Introduction: Your Body's Hidden Symphony

Ashaki is the thirty-three-year-old daughter of a wealthy Black CEO of an IT consulting firm in Los Angeles. She doesn't like to admit it, but she lives at home with her parents. Ten years earlier, just shy of graduating from USC, she was hospitalized and diagnosed with bipolar disorder, for which she's been taking three medications a day for ten years.

What does Ashaki have in common with Luke, the twenty-eight-year-old former coal miner in West Virginia, a White guy, who has been on food stamps and unemployment for two years since being laid off from the mine? He dropped out of high school in tenth grade, and neither of his parents made it past eighth grade.

And what does this former coal miner have in common with Yoko, the forty-five-year-old tenure-track East Asian languages professor who is a happily married (most of the time) mother of two? A woman of Asian heritage. As a child she was repeatedly beaten by

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her drunk stepfather during third and fourth grades and was raped three times by her first cousin during eighth grade, while her parents lived in Singapore for a year doing mission work. Recently her panic attacks have been well controlled with therapy and medications.

And what does this professor have in common with Arnold, the fifty-year-old White male British civil service accountant who worked for twenty years in London at Whitehall as an administrative officer, never advancing above a lower-level position? Three times he tried for promotions but never made it.

In spite of their differences in age, race, gender, geography, health, and social status, each of these people stands a high risk of dying young.

What sets them on a fast track to dying young? Each of them represents a common group of people who live with persistent or periodically high levels of toxic stress.

Severe mental illness, even among the wealthy and well educated, such as the daughter of the Los Angeles businessman, takes a decade or two off life expectancy.[1] As a Black woman, her exposure to racial discrimination may also add to her burden of chronic stress and risk for early death.[2]

Poverty, both rural and urban, shortens life. Poverty exerts its relentless demands early in the lives of children and persists during their formative years, day after day.

Childhood trauma raises the risks for heart disease, diabetes, severe mental illness, suicide, and early death.[3] These health effects appear early in adult life for people of all races, classes, and nationalities.

And *low social rank* in a tight social order such as the British civil service predicts more chronic illness and early death.[4] This health effect of low social rank has also been observed in animals with complex social hierarchies.

Each of these risks for a shortened life comes to us from sound population studies since the turn of the century. These studies of

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the social and psychological determinants of physical health present us with alarming associations between events that took place over many years and the later development of physical illnesses severe enough to cause early death.

How can such different challenges for these people lead to a common pathway toward early death?

Severe mental illness, the threat of discrimination of any kind, poverty across generations, the lingering costs of childhood trauma, and the oppressive pressure on the lower ranks of any tight social order provide us with just a few examples of the persistently demanding stressors that may take a sizable chunk of years off our lives. Unlike a traffic accident, an argument, or winning a gold medal, these stressors don't strike and then fade. They hang on with a grip that won't let go.

The list of potential long-lasting stressors is lengthy: incarceration, homelessness, threatening relationships at work or at home, caretaking for a family member with a debilitating condition, job mismatches, sleep deprivation, exposure to pollution, high-crime neighborhoods, substance abuse, culture clashes for immigrants, worry habits and ruminations, loneliness, living alone, chronic pain, and any chronic physical or mental illness.[5]

Any one of these relentless stressors can strain our body's resources over the years, especially if it hits during critical periods of development, such as early childhood or during the frailty of the elder years. The trouble accelerates when these chronic stressors come in bunches, as they often do. Illness leads to poverty, immigration leads to compulsive worrying, job mismatches lead to sleep deprivation, which leads to substance abuse, which leads to threatening relationships at home. One burden becomes many, a train of troubles. No wonder our train of troubles sometimes seems impossible to stop once it gets rolling.

Why do acute stressors generally not cause illness, but chronic stressors can make us sick and hasten death? Why do the sections

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of the orchestra (our organ systems) continue to play out of tune during chronic stress?

The key paradox here is that acute stressors, if brief, tolerable, and infrequent or predictably regular, help keep our stress response systems fit, tuned up to handle the demands of daily life – a flat tire on the way to work or the babysitter is late. This is good stress because it helps regulate the stress response system, just as regular gentle exercise strengthens and regulates specific muscle groups.

On the other hand, any pattern of stressors that interferes over many months or years (caregiving long term for a loved one, a bad boss and you're stuck in a job you can't leave, childhood trauma and abuse, for example) without allowing the marvelous capacity of our stress response system to recover and self-regulate – any pattern that reduces our resilience – tends to lead eventually to illness.

The Mystery of Toxic Stress

Toxic stress is a black box – a mystery how we end up trapped in it and a mystery how to work our way out. Our COVID-19 pandemic brought the experience of toxic stress into every home, school, and workplace, raising questions once again about the seemingly random ways that stress strikes our bodies and minds, and the ways that resilience often rescues us.

And toxic stress is a mystery not only to those who struggle with stress-related conditions, but all too often toxic stress mystifies the doctors who help them manage these conditions.

What determines who falls ill and who survives or thrives? Why have minorities, the obese, and people with preexisting conditions been among the most vulnerable to severe and lethal COVID-19 infections?

For some this pandemic has delivered the very definition of toxic stress – persistent demands that appear to exceed our resources – and death for millions, more rapidly than any war. For others more

lucky or resilient, the coronavirus threat has meant no more than a mild illness or the inconvenience of a miraculous vaccine. For all of us, novel uncertainties about jobs, school, and healthcare ruled our daily lives during this pandemic.

On the other hand, when what threatens us is a predator, a storm, or an argument between siblings about who gets the popsicle, we usually fare well enough. Most of us most of the time face these threats; we manage them, the threats pass, and we recover to face the next hurdle. In fact, clearing these hurdles teaches us, makes us stronger, and builds our resilience. What would we be without them? Managing these kinds of acute stressors grows our resilience by fine-tuning our stress response systems.

But other patterns of stress can cripple us with illness, crush our souls, or kill us young.

Like global warming, the alarming rise in rates of stress-related conditions over the past half-century around the world may be the price we are paying for our high-energy living in the form of these diseases: obesity, diabetes, heart disease, depression, addictions, and autoimmune disorders. What is this trick of nature that turns years of toxic stress into Crohn's disease for one person, multiple sclerosis for another, a heart attack for another? Can a pattern of toxic stress exhaust a pancreas, plug a coronary artery, or inflame an intestinal wall? And what makes some lucky survivors of toxic stress resilient to diseases of any kind?

If you prefer living well to the alternative, it helps to understand the difference between the kinds of stressors that make us grow and the kind that cripple or kill us young. It helps to understand how our stress response systems work and how they fail. Here we are, creators of space shots to Mars, the Internet, and iPhones, yet most of us are still in the dark about the mysteries of our stress response system and the kinds of toxic stress that make us ill.

The hero of this book is our magnificent stress response system, which operates beneath our awareness, like an orchestra of organs

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playing a hidden symphony, seemingly without effort when we are healthy. What is this hidden symphony, and how does it work, and how does it slip out of tune?

The neuroscience of stress is comparatively young – some say fifty years – and has not yet seeped into the clinical practice of medicine or into our popular culture. In this book, I define the neuroscience of stress as the study of the ways the nervous system coordinates with the other major organ systems to respond to the stressors of daily life.

The Stresses of High-Energy Living

Life is tough, always has been. Evolution has given us a stress response system that is remarkably adapted to coping with many kinds of stressors. And relative to our ancestors, most of us live longer and healthier lives than they did. But in the last century's blink in evolutionary time, our sudden escalation in energy consumption around the world has created stressors that evolution could not anticipate.

- Our sleep can now ignore the day–night cycle.
- We travel enormous distances at great speeds with unlimited frequency.
- Many of us organize our social lives now without villages or extended families to contain us.
- Our volume of communications has risen exponentially, yet many of us cope with loneliness that was unimaginable a century ago, when it was harder to lose touch with those who cared about us.
- Our options for addictive stimulations have never been greater.

These are just some of the novel forces that have conspired to create modern forms of toxic stress despite our having access at the same time to more resources than ever before. We are both blessed and cursed by our high-energy living.

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In this book, I focus on the central but often overlooked role of our stress response systems in our most common and costly illnesses, such as diabetes, heart disease, depression, and obesity. Stress is a hot topic in our culture, but a blind spot in most branches of medicine. Most doctors ignore stress or pay it only lip service. Standards of treatment for diabetes and heart disease promoted by our leading medical organizations hardly offer a whisper about stress as a risk factor or a target for treatment.

Yet we know from decades of good neuroscience that severe or persistent stress raises the risks for these common long-lasting illnesses, and toxic stress makes most illnesses harder to treat. We also know that exposure to a lot of adverse experiences in childhood is among the strongest predictors of physical and mental illness in adulthood.

What chance do we have to prevent and manage these illnesses if we don't learn to "see" toxic stress, measure it, and treat it?

Long after persuasive mountains of scientific data have made the case for changing our views about stress, many of us persist with our traditional views of how our bodies work. The culture of modern medicine is built around specialty areas (cardiologists look at the heart, orthopedists fix knees, oncologists treat cancer, for example) with economic investments and turf to protect. The stress response system, as we shall see, respects none of these turf boundaries, and it rules at every level of organization from genes to cells to tissues to organs to individuals to social groups.

And the Big System Is Not Well

Surrounding our individual stress response systems, there is the bigger system of healthcare where we get help. How does the healthcare system determine the ways we treat stress-related conditions? This is a simpler question to answer in countries where

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healthcare is delivered through a single national health service. In the US, by contrast, where many of the healthcare systems are run as businesses, it is difficult to understand the many ways the many big systems affect our individual stress responses.

The US has consistently ranked in the mediocre range on most international studies of effective population healthcare.[6] The US healthcare culture has, in general, also given low priority to primary care doctors who potentially have the greatest influence on the long-term health of their patients, resulting in low pay and high burnout rates for primary care.

And the US government safety net has picked up the costly pieces neglected by the for-profit and not-for-profit parts of the system, such as the uninsured, the underinsured, those bankrupted by healthcare bills, those denied coverage due to preexisting conditions, and those with chronic mental illnesses. The US healthcare system's problem list is long and expensive, and unique among developed countries.

Paul Starr, professor of sociology and public affairs at Princeton University and former senior healthcare advisor for the Clinton administration, reminds us that the US spends 17.6 percent of its gross domestic product on healthcare, about double the average of 9 percent across other economically advanced societies.[7] The US spends more to get less in terms of good results, and it is the only major advanced society without a national healthcare system. The only partial advance in healthcare reform on a federal level in the US has been the Affordable Care Act of 2010, the target of over fifty efforts to repeal it, all of them unsuccessful (as of 2023).

As we will see in more detail in later chapters, this system of silo-minded, specialty-driven, procedure-focused healthcare for commercial gains tends to ignore improving outcomes for the stress-related disorders that require collaborations across disciplines to achieve incremental gains that prevent and mitigate our most costly common conditions. The US healthcare system

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reminds us that big systems can present barriers to effective care for stress-related disorders.

Narrowing the Gap

This book tells the stories of people who eventually triumphed over multiple illnesses, beating the odds at a considerable cost by developing a resilience regimen that reversed or slowed the course of these conditions.

I have spent my career providing psychiatric care in medical settings, and I have watched with wonder over the past forty years as the gap between psychiatry and medicine narrowed – a narrowing that has been both painfully slow and promisingly persistent. I have focused my career on this narrowing interface, trying on a daily basis to translate advances in neuroscience into treatment plans that work for patients and their healthcare providers, which in this book means doctors, nurses, and other allied health professionals.

This book profiles the clinicians, the scientists, and the programs that have helped people along the path from toxic stress and illness to health. I explain how the science of the stress response system emerged in fits and starts over the last half-century, building the case for clinical relevance while the practice of medicine often looked the other way.

Fortunately, the tide is changing. In recent years key voices in the reform of healthcare in the US and around the globe have spoken up about the central role of toxic stress in our current epidemics. And in some places the practice of medicine is changing to meet this challenge.

I explore the key dilemmas we face as patients, as providers of healthcare, and as healthcare systems – in the US, quirky like no other system in the world – in our approaches to stress and illness.

Many dilemmas are shared by all nations and cultures, and some pertain to particular nations. Why is the US so peculiarly behind the rest of developed nations when it comes to managing stress-related conditions and saving lives?

My purpose in this book is to sharpen our focus on this mysterious and often invisible thing we call stress, and to clarify how we can think about stress in ways that lead to more effective approaches to common illnesses. Like volcanoes in the ocean, most of the troubles that erupt in our stress response systems lie deep beneath our awareness and go undetected until they take the form of major illnesses.

This book calls for nothing less than a frame-shift, a clearer way of seeing the workings of our stress response system and seeing how dysregulations of that system lead to illness. No book can make this shift in thinking alone, but a good book can guide us to change the way we look for toxic stress and change the way we practice caring for these illnesses.

The overlooking of stress in medicine is a phenomenon of cultural blindness that is similar to our culture's overlooking of global warming. Just as we are waking up to the environmental costs of our high-energy living, we are waking up to the physical and psychological costs as well. There are good reasons why we have not understood our stress response systems as well as we need to, and good reasons why now more than ever we urgently need to face this challenge of toxic stress, both on a personal and on a public health level.

This book aims to show us how we can begin to meet that challenge on an individual level, how we can develop the resilience we need to identify and treat or prevent stress-related conditions. For anyone who is curious about the culture of medicine and healthcare and for anyone fascinated or troubled by the enigma of toxic stress, this book will open that black box and show us the process that transforms distress into a failing heart, brain, or

pancreas. And it will show how we can participate in a journey that can move us from reluctant victim to informed expert in our own conditions.

What You Will Learn from This Book

Chapter 1 orients you to the key dilemmas we face in the way we approach stress in our stimulating and consuming culture, in the US and around the world. Recognizing that stress comes in many forms – good, tolerable, and toxic – this chapter describes the size of the problem of toxic stress in a variety of settings and our difficulties identifying the stressors that hurt us.

Chapter 2 spells out why toxic stress remains invisible to most of us, including your healthcare providers. This blind spot is all the more fascinating in the context of the magnitude of the problem of toxic stress, which contributes substantially to poor performance on the major indicators of public health, including death rates.

One complicated and inconvenient truth for modern medicine around much of the world is that we have developed an epidemic of stress-related conditions. This epidemic has been building for decades and will be around when COVID is gone or at least under better control.

Think of the mysterious rise in rates of suicide, depression, and PTSD (posttraumatic stress disorder) over the last three or four decades, beginning in the 1980s. Then think about the rises during the same period of rates of obesity, substance abuse disorders, and ADHD (attention deficit disorder). Then think about the sharp rise in rates of diabetes – now 37 million or one in ten US citizens have diabetes, and a third of our population is on that path with prediabetes. Over half of us are obese. That's never happened before. And it's happening in developing countries now too.

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While much of our population is living longer and healthier, too many of us are dying younger. The health gap is widening around the globe.

Another complicated truth – the one that requires this book – is that the stress response system, especially the human kind, is a complex system of systems. Ours is so complex that most doctors avoid thinking about it. We're more comfortable focusing on one organ system or one set of problems.

Medical specialists like me prefer a turf we can know. Trying to understand the stress response system poses the same difficulties as trying to understand global warming or global economics, two other examples of complex systems of systems. If you find this hard to believe, try asking your doctor on your next visit to talk to you about how your stress response system is doing.

Chapter 3 may help with that conversation. It spells out some of the difficulties that stress neuroscientists have faced when studying the stress response system, and it alerts you to some of the difficulties we all run into as we talk about stress in our everyday lives. This chapter cautions us against oversimplifying the story.

No single factor – and certainly not toxic stress – "causes" our most common chronic illnesses. Instead, multiple factors, including toxic stress, drive these processes over long periods. This chapter establishes some terms and frames the journey for exploring how toxic stress drives illness over the lifespan and helps us understand what it takes to develop resilience and keep it.

Our stress response system works well under the best of health, when we're most resilient. As we grow from infancy through adulthood, this complex system of at least nine organ systems develops resilience through redundancy, with plenty of overlap, so one system can support another under strain. In chapter 4, we see what happens from head to toe, whether you're an office worker navigating the demands of daily life or a tipsy lush hearing a scuffling noise in a dark alley.

And in chapter 5 we take a fanciful look at the hidden symphony and see what happens in Usain Bolt's stress response system during his ten-second sprint as the world's fastest human. He is one of the master conductors of the stress response system, with his speed as proof of his prowess. An appreciation of the orchestration required to mount this everyday miracle provides the background for understanding the way persistent and severe stressors disturb this process.

Chapter 6 spells out the features of the dysregulated stress response system that distinguish it from the healthy system. Here, most of all, is where it pays to appreciate the current state of what stress neuroscience can tell us, and what we still need to know. Like oceanographers aware of the enormity of our uncharted waters, we know we have just a few good maps of a few aspects of the stress response system. By focusing on some of the better-studied pathways by which your experience of toxic stress transforms into an illness or disease, we can appreciate the need to think about multiple organ systems over long periods of time, often a lifetime, and to understand the biological, psychological, and social aspects of stress.

Once we appreciate the complexities of the dysregulated stress response system, we can begin to understand how toxic stress turns into illness. Chapter 7 describes six pathways: genes and epigenetics, adverse childhood experiences, high-risk health behaviors, autonomic imbalance, hormonal turmoil, and low-grade inflammation. And each one of these pathways may weave through the others, eventually creating a Gordian knot of dysregulations that may be experienced by you as fibromyalgia, depression after a heart attack, or a perplexing and debilitating tremor in your hands and legs.

Toxic stress, like global warming, is a state of imbalance and impairment in a system that has lost its ability to reset itself. It's brittle now, instead of flexible and resilient and self-regulating. This is just one reason why it makes sense, when evaluating one

medical problem in one organ system, to look for related problems in other organ systems or other aspects of a person's psychological or social life.

How fast or slow does this process of dysregulating the stress response system go until a disease emerges? Chapter 8 builds a model for how this process works over the lifespan. One of the lessons is that the apparently sudden onset of diabetes or heart disease in our fifties or sixties can often be traced to subtle dysregulations that began years before, even decades before, invisible to the unsuspecting and asymptomatic (no apparent symptoms). And the pace with which we develop many common disease processes is accelerated by persistent stressors.

Toxic stress accelerates illness and speeds up aging. Are you on a fast track to future illness and early death? And when is the best time to intervene? The answers are not simple, but they begin with knowing the questions to ask.

And answering those tough questions begins with measurement. Good management in all branches of medicine begins with good measurement. One of the biggest barriers to recognition, prevention, and treatment of stress-related disorders has been the troubled waters of stress measurement.

Chapter 9 describes the dilemmas faced by anyone who tries to carefully measure the stress process to guide clinical care. Some of these dilemmas are rooted in the complexities of the stress response system itself. And this chapter describes the options for simple stress measurements available to you and your doctor right now.

More than ever before, most of us now have access to devices that can measure aspects of our stress response systems (you may already have a Fitbit or Apple Watch on your wrist or a smartphone in your pocket) – processes that are otherwise invisible to us – and we now have apps to help us make sense of these new data.

More important than any single measurement of stress is the stress profile, as we see in chapter 10. Modern medical practice

depends heavily on profiles, but so far we have no standard stress profile. This chapter presents a few of the options for creating a stress profile that can guide your decisions about risks and treatment planning. It then distills the complexities of stress measurement to three types of assessments: subjective distress, lifetime exposures and responses, and physiologic measures of toxic stress responses.

This chapter discusses the need for psychological consulting services that provide stress profiles, similar to the services that currently provide neuropsychological profiles for people with learning disabilities, head trauma, or early dementia, for example, to guide their treatment plans. For the one in five of us who has been exposed to toxic stress, this stress profile could provide the starting point for a personalized approach to reducing our risks for stress-related illnesses.

Of course, there's no point in creating a stress profile unless we believe we can do something about it. Can you do anything about your specific collection of financial, social, and physical troubles? Many of the most oppressive sources of stress, such as poverty, crime, pollution, childhood trauma, and abusive family members, appear beyond our control. Is it possible to retrain a dysregulated stress response system and regain some sense of resilience after being sick with a severe condition? How long does that process take?

Chapter 11 describes five programs that have been well studied and widely used in some medical settings. Each of these programs exemplifies the effective retraining of specific aspects of the stress response system and the slowing or reversing of the course of an illness. All of them, as well as the emerging trend toward what we now call Lifestyle Medicine, depend on mastering the puzzling process of changing entrenched high-risk health behaviors, sometimes in the context of treatment with medications or surgery. These examples teach us what we can expect to invest in these approaches and what we can expect to reap as health benefits.

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Where should people with stress-related health conditions go for help? What might you do differently now if you and your doctors can add up the multiple toxic stressors in your life? Most often the best place to begin and end is with your primary care doctor. Depending on your stress profile and the conditions you're managing, you may see a number of specialists along the way, but if you suspect that stress plays a guiding role in your health, start with your primary care doctor.

You don't have to imagine how that conversation might go. In chapter 13 I present ways you can have that conversation with your doctor. The more you understand the stress lingo, how the stress response system works, and how stress-related illnesses develop, the better these conversations will go.

In the final chapter I take a look forward at what we can do next to improve how we manage toxic stress. As individuals we can create more effective conversations about stress and illness and we can practice habits that help retrain our stress response systems after periods of dysregulation. As nations debate public health priorities, I argue that the time has come to put toxic stress at the top of the list. We can no longer ignore the size and the health impact of our current burden of toxic stress and stress-related conditions.

In the appendix of this book, I imagine what the ideal Resilience Center would look like and how it would function. With such centers, we can relieve the public health burden of toxic stress and common stress-related conditions. Such treatment centers could play a role in a larger public health initiative targeting toxic stress. Imagine that!

Let's begin this journey with a day in the life of Ted Daley, just a regular guy who is unselfishly helping scientists understand toxic stress.