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NAOMI WATTS

The Menopause Brain



The new science
for women to navigate
midlife, and optimise
brain health for later years

LISA MOSCONI PhD

NEW YORK TIMES BESTSELLING AUTHOR

Lisa Mosconi, PhD, is an associate professor of neuroscience in neurology and radiology at Weill Cornell Medicine and the director of the Women's Brain Initiative and the Alzheimer's Prevention Clinic at Weill Cornell Medicine/NewYork-Presbyterian Hospital. A world-renowned neuroscientist with a PhD in neuroscience and nuclear medicine from the University of Florence in Italy, Mosconi was listed as one of the seventeen most influential living female scientists by *The Times* and called 'the Mona Lisa of Neuroscience' by *ELLE* International. She is the *New York Times* bestselling author of *The XX Brain* and *Brain Food*.

PRAISE FOR *THE MENOPAUSE BRAIN*

'Dr Lisa Mosconi is my go-to for insightful guidance on the brain during menopause.'

Naomi Watts

'Now that you have this book, you will not have to navigate perimenopause, menopause, or even your postmenopausal life alone.'

Maria Shriver

'Ladies, your brain needs to read this book.'

Dr Linda Dear, Menodocor

'Wish Dr Lisa's book was around when I went through my menopause nightmare. *The Menopause Brain* is a must read for EVERYONE not just women.'

Susie Elelman AM, author, TV and radio broadcaster

'Dr. Mosconi's book serves as a rallying cry for embracing this transformative period with knowledge and empowerment.'

Mary Claire Haver, MD, author of *The Galveston Diet*

‘Highly recommended for women who want to actively participate in preserving their brain’s health as they approach and progress through perimenopause and menopause.’

Avrum Bluming, MD, co-author of *Estrogen Matters*

‘Dr. Lisa Mosconi expertly guides us so that we do not feel alone in this journey, providing us with hope and achievable, empowering solutions drawn from her pioneering research, holistic training, and personal experience.’

Tamsen Fadal, author of *The New Single*

‘When it comes to menopause, it feels as if we have no information, misinformation, or what’s out there is too chaotic and conflicting to make sense. For every woman living any phase of menopause, this is your required reading.’

Lisa Genova, bestselling author of *Still Alice*

‘Delivers the comprehensive, science-backed information we need about menopause.’

Jolene Brighten, NMD, FABNE, bestselling author of *Beyond the Pill*

‘Dr. Mosconi is finally answering the questions that have been ignored for far too long. *The Menopause Brain* is deeply researched, yet accessible, and provides the gold standard for understanding the role of oestrogen in the female brain.’

Sharon Malone, MD, author of *Grown Woman Talk*

‘*The Menopause Brain* gives you the tools you need to make sure that your beautiful mind is vibrant and that your brain stays healthy.’

Aviva Romm, MD, author of *Hormone Intelligence*

‘Long misunderstood, menopause gets a fresh narrative in *The Menopause Brain*. Filled with groundbreaking research and actionable advice from a leading neuroscientist, this book is essential reading for anyone navigating this transformative period.’

Ellen Vora, MD, author of *The Anatomy of Anxiety*

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*To all women—our ancestors, our descendants,
and all of you blazing the trail with me as we speak.*

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FOREWORD

I AM SO HAPPY that you picked up *The Menopause Brain*. Good for you. You just did yourself and your brain a huge favor! Now that you have this book, you will not have to navigate perimenopause, menopause, or even your postmenopausal life alone. You now have at your fingertips the most up-to-date information about what is happening to your brain and your body—and why. What a gift!

This book is crucial because every woman, if she lives long enough, will go through menopause at some point in her life. And every woman will wonder why, in addition to losing her period and fertility, she may be experiencing sudden heart palpitations, anxiety, depression, lack of concentration, hot flashes, night sweats, mood swings, and sleep disturbances. The list of symptoms is long and varied. Menopause is a function of the brain that plays havoc with a woman's body and her outlook on life. Indeed, all of these erratic emotions and symptoms can make a woman feel crazy if she is not reassured that they are normal. This book will do exactly that.

I wish this book had been around when I was going through perimenopause and menopause because for millions of women like me, when *The Big M*, as I call it, came knocking, we were given little information to guide us forward. So women of my generation felt unseen and unheard by healthcare professionals who weren't educated in this space and didn't have the research to help guide us through the confusing, often chaotic symptoms we were experiencing. Instead, we weathered the turbulence, while living in a culture that intimidated women at midlife were prone to going crazy. This book is testimony to progress.

A few years ago, I was honored to write the foreword to Lisa's book *The XX Brain*, and now I am thrilled to write the foreword to this book as well. In *The Menopause Brain*, you have the most current science and the best practical guidance available, and it comes from a researcher who is not only an innovative and visionary thinker but someone I now consider a friend for life.

I first met Lisa in 2017, when I was looking for research to help answer the questions of why women are twice as likely to develop Alzheimer's as men, and why women of color are at even higher risk for the disease. Finding almost no research available motivated me to start my nonprofit organization, the Women's Alzheimer's Movement (WAM), and it has driven my quest ever since to learn about women's brains throughout the lifespan. Meeting Lisa along this journey was a game changer. She was one of the first scientists to show the impact of menopause on a woman's brain at midlife, and to discuss the brain's response to menopause in general. Lisa had just published the first study showing that women's brains become more vulnerable to Alzheimer's in the years before and after menopause. She was among the first researchers who not only described how a woman's brain changes physically and shrinks during menopause, but developed the technology and research to show the process in action. Thanks to Lisa and other like-minded scientists dissatisfied with the lack of research on women's brain health, a movement began that aimed to study the unique impact of sex hormones such as estrogen on women's health. I was delighted to help fund some of that research through the WAM Research Grants, which are awarded to scientists looking at the role of gender as a risk factor for Alzheimer's.

It's a sad fact that despite the prevalence of menopause symptoms and its potentially serious consequences on long-term health, research into menopause has historically been underfunded and overlooked, right alongside women's health in general. For Black women in particular, the health consequences of this oversight are even more dire, and the road through menopause often longer and harder. There is no excuse for ignorance.

My mission now is to make up for lost time, for the neglect in funding that has led to a historic gap in our understanding of women's health. It's why in 2022 we joined forces with one of the world's top-rated healthcare systems to become WAM at Cleveland Clinic. I'm proud to say WAM remains the preeminent organization for women and Alzheimer's, made all the stronger by now having partners leading the field in medical research and excelling at delivering the best clinical care available. In 2020 we made history together when we opened the first Alzheimer's Prevention Center designed just for women at the Lou Ruvo Center for Brain Health in Las Vegas. Now we are working on a shared mission to make Cleveland Clinic a premier holistic center for women's healthcare where every patient feels seen and heard.

My focus is on continuing to support all those around the world who, like Lisa, are researching what is happening to women's brains during midlife, while also ensuring that women everywhere get the valuable information they need to take control of their health during these critical decades. And it's not just women who need to have this information but their doctors, friends, and families as well. This book is a guide for us all, and I hope it is studied by those teaching medicine and those practicing it. I encourage women to remember that they can make a difference to their own health. I hope they will visit their healthcare providers with this book and its research in hand, and together formulate a plan that will deliver them the best medical care they need and deserve to set them up for lifelong health.

So empower yourself with this knowledge, share it with women you meet along the journey. Become what I call an "architect of change"—someone who brings about the change they want to see in the world. Your brain is your biggest asset. Care for it well so it may last a lifetime. I promise it will be the best investment you can make in your future health.

—Maria Shriver

PART 1

THE BIG M

1

You Are Not Crazy

“AM I LOSING MY MIND?”

Between the ages of thirty and sixty, many women will wake up one morning and wonder what hit them. Whether it's uncontrollable sweating or a barrage of brain fog and anxiety, any one of us can be confronted with an onslaught of peculiar changes sudden enough to, quite literally, make her head spin.

It might be a sense of disorientation, where you find yourself doing increasingly absent-minded things, like entering a room only to wonder what made you go there in the first place. Belongings may be misplaced, with milk cartons finding their way into cabinets and cereal boxes ending up in the fridge. Communication can also become a challenge. Moments of sheer panic may arise as you struggle to come up with that word on the tip of your tongue or draw a blank on something you just said, losing your train of thought. Emotions, too, can be all over the place, as if a heavy darkness is causing you to weep for no clear reason—only to be replaced a moment later by waves of irritability or even anger. And just when you hoped a good night's sleep might resolve these issues, sleep becomes elusive. Like a fickle ghost, it visits sporadically throughout the night, or may not appear at all. With the

rapid-fire onset and the intensity of these unexpected changes, it's no wonder many feel as if their own bodies are betraying them, throwing any woman into a tailspin of questioning herself, her health, and even her sanity.

Perhaps you don't recognize any of these symptoms—yet. Most likely, though, you've heard about them before. From girlfriends, from your mother, from googling late at night when you can't sleep . . . again.

We now have a name for it: menopause brain.

More often than not, the answer to the phenomena so many women experience in midlife is nothing more, but also *nothing less*, than menopause.

Menopause is one of the best-kept secrets in our society. Not only has there been no proper education or culture of support around this rite of passage common to all women, but often, menopause isn't even discussed within families. What's noteworthy is that even when there is some information or wisdom that's shared, it's generally not centered around the most prominent aspects of the transition—namely, how menopause impacts *the brain*.

As a society, insofar as we have understood menopause at all, it's generally only half of what it's all about—the half that pertains to our reproductive organs. Most people are aware that menopause marks the end of a woman's menstrual cycle and, therefore, her ability to bear children. But when the ovaries close up shop, the process has far broader and deeper effects than those associated with fertility. Far from the spotlight, menopause impacts the brain just as much as it impacts the ovaries—directly and powerfully, and in ways we are only beginning to gather real data about.

What we do know is that all these baffling symptoms—the heat surges, the feelings of anxiety and depression, the sleepless nights, the clouded thoughts, the memory lapses—are, in fact, symptoms of menopause. The real kicker, however, is that they don't originate in the ovaries at all. They are initiated by another organ entirely: *the brain*. These are, in fact, *neurological* symptoms that come from the ways that

menopause changes the brain. As much as your ovaries have their role in this process, it's your brain that's at the wheel.

Does that make your worst fear real? Are you truly losing your mind?

Not at all. I am here to reassure you that you are **not** going crazy. Most important to note: you are not alone in this, and you are going to be okay. While menopause does indeed impact the brain, that doesn't mean the problems we experience are "all in our head." Just the opposite.

THE HIDDEN SCALE AND IMPACT OF MENOPAUSE

In our youth-obsessed culture, where it's not outright dismissed, menopause is either dreaded or derided. Not only is there no acknowledgment of menopause as a noteworthy landmark in a woman's life, but as it is historically perceived in the extreme negative, menopause comes with the stigmas associated with ageism, the demise of one's vitality, and even the end of our identity as women. Mostly, however, menopause is framed in silence, sometimes even secrecy. Generations of women have suffered under misinformation, shame, and helplessness. Many remain reluctant to discuss their symptoms for fear of being judged, or strive to hide them. Most don't even realize that what they're experiencing has anything to do with menopause in the first place.

All this confusion isn't just unfair. It constitutes a significant public health problem, with far-reaching consequences. Let's look at the numbers:

- Women are half of the population.
- All women go through menopause.
- Women of menopausal age are by far the largest growing demographic group. By 2030, 1 billion women worldwide will have entered or will be about to enter menopause.
- Most women spend about *40 percent of their lives* in menopause.

- All women, menopausal or not, possess an organ that has been largely ignored: the brain.
- Over three-quarters of all women develop *brain symptoms* during menopause.

Out of sheer numbers alone, menopause should be a major sociocultural event and the subject of extensive investigation and deep knowledge. Instead, whether we remain focused on the unpleasant symptoms or psyched out by the perceived lessening of our female powers, the current perception of what menopause means is fixated on the many pitfalls of this life event. Meanwhile, from a scientific and a medical perspective, it's a discipline without a name.

The Problem of Western Medical Frameworks

Thanks to how genuinely uninformed we are about menopause, too many women are caught completely off guard, feeling betrayed by their body *and* their brain—not to mention their doctors, too. While hot flashes are generally recognized as a “side effect” of menopause, most doctors simply won't make the connection between menopause and its other symptoms such as anxiety, insomnia, depression, or brain fog. This is especially the case for women under fifty, who are typically sent home with a prescription for antidepressants, their concerns dismissed as a by-product of their psychology, a sort of female existential crisis. Why is that?

Western medicine is well known for its siloed, non-holistic frameworks, in which the human body is evaluated in terms of its individual components. For example, people with eye problems go to an eye doctor, and those with heart problems go to a cardiologist even if the heart problems led to the eye problems. As a result of this extreme specialization, menopause has been pigeonholed as “an issue with the ovaries” and consigned to ob-gyn territory. Anyone who's been there, however, knows that ob-gyns don't do brains. Educated like every other doctor to specialize in specific body parts—in this case, the

reproductive system—they aren't trained to diagnose or manage brain symptoms in the first place. But also, many ob-gyns are not trained to manage menopause at all. Today, fewer than one in five ob-gyn residents receive formal training in menopause medicine, which often consists of a mere few hours in total. Perhaps unsurprisingly, 75 percent of women who seek care for menopausal symptoms end up not receiving treatment.

On the other hand, brain doctors—neurologists and psychiatrists, among others—don't handle menopause, either. Given these divided frameworks, it's no surprise that the effects of menopause on brain health have been neglected, leaving these issues to fall into the cracks between rigidly defined medical disciplines.

Here's where brain scientists come in handy. I am one of them, holding a somewhat unusual PhD in neuroscience (the study of how the brain works) and nuclear medicine (a branch of radiology that uses imaging techniques to examine the brain). But what really sets my work apart is that I have made it my life's work to study and support *women's* brains. Specifically, I am an associate professor of neuroscience in neurology and radiology at Weill Cornell Medicine in New York City, where I apply this background at the intersection of all these disciplines and women's health. To this aim, in 2017, I launched the Women's Brain Initiative, a clinical research program entirely and unapologetically dedicated to understanding how brain health plays out differently in women than in men. All day every day, my team studies women's brains—how they work, what makes them uniquely powerful, what makes them uniquely vulnerable. At the same time, I am the director of the entire Alzheimer's Prevention Program at Weill Cornell Medicine/NewYork-Presbyterian, which allows me to integrate my research on women's brains with the clinical practice of evaluating and supporting cognitive and mental health for the long run.

Years of research have made clear to me that caring for the health of the female brain requires a careful understanding of how it shifts and changes in response to our hormones, especially during menopause. So one of the very first things I did after launching these

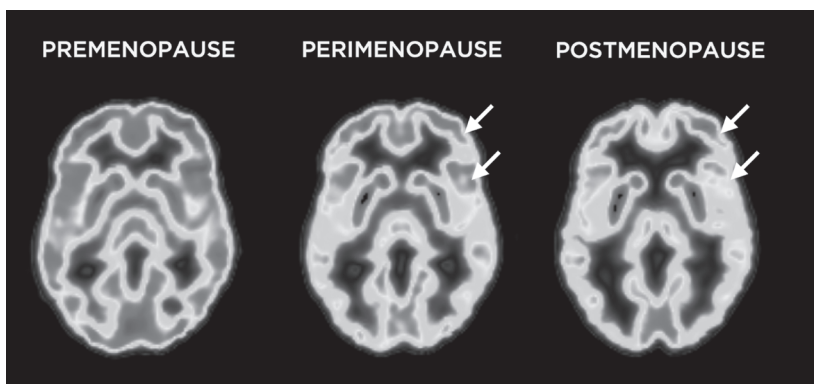
programs was to pick up the phone and call the ob-gyn department. From that day on, we've been collaborating with some of the best menopause specialists around, as well as top-tier ob-gyn surgeons and oncologists. Together we set out to answer the question we didn't see enough professionals exploring: *How does menopause impact the brain?*

THE BRAIN ON MENOPAUSE

When I started studying menopause, I quickly realized two important facts. First, very few brain studies looked at menopause at all. Second, the few that did were focused on women who were well past menopause, often in their sixties and seventies. In other words, menopause has been studied in terms of its impact on the brain *after* the fact—more like a product than a process.

My team and I have focused instead on what leads to those outcomes, up to and through menopause. To give you a sense of how dire the situation looked when we started, there wasn't a single study that examined women's brains before and after menopause. So we rolled up our sleeves, turned on the brain scanner, and set out to explore this new frontier. As of today, we've made significant progress in demonstrating that women's brains age differently from men's brains, and that menopause plays a key role here. In fact, our

Figure 1. Brain scans before and after menopause



studies have shown that menopause is a *neurologically active process* that impacts the brain in fairly unique ways.

To give you a sense of this, what you see on the previous page is a type of brain scan generated by a functional imaging technique called positron emission tomography, or PET, that measures brain energy levels. Brighter colors indicate high brain-energy levels, while the darker patches indicate a lower energy turnover. (For full-color imagery, see my website: <https://www.lisamosconi.com/projects>.)

The image to the left shows a high-energy brain. It is a perfect example of what you want your brain to look like when you're in your forties—vivid and bright. This brain belongs to a woman who was forty-three years old when scanned for the first time. Back then, she had a regular cycle and no symptoms of menopause.

Now look at the scan labeled *postmenopause*. That's the same brain just eight years later, shortly after the woman had gone through menopause. Do you notice how this scan looks darker overall than the first? That change in luminosity reflects a 30 percent drop in brain energy.

This finding was far from being an isolated case; many women enrolled in our research program exhibit similar changes, whereas men of the same age do not. So what you see here are intense shifts that seem specific to the female brain going through menopause. While these changes can account for feeling worn out or simply out of sorts (as many can attest to, menopause fatigue is nothing to sneeze at), they sink more than your energy. They can also impact your body temperature, mood, sleep, stress, and cognitive performance. And guess what? Most women can *feel* these changes. When there are marked biological changes at play, resulting in actual modifications of the brain's very chemistry, one can't help but notice them.

The aforementioned study was only the tip of the iceberg. Over time, our investigations yielded a treasure trove of data, demonstrating that it's not just brain energy that changes during menopause but that the brain's structure, regional connectivity, and overall chemistry are also impacted. All of this can make for a profoundly mind-blowing, mind-body experience. Perhaps less obvious without a brain scanner is that these changes don't occur after menopause—they start before it,

during perimenopause. Perimenopause is the warm-up act to menopause in which you start skipping periods and symptoms like hot flashes tend to make their first appearance. Our research shows that's exactly when the brain is going through the most profound changes, too. The best way I can explain this phenomenon is that the menopause brain is in a state of adjustment, even remodeling, like a machine that once ran on gas and is now switching to electricity, challenged to find work-arounds. But mostly, these findings are scientific evidence of what scores of women have been saying all along: **menopause changes your brain**. So if you've ever been told that your symptoms are just stress-related or "part of being a woman," here's the proof that all you've been experiencing is scientifically valid and viable. The brain is at the crux of the matter, not your imagination.

How Science Can Help

Over the years, I've spoken to countless women in various states of distress due to menopause, especially as related to their brain symptoms (whether they could articulate these or not). Many have told me that one of their steepest challenges was finding information they could not only readily consume but also trust. Hearing and listening to their need for knowledge and support made me realize that every woman deserves accurate and thorough information about menopause. Peer-reviewed science ensures that the ideas are valid, but academic journals are not an efficient way to provide this information to the hundreds of millions of women in the real world.

The Menopause Brain grows out of my commitment to empowering women with the information they need to experience menopause with knowledge and confidence. Understanding what's happening inside your body and brain before, during, and after menopause is crucial to understanding *yourself* before, during, and after menopause. It is just as crucial to take charge of your changing healthcare needs and reclaim your agency during this important life transition.

Thus far, menopause has been painted as an ill-fated, flat-out scary roadblock ahead, coming for us one by one. Most of what's been written

about menopause, from the scientific literature to online sources, focuses on coping or dealing with it, if not even rebelling against it. The vast majority of research on the topic has also been focused on what can go wrong with menopause and how you can “fix it.” “What’s wrong with that?” you may ask. Underlying this approach is the assumption that we can’t hope for better than surviving menopause. By treating this life event strictly in a biological context, Western medicine has emphasized its downsides and minimized its significance. But when you look at menopause from an integrative perspective, there is much more at play. In reality, the hormonal changes that provoke menopause and its symptoms are simultaneously fostering the development of new and intriguing neurological and mental skills—ones our society blatantly chooses to ignore. The hidden powers of the mind on menopause are the highlights that never make the headlines, powers that all women should be aware of. Such awareness leads to new means of navigating menopause, and ultimately womanhood itself.

To this end, the book is divided into four parts:

Part 1, “The Big M,” provides the foundational elements needed to understand what menopause is and isn’t, from a clinical perspective; how it impacts the brain; and how we fail to recognize this crucial connection.

Part 2, “The Brain-Hormone Connection,” discusses the role of hormones for brain health and how this interplay is critical in understanding menopause. Here, we take a deep dive into understanding how menopause operates within the body and brain, which is not just about deciphering the “what” but also the “why” of menopause, placing it within a broader context. To do so, we will examine what I call the Three P’s: puberty, pregnancy, and perimenopause. These are all pivotal times during which our brains, hormones, and the give-and-take between them change dramatically. Knowledge of the similarities between the Three P’s is key to recontextualizing menopause as a natural stage in a woman’s life—a moment that, just like the others, can provoke vulnerability as well as resilience and positive change. However, if your immediate interest lies in finding solutions and seeking ways to feel better, feel free to skip to part 3, where we focus on practical

strategies and guidance. Part 2 will be there for you whenever you're ready!

Part 3, "Hormonal and Nonhormonal Therapies," is a deep dive into hormone replacement therapy, as well as other hormonal and non-hormonal options for menopause care. We will then review anti-estrogen therapy for breast cancer and ovarian cancer, and the effects of "chemo brain." Finally, while throughout the book I use the term "women" to refer to individuals born with a so-called female reproductive system (breasts and ovaries), not all people who go through menopause identify as women and not all people who identify as women go through menopause. In recognition of the diverse experiences and identities within the context of menopause, we will discuss gender-affirming therapy for transgender individuals, which includes methods to suppress estrogen production.

Part 4, "Lifestyle and Integrative Health," discusses key validated lifestyle and behavioral practices designed to address the symptoms of menopause without prescription medications, while also supporting cognitive and emotional health. Although you might feel like your brain is all over the place, you do have control over your lifestyle, environment, and mindset—all of which can impact your experience of menopause in return. There is a way to be empowered by embracing and caring for menopause; as we do, a wealth of new possibilities is made evident.

Ultimately, this book is a love letter to womanhood and a rallying cry for all women to embrace menopause without fear or embarrassment. It's the foundation to celebrate our own signature brand of brainpower, to appreciate the intelligent adaptations our bodies and brains make over the course of a lifetime, and to enjoy our journey to optimal lifelong health. I hope the information contained in this book will spur many a discussion, not only about the multifaceted topic of menopause but also about the way in which we have dismissed and marginalized various important parts of our population at large. This is crucial not only to shift the conversation about menopause but also to reinvigorate the voice of the "forgotten gender"—individually, and as half the world.

2

Busting the Bias Against Women and Menopause

SEXISM AND NEURO-SEXISM

This book is a neuroscientist's take on the ups and downs of menopause. Before we reveal the future of the field, however, it's useful (albeit a bit dismaying) to review the cultural and clinical perspectives on menopause to date. I warn you that retracing some key sociohistorical steps on the topic might leave you feeling gloomy at first. After all, the combo of culture and conventional medicine is the reason we equate menopause with "ovarian failure," "ovarian dysfunction," "estrogen depletion," and another slew of negative outcomes. But stick with me; I promise that if we draw from modern science, there's a very different and more balanced story to tell.

From a cultural perspective, however, the outlook is unequivocally dim. If we dig a little deeper, it's clear that many of the demeaning stereotypes around menopause originate from a broader negative understanding of women* as the "weaker sex." If we start with the

* Throughout the book, for the sake of simplicity and based on the long-standing biological definition of the female sex, I use the term "women" to refer to individuals who were born with two XX chromosomes and possess a female reproductive system (including breasts and ovaries). However, there are individuals who fit within this biological framework but do not identify as women, and there are also individuals who

age-old sense that women are physically more fragile than men, this reference is also applied to our brains and intellect in the form of what we now call *neuro-sexism*—the myth that women’s brains are inferior to men’s brains. So before we can even address the complexity of medical frameworks for menopause, we need to address the complexity of the same frameworks for women as a whole.

However astoundingly flawed the doctrine of female inferiority may be, it’s nothing short of the backbone of modern science. According to Charles Darwin, the father of modern biology, “a man attains a higher eminence, in whatever he takes up, than can women—whether requiring deep thought, reason, or imagination, or merely the use of the senses and hands.” This theory gathered momentum and proliferated unchallenged throughout the nineteenth century, when male scientists made an “impressive discovery.” They realized not only that women’s heads were anatomically smaller than men’s but that women’s brains weighed less than men’s as well. This was an era in which the biological premise that “bigger is better” reigned supreme. Therefore, a woman’s slender brain was conveniently interpreted as a sign of lack of intelligence and mental inferiority. The pundits of the day were quick to correlate that with a lack of aptitude for a variety of tasks. For example, George J. Romanes, a leading evolutionary biologist and physiologist of the time, went on to say this: “Seeing that the average brain-weight of women is about five ounces less than that of men, on merely anatomical ground we should be prepared to expect a marked inferiority of intellectual power in the former.” These assumptions were by no means unique, as most intellectuals back then were perfectly comfortable embracing an interpretation that suited the status quo. Those “missing five ounces” of women’s brains were thus used to justify the difference in the social status between men and women,

were not born with these characteristics but do identify as women or as female. The biological response discussed in this chapter is independent of gender identity and rooted in physiology. Chapter 12 is focused on discussing the diverse experiences of individuals beyond the traditional biological definitions.

cementing the denial of women's access to higher education or to other rights that might have rendered them independent.

I'm going to go out on a limb here and guess that the following goes without saying: the fact that, on average, men's bodies are larger and heavier than women's might have made the observation that their heads were more or less made to match a no-brainer (pun intended). If one has a bigger body, the skull and the brain within should be bigger as well. In fact, once head size is taken into account, the fabled brain-weight difference disappears into the thin air whence it came.

Just the same, for centuries, women's brains continued to be weighed and found wanting, keeping women out of universities and prestigious jobs. Eventually, female scientists and human rights activists joined forces to denounce how such biased interpretations were nothing more than political weaponry subverting women's efforts to attain equity and equality. Thanks to their efforts, the brain-weight intelligence theory was fully debunked in the early twentieth century. The later advent of brain imaging fostered further progress in dispelling many of the base assumptions behind neuro-sexism, leveling the playing field once and for all.

Or has it?

Today, while overtly sexist statements no longer have a place within the scientific community, many argue that neuro-sexism is still alive and kicking. The thing is, in many respects women's brains do differ from men's. We'll talk more about this in just a moment. For now, I want to point out that disparities between the genders are too seldom used to modernize medical care, and far too often used to reinforce demeaning gender stereotypes instead. Consciously or not, we are coerced into gender roles from birth, further fed by pop science claims about how our "Venus/Mars" behaviors differ due to our brains. It may start with the age-old tradition of accessorizing our infants in pink and blue, but it ends with the propagation of rigid, derogatory biases that relentlessly cast women as the lesser gender.

As it now stands, we face a triple challenge: sexism, ageism, and *menopause-ism*. From the moment we are born, the message from our

society is that we are lesser as women, if for no other reason than the fact that men are bigger and stronger. But these baseline beliefs proliferate in ways both subtle and not as we traverse the playground, the classroom, and the workplace, culminating in middle age. In this timeline, menopause is the final blow. After women endure decades of messaging that undermines them, here it is yet again, another fundamental female physiological process reduced to evidence for weakness and disease. Viewed through a dark patriarchal lens, in addition to the widely held belief that a woman's age renders her less attractive, the loss of utility in bearing children is an additional unwelcome cultural tax—one that only adds fuel to the fire of inferiority, physically, mentally, personally, and even professionally.

While there is a shortage of reliable science regarding menopause, there is certainly no lack of misleading claims or even misogyny surrounding this topic. In popular culture, menopausal women have often been portrayed through a distressing lens of erratic moods and explosive rages. We're all too familiar with the stereotype of the belligerent menopausal woman, tormented by hot flashes and mood swings, depicted as causing turmoil for her unfortunate and exasperated husband. This view is nothing new. It is deeply rooted in centuries, even millennia, of deep-seated patriarchal mistrust of female bodies. Ready for this?

MENOPAUSE AND THE ANTI-MENOPAUSE MOVEMENT

The first scientific references to menopause originate around the year 350 BC, when Aristotle first observed that women would stop having menstrual discharge sometime between the ages of forty and fifty. However, given that lifespans were shorter back then, not many women had the opportunity to traverse the whole of menopause and live to tell the tale. Besides, in ancient Greece as well as in many other ancient civilizations, a woman's value was linked to her ability to bear

children. Those who could no longer do so were evidently not worthy of much interest or study.

Aside from some vague mentions, menopause remained basically invisible to medicine until the nineteenth century. Right around the time male physicians “discovered” women’s brains, they also stumbled upon another disconcerting phenomenon: menopause. It might have been overall progress in scientific inquiry, or perhaps that more women were living long enough for menopause to not be ignored, but doctors eventually realized menopause wasn’t some kind of freak accident. By then, there were indeed colloquial expressions for menopause all over Europe, such as “women’s hell,” “green old age,” and “death of sex.” The word *menopause*, though, entered our vocabularies only in 1821, when French physician Charles de Gardanne came up with the term, borrowing from Greek *men* (month) and *pauein* (to cease or stop), indicating the time at which a woman’s period ends.

On brand for those times, the realization that menopause was something worth addressing led clinicians to build a framework for it . . . as an actual disease. A remarkable number of medical conditions, ranging from scurvy to epilepsy and schizophrenia, were readily blamed on this baffling new condition. This should come as no surprise considering the general mindset was that some obscure connection between the uterus and the brain rendered women susceptible to madness, or *hysteria* (from the Greek word *hystera*, meaning uterus). For instance, what we now refer to as premenstrual syndrome (PMS) was thought to be caused by the “suffocation” of the womb filling with blood, or even the upward migration of the womb within a woman’s body to suffocate *her*. Clearly, they argued, this unhealthy link will also result in “climacteric insanity” after menopause.

Consequently, drastic and often highly toxic practices emerged to deal with the rebellious wandering womb. Hypnosis, vibrating devices, and blasting the vagina with a jet of water are just a few well-documented techniques. Opium, morphine, and lead-based vaginal injections are others. Then physicians came up with an even more

radical solution: surgery. They argued that if the womb was diseased, it should be removed. In hindsight, we now know that *hysterectomies* (the surgical removal of the uterus and ovaries) plunge a woman into menopause almost overnight, potentially worsening its symptoms altogether. So as surgery only exacerbated issues, the asylum beckoned instead. Accounts abound of how women experiencing symptoms of menopause were wrongly diagnosed as “crazy” or “demented,” and as such, were locked up in mental institutions. The truth is that these women likely suffered such tragic ends due to the misguided treatments administered by their own doctors.

Fast-forward to the twentieth century. As women gained lifespan, suffrage, and cultural power, menopause finally came to be understood as worthy of medical attention, as opposed to institutionalization. One of the most significant contributions to this shift in perspective came in 1934, when scientists discovered the hormone estrogen. Notably, the term *estrogen* itself was derived from the Greek *oistros*, which means frenzy or mad desire—further reinforcing a historical trend to frame female physiology through the lens of mental instability. Nonetheless, as science moved forward, the link between loss of estrogen and menopause was also found—which led only to updating the definition of menopause to be a disease of “estrogen deficiency.” By extension, estrogen became a magical elixir of youth in people’s imagination, and as such a profitable drug. Pharmaceutical companies jumped at the opportunity, and estrogen replacement therapy quickly became the treatment of choice for menopause. As recently as 1966, Robert A. Wilson, MD, author of the national bestseller *Feminine Forever*, declared the condition “a natural plague,” calling menopausal women “crippled castrates.” But, Wilson wrote, with estrogen replacement, a woman’s “breasts and genital organs will not shrivel. She will be much more pleasant to live with and will not become dull and unattractive.” Later, and perhaps unsurprisingly, evidence emerged that the influential book had been backed by pharmaceutical companies. Not all the propaganda was explicitly sponsored, though—it just spread across culture like wildfire. David Reuben’s *Everything You Always Wanted to*

Know About Sex but Were Afraid to Ask (1969) had this to say: “Once the ovaries stop, the very essence of being a woman stops.” He added that “a postmenopausal woman comes as close as she can to being a man,” correcting, “not really a man, but no longer a functional woman.” Little by little, the idea that menopause was an estrogen deficiency syndrome took hold, and it is still common in medical textbooks and practices today.

On the other hand, the actual mechanisms by which estrogen impacts mental health are a strikingly modern discovery. Only in the late 1990s did scientists make a powerful breakthrough: our so-called sex hormones were key not just for reproduction but for *brain function* as well. In other words, the hormones inextricably involved with our fertility, with estrogen leading the charge, turned out to be just as crucial in the overall functioning of our minds. To give you a sense of how recent a finding this is, men had walked on the moon thirty years prior. During those same thirty years on earth, scores of women had been taking hormones in spite of the fact that nobody had a clue about how estrogen really worked from the neck up.

MEDICINE AND BIKINI MEDICINE

Which brings us back to the twenty-first century. Today, menopause is strictly ob-gyn territory, and the connections between our reproductive system and our brain are no longer demonized but are mostly unaddressed. At the same time, in a bizarre turn of events, most scientists now accept that sex hormones are important for brain health, but also believe men’s and women’s brains to be roughly the same, except for some functionalities involved in reproduction.

Enter one of the major healthcare challenges of our times: bikini medicine. Bikini medicine is the practice of reducing women’s health to those body parts found beneath a bikini’s confines. It is saying that, from a medical perspective, what makes a woman “a woman” is our

reproductive organs and nothing more. Aside from those organs, men and women have been studied, diagnosed, and treated in the same exact way—as if we were all men. This, as it turns out, is not only counter to reality but also destructive in guiding medicine and science to protect women's brains, including those in menopause.

In the simplest terms, the vast majority of medical research has used the male body as its exclusive prototype, “boobs and tubes” notwithstanding. On top of that, as recently as the 1960s, the FDA made it standard practice to deny women of childbearing potential access to experimental drugs and clinical trials, claiming that doing so avoided any potential adverse effects on the fetuses. The phrase *woman of child-bearing potential*, however, was taken to mean “any woman capable of becoming pregnant,” not solely those who were. This meant that any woman from the age of puberty through menopause, regardless of sexual activity, use of contraceptives, sexual orientation, or even any desire to have a child in the first place, was excluded from clinical trials. Where women's brains had been dismissed for centuries as flawed, they were now being rendered invisible for other reasons entirely.

This woman-wide ban was enforced well into the nineties, which means we have decades of medical research based on nearly male-only samples. Shockingly, this is true right up to the present day, as countless drugs have been put on the market that have never actually been tested on women. In fact these drugs often haven't been tested even on female animals. The vast majority of preclinical studies still use only male animals, arguing that variability in sex hormones may “confound empirical findings.” This profoundly biased unisex system has been supplying the medical field with data that either doesn't apply or, at best, applies inconsistently to an entire half of the world's population.

Given that the male-dominated medical system has a long history of vilifying menopause while sidelining the study of women's brains, *and* that research has been done mostly on men, *and* that men don't go through menopause, it's really no surprise that the effects of

menopause on brain health have remained a mystery—a mystery “solved” with stigma and stereotypes rather than with facts and information. To state the obvious, this has had a catastrophic effect on medical research on the whole, and on the field of women’s health in particular.

The consequences are especially clear when it comes to the health of our brains. Because the truth is, women’s brains are not the same as men’s brains. They are hormonally, energetically, and chemically different. While these differences have no deterministic effects on intelligence or behavior and should never be used to reinforce gender stereotypes, they are crucial to supporting brain health, *especially* after menopause. For some statistics most people aren’t familiar with, women are:

- Twice as likely as men to be diagnosed with an anxiety disorder or depression.
- Twice as likely to develop Alzheimer’s disease.
- Three times more likely to develop an autoimmune disorder, including those that attack the brain, such as multiple sclerosis.
- Four times more likely to suffer from headaches and migraines.
- More likely to develop brain tumors such as meningiomas.
- More likely to be killed by a stroke.

Notably, the prevalence of these brain conditions changes from broadly equal between men and women *before* menopause to a 2:1 or higher female-to-male ratio *after* menopause. As for the impact of this change, a woman in her fifties is twice as likely to develop anxiety, depression, or even dementia in the course of her lifetime as she is to develop breast cancer. Yet breast cancer is clearly recognized as a women’s health issue (as it should be), while *none of the brain conditions above are*. And since breast cancer fits within the “bikini medicine” framework, research and resources have been appropriately devoted to

curing it, while hardly any effort has been directed toward menopause care for brain health.

Let's be clear that menopause is not a disease and doesn't *cause* any of the mentioned illnesses. However, the underlying hormonal changes can put a targeted strain on many organs, including the brain, especially when ignored or left unattended. For most women, this can lead to various well-known symptoms such as hot flashes and insomnia. For others, menopause can potentially trigger severe depression, anxiety, or even migraines. For others still, it might be a higher risk of developing dementia down the line. So while the notions of hysteria and womb suffocation were made up, these risks are real. They call for a clear, urgent response: comprehensive research and effective strategies necessary to address the impact of menopause on the brain. Not only do we need help minimizing those initial symptoms, but it's time to accelerate our understanding to prevent the development of more severe issues in the future. Women's medicine must raise its sights—not only beyond the bikini but beyond reproduction as a sole goal. It's time to take an honest and rigorous look at what's happening in women's bodies and brains as a whole, and to fully acknowledge the systemic impact of menopause in the mix.

OUR BODIES, OUR BRAINS

Thus far, we have been looking at the effects of scientific knowledge (and ignorance) at systemic and cultural altitudes. Historically, women have been nothing short of tortured, both physically and psychologically, in the name of menopause. We've been made to believe that menopause can render a woman medically insane, while women of menopausal age and beyond have been rendered invisible in society. This is dangerous, as culture has a powerful effect on how we understand and experience menopause itself—and Western culture has conditioned us to see the symptoms surrounding it as the only meaningful aspects of this transition. While things have certainly improved over

time, this trauma has embedded itself into the collective unconscious, influencing not only how a woman is perceived but also how we at times perceive ourselves and our self-worth.

Many women have direct individual experiences with the effects of these frameworks, and not just when going through menopause. Thanks to the one-two punch of bogus beliefs and outdated conventions covered above, our health concerns are routinely downplayed or dismissed. In cardiac care and pain management, for example, it's now a well-documented phenomenon that female patients are much more likely than male patients to be sent home and not treated at all, resulting in poorer outcomes. How does this play out? When they are in pain, women are more likely than men to be told their pain is psychosomatic, hypochondriacal, or stress-related. This sounds like the nineteenth century, but it's happening right now, all too often culminating in a prescription for antidepressants or psychotherapy rather than targeted care.

Given these tendencies, I'm sure you can imagine (or recall) the response to any issues related to menopause being treated as fabricated or unimportant. More broadly, healthcare professionals have often engaged in a disheartening form of medical gaslighting, where they have historically downplayed women's health issues as a whole, and specifically neglected women's concerns around their mental health. As patients, we can therefore grow accustomed to downplaying our own symptoms in turn, for fear of appearing silly or oversensitive or even to avoid being patronized. Unfortunately, brushing off a woman's symptoms can lead to delays in diagnosis and treatment, potentially costing us our quality of life and, if we're unlucky, worse.

As women, we've been taught to fear our hormones and doubt our brains. Women's brain health remains to this day one of the most under-researched, underdiagnosed and undertreated fields of medicine. Not to mention underfunded. Women in menopause in particular have been underrepresented and underserved not only in medicine, but also in culture and media. This is seriously overdue for

a change—one that I hope science will help bring forth, this time to *support* women instead of harming them.

In this chapter, we address the persistent issue of gender bias in medicine, particularly the exclusion of women, and the inadequate representation of various demographics within the existing research. The glaring neglect of menopausal women in scientific studies is further exacerbated by the insufficient inclusion of women of color, individuals from diverse socioeconomic backgrounds, and those with differing gender identities, among other important factors. This lack of representation is detrimental to us all. Just as it is fundamentally flawed to consider women and men as medically identical, it is erroneous to assume that all women share the same access to well-informed doctors, fitness centers, or nutritious food options. The disparities in access and resources can lead to negative outcomes for brain health, which may in turn affect the experience of menopause. Despite the significance of these considerations, there is a surprising absence of research examining how these factors play out in real-life situations. In an ideal world, accurate information and effortless access to necessary resources and specialists would be available for optimal care throughout our lives. However, given that our world is far from perfect, this book aims to bridge some of these gaps and tackle potential challenges specifically related to menopause. As a scientist, I strive to ensure that my own research addresses these concerns and actively advocate that other investigators adopt a similar approach and interest. By addressing these disparities, we hope to foster a more inclusive and comprehensive understanding of the neuroscience of menopause for all.

In this spirit, I'd like to remind everyone that the field of women's health advances as women's rights evolve. Generations of women have fought for us to have access to healthcare, to be included in clinical trials, to benefit from higher education, and to be acknowledged as lauded contributors in society. Nonetheless, we still strain under the yoke of income, power, representation, and healthcare gaps. It's time to take down the last taboos regarding our bodies *and* our brains and,

in doing so, create a culture of understanding, acceptance, and support around menopause. While the work of overcoming the stigma does not fall upon women alone, speaking out loud in our collective voice has the power to yield significant impact. This is a legacy we could be proud to pass onto our daughters and granddaughters, lightening the load for generations to come.

3

The Change Nobody Prepared You For

WHAT IS MENOPAUSE?

After years of discussing menopause with patients, healthcare providers, and the media, I realized there's a great deal of confusion and *misinformation* about menopause. Two things can help bring clarity and reduce worry: (1) clarifying what menopause is and isn't, and (2) separating fact from fiction. Our ideas arrive to us and are transmitted through language. So let's start by looking at terminology, not necessarily as it is commonly used in conversation but rather the way it is used in clinical practice. The most important concepts are summarized in table 1 and described below.

• • •

Table 1. Glossary: What You Need to Know About Menopause

TERMINOLOGY	MEANING
Premenopause, or reproductive stage	The whole reproductive period before the menopause transition.
Menopause transition	The period before menopause when the timing of the menstrual cycle wobbles and the hormonal and clinical symptoms of menopause begin.
Menopause	The ending of the menstrual cycle. Clinically speaking, the menopause transition is complete after twelve consecutive months since the final menstrual period. There are different ways menopause can occur: it can be spontaneous or induced (see below). All women go through one or the other.
Perimenopause	A phase that starts toward the end of the menopausal transition and continues into the first year after the final menstruation period. You've exited perimenopause and begun menopause once you've had twelve consecutive months without a period.
Postmenopause	The stage starting twelve months after the final menstrual period.
Spontaneous, or "natural" menopause	Menstruation stops when the ovaries run out of egg cells and the production of estrogen and progesterone declines, as part of the aging process. The vast majority of women worldwide will enter menopause aged forty-nine to fifty-two years. Age can differ based on geographical location and ethnic background.
Early or premature menopause	Menopause occurring before age forty (premature) or forty-five (early). It can occur as a result of: ■ Genetic factors ■ Polycystic ovary syndrome (PCOS) ■ Autoimmune disease ■ Infections ■ Surgery ■ Medical treatment
Induced menopause	Menstruation ends due to the surgical removal of the ovaries (<i>oophorectomy</i>) or the lapsing of ovarian function due to medical procedures such as chemotherapy or radiation.

(continued)

TERMINOLOGY	MEANING
Surgical menopause	Menopause provoked by surgical procedures. It can occur at any age as a result of: ■ Bilateral oophorectomy: both ovaries are removed. ■ Bilateral salpingo-oophorectomy (BSO): both ovaries and fallopian tubes are removed. ■ Total hysterectomy: the uterus, cervix, ovaries, and fallopian tubes are removed. ■ Note that a partial hysterectomy (removal of the uterus but not the ovaries), ovarian cyst removal, or endometrial ablation does not cause menopause but can affect blood flow to the ovaries, prompting menopausal symptoms at an earlier age.
Medical menopause	Menopause provoked by medical treatments that cause temporary or permanent damage to the ovaries. It can occur at any age, often as a result of: ■ Radiation or chemotherapy ■ Estrogen blockers (tamoxifen): medications that block estrogen's action in specific tissues ■ Aromatase inhibitors: medications that stop estrogen production throughout the body ■ GnRH agonists: medications that keep the ovaries from making estrogen and progesterone, thus stopping ovulation

In medical terms, menopause is the one-year anniversary of your *final menstrual period* (FMP). Long story short, it is confirmed only once you have missed your period for a year or more, which means a yearlong waiting game is required before you can deem your final period genuinely *final*. Then, and only then, are you officially postmenopausal.

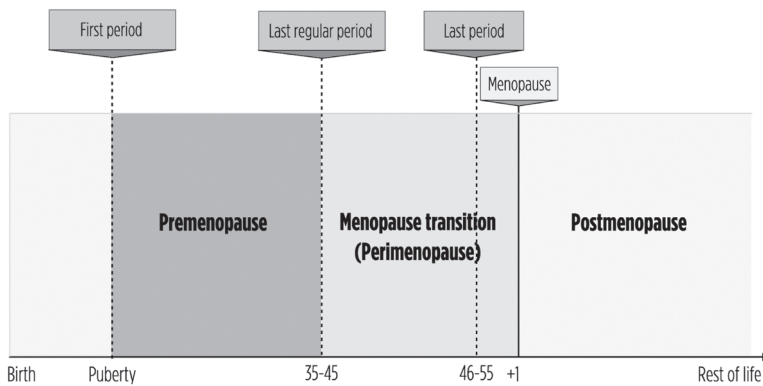
While this makes sense from a clinical perspective, this framework can be quite confusing in real life, and for good reason. This description of menopause implies that one will experience a singular moment that starts on a specific day, much like menstruation did some decades prior. You'd think that one day you suddenly stop having your period, and that's that. Many women who have gone through menopause might utter a wry chuckle at this, knowing better. In actuality, menopause is not a day that arrives but a dynamic and sometimes lengthy

process that can span many years. It is also a time during which whatever your previous sense of normalcy has been, it's now in a state of flux and change.

How Menopause Unfolds: Ages and Stages

The complexity of the menopause transition is just starting to be formalized in medical textbooks, some of which now describe menopause as coming in several phases. In more succinct terms, we are looking at three main stages: premenopause, perimenopause, and postmenopause.

Figure 2. The Three Stages of Menopause



As shown in figure 2:

► PREMENOPAUSE

As long as you have a regular cycle, you are in the “reproductive” or premenopausal stage. It starts with puberty and ends as the menopause transition begins.

► PERIMENOPAUSE

Once your period starts becoming irregular, you’re entering the menopause transition, which is often called perimenopause. At first, your

period might go a little wonky. It might show up early or late, be longer or shorter, get more or less painful, or be heavier or lighter. In other words, it won't be consistent—everything is up for grabs. And then at some point it won't show up at all for two months or more. At this time, symptoms like hot flashes, as well as possible shifts in sleep quality, mood, and cognition are more likely to flare up, and even the bravest among us may feel they've stayed too long at the fair. The average age that perimenopause starts is forty-seven years, but it varies depending on ethnicity, genetics, and lifestyle factors. The transition usually lasts four to eight years, but can be as long as fourteen years.

► POSTMENOPAUSE

A full year after your final menstrual period, you are considered postmenopausal. However, let's say you don't have a period for a year, and then, boom, you suddenly have a surprise one—the clock resets, and you are once again in perimenopause! Back at square one, you will again work toward the postmenopausal stage. Importantly, symptoms typically start to recede or disappear a few years after the final menstrual period, though this is not always the case. Most women experience menopause between age forty and fifty-eight, and the average age at menopause is fifty-one to fifty-two. However, the exact timing varies widely from person to person. Additionally, this map applies only to women undergoing *spontaneous* menopause, which occurs when menstruation stops in midlife as a result of the endocrine aging process. Many women experience menopause at younger ages and for different reasons.

► EARLY OR PREMATURE MENOPAUSE

Some women develop menopause before age forty-five (early menopause) or even before age forty (premature menopause). About 1 to 3 percent of women who experience early or premature menopause do so due to the ovaries producing low levels of reproductive hormones, a condition known as primary ovarian insufficiency (POI). Other women experience menopause prematurely or early because of

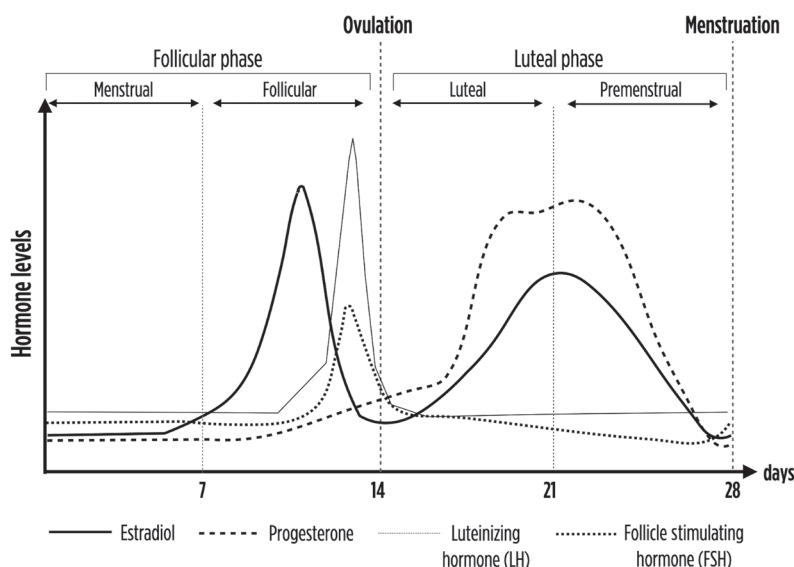
autoimmune or metabolic disease, infection, or a genetic cause. However, the most common causes of premature or early menopause are surgery and some medical treatments. In this case, menopause is called *induced*, and differs from spontaneous menopause in many ways.

► INDUCED MENOPAUSE

Many women undergo induced menopause, which is when ovulation ends due to either the surgical removal of the ovaries (*oophorectomy*) or the lapsing of ovarian function due to medical procedures such as chemotherapy or radiation. Women who have their ovaries surgically removed while still having a menstrual cycle will find themselves in menopause soon after the intervention. Women whose ovaries stop working for other medical reasons can also develop menopause earlier in life. This is referred to as medical menopause. Surgical menopause may come on very quickly, whereas medical menopause can happen over a time frame of weeks or months. It's important to note that a *partial*, or simple, *hysterectomy*, where the uterus is removed but the ovaries are left in place, will stop menstruation but not ovulation. As such, it will not prompt early menopause. However, hormonal production may decrease, and blood flow to the ovaries may be reduced, too. This may prompt the symptoms of menopause earlier than expected.

How Does Menopause Happen?

To fully appreciate what our bodies experience during menopause, we first need to clarify how hormones function before menopause. During our reproductive years, an intricate dance of hormonal feedback loops occurs approximately every 28 days. The main sex hormones involved are estrogen (the technical term is *estradiol*), progesterone, follicle-stimulating hormone (FSH), and luteinizing hormone (LH). As you can see in figure 3, they rise and drop at varied points during the menstrual cycle, spanning from the first day of your period through the day before your next period.

Figure 3. Sex Hormones During the Menstrual Cycle

The first half of the menstrual cycle is called the *follicular phase*. At this time, the hormones FSH and LH rise to stimulate the growth of several *follicles*, each containing an egg cell from the ovaries. As the follicles grow, estrogen prompts the growth of the uterine lining to provide the egg with the support it needs to host a baby. Once estrogen levels are sufficiently high, a surge in LH causes the so-called dominant follicle to burst and release the mature egg into the fallopian tube. This process is known as *ovulation*, which occurs mid-cycle. That's when pregnancy is most likely to occur.

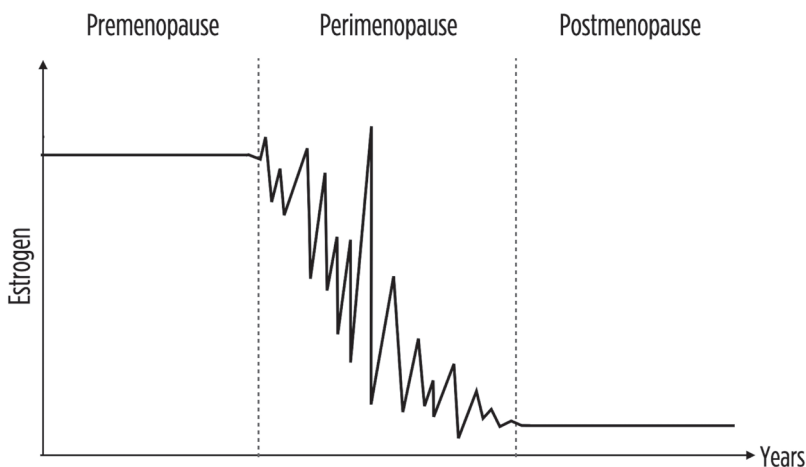
The second half of the cycle is called the *luteinizing phase*. If pregnancy has occurred, estrogen and progesterone remain high to prevent the womb's lining from being shed so the placenta can develop. If pregnancy has not occurred, these hormone levels drop instead, prompting the uterus to shed its lining, cuing menstruation.

Although the menstrual cycle is relatively complex, all generally goes to plan as long as these hormones are on the same page, supporting and regulating one another in harmony. That is, until a major event occurs to disrupt this fine-tuned balance: the arrival of menopause.

When a woman is transitioning toward menopause, her ovaries run out of eggs and start producing less estrogen. However, this isn't a linear or steady process, as estrogen doesn't give up so easily.

As you can see in figure 4, estrogen's concentration doesn't drop all at once but can fluctuate wildly as it declines. While not all women exhibit these changes, the "before menopause" part of the graph looks broadly flat. That's because estrogen concentration remains consistent thanks to its levels rising and falling at a regular rhythm with the menstrual cycle. The "after menopause" graph is also virtually flat, as estrogen levels are steadily low at this stage. But the "during" graph looks like the output of a seismograph during an earthquake. As the length and frequency of the menstrual cycle become increasingly irregular during the menopause transition, estrogen's dramatic peaks and valleys make its concentration fluctuate just as widely. Estrogen is not the only hormone that's having ups and downs. As the feedback loops that were so carefully regulating all sex hormones go out of synch, progesterone eventually bottoms out, while FSH and LH increase instead. This hormonal roller coaster can create or contribute to the seemingly random and often unpredictable physical and psychological repercussions many women experience during menopause.

Figure 4. Estrogen Concentration Before, During, and After the Menopause Transition



So now we're looking at two ways that the clinical framework for menopause can make the whole process confusing. First off, menopause doesn't happen overnight. Second, while all women experience menopause, every woman's experience is different. Each of us has a unique hormonal fingerprint, a unique reproductive system, and a unique brain. While this individuality has yet to be formalized in medicine, it's clear that both the timeline and the symptoms of menopause can vary greatly from person to person. All of this has led not only to lack of clarity among patients, but also to some widespread inaccuracies around menopause itself, which we'll now proceed to debunk.

MENOPAUSE FAQs

Is menopause an illness or a disease?

Menopause is a physiological stage of life. While the symptoms may not feel normal and the actual challenges surrounding it can feel anything but ordinary, menopause is not an illness, a disease, or a pathological condition. It is a transition. It doesn't need curing or fixing. It does need addressing and managing, if necessary.

Does menopause happen when you're old?

Most women develop menopause in their forties and fifties. On average, menopause occurs around age fifty-one to fifty-two, which is not old by any standards. Besides, recent studies indicate that the actual average age of menopause across the globe is forty-nine, so even earlier. As mentioned already, the exact timing also varies widely from person to person, spanning from the late thirties to the early sixties.

Are blood tests necessary to diagnose menopause?

Since periods become less frequent during the menopause transition and one gets more used to missing them, it may be

hard to know when they've stopped for good, leaving many women wondering if they're in menopause or not. I am often asked if there's a simple hormone test that can tell if you're nearing menopause or are already past it. The answer is no. Blood tests can be helpful but are not necessary to diagnose menopause. If you suspect that you're in perimenopause or want to know if you're past menopause, the best thing to do is to have a complete medical examination by a qualified health-care professional. The diagnosis is based on age, medical history, symptoms, and period frequency. Blood work can be used as supportive information, but more often than not, it isn't needed.

Generally speaking, hormone tests are unnecessary to tell if a forty-seven-year-old woman with irregular periods is in perimenopause (most likely she is), or if a fifty-eight-year-old woman with no period for years is postmenopausal (most likely she is). Testing is instead recommended to evaluate fertility problems or when periods stop at an early age, as with POI. Another reason to test is for polycystic ovary syndrome (PCOS), a hormonal condition that can impact menstrual regularity and fertility. Labs may also help determine menopausal status for women who no longer have a period due to medical interventions. These include a partial hysterectomy (the surgical removal of the uterus but not the ovaries) or an endometrial ablation (a procedure that removes the lining of the uterus). These procedures stop your menstrual period but don't stop ovulation. In this case, the occurrence of menopausal symptoms is the first indication of menopause, with blood work providing supporting evidence. In such cases, the levels of estrogen and other hormones, chiefly FSH and another hormone called inhibin B, are measured. Inhibin B regulates FSH production, and it can serve as a marker for ovarian function and follicular content. Normative values are in table 2. When estrogen and inhibin B are low, FSH is high, and a woman has not had a menstrual period for a year, it is

generally accepted that she has reached menopause. However, a single lab test can be tricky because these hormones may be lower today and higher tomorrow. Their range is quite wide, too. Additionally, a high FSH level in a woman who is having hot flashes and is missing her period does not eliminate the likelihood that she is still in perimenopause. Blood tests are particularly tricky for women in perimenopause, since the hormone levels change throughout the cycle, and the cycle is now irregular, which only increases the variability. In addition, contrary to popular belief, estrogen levels fluctuate widely in perimenopause, sometimes ending up being *higher* than expected rather than lower. Also keep in mind that hormonal contraception such as the pill and some IUDs can stop menstruation and affect the accuracy of the FSH test, making it difficult to determine whether one is past menopause or not.

Table 2. Laboratory Tests for Menopause: Reference Ranges

	PREMENOPAUSE			POSTMENOPAUSE
	Follicular phase	Ovulation	Luteal phase	
Estradiol (pg/ml)	12.4–233	41–398	22.3–341	<138
Progesterone (ng/ml)	0.06–0.89	0.12–12	1.83–23.9	<0.05–0.13
LH (mIU/ml)	2.4–12.6	14–95.6	1–11.4	7.7–58.5
FSH (mIU/ml)	3.5–12.5	4.7–21.5	1.7–7.7	25.8–134.8
Inhibin B (pg/ml)	10–200			<5

Can blood tests predict when you’ll go through menopause?

Blood tests cannot predict when you’ll go through menopause. When it comes to menopause, there’s only one given: at some point, your ovaries will run out of follicles, and you

will go through it. Everything else is like that randomly appearing repair person—a bit hard to anticipate. So no, there is no surefire way to predict when you will go through menopause, and certainly not by using blood tests. Rather, your best indicator is . . . your mother. If your mother reached menopause early, late, or somewhere in between, you could eye your calendar with some degree of confidence. The experience and symptoms of menopause are also somewhat similar between mother and daughter, so it is helpful to have this conversation sooner rather than later. Another great indicator of what your menopause will be like, however, is you. The way you experienced puberty and, later on, pregnancy if you have been pregnant, can offer important insights into your menopause journey. We will explore this concept in part 2, but for now consider this: if you experienced mood swings, irritability, or changes in emotional state during puberty, and more so during pregnancy or postpartum, there's a higher chance that you may experience mood disturbances during menopause, too. Similarly, if you experienced hot flashes, sleep difficulties, or brain fog with these reproductive milestones, there is a higher likelihood of encountering them again during the transition to menopause. That said, your experience of menopause is influenced and can be changed by many other factors such as your lifestyle, environment, medical history, and cultural beliefs.

Are blood tests necessary to decide whether hormone replacement therapy (HRT) is indicated?

Blood tests are unnecessary for those aiming to use hormones for symptom relief. This is because we are not treating hormone levels. We are treating the symptoms of menopause, which do not correlate with hormone levels. You may have symptoms even if your hormones are within normal range, and you may have very low estrogen and no symptoms.

Are saliva and urine tests as good as blood tests?

A blood test is the only accurate test for hormonal levels. Saliva and urine tests are often offered to evaluate reproductive hormones but are less precise than blood tests and are not recommended in clinical practice. The well-known DUTCH test (Dried Urine Test for Comprehensive Hormones) is also less reliable than a blood test.

Can HRT be used before menopause?

HRT can be used both before and after menopause. HRT before menopause is typically prescribed to address specific conditions such as POI and other medical indications. Unfortunately, among women without these indications, healthcare providers tend to prescribe HRT only after menopause has occurred, rather than during the perimenopausal phase. From a scientific perspective, HRT was developed to be used in presence of active symptoms, which can be more frequent and disruptive before menopause than after. The decision to use HRT, its timing, and duration should be based on each patient's individual circumstances and needs.

Are there different types of menopause?

There are different types of menopause, chiefly spontaneous and induced menopause, which occur for different causes such as surgery, radiation, or chemotherapy. They are summarized in table 1.

Is it safe to have the ovaries removed?

Oophorectomies are often performed as part of a hysterectomy (when the uterus is removed), the second most common major surgery performed on women in the United States, with only the C-section topping it. Oophorectomy is a first-line treatment for ovarian cancer. Ovarian cancer still kills 14,700

women every year in the United States alone. Removing the ovaries along with the fallopian tubes by means of a procedure called bilateral salpingo-oophorectomy (BSO) is of established clinical benefit when ovarian cancer is found or suspected. It can also be done preventatively in women with a family history of ovarian cancer or proven genetic predisposition, such as specific BRCA gene mutations, and those with medical conditions known as Lynch syndrome and Peutz-Jeghers syndrome. We'll talk more about this in chapter 11.

For now, it's helpful to note that roughly 90 percent of all hysterectomies, which often include the ovaries, are performed for reasons other than cancer. These "benign" conditions include endometriosis, fibroids, benign tumors, cysts, ovarian torsion (the twisting of an ovary), and tubo-ovarian abscess (a pus-filled pocket involving a fallopian tube and an ovary). In such cases, whenever possible, it is common practice to conserve the ovaries during a hysterectomy in women who have normal functioning ovaries. This is because, while oophorectomy is a low-risk procedure, it inevitably results in induced menopause. Therefore, it is a delicate intervention with potential long-term health risks, requiring counseling and a thorough weighing of risks and benefits. In addition, there is accumulating evidence that ovarian cancer may originate in the fallopian tubes, and removing the tubes without the ovaries has been shown to substantially reduce that risk without prompting menopause. Current guidelines for ovarian conservation are summarized in table 3.

There is also some confusion on whether preventative oophorectomies are beneficial to postmenopausal women. While this is a subject of debate, the ovaries continue to make small amounts of estrogen for years after menopause. The ovaries also continue to make two other hormones, testosterone and androstenedione. Muscle and fat cells convert testosterone and androstenedione into more estrogen. Some studies

indicate that for women without contraindications, ovarian preservation after menopause might still lower the risk of osteoporosis, heart disease and stroke later in life. As a result, current guidelines recommend ovarian conservation for postmenopausal women with no genetic or additional risks who are undergoing hysterectomy for benign reasons (see table 3).

Despite these revised guidelines, over half of all American women undergoing hysterectomies for these benign reasons still have their ovaries removed along with their uterus. Twenty-three percent of American women aged forty to forty-four and 45 percent of those aged forty-five to forty-nine are still counseled to undergo elective BSO at the time of hysterectomy for a benign (noncancerous) condition.

So if you ever find yourself in a situation where you need to have the uterus removed and the surgeon is suggesting that your ovaries be removed, too, but you don't have ovarian cancer or a genetic predisposition, make sure you discuss the pros and cons of this procedure, considering all aspects of your medical and family history, and clarify why they are recommending it. Keep in mind that there are situations where oophorectomy is indicated even in absence of cancer or cancer risk, and other situations where ovarian conservation is more appropriate.

To be absolutely clear, nobody is telling patients to decline necessary treatment. The point is that oftentimes the possible risks resulting from these surgeries are not made sufficiently clear to patients. "I wish I had known" is something I've heard way too many times. It's important to understand what these procedures involve, both in the short and long term, and what treatment options are available, so that each and every woman can make an informed choice for herself and her own health.

Table 3. Bilateral Salpingo-Oophorectomy (BSO): Current Guidelines

Indications for BSO	Suspected or confirmed gynecological malignancy
	Risk reduction surgery (BRCA1 and BRCA2 gene mutations, Lynch syndrome, Peutz-Jeghers syndrome, and a strong family history of ovarian cancer) only after completion of childbearing and over the age of thirty-five
Other indications for BSO	Chronic pelvic pain
	Pelvic inflammatory disease
	Severe endometriosis
Considerations for ovarian preservation	Premenopausal women without genetic predisposition to cancer
	Women with no significant family history of ovarian cancer
	Women with no adnexal pelvic pathology (a lump in tissue near the uterus, usually in the ovary or fallopian tube)
	Postmenopausal women with no additional risk factors

Does menopause affect a woman only physically?

Most certainly not. Menopause is a mind-body experience. When hormones change, we change too. Menopause isn't just a reproductive phenomenon; it impacts a woman's thoughts, feelings, self-image, and behavior. In the next chapter, we'll clarify how many of the symptoms of menopause are in fact a reaction to the brain's own menopausal journey.