**The Natural History of a Clinical Geneticist: A Case Report.**

*by Margaret Nowaczyk*

The natural history of a disease is defined as the course a disease takes from its pathological onset until its eventual resolution through complete recovery or death.


**Susceptibility**

*The state of being predisposed, liable, or sensitive to the effects of an infectious disease, allergen, or other pathogenic agent; lacking immunity or resistance.* [Dorland’s Medical Dictionary, 28th edition, 1994]

When I was five, I bugged my parents to buy me *A Walk in the Depths*, a marine biology book I saw in a bookstore window in Gliwice, my hometown in southern Poland. In the early dusk of a winter afternoon, the bookstore display window shone like a huge aquarium. Mesmerized by the cover photo of a sea anemone and a hermit crab under a dome of blue waters, I insisted and cajoled, possibly threw a tantrum, until my father bought it two days later, bringing it home for me. I spent hours poring over the slim volume even though I couldn’t quite read yet, gawking at photos of jellyfish with see-through blood, chalky microscopic diatoms, and pink-tentacled octopuses.

After I learned to read, I entertained myself by flipping through the pages of my
mother’s tattered *Little Encyclopedia of Health*, often stealthily, because there were diagrams of human sex organs in there. My mother had pried it from my unyielding hands saying: “You’re too young for this,” but not before I noticed several stiff and ragged edges poking from deep in the book’s gutters: remnants of photo plates cut out with manicure scissors.

“What was here?” I asked.

“Terrible pictures that I couldn’t look at,” my mother said.

“Pictures of what?”

“Hydrocephalus and kids with other diseases. Awful.”

I tried to imagine what hydrocephalus—“waterhead” in Polish—looked like, but I couldn’t quite picture it. The image must have been horrific for my mother to butcher the book so, I thought, and for weeks afterward, monstrous heads squirting water from their ears and eyes and nostrils inhabited my imagination, especially before I fell asleep.

Several years later, I found an unmaimed volume in a neighbor’s bookcase and, my heart thumping in my throat, I searched for the photos that had disturbed my mother so. I found a much less frightening image of a toddler lying in a crib, his skull ballooned and tufted with sparse hair, his eyes half-hidden by the lower eyelids, the irises sunsetting. Our imagination outdoes itself when confronted with the unseen unknown, furnishing monstrous grotesques and horrific freaks.

In grade four, I loved biology, and in grade seven, chemistry; then, in grade eight, like most thirteen-year-olds, I was fascinated by human biology, but unlike most of my classmates, my interests weren’t centred on the reproductive system—I wanted to know everything there was to know about the human body. On a test, I described the structure
of the eye in such meticulous detail that I ran out of time to answer the remaining questions. The teacher took pity and marked the single question as if it had been the whole test. I got the top mark in the class but with a stern, “Don’t dawdle,” scribbled across the top of my paper.

At the end of summer 1980, after I finished grade ten, my family left Poland: my father didn’t want his two daughters (and himself) languishing under communism any longer. After a six-month emigrant limbo in Austria when we didn’t know in what country we would end up and when or even if we would be allowed to leave, we landed at Toronto’s Pearson Airport on a frigid, grey March afternoon. In spite of having finished two years of English immersion in my Polish high school, my expressive language was so poor that I concluded I would only succeed in the sciences and math with their multiple-choice questions and international languages of symbols. How could I write essays in humanities if I couldn’t even speak?

Two years later, when I was accepted into the Faculty of Arts and Sciences at the University of Toronto, my choice of major was a no-brainer: biochemistry specialist degree, a marriage of my two earliest loves. To this day, organic chemistry remains my favorite subject: the chemical equations are rational and balanced, the naming system of organic molecules impressively logical. Thrilled to be finally be learning how the human body worked, I memorized the Krebs cycle of cellular energy production and the intricacies of protein synthesis. Molecular biology and the study of DNA synthesis and replication, came a close second. The DNA structure enchanted me with its beauty, the genetic code by its simplicity: life itself written large, its secrets spelled out.
Exposure

The condition of being subjected to something, as to infectious agent, extremes of weather or radiation, which may have a harmful effect and result in pathological changes or disease. [Dorland, Op. cit.]

After I was accepted into medical school, I began collecting rare—the “weird and wonderful” in the medical student vernacular—diseases. In a little red notebook, I jotted down “Kallman syndrome”: anosmia and underdeveloped genitalia; and “Alport syndrome”: deafness and kidney failure. My brain glommed onto these random associations as I wondered what underlying mechanism might tie together lack of smell and sex, problems with hearing and producing urine. But our clinical instructors warned us sternly against diagnosing the rarest of the rare diseases: “When you hear hoofbeats outside the window, think horses, not zebras.”

My professional epiphany blazed during our second-year genetics course: genetics was all about strange and rare diseases. Most of them affected children. Many were biochemical. Cue in metabolic genetics, the study and management of inborn biochemical disorders that seemed custom-tailored for me. And since I had already decided that I wanted to be a paediatrician, at that moment I knew I had found my destiny.

The genetics course director, professor Huntington Willard III, PhD, was disliked by most of the class and actively hated by the rest because he demanded that we answer questions on assignments and exams using grade-six language as if we were talking to patients in our future offices. Genetic conditions were so rare, a general physician would likely never see one, but there was a method behind his madness.
“Patients need to understand what’s wrong with them,” I said. “Everybody has heard about pneumonia or diabetes, but hardly anybody knows anything about genes.”

My classmates’ indignant glares shut me up. “He’s not even an MD!” many said, as if that disqualified Willard from teaching clinical medicine.

It was damn hard to learn the biochemical composition and the structure of the double helix and the principles of human inheritance patterns, but having to explain them in layman’s terms elevated the challenge to a whole new level. Reciting: “Each original DNA strand serves as a template for the synthesis of its counterpart in a semi-conservative fashion” demonstrated mastery to our peers and teachers, but explaining the genetic code with an analogy of DNA as a library with chromosomes as bookcases, genes as chapters in books, and mutations as spelling errors required so many more words that we often had to ask for extra exam booklets for our answers. At the time, I didn’t realize that explaining the patterns of inheritance in plain English was what geneticists did every day.

**Prodrome**

*An early symptom indicating the onset of a disease or illness.* [Dorland, Op. cit.]

During my first summer job as a medical student, I worked at Bloorview Hospital in Toronto’s northern suburb, a two-storey, fully accessible rehabilitation hospital overlooking a verdant ravine. The facility cared mainly for children with cerebral palsy and spina bifida, but patients with other neurological conditions, many undiagnosed, lived there as well. One lunch hour in its medical library, I discovered the first edition of
Wiedemann’s *Atlas of Clinical Syndromes: A Visual Aid to Diagnosis*, an illustrated compendium of rare and unusual conditions. Heart pounding behind my sternum, I spent the afternoon staring at black-and-white photographs of misshapen skulls, hands without fingers, genitals that appeared neither male nor female. And, looking at a photo of a squat young man in his underpants, his legs disproportionately short and thick, flesh bunched up above his knees and elbows as if in fetal life he had grown his skin several sizes too large for his skeleton, I remembered with a start the untidily cut photograph plates from my mother’s *Little Encyclopedia of Health*.

Pages and pages of such photos. As I lifted each new leaf, my throat clotted, my heart rate doubled, but the physical sensations diminished as I continued to flip through the book’s pages. Upper lips cleft into three fleshy nubbins, pulled up to reveal misaligned teeth and the nasal cavity, did not bother me anymore, nor did the lobster-claw hands and clubbed feet. A frisson shuddered through me when I encountered a cloverleaf skull with eyes extruded from their too-small orbits, but even that sensation passed after viewing the photo several times.

That summer, my supervisor expected me to write up the results of my summer research and to prepare it for publication. And I did—for the first time in my life I was writing in English, putting words together into phrases and sentences and arranging them on the page. I never imagined that it would be so satisfying and enjoyable nor that I would be able to actually do it. I loved looking up new words, their meaning and spelling, their etymology, I even enjoyed learning the proper way to punctuate. When my article was published a year later, I knew that I had been bitten by the publication bug. I have not stopped writing medical articles ever since.
Spectrum of Disease

The onset of symptoms marks the transition from subclinical to overt disease. In some people, the disease process may never progress to a clinically apparent illness. In others, the disease process may result in illness that ranges from mild to severe or fatal. [Centers for Disease Control and Prevention. Principles of epidemiology, 2nd ed. Atlanta: U.S. Department of Health and Human Services; 1992]

After I finished the coveted paediatric residency at the Hospital for Sick Children in Toronto, I began a clinical genetics fellowship there. Sick Kids had always been the best place in Canada and one of a handful in the world to learn about rare diseases—a diagnostic and treatment centre for children from the entire country and a leading genetics research hub: the genes for Duchenne’s muscular dystrophy and cystic fibrosis were discovered there in the late 1980s.

Again, I flipped through photographs of syndromes and malformations in dog-eared textbooks and atlases but with a difference: I was no longer a morbid freak but a dedicated student of dysmorphology, the study of the subtle facial changes that delineated syndromes. Over and over again, page after page, photograph after photograph, just to imprint the images onto my retinas and hippocampus. Later, this helped me recognize and diagnose the rarest—the once-in-a-lifetime—cases. I became an expert in recognizing the strangest constellations of physical signs and symptoms and putting the puzzle pieces
together—I hunted the zebras that we had been warned against in medical school. I wanted to name them, *to diagnose*. Nothing else mattered.

As I examined newborns and children with genetic diseases, the conditions afflicting them soon lost the carnival value of the atlas photos. Concern and compassion replaced curiosity; the children were no longer oddities to stare at but individuals, even if at a deeper, chthonic level the scientist in me remained fascinated. I congratulated the parents on their babies’ births and told them that the children were beautiful. Not to prevaricate but because they were: a newborn girl flashed huge, pellucid blue eyes above her cleft upper lip; a boy with Rubinstein-Taybi syndrome blinked the longest eyelashes in the clinic.

To a question on an admission interview for a genetics fellowship—When does a severely malformed fetus stop being human?—I had given an immediate response: Never.

I reveled in the hunt for clues, the detective work, the feeling of accomplishment when all the pieces fit. My brain tingled when I diagnosed Angelman syndrome upon glimpsing a young girl’s wide smile and flapping hands from across the waiting room in my clinic. Sometimes, I did it in my head, in a flash of recognition; sometimes with the aid of computer databases and textbooks. However I did it, it always thrilled me when the molecular testing confirmed my clinical diagnosis. I lived for that validation.

**Complications**

*An additional disorder or condition that develops during the course of an existing one,* frequently in plural. [Oxford English Dictionary; http://www.oed.com/]
Once when I was still in training, something had gone amiss in the chain of prenatal diagnosis, somewhere between suctioning a sample from the fetus by amniocentesis, shipping its cells to a research lab in Wisconsin, and growing them there to be tested. The diagnostic mistake resulted in the birth of a second daughter with an exceedingly rare cellular storage disease that caused blindness, deafness, paralysis, intellectual disability and death before a third birthday; her parents had already lost a two-year-old to the same disease. The girl, a beautiful, tawny-skinned and curly-haired infant, lay in her mother’s lap like a marionette with cut strings. The mother’s voiceless grief as she held her doomed daughter screamed louder than the father’s livid “What the fuck happened?!”

The attending physician started to cry and I watched her, bewildered. Later, the physician said with the air of imparting wisdom to a tyro: “Put on the waterworks and they will never be mad at you,” stunning me into a confused silence. My emotions always on my sleeve, I didn’t think that I could ever be that calculated.

I saw my first fetus during rounds with a senior geneticist, a kind and gentle man with a wonderful manner with his patients. As he rushed through a stainless-steel door in the pathology department, I thought nothing about following him. He unwrapped a small bundle he had just lifted from an industrial size refrigerator: a glistening red fetus emerged, its tiny hands folded over its chest, a hospital bracelet hanging off its left foot. The head looked much larger than expected for its size, but otherwise it did not look abnormal to me. My heart banged to be let out, but I didn’t gasp, I didn’t blink. The geneticist briefly examined the fetus’s mouth, anus, genitalia, hands, and feet. He didn’t describe the features, only said, “Trisomy 18, nineteen weeks,” as he gently wrapped the
baby up again. The pregnancy was terminated because of the severity of the genetic diagnosis. He never asked if I was okay.

No matter how shaken or upset, I never discussed with my supervisors anything other than the making of the diagnosis—the pertinent medical history, the clinical findings, the thought processes, the tests to be ordered—and the management plans. Patients came and went, some died, very few improved, but the senior physicians always remained cool, aloof and professional. I wasn’t going to show any weakness that might ban me from their club. I bottled it all in.

After passing my genetics fellowship exam in 1996, I began working as an attending clinical geneticist in the pediatric teaching hospital at McMaster University. No more supervision from senior physicians, no more training wheels.

I shared the general genetic service and supervision of genetic counselors with a senior geneticist, but for almost nine years I alone managed the prenatal diagnosis consultations. The decisions made in prenatal genetics are truly life-and-death: because of them, some lives never materialize. A couple chose to have a girl whose every bone was crooked or shortened or bent on the prenatal ultrasound and who couldn’t breathe on her own and would never learn to walk or feed herself or wipe her own bum. They named her Savannah Rose. Every time I saw her little misshapen body splayed in the middle of an ICU bed ten times too large for her, a thick corrugated tube snaking from her throat to a ventilator, my heart broke a little. Her face so deformed, she was the only baby that I could not call beautiful. But I supported all the parents no matter what they decided: non-directive counseling, the dogma of clinical genetics, had been drilled into me during my
training. The geneticist provides the most accurate information, the parents decide. No judgment.

As befitted an academic physician, after seeing patients, often at nights, I wrote case reports of the rare or unknown conditions I saw in clinics and published them in genetics journals; I presented papers at medical conferences; I climbed the academic ladder. Even if the days were long and the cases difficult, even if occasionally I struggled with the workload and sleep deprivation, I loved my work. But with time, prenatal diagnosis ate me alive.

Outcome

*Clinical disease ends when the patient recovers, develops a permanent disability or dies as a result of the disease process.* [Merrill RM, Introduction to Epidemiology, 5th edition, 2010]

Justin was fifteen years old, unable to walk or talk, still in diapers, his thin limbs pretzelled onto themselves. The neurologists and ophthalmologists weren’t sure if he could see; we knew that he was deaf. His face flat as a pancake, he didn’t have a recognizable syndrome; all his genetic tests had come back as normal; at international conferences where I had presented his findings, other geneticists were as stumped as I was.

Justin and his mother came that morning to review new genetic tests that might diagnose his condition. But as I sat there watching him for new clues, a long-held
suspicion coalesced into a truth: for some patients—and for some parents—naming the disease simply didn’t matter. Justin was Justin. No point in poking him with needles for more blood or spinal fluid, in taping a bag over his penis to collect urine, or in sedating him for yet another brain MRI. His mother agreed, relieved that she would not have to hold him down for yet another test. A diagnosis wouldn’t change anything for her or for him. She simply wanted to talk and I listened.

She told me about her husband who’d left, unable to deal with the constant care that Justin required. About her fourteen-year-old daughter with ADHD who balked at babysitting her older brother. About her own chronic tiredness and depression. About her boss who confronted her the other day about her frequent days off. As I listened to her, I realized that this conversation helped her more than the long-sought-for diagnosis might have.

Of course, I continued to search for diagnoses in other patients—for prenatal cases, for newborns with unexpected anomalies, for toddlers with intellectual disability. I counselled parents and patients’ siblings worried about recurrence. But now, instead of ordering every new test or investigation or rushing off to look things up in books or online, I sat and I listened first.

In the winter of 2007, I enrolled in a creative writing course. After I had published that research article from my summer job at Bloorview, I experienced a temporary delusion of wanting to be a writer—a “real writer,” a writer of short stories and novels. I never pursued it. It seemed too selfish, too frivolous, too self-absorbed. Besides, who was I to write—writers were a different species of humans, sojourning on an another, rarefied plane of existence. But now, every Thursday afternoon, I wrote about lace spilling from
my Silesian nanny’s lap as she crocheted the blindingly white, gossamer-thin cotton thread into tablecloths and curtains; about the soughing Baltic pines swaying above me as I traipsed through the forbidden dunes searching for nuggets of amber; about the cicatrix of my navel and its connection to my own prenatal life. I crafted sentences, naming my feelings and telling stories, incredulous that I could do it at all and even more so that I was doing it in English. This was not medical writing: the facts and nothing but the facts; this was deep work, excavating emotions and dressing them in words. And when I wrote about Savannah Rose for one of my class assignments, I remembered that in the past, whenever things got tough, I did write: about my father’s heart attack during my last year of medical school, about my own prenatal ultrasound when I had thought for two horrific minutes that my unborn son had Down syndrome. Unbeknownst to me, somewhere along the way, I had become a writer.

In 2011, I flew to New York City to attend a workshop in narrative medicine at Columbia University. I loved the idea that studying literary texts improved doctors’ diagnostic skills; I suspected that it would promote empathy and prevent burnout. Narrative medicine is the brainchild of Rita Charon, an internist who, after several years of seeing patients in her office, realized that what they needed the most was for her to listen to their complicated narratives told in words, gestures, silences, physical findings, heart tracings, radiographs, and blood tests, and to cohere them into a whole. To make sense of their stories and to act on in. Soon, she realized that as the study of literature made her a better listener, she became an even better doctor.
For one of the workshop’s small-group sessions, I had brought the piece I had written about Savannah four years earlier, the feelings as fresh as when I first examined her. Rita happened to be assigned to our room for this session.

I began to read. “I saw Savannah today. Yet another of my professional successes. A fifteen-pound grotesque of foreshortened limbs, crooked vertebrae and blown up skull. Not a single straight bone in her eight-year-old body. I have known her since before she was born, when the gray-and-black images coalesced to reveal a malformed spine, bowed arms and legs and bent ribs. My many attempts to paint a realistic and warning picture fell on deaf ears; her parents actually tell all that I am the only doctor who never gave up on her.

Now, after almost a year in intensive care units, after many times spent in the hospital with a breathing tube and on ventilator support—her chest and lungs are too small, you see, she is still receiving oxygen by a hole in her throat—her mother tells me that she is learning to speak in sentences—very short ones because of the breathing problems, and she is learning to use a motorized wheelchair. She loves her eighteen-month-old brother Jack who is already bigger than she is. With her squinty little eyes with cataracts and crooked yellowed teeth, she looks so miserable.

What have I done?”

I put my notebook down. My pulse banged in my ears in the silence that filled the dingy seminar room. Did I just read it out loud, I wondered, in a panic. What will the group think of me? What will Rita?

“What did you hear?” Rita asked the room.

“How much she is hurting,” Thomas, an internist from Long Island, said. “How it
“How much she cares,” Nadia, a gerontologist from D.C. sitting across the table, said. She smiled at me.

“How can she make it better for herself?” Rita asked.

“She can’t change the memory,” Krisann, a psychologist from Galveston, said, “but she can change how she looks at it.”

Rita peered at me sideways, head tilted like a curious bird. Something shifted in my chest.

“It feels so...so great to have read it,” I blurted out, my voice shaking. “It made such a difference that you all listened.”

Rita’s eyes held mine.

The thick brick wall I had built around the hurting part of my brain cracked. I inhaled a shuddering breath. Her words, their words, reflected my pain and supported me. The clenched muscles in my back relaxed, my shoulder blades slid down my back. The brick wall lay at my feet, demolished. I had been heard.

“See?” Rita said, her warm grey eyes on my face. “You made room for more.”

On the way home from New York City, sitting in the Buffalo airport that evening waiting for the hired car to take me back across the border to Hamilton, I wrote frantically. I could have flown home without the airplane, I felt so unweighted. All the feelings, all the emotions I had been bottling up for years just geysered out.

The guilt over Savannah had haunted me for over a decade yet I never shared it with anyone. It hurt constantly, like sharp pebbles I couldn’t remove from my shoes.
I balanced my notebook in my lap and wrote and wrote and wrote. I wanted to capture this feeling of lightness in a net of words. I had found my “tribe”—people who understood and accepted me without judgment, and respected me even when I revealed my personal and professional worst.

My notes were a jumble of scribbles, flattened by speed as they poured out; the paper ridged by the pressure of my ballpoint pen: “I have room in my chest, I have space in my stomach. I did not realize how Savannah bore into me, how she became a part of my marrow and of my brain.”

And I knew then and there, next to the squeaking luggage carousels in the dingy Buffalo airport’s arrivals hall, that I would not stop writing.

Forty years after the photographs in the Little Encyclopaedia of Health captured my imagination, I continue to diagnose genetic diseases and counsel patients and their families about inheritance patterns and recurrence risks. I have not stopped writing articles and presenting papers at genetics conferences. I still love nailing a diagnosis as much as I loved catching those zebras in medical school. But now, I also take care of myself.

I listen. And write. I have made room for it.