# EXPERIMENTAL MAN: What one man's body reveals about his future, your health, and our toxic world

## By David Ewing Duncan



***Contents and Excerpt from Book***

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# INTRODUCTION

All Life is an experiment. The more experiments you make, the better.
— RALPH WALDO EMERSON

# A fish and mercury story

When the halibut on my hook broke the surface, writhing in a splash of seawater, I was thinking less of this fish's fate than of my own. Considering that I planned to kill and eat it, this might seem cruel. Yet this flat, odd-looking creature had tucked inside its fat and muscle cells a substance as poisonous to me, if this fish becomes my meal, as it could be to him — methyl mercury, the most common form of mercury that builds up inside people (and fish). At the right dose and duration of exposure, methyl mercury can impair a person's memory, ability to learn, and behavior. Even in small doses, methyl mercury can cause birth defects in fetuses exposed to it in the womb and in breast-fed newborns whose mothers'milk is laced with tiny amounts of this heavy metal.

Scientists have assured me, however, that a single halibut contains nowhere near a dosage that might cause harm. These are the same scientists who admit that no one knows for sure what the threshold dose is that causes this toxic metal to subtly poison cells in the brain and the liver, two organs where it tends to accumulate.

I'm fishing from the bow of the *Osprey* , a tiny, open-decked trawler, as part of an experiment that started a few days earlier when I gave up 9 milliliters of blood and enough pee to fill a tiny cup. The idea is to test my normal level of methyl mercury — the background level that I typically have in my body from living on Earth in the twenty-first century, in the city of San Francisco, California — and then to give up more bodily fluids after I have eaten today's catch for lunch and a store-bought swordfish on the same day for dinner. Would my level rise?

I live just a few miles south of Bolinas, California, where we are now bobbing just off the coast above a field of kelp where halibut troll for food. The kelp is also a repository of lost hooks that landlubbers ike me tend to lose when we lamely snag them on the leathery plants and the hooks have to be cut loose — so says the *Osprey'*s skipper and sole member of her crew, Josh Churchman. Fifty-something and stubbly bearded, with graying hair and a faded baseball cap, Churchman has been fishing solo for more than three decades on this twenty-four-foot vessel with a steering cabin large enough to fit a single person. He let me come along because he's worried about mercury in the fish he catches and regularly eats and because he loves the company. He hasn't stopped talking since we motored out here from the Bolinas Lagoon a couple of hours ago.

Methyl mercury gets into these fish from coal-burning power plants that rim the northern Pacific, from the United States and Mexico to Japan and China. Expelled from tall stacks, mercury is carried in the upper atmosphere until it rains down over the eastern Pacific Ocean, where microorganisms transform it into methyl mercury. It then moves up the food chain after being absorbed by plankton that is eaten by small fish. They are gobbled up by larger predators, as each bigger fish accumulates more mercury with every meal — including the halibut that was now tiring and allowing itself to be reeled in as Churchman leaned far over the gunwales with a net.

In my "before" test for mercury, I had registered a level of 4 micrograms per liter ( _ g/l), safely below the Environmental Protection Agency (EPA) threshold of 5.8 _ g/l. (This is the same as saying parts per billion, a very small amount.) In a previous "before and after" test, I had registered 5 _ g/l, the difference coming because mercury, like all toxins, stays inside the average person only as long as it takes the body to expel it — a process that depends on the chemical and

on people's different physiologies. For instance, phthalates, which among other things make plastic soft and malleable, dissipate in the human body in only a few hours. Other chemicals, once on board, stay for years, such as perfluorinated acids (PFOAs), the hard, nonstick material in Teflon and formerly in Scotchgard fabric protector. Mercury stays in most people's bodies for 30 to 40 days, although constant exposure to the toxin means that levels re-up each day, keeping a steady background level of the sort that I had registered. Since I had not consumed fish in several weeks when I had my first round of blood and urine collected—fish are the major source of mercury exposure in humans—my level most likely came from the air and the water and from eating other food.

I planned to do much more than a simple before-and-after test. In a first-time experiment for an individual, I was going to investigate how well my body defends itself from the harmful effects of mercury. Not everyone responds to methyl mercury in the same way. Some people take more than the usual 30 to 40 days to expel this noxious metal from their bodies, with a few taking up to 190 days, which greatly increases their chances of suffering permanent physical and mental damage. These differences suggest a strong genetic component, says Karin Broberg, an environmental toxicologist who specializes in mercury exposure at Sweden's Lund University. This led me to investigate what is known about genes that make one susceptible to methyl mercury and to see whether I could track down genes inside my body that might confer a higher-than-average risk.

My methyl mercury tests are the opening salvos in a large battery of tests I plan to take for this book, exploring four major areas: genes, environment, brain, and body. In essence, I hope to answer two questions: how healthy am I, and what can the seemingly endless profusion of new high-tech tests for various diseases and traits tell me about my health in the present and for the future?

Wondering when we might get sick or die, which is at the heart of question one, has always been part of the human condition. This goes for people with no obvious ailments as well as for the ill. The second question is made possible only by a new precision in acquiring information about ourselves that was unavailable until recently, when technology began to produce its contemporary wonders, from the X-ray machine, invented more than a century ago, to the cracking of the human genome,[i] which was completed in 2003.

These discoveries and many others have revolutionized modern medicine, allowing physicians to give more accurate diagnoses and researchers to have better tools to delve into the secrets of how the body works. Technological advances also usher us closer to the long-sought goal of truly personalized medicine, where diagnoses and treatments — everything from diet and exercise to pills and surgery — will be customized to individuals based on their own genes, environmental input, and other factors specific to them. This is a radical departure for a medical system that has been largely based on lumping people into groups by age and sex and by such broad factors as whether one smokes or drinks. These categones are important but do not offer truly individual insight.

We are witnessing the beginning of a new era of medicine, when healthy people will get a personal snapshot of their bodies — organs, cells, DNA, proteins, and a whole molecular universe of other tiny structures — cross-referenced with environmental input that ranges from heavy metals and other pollutants to stress, food, gravity, and ultraviolet rays from the sun. Changes in diet and lifestyle, in medications, and in other treatments will be tailored to an individual's specific profile, instead of physicians resorting to the one-size-fits- all medicine that is often practiced today.

A raft of new technologies will help make this happen, creating a world where a doctor's exam will include a quick scan of our bodies that reveals hundreds or thousands of bits of data seamlessly integrated by a computer into a health scorecard. (You Trekkies, think of the sick bay on the starship *Enterprise*). Or maybe we'll have our own handheld devices—let's call it an iHealth (with apologies, or perhaps a suggestion, to Apple)—that will keep track of our genomes plus the most recent scans of our brain and body, while inputting real-time environmental data about what we are exposed to as we walk around, eat, and work: levels of mercury and benzene, say, and exposure to UV rays. This information will be synced up at home with sophisticated biomonitors that record daily levels of thousands of chemicals, proteins, and other substances inside us. Our iHealth will download the data, calculate our current health, and determine up-to-the-minute probabilities of acquiring various diseases and exposures, while assessing risks all day long for everything from walking out of our front door into an outside environment teeming with hidden chemicals to eating a steaming piece of halibut. While we're waiting for all of the data to sync, we can play a game, check our e-mail, or watch a video on a futuristic version of YouTube.

The impact on humanity of such a device, and the intimate information it will provide, cannot be fathomed, much as people in the midtwentieth century had only an inkling of the affects antibiotics, when they were invented in the 1940s, would have on future generations. They could not have imagined that diseases such as tuberculosis and whooping cough that terrified them and cut lives short would largely disappear in the West, and that millions of people would remain alive and vibrant (and receiving Social Security) well into their seventies and eighties. I suspect some people already inclined to fret over their health will be terrified to go outside while others will love having the information. Everyone will worry about health hackers and new forms of identity theft that make today's fears seem quaint by comparison.

My experiment aims to explore clues hidden deep inside a typical, healthy person — me — that might flag a future heart attack, diabetes, or dementia. It explores the biology behind behaviors in my head, such as risk taking, greed, anxiety, and even religious belief — and what in the environment might trigger certain actions and feelings or some dreadful neural malady. Most of the tests I have taken are in the early stages of reliability and offer an incomplete assessment of an individual's health. But the potential is there. Most of them are also unavailable to the public. I had to persuade dozens of labs and companies to allow me to partake. A few did so only after I agreed to underscore that their research is still preliminary; a very few said no thanks because of cost or a lack of time in their schedules, or because their experimental protocols required that their subjects, and results, stay anonymous. A few worried that erroneous or preliminary results might cause me unnecessary anxiety or even harm if I am compelled to act based on a sketchy finding — such as taking a drug that has side effects.

I can reveal enough of my findings to confirm that I am not a lunatic for wanting to subject myself to this investigation, inasmuch as modern medical science is able to determine such things. Yet I seriously wonder whether I possess an undiscovered Pandora gene that makes me insatiably curious in a manner that might get me in trouble. I do have a DNA marker on the DRD4 gene that supposedly predisposes me to taking risks, although the study that made the association between this gene and risky behavior is preliminary and needs to be confirmed. Another gene that investigators might want to look for is a narcissism gene — a hypothetical patch of DNA that predisposes humans to gaze back lovingly at their own reflections, as the original Narcissus did in the ancient Greek myth. My investigation, however, is not intended to be an exercise in self-absorption — though for some, indulging in a high-tech perusal of their

body might be. I plan to peek beneath my reflection, an exercise that I suspect will reveal unpleasant realities about how I might get sick or die and undoubtedly a blemish or two.

Another motivation I have for writing this book is frustration. As a journalist trying to explain science to nonscientists like myself, I've noticed a tendency for readers'attention to stray when stories get overly technical or abstract. *Experimental Man* is an effort to humanize science by having a real person with a family and children intimately participate in leading-edge technologies, using the experience both as a tool to better understand the science and also to assess the usefulness of tests that will be available to everyone in the next few years.

We are about to acquire profound new powers of knowledge about ourselves, possibly more than we want to know. This data will impact and change lives; it will alter personal and family dynamics; it will confront us with ethical dilemmas, such as how we keep information private and who gets to use new medicines and other goodies that might extend the human life span or cure cancer. Like Pandora, it might also unleash plagues and monsters, although I don't think it has to.

Back on the *Osprey* , Josh Churchman scoops up my halibut in his net and drops it on the deck. After he stabs it and drains some of its blood, we fish for another hour or so amid whitecaps and a steady, chilly wind before heading back to Bolinas Lagoon with a second halibut and a rockfish. As the little boat rides up and down over the waves and the twin outboard engines roar, I wonder what my tests will reveal about my susceptibility to mercury. Do I have a super-gene deep inside me to fend off heavy metals or not? I know that I will die of something, someday, but I seldom give it much thought. Yet I wonder, Have I been born with the best genetic and physiological armor that evolution can provide?

A few days later I eat the halibut I caught, cooked with melted butter and basil, and later the same day the swordfish steak I bought, grilled with lemon juice. The next morning I have another 9 mm of blood drawn and give up another container of urine at the University of California at San Francisco, where my internist, Josh Adler, is the physician overseeing the testing for this book. I also put uneaten chunks of both fish on ice and mail them in a cooler to environmental biologist Robert Taylor at Texas A & M to measure how much mercury each has inside its body.

Soon after, Josh Adler e-mails me the test results. With just those two meals, my mercury level (most of which is probably methyl mercury) has spiked upward from 4 _ g/l to 14 _ g/l, more than doubling to well over the EPA's recommended level of 5.8 _ g/l. These results were even more dramatic than when I ran the same test on store- bought fish caught in the Pacific for a 2006 *National Geographic* story on environmental toxins. That before-and-after test took me from 5 _ g/l to 12 _ g/l, a bump up that prompted pediatrician and mercury expert Leo Trasande of the Mount Sinai Medical Center in New York City to scold me about running a "fish gorge" experiment.

"No amount of mercury is really safe," Trasande says, although my results as a fifty-year-old white male are far less significant than they would be for children or for women who are of childbearing age. "Children have suffered losses in IQ at 5.8 micrograms."

After my first "gorge," Trasande had advised me to avoid repeating the experiment. I didn't tell him that I did it again.

The fishes'exposure levels came later from Texas A & M's Robert Taylor. My halibut carried more than three times the average level recorded in a 1997 FDA investigation. The swordfish registered a level that is two and a half times above the average for swordfish in the same study.

Armed with my onboard methyl mercury data, I go hunting for genes tucked into my cells that might influence whether I will follow Leo Trasande's advice on eating large fish in the future. This search begins with an e-mail to Trasande, who tells me that as a clinician he is not aware of human genes that are affected by mercury or of tests to determine a patient's genetic proclivities for coping with heavy metals. So I turn to animal toxicologists, who have identified several relevant genes in rodents, fish, dogs, dolphins, chickens, and fruit flies. Matthew Rand, a mercury toxicologist at the University of Vermont, has shown in flies that mercury binds to cells, including neurons, and interferes with receptors that send signals to the cell controlling how it develops, replicates, and dies. Rand says that Trasande is right about the lack of studies on mercury-gene interactions in humans, although he later corrects himself when he recalls a study by Karin Broberg and her lab in Sweden. In 2004, her team ran a study on 365 people to see whether ethyl mercury, a close cousin of methyl mercury, caused a reaction in several target genes that are involved with ridding the body of unwanted chemicals. She concluded that mutant variations of two genes did affect a critical system for flushing cells of toxic metals, such as mercury, cadmium, and arsenic.

Called GCL and GSTP1, these genes help produce enzymes such as glutathione-S-transferase that maintain levels of glutathione, a first line of defense in cells for expelling metals, among other things. Too little glutathione causes metals to stay in cells longer, according to Broberg, adding to the potential for damage, particularly in neurons. "These findings suggest that GCL polymorphisms [variatons] that affect glutathione production also affect methyl mercury retention," she wrote me in an e-mail, "and that GSTP1 may play a role in conjugating [chemically joining] methyl mercury with glutathione." Broberg's lab has identified a specific spot within the DNA sequence of GSTP1 that when mutated signals a slower elimination of ethyl mercury. In genetic-speak, this means that a single letter in the genetic code — in the Gs, Ts, Cs, and As that are used like an alphabet to describe the DNA inside us — is probably different for people who produce less glutathione. They have an "A" where most people have a "G" and presumably expel mercury at the normal rate.

Fortunately, when I checked my genetic results, I came up with the normal "G," meaning that my cells most likely expel methyl mercury in the 30-to 40-day range, rather than in the more dangerous 190-day end of the spectrum.

Even if my genes did contain the "bad" variation for GSTP1, there is a simple solution to avoiding this toxin: limit my consumption of large, predatory fish. According to experts, small fish have less mercury and are probably safer. Older fish also have higher concentrations of mercury. Unfortunately, eliminating or reducing the source isn't possible for most other pollutants that we breathe, eat, drink, and absorb through our skin, whether we want to or not, including new manmade chemicals such as the phthalates I mentioned and the PFOAs in Teflon. These and thousands of other manufactured compounds we use in everyday products do not appear in nature and have entered our environment so recently that our genes, cells, brains, and bodies have not yet evolved specific mechanisms for coping with them. I suspect that some of us will develop adaptive defenses for these chemicals. In the meantime, we need to better understand the genes, the neural architecture, and the organs each of us has been born with: our strengths and vulnerabilities as our bodies and minds are daily faced with environmental input that ranges from trace levels of metals to the stresses and joys of life that make us happy, blue, crazy, angry, and ecstatic.

This is my journey in this book: to discover what one person can find out about his body as it interacts with the world, including, as I have my DNA scrutinized and my brain scanned, why I might be crazy enough to want to take all of these tests in the first place.

# Your host

I'd like to introduce you to the main character in this book: me. Not *me* in the sense that I am going to bore you with details of my modest accomplishments. I have not conquered countries, held high office, or founded a multibillion-dollar company. The *me* here is the physical person who is not too different from you, the parts that one might disassemble like a machine to see how the programming and all of the pieces are working as I turn fifty years old.

Your host — the human guinea pig telling this story — is a father of three children, ages fourteen, twenty, and twenty-two; he is an older brother to his only sibling and the son of a mother and a father in their late seventies who are both in good health. This book is in part their story, too, the connection to a continuum of generations that stretches far back in history and will project forward into the future through my daughter and two sons. To make this link for *Experimental Man* , I have had genetic profiles run of my parents; my forty-nine-year-old brother, Donald; and my twenty-year-old daughter, Danielle.

But this physiological and hereditary "me" — the bundle of tissue, organs, sensors of environmental cues, cells, and genes — isn't the full story I plan to tell. This is the functional part, the mechanistic me. This is also an experiment about what happens to my mind (as opposed to my physical brain—the tissue that will be tested) and my emotions and to my conception of self as I learn the results of my investigation — if I have a reaction at all. This is the mental "me" that gets up each morning with an innate sense of who I am, how I feel about myself, and my place in the world: that package of hopes, fears, euphoria, loves, hates, needs, and resolutions that shifts and changes and underlies my days and nights as I interact with the world. As Fyodor Dostoyevsky wrote in *Notes from Underground*: "There are . . . things which a man is afraid to tell even to himself, and every decent man has a numberof such things stored away in his mind."

Underneath this fluctuating interface with our environment and other people is a multilayered self-conception that each of us has deep down, aspects that we like and hate about ourselves: weaknesses, anxieties, and hidden reserves of strength. We are healthy or sickly, risk takers or not, shy or outgoing, generous or miserly. The outer layer of our self-conception is what we prefer to present to the world — our cool and confident public persona. The next layer down consists of the "selves" we share with our families and friends. These can include behaviors that we are proud of but also those that we view as deficits, such as a quick temper or a lack of humor, that others either like about us or tolerate or loathe. Deepest of all are the selves that we share with no one — our secret selves, our ids that ruminate about failures, expectations dashed, loves lost, flaws, and proclivities that we don't want to admit even to ourselves.

One of my hidden secrets since I was a boy is an intense and occasionally debilitating social anxiety, a shyness and a fear that I'll say or do something that will make me seem like an idiot — or that will upset or disappoint people I care about. In my early teens, I was terrified to raise my hand in class, and several times I vomited from nerves before or after piano recitals and plays in which I was acting. When I was a young adult, I fumbled and fidgeted around women I was attracted to and men whom I wanted to impress, and I felt the blood rushing through my head when I needed to be smart and articulate with teachers, my parents'friends, and, later, as a young journalist, with editors and subjects. Possibly, these anxieties were normal, but to me, they were sometimes terrible. And yet I also have extrovert tendencies and have spent my life taking risks professionally as a reporter and physically as a foreign correspondent who has covered conflicts and lived in dangerous areas of the world. In my twenties, I bicycled around the world

and then from Cape Town to Cairo in Africa. This seeming contradiction of the shy risk taker has been reconciled over years of forcing my timid side to give way to the extrovert. Today I regularly give lectures, and I love nothing more than visiting tumultuous areas of the world or hurtling down a steep mountain on skis. I have learned to overcome my anxieties, yet they are still there, buried deep inside, along with a now low-grade fear that they will emerge at some inopportune moment that will cause me great embarrassment.

The one person who knows the truth is my mother, who suffers from more severe anxiety and occasionally has panic attacks that require medication. We will investigate whether her genes are the source of my own milder condition.

I relate this not because anyone should care about my details, but because we all have inner secrets that we closely guard, fearing they will be discovered. I'm mentioning it now because, as I contemplate my tests, I am rather absurdly anxious about being anxious. I feel old fears rising that the tests might expose an abnormality in my genes or my brain that will disturb or shatter the carefully wrought self-conception — or self-deception — that my anxious days are over.

Another thought as I launch this project is my oft-stated contention that I am a fatalist who gives little thought to how and when I will get ill or die. But is this true? Am I really so cavalier about my future health, figuring that when my time comes, it comes, and there is no point in worrying? Or is this more self-delusion? I come from a mostly long-lived family that suffers from few obvious genetic diseases. My grandmothers died well into their eighties. My father's father died in 1972 at age sixty-seven, after having been misdiagnosed with non-Hodgkin's lymphoma. He was subjected to the crude and highly toxic chemotherapy of that day and died of a heart attack, probably exacerbated by the treatments. My mother's father died of a rare form of small bowel cancer at age sixty-eight. Several aunts and uncles in my grandparents' generation lived past eighty and some past ninety, with a brother of each grandfather living to age ninety-three. This was when life expectancy was less than it is today. A great-great-aunt named Effie on my father's side lived to be 102 years old — I visited her in a retirement home when I was small, and she gave me homemade cupcakes. I had a great-aunt who lived into her nineties who suffered from dementia that was probably Alzheimer's disease and one ancestor in my great-grandparents ' generation who died young of cancer, but she lived long ago.

Other than my brother — the sole member of my family afflicted by a genetic disorder that grew serious only in recent years, as I'll explain later in this book — the general good health of my loved ones, especially my parents, has enabled me to form a powerful self-belief about my physical well-being and an anticipated long life. If I had come from a family with a history of grave illness or relatives who died young, I would have a very different outlook. I have a friend who tells me he wakes up every morning convinced he will die that day or perhaps the next, or that he will be diagnosed with a fatal ailment. Both of his parents died young — his father of a heart attack and his mother of breast cancer. He says he would be very selective about the tests I'm taking for *Experimental Man.* "I might be okay with taking tests for diseases that have good treatments," he told me. "But tests for diseases that have no treatment? Forget it. I don't want to know." Geneticist Jonathan Rothberg, a pioneer of gene testing and sequencing and the founder of several biotech companies, has Huntington's disease running in his family. He tested negative, but his cousin did not — and committed suicide rather than face a disease that as a carrier she had a 100 percent chance of contracting as she grew older. Most DNA tests do not have this much predictive power, however; a “positive” for a mutation in most cases means an increase in risk, not that a person will actually get a disease.

Despite my nonchalance, I like to feel healthy, and I have always been mildly obsessed with exercising regularly. This has less to do with a sense of mortality than a realization that I feel out of sorts if I go a day or two without riding my bicycle or visiting a gym. As I grow older, I have given more than a passing thought to what I eat, having spent the last few years casually following a low-carb, high-protein diet that I have discovered during this investigation might one day kill me, given my genetic and physiological make-up. I have since discontinued this diet, a story I'll describe later in the book.

Susan Sontag, in *Illness as Metaphor*, wrote that illness is as much a part of life as good health is. "Illness is the night-side of life, a more onerous citizenship," she wrote. "Everyone who is born holds dual citizenship, in the kingdom of the well and in the kingdom of the sick. Although we all prefer to use only the good passport, sooner or later each of us is obliged, at least for a spell, to identify as ourselves citizens of that other place."

As your guide on a voyage into the day-side of Sontag's equation, the part of life that is healthy, I will explore secrets and clues, ultimately trying to see whether it is possible to predict when a shadow might fall on the kingdom of the well I've been lucky enough to inhabit for fifty years. Thus, the night-side of Sontag's dual kingdom will hang over the narrative and in many ways drive it. As Sontag says, no one has yet figured out how to deny the night-side of our citizenship, although at the end of this book I will discuss the possibility that science may be able to extend the daylight, perhaps for a very long time.

# Checkup with my internist (the plan and three rules)

Before plunging into my tests, I visited my internist for a routine exam to establish a baseline of my health according to today's standard practices. On a bright day in June I met with Josh Adler, a fortyish general practitioner on staff at the University of California at San Francisco. He is also the medical director of its ambulatory care clinic, a building crowded with patients, white-coated physicians, nurses, and attendants pushing wheelchairs. Some patients look ill, others nervous, several healthy, and a few bored with waiting. Intravenous devices on stands, portable X-ray machines, defibrillators, and computers tucked here and there in hallways and on desks barely hint at the high-tech arsenal of cutting-edge technology available at this world-class medical center in the early twenty-first century.

Behind closed doors, deeper in the complex, are magnetic resonance imaging machines, catheterization labs, and high-resolution ultrasound scanners. But virtually all of this is reserved for the ill or those with current medical conditions. For the healthy, the procedure for getting a physical isn't markedly different from what my grandparents and perhaps their grandparents would have recognized: a small room smelling faintly of antiseptic with a blood pressure device and the stethoscope wrapped around a doctor's neck. One small difference is that Josh uses a digital thermometer to take my temperature, which is a normal 97.8 degrees Fahrenheit.

Josh's exam room is on an upper floor of a clinic built on a ridge with a dramatic view of Golden Gate Park and the Pacific Ocean. On a very clear day, the floor-to-ceiling windows give an impression of a building floating high above the treetops in the park. Far off in the distance to the north I can see the light gray cliffs of Bolinas, where a few weeks later I will go fishing with Josh Churchman.

Josh Adler says hello and leads me into the exam room. One anomaly in this physical is the extra time he gives me to chat about my project. Normally, in this age of managed care, he would have to be thorough but quick. I will be returning to him several times during the next year to show him my Experimental Man results and to get his impression as an internist on the front lines of medicine. What did he think was useful in my tests? What had he been trained to deal with, and what were the possible dangers in any of the testing or in the results?

Josh is lean, with longish unkempt hair, clothes that look slightly frumpy, and glasses with a frame the size of those old "aviators" people wore in the 1970s. He exudes empathy and intelligence, which combine with his slightly rumpled look to make me, as a patient, feel as if I have a doctor who cares far more about me than about fashion and will be there for me even late at night if I need him. Josh smiles a lot and patiently waits for me to finish talking. Unlike those physicians who seem harassed and busy, he is calm and unhurried.

Josh has strong opinions about my project. Mostly, he thinks I am delving into technologies and tests that are still a work in progress and are not yet ready to be useful for healthy patients. Like many physicians, he hopes the project will be helpful as an investigation into the state of the technology, but he thinks I'll find little of value.

"I think the technology is exciting, but our ability right now to collect data far exceeds our ability to know what to do with such information. We are in a phase where we are able to collect data about human beings without any real sense of how to use this information in a way that would help a person or change his or her life. For instance, I'm trying to figure out how to guide my patients through certain genetic tests, which produce results that are sometimes hard to interpret."

"Do you have people asking you about genetic tests?"

"Not that many. I do have people asking me about genes for Alzheimer's, breast cancer, and colon cancer — I think there is some science behind these tests and a lot of media attention, so people ask about them. What people really want to know is that they're not going to get these diseases. But very few of these tests can predict that."

Take the BRCA tests for breast cancer, he says. Mutations of the BRCA1 and BRCA2 genes are carried by 5 to 10 percent of breast cancer patients. Patients with breast cancer in their families often take the tests, but having the gene does not mean a person will ever get breast cancer. Also, 90 to 95 percent of the people with the disease do not carry the gene. "Testing positive for the BRCA genes gives a person an increased risk of getting breast cancer," says Josh. "Trying to explain this to people is difficult, and to help them make choices about what to do. In many cases, if there is no physical sign yet of the disease, it is helpful because we can keep a close eye to see whether it develops."

Many other tests are next to useless, he says. "Most of them are association studies that give a person a slightly elevated risk factor for something like diabetes. But I can tell you that without a genetic test. A person's diet, age, and family history tell me more than a genetic test. What people want is a yes-no answer, and they will not get this with these tests."

Josh is wrapping a blood pressure cuff around my arm as he talks. He pumps it up with air and watches the metallic liquid in the device rise and fall.

"Your blood pressure is slightly elevated," he says. "But that's not unusual when people come to visit their doctors. On the other hand, you're reaching an age when blood pressure begins to go up in about twenty- five percent of people. We'll keep an eye on it."

"Is there any danger in taking these tests?" I ask him as he begins my ear exam.

"The genetic tests aren't dangerous," he says, "but the scanning could be. You have a small radiation risk with some of the CT scans. But the real danger involves taking the next step beyond the test. What happens with most of these tests is that we won't know what they mean, and there will be the possibility that there is something serious. You might come to me with a CT scan with a nodule on your liver. Could it be cancer? It's unlikely, but we don't know. The next step to find out for sure would be a biopsy, and that could be dangerous — there is a small chance of infection, bleeding, or accidently making a perforation, like poking a lung. So I see my job here as protecting you from getting hurt."

"To make sure you as the physician do no harm, as Hippocrates said?"

"Exactly."

He tells me that my ears look fine and checks my eyes and throat. He asks me to lie down on my back.

"Turn your head on the side," he says. "This is a very low-tech test to see if there is pressure in your jugular vein, which would indicate a problem with your heart." He listens for a moment. "It's particularly important to contrast the tests you're taking with the more obvious and simple aspects of health care," he continues as I sit up. "You don't need a genetic test to tell you to eat healthy — though some people may need a test to convince them to do this. Don't smoke, and be sure to exercise, get a good night's sleep, eat plenty of vegetables. These are things that really do make a difference."

"And we don't need those fancy tests to tell us this," I comment. "Which makes me wonder if after all of these tests, I'll basically learn what I already know: that I should eat right, exercise, and sleep well."

"It wouldn't surprise me," he says.

We're both quiet again as he uses his — very cold! — stethoscope to listen to my insides. "Breathe deep and hold it," he says several times, doing the "hmmm" routine that doctors must have done to the mild frustration of patients since the invention of the stethoscope. About this time, Josh is called out of the room for a moment, and I'm left alone in my boxer shorts sitting in that tiny room. It is an odd moment that leaves me feeling abruptly vulnerable. I am in my underwear in a strange little room with no windows, the supplicant to the learned man in the white coat who at this moment has an enormous amount of power over me, to inform me whether he thinks I am sick. He is the augur in this room, the expert who can with a few words about an unexpected finding change my life and my conception of myself.

My confidence in my health and in running tests for this book is dipping, and I feel a pang of apprehension — an ever-so-slight wish not to be here, to take the risk that my personal vision of myself might be challenged.

Josh returns and apologizes for having to step out. He tells me that everything looks fine — so far. "We'll get the chemistry back in a few days, but I don't expect much there, either."

I let myself exhale and then jump back into reporter mode, remarking that the exam seemed remarkably low tech. Other than the stethoscope and the blood pressure device, much of the exam could have been done by the ancient Greeks.

"Perhaps, though I'd like to think we have learned a few things since then. It's more along the lines of an exam that developed in the past two or three hundred years, with much knowledge added since then, though the critical part of the exam is still the patient history — the conversation about how you feel, your family's history of illness, and so forth. This leads to about seventy-five percent of the diagnoses we make. The rest of it, including blood tests and the rest, is a lesser part of it."

"Do you think that will change with all of this new technology and knowledge?"

"It already has changed in certain arenas, in diagnosing things like prostate cancer or presymptomatic diabetes with various blood tests. Although in the history we try to identify who is at risk."

Josh had already taken most of my medical history and had come up with an unremarkable story that says I'm basically healthy. The only significant ailment I have had is a disk in my back that was herniated twelve years ago. They didn't operate, I tell Josh, but it took me six months to recover with physical therapy, and the back still bothers me now and then.

"So, Doc, what is my prognosis?" I ask when he is finished.

"Based on your physical and your family history, you are not at risk for any major disease that I can identify," he says. "Everything was normal in your exam, except your blood pressure — which we will watch, though I'm not overly concerned. Otherwise, the prognosis for you living a long and healthy life is quite good."

Josh orders a typical regimen of tests: white blood cell count, hematocrit count, and blood sugar. He suggests an EKG for my heart, which uses electrodes attached to my chest to check the electrical action of my beating heart, just to be sure the blood pressure isn't indicating something more serious than he thinks.

"At this point, you could order many more tests if you wanted to, right?" I ask. "Setting aside cost for a moment, why wouldn't you test me for anything that's not dangerous?"

"As I said, the only important clues in this exam would be from the family history," he says. "There also is no evidence that you are functionally declining. Beyond this, there is no way to know your risk, except as an average risk. I don't see a need to subject you to endless batteries of tests for no reason. It is costly, and we need to reserve them for people who really need them."

A few days later I get back my lab results, and everything is normal except my cholesterol. It's 209 — slightly over the threshold of normal, which is 200 or less. Josh says not to worry. "We'll watch it," he says. "Cut back on meat and fatty foods."

"So I'm still healthy?" I ask, feeling that vulnerability creeping in again.

"You are not going to die today."

Fundamentally, I trust Josh Adler that I'm fine — a prognosis that fits in nicely with my core belief that I'm healthy. But I'm about to find out much more about myself than Josh can tell me — information that may give me some useful advance warning about Sontag's nighttime side of life but might also frighten or confuse me. For some people, knowing vast quantities of information, much of it incomplete and a work in progress, about risk factors and possible outcomes could plunge them into a kind of twilight between the kingdoms of the sick and the well.

The plan of my investigation and of this book is divided into four parts — genes, environment, brain, and body, with a short epilogue called "eternity" that will have a surprise result for me concerning my longevity and will assess technologies that may radically increase life span. Each of these sections will contain personal stories that could be your stories, too — my life's experience as a human organism and how the secrets inside my genes, cells, and organs have influenced my own and my family's lives. I'll weave in as much science as I think the reader can bear, while also pondering the usefulness and meaning of my results, the science, and what they might mean for society.

Section 1, about genes, will describe the current state of the science for hunting down genes and DNA markers that have been associated with diseases and other traits. These are variations from the norm that contribute to why some of us get sick from a specific disease and others don't. I will be tested for millions of genetic markers and hundreds of genes and will find out what mutations I have, along with my parents, my brother, and my daughter. I will also delve into genes that link me to my immediate past with my ancestors and to more ancient and primordial times, as the history inside my genome spirals backward in time to a DNA record of the earliest forms of life.

In section 2, I'll test levels of hundreds of manmade chemicals that I may have accumulated just from living on Earth — pesticides, plasticizers, flame retardants, heavy metals, and much more. I'll assess the impact of stress and the wear and tear on my body of living in the twenty-first century. As I did in my fish story, I'll delve into how these environmental factors interact with my genes and my body to create a profile of my defenses against potentially toxic input. I'll travel to places where I have lived and may have been exposed to certain chemicals, and I'll spend time trying to collect data as best I can on the environmental factors I have encountered.

In section 3, I'll peer inside my brain and have scientists whom I'm working with build a schematic of my brain's architecture. I'll put my head into magnetic resonance imaging machines — MRIs — logging more than twenty hours in the coffinlike tubes of these scanners, while neuroscientists run amok inside my noggin, testing me first for diseases such as Alzheimer's and then for how my brain responds to everything from fear and anxiety to hip-hop and Beethoven. I'll be tested for, among other things, my sleep patterns and cognition levels and how my brain makes decisions, takes risks, and even believes or doesn't believe in a supreme deity.

Section 4 will link together the previous three sections and will add results from tests, scans, and analyses of my body, including a fullbody computed tomography (CT) scan and even a breakdown of the proteins in my blood. I asked several researchers to run my tests with

sophisticated programs that model my heart to predict future disease, such as when I might get a heart attack. Assembling the pieces of the puzzle that is me — all of the tests — is an attempt to take a holistic look at a single person. Because most of the tests come out of disciplines that focus on one field, such as genetics or neuroscience, I didn't expect that much of this would fit together. But it did in a preliminary way, an example being the fish experiment, which incorporated genes and the environment and could have also tapped into my brain if I had wanted to look for neural damage from mercury. Although I'm willing to get virtually any test, this seemed unnecessary, given my minute exposure levels and my thankfully normal genetic profile for the GCL and GSTP1 genes.

I started with three rules for this project, following Josh Adler's advice. First, all tests would be done under the supervision or with the knowledge of a physician. Second, if my tests revealed any medical condition that needed to be acted on, I would follow through with appropriate therapies and interventions. And finally, my tests would be passive and cause me no physical harm. I conducted no self-experiments of the sort performed by Australian scientist Barry Marshall, who swallowed a broth of bacteria to prove that these critters cause ulcers, a stunt that proved his hypothesis, garnered him a Nobel Prize — and gave him ulcers, which were cured using antibiotics. Nor am I trying to emulate John Paul Stapp, who rode in a rocket sled traveling at the speed of sound and then abruptly stopped to test the impact of great force on the human body. The most dangerous test I'm taking is a CT scan, which exposes me to about twice the radiation in a complete body scan than the amount I absorb from the sun and other natural sources in a year. I also knowingly exposed myself to mercury for my fish tests, despite the admonition from Leo Trasande at Mount Sinai not to do this.

Josh Adler agrees about the fish gorge test. When I tell him what I have done, he looks at me with a genial expression of disapproval that reminds me of Marcus Welby, a kindly doctor on television when I was a kid. Josh says, "Can we not do that again? Promise?"

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[i] For a definition of “genome” and other scientific terms, please consult the glossary.