-putting perceptions seemed to retreat as the class bell tolled, so I shrugged them off. I did not attach significance or words to these nebulous symptoms. I should have noticed them as precise warning signs, sensory missives from my failing body that communicated I was, quite literally, spontaneously rupturing at my seams.

"Hey, Elly. It feels like a cold morning for a river walk. Want to wander toward Oxford Street and see where we end up?" Olivia grinned.

"Sure, that sounds great. Also, I don't want my brace to become a proverbial elephant in the room between us. I have a connective tissue disease called Ehlers-Danlos syndrome, which, in everyday English, means that my body is effectively unglued. I frequently dislocate my limbs by doing routine tasks, such as waking up in the morning, putting my shirt on, brushing my hair—you name it. I just wanted to be up front about it, so it does not come across as a taboo third rail. I know it sounds pretty surreal, but it's my life. This morning, my shoulder dislocated, hence this lovely purple straightjacket." I gestured my left forefinger at my brace and slanted my attention toward Olivia. She gave me an encouraging expression, and her face was fraught with a unique variety of support deprived of pity. The wind twisted between us like an invisible sheet.

"Thanks for being so upfront about it. I can't even begin to imagine what it must be like to live with a condition like that. You don't have to feel strange at all about what you have to put up with. In fact, I think it makes you even more extraordinary than I already supposed you were. You contribute so many thoughtful comments and questions to Dr. Ruvolo's class. But, dealing with all you put up with makes what you say all the more powerful. Also, Elly, everyone struggles with their own stuff. By the way, did you manage to obtain a copy of *NeuroTribes*? If not, I can lend you mine." I eyed Olivia's mouth as it shaped itself into words. Until that nippy morning, I was completely irresolute about the type of response I wanted my coming out to rouse or how I fancied people should coordinate the creases on their faces when I alerted them of my EDS. Beside Olivia, I felt an unexpected rush of aplomb. My teeth quit excavating harsh shapes into my lower

lip, and my gaze softened as if the blue tent of sky blurred into a pastel drawing.

"Because of my unstable shoulder, it's tough for me to physically hold a book, but I downloaded the audio version of *NeuroTribes*. I love it. The nearly concurrent discoveries of Leo Kanner and Hans Asperger hit me as particularly fascinating. I found it curious that they came to radically different conclusions about autism because of the spectral nature of the disease and where their respective patients fell on the continuum. I know you study neuroscience, and I overheard you tell someone in the seminar that you work in a lab. What type of research are you conducting?" Her countenance gleamed in the fractured sunlight as it soaked through the tree branches overhead.

"I study the escape reflex of zebrafish in the Engert Lab to understand the neuronal algorithm implemented during goal-directed behaviors, such as avoiding a barrier in a water-filled compartment." Olivia fetched her phone out of her left pocket, revealing what appeared to be a progressive electronic work of art.

"What's that? A depiction of a moonless night sky with red stars?" Olivia erupted into laughter.

"No, silly. It's a confocal image of a zebrafish's hindbrain. But you are right on with your description. I laughed because that's exactly the reaction my father had to it."

"Well, perhaps we are related. Or, at a minimum, perhaps I'm related to your father." Olivia gave me a genial wink.

"I feel like we're related too, Elly. There's a sense of knowing I feel with you." I felt an unadulterated grin wipe itself onto my face.

"So, how did you become interested in neuroscience to begin with?" I felt Olivia examine me with an inner understanding of someone who did not need to read up to speed on the litany of my misadventures to fathom who I was.

"Well, my mother is a painter. My father designs furniture. So, science, *per se*, does not really run in my family. In high school, I loved physics. I think my dedication to neuroscience was driven by my deep interest in the human experience as a lover of art and literature.

Neuroscience, to me, is a form of physics because it boils down to our innate ability to understand the physical world. As I got interested in the visual system and its ability to create optical illusions, I realized that my mother's artistry is itself a form of neuroscience. Artists rely on our naïve physics by using color, shape, shadow, and line to evoke emotion and direct attention." Olivia rotated her face toward me as she offered me a synopsis of her life. Her words vibrated into me with a guileless sincerity.

"I never met someone like you, someone who reminds me of the best parts of myself. I share your blended passion for literature and science. Do you also enjoy writing?" I suddenly realized that I was clueless with regard to where we were or where we were headed. Ambling beside Olivia felt like letting the whole of me slide into a meditative trance from which I never wanted to retreat.

"Yeah, I like writing. Do you?"

"I start most mornings by writing a poem. It acts like a sort of windshield wiper that runs across the inside of my mind, clearing

out the thoughts that won't serve me well in the upcoming day." Olivia exuded a hasty grin.

"Can I see some of your poems? I understand if you don't want to share them, of course." Cool ether dashed into my eyeballs, and I felt my eyelids stretch apart with glee.

"I would love that. I will send them as soon as we get unlost from wherever we are."

The following semester, Olivia accompanied me to my History of Science section. After we mounted the red stack of stairs before Sever Hall, we wove our arms about each other. I turned about-face as Olivia departed into Harvard Yard. I could not have known that I was parting from anything other than my best friend, whom I anticipated encountering the next day. I could not have known that this was the beginning of an end for me, that the waistband of my EDS was being pulled tighter and tighter around me until it would come close to taking my life.

I ventured into my classroom and occupied a seat in the room's rear. I inclined over my notebook, filling pages with scraps of comments. My head began to feel unnaturally heavy. My eyelids flickered to a close, and the dull roaring sound recrudesced. Rapidly, I felt wholly unqualified to hold my head over my shoulders. I paddled my chair against the wall behind me and leaned my head against it. If I squinted, I could read my instructor's lips, but his words were no longer coherent. Or, perhaps, my auditory neurons did process, but they were drowned out by the resonant rattle my body created as my cerebrospinal fluid trickled out, disturbing the homeostatic pressure in my inner ears. I felt

my body incrementally skate off the seat, but I could do nothing to halt its downward motion. I heard thundering footsteps lurch in my direction. Then, my whole world went a dizzying black.

I stirred awake in Beth Israel Deaconess' emergency room. My mother's fingers caressed the soft inside of my left forearm. Intravenous hydration seeped through a narrow tube that fed into my right arm. She reported that the attending physician deduced I had a case of simple dehydration. I would need to remain joined to the IV pole overnight to replenish my fluids. I felt my brain resume thinking and my head recover into something I could carry as electrolyte-rich fluid sped into me. The following morning, I continued pushing through junior year and went on to be designated a John Harvard Scholar. I went on as though nothing was the matter until it was. I went on not knowing that my Elly-ness was percolating out of me drip by drip, day by day, until I would find myself, once again, raided of a life that I would soon learn I could not trust.

21
Coding my way through coffee and biohacking my way through life

I may have a disease, but I am far greater than any one label,

far more powerful and more overflowing than any one box, any one division.

I leap into days, stop the bleeding, fix the disjointed limbs, and move onto what matters.

I am my own doctor, my own healer, my own advocate, my own consolation, my own inspiration. There is more to me than I know.

The linen sofa sank under me, and my head was pegged against Rebecca's psychotherapy license on the wall. I was clad in my athleisure that stabilized my patellae, my right hip, and my right shoulder while buttressing my fictional alter ego who ran track, my counterpart whose body functioned in accordance with her will. Packaged compactly in a medical-grade compression track-suit, my subterfuge probably appeared like a convincing act. However, with my neck secured in a cervical collar, my disability was in plain sight.

I fastened my gaze on Rebecca's wide sapphire eyes, earnest smile, and sleek brown waves as she sat in the armchair opposite me. Initially, I could not detect the black plastic hearing aids magnetically tacked to her scalp and was unaware that an expanding blind spot was located in the center of her visual field. Like my EDS, Rebecca's Usher syndrome, a progressive genetic disease that caused her to lose her vision and her hearing, was almost imperceptible.

"I hate that my world feels so unstable. I am a rising senior at Harvard, and my college experience is nothing like I expected it to be. I've never attended a social gathering or party.

When my geneticist communicated that her EDS patients often don't make it through college, I did not initially believe her. But now, I understand why EDS makes college so challenging to complete. My right shoulder dislocates so often that it compromises the alignment of my cervical spine. I used to wear my braces with a sense of ironic pride that I was finally being seen by others, but this material around my neck is only making me feel vulnerable and like I want to cry for myself. But I'm frightened if I start lamenting, I will never stop and that my whole life will pass me by while I mourn for what I've lost. I was supposed to participate in a science research program through the Harvard Stem Cell Institute this coming summer, but that feels like a pipe dream now. I hate the total absence of control that comes with EDS." I unleashed a reticent weep. I perceived Rebecca's eyes gloss over with liquid anguish for me, for her own disabilities, and for the rapport that expeditiously took shape between existences neither of us wanted to assume, between genetic mutations branded into our cells

like microscopic tattoos that bloomed into nightmares from which we would never awaken.

"El, I know better than to undermine how unfair and aggravating our realities are. In modern parlance, we toss around the word recover. We speak about recovery in terms of alcoholism or addiction. But we also, inevitably but detrimentally, extend it to conditions like ours. When we say the word recover, we are implicitly harkening back to a previous mode of being. We will never be able to return to anything as it was. We may feel closer to that illusion on some days, but we will never recover. Does that make sense to you?" From the inception of our relationship, Rebecca abbreviated my name to the household El and pluralized her personal pronouns, spinning my disease into ours. Almost instantaneously, she felt more related to me than my own family.

"Yes, I get that. But the issue I have with that idea is in regard to my father, who wants so tremendously to have faith that I will recover, to believe the person I was before my diagnosis will resurface. I fear that I will always be a disappointment to him because I'm unable to live out the life he wants for me. I can't even physically partake in schoolwork or science right now because of my neck. I know that having children may be lethal for someone with my disease, but I also know that I could never stomach adopting kids and hiring help to care for them. That would never feel right to me."

"So, El, does that mean that what you want is not worth trying to reach for at all?" Rebecca's question rang with biting insistency. I could not construe whether it was lobbed at me, at herself, or onto our mutual middle ground.

"I don't know. Some experiences feel like I may as well not participate in them at all. For example, I've essentially given up on attending Friday night dinners when I'm home. It's too challenging for me to listen to tidbits of my brothers' conventional work weeks and to their weekend plans to go for bike rides or runs, activities that my body will never again tolerate. I hate to say this, but it makes me nauseous to assemble myself beside my able-bodied family and watch them eat food I will never be able to consume and sit on chairs that would dislodge my hips out of socket. I force myself to sit beside them on my exercise ball in my compression gear for my parents' sake. My parents want me to be there, to at least pretend that I am right where I belong. I don't know what lies in store for me in terms of science and if a lab environment could adapt to my physical limitations." A considerate grin kneaded itself onto Rebecca's face as she shook her head in empathy.

"No one will ever match what we go through. That is not to say that we chose this life for ourselves—but that there is a very real part of us that other people just don't get. We live in a world where we are constantly comparing ourselves to others to understand where we stand on normative scales. This almost subconscious process can be really injurious. When I observe young girls with Usher syndrome who are still, unlike me, able to drive on their own, I feel a sense of dejection toward what used to be mine. There are tons of things I want to do, but I will never be able to do them the way I initially intended. I always consider, if I hadn't had my accident, in which I broke roughly all of the bones on my left side, would I run a marathon? I used to live for that sense of physical triumph, but I could never do that

now, given my injuries. I had no idea that the trauma my body incurred from that one incident would endure for the remainder of my life. There is nothing we can do to alter our situations, and that's frustrating." Rebecca's voice wavered, and her cerulean eyes glossed over. Tears slipped down my cheeks into my cervical collar.

"I feel exactly the same thing about my own life. I always catch myself reflecting on my medical leave from college during my freshman year. A voice in my head goes on the following rant: If I wasn't misinformed by a doctor that my heel was fractured, if I didn't hobble on crutches for months on my right side, and if I hadn't remained in bed for months that followed, would I have suffered this downstream effect of dislocations that won't stop? Would my right shoulder still be dislocating each night? Would I be in a neck brace right now? Like you, I feel like I'm paying the cost for something I never could've foreseen." I wept uncontrollably. I felt my grief leech into my bones like a dormant cancer that was finally metastasizing its way through me.

"El, there's no trajectory for us. No one knows what our fate will be. We don't have any sort of conventions to turn to or people to look at to tell us what we can become. But El, you are not alone. You need to let yourself feel these emotions." I sped my eyes back and forth across Rebecca's face, and an epiphany seemed to dock somewhere between my shoulder blades like a poem that scripted itself spontaneously in full inside my head.

"You, Rebecca, are giving me someone to look to." As we assembled ourselves upright, I reached to embrace this familiar stranger who would swiftly prove herself to be a confidant without whom

I never would have had the courage to seize control over my narrative from the custody of EDS.

I returned home from junior year at Harvard with my elbows fanned out like wings and my head firmly pressed between my palms. My orthopedist in New York attributed my carriage to cervical spine instability and prescribed a neck collar. He forbade me from hunching over tissue cultures in the Wagers Laboratory, where I was to complete my internship through the Harvard Stem Cell Institute. Once again, a barricade seemed to develop between my faltering body and my scientific aspirations.

The Tuesday after my conversation with Rebecca, I phoned Albert, my mentor to be in the Wagers Lab. With the exception of a succinct email correspondence, I personally met with Albert only once on one occasion to outline the gist of my summer project. When we convened in April and I mentioned my EDS, Albert explained that his research into Duchenne muscular dystrophy was motivated by his brother, who was succumbing to this debilitating disease. He tacitly understood my physical limitations. I promptly realized that for him, scientific success did not boil down to publishing articles and cachet, but rather amounted to reversing, or at least to decelerating, disease pathophysiology.

"Hey, Elly. What's up? I'm in between experiments in the mouse facility, but I have a few moments to chat." Albert's syllables were clipped and he breathed heavily into his end of the line.

"Well, I was thrilled to be admitted to the program and to work with you. Unfortunately, my physical health has taken a

bad turn recently. My right shoulder has been dislocating frequently and has been pulling on my neck and head, which has been causing me considerable pain. My orthopedist advises that I do not partake in benchwork this summer. I hate that I have to relay this news to you. I was so excited to work with you, but my physical limitations are forcing me to change course." My voice cracked under the weight of my words. I felt like I was trying to communicate under water. I sniffed into the receiver and tears rolled down my jaw. The line went flat for a few seconds.

"Elly, I'm so sorry to hear about your recent struggles. Your health is the top priority, and only you and your doctors will know what's best. But I enjoyed our conversation earlier in the term and was inspired by you so much that I am determined on my end to make this summer work for you in whatever way I can." Albert's tone became measured.

"But how could I engage in lab work without further compromising my neck and shoulders?" My stomach churned. Moist heat crept down my spine and thighs, marinating me in a mundane bout of dysautonomia.

"What if we tried to give you a strictly computational project for the summer—so no physical benchwork at all. I have some RNA sequencing data that you can help me analyze. You could learn programming skills and have an actual dataset on which to focus. There will be no pressure to get this done by any timeline since it's a secondary project that I'm not focusing on for the next few months. You can work on it as you feel able. Also, doing computer work can be done at home on days you aren't

feeling as great, or in the lab when you feel up to it. I really want to help you, Elly! But, first and foremost, I want you to do what's best for you, of course." Albert's gracious proposal ran through me like a satisfying electric current that seemed to fuel each of my mitochondria with radiant electrons, a sensation that I previously assumed only came packaged in a Bulletproof bottle. The silence that accumulated between us began to feel dense, and I felt an impulse to speak.

"I'm sorry for my pause. I'm crying tears of joy. I thought I had to forego this opportunity.

I really appreciate your support and time. I can't wait to become a coder." I quickly felt very light on the inside. For the first time, I overcame my body and the flashing tennis scorecards in my head read: Elly to EDS, fifteen-love.

In my neck brace and compression getup, I trained to Cambridge with my mother. After entering my studio on Concord Avenue, my mother crammed my ergonomic tabletop podium, my MacBook, a wireless keyboard and a mouse, and a two-month supply of my midday cocktail of supplements into durable shopping bags. She caught hold of my gaze as I retrieved water from the refrigerator and shot me a pensive half-smile.

"Bel, let's head over to the lab with your supplies. I need to depart for the train home in just under an hour. Also, grab a few collagen bars from your cabinet so you will have snacks there. I will carry your extra physioball, so your hips won't ache or sublux in the lab." I responded with a spirited nod.

Albert awaited our arrival on the third floor of the Bauer research complex.

"Hey, Elly. It's so wonderful to see you. And I'm guessing that you must be Elly's mother." Albert extended his hand toward my mother, and she gave it a dynamic shake.

"Yes, it's lovely to finally meet you. My husband and I are so taken by your compassion toward Elly, given her circumstances. It means a lot to all of us." My mother's voice wobbled. I intuited that she was undertaking the daunting task of balancing her words over a growing aggregation of tears at the base of her throat.

"Of course. It was not even a question in my mind. Elly is such a strong student, and I want to do everything in my power to ensure her scientific success, despite the daily setbacks she faces due to her EDS." I observed Albert's eyes jog back and forth between my mother and the gray inflated ball in her arms.

"Albert, I hope it's alright that in addition to my laptop, my mother brought a desk raiser that elevates my computer to eye level to help me avoid further neck strain and an exercise ball to help me dodge any hip subluxations. Sorry that I come with a ton of paraphernalia." Albert produced an expansive hospitable grin. I felt my mother's sensitive arm loop itself about my upper back, a physical cue that corroborated the thoughts that raced telepathically along invisible tracks between our brains. Her tender fingers imparted something to the effect of "disown your shame, El. You have zero reason to feel embarrassed about communicating your body's needs."

"Elly, if it would make you feel more comfortable, I would be more than delighted to swap out my chair for a ball as well. I think I could even convince most people in the lab to follow our lead.

Then, you would not be alone." Albert's words shot through me like an unfamiliar melody I instinctively took to, like a fresh track I wanted to listen to repeatedly. I had yet to confront a researcher who demonstrated an overarching faith in me, EDS included.

Albert guided me to my workstation and sat in a chair beside my ball. He transferred a textbook entitled *Practical Computing for Biologists* onto my raised desk. I studied Albert, and his charismatic smile rematerialized. I eyed the transparent barrier to my left between the office desks and the wet laboratory. I felt a strong yearning to meander across the glass threshold and to pipette something somewhere without speculating if my thumb would dislocate, if my neck would throb, or if my shoulders would come out of joint. But science could not transpire on my own terms, not if I did not want to disassemble into my constituent parts. A subtle sense of loss eddied about in my chest. I denied the tears that almost slipped out of me.

"So, Elly, this textbook is going to be your companion as you teach yourself C, R, and Python computational languages, each of which is necessary for different phases of the pipeline you will use to analyze the RNA-sequencing data. I am interested in identifying early-acting mechanisms that activate muscle stem cells to regenerate skeletal muscle following muscle injury. If we can pinpoint potential transcription factors and gene networks that must be turned on for muscle repair to occur, we may be able to isolate genes that need to be upregulated in the context of aging and Duchenne muscular dystrophy. In both of these conditions, early-activating muscle stem cell processes are dysregulated. The RNA-sequencing data I'll forward to your email is the result of an

experiment I performed in injured versus uninjured mice. As I isolated muscle stem cells from the mice soon after inducing muscle injury, I suspect that the injured mice will exhibit a unique genetic profile due to early-acting drivers of muscle regeneration at play. I want you to determine which genes are differentially expressed in the samples derived from injured versus uninjured mice and to identify transcriptional regulators responsible for these enriched genes." While he clarified my task, Albert threaded an arm across an adjacent counter in the direction of a stack of typing paper. With red ink, he composed a series of diagrams denoting muscle stem cells' transition from quiescence to activation and, finally, to skeletal myoblasts. After approximately ten minutes of rapid penmanship, Albert settled his fist onto the table and searched me patiently, pending the instant when his words clicked into understanding.

"That all makes sense to me, and I'm really excited about this project. I also read through your manuscript, which provided me with useful background information."

"Elly, that sounds great. You pick things up so quickly. I'm impressed. Don't hesitate to bother me with any questions." Albert retreated into the laboratory to dissect the shin muscle from a mouse. I felt my jaw unclench and an unexpected anticipation work its way into me. EDS may have mutated my affiliation with science, but it did not terminate it altogether. Almost reflexively, like a benediction I whispered into my own ears, I felt myself mouth "I can walk. I can see. I can beat CRPS. I can do anything."

Within my first week in the lab, I polished off *Practical Computing for Biologists*. I began funneling Albert's dataset through the

computational workflow, submitting Python scripts to the Harvard server, and coding my way through my assignment with a natural facility that felt like it was ingrained into my genome along with my EDS. Roughly six out of seven mornings, I arose with my right arm dislocated and electric pain raged across my right chest. I shunted my slack arm into place and hovered on the brim of my mattress. I was primed to exact my sense of self-control, however illusory it was. I ambled to my kitchenette and twisted my way into upward of fifty supplement bottles containing ingredients that enhance muscle recovery, including D-ribose and creatine. Armed with my mugful of capsules, I sipped on Bulletproof cold brew and inputted one line of code after another as though I were composing an orchestral oeuvre that crystallized almost mechanically into being. Because the Harvard supercomputer flooded my inbox with notifications that my script was processed or that I was occupying more than my fair share of memory on the server, I felt uncharacteristically in demand that summer.

While I coded between the hours of six and nine, Bulletproof Radio sounded in the background, streaming Dave Asprey's interviews with researchers, including Dr. Dominic D'Agostino and Dr. David Sinclair. In the company of my computational pipeline and Asprey's podcast, I entered into an idyllic delirium filled with the persuasion that my EDS and I could be biohacked and debugged like the programs I ran.

On July 1, I entered the Wagers lab in my compression uniform and neck brace following my morning routine. Given my shoulder instability, I strapped a black fanny pack about my waist as a surrogate backpack. Sia's "Unstoppable" trickled through my

earbud wires, and euphoric vibrations coursed through my neurons. My tennis shoes broke into an unwieldy caper through Harvard Yard. I refused to tone down my gambol when pedestrians eyed me like the mutant being I was, and I disregarded their sardonic expressions. Living with a chronic disease had molded me into an expert at blocking out outside opinions and expectations. I was determined to live to the maximum, however preposterous I appeared, when my limbs were located in their respective sockets.

While I keyed code into a text editor that morning, I overheard muffled conversation circulate about the lab. The lab coordinator, Jamina, shuffled in and out of researchers' cubicles with a paper in hand. As she passed my workstation, I stole a glance at the document tabulated with each lab member's surname, beside which Jamina notated yes or no. I scrolled my eyes down to the row that read Katz and noticed that no was printed in the adjacent column. I returned my stare to my MacBook screen, but the nearly completed R script looked shockingly foreign. I concluded that I should excuse myself for a lavatory break even though I did not need one. As I navigated to the hallway restroom, Albert spied me and pronounced my name. I felt my quadriceps seize in a paroxysm of fear. For a brief minute, I lingered in my tracks and mentally skimmed through the week for any errors for which I could be held accountable or even reprimanded. I rested a palm over my rib cage and felt it expand and contract as atmosphere came into me and departed.

"Hey, Elly. I wanted to talk to you. I know you probably heard the hubbub in the lab this morning. I want to be open with you about it. We have a laboratory-wide rafting trip coming up.

I know with your EDS, that type of outing probably sounds like going to Venus. I told Jamina to be discreet about asking people if they can attend. I did not, in any way, want you to feel left out. I just didn't want to throw it in your face. I hate that you can't be there with us. I hate that this world is not as accommodating to your body as it is to the rest of ours." My upper lip trembled in an emotive slurry of relief. I was astonished by Albert's impassioned concern and felt a twinge of personal bereavement.

"I'm overwhelmed by your thoughtfulness. I'm so accustomed to recusing myself from activities of that sort that they don't even really faze me anymore as exclusionary. It means a lot to me that you care enough about my limitations and their emotional consequences to say something to Jamina." My words wavered as they poured out of me in shaky spurts. Albert's degree of forethought on my behalf felt fantastically alien.

"How does it work for you here? Do people just learn to stop asking you if you want to do things or attend events? Doesn't it hurt you that they have to tiptoe around you? How do you cope with all of that?" Before Albert, no one at Harvard had directly questioned how my EDS warped my social and emotional life. He motivated me to realize that I could uncork my solitude, my pain, and my anguish and let myself spill freely into someone else without feeling mortified that I was me.

"Yeah, I guess people learn over time to stop asking. But, thankfully, I'm not what anyone would call popular, so I didn't have many offers to lose to begin with. Between my coursework, my best friend, Olivia, and putting my body back together, I don't have much time to gripe about what I've lost or never had. And,

also, I think I'm happier than most people I know because the small things that most people overlook, like waking up without dislocated limbs, are magnified for me. My life is far from normal, and I know that will always be the case. But, somehow, I've learned to love it and to make of it what I can."

As I sifted through Dave Asprey's blog that evening, I stumbled on a post about whole body cryotherapy, which involves exposure to negative 266 degrees Fahrenheit for three minutes in a cryochamber. In the article, Asprey synthesizes genuine scientific reports to advance his claim that cryotherapy accelerates muscle recovery, curbs pain, and, most intriguingly, ramps up collagen production and slows its degeneration. This burst of exposure to extreme cold triggers the production of anti-inflammatory cytokines and norepinephrine in addition to antioxidants, including superoxide dismutase and glutathione, that suppress oxidative stress. Furthermore, as skin temperature plummets to roughly 41 degrees Fahrenheit, the body falsely assumes that it must increase collagen production to repair the outer layer of skin. Cryotherapy also inhibits collagenase and cortisol, both of which break down collagen. I queried "cryotherapy in Boston" on Google and booked a session for an hour later.

As I mounted two steps to the cylindrical chamber, I witnessed frigid clouds gather around me like an aerial wedding dress. My whole body numbed into a glacial narcotic stupor until I felt nothing at all. My pain receded into the liquid nitrogen-infused vapor, and my EDS seemed to melt into a three-minute sabbatical. I would voluntarily enclose myself in this human freezer thrice a week and perceive my spasms, bruises, and agony fleetingly

drain out of my pores, provisionally purging me of everything I never wanted.

On Saturday mornings, Olivia and I rambled for miles down Massachusetts Avenue until our weary feet remonstrated. As I drifted toward Olivia's rental apartment that August before my senior year, I sensed that my cranium felt unnaturally heavy and applied manual traction at the base of my skull, suspending the underside of my jaw against my thumbs. I was completely unaware that I was leaking. I considered my EDS on a limb-by-limb basis without even postulating that I could spontaneously rupture internally and that I could dislocate a part of me I could not brace. I sustained this awkward posture for five blocks, at which point my right shoulder clunked out of socket. I felt my dizzying body fall against a white fence. I hoisted my right arm in my left fist and shoved it into the joint. I heard myself panting.

I deliberated messaging Olivia and canceling our outing, but I quickly dissuaded myself from doing so. If I could not cope with my piecemeal self in Olivia's company, I feared that I would wind up miserably isolated, that I would effectively concede to my EDS, and that my sense of self-mourning would thicken until it smothered my resolve. On an almost cellular level, I realized that I had to repress the crushing urge brought on by chronic illness to shut out the world, to retreat into the glaring darkness of pain, and to bisect myself from a reality that seemed excruciatingly normal and out of reach. I plodded across the street to Olivia, whose expression was contorted in apprehension. She wore a sham smile and appeared as if she was posing for a photograph against her will.

"What's wrong, El? You look distraught." Olivia cautiously coiled her arms about me, and my neck brace bumped up against her shoulder. I instantly felt unnervingly fragile.

"I'm alright. I just had a tough walk over here. My shoulder dislocated, and I felt faint. I'm doing much better now though. Do you have a directional preference for our walk?" Olivia gave me a merciful grin.

"Well, fill me in. How was your week? Is the computational work going well?" As she studied me, genuine flickers of interest took shape in her focused pupils.

"It was great, actually. As you know, at the outset of the summer program, I sulked over the idea of abstaining from benchwork and had zero proficiency in computer science. I second-guessed my ability to pick up a new skill set, but I'm truly enjoying my project. I've become an unexpected computer geek who wakes up and goes to bed writing code. I think programming has given me a profound sense of self-control. The process of scripting, running, and debugging code is so therapeutic for me. It makes me feel like I can rise above my detaching body, like biology is one long logical program. I'm almost done with my entire project, and only half of the internship has elapsed. Also, Albert is really enthusiastic about my findings and believes that I may have hit on a novel stem cell renewal pathway. But how are you? Are your zebrafish behaving? How is your English boyfriend settling into his internship at MIT?" Olivia's beam unfolded into a full-toothed smile as I recapped my week. I chased her gaze until our eyes locked into understanding, and I emitted an amused smile.

"Overall, the zebrafish experiments are going well. To identify the circuits that give rise to avoidance behavior, I'm trying to ablate a nerve fiber that I hypothesize is primarily responsible for the escape reflex. The hiccup is that when I administer the neurotoxin that ablates the neuron, many of the zebrafish die, which clearly poses a challenge for completing the experiment. Callum is thriving at MIT. Last night, he apparently played limbo with his colleagues, which seems like a fairly good barometer that things are going well for him." In step with Olivia's transition from the topic of annihilating zebrafish neurons to her boyfriend, Callum, her expression remodeled itself. I watched merriment stretch itself like a banner over her cheeks and suddenly sensed that we were extremely far away from each other.

"Olivia, do you think a guy will put up with me? I want what you and Callum have with each other. I just don't know if it's realistic to expect that of myself. I don't know if I can hope for someone to love me enough to overlook my haywire physical constitution." Olivia twisted her forearm about my elbow, twining us into one entity. I gave her a meek look, and she swiped a forefinger through an errant tear on my left cheekbone. I gaped at my able-bodied best friend whose shoulders were firmly lodged in their sockets, who could select her own apparel without gambling away her joint stability, and whose body functioned as a container for her brilliance rather than as an authoritative impediment. In the suffocating silent heat, I marveled at Olivia's seemingly supernatural power to sense my pain she could not feel and to occupy the emotions that hitched a ride with my EDS.

"Elly, quit doubting yourself. Your EDS is not you. Sure, it's a huge part of you. But you outgrow it because of how you respond to

it, how you continue to shape such a meaningful life through poetry, science, and everything in between. When I'm with you, I'm not with a disease or a patient. I'm with a remarkably resilient person who I love. Trust that other people, guys included, will take to you like I do." Olivia hesitated on the pavement and took hold of my left hand.

"Sometimes, I feel like my EDS is a nemesis conjoined to me from birth that is using up all of my air supply. Your words mean a lot to me. On an important digression, how is your Rhodes application progressing?" We continued our promenade down Massachusetts Avenue, and the sun-choked heat liberated beads of sweat at our temples. I eyed Olivia, who would score a Rhodes Scholarship in England, which she would follow with a doctorate in cognitive neuroscience. An instinctive pang of envy stitched itself into the lining of my stomach. My physique was not intended for overseas travel, for barometric swings that prompted my abdomen to distend and my rib to dislocate, for residing across the Atlantic from my mother, and for conducting benchwork for a summer, let alone for a three-year span.

"Yes, the application is going well. I finished the personal statement last night. If I make it through the first cut, can I count on you to write on my behalf? The nomination committee requests a letter from a friend about your character." I glanced at Olivia without feeling like I was looking into the reflection of what my life was not. I did not, *per se*, abnegate my EDS or lock it behind a trapdoor inside my brain. Instead, I heeded a persistent internal voice that entreated, "Restrain yourself from internalizing your best friend's excitement as your own sorrow. See Olivia for herself, take pride in her promise, and put yourself aside." I waded

speechless through the sagging heat until my homunculus concluded her sage council.

"I would, of course, be delighted to write about you. It sounds like a great excuse to brag about one of my favorite humans." She did not revolve her head toward me, but I could feel Olivia's smile jell into place as she clenched my hand securely into her fist. I was well aware that what was stated between us was not all that was said. I knew that our sentiments spilled into each other, that there was a knowing, a sort of emotive sign language that articulated itself in the summer air like the hushed flight of a sparrow overhead.

After the close of my internship in early August, I phoned my parents to report that I would remain in Cambridge until the launch of my senior year later that month. My EDS furnished me with an infinite catalogue of credible alibis, ranging from my hip instability in vehicles to aggravating my daily routine of dislocating, relocating, and rehabbing my limbs. Almost instantaneously, my father admitted that my inventory of excuses was sound and that returning to his Manhattan apartment may retard my physical progress. He disconnected from our brief conference call to resume his work. My mother's end of the connection flatlined.

"Bel, I sense that you're not being straight with me. I understand all of the physical challenges that are par for the course with any sort of travel for you. But what's really behind your determination to stay in Cambridge for the next two weeks?" My mother's words prompted a dazed nausea to settle at the back of my knees and work its way up my spine. Perched on my physioball in my studio, I felt my stomach distend.

"I hate to say this, mom, but your home has become a charged place for me, a sort of hall of mirrors that reflects my history and my past agony, which happen to be the very things I am trying to leave behind. It's not just about my past but about my present and future. My disease is not like a cancer that can be put into remission; it's a lifestyle that I have to create for myself.

When I'm home, I despise my life because I see what's outside of its purview, from children of my own, to cycling, to dining out, and to paying forward everything you have instructed me by example to my own daughter. It also pains me deep in my guts to consider that you lived an entirely normal life before I entered into this world. I know you feel my pain to the pinnacle that it is possible for another person to do so, but EDS is *my* life. I need to figure it out for myself." My mother's inhales deepened as I detailed the raw edict of what it meant to be me, to be permanently corralled into the role of a patient in an otherwise healthy family, to be forging an existence out of my EDS.

"El, I know all of that. As painful as your words are, I get where they come from. I respect you for working so hard to create a life for yourself. I know it's never going to be anything like the one Dad and I have built, and I appreciate the inordinate amount of losses you suffer again and again each time you return home." My mother's syllables were slurred.

"Mom, I certainly don't want you to view me as a victim or feel bad for me. Sure, I may be mutated, but that does not mean that my life has been flushed down the drain. I'm planning to have a limited but, nonetheless, epic life. Just you wait and see."

I perceived a pithy pause formed between us as my mother processed my words.

"El, that's exactly why I'm never going to give up on you. I'm so honored to be your mother." My mother's words steadied, and she sounded like she was grinning.

Aside from the mundane retinues of tourists, Harvard Yard was deafeningly quiet during the two weeks that followed. Olivia retreated to her Pennsylvania home, and I found myself entirely at my own disposal. EDS had shaped me into something of a virtuoso at solitude. I strayed through Cambridge with earbuds screwed into my cranium, listening to Rebecca Alexander's *Not Fade Away*. I assured myself that I, too, would one day pen a memoir and frame my life into the semblance of something that could be dissected into a beginning, middle, and end. I passed my mornings writing poetry, solving unassigned genetics problems in the margins of a tattered textbook, and freezing myself in the cryotherapy chamber. This was as asymptotic as I would get to a vacation without jeopardizing my baseline well-being. I knew better than to hope to revisit Rome or Israel. I knew better than to bemoan my quotidian shoulder dislocations and my neck brace.

When classes commenced, I poised myself on my conspicuous exercise ball in my neck brace and compression attire. I felt like a biological pariah in my genetics classroom brimming with able-bodied undergraduates. I felt my toes tremble in my sneakers, and a dizzying vertigo haze over my field of view. A buzzing shot through my ears, and my thoughts halted. I felt my eyes flit open and shut and my cheekbones sink into me with the weight of

solid lead. I felt a swift sense that I was ending, that a final period was branding itself on my life.

I somehow managed to direct myself to my apartment. My knees threatened to give way beneath me on several occasions, and I clenched my skull between my palms. I did not halt to repair myself when my right shoulder dislocated. I was not even conscious enough to cry, to react to the pain my neurons transmitted along my brachial plexus. As soon as I ventured into my studio, I wound myself into something small on the wooden floor. I felt myself mouth the Shema prayer to a God I rejected, mourning for a being that I sensed was whittling down into nothingness, mechanically acting as my own spiritual guarantor. I fumbled for my iPhone in my pocket and felt my fingers innately press themselves into my mother's voice. I teetered in and out of oblivion for the next four hours. I felt my parents scoop me up, pack me into compartments that transported me home, and unmoor me from Harvard Yard, from a hemmed-in existence I reckoned I could survive.

22
Learning to live with adversity

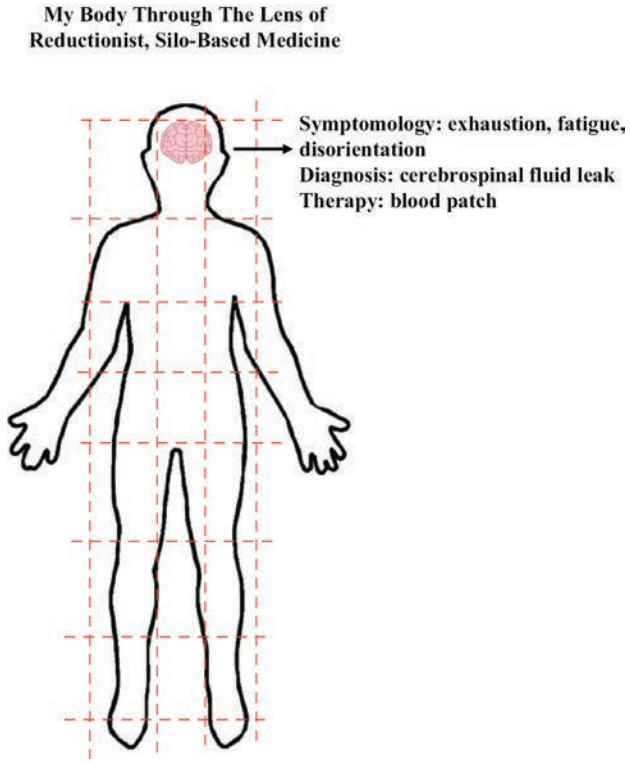
I am broken but have never been more whole. I am out of sorts but at peace.

I am a graceful paradox, undaunted by fragments that do not cohere into sense, unafraid of living in pieces. I am an active collage and am complete where it matters most, to myself.

I tie experiences into memories that taste sweet on my tongue, forge connections within and without, and lace the pieces of my being with meaning, no matter how piecemeal, how incomplete.

"Elly, I'm about to introduce the blood drawn from your arm into your epidural space. The clotting factors in your blood should almost immediately patch up the hole in the lining of your spine responsible for your CSF leak. I'm starting the injection now. You may feel radiating pressure along your spine." As I rested, face-down, on the operating table, I deliberated the harrowing truth that I was shockingly mortal, a creature I would never master into predictability.

A warm pressure spread up my spine, which I sensed was speedily expanding in diameter. I felt like a botched chemical reaction nearing spontaneous combustion. Swiftly, the



thought process that was suspended in my genetics classroom resumed; I imagined ions flowing into and out of my neurons and neurotransmitters gliding across synaptic clefts, revving me up again.

"The procedure is complete. But as I mentioned, your leak was spontaneous. Your EDS causes the connective tissue sheathing your spine to be friable. Hopefully, this will be a one-time ordeal. But patients with your condition sometimes require more than one blood patch. I would advise you abstain from any activities that put stress on the dura, such as running. If you do not feel dizzy now, try to sit up." Even though the anesthesiologist had just expelled a syringeful of my blood from my arm and plunged

its contents into my back, the equation of my being was far from balanced.

Unlike my right shoulder, which dislocated during specific activities, my CSF leak ensued without cause. I lamented its lack of logic. If I could not isolate the trigger of my nearly lethal leak, I indubitably was unqualified to prevent its recurrence. I waited for my head to settle into something inhumanly cumbersome. A petrified shiver sped along my arms. My cranium felt decadently light. I tossed a glance at the physician and mumbled, "thank you for returning me to myself." I would soon accept, however, that I was not returning to anything but was beginning anew from the severe starting point that I could control almost nothing, save for my own narrative.

A week after my internal plumbing was restored, I parted with my neck brace. My cervical spine pain, I then suspected, was only a side effect of my leak. While my neck pain dissipated, my shoulders continued to dislocate almost daily.

The next Tuesday morning, my mother accompanied me to Weill Cornell. As we walked to the waiting area, Dr. Gellhorn approached us.

"Welcome back, Elly. How are you doing today? Follow me back to my office so we can begin." Dr. Gellhorn's lips parted into a slight but kind smile.

"Well, I'm proud to report that I'm no longer leaking internally. But, as my mother probably informed you through her emails, my shoulders, especially my right one, dislocate often. I know that surgery in patients with EDS is risky in terms of bleeding and healing, and I want to do everything in my power to avoid

surgical intervention." The physiatrist guided me to an examination table.

"Elly, not leaking is definitely an upside. I agree with you about dodging surgery. I am going to inject something called AmnioFix into your shoulders. It is a sterilized powder derived from dehydrated human placental amnion and chorion membrane. It contains growth factors and specialized proteins that enhance tissue repair. I think it may reduce your shoulder pain and potentially stabilize your joints." Dr. Gellhorn's stare bounced from me to my mother as he spoke.

"So, basically, you want to inject a random person's placenta into my shoulders?" Dr. Gellhorn and my mother broke into peals of laughter. I organized my face into an amused grin and continued my extemporaneous comedic act.

"Just so you know, I am 110 percent game for that. It will be the closest I will ever come to carrying an actual component of a fetus. As you know, having children can be lethal for someone with my disease, so I'm glad I will get to sample what it feels like to bear a syringeful of someone else's placenta in each of my shoulders." My mother slid her palm onto my lap, twining her fingers about mine, communicating that I was not obligated to turn my disease into a parody. Dr. Gellhorn withdrew from the room to prepare the injectables.

I felt my self-travesty morph into lament. I contemplated whether my grief would crouch inside me like a lifelong vestigial organ or if I would eventually rid myself of it in full. Before Dr. Gellhorn reemerged, I flicked through my painful memories in my mental flipbook and realized that my suffering was a critical part

of me that I would probably never outgrow. I vowed to myself that I would live with the adversity that rang through my tenses and strive to respond to it with a perpetual internal echo of Sia's "Unstoppable."

After my shoulders were infused with donor placental membrane, I observed my mother hail a taxi outside. A cab swerved toward her, and she motioned for me to enter the backseat. I tarried on the curb and scanned my mother as though she were a recondite passage in the Bible. I beheld her cheerful grin that looked too gullible and sincere for a sixty-year-old face, an expression I wanted to cut and paste onto my own twenty-four-year-old cynical countenance. I felt the volume of polluted atmosphere between us as if it were an insurmountable hurdle dividing my skepticism from my mother's faith, a marginal but, nonetheless, real space that segregates the chronically ill from their mothers who double as their healthcare proxies and unmatched confidants. After a long two minutes, I folded myself beside my mother in the car and felt her examine me.

"Bel, why did you respond to Dr. Gellhorn the way you did? What compels you to turn your disease into a humorous skit?" My mother's expression flattened into resignation. As a solitary tear washed down her jaw, I sensed that she intuited my reply before her question escaped her.

"I think I'm still trying to come to terms with my EDS and with what it means to translate my invisible disease into a language accessible to able-bodied people. I don't want to scare people, even my own doctors, away from me by feeling sorry for myself or speaking histrionically about my life. My humor is not meant to

demean my EDS or the lifestyle sacrifices I have to make because of it. Instead, laughing functions to lighten the emotional burden I have to bear and to create a sort of expressive bridge between me and my world. I already feel sufficiently like a science experiment gone awry. I don't want to look back on my life and feel like I've succumbed to my fragile tissues." I slanted my glance to meet my mother's. Her face leaked mascara. I felt my own sadness drip down my cheeks.

"You know you are never alone, love. I hate that your life has to be so uncanny and painful. I hate that you have to transform your hardship into mirth, but I am awed that you are able to do that. I can't help but feel guilty when I look at you, like I somehow built you gene by gene and did wrong by you. You deserve so much more than this." I reclined my head against my mother's shoulder and felt myself descend into the one entity I would always trust would never dislocate no matter what.

"Mom, I know that we are in this together. But, please, your guilt only harms me. I promise you this—I would take EDS for a Karin Katz any day if genetics worked like a quid pro quo business transaction. I would always choose you."

The following afternoon, I made for Rebecca's psychotherapy practice. Wintry gusts wrapped against my face, but my sensory receptors seemed to have an attention deficit disorder of their own about the weather. Between my compression gear and my skin, a film of sweat developed. I shrugged my way out of my puffer and knotted it at my waist. In outdoor air falling to thirty degrees Fahrenheit, I probably appeared like a runner cooling down from a sprint instead of an EDS patient with dysautonomia.

I fished my iPhone out of the side pocket of my leggings and fingered my way through Spotify to Sia's "Alive." As though it had a will of its own, my mouth mimed "I was born in a thunderstorm. I grew up overnight. I played alone. I played on my own. I survived." As Sia reprised "you took it all, but I'm still breathing," I was overcome by a triumphant ecstasy and my stroll broke into an artless frisk. I had been painfully robbed of the life I expected but was more than breathing. I was moving forward with an inner composure I presumed my EDS would never sanction. I felt myself come to the surface of my flawed connective tissue and sensed an unexpected pleasure with the person I was becoming.

Inside Rebecca's office, I advanced toward the physioball stored in the far corner for my routine visits. I studied the edges of Rebecca's smile, the compassion in her cerulean eyes, and her overarching authentic allure. I felt her zooming in on me with her residual ten degrees of central vision. Our eyes met in the small space between us, and I peeled back some inner lining and let my vulnerability breathe itself into words.

"I'm starting to feel scared about resuming Harvard. I don't know how I'm ever going to trust my body again. When my EDS was a matter of my limbs sliding out of and into their sockets, it at least felt manageable. But the fact that I can leak without even knowing I am doing so frightens me. I try to persuade myself that I will read my biological signals faster if this happens again, but I'm honestly not sure I will ever have the handle I want on all of this." I sensed my eyes as they gradually welled up.

"El, we will have days that are easier, and we will have days that are harder. It's the total lack of ability to know when those days

are going to come, and they come so suddenly and unexpectedly, which makes what we deal with intolerable. It's like I told you, every time I cross the street I think: This is it. No matter how many times I look from side to side, I still miss things or have accidents. It is that absolute uncertainty and vulnerability that is both incredibly humbling, terrifying, and real all at once. But El, I honestly have never met anyone your age who has the type of insight, intellect, and ability that you do. It's impossible to know who you inherently are without EDS. Your EDS has undoubtedly been incredibly formative in your person, but I also wish I could have you in my office as a fly on the wall. I wish you could listen to the drama and insecurity that takes place in here when I talk to other girls your age who are, for the most part, riddled with shame, guilt, and self-doubt. When I think of you, there is no world in which I would want to live with EDS, but my other twenty-four-year-old patients do not have it easy either." Rebecca steadied her gaze on me.

"Rebecca, I can't feel insecure like other girls my age. If I did, I would not know how to survive. I don't have mental room for those kinds of feelings when I'm dealing with putting my body back together every day. But I think what is consuming me about returning to Harvard is not only the physical aspect of EDS but a deep sense of loss. I feel like there is not a clear path for me anymore. I'm trying to see where I'm physically able to take myself, to tease apart what it is I can do in the world without compromising my body. Before this leak, I would sit in classes with the agenda of pursuing a PhD in genetics. Even when I suffered my first series of dislocations during my leave of absence as a freshman and returned to Harvard, I had this flicker of intuition that

I could somehow fit myself into what I wanted and make it work. Now, it feels like that sentiment is gone. On the other hand, I feel an imperative to take my experiences and do something constructive with them like you have. I have dealt with the psychological consequences of illness, and I know I want to help other people to do the same." For the first time, when I considered my future, I perceived my EDS as an asset, not as an impediment. My gaze softened on Rebecca, and, in her, I realized who I wanted to be and where my EDS could lead me.

"But El, I don't want you to feel like you are conceding your passion for science and being forced down my career path because of EDS." Rebecca tossed me an inquisitive expression and slipped a fist into her jean pocket. At that point, she knew what my recurrent strife and fear of my future prompted me to block out; Rebecca realized that I would not permit my EDS to win over what I would become, that the scientist in me was not going to abdicate her ambitions. But she also knew better than to question what I thought would be my calling. Neither of us could have foreseen what my EDS had in store for me next.

"If I hadn't met you, I might feel like I was giving in by wanting to be a psychologist," I rejoined with haste. She secreted a look of disbelief and tucked her hair over her ears. I focused on the black plastic protruding from above her ear that processed my words into digital sound bites for her auditory cortex, bypassing her eroding connections between her internal and external worlds.

"Why is that El?" Her words were punctuated with incredulity.

"When I used to talk to psychologists in the past, I often felt like I was giving an emotional performance that sounded outrageous

even to me. Because you go through parallel but different experiences, you give me the sense that I can build a life, however different it is from my ten-year-old expectations. I want to construct a life and a career that is not defined by my EDS but that I develop *because* of my EDS. I feel like I have to find callings that make me want to wake up every day, relocate my shoulder back into its socket, and tell myself, 'this is my disease. I'm going to use it to my advantage in ways that make me feel whole.' I've been alive close to twenty-five years and have never come across anyone like you. From age ten, when I got my first back brace, I felt a sense of shame about my body. From there, the same self-effacing sentiment cropped up each time my body collapsed. Even in Harvard classrooms on my physioball, I felt embarrassed, like I was a spectacle to my peers. Because my disease is invisible—it's not like I have casts, crutches, or any manifestly disabled emblem that people can point to and understand—I look pretty normal in my compression garments and kinesiology tape." I threaded my fingers into each other on my lap, composing myself into a creature who could, despite her dislocating limbs, rein herself into sanguine unity.

"It's not like you're ever going to be fully at peace with the hardship that happens to you, and you're always going to go through hard times, like when you dislocated your hip in the Uber last week. That is a part of EDS, but it is also a part of being human. Unfortunately, if there is a spectrum of experiences, you, like me, reside at the extreme end of the continuum in that our sense of loss far surpasses that of the average person. That is both distressing and incredibly humbling. Of all people, we are not people who need to be humbled, but you are developing your

level of comfort with your circumstances. The more comfortable you are with the uncertainty of it all, the more comfortable other people will be with it. You are slowly going to develop a support system that includes people like Olivia. The people you choose to let in are not going to see your EDS as something that makes you super weird, but they will see it as a part of you that makes you superhuman. Superhuman not because of everything you go through and the ways in which you literally put yourself back together but because of the fact that you are repetitively exposed to hardship and you continue to push forward and to excel even though you experience tremendous suffering. Writing your thesis, El, is giving you the opportunity to finally be seen for the magnificent and resilient person you always were, EDS and all." I suddenly felt electrified by self-acceptance, by an inner mettle invincible to my defective genes, by the instinct that I would walk myself wherever my feet could carry me and relocate my limbs in their sockets again and again with as much fortitude as I could muster.

23
Editing my environment

My mitochondria are cranking out ATP,

shuttling energy to swollen limbs, to bruised legs, to unhinged shoulders. My factory is in full force; each cell dances to logical recurrent cycles, regenerating something new out of used building blocks.

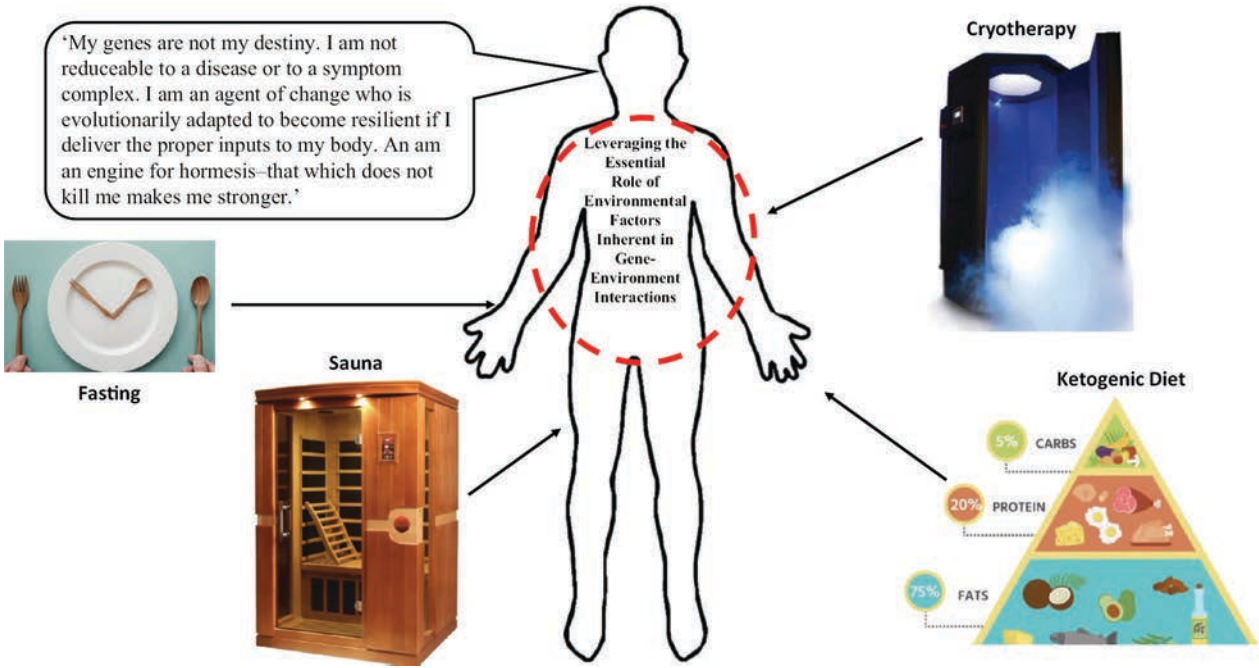
There is a rhythm, an intracellular pulse, as breath becomes fuel.

Among the recognized 14 subtypes of EDS, 13 are deemed rare as each occurs in a maximum of one out of 2,000 individuals and are collectively due to 22 genetic variants that disrupt collagen pathways. While its genetic basis continues to evade researchers, hypermobile EDS (hEDS) accounts for 80 to 90 percent of EDS cases. Scientists, including Clair Francomano, Brad Tinkle, Joel Hirschhorn, and Fransiska Malfait, hypothesize that hEDS is associated with multiple genes, each of which exerts a small effect, and environmental factors (Malfait et al. 2020; Tinkle et al. 2017; Scicluna et al. 2021).

Cases of hEDS have been linked with mutations in genes, such as *COL3A1*, *LZTS1*, *TPSAB1*, *TNXB*, and/or *KLK*. The Hypermobile

Inverting the Western Medical Paradigm: The body is an interconnected functional network influenced by lifestyle, genetics, physiological processes and psychosocial factors.

'My genes are not my destiny. I am not reduceable to a disease or to a symptom complex. I am an agent of change who is evolutionarily adapted to become resilient if I deliver the proper inputs to my body. An am an engine for hormesis–that which does not kill me makes me stronger.'



Ehlers-Danlos Genetic Evaluation (HEDGE) study, the first hEDS genome-wide association study (GWAS), is currently ongoing with the aim of correlating phenotype—based on Beighton Scoring and clinical questionnaires—and genetic predispositions. I am one out of 1,000 participants enrolled in the HEDGE study. However, even if the GWAS analysis culminates in the identification of multiple genetic variants associated with hEDS symptomatology, these loci will likely only aggregately explain a relatively insignificant percentage of the phenotype. The latter phenomenon, known as the missing heritability problem, often occurs in the context of polygenic traits, such as height and cancer.

Though complex genetic diseases, as of today, are challenging, if not impossible, to approach through gene therapy or gene-editing perspectives, the role of the environment in these conditions presents an opportunity for intervention. The correlation between hormonal shifts and hEDS manifestation in females, who comprise roughly 80 percent of hEDS patients, emphasizes that hEDS symptoms stem from the body's dynamic response to internal and external stimuli (Tinkle et al. 2017). The role of the environment—the endogenous and exogenous milieu—in hEDS pathophysiology further suggests that this form of the syndrome is multifactorial in origin.

The burgeoning field of epigenetics probes how environmental exposures throughout one's life, collectively referred to as the exposome, regulate gene expression, RNA signatures, and DNA methylation patterns. Determining the effect of the environment in hEDS must account for the timing, source, mode of entry—dietary, respiratory, or transdermal—and type of

exposure—chemical, biological, and/or psychological. While ascertaining the genetic etiology of hEDS is daunting, identifying the environmental factors and the gene-environment interactions at play appears to be an equally, if not more, overwhelming undertaking. Given that scientists worldwide have homed in on several, as of today, unpublished variants in my genome (I am not at liberty to disclose) that may contribute to my hEDS, I am confident that my condition is polygenic. My mutant *TNXB* and *KLK* likely only partially explain my genetic underpinnings.

Furthermore, in addition to the nuclear genome, mitochondrial DNA may be a culprit in the etiology of EDS due to the crosstalk between the mitochondria and the autonomic nervous system (Wilson & Tonk 2020). Mitochondria are predominantly thought of as regulators of cellular metabolism reliant on oxidative phosphorylation to generate energy in the form of ATP. These organelles are also central to the production of reactive oxygen species (ROS), fatty acid metabolism, epigenetic reprogramming, and metabolic shifts responsible for the activation and differentiation of muscle stem cells following muscle injury, the latter of which is central to the muscle-building process.

Golder Wilson and Vijay Tonk's (2020) case study revealed mutations in mitochondrial genes, such as *MT-ATP6*, that disrupt ATP synthesis and cause a cycle in which lax connective tissue leads to blood pooling in the legs and reduced blood flow to the brain, thereby triggering dysautonomia, which, in turn, provokes gastrointestinal issues, postural-orthostatic tachycardia, and mast cell activation (Wilson & Tonk 2020). Chronic autonomic nervous system dysfunction, according to

the subject's muscle biopsies prior to and following exercise, impairs sensorimotor neuron transmission, thereby inducing small fiber neuropathy and a reduction in tissue and muscle strength, which ultimately compounds connective tissue laxity. The link between EDS and mitochondria strongly suggests that enhancing mitochondrial function, expediting the elimination of impaired mitochondria via an autophagy process known as mitophagy, and boosting mitochondrial biogenesis may improve EDS patients' quality of life.

Research and my own personal journey validate that hEDS, like many chronic conditions, takes a toll on the psyche. According to survey-based studies from 1994 to 2021, patients with my condition are more prone to anxiety disorders, depression, and suicidality than healthy controls (Bulbena et al. 2017; Baeza-Velasco et al. 2021). These psychological consequences, which breed anger, fear, and sorrow, give rise to biological distress—the body becomes incapable of managing the overstimulation of the nervous system, cortisol levels surge, and patients face a lack of self-control. However, not all stress is detrimental.

Unlike distress, eustress—brief exposure to a stimulus driving a moderate stress response that encourages cellular and psychological resilience by expanding one's "comfort zone"—is pivotal to evolutionary adaptation and promotes personal growth (Korte et al. 2005). Biological resilience, known as allostasis, is defined as an organism's capacity to turn on and off mediators involving the autonomic nervous system, inflammatory and immune biomarkers, and cortisol in response to a perturbation from homeostasis. At its core, life boils down to stress adaptation; humans are constantly bombarded by internal toxins, such

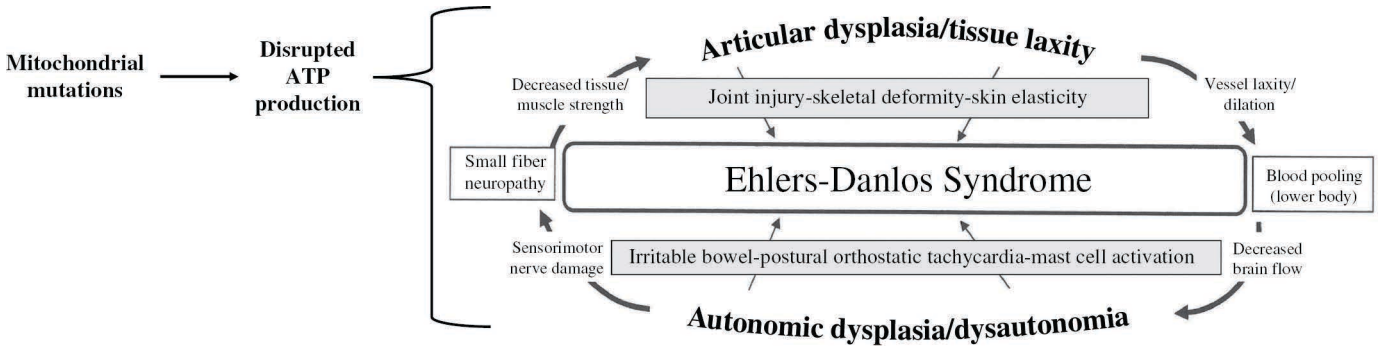


Figure 23.1: *Interaction between mitochondrial dysfunction and Ehlers-Danlos syndrome (EDS).* Mutations in mitochondrial genes may contribute to EDS and its associated comorbidities by interfering with ATP synthesis. The latter potentially causes blood pooling in lower extremities, which can, consequently, elicit dysautonomia, gastrointestinal symptoms, postural-orthostatic tachycardia, and mast cell activation syndrome in a cyclical fashion.

Adapted from "Mitochondrial Dysfunction Contributes to Ehlers-Danlos Syndrome—A Patient Presentation," by Wilson, G., & Tonk, V., 2020, *Journal of Biology and Life Science*, *11*(2), 192.

as ROS generated during ATP synthesis, and external chemicals, such as air pollutants. Evolutionarily conserved gene networks have been observed in fruit flies, roundworms, zebrafish, mice, humans, and other species that are activated to manage stress, which leads to a net resilience effect (Kültz 2005). Because of organisms' genetic pathways that respond to stress, life on earth persisted in the wake of volcanoes, Ice Ages, asteroids, and worldwide pandemics.

In conjunction with psychosocial and linguistic adaptations that enabled *Homo sapiens* to acclimate to harsh climates, reconstruct habitats, and forge communities, our species' resilience is also physiological. Hormesis—the Greek term coined in 1888 for "rapid motion" or "eagerness"—is a biphasic reaction to mild stress via which injury prompts biological adaptation that renders the body more resilient than it was prior to the eustress exposure, like exercise.

Despite possessing a sophisticated thermoregulatory system mediated by the hypothalamus, modern humans rarely experience environmental hormesis. Over the past several thousand years, thermal stress, a mainstay in primate existence for millions of years, was quickly removed from the human lifestyle. Such a rapid shift may predispose modern humans to disease as the thermoregulatory system and the brain do not experience enough thermal stressors, thereby leading to compromised central nervous system function (Flatt & Heyland 2011; Rattan 2019; Sun 2020; Birringer 2011).

In *Antifragile: Things That Gain from Disorder*, Nassim Nicholaus Taleb (2012) explores hormesis, which he refers to as antifragility

(Taleb 2012). As per Taleb, fragile entities are devastated under pressure, resilient entities can withstand stress and remain unchanged, and antifragile organisms adapt to stress and become stronger, from cellular and mental perspectives. Mark Mattson, a Professor of Neuroscience at Johns Hopkins University, and associates demonstrated the latter by showing that healthy cells react to bioenergetic stress signals by upregulating DNA repair enzymes, antioxidants, and neurotrophic factors, such as brain-derived neurotrophic factor (BDNF) (Mattson 2012; Raefsky & Mattson 2017; Mattson et al. 2018; Calabrese et al. 2010).

While he possessed no scientific credentials, Friedrich Nietzsche captured the concept of hormesis in his statement "that which does not kill us makes us stronger" (Gems & Partridge 2008). While it may be impossible, as of 2021, to apply gene editing technology in the setting of polygenic diseases like hEDS, patients can wrest back some of their control over their circumstances by modifying their external and internal environments to enhance their resilience by experiencing eustress. To this end, I have embraced my dual roles as scientist and specimen and strive to do everything, within reason, in my power to embody Taleb's notion of antifragility. My incorporation of sauna and cold immersion—forms of environmental hormesis—into my therapeutic regimen has expedited my healing from setbacks and has enabled me to become stronger, both psychologically and physically. By willfully subjecting myself to incremental doses of stress, I become less biologically vulnerable and emotionally reactive to the inevitable regular traumas that are a part of living with EDS. Hans Selye, the pioneering scientist of stress theory, remarked, "It's not stress that kills us, it is our

reaction to it" (Rice 2011, 384). Prior to experiencing heat or cold shock, I repeat this internal mantra: "You are in control of this small, yet incredibly powerful practice. You can dictate the temperature and duration. You are enabling yourself to gradually become antifragile, despite your fragile connective tissue. Do not fear these temperature shifts but embrace this stress for it will strengthen you in return."

Exogenous hormesis

Exposure to high heat in the sauna prompts dynorphin release from presynaptic neurons with the aim of returning body temperature to homeostasis. In contrast to endorphin, dynorphin, upon binding to kappa opioid receptors, induces temporary feelings of distress and dysphoria (Patrick & Johnson 2021). This thermoregulatory control pathway alters the brain's perception of endorphins, endogenous opioids responsible for the sensation of pleasure and the body's pain response. Dynorphin release increases the number and sensitivity of mu opioid receptors to endorphin, thereby enhancing the postsynaptic response to subsequent endorphin release, which, in turn, eases depression and anxiety (Shetty, et al. 2015). I experience this feedback loop on an almost daily basis; my heightened sensitivity to endorphins following my sauna exposure ameliorates my pain and fear secondary to my routine dislocations. The sauna not only lessens my EDS-related depression from a physiological perspective but also offers me a semblance of control over my circumstances by affording me the opportunity to heal myself.

A randomized, double-blind control study indicates that such postsynaptic remodeling is enduring. Clemens Janssen and

colleagues (2016) subjected 30 participants with depression to a single session of whole-body hyperthermia during which core body temperature was elevated to 101.3 degrees Fahrenheit (Janssen et al. 2016). Within a week of treatment, the subjects experienced an antidepressant effect that endured for six weeks after the single exposure. Furthermore, Tanjaniina Laukkanen (2015) and collaborators' longitudinal study followed 2,315 middle-aged Finnish males for 20 years and found a linear correlation between increased sauna frequency and duration and up a 37–40 percent reduction in all-cause mortality—including cardiovascular disease, neurodegenerative disease, respiratory disease, and cancer—irrespective of other lifestyle factors and age (Laukkanen et al. 2015). Given the extensive amount of time during which my disease prevents me from fully engaging in life, I readily welcome the potential that my regular sauna practice may extend my healthspan.

Heat shock proteins (HSPs), a conserved family of proteins present in each cell, are essential for protein synthesis and structural maintenance. Creating ATP gives rise to ROS, which continuously damage protein structure. Consequently, these malformed proteins' half-life is extended, enabling misfolded proteins to accumulate inside and outside of the cell and lead to diseases, including Alzheimer's disease, Parkinson's disease, and Huntington's disease. Sauna use activates the heat shock response system, thereby upregulating HSPs that repair damaged proteins. Paul Hafen (2018) and colleagues examined the effects of two hours of heat exposure for six consecutive days on 20 subjects, who demonstrated an increase in HSP70 and HSP90 by 45 and 38 percent, respectively (Hafen et al. 2018; Khazaeli et al. 1997).

Furthermore, the authors found a 28 percent increase in the participants' mitochondrial function and amplified expression of genes, such as peroxisome proliferator-activated receptor gamma (*PPARG*), requisite for mitochondrial biogenesis (Hafen et al. 2018). Reputable EDS experts, such as Dr. Pradeep Chopra, speculate that the neuropathic aspects of EDS may be due to mitochondrial dysfunction. Because my body is constantly repairing its connective tissue, a process dependent on a steady influx of ATP, I aim to optimize my mitochondrial efficiency.

In addition to directly impacting HSPs, heat stress turns on evolutionarily conserved gene networks included in the body's stress response system. Sauna therapy use activates *Nrf2*, a master regulator of the redox state in the cell that protects the cell from the damaging ROS by turning on cytoprotective, anti-inflammatory, antioxidant, and detoxifying genes—*heme oxygenase-1 (HO-1)*, *NAD(P)H:quinone oxidoreductase 1 (NQO1)*, and *glutathione peroxidase (GPx1)*, among others. For example, Nrf2-dependent upregulation of heme oxygenase-1 (HO-1) during heat exposure degrades the heme, a pro-oxidant, into anti-inflammatory carbon dioxide and bilirubin, an antioxidant. Nrf2 also downregulates inflammation by preventing the production of proinflammatory cytokines, including, but not limited to, interleukin (IL)-6, IL-1α, and inducible nitric oxide synthase (NOS2) (Vomund et al. 2017; Patrick & Johnson 2021).

Another transcription factor, forkhead box O3 (FOXO3), is upregulated during the body's reaction to heat. FOXO3 promotes the expression of genes that mend damaged DNA before a cancerous mutation takes root and genes that stimulate cell death in cases where cancer-causing mutations have already occurred.

Throughout the aging process, cells, like proteins and DNA, accumulate damage until they become senescent—cells incapable of proper function but persist, secreting proinflammatory molecules that compromise adjacent cells. FOXO3 turns on antioxidant genes that protect cells from succumbing to this fate. Furthermore, in the event that the cell becomes senescent, FOXO3 upregulates autophagy-promoting genes to destroy malfunctioning cells, thereby increasing longevity. This master transcriptional regulator not only manages senescent cells but also activates genes associated with stem cell function that facilitate regeneration and repair. Although *Nrf2* and *FOXO3* have yet to be researched in the setting of EDS, my daily sauna experience encourages me to speculate that the combined antioxidant, anti-inflammatory, and cytoprotective gene networks activated by these transcription factors accelerate my recovery and improves my resilience (Renault et al. 2011; Webb & Brunet 2014; Fitzwalter & Thorburn 2018).

Heat adaptation also decreases the basal level of protein degradation that occurs during physical activity, which leads to net muscle hypertrophy. This phenomenon is, in part, due to the fact that heat stress increases the production of growth hormone, which inhibits protein breakdown. Growth hormone's anabolic properties are mainly due to its effect on insulin-like growth factor 1 (IGF-1), which stimulates skeletal muscle development by inhibiting the FOXO pathway that degrades muscle and by activating the mammalian target of Rapamycin (mTOR) pathway responsible for sensing amino acids and synthesizing protein. A 1986 study of 17 subjects demonstrated that two one-hour sauna sessions per day for a week upregulated growth hormone

by 16-fold over baseline on the third day. Growth hormone remained elevated for hours following sauna use (Leppäluoto et al. 1986; Selsby et al. 2007; Naito et al. 2000; Hannuksela & Ellahham 2001; Hafen et al. 2019; Selsby et al. 2005). Maintaining muscle strength is pivotal to my well-being; because of the laxity of my connective tissue, my body depends on muscle tone for joint stability. Following my physical therapy sessions with an hour in the sauna boosts the development of my skeletal muscles due to the surge in anticatabolic growth hormone in conjunction with the other benefits associated with mild heat stress.

Another form of environmental hormesis that has improved my mental and physical resilience is cold stress—brief bursts of extreme cold-water immersion or cryotherapy (WBC)—which also turns on evolutionarily conserved gene networks associated with the stress response system. In ancient times, cold hydrotherapy was a means of equilibrating the body and mind; Hippocrates asserted that cold-water therapy "allays lassitude" (Hippocrates 400 B.C.E., Part 18). Hank Jedema (2008) and his collaborators elucidated the mechanism underpinning Hippocrates' conviction (Jedema et al. 2008). The researchers demonstrated that cold exposure has a pronounced impact on norepinephrine release into the bloodstream, where it functions like a hormone, and into the locus coeruleus (LC) in the brain, a critical neuromodulatory system involved in attention, emotion, motivation, and focus.

To understand the temperature and duration requirements for cold immersion to exert a hormetic response, Petr Šrámek (2000) and colleagues' study enrolled male subjects who submerged in

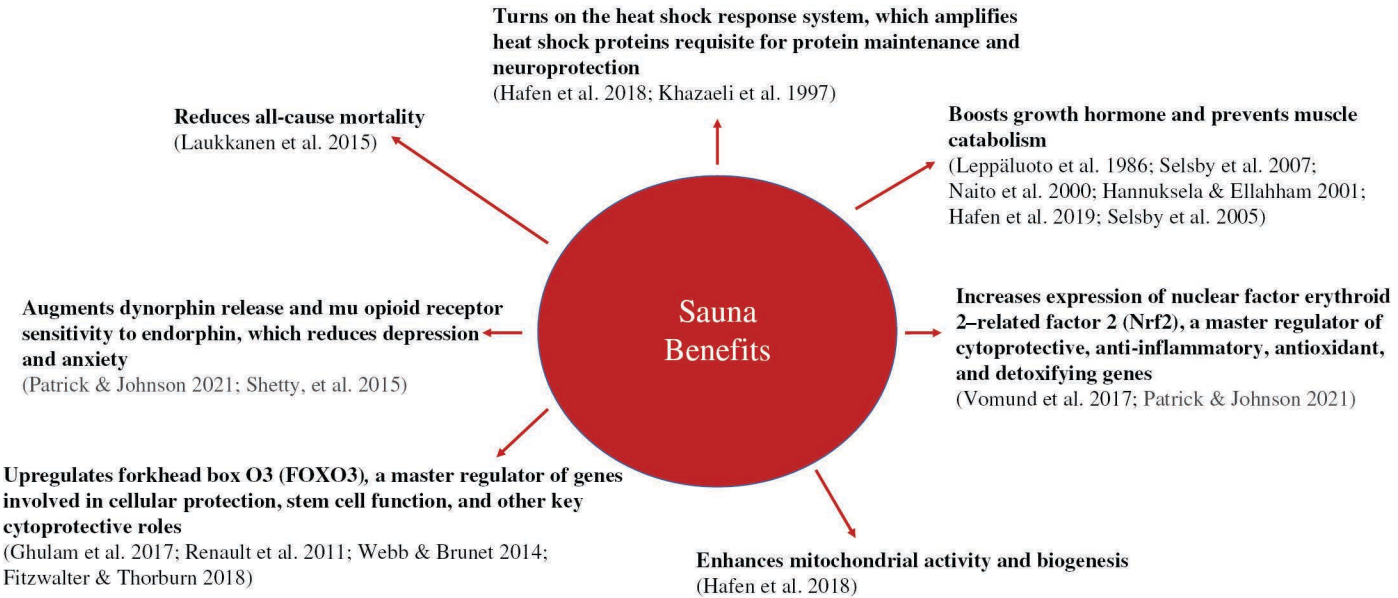


Figure 23.2: *Overview of Sauna Benefits*

water ranging from 14–32 degrees Celsius for an hour; only the participants immersed in the 14-degree-Celsius water showed a reduction in rectal temperature and an increase from baseline in norepinephrine by a staggering 530 percent (Šrámek et al. 2000).

However, one does not need to withstand cold temperatures for an hour to trigger the body's autonomic stress reaction. As the temperature falls, the amount of time requisite to stimulate these hardwired mechanisms decreases. In their study of 40 healthy males, Julien Louis (2020) and his associates found that a single two-minute WBC session at negative 110-degree-Celsius was sufficient to activate the autonomic system and to cause norepinephrine levels to climb (Louis et al. 2020). Interestingly, after five consecutive exposures, the subjects' autonomic response significantly declined relative to that after the initial session, which suggests that recurrent cold exposure modulates hardwired stress-resistance pathways. Throughout my two-year experience with daily extreme cold therapy, I noticed an increase in my tolerance to cold hormesis. Initially, I shivered uncomfortably through twenty seconds at negative 90-degree-Celsius but gradually acclimated, over the course of a year, to withstand three minutes at negative 160-degree-Celsius. Currently, I welcome this three-minute routine daily, and my body no longer shivers or protests in any way; in contrast, during this protocol, I experience a sense of euphoria as pain leaches out of my body and a satisfying sense of levity both physically and mentally.

By activating the innate fight-or-flight response mediated by the sympathetic nervous system, cold exposure robustly increases circulating norepinephrine. To ascertain the effect of WBC as an adjunct treatment for depression, Joanna Rymaszewska (2020)

and her collaborators conducted a randomized controlled trial (Rymaszewska et al. 2020). The study included 92 adults reliant on antidepressants to manage depressive episodes who were randomly assigned to the experimental or to the control cohorts. While the former group was subject to 10 WBC treatments at approximately −160 °C, the latter subset was exposed to -50 degrees Celsius, a cold but not cryogenic temperature. Based on self-reported depression rating scales and clinical psychiatric reports that accounted for quality of life, affect, and self-acceptance, the researchers concluded that, in conjunction with pharmacological intervention, WBC, relative to exposure to −50 °C, enhances well-being in depressed individuals. The authors speculate that WBC may exert such benefits because of its capacity to modulate immune molecules, or cytokines, that may be the culprit in depression, anxiety, and chronic pain disorders.

Like sauna-mediated endorphin sensitization, WBC, by raising norepinephrine systemically, may offer EDS patients a means of becoming psychologically antifragile. Following WBC, I notice a marked improvement in my mood, energy, and psychological staying power to mentally cope with whatever EDS setbacks I face for the remainder of the day. Joanna Rymaszewska and associates' supposition that WBC alleviates depressive symptoms by rebalancing immune modulators is certainly consistent with my experience. In addition to enhancing my mental state, WBC eases my chronic pain, which is potentially due to inflammation.

The sensation of improved energy following extreme cold exposure is, at least in part, due to the therapy's effect on mitochondria. In response to cold shock, the body generates heat by ramping up metabolic rate in muscle tissue, which leads to

muscle contractions, a process known as shivering thermogenesis. A parallel reaction to cold shock, known as non-shivering thermogenesis, occurs in fat tissue. Norepinephrine, which increases by two- to five-fold depending on the temperature and duration of cold exposure, upregulates the expression of uncoupling protein 1 (UCP1), which uncouples the electrical gradient in the mitochondria essential for ATP synthesis (Von Bank et al. 2021). In response, UCP1 increases metabolic rate through mitochondrial biogenesis—the generation of more mitochondria—in adipose tissue.

A human-based study supports prior rodent research findings that inhibiting norepinephrine receptors prevents mitochondrial biogenesis in fat tissue (Saito et al. 2009). Thus, cold shock boosts metabolism to return body temperature to baseline by activating the sympathetic nervous system and upregulating norepinephrine, which is necessary for mitochondrial biogenesis in fat tissue (Young et al. 1982).

While mitochondrial biogenesis in adipose tissue is mediated by norepinephrine, this phenomenon in skeletal muscle is dependent on peroxisome-proliferator-activated receptor-γ coactivator-1 (PGC-1α). According to James Broatch, Aaron Petersen, and David Bishop's (2018) review article, cold thermogenesis in muscle tissue degrades ATP into adenosine monophosphate (AMP), which increases the production of adenosine monophosphate-dependent protein kinase (AMPK), an enzyme that upregulates PGC-1α in response to cold stress (Broatch et al. 2018). PGC-1α, the master regulator of mitochondrial biogenesis, determines muscular oxidative capacity and motor neuron adaptations secondary to physical activity (Shute et al. 2018). William Southern

(2019) and collaborators showed that in the context of a mouse model of volumetric muscle loss (VML), myofibers are incapable of regeneration and mitochondrial respiration is impaired (Southern et al. 2019). However, in transgenic VML mice programmed to overexpress *PGC-1α*, the authors noted a near-complete normalization of muscle mass. The researchers conjecture that *PGC-1α* upregulation is protective against muscle cell death and that this transcription factor enhances the stability of the pre-synaptic neuromuscular junctions, thereby promoting muscle strength and endurance.

In conjunction with norepinephrine and *PGC-1α*'s pivotal roles in mitochondrial biogenesis, I hypothesize that boosting PGC-1α expression via WBC in EDS patients may aid in skeletal muscle maintenance. Through recurrent episodes of prescribed stillness following injuries, I have learned over and again that maintaining skeletal muscle mass is key to well-being in hypermobile EDS.

In addition to improving mood, mitochondrial function, and muscle strength, cold hormesis promotes analgesia by re-equilibrating immune molecules, known as cytokines. Dysregulation of cytokines, central sensitization, and hyperalgesia are hallmarks of several chronic pain conditions, including fibromyalgia (FM) and EDS. Given the overlap in psychological and pain processes associated with the latter conditions, perhaps Philipp Klemm (2021) and collaborators' findings are transferable to EDS cases (Klemm et al. 2021). In their study, the researchers probed the impact of six WBC sessions on 23 FM patients and 30 control subjects to assess the effect of cold stress on pain levels and cytokine profiles. They noted a reduction in self-reported pain and disease symptoms following three sessions. Unlike in

healthy controls, levels of IL-1, IL-6, and IL-10 cytokines shifted significantly throughout the study in FM patients. While IL-1 and IL-6 are typically disproportionately elevated in FM and may explain the myalgia and heightened pain present in FM cases, IL-10 is commonly reduced relative to baseline in this patient population. IL-10, in contrast to IL-1 and IL-6, lowers inflammation by regulating the activity of substance P—a neuropeptide implicated in the transmission of pain signals—to improve pain threshold and to downregulate pro-inflammatory IL-1, IL-6, and tumor necrosis factor alpha (TNF-α). While the pain-reducing influence only lasted for three months after the study was discontinued, WBC offers temporary analgesia by altering cytokine levels in FM patients. This shift in immune modulators may also improve FM patients' mood, as Joanna Rymaszewska and her colleagues suggested in their aforementioned study.

Though the combined activity of extreme bouts of hot and cold hormesis has yet to be rigorously investigated, biochemist Dr. Rhonda Patrick (2020) considers these two modalities to be synergistic (Patrick 2020). Anecdotal evidence and her own self-experimentation prompt Patrick to posit that experiencing cold shock following heat exposure amplifies the positive impacts of the sauna therapy alone because both modalities stimulate overlapping gene networks. While it activates heat shock proteins (HSPs) to a lesser degree than does the sauna, brief cold immersion increases the expression of HSPs, such as cytoprotective HSP70, that clear protein aggregates and maintain the integrity of the cellular cytoskeleton (Wei et al. 2018; Sonna et al. 2002). My personal regimen bolsters Patrick's hypothesis. I typically enter the sauna with EDS-related symptoms, including

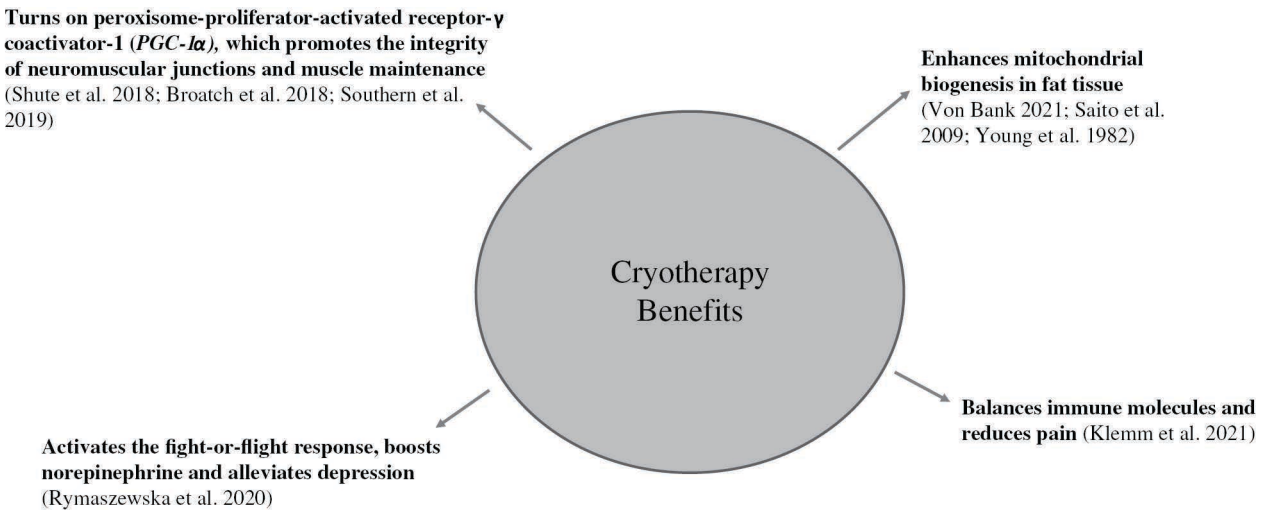


Figure 23.3: *Overview of Cryotherapy Benefits*

gastroparesis, nerve pain, dysautonomia, muscle soreness, and emotional distress, all of which transiently vanish after an hour in the sauna followed by three minutes of cryotherapy.

Endogenous hormesis

Since the gene networks governing hormesis are present in eukaryotic kingdoms—yeasts, fungi, plants, protozoa, and animals—Dr. David Sinclair, a professor in the Department of Genetics at Harvard Medical School and Dr. Konrad T. Howitz, the Director of Molecular Biology at BIOMOL Research, realized that humans can leverage stressed plants to induce molecular hormesis. In their seminal article, Sinclair and Howitz (2008) coined the term xenohormesis, meaning interspecies hormesis, to explain how plants produce phytochemicals in response to stress that may confer health and selection benefits to mammals and fungi that ingest them (Howitz & Sinclair 2008). Because plants are stationary organisms, they are unable to react to pathogens, parasites, or environmental threats by fleeing; instead, these eukaryotes evolved a broad spectrum of toxic defense chemicals, or phytochemicals, to handle stressors. For example, beans produce lectins to ward off insects and tobacco crops secrete nicotine to deter grazers.

When we consume stressed plants, our bodies identify their toxins, thereby activating the hardwired hormetic cascade via which we adapt to thermal stress discussed above. Research continues to critique the Western diet on account of its highly processed foods and its caloric surplus. Philip Hooper, an endocrinologist at the University of Colorado, argues that "there's true mutualism. We're in this together, the plants and us" (Velasquez-Manoff

2014). In line with the profound impacts of heat and cold shock on human biology, xenohormesis research advances the significance of epigenetics; genes are not the sole determinants of our fate. Health is a matter of expressing certain genes at specific levels at the proper time; resilience is contingent on how we interact with the external world. My mutations are not my destiny. I have a lifelong disease that I know will provoke future setbacks and engender a temporary sense of overwhelming defeat. But simultaneously, I know that I am far more than the errors in my genome once led me to believe. In becoming my own N-of-1 trial, I cultivate self-empowerment as I glean actionable information on the science of environmental as well as xenohormesis.

Sinclair and Howitz's (2008) paper reveals how plant toxins, or polyphenols, including resveratrol, curcumin, and EGCG, beneficially modulate mammalian gene networks to reduce inflammation, improve energy metabolism, and promote antifragility (Howitz & Sinclair 2008). Consumption of resveratrol increases ROS release, which activates NAD-dependent deacetylase sirtuin-1, which regulates transcription factors and associated pathways—including but not limited to *FOXO*, *PGC-1α, nuclear factor-κB* (NF-*κB*), and *DNA-binding subunit 70* (*Ku70*)—that enhance stress resistance, autophagy, mitochondrial biogenesis, mitophagy, hemostasis, and survival. One of curcumin's mechanisms of action, for example, involves its direct inhibition of cyclooxygenase-2 (COX-2), an enzyme that stimulates the release of prostaglandins, hormone-like proinflammatory compounds. While a small dose of a myriad of plant toxins have been scientifically validated to optimize human physiology and even to treat conditions, such as diabetes, rheumatoid arthritis, and

cardiovascular disease, my self-experimentation with plant compounds throughout the past three years leads me to home in on two such phytochemicals, curcumin and sulforaphane, because of the profound impact they continue to have on my health.

As mentioned above, inflammation is commonly thought of as a primary culprit in chronic pain conditions. Researchers have yet to probe the therapeutic effects of curcumin, the key curcuminoid found in the rhizomes of turmeric, on EDS pathophysiology. However, EDS experts, such as Dr. Heidi Collins (2017) and Dr. Christopher Centeno (2020), endorse supplemental turmeric as a means of downregulating inflammation in EDS (Collins 2017; Schultz 2020). Numerous in vitro and in vivo studies corroborate curcumin's capacity to reduce inflammation in the setting of arthritis, asthma, cardiovascular disease, and diabetes (Aggarwal & Harikumar 2009; White et al. 2019). Inflammasomes consist of protein complexes that control host responses to pathogens, physiological danger, or damage by secreting proteolytic and proinflammatory enzymes, such as caspase-1, and cytokines IL-1β and IL-18. Once these protein complexes are activated in response to structurally diverse damage-associated molecular patterns (DAMPs), like surplus glucose or toxins, they induce a rapid cell death process known as pyroptosis (Yang et al. 2019). The most well-characterized inflammasome is the nucleotide-binding domain and leucine-rich repeat-containing receptor with a pyrin domain 3 (NLRP3) inflammasome that is implicated in type-2 diabetes, Alzheimer's, and other inflammatory chronic diseases. Upon binding to apoptosis-associated speck-like protein with a caspase recruitment domain (ASC), NLRP3 induces ASC oligomerization to form protein structures called ASC

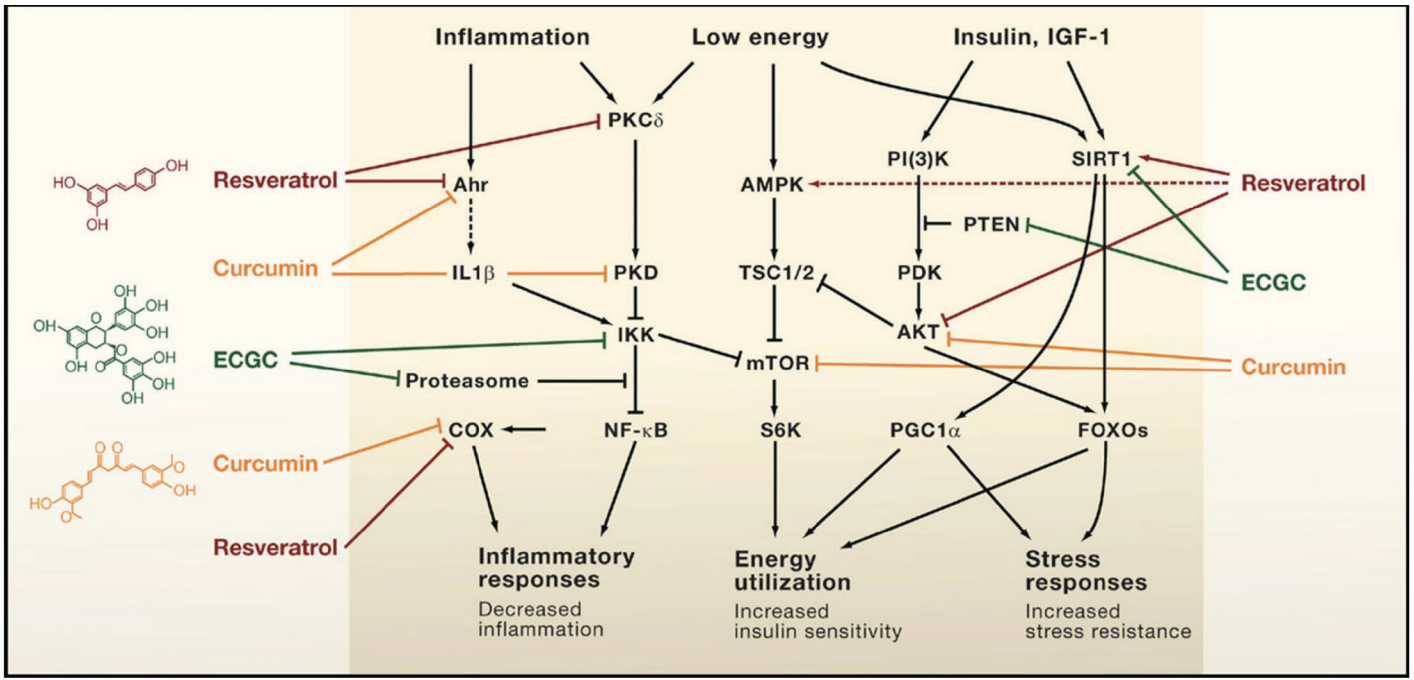


Figure 23.4: *Xenohormetic Effects of Polyphenols on Mammalian Enzymatic Pathways.* Compounds, including resveratrol, curcumin, and epigallocatechin-3-gallate (EGCG), derived from plants, modulate human physiological mechanisms to

confer health benefits. These molecules affect overlapping pathways regulating inflammation (aryl hydrocarbon receptor (AHR), interleukin 1 β (1L-1β), nuclear factor kappa B (NFkB), IκB kinase (IKK), protein kinase D (PKD), protein kinase C (PKC), cyclooxygenase (COX)), cellular energy (adenosine monophosphate-activated protein kinase (AMPK), tuberous sclerosis (TSC), mechanistic target of rapamycin (mTOR), ribosomal S6 kinase (S6K), and the stress response Insulin-like growth factor 1 (IGF-1), phosphoinositide 3-kinases (PI(3)K), dehydrogenase kinases (PDK), protein kinase B (AKT), peroxisome proliferator-activated receptor-gamma coactivator (PGC)-1alpha, sirtuin 1 (SIRT1), forkhead box transcription factors (FOXOs)) to boost organismal resilience. Note that arrows indicate interactions that activate signaling pathways, and blunted lines denote interactions that inhibit pathways.

Adapted from "Xenohormesis: Sensing the Chemical Cues of Other Species," by Howitz, K. T., & Sinclair, D. A., 2008, *Cell*, *133*(3), 388.

specks. In their paper, Haipeng Yin (2018) and collaborators used a mouse model to explore the anti-inflammatory effect of curcumin on the production of IL-1β and on NLRP3 inflammasome function (Yin et al. 2018). To this end, the authors fed curcumin to wild-type (WT) mice and to *Nlrp3*-deficient mice. While curcumin significantly reduced IL-1β levels in WT mice, this finding was not reproduced in *Nlrp3*-deficient mice, thereby implying that the NLRP3 inflammasome is a critical mediator of cytokines and of curcumin's anti-inflammatory properties.

Another study by Yannong Dou (2018) and colleagues investigated an alternate mechanism associated with curcumin in a rat model of collagen-induced arthritis (CIA) (Dou et al. 2018). CIA, in addition to causing degradation of connective tissue, shares other features with EDS, including dysregulation of the autonomic nervous system (ANS). The ANS mediates cytokine synthesis by way of the cholinergic pathway consisting mainly of the vagus nerve, the neurotransmitter acetylcholine, and acetylcholine receptors. The vagus nerve connection between the gut and the brain likely explains how dysautonomia in EDS, among other conditions, leads to and/or causes gastrointestinal symptoms. In their study, the authors explored the role of curcumin on the cholinergic system and found that in WT rats this phytochemical decreases sympathetic activity and increases parasympathetic activity, thereby reducing the fight-or-flight response and improving rest and digest processes.

Interestingly, Yannong Dou and associates' results were not duplicated in rats subject to a vagotomy—an operation in which the vagus nerve is severed—which strongly suggests

that curcumin's activity is dependent on the gut-brain axis. In WT rats, curcumin dosed at 100 mg/kg led to a reduction in proinflammatory TNF-α, IL-1β, IL-6, and IL-17A; vagotomy in these rats, however, even in the presence of curcumin, reversed these anti-inflammatory effects.

The manifest connections between the autonomic nervous system, cytokines, the gut, and chronic pain are frequently corroborated by researchers in the context of diseases ranging from Parkinson's disease to colitis. Furthermore, affect and digestive symptoms commonly co-influence each other. Diego Bohórquez (2010) used an electron microscope to observe that enteroendocrine cells found on the lining of the gut had protrusions akin to synapses, prompting him to question if these cells could, like neurons, transmit electrical messages to the brain.

Bohórquez later witnessed enteroendocrine cells secrete neurotransmitters and communicate to vagal neurons within 100 milliseconds, thereby cementing the gut-brain axis from a hypothesis into scientific truth (Underwood 2018; Kaelberer et al. 2018).

In light of Bohórquez's findings, the fact that hEDS is often comorbid with dysautonomia, postural orthostatic tachycardia, mast cell activation syndrome, and gut dysmotility is not surprising. Given the bidirectional crosstalk between the gut and the brain, I often find it challenging, if not impossible, to localize the origin of one of my particular symptoms; did the pain and inflammation in my right shoulder trigger my latest episode of mast cell activation syndrome? Or, alternatively, did the mast cell reaction in my gut stem from consumption of a histamine-releasing food, which dysregulated my cytokine profile systemically, and, in turn, caused the heightened pain in my shoulder?

My joint dislocations and chronic pain typically go hand-in-hand with gut and autonomic dysfunction. Ingesting 1,500 mg of curcuminoids each day for the previous year has been, to date, one of the few remedies that has eased my chronic joint pain, my autonomic dysfunction, my gastrointestinal issues, and my depression. Both 2018 publications mentioned above and my positive reaction to curcumin indicate that by altering cytokine levels regulated by the NLRP3 inflammasome or by the ANS by way of the vagus nerve, curcumin can downregulate inflammatory processes and thus mitigate pain, depression, and gut symptomatology.

Sulforaphane (SFN), another xenohormetic compound I have been consuming in supplement form each morning for the past three years, has profoundly reduced my neuropathic pain and my anxiety. An isothiocyanate, SFN is produced from the precursor glucoraphanin present in cruciferous vegetables and especially abundant in broccoli sprouts. SFN boosts levels of nuclear factor erythroid 2–related factor 2 (Nrf2), a transcription factor discussed above that has been documented in publications from 2011 to 2017 to mitigate inflammation, nerve pain, anxiety, and depression in several animal-model and human studies. Pablo Ferreira-Chamorro (2018) and collaborators aimed to identify SFN's effect on Nrf2's capacity to reduce depression and pain in a mouse model of neuropathic pain (by surgically inducing sciatic nerve constriction) (Ferreira-Chamorro et al. 2018). The researchers either fed the mice SFN or a control solution. They demonstrated that SFN, unlike the

sham compound, blocked the mechanical and thermal pain sensitivity in the injured mice.

To elucidate SFN's mechanism of action, the authors investigated SFN's impact on the levels of Nrf2, HO-1 and NQO1, antioxidants, and on CD11b/c, a marker of microglial activity. Microglia are specialized immune cells localized to the central nervous system that exacerbate long-term pain by upregulating proinflammatory molecules like COX-2 and interleukins. While nerve injury-mediated oxidative stress induces a reduction in Nrf2 and HO-1, SFN, by mitigating ROS, caused the expression of these proteins to return to baseline, thereby leading to a reduction in pain. Pablo Ferreira-Chamorro and collaborators also aimed to understand SFN's anti-inflammatory activity modulated by microglia. The authors showed that SFN prevents microglial activation in the spinal cord in injured mice, which, in turn, diminishes neuropathic pain.

Because my EDS impairs my connective tissue systemically, including my nerve sheaths, the majority of my pain is neuropathic. My multiple shoulder dislocations led to brachial plexitis and ulnar neuropathy; my CSF leak caused occipital neuralgia; my ankle dislocations spurred tarsi tunnel syndrome; and my temporomandibular joint instability triggered trigeminal neuralgia. As EDS patients, including myself, experience an adverse reaction to opioids, ranging from hyperalgesia to gastrointestinal dysmotility, identifying natural compounds with minimal to zero side effects is critical to my pain management. BrocElite's stabilized bioavailable sulforaphane capsules markedly decrease my nerve pain and improve my mood, even during and immediately

following a dislocation or injury. Recently, for the sake of testing the effects of SFN on my well-being, I excluded it from my daily supplement cocktail for three consecutive days, during which my pain noticeably increased and I felt more depressed than usual. In conjunction with curcumin, SFN upgrades my quality of life and permits me to live to my fullest potential, despite EDS.

Environmental hormesis and xenohormesis not only stimulate autophagy pathways responsible for cellular waste disposal, but the benefits of these mild stressors are contingent on functional autophagy (Malta et al. 2019). Autophagy-related genes (ARGs) trigger the formation of autophagosomes, vesicles containing dysfunctional proteins, subcellular constituents, and even damaged stretches of the genome that fuse with lysosomes—subcellular compartments filled with degradative enzymes—to create autolysosomes. In turn, autolysosomes facilitate the degradation of the sequestered molecules and organelles. Autophagy thus promotes the recycling of aged or impaired components of the cell to generate new molecules and energy. In addition to ARGs, this evolutionarily ancient mechanism is governed by highly conserved gene networks, primarily by mTOR signaling, present in organisms ranging from yeasts to humans. The transcription factor EB (TFEB) is a critical ARG that translocates to the nucleus in response to hormesis to activate genes required for lysosomal biogenesis, autophagosome formation, and lysosomal fusion.

Caroline Kumsta (2017) and collaborators' paper reveals the intimate link between autophagy and hormesis in the form of thermal stress (Kumsta et al. 2017). The authors exposed two classes of the model organism, *Caenorhabditis elegans* (*C. elegans*)—one

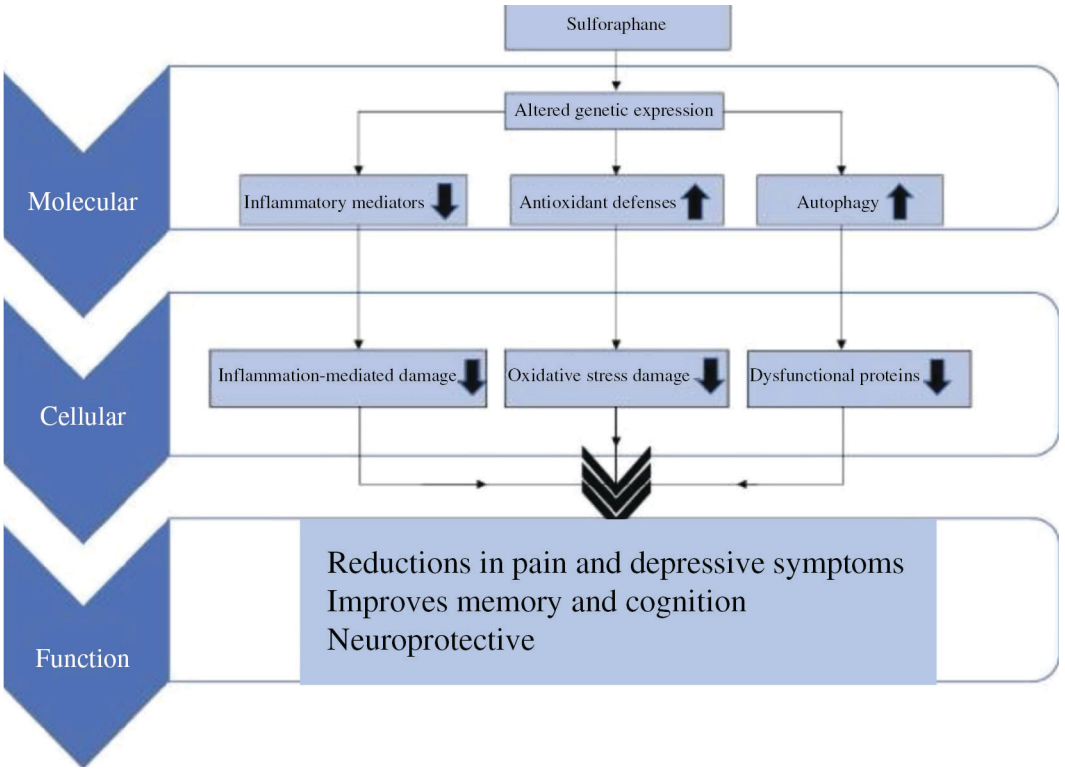


Figure 23.5: *Impact of Sulforaphane on the Nervous System.* Sulforaphane reduces pain and depression, enhances mental acuity and recall, and confers neuroprotection by acting on genetic pathways that decrease cellular damage and protein aggregation.

Adapted from "The Neuroprotective Mechanisms and Effects of Sulforaphane," by Klomparens, E. A., & Ding, Y., 2019, *Brain Circulation*, *5*(2), 80.

wild-type (WT) subset and another group programmed with a *Tfeb* (the homologue to the human *hlh-30*) loss-of-function mutation—to heat shock at 36 degrees Celsius. While the WT *C. elegans* turned on several green fluorescent protein (GFP)-tagged ARGs, the mutant class failed to activate autophagy pathways central to the life-extending and health benefits associated with hormesis.

However, thermal stress resilience not only hinges on functional autophagy, but ARGs are essential to thermoresistance. To show the latter, the researchers developed a *C. elegans* model of neurodegeneration in which organisms overexpress Polyglutamate (PolyQ)-containing proteins that aggregate in the cell and accelerate aging. When these modified *C. elegans* were subject to heat, the organisms exhibited a reduction in PolyQ deposits dependent on heat shock factor 1 (*HSF-1*), a key autophagy gene upregulated in reaction to heat shock. Furthermore, in another genetically programmed *C. elegans* line that led the animals to overexpress HSF-1, ARGs were upregulated; silencing these ARGs diminished the increased stress tolerance and survival relative to baseline observed in *C. elegans* overexpressing HSF-1. Collectively, these results imply that autophagic pathways and antifragility, as demonstrated in the setting of heat shock, are codependent. To augment the anti-inflammatory, analgesic, antidepressant, cytoprotective, and life-extending effects of my hormetic regimens, I boost my autophagy, among other pathways, through fasting, another form of hormesis.

Rather than functioning as a binary on-off switch, autophagy is a degree-dependent state chiefly mediated via sirtuin (SIRT) and mTOR signaling. Eukaryotic cells contain seven SIRT enzymes,

three of which, SIRT1, SIRT6, and SIRT7, reside in the nucleus. To remove functional epigenetic marks, known as acetyl groups, from proteins, SIRTs consume the energy-rich nicotinamide adenine dinucleotide (NAD+), and SIRT abundance is governed by the cell's metabolic state. As mentioned earlier, mTOR is an enzyme whose activity is modulated by hormones, glucose, and amino acid availability, which determine if the cell enters growth mode or autophagy. mTOR is composed of two complexes, mTORC1 and mTORC2. In accordance with Gavin Yong-Quan Ng (2019) and colleagues' review paper, I will focus on SIRT1 and mTORC1, the main drivers of autophagy and other pleiotropic effects of fasting. During fasting, the cell responds to the reduced influx of energy by decreasing blood glucose, hormones, including IGF-1, and mitochondrial respiration, the latter of which boosts levels of adenosine monophosphate (AMP)—a byproduct of ATP metabolism—relative to ATP and NAD+. As a result, adenosine monophosphate-dependent protein kinase (AMPK) and SIRT1 are activated and directly promote the transcription of cellular autophagy genes by modifying epigenetic tags to render specific segments of chromatin more accessible to transcriptional machinery. AMPK also indirectly promotes autophagy by inhibiting mTORC1, which itself inhibits autophagy.

Homo sapiens are evolutionarily programmed to fast. Prior to the advent of the Neolithic era, members of the genus *Homo* were vulnerable to cycles of feast and famine, ranging from hours to weeks, dictated by food availability (Mattson et al. 2017). Just as humans developed hardwired mechanisms to cope with thermal stress, they were also forced to adapt metabolically to

persist during famines psychologically, physically, and cognitively. Episodes of nutritional deprivation were often accompanied by necessary physical exertion in order to hunt. By learning to store energy in adipose tissue, as opposed to in the form of carbohydrates and proteins, *Homo sapiens* effectively amassed a ready supply of fuel that facilitated survival. In fact, this capacity to burn fat to generate energy, a metabolic strategy that leads to the production of ketone bodies, permits our species to function at peak performance cognitively and physically. It is due to this 'thrifty genotype' adaptation, Mark Mattson, Valter Longo, and Satchidananda Panda, among other scientists, posit that our species endured (Anton et al. 2018; Longo & Panda 2016).

Humans inherited genetic pathways primed for temporary food scarcity and concurrent physical activity (Mattson et al. 2017). However, due to humanity's current overconsumption of food and sedentary lifestyle, our species currently faces what biologists dub an evolutionary mismatch—evolved traits that were originally advantageous are now maladaptive on account of environmental shifts. This phenomenon is mediated by epigenetics as environmental conditions, like the various hormetic stressors discussed previously, modulate gene expression patterns and, in turn, influence phenotypes. Studies conducted on identical twins show that different environmental circumstances alter disease vulnerability and other traits between these siblings who share 100 percent of their genome.

Frequent consumption of carbohydrates and amino acids, especially leucine, leads mTOR to be constitutively active, which means that one is constantly synthesizing protein and remains

in growth mode. While this steady state of mTOR activity is essential for fetal development and maturation, it is deleterious, and can induce early aging, cancer, neurodegenerative diseases, among other life-shortening conditions in adulthood. mTOR is an example of biologist George Williams's hypothesis of antagonistic pleiotropy—a single gene responsible for a phenotype that is both beneficial and harmful to the organism depending on its time of expression (Schmeisser, K., & Parker 2019). In the case of mTOR, this hypothesis is known as the trade-off theory of aging whereby the genetic program responsible for cellular senescence and aging is essential during development. In his groundbreaking book entitled *The Switch*, scientist James Clement delves into how we can strike a balance between mTOR and autophagy through fasting and diet to stave off the diseases that plague modern times (Clement 2019).

In addition to boosting autophagy, fasting exerts other hormetic benefits by activating evolutionary programmed gene networks that facilitate cellular resilience and repair discussed previously in relation to thermal stress and xenohormesis. In their review article, Gavin Yong-Quan Ng (2019) and associates explain that fasting-induced SIRT1 activity is mediated by NAD+ and by FOXO3, a master regulator of stress resistance genes upregulated in the context of fasting (Yong-Quan Ng et al. 2019). Upon activation by NAD+ signaling, SIRT1 coordinates the expression of genes, known as peroxisome proliferator-activated receptor (PPAR) genes, that increase fat mobilization and degradation to generate ketone bodies. SIRT1 also functions as an inhibitor of NF-κB, a transcription factor that promotes the expression of

proinflammatory genes. In conjunction with NAD+ levels, SIRT1 is regulated by FOXO3's interaction with tumor protein (TP53/p53)—a protein responsible for detecting and responding to DNA damage—at the SIRT1 promoter. According to Suchitra Gopinath (2014) and collaborators' investigation, *FOXO3*, which is expressed in quiescent muscle stem cells are vital for stem cell self-renewal (Gopinath et al. 2014). The authors deleted *FOXO3* in mouse muscle stem cells and used histological and transcriptional analyses, which showed the stem cell's propensity to differentiate and that Notch signaling—a primary pathway that maintains stem cell quiescence—was downregulated. When the authors programmed the *FOXO3*-deficient cells to overexpress the Notch intracellular domain, they were able to rescue the self-renewal capacity of muscle stem cells. The researchers' data implies that by triggering the Notch pathway, FOXO3 sustains muscle stem cell quiescence essential for adult muscle regeneration. My routine 16 to 24 hour fasts, which I extend up to 48 hours immediately following a procedure or dislocation, accelerate my recovery time and, thereby, reduce the amount of time I have to remain bedridden to heal. By fasting, I am upregulating *SIRT1*, which indirectly inhibits inflammation, and *FOXO3*, which promotes the self-renewal of my muscle stem cells that are essential for tissue repair.

Independent of SIRT1 and NAD+ levels, fasting profoundly affects mitochondrial biogenesis and mitophagy. The low energy status in the cell boosts NRF2, which enhances antioxidant gene expression and mitochondrial biogenesis. Sanaz Mehrabani (2020) and associates' meta-analysis on the links between fasting and mitochondrial function suggests that fasting governs

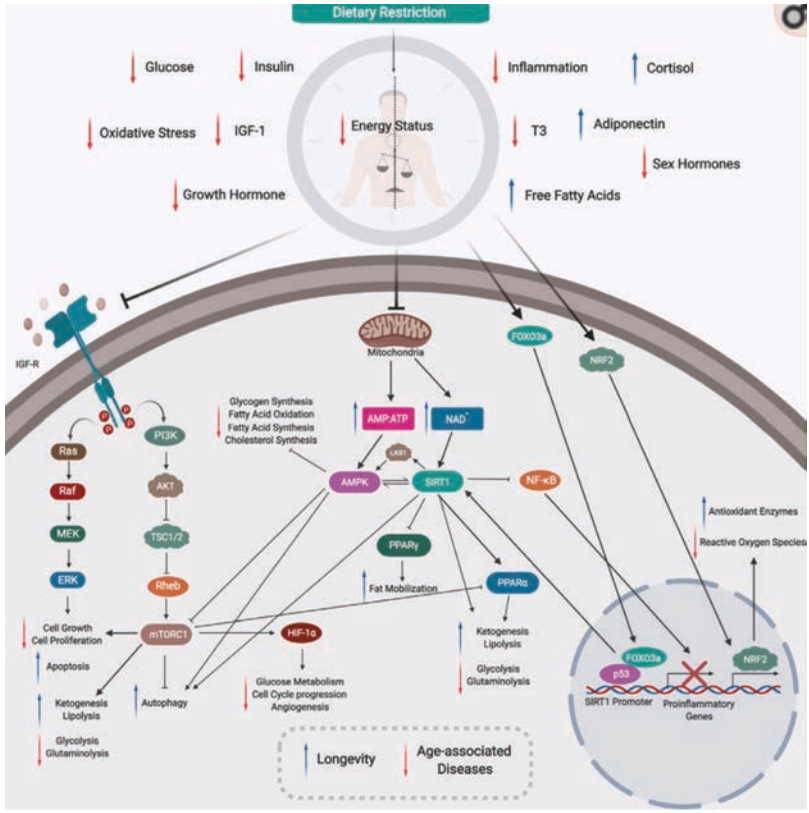


Figure 23.6: *Mechanism of Dietary Restriction (DR).* During DR, there is a reduced energy status within the organism, resulting in corresponding decreases in blood glucose, insulin, insulin growth factor 1 (IGF-1), growth hormones, sex hormones, and T3 thyroid hormones. Also, DR induces a reduction in both oxidative stress and inflammation. Following DR, there are increases in free fatty acids, adiponectin, and cortisol. A lower cellular energy status will lead to reduced mitochondrial activity and aerobic respiration, increasing the adenosine monophosphate (AMP): Adenosine triphosphate (ATP) ratio and nicotinamide adenine dinucleotide (NAD+) levels. Two major cellular nutrient and energy sensors, adenosine monophosphate kinase (AMPK) and sirtuin 1 (SIRT1), will then be activated, respectively. Activated AMPK will inhibit glycogen synthesis, acetyl-coenzyme A carboxylase 1

and 2 (ACC1, ACC2), and 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) to drive a reduction in fatty acid synthesis, oxidation, and cholesterol synthesis. Activated SIRT1 can enhance ketogenesis and lipolysis, and downregulate glycolysis and glutaminolysis. These effects may also be due to an activation of peroxisome proliferator-activated receptor alpha (PPARα), reflecting direct and indirect functions of SIRT1. Activated SIRT1 can also repress the activity of peroxisome proliferator-activated receptor gamma (PPARγ) to modulate lipid metabolism and enhance fat mobilization in white adipose tissue during DR. Activated SIRT1 can inhibit nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) activity, inhibiting the expression of proinflammatory genes. SIRT1 activation is dependent on the increased interaction between forkhead box O3 (FOXO3a) and p53 at SIRT1 promoter sites. The physical interaction between FOXO3a and p53, and the subsequent activation of SIRT1, play important roles in repressing cell growth and proliferation. Notably, SIRT1 activation can activate liver kinase B1 (LKB1), which will further activate AMPK, thus creating a positive feedback loop. Reduced levels of insulin, glucose, and growth hormone downregulate insulin and IGF-R signaling pathways, inactivating the RAS/MAPK axis, repressing cell growth and proliferation, and promoting apoptosis. Repression of IGF-R signaling will include the phosphoinositide 3-kinase (PI3K) pathway, and inhibit downstream mammalian target of rapamycin complex 1 (mTORC1), promoting autophagy. Inhibition of mTORC1 can also occur via activated AMPK in response to DR. Decreased mTORC1 function can promote ketogenesis and lipolysis, and repress glycolysis and glutaminolysis. Moreover, the corresponding decreased function of mTORC1 also inhibits hypoxia-inducible factor 1 alpha (HIF-1α), which downregulates key biological processes such as glucose metabolism, angiogenesis, and cell cycle progression. The nuclear factor erythroid 2-related factor 2 (NRF2) pathway is also triggered by DR, which helps to increase production of protective antioxidant enzymes and mitochondrial biogenesis to reduce

reactive oxygen species (ROS) activity. With lower levels of ROS, there will be reduced DNA damage and maintained genome stability. Lower energy status will prime cells to low-intensity stress, and this hormetic mechanism will stimulate better management of stress, upregulate DNA repair genes, as well as shifting toward a preferred setting of maintenance and repair (not shown). Overall, DR can act via these mechanisms to counter age-associated diseases and induce longevity.

Reprinted from "Dietary Restriction and Epigenetics: Part I," by Yong-Quan Ng et al., 2019, *Conditioning Medicine*, *2*(6), 287.

the expression of mitophagy (mitochondrial autophagy)-related genes—including *PTEN-induced kinase 1* (*PINK1*), *Parkin*, *ubiquitin*, and *SIRT3* (Mehrabani et al. 2020). In their study of fasted mice, Sunmi Seok (2018) and collaborators identified SIRT3 as a critical mitochondrial deacetylating enzyme that protects the cell from ROS (Seok et al. 2018). Dysfunctional mitochondria are at the root of several diseases that are also associated with overstimulation of mTOR, such as diabetes, cancer, and neurodegenerative conditions.

Moreover, Heather J. Weir et al.'s (2017) publication strongly suggests that mitochondrial dynamics are essential to fasting's capacity to increase AMPK and healthspan (Weir et al. 2017). Just as my stillness following setbacks only begot further injuries and pain, mitochondrial stagnation prevents fasting from exerting its positive effects; in the Harvard School of Public Health's news release, the senior author of the study, William Mair noted, "Our work shows how crucial the plasticity of mitochondria networks is for the benefits of fasting. If we lock mitochondria in one state, we completely block the effects of fasting or dietary restriction

on longevity". During my daily 16 to 24 hours of fasting period, I feel more focused and energetic than I do following a meal due to the cytoprotective effects, mitochondrial biogenesis, and mitophagy associated with abstaining from food. Because I consume xenohormetic supplements and practice hot and cold shock while fasting, I activate these strategies' overlapping genetic pathways with the aim of amplifying the accompanying hormetic benefits to become stronger through stress.

While my routine fasting robustly increases my mitochondrial function and energy, its pain-alleviating impact is, from the vantage point of an EDS patient, its greatest asset. The cumulative effect over the past decade of my frequent joint dislocations, gastroparesis, neuropathies, and other injuries renders chronic pain a mainstay in my life. Throughout my 16- to 24-hour fasts, and especially during my extended fasts, my chronic pain diminishes, and I am able to channel the focus it usually consumes into constructive endeavors, like writing my senior thesis.

In contrast to acute pain sensation—a reflex mediated by peripheral sensory neurons animals evolved as an adaptive mechanism in response to danger—chronic inflammatory pain is maladaptive and is partially due to central nervous system activation.

Amber Alhadeff (2018) and colleagues' study examines how the neural circuits that mediate hunger also modulate chronic pain (Alhadeff et al. 2018). The authors first exposed mice to 24-hours of fasting and tested the animals' pain behaviors. To mimic chronic pain, the researchers injected formalin, a chemical that causes acute pain within zero to five minutes and chronic pain within 15 to 45 minutes, into mice's paws. Acute pain

behavior was assessed by subjecting the mice to a hot plate or to mechanical stimuli. Relative to fed control mice, hungry mice were significantly less reactive to long-term inflammatory pain; according to the authors, fasting "almost completely abolished inflammatory pain responses, mimicking the effects of anti-inflammatory painkillers (Alhadeff et al. 2018, 149)." Hunger, however, did not alter the mice's acute pain behavior, which suggests that hunger only modulates the maladaptive, not the adaptive, pain response.

In order to identify the neurons involved in hunger and chronic pain, Amber Alhadeff et al. systematically inhibited and activated clusters of hunger-regulating neurons that project from the hypothalamus to the hindbrain and express agouti-related protein (AgRP). The researchers discovered a subpopulation of roughly 300 AgRP neurons responsible for the hunger-dependent analgesia, an effect dependent upon neuropeptide Y (NPY) signaling on NPY1 receptors on hindbrain neurons. Injection of NPY into the region of the mice's hindbrain containing the AgRP neuronal projections was sufficient to eliminate, chronic, but not acute, pain, irrespective of food consumption. Inhibition of NPY1 receptors in fasted mice reversed the hunger-mediated analgesia. Moreover, subjecting hungry mice to acute pain or food markedly decreased AgRP neuronal activity. In sum, these findings elucidate that fasting, by stimulating AgRP hunger-related neurons mediated by NPY, profoundly eases maladaptive chronic, but not adaptive acute, pain behavior.

Notwithstanding the evolutionary gap between mice and humans, human clinical trials continue to reveal the positive

impacts of fasting on chronic pain, fibromyalgia, and metabolic diseases among other conditions. My own lifelong N-of-1 study suggests that Amber Alhadeff and associates' findings hold merit in the setting of EDS. If I tear a ligament or sustain a fracture during my prolonged fasts, I notice that my acute pain sensation remains heightened, my long-term pain is remarkably reduced (compared to when I experience an injury during my eating window). Abstaining from food intermittently, like thermal hormesis and xenohormetic compounds, is a profound form of eustress that boosts autophagy, stem cell function, cellular stress resistance, mitochondrial function, energy, and mitigates chronic pain. Through its hormetic benefits and the sense of self-control it offers, fasting empowers me, both physically and spiritually.

Intermittent fasting, however, like any other form of hormesis, when taken to the extreme of chronic nutrient deprivation, causes eustress to become distress and leads to malnutrition and fragility. Thus, while I value the benefits of forgoing food temporarily, I acknowledge that fasting, especially for those with eating disorders, may be counterproductive. To enhance the lifestyle practices discussed in this chapter, I view my nutritional intake as a form of medicine; I have experimented with and documented my physiological responses to over a dozen regimens—from the low FODMAP diet to the autoimmune paleolithic protocol. For the past two years, I have adopted a traditional ketogenic approach that continues to improve my quality of life more than any other eating plan I have attempted thus far.

The ketogenic diet is defined by the binary presence or absence of a biomarker, known as ketone body (e.g., acetoacetate,

beta-hydroxybutyrate, or acetone), which is produced from fatty acids by the liver and can cross the blood-brain barrier (Greco et al. 2016). Achieving the state of dietary ketosis requires eating a macronutrient ratio that is high in fat calories (65–90 percent), adequate in protein (15–25 percent), and restricted in carbohydrates (< 5 percent). Like glucose, ketones are a source of biological fuel to generate ATP. For good reason, sugar-containing foods continue to be lambasted as causative agents of chronic disease. Reliance on glucose alone as a starter molecule for ATP synthesis leads to the overproduction of ROS, which results in inflammation and can set the stage for or, in my case, exacerbate chronic illness.

Dr. Oliver Owen and Dr. George Cahill's research at Harvard in the 1960s involved fasting overweight subjects for 40 days (Felig et al. 1969a; Cahill et al. 1968; Felig et al. 1969b). In doing so, these scientists demonstrated that prolonged fasts cause ketone bodies to, almost completely, replace glucose as the brain's primary fuel. Dr. Richard Veech, who was mentored by Dr. Cahill, recognized beta-hydroxybutyrate (BHB) as a "superfuel" (Veech 2004; Veech 2014). To this end, he measured redox potential energies in the liver, heart, and brain in both fasted and fed states. Dr. Veech's analysis led him to conclude that one of the ketone bodies, BHB, was metabolically superior. Scientific studies over the last five years have elucidated that ketone bodies not only function as "superfuels" but also serve as potent signaling molecules that favorably regulate processes including inflammation, mitochondrial biogenesis, and muscle catabolism by activating biological stress pathways (Newman & Verdin 2014; Puchalska & Crawford 2017).

Elevated circulating BHB secondary to fasting, endogenous ketosis, or exogenous ketones, suppress inflammation. Yun-Hee Youm (2015) and colleagues determined that BHB exerts this effect by, like cryotherapy, inhibiting the NLRP3 inflammasome (Youm et al. 2015). The authors assessed human monocytes—a type of white blood cell—before and after exposure to BHB and found that BHB modulated NLRP3-dependent cytokines IL-1β and IL-18. To assess BHB activity *in vivo*, the authors used mouse models of Muckle-Wells Syndrome (MWS), Familial Cold Autoinflammatory Syndrome (FCAS) and urate crystal-induced body cavity inflammation, all of which stem from mutations in NLRP3-encoding genes that render the complex constitutively active. In the setting of these disease models, consumption of BHB markedly decreased the release of proinflammatory caspase-1 and IL-1β from the NLRP3 complex. Yun-Hee Youm and associates' results indicate that the anti-inflammatory effects of ketosis are, at least in part, due to BHB's inhibition of the NLRP3 inflammasome. The authors showed that by blocking potassium ion efflux in bone marrow-derived white blood cells, ASC oligomerization, which is central to NLRP3 assembly, and ASC-dependent speck formation, BHB downregulates inflammation.

In conjunction with blunting NLRP3-dependent inflammation, BHB impacts the epigenome to reduce inflammation and oxidative stress. Brianna Stubbs et al.'s review article (2020) on the therapeutic potential of ketone bodies in COVID-19 cases (due to the link between inflammation and the virus) summarizes BHB's function as a class one and class two histone deacetylase inhibitor (HDACis)—enzymes that facilitate chromatin opening— to allow for favorable gene expression, even in the context

of a persistent molecular pathology (Stubbs et al. 2020). Based on previous research, the authors suggest that BHB upregulates oxidative stress-resistance genes *FOXO3* and *Mt2* by dampening HDAC1 and HDAC2 at the respective promoters associated with these genes. Furthermore, BHB directly stimulates Nrf2 and, in turn, triggers the expression of antioxidant response elements (AREs) that promote cytoprotection. BHB also mitigates inflammation by reducing NF-kB-mediated cytokines TNF-α and IL-6, according to Cassandra Forsythe (2008) and collaborators' study in which overweight subjects were either administered a low-carbohydrate or a low-fat diet (Forsythe et al. 2008). Living with a chronic disease, like EDS, causes my inflammatory markers to be elevated above baseline. Adhering to a ketogenic diet presents me with the empowering opportunity to diminish, at least to a certain extent, inflammation secondary to recurrent joint dislocations. Two weeks into my ketogenic diet experiment, I recognized a profound improvement in my systemic chronic pain that I augment following dislocations or during episodes of severe pain by ingesting a bottle of TdeltaS ketone ester—a supplement developed at Oxford University containing 25 grams of bioavailable BHB.

BHB's pleiotropic effects also influence mitochondrial activity. While elevated mitochondrial ROS (mtROS) are detrimental, basal levels are adaptive and stimulate hormetic pathways involved in cell replication, differentiation, resilience, and immunity. This phenomenon, referred to as mitohormesis, is a promising mechanism that improves mitochondrial function. A study by John Newman (2017) and collaborators subjected mice to a ketogenic diet—90 percent of calories came from fat and 10

percent from protein (Newman et al. 2017). Blood assays and gene expression analyses revealed that relative to mice fed a non-ketogenic low-carbohydrate diet—75 percent of the calories came from fat, 15 percent from carbohydrates, and 10 percent from protein—mice that consumed a ketogenic diet exhibited raised blood BHB levels and increased peroxisome proliferator-activated receptor α (PPARα)-associated genes that induce mitohormesis and mitochondrial biogenesis. These findings suggest that BHB upregulation in the setting of a ketogenic, but not a low-carbohydrate diet, modulates PPARα signaling. Eating in accordance with stringent ketogenic macronutrient ratios has robustly increased my energy. The synergistic effects of my intermittent fasting and my ketogenic diet significantly reduce, and even periodically eliminate, my EDS-related fatigue and brain fog due to the mitohormetic effects associated with these lifestyle practices.

Andrew Koutnik (2020) and colleagues provided evidence that BHB and AcAc impede muscle protein breakdown directly as well as indirectly by inhibiting inflammation, a cause of muscle degradation (Koutnik et al. 2020). They analyzed ketone levels, muscle tissue biopsies, tumor biomarkers, and immunoinflammatory indicators in the setting of a mouse model of cancer cachexia (the experimental group), or muscle wasting, relative to these variables in healthy control mice. First, the authors established that the experimental subset of mice demonstrated heightened proinflammatory serum markers, including TNF-α and IL-10, and muscle degradation, hallmarks of cancer cachexia. After feeding a subpopulation of the afflicted mice a ketone diester (KDE), the researchers observed decreases in tumor size, inflammatory

markers, and skeletal muscle wasting. These results shed light on ketones' distinct anti-catabolic effects, which the authors speculate are partially due to KDE's ability to downregulate cytokines by modulating the NF-kB pathway and the NLRP3 inflammasome (in addition to other proinflammatory cascades). Thus, ketones—generated endogenously through diet and/or fasting or administered exogenously in the form of ketone esters or salts—may be applied to several disease processes, including Duchenne muscular dystrophy, age-related sarcopenia, and even muscle loss due to EDS. With the goal of optimizing my muscle strength, I continue to revise my supplement and dietary protocol that includes ketosis, ketone supplements, creatine monohydrate, amino acids, and various cofactors linked to metabolic processes that I ingest prior to and following physical therapy. Throughout the previous two years, I have witnessed my body rebound faster than ever before from setbacks and have developed my skeletal muscular strength, which has, to a significant extent, enhanced my joint stability and capacity to physically engage in my world.

While my EDS-associated mutations cause my connective tissue to be lax and predispose me to injuries that cause my trust in my own biology to falter over and again, I refuse to play the victim in my own narrative, to transform my diagnosis into self-loathing. My existence inevitably feels saturated with a sense of loss over a life I once surmised was mine for the taking—from the ability to bear my own children to participating in the mainstream college social scene. It has taken seven years for the reality of my EDS to set in and, occasionally, I still sense that I am acclimating to unfamiliar terrain, adapting psychologically and physically to circumstances that I assume during their unfolding will break me into

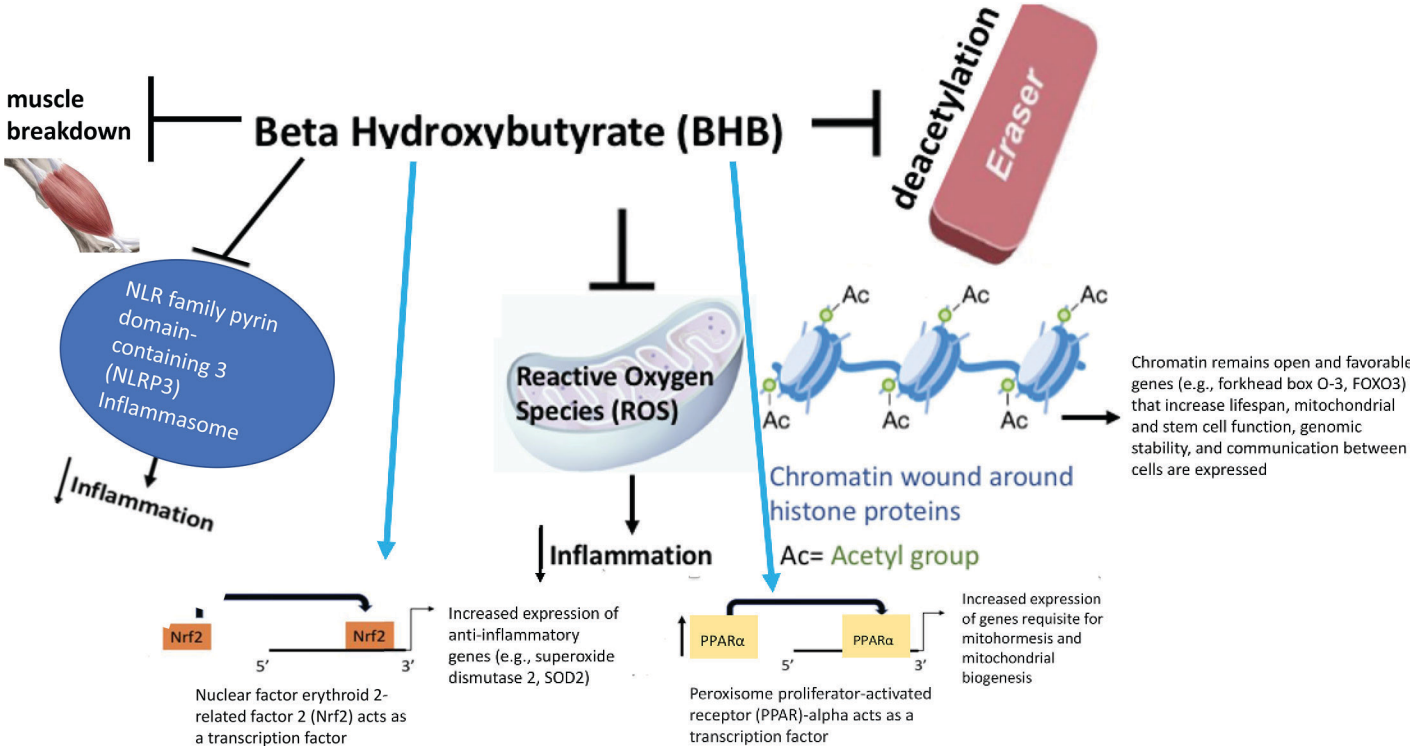


Figure 23.7: *The ketone body beta hydroxybutyrate (BHB) exerts beneficial physiological effects.* BHB directly inhibits histone deacetylation, thereby exposing favorable genes to transcriptional machinery. This ketone body also suppresses inflammation and muscle catabolism. Note: Black blunted lines indicate pathway inhibition, and blue arrows indicate pathway activation.

shards I will never again assimilate into something whole. But I do. I turn on my inner scientist to marshal as much control as my EDS permits. Just as I was born with my EDS genes, I inherited astonishing genetic stress-response pathways. Despite my fragile internal connections, I am becoming resilient, and even antifragile, by fine-tuning my environment through hormetic habits that will enable me to rebuild myself in the wake of whatever my future holds in store.

24
Curses and blessings of COVID-19

There is part of me that always knew my EDS did not equate to torn dura or fractured spines, an inner knowledge that, for me, recovery was but a word.

As COVID-19 skyrocketed cytokines and constricted airways, my pandemic had little, if anything, to do with immunity.

Trapped in a human reenactment of Schrödinger's cat, I was alive, yet not.

Dead, yet not,

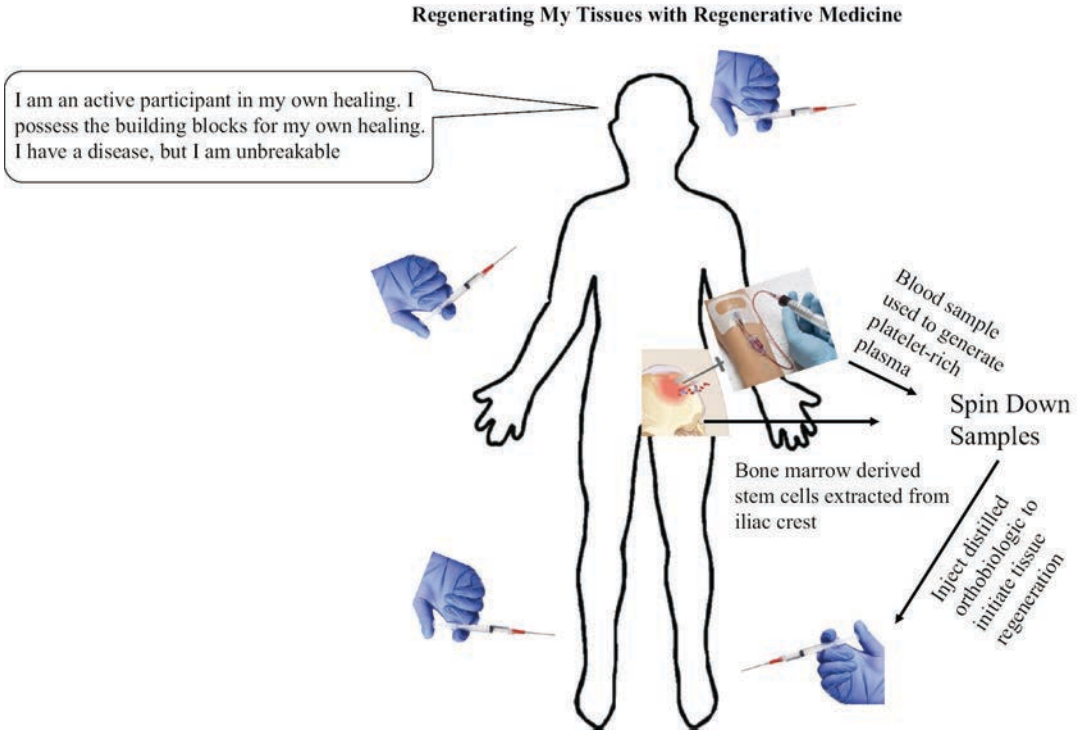
locked in a quantum mechanical middle ground, a head-to-toe breakdown even I, after all of my hardships, could never have anticipated.

In a cruel version of locked-in syndrome, my tibial tendons ruptured,

bones dislocated in my feet, my left hip sank out of socket,

my shoulders descended out of overtaxed capsules, the facets in my cervical spine slid out of alignment, shuttling electric pain through my scalp,

and my jaw felt like it was shut down with heavy-duty wiring.


Regenerating My Tissues with Regenerative Medicine
I am an active participant in my own healing. I possess the building blocks for my own healing. I have a disease, but I am unbreakable
Blood sample used to generate platelet-rich plasma
Spin Down Samples
Bone marrow derived stem cells extracted from iliac crest
Inject distilled orthobiologic to initiate tissue regeneration

I assumed that my EDS could temporarily rob me of a limb or two, but never knew that it could swallow me whole,

leaving me barren of everything,

save for watching the slow seepage of time, moments I did not have to waste, and a crushing sense of loss and defeat.

"Mom, I can't walk any further. My feet are really hurting, and the nerve pain in my skull is piercing." I witnessed bodies zoom past me and heard the thumping of sneakers sloshing against Central Park's grimy Bridal Path. I felt a queasy blend of envy and fear collect at the base of my throat.

"What's wrong, Bel? We only just left home." Her voice, tremulous with trepidation, was muffled into an almost whisper beneath a surgical mask, a trademark of pandemic life. Arrested in my tracks by pain running from my insteps up my calves, I experienced a sudden onslaught of grief. I craved to move like the joggers that dashed by me but knew that my body would never fit that mold, nor any template of mainstream human life. I observed my mother's face coordinate itself into lines of worry.

"I don't know what's going on, Mom. All I know is I can't walk any further. My knees are giving way from the pain in my legs." I pressed myself against my mother, looping my left arm through her right one. A popping noise—like a firecracker or a shotgun emission—resounded into the sliver of space between us; my simple act of dependence, of shifting my weight onto my mother, caused my left shoulder blade to clunk out of socket. So accustomed to the sounds of my dislocating limbs, neither of us flinched. We stood in silence, sentry to my failing body.

A gray sheet of cloud obscured the blue lingering in the February sky. My mother studied me. I could feel my own building panic work its way into her. Sporadic droplets of rain bled into my mesh sneakers. Rivulets of sadness and weather rolled into our face masks. Muted by overwhelming distress, I limped the two blocks home to our apartment. In that moment, I could not have foretold that I would not resume walking for a listless fourteen months. Only in retrospect, do I realize that my past tribulations served as a sort of testing ground—training in emotional and psychological catabolism and anabolism—that would offer me sufficient stamina for the course ahead.

My amplified occipital neuralgia following my blood patch in 2019 was not, as doctors encouraged me to presume, a side effect of the procedure, but was, in fact, a symptom of the cerebrospinal fluid (CSF) leak itself. The anesthesiologist's injection of ten cubic centimeters of blood into my epidural space was inadequate to completely fill the column of my dilated dura. At the outset of the COVID-19 pandemic, my body intuited the mandated lockdown on a cellular level. CSF continued to seep out of me. As though a spell was cast, I came comprehensively undone. Because the partial patch seemed to revive neural circuits in my brain, transporting me from my comatose-like state to solving genetics problems, I naively packaged my leak into a past nightmare.

Caught in a personal lockdown that did not come with the promise of an expiration date, I struggle now, as I did at the time, to deduce the cause and effect underpinning my downfall. Did my ongoing CSF leak destabilize my cervical spine, left scapula, and right shoulder, thereby perturbing my balance, which, in turn, threatened my lumbar spine fusion and the integrity of my

feet? Or, instead, did the logic of the Rube Goldberg machine that was my body flow in the reverse direction? Did my unstable naviculars and my flat feet spur my collapse? The mathematician in me was incapable of plotting my logical regression curve; my inner geneticist was ill-equipped to decode the gene networks at work as my body gave way at age 26.

An uneasy blend of paralyzing dread settled over me, masking all other emotions. I did not cry, laugh, nor feel much of anything, save for numbness, for fourteen months. 2020 seemed like one long excruciating blur. My body was in a constant state of emergency as one setback spiraled into others. While my anguish probably came in spurts, I was impotent to even articulate it in shrieks and whimpers because doing so would only exaggerate my neck and nerve pain. Moreover, my cervical instability caused temporomandibular joint (TMJ) discomfort. Each word came at a high cost; full-fledged emoting in the form of laughter or tears was out of my budget. So, I suppressed all of the feeling I could, exchanged words with my parents for gestures, and locked out Rebecca and Olivia. I focused on the one skill my illness had sharpened into a fine blade over the years. I held fast to the problems that came with neat solutions.

Ironically, the timing of the COVID-19 pandemic was, in my case, a blessing. My physical decline—from my limited talking to my inability to sit or walk for long durations—rendered me too disabled to return to Cambridge to resume Harvard. However, social distancing protocols encouraged Harvard to substitute in-person lectures with remote learning. As I tended to my faltering body, I could manage a partial course load without fretting about my

physioball and desk raiser, accommodations concealed behind Zoom's purview. I reenrolled in Genetics and Genomics, the course that my CSF leak forced me to abort in 2019.

In contrast to my emotions, I could not ignore the throbbing pain in my head, neck, back, and feet. I felt like someone somewhere had pulled the plug responsible for my nervous system function, like my entire being was rioting against me, and like I was backsliding into a conglomeration of all of the ill phases that haunted my history. I was at a stalemate against the almighty EDS. So, I channeled all of the anguish, sorrow, and disquiet into genetics problems that did not concern my mutant genes. I calculated covariances, mutation-selection balances, and Hardy-Weinberg equilibria from dawn until late into the evening. I reserved my restricted seating and talking time for class, a daily hour during which my personal torment seemed to recoil and my synapses fired solutions to problem sets at warp speed. I no longer relied on my calculator to compute Bayesian posteriors. Even in the midst of my leaking dura, my mind astounded me as it multiplied and divided large sums and analyzed data in problem sets. I turned my raging pain into intellectual fuel, grasping hungrily at whatever control I could.

Because my TMJ discomfort escalated as the day progressed, I retreated into my locked-in state—incapable of walking, sitting, talking, crying, or laughing—in the interludes between class. I communicated solely with my parents in an impromptu sign language, gesticulating here and there, attempting, and often failing, to translate my thoughts into comprehensible pressing needs to use the restroom or to prepare something to drink. The articulate poet in me vanished. Even if I could physically withstand more seated time to write, I feared the words and withheld sentiments

that would spill out of my fingertips, unbidden. Instead, I passed the rest of the day bedridden as I mentally worked through problem sets and supplemental questions projected from my laptop onto my bedroom ceiling. While I was an introvert, I was not alone. I exchanged emails almost daily with my genetics instructor, Professor Daniel Hartl, regarding topics including recombination events, epistasis, inbreeding coefficients, CRISPR, and my EDS.

Like Professor Ruvolo and Albert, Professor Hartl offered me more than prompt explanations and affirmations of my understanding. Despite the remote nature of our correspondence, Professor Hartl viewed me holistically; he simultaneously sympathized with my personal hardships and recognized my passion for genetics. To him, I was a student who happened to be a patient, rather than the inverse. For his capability to see through the thick veneer of my EDS into the scientist I strove to become, I am eternally grateful. It is because of Harvard faculty like Professor Hartl that I would ultimately muster the courage to pursue science, despite my illness. Infrequently, acutely after a dislocation or during episodes of severe pain, I emailed Professor Hartl to inform him that I was unable to attend class. Our communication was in keeping with the following set of emails:

"Professor Hartl,

I have sadly been up all night with neck pain, blurred vision, and recurrent bilateral shoulder dislocations that have caused terrible nerve pain when I sit. I sadly do not think I can make it to class this morning, despite my desire to do so. I am sorry for the inconvenience. My body is so unpredictably challenging.

Best, Elly

Dear Elly,

I'm very saddened to hear that you are struggling so hard and so heroically with your disability. I am so enjoying having you in the class. I've been teaching long enough to know that having a student like you is a privilege. You really think, and think deeply, and you enjoy thinking. That kind of curiosity is a rare and wonderful gift, and I am privileged to be your mentor. My thoughts and prayers are with you.

Dan Hartl

Hello again,

I just wanted to express my gratitude for all of your time and support. It means so much to me to have a teacher like you who is, at once, sensitive to my situation and who also sees beyond my illness into who I really am and my passion for learning.

Best, Elly"

At the conclusion of the term, Genetics and Genomics students completed a final project that involved formatting an interview with a scientist into a podcast. As the term progressed, however, my physical status deteriorated to the extent that opening my mouth wide enough to drink water caused excruciating TMJ pain. My meals then, as they do now (due to ongoing neck issues), consisted of blended concoctions of bone broth, avocado, olive oil, and protein powders. Given my predicament, Professor Hartl suggested that I conduct a written, rather than oral, interview.

My final project presented me with the unique opportunity to weave together my passion for nutritional approaches to disease and the topics covered in Genetics and Genomics. I decided to

interview a long-standing hero of mine, Dr. Dominic D'Agostino, a leading scientific authority on ketosis and its use cases in the settings of disease and extreme environmental conditions. He is a tenured professor at the University of South Florida in the Department of Molecular Pharmacology and Physiology and a researcher at the Institute for Human and Machine Cognition (IHMC). After reviewing my interview in *O, The Oprah Magazine* and my publication in *The Jewish* Journal, Dr. D'Agostino expressed interest in my story and dedicated ample time to respond to my questions on the ketogenic diet as it pertains to genetics, epigenetics, and EDS, as indicated in the email below.

"Elly,

It was my pleasure and very interesting for me to hear your story. We can post this on my blog and feature you as a guest writer. I admire your determination to endure, thrive, learn and educate others about EDS.

Very best, Dom"

Along with my written transcript, I sent the following to Professor Hartl:

"Thank you for presenting me with such a wonderful opportunity. Your course has truly rescued me emotionally from what I am going through physically by affording me one sector of my life that I can understand and control. I cannot thank you enough."

In response, Professor Hartl wrote:

"I'm really impressed with how much you have learned about the ketogenic diet and how it affects metabolism and its applicability to all sorts of conditions that I would not have guessed. I very much

enjoyed reading your paper. The projects in OEB50 are not graded, but if they were this one would get an A. Excellent work."

(My feature article on Dr. D'Agostino's blog, released in March 2021, is accessible via this link: https://ketonutrition.org/ketogenic-diet-for-ehlers-danlos-syndrome-eds/)

Despite my success in genetics class, I was soon forced to face the reality rooted in my own genome. As the term came to a close, my body continued to fall into disrepair from head to toe. MRIs of my spine, feet, and jaw revealed misaligned and unstable vertebral bodies, torn tibial tendons, dislocated tarsal bones, and adhesive capsular restriction of my TMJs. Moreover, as my CSF leak evolved, my head once again felt like a boulder, my vision disintegrated into incoherent fragments, and my thoughts seemed to come to a standstill. During a blurred haze of doctors' appointments, I learned that I had Bertolotti syndrome—a congenital defect in my lumbar spine due to an enlarged transverse process—and required surgery on my feet, back, neck, and jaw. Meanwhile, my CSF leak progressed without a formal diagnosis. In spite of my muddled thought process, I was doggedly averse to more operations; my spinal fusions had instructed me that surgical interventions came with too many risks and side effects secondary to the tissue fragility associated with EDS. If my status as a scientist and patient had taught me anything, it was that it motivated me to be my own experiment and advocate. By 2021, I did not trust Western medicine to prescribe an optimal course of treatment, so I charted my own. My research into the science of stem cells, in addition to my work with Albert, led me to conclude that, with the aid of a regenerative medicine physician, I could rebuild myself cell by cell.

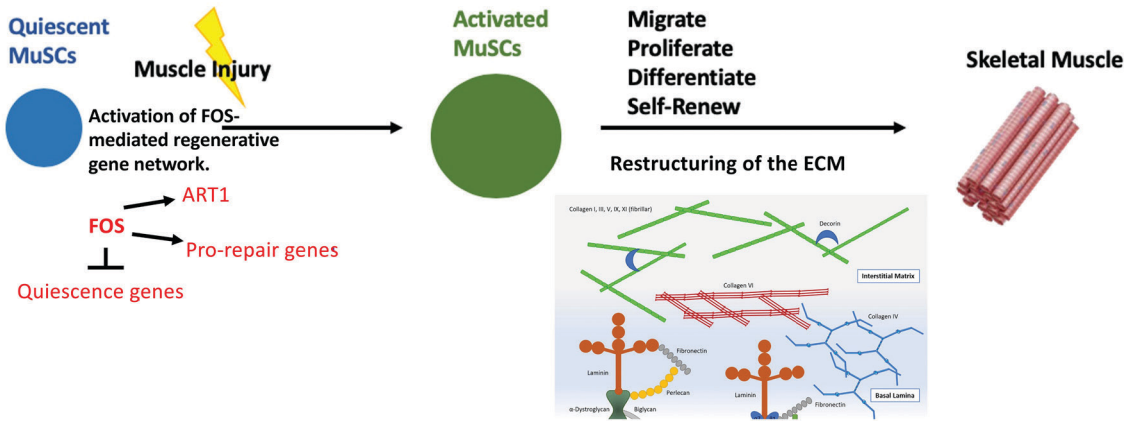


Figure 24.1: *Polarization of macrophages.* Macrophages polarize into two broadly classified phenotypes based on their cytokine environment exposure. Macrophages exposed to inflammatory cytokines (tumor necrosis factor alpha (TNF-α) and interferon gamma (IFN-γ)) polarize to an M1 phenotype. The M1 macrophages are inflammatory in nature and produce additional inflammatory cytokines (e.g., TNF-α, interleukin (IL)-1, IL-12, IFN-γ). These cells are thought to be responsible for scarring and fibrosis. In contrast, exposure to anti-inflammatory cytokines (IL-4, IL-13) will polarize macrophages to an anti-inflammatory M2 phenotype. The M2 macrophages produce additional anti-inflammatory factors (IL-10, interleukin-1–receptor antagonist (IL-1RA), arginase, transforming growth factor-β (TGF-β)) and in turn are thought to be responsible for regeneration, rather than scarring and fibrosis. Red indicates inflammatory factors, blue coloring indicates anti-inflammatory factors.

Reprinted from "Mesenchymal Stem Cell Therapy on Tendon/Ligament Healing," by **Chamberlain et al., 2017,** *Journal of Cytokine Biology,* ***2*****(1), 112.**

Regenerative mechanisms

Albert Almada and collaborators (2021) identified the function of an oncogene called *FOS*, a pro-regenerative master regulator that is transiently activated in mouse muscle stem cells within 90 minutes following muscle injury (Almada et al. 2021).

Muscle stem cell state—from quiescent to activated—is contingent on the cells' transcriptional profiles. For example, a hallmark of quiescent, or non-dividing, stem cells located under muscle fibers' basal lamina is their expression of paired box 7 (*PAX7*), and muscle damage turns on myogenic determination factor 1 (*MYOD1*), which facilitates stem cell activation, proliferation, and myofiber regeneration. As per my mentor's research, FOS regulates dozens of genes, such as ADP-ribosyltransferase 1 (*ART1*), which is integral to initiating stem cell-mediated repair. Almada et al. showed that *FOS*-knockout stem cells transition from dormancy to an activated state more gradually and demonstrate inferior regenerative capacity relative to *FOS*-expressing stem cells. Based on these findings, perhaps upregulating the human analogue of *FOS* either epigenetically or using gene-editing technology in patients, like myself, who constantly face skeletal muscle injury following dislocations and other insults would boost efficient skeletal muscle repair and, thereby, expedite the healing process. Combined with intracellular signals, such as *FOS*, the extracellular matrix (ECM), according to Robert Csapo, Matthias Gumpenberger, and Barbara Wessner's (2020) review article, is a key regulator of muscle growth, regeneration, and function. Specifically, current research shows that muscle stem cell fate is, in part, dictated by chemical and mechanical signals

transmitted between the stem cells and their niche. Activation of muscle stem cells induces restructuring of the cell's ECM; during this process, proteins that comprise the ECM, laminin-α1 and laminin-α5, are secreted into the basal lamina layer of the ECM. Furthermore, rodent studies have shown that muscle stem cells express ECM-associated collagen proteins to sustain dormancy and thus maintain the muscle stem cell pool for future repairs. In light of the interplay between muscle stem cell activity and the ECM and between my form of EDS and ECM dysregulation, it is possible that my skeletal muscles' regenerative capacity is diminished from baseline. As such, because my ECM-related mutations may downregulate my body's capacity to heal itself (perhaps by reducing my quiescent muscle stem cell count), regenerative injections, including bone marrow-derived stem cells and platelet-rich plasma (PRP), may help to incite, or to accelerate, muscle repair by amplifying my reservoir of muscle stem cells.

Regenerative medicine

Regenerative medicine injections not only deliver stem cells and growth factors to damaged tissues to initiate cellular repair and renewal but also stimulate ECM restructuring. While our bodies continually demolish and regenerate cells to maintain cellular health, EDS patients, as described in Chapter 2, are genetically programmed to perturb this balance by stimulating cellular destruction at the cost of renewal. As such, regenerating tissue through therapeutic injections may permit EDS patients to transition toward a more reparative state, which may promote the re-equilibration between anabolism and catabolism in these cases. In their article, Liborio Martini (2017) and collaborators studied

the impact of platelet-rich plasma (PRP), a form of regenerative intervention to be elaborated on below, in patients with knee osteoarthritis (Martini et al. 2017). In healthy individuals, the cartilage ECM maintains a dynamic equilibrium via which cartilage cells, or chondrocytes, are broken down and rebuilt to sustain cartilage structure and function. However, in osteoarthrosis, ECM-degrading enzymes are, as in the context of EDS, upregulated relative to proteins involved in regenerating chondrocytes, thereby unleashing an inflammatory cascade. After an injection of PRP, patients with osteoarthrosis exhibited reduced pain because the intervention alters the joint microenvironment by introducing chemical signals that protect the ECM from harmful inflammation and prompt collagen and ECM regeneration, thereby bolstering connective tissue (Chamberlain et al. 2017).

According to physiatrist Dr. Ross Hauser, the director of Caring Medical, a regenerative medicine clinic that treats EDS, restoring ECM integrity is central to tissue repair and EDS-related symptom mitigation (Hauser 2021). In his clinic, Dr. Hauser has successfully treated hundreds of EDS patients, who experience pain relief and joint stability after his injections. While further research that explores the impact of regenerative medicine in EDS patients is necessary to fully understand and appreciate the mechanisms at work in this patient population, doctors at regenerative medicine practices such as Caring Medical and The Centeno-Schultz Clinic (founded by Dr. Christopher Centeno and Dr. John Schultz) have had successful outcomes in EDS patient populations (Schultz 2019). The currently presumed mechanism is that regenerative agents ameliorate EDS pain, thicken lax ligaments and tendons, and strengthen joint capsules.

In the 1950s, Dr. George Hackett set the stage for the field of regenerative medicine. Dr. Hackett developed a concentrated hypertonic dextrose solution, referred to as prolotherapy, that has since been repeatedly proven to improve joint function, connective tissue structure, and pain control. In 1989, Dr. Robert Klein validated prior animal-based studies that showed prolotherapy's capacity to augment ligamentous mass. Following prolotherapy treatment in human subjects, Dr. Klein (based on biopsies taken before and after his injections) noted a roughly 60 percent increase in collagen fiber and ligament thickness (Reeves et al. 2016; Hackett 1958; Klein et al. 1989). Despite its documented success, prolotherapy is frequently insufficiently potent (especially in EDS cases) to offer enduring symptom relief and thus commonly serves as a diagnostic tool, rather than a long-term strategy. In contrast, autologous alternatives, which fall under the umbrella of 'orthobiologics,' like bone-marrow aspirate concentrate (BMAC) or PRP, are thought to confer prolonged joint stability, pain reduction, and enhanced function. My life-changing personal experience with regenerative medicine in the care of Dr. J, who completed her fellowship at The Centeno-Schultz Clinic, corroborates that BMAC and PRP injections can alleviate EDS symptoms and restore quality of life in patients with my condition (Schultz 2019).

BMAC is one source of mesenchymal stromal cells (MSCs), multipotent cells originating from the mesoderm and neural crest. Stromal cells, previously referred to as stem cells, mainly drive tissue regeneration by replacing impaired cells and by releasing molecules and extracellular vesicles that stimulate a hormone-like response, known as the paracrine effect, that

promotes cell-to-cell communication between stem and differentiated cells (Assis-Ribas et al. 2018; Harrell et al. 2021). Paracrine and growth factors— vascular endothelial growth factor (VEGF), transforming growth factor beta (TGF-β), and IL-1β, IL-6, and IL-8—induce angiogenesis, cellular proliferation and differentiation and downregulate inflammation. *In vitro*, MSCs can differentiate into several connective tissue cell lineages— adipocytes, osteocytes, chondrocytes, tenocytes, and myoblasts. These multipotent cells are promising therapeutic agents in the setting of several degenerative musculoskeletal and inflammatory conditions. MSCs downregulate inflammation by modulating genes relevant to EDS pathophysiology, including matrix metalloproteinase (MMP) and tissue inhibitors of metalloproteinases (TIMP) implicated in ECM stability, tumor necrosis factor alpha (TNF-α), and interleukins (ILs), among others (Pittenger et al. 2019).

Tendons and ligaments, which attach muscle to bone and bone to bone, respectively, are fibrous connective tissues responsible for maintaining musculoskeletal architecture. Following injury or damage to these structures, a process of inflammation, tissue granulation, and collagen production reestablishes connective tissues. The initial inflammatory phase primarily involving immune cells known as M1 and M2 macrophages, however, weakens the resultant tensile strength of tissue (relative to that of the original tendon or ligament) secondary to the development of scar tissue and impaired collagen fiber organization. In their study, Connie Chamberlain, Erin Saether, Erdem Aktas, and Ray Vanderby (2017) probed MSCs' impact on immune cells during the healing process (Chamberlain et al. 2017). The authors found that MSCs exert a reprogramming effect on

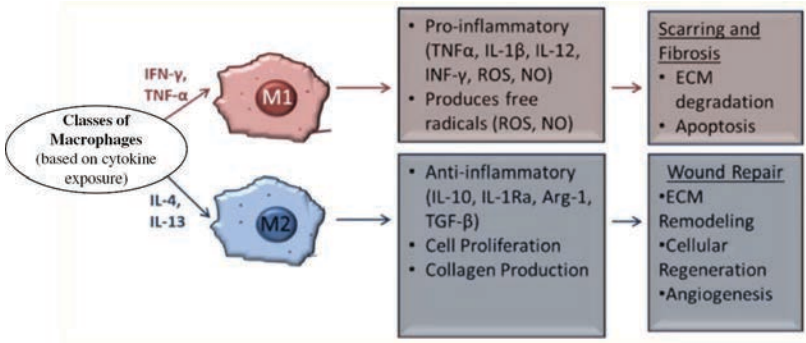


Figure 24.2: *Overview of orthobiologic treatment effects*

pro-inflammatory M1 macrophages by altering their phenotype to anti-inflammatory M2 cells. Whereas M1 cells secrete proinflammatory molecules and free radicals, both of which contribute to tissue fibrosis, cell death, and ECM degradation, M2 macrophages release IL-10 (along with other anti-inflammatory molecules) and foster collagenous and cellular development, thereby promoting wound healing and ECM remodeling. Furthermore, in vitro experiments in which macrophages were incubated with MSCs isolated from bone marrow led to increased expression of anti-inflammatory factors associated with M2 cells and markedly reduced levels of proinflammatory IL-12 and TNF-α.

To understand how MSC dosage following ligamentous injury impacts inflammation and tissue strength, the researchers subjected rats to medial collateral ligament injury, which they treated either with a low dose (1×10^6) or high dose (4×10^6) of allogenic MSCs—stem cells derived from a healthy donor, rather than extracted from the mice (autologous) involved in the study. Unlike the low dose mouse subset, which demonstrated a notable decrease in M1 cells and augmented ligamentous strength,

the high dose population exhibited lowered quantities of M2 cells and slim to no improvement in tensile strength. The authors speculated that the increased inflammatory response and lack of healing in the high dose group resulted from the use of allogenic, not autologous, stem cells, a hypothesis that has been supported by previous mouse model studies. Based on the researchers' data, MSCs chiefly exert healing effects by modulating macrophage phenotypes to mount an anti-inflammatory response responsible for cellular regeneration and ECM remodeling necessary for connective tissue repair. Given these results, MSC-mediated tissue recovery, inflammation, and ECM restoration are clearly interlinked. As such, my elevated levels of inflammation and ECM dysfunction, hallmarks of my EDS, may diminish the therapeutic potential of my MSCs. My routine hormetic practices that blunt inflammation (discussed in the Chapter 23), however, hopefully prime my autologous stem cells to boost my M2 to M1 macrophage ratio, thereby encouraging ECM remodeling, cell proliferation, and connective tissue regeneration, despite my mutant genes.

Just as autologous stem cell injections harness the body's endogenous healing capacity, platelet-rich plasma (PRP) therapy is an orthobiologic treatment that triggers overlapping paracrine and growth factor-dependent cascades. Since 1972, a robust number of animal-based studies and human clinical trials continue to support the use of PRP in the setting of orthopedic and sports injuries involving the rotator cuff, meniscus, Achilles tendon, medial collateral ligament, among other tendinopathies, joint arthritis, cartilage defects, and muscle pains. According to Yiqin Zhou and James Wang's (2016) review publication, more than 86,000 athletes per

year who sustain connective tissue and muscle injuries are treated with PRP in the United States and Europe (Zhou & Wang 2016).

According to the American Red Cross, PRP consists of a blood plasma sample containing more than two-fold the number of platelets relative to baseline. Venous blood is made up of red blood cells (RBCs), white blood cells (WBCs), and plasma—the acellular fraction of blood harboring platelets and growth factors. Platelet activation relies on the degranulation of constituent alpha granules that degranulate upon interaction with collagen or other ECM proteins and secrete growth factors—connective tissue growth factor (CTGF), platelet-derived growth factor (PDGF), TGF-β, VEGF, insulin-like growth factor (IGF), fibroblast growth factor (FGF), epidermal growth factor (EGF), and proteins that initiate a paracrine effect to enhance ECM formation, cellular division, collagen formation, muscle and tendon regeneration, angiogenesis, and overall cellular protection and repair (Cole et al. 2010; Alves & Grimalt 2018).

In their review article on the topic, Ting Yuan, Chang-Qing Zhang, and James Wang (2013) explain how PRP improves tendon and ligament healing by leveraging the aforementioned growth factors as well as by prompting tendon stem cells (TSCs) to differentiate into collagen-producing tenocytes. Furthermore, the authors discuss Yoshiteru Kajikawa (2008) and colleagues' findings demonstrating that PRP injections into injured rodent patellar tendons lead to a greater recruitment of circulating stem cells and collagen synthesis compared with injured control rodents not subject to PRP intervention. The 2013 review article mentioned above describes how the preparation of PRP is based on

the premise that plasma, platelets, RBCs, and WBCs have different specific gravities (Yuan et al. 2013). In turn, these elements within blood segregate through a centrifugation process, the duration of which and the number of spins determine the resultant relative quantities of these blood products. Although the International Cellular Medical Society devised and revises PRP guidelines for practitioners, the heterogeneous sample preparation methods and disparate patient injuries cause high-powered, rigorous scientific studies to lag behind PRP's anecdotal evidence and its clinical use. Jeremy Magalon and collaborators' 2014 study advances a positive correlation between platelet and growth factor abundances (Magalon et al. 2014). However, as in the case with excessive hormesis, Emily Sundman, Brian Cole, and Lisa Fortier's 2011 publication suggests that more platelets come at the cost of more WBCs, otherwise known as leukocytes (Sundman et al. 2011). Specifically, the authors showed that augmenting platelet content boosts neutrophils, WBCs that increase MPP-9 (matrix metalloproteinase-9), and IL-1, thereby promoting ECM and connective tissue catabolism and delaying healing, unlike leukocyte-poor PRP.

In their experiment, Yohei Kobayashi (2020) and associates used a mouse patellar tendon injury model to explore the efficacy and molecular underpinnings of PRP therapy (Kobayashi et al. 2020). After surgically inducing the tendon injury in 20 case mice (subject to PRP derived from a healthy mouse) and 20 control mice (subject to platelet-poor plasma (PPP) or supernatant isolated from the healthy mouse's whole blood sample), the authors analyzed histological assays on a biweekly basis for eight weeks following treatment. While the vascularity score was significantly

higher at the two- and four-week marks in the PRP-treated mice relative to the control mice, the collagen arrangement score was robustly reduced in the PRP group at eight weeks compared to that of the control group. These findings strongly suggest that PRP intervention augments angiogenesis during the early healing phases and protracts collagen fiber reorganization subsequent to injury. Overall, the PRP group demonstrated accelerated recovery compared to control subjects at the six- and eight-week benchmarks, as measured by the FT-ratio—the ratio of collagen fibers to the total tendon tissue. The scientists also quantified the levels of growth factors, PDGF, VEGF, and TGF-β1, central to tissue recovery, which were statistically significantly elevated in experimental mice. Therefore, like stem cell therapy, PRP upregulates the body's innate aptitude to heal itself.

While research continues to corroborate the value of PRP in the tissue repair process, the divergent preparation protocols and the heterogeneous use cases render most of the evidence behind PRP's success circumstantial. Because hEDS is a spectrum disorder, rather than a binary Mendelian disease, it is challenging, if not impossible, to conduct a randomized controlled trial on patients with my form of the condition (especially given the current lack of genetic insight into the syndrome). Despite the dearth of scientific research, however, regenerative and EDS clinicians recognize the healing potential of PRP and stem cells in EDS pathophysiology. In addition to the regenerative medicine facilities mentioned above, Dr. Ellen Elias and Dr. Dennis Roop spearheaded a collaboration in 2019 to investigate EDS at the Gates Center for Regenerative Medicine at the University of Colorado (Keener 2020). Thus, although orthobiologic treatment may be cost-prohibitive for

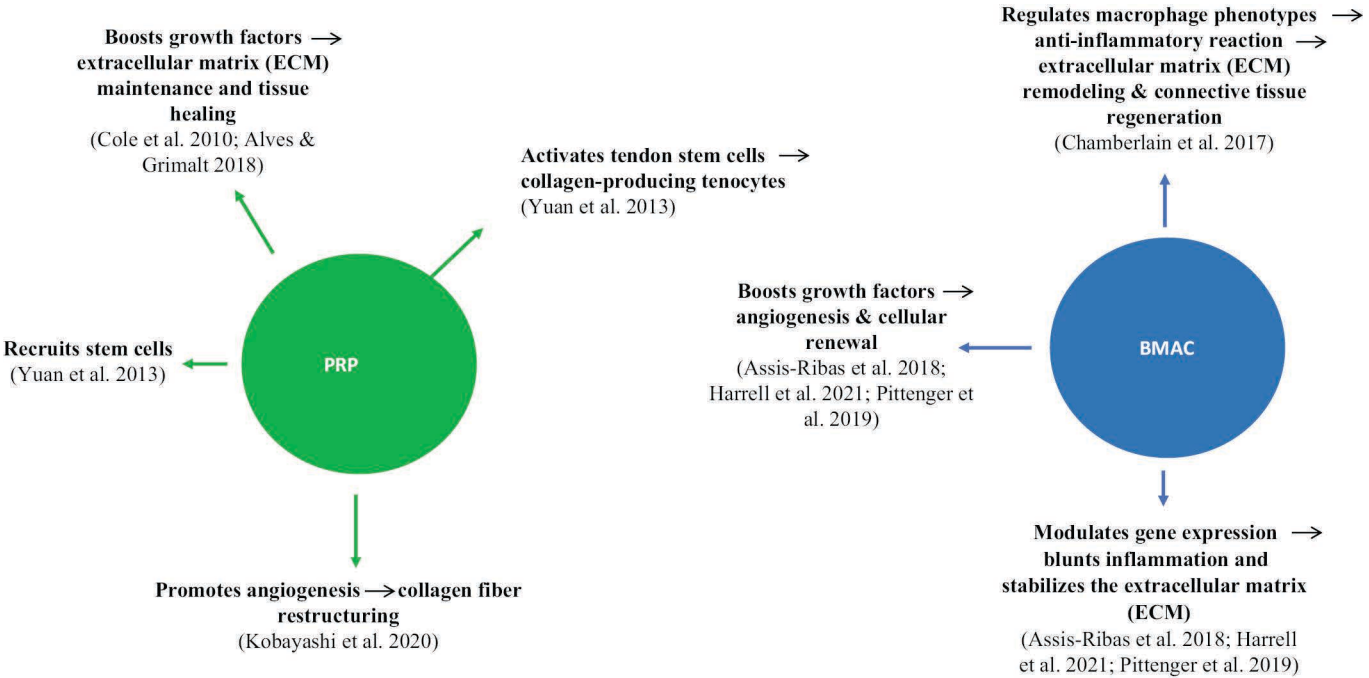


Figure 24.3: Overview of orthobiologic treatment effects

many patients (as it is not covered by insurance), the growing collection of animal-model studies, clinical trial outcomes, anecdotal reports from patients like myself, and the application of funds to further probe the mechanisms and success associated with autologous stem cells and PRP are compelling. Without these two therapies, I would have likely succumbed to several fusion operations, which would have, based on my history, begotten stillness and additional setbacks that may have forever compromised my ability to walk, talk, sit, or emote—routine biological functions that most 16- and 26-year-olds are healthy enough not to consider, but, for me, are blessings I will forever hold dear.

My cellular regeneration

Like remote learning, Dr. J's presence in my life was a profound silver lining of the COVID-19 pandemic. It is because of her persistent belief in my failing body that I would not only find myself sitting, talking, and walking beside Rebecca in 2021 but that I would ultimately pursue graduate work in stem cell and regenerative biology. By regenerating my body, one segment at a time, Dr. J reinstated me into my orbit, into science and into the world beyond the prison of my EDS.

In January 2021, it became apparent that resuming Harvard, even remotely and on a part-time basis, was out of the question. My jaw quivered painfully with each word I emitted, my feet could no longer withstand the few paces from my bed to my bathroom, both shoulders dislocated at the slightest provocation, my left lower back discomfort made sitting insufferable. On top of my physical decompensation, my mind slid out of calculating covariances and

into a catatonic drug-like state. I no longer had my small, yet significant, sense of control that I possessed on Zoom with Dr. Hartl. My days blended into each other. A leaden blanket of sleep steadily stole away my daylight and my nights. Someplace, in the hazy periphery of my consciousness, I knew I was leaking.

While specialists had evidently convinced my mother that surgically removing the adhesions in my TMJ capsules, fusing the dislodged bones in my feet, stabilizing the extra vertebral body in my lumbar spine, and manually repairing my damaged shoulder capsules was in my best interest, I was firmly opposed to further operations. I pleaded with my mother to investigate regenerative medicine alternatives. My encouragement led her to discover Dr. J, whose practice is a mere block away from my apartment and who only returned to New York due to circumstances set in motion by the COVID-19 pandemic.

As my mother pushed my wheelchair into Dr. J's office, I felt my face crease into a weak smile under my surgical mask. An unexpected burst of hope rippled through me. I did not need to visualize Dr. J's expression, tucked beneath an opaque face shield, to intuit her compassion and empathy. Her naturally wavy blonde hair was arranged into a neat bun. She squatted to meet my eyes.

"Elly, it is nice to meet you. I know you have been going through a tremendously difficult time for the past year. But, I want you to know that my training involved working with several patients with EDS. I think that I can help you." Dr. J's eyes crinkled into half-moons. She was beaming at the prospect of restoring my ruined body. Part of me feared what her treatment entailed, but most of

me knew I had nothing to lose by trusting this gentle and brilliant physician. I nodded in assent until she continued.

"First, I want to tackle the ligaments and bony unions in your feet. From my experience with EDS cases, I know that you are not a mainstream patient. I learned that administering injections at the enthesis, the location of attachment of tendons, ligaments, or connective tissue to bone, will yield the greatest success. My plan is to do a few test injections with dextrose-based prolotherapy in your feet. If these injections offer short-term relief, that will tell me that you are a good candidate for bone marrow stromal cells in these locations. Afterward, I hope to do the same with your shoulders and lumbar spine, but with PRP, not bone marrow. Your feet are my greatest concern. I will address your jaw capsular restriction last and am developing a procedure I can try instead of the arthrocentesis surgery proposed to you. I am with you in your conviction to avoid surgery." Dr. J maintained her crouched posture as she spoke, never once breaking eye contact with me.

"That all sounds great, Dr. J. We are so glad you moved to New York and our fingers are crossed that you can help Elly." My mother's voice juddered over her words. Unfamiliar with the details of regenerative medicine, my mother was out of her medical element. She laid a palm on my shoulder and gave it a tender squeeze before escorting herself to the waiting area. Dr. J stood erect, approached a side table, and began filling syringes with clear fluid.

"So, Elly, do you like music? I am going to give you a towel to squeeze as the feet are extremely sensitive to the injections. Pain and pressure are expected, but I will let you know what I am

doing as we proceed." I bit into my upper lip, suppressing alarm that quickly evaporated. I was, after all, more afraid of not being fixed, of living in pieces, than I was of the acute pain required to put me back together.

"I love music, actually. I can handle the pain." I hardly recognized my voice, which was so subdued, so devoid of verve, and so terrified that my disrepair was permanent. Dr. J positioned herself before an ultrasound machine and maneuvered a small probe along the hodgepodge of disjointed bones and severed ligaments in my feet.

"What are you studying at Harvard?" With her attention focused on the monitor, I could tell she attempted to divert mine away from the broken black-and-white landscape of my feet.

"I mainly study genetics and math, but I am also earning a minor in a field that combines psychology and neuroscience," I lilted, springing back to life as Harvard came to mind.

"What did you study as an undergrad?" I went on, encouraging myself that this considerate doctor was worth knowing and inviting into my world.

"Actually, Elly, I studied art in college. But, strangely, I think that pursuit has made me into a better doctor. Decoding images, like ultrasound, causes me to use a lot of what I learned about visual art and shadow." A mental image of Olivia leapt into my mind. Dr. J's words reminded me of Olivia's sentiments on the links between art and science. I already venerated this physician, and she had yet to treat me. A familiar Shawn Mendes song began to stream softly through the examination room. His words "*Help me, it's like the walls are caving in. Sometimes I feel like giving up.*

But I just can't. It isn't in my blood" felt like they sank into my core, replacing my self-loathing and distrust with an unyielding confidence that I could, yet again, be revived.

Tears aggregated and blurred my field of vision. I shut my eyes, focusing only on Mendes' words as needles pierced the bottom of my foot and inner ankle. Nerve pain radiated through my feet as Dr. J injected my tarsal joints. The towel rested limply in my palms. My jaw clenched in protest. My heart rate skyrocketed; I heard blood pulse in my inner ears. "Breathe in trust, and breathe out dread," I whispered to myself. "You are being helped, your walls are being rebuilt, and you are never ever giving up. It isn't in your blood."

"Elly, you are a trooper. I'm done. You should experience some pain relief and perhaps be able to walk a bit more comfortably around your apartment. The fluid I injected should temporarily secure the bones in your feet in place. We will take it one step at a time together."

As I arose from my prone position on the examination table, Dr. J and everything in my purview doubled. I observed two of her as they examined me with apprehension. Four blue eyes swept across my face. My head suddenly felt heavy. I reclined back onto the table. Dr. J's slender fingers wrapped around my wrist to assess my pulse. I heard my mother's heels clatter into the room.

"Dr. Katz, Elly did great with the procedure, but I am confident that Elly is dealing with more than EDS dislocations. Her heavy eyelids and need to lie down encourage me to presume that she has another CSF leak. Alternatively, perhaps the initial leak never truly sealed over due to the low volume of the blood patch. Either way, I'm sending Elly to an EDS and CSF expert. We need to sort this

out before any regenerative work can really have the profound impact I want it to on Elly's body." Before she even concluded her remarks, I knew that Dr. J was correct. My halted thoughts and inability to sit upright were trademark symptoms with which I was all too acquainted. The reality that CSF continued to drain out of my dura was petrifying, but I was more scared of permitting the leak to continue. It is because of Dr. J's keen insight into my body that my CSF leak, which likely persisted for upward of two years, was finally addressed adequately the next day.

The following week, Dr. J began to reconstruct me. She glued the jigsaw puzzle of my feet back together with stem cells isolated from my bone marrow, addressed my unstable shoulders, lumbar spine, and neck with PRP, and innovated an ingenious technique involving dilation of my TMJ capsules with platelet lysate—an anti-inflammatory serum composed of lysed platelets derived from venous blood—to sidestep arthrocentesis surgery. While each of these procedures was followed by two to five days of acute pain as my internal inflammatory and healing cascades went to work, within eight weeks, my body gradually returned to me. I transitioned through the familiar stages from wheelchair, to walker, to legs that, to this day, I still hesitate to trust. After 15 months of emotional silence, I Zoomed with Rebecca. Once her face came into view, unwept tears pooled in my eyes. Whether I was finally feeling the loss of control and time I suppressed for over a year or euphoric about my steady reintegration of my world into something coherent, I could not tell. Behind our computer screens, we sat together, half a mile apart. I watched her face as it creased and slackened. I was afraid of what was yet to come, of a future on

which I could not get a wet read, but I was galvanized by the fact that I was back, that Dr. J had put my pieces and my frayed edges back into someone I wanted to own.

If my EDS diagnosis had been handed to me years earlier, it is challenging to foretell which iatrogenic disasters I would have been fortunate to mitigate or even to sidestep altogether. It is, more broadly, impossible to know who I would be without each of the scars—my patchwork of physical and emotional pain—I carry into my future. However, as a patient who lives, much of the time, in the porous nexus between illness and relative wellness, I hope the EDS diagnostic process is expedited in the future and that EDS patients become easily visible to mainstream medicine. Not only are Western physicians partially at fault for my excruciatingly circuitous journey through misdiagnoses and physical hardship, but the system at large is to blame for placing far too much stock in static biological snapshots—vital signs, bloodwork, punctuated check-ins—that can never do justice to a constantly adapting organism. In the case of a disease like EDS, medicine is far more of an art than a science and demands a more complete integration across time and data structures to assess well-being and to coordinate and recalibrate healthcare plans. Leveraging continuous tracking devices, omics platforms, phenotyping, and machine learning algorithms from the moment a patient begins to experience symptoms would facilitate accelerated diagnoses and may lead zebras, like me, to be seen decades earlier. Incorporating large longitudinal datasets that interrelate genetics, epigenetics, transcriptomics, lifestyle factors, among other variables into medicine would also contribute to

disease discovery and therapeutics by clustering patients with similar clinical presentations and/or genetic predispositions. To this end, artificial intelligence-assisted platforms that diagnose rare diseases, like Dx29, correlate phenotyping, genotyping, and scientific reports to evaluate mutations and possible pathologies, both novel and known. Moreover, as biosensing wearable devices, such as BioIntelliSense's BioButton that provides continuous vital sign monitoring, infiltrate the marketplace, precision preventative medicine will become a reality in which individuals can modify their lifestyle practices to optimize wellness long before illness takes root. In tandem with these innovations, however, new challenges—from cyber privacy and data accessibility to disentangling signals from noise in these databases—will arise that should be anticipated and prophylactically addressed by healthcare and other allied authorities.

Even in the face of my indeterminate prognosis and absence of treatment options, I would opt to be equipped with knowledge of my illness as early as possible; at the very least, a faster diagnostic route would have offered me more time to live with the understanding that my path would be paved with continuously shifting goalposts and with utter uncertainty as to what lies on the other side of each hardship. As technology continues to infiltrate medical practice, zebras will hopefully begin to trend toward extinction. The evolving patient data matrix may render EDS far easier to identify. Hoof beats may all eventually belong to horses of different shades, rather than to organisms warranting arbitrary degrees of notice or neglect.

Hope is a strange emotion that even during my most trying setbacks I find challenging to strangle. Despite EDS, I plan, I imagine,

I map out a life that I intend to occupy. So, as my recovery proceeded with Dr. J's continual intermittent interventions, I contacted Albert, who had since accepted a faculty position in the Stem Cell and Regenerative Medicine department at the University of Southern California. Dr. J, who unleashed my body's endogenous zest to heal itself, championed me to pursue science. EDS would forever be on the margins of my life, but it did not always have to occupy center stage.

I emailed Albert to notify him about my recent hardships, about the marvelous about-face Dr. J had performed on my body, and about my desire to follow in his stead to USC to pursue a master's in regenerative medicine. As one of my staunchest advocates, Albert responded: "*I will support you in any academic endeavor you choose, and I am more than happy to give you the strongest recommendation possible for the program in stem cell biology and regenerative medicine at USC. You are brilliant, Elly, and have so much potential! I will always be here to help you navigate your academic career. Please keep strong!*"

I would resume my grip on life, no matter how afraid I was to yet again begin to trust a body that I knew would let me down over and again. I would go on to USC's program following graduation and become a scientist outside the limits of my own self-experimentation. But first and foremost, I would remain the product of optimism in the face of hardships, a bona fide professional at getting back up again, fists pumping the air, no matter how many times I fell.

Epilogue

Elly's tenacity, brilliance, determination and optimism remained her dear intimate friends into the year 2026. She never attended USC's program, but was admitted both to labs at Technion in Haifa and to the Biological and Biomedical Sciences (BBS) Program at Harvard Medical School. She opted to join the BBS program and was going to perform her PhD in Dr Galloway's lab. The focus of Dr. Galloway's lab is to understand how tendons and ligaments develop and regenerate. Her lab addresses the questions: How are tendons and ligaments formed and what goes wrong during injury and disease? She dreamed of becoming better positioned to create more targeted therapies to treat human disease affecting tendons and ligaments. How Elly could have excitedly contributed to this work, so personally motivated, by her Ehlers Danlos Syndrome. She loved Jenna Galloway.

Sadly, Elly never made it to that lab. Her body was in excellent shape but for the stability of her neck in the aftermath of a careful physician's injections to stabilize many large and small joints of her extremities. That female physician relocated; hence, she referred us to a new clinician. Elly required an injection, which the second physician performed, of PRP into ligaments and facets to stabilize her upper neck, a series of injections she had in January 2022, which provided much improvement and stability. After that procedure in January, Elly no longer required a neck brace and was able to flex, extend, and rotate her neck with ease. However, it was only transiently successful. The injections

needed to be repeated again in the fall of 2022. We did not know if it would be a mere "band aid" stabilizing her neck for a brief interval or if it could be a potential cure, but after consulting with many cervical spine surgeons, each suggested that because she did so well with the injections in January of that year, we should try them again, as a surgical cervical fusion, especially in a patient with Ehlers Danlos Syndrome, can be quite complicated. EDS patients do not heal easily.

Tragically, the physician was in a hurry that day and missed the superficial targets, despite fluoroscopic guidance. His needle went too far, and he injected concentrated PRP, which is very proinflammatory, into her medulla (a critical part of her brainstem) and into her cervical cord.

As Sir William Osler, the famous father of modern medicine, once said, "More people are killed by hurry than by disease."

Elly fought for almost four years because she was a survivor, powerful, in love with life, and determined to regain whatever functions she could. But her body became a cage confining her to a wheelchair, and she lost control of almost every normal physiologic function. Her bowel and bladder did not work properly; she suffered from severe vestibular dysfunction and lost all sensation and proprioception on the right half of her body. She lost the right side of her once stunning smile, hearing in her right ear, and her vision was compromised. She lost taste, appetite, thirst, smell, and so much more.

Stripped of sensation and function and symmetry in her words, she lost her resilience. What she sustained was "endurance," forced to endure what she must and sacrifice her dreams.

She did pivot and became a poet, authoring a memoir a year after her stroke entitled *From Scientist to Stroke Survivor: Life Redacted*, a best seller on Amazon and with her academic publisher Lived Places Publishing. She has a collection of poetry coming out in October 2026 entitled *INHERITANCE*.

She wrote a piece in her upcoming book that explained the power poetry gave her to endure.

The Sabbath

To be a poet, one must earn two credentials. To be a poet is to revere silence, to generate a devotional to soundlessness at the origin of sound—the womb of the word. To be a poet is to hear solitude as privilege, a heightened state of ritual, not as right. Adam arrived here alone. At the center of noise and relational input streams of bygone sensoriums, one eschews their absence. I was one of the one, regarding noise above noiselessness, company above the silo of self. The shrill tilt of my stroke struck me into emptiness of other voices, wattage of data from the cloud that's no cloud. In the igloo of self-enclosure in a dismantled body and a thrashing soul, I didn't know what I know—that my womb foreclosed to children opened to procreate the etymology of poetics. As a teenager, I turned over worn leather prayer books in my hands like stones smoothed across generations of waves, generations of Jews I emulated—seduced more by the solace in the careworn texture of the Siddur, the Biblical characters, than by prescriptions to God. In flashes, letters let me in. Disability cracked words wide-eyed. I broke. They broke. Now, each keystroke of the tongue, vocal cords

> crackling and backpedaling, is a breaking out of, a breaking into what my stroke scorched inside—a profound respect for silent solitude, for growing a poet across two years at the moment I supposed my ashes were infertile, at the moment I supposed I had grown beyond where there was anything left to grow.

Sadly, Elly's body was deteriorating constantly after the injury to her brainstem and spinal cord. Her bio hacks stopped working. Hope was stripped away, and in August 2026 she died at home quietly and peacefully in the company of her adoring parents.

How much she could have and would have contributed to science and to creative writing is beyond the scope of what anyone can imagine.

Elly will be forever missed by all who really knew and understood how powerful she was. So unique. So brilliant. So sensitive. So positive.

She desired to remain on planet Earth for as long as she possibly could.

She loved this life passionately. Elly was a survivor who had to fight against impossible odds. She never gave up until the very end. Her bravery was astounding. I will forever miss my daughter, my muse, my best friend, my inspiration for infinite grit and joy.

Karin Charnoff-Katz (her mother)

Glossary

Adenosine monophosphate-dependent protein kinase (AMPK): An enzyme that regulates cellular energy homeostasis

Adhesive glycoproteins: Proteins abundant in ECMs

Agouti-related protein (AgRP): Neuropeptide released by neuropeptide Y-containing (NPY containing) neurons in the brain

Antagonistic pleiotropy: A phenomenon in which a gene leads to a beneficial phenotype in early life but a deleterious phenotype in later life (e.g., *trade-off theory of aging)*

Antioxidant response elements (AREs): Cis-acting enhancers that regulate transcriptional profiles in cells exposed to stress

Apoptosis-associated speck-like protein with a caspase recruitment domain (ASC): A protein that is a proxy of inflammasome activation

Autophagy: The cellular 'self-eating' process of degrading and recycling subcellular components

BRAF-V600E: A mutation in the *BRAF* gene, normally involved in cell signaling and growth, that encodes a protein that accelerates the growth and metastasis of cancer cells

***BRCA1*:** A tumor suppressor gene that encodes a protein responsible for repairing DNA damage

Cadherins: Transmembrane proteins involved in cell-cell adhesion

Caspase-1: A protease that regulates the effect of IL-1β

Central sensitization: Hypersensitivity to stimuli

Cerebrospinal fluid (CSF): Fluid surrounding the central nervous system

Collagen: A primary structural protein in the ECM involved in stability

Cyclooxygenase-2 (COX-2): An enzyme that catalyzes the production of prostaglandins, which impact all physiological processes through interactions with G-protein-coupled receptors (GPCRs)

Cytokines: Proteins that function as signaling molecules

Damage-associated molecular patterns (DAMPs): Molecules secreted by damaged cells that interact with pattern recognition receptors (PRRs) to activate the innate immune system

Desmosomes: Membrane domains involved in cell-cell contact and adhesion

DNA-binding subunit 70 (Ku70): A DNA repair protein

Dysautonomia: Dysfunction of nerves responsible for nonvoluntary functions (e.g., heart rate, sweating, and blood pressure)

Dural ectasia: Expansion of the dura

Dynorphin: An opioid peptide that binds to kappa opioid receptors in the central nervous system to modulate the stress response, emotion, learning, memory, and pain perception

Elastin: A key ECM protein responsible for tissue resilience and elasticity

Extracellular matrix (ECM): A three-dimensional intricate network of macromolecules

Fibroblasts: A connective tissue cell type that releases collagen

Forkhead box O3 (FOXO3): A transcription factor that acts as a master regulator of cellular events (e.g., apoptosis, metabolism, stress resistance, and longevity)

Haploinsufficient: Describes genes when one copy of an allele is not sufficient for wild-type function

Heat shock factor 1 (HSF-1): An inducible transcription factor implicated in the stress response

Heat shock proteins (HSPs): A protein family synthesized in reaction to stress

Hormesis: A biphasic dose-dependent reaction to a substance

Inflammasome: Receptors of the innate immune system that elicit an inflammatory response

Insulin-like growth factor 1 (IGF-1): A hormone that exerts anabolic effects

Interleukins (ILs): Cytokines involved in cell motility, growth, differentiation, and inflammation

Kallikreins (*KLKs)*: Genes that encode for serine proteases

Kappa opioid receptors: Receptors present in the central nervous system that mediate the effects of opioids

Ketone bodies: Energy substrates (e.g., beta-hydroxybutyrate (BHB)) produced by the liver

Laminins: A glycoprotein located in the ECM

Locus coeruleus (LC): A norepinephrine-secreting nucleus located in the brainstem

M1 and M2 macrophages: Macrophage phenotypes involved in tissue healing and wound repair

Mammalian target of rapamycin (mTOR): A protein kinase that detects/integrates amino acid signals and regulates the balance between cellular growth and resource conservation

Mast cell activation syndrome (MCAS): Hyperreactivity of mast cells that causes hives, gastrointestinal distress, swelling, and reduced blood pressure

Matrix metalloproteinases (MMPs): Proteases in the extracellular environment that regulate protein degradation

Mitochondrially encoded ATP synthase membrane subunit 6 (*MT-ATP6*): Gene that encodes for a protein subunit of ATP synthase

Mitophagy: Mitochondrial autophagy

Myofibroblasts: Fibroblasts with muscle-like properties involved in matrix development and degeneration

Myoblast: Muscle precursor cell

Myogenic determination factor 1 (MYOD1): A protein that regulates muscle differentiation

Neuropathic pain: Pain in reaction to nerve damage

Nicotinamide adenine dinucleotide (NAD+): A coenzyme/substrate essential for cellular metabolism

Nociceptive pain: Pain in reaction to a stimulus

Notch signaling: An evolutionarily conserved cell signaling pathway integral to embryonic development and neurogenesis

Nuclear factor erythroid 2-related factor 2 (Nrf2): A transcription factor that regulates over 1,000 cytoprotective genes (e.g., heme oxygenase-1(*HO-1*), NAD(P)H:quinone oxidoreductase 1 (*NQO1*), and glutathione peroxidase (*GPx1*))

Nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB): A transcription factor responsible for several immune, inflammatory, developmental, and cell cycle-related processes

Nuclear pore complexes (NPCs): Protein complexes spanning the nuclear envelope that control the bidirectional movement of molecules between the nucleus and cytoplasm

Nucleotide-binding domain and leucine-rich repeat-containing receptor with a pyrin domain 3 (NLRP3) inflammasome: A critical component of the innate immune system that acts as a pattern recognition receptor (PRR)

Orthobiologics: Substances used to augment/accelerate tissue healing (e.g., platelet-rich plasma (PRP), prolotherapy, bone-marrow aspirate concentrate (BMAC), and platelet lysate) by recruiting growth factors (e.g., vascular endothelial growth factor (VEGF) and transforming growth factor beta (TGF-β))

Paired box 7 (*PAX7*): A gene that encodes a transcription factor involved in stem cell differentiation

Paracrine signaling: A type of cell-cell signaling by which a cellular signal causes changes in adjacent cells and alters their phenotype

Pattern recognition receptors (PRRs): Receptors capable of identifying molecular structures on dying cell surfaces and pathogens that require the attention of the immune system

Peroxisome-proliferator-activated receptor-γ coactivator-1 (PGC-1α): A transcription factor that activates genes responsible for mitochondrial biogenesis and energy metabolism

Peroxisome proliferator-activated receptor gamma (PPARG): A receptor that modulates cell differentiation, anti-inflammation, and cell death

Piezogenic papules: Papules on feet and wrists caused by fat herniation through the dermis

Polyglutamine diseases: Neurodegenerative diseases resulting from expanded polyglutamine (CAG) tracts in specific genes

Polyphenols: Plant compounds (e.g., resveratrol, curcumin, and sulforaphane (SFN)) that may confer benefits

Proprioceptors: Sensory receptors located in muscles, tendons, and joints that react to internal position and motion cues

Proteoglycans: ECM proteins

Protocadherins: Most abundant mammalian subclass of cadherins implicated in embryonic development, carcinogenesis, and tissue regeneration

PTEN-induced kinase 1 (PINK1): Mitochondrial protein kinase that protects cells from stress-related mitochondrial damage

Pyroptosis: Proinflammatory signaling-induced cell death

Reactive oxygen species (ROS): Highly reactive oxygen derivatives

Senescent: A cell that is not mitotically active but remains metabolically active

Sirtuins (SIRTs): A highly evolutionarily conserved group of signaling proteins that regulate metabolic processes and are associated with life extension

Substance P: A neuropeptide that acts as a neuromodulator and neurotransmitter and is involved in pain perception

TNXB: A gene that encodes tenascin X, a protein expressed in connective tissue that regulates collagen fiber assembly

Transcription factor EB (TFEB): A transcription factor that serves as a master regulator of autophagy and metabolism

Tumor necrosis factor alpha (TNF-α): An inflammatory cytokine secreted during acute inflammation that leads to signaling cascades culminating in apoptosis or necrosis

Uncoupling protein 1 (UCP1): An inner mitochondrial membrane protein involved in non-shivering thermogenesis. When activated, UCP1 facilitates inner membrane proton conductance and leads to the uncoupling of respiration from ATP synthesis

Wingless and int-1 (Wnt) pathway: Evolutionarily conserved signal transduction pathway

Xenohormesis: The hypothesis that certain molecules derived from stressed plants exert beneficial effects in humans

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