

The American Institute of Stress

# CONTENTMENT

*Connecting the Relationship Between Stress, Health and Longevity*

**Volume 12 Number 3**

**Fall 2023**

## Connecting Stress with the Immune System



*Inside: The Immune System-Stress Connection – Use It to Thrive!*, By Cynthia Ackrill • *The Stress-Cancer Connection*, By Brandon LaGreca  
• *Connecting Gut Microbiota, Stress and the Immune System*, By Stephanie Maxine Ross • *Guided Imagery: An Evidence-Based Approach for Cancer Immune Function – Exploring the Potential of the Infinite Holistic Image Model*, By Marcia Uddoh



The mission of the nonprofit American Institute of Stress is to improve the health of our community and the world by setting the standard of excellence of stress management in education, research, clinical care and the workplace. Diverse and inclusive, AIS educates healthcare practitioners, scientists, and the public. AIS is the only Institute in America solely dedicated to providing information, training and techniques to prevent and reverse human disorders related to stress, and to improve the quality of life and increase longevity through building resilience to stress. Credentialed AIS members provide leadership to the world on stress related topics.

Your source for science-based stress management information

# CONTENTMENT

We value opinions of our readers.

*Contentment* is a quarterly magazine published in Spring, Summer, Fall and Winter with news and advertising designed with the general public in mind. It appeals to all those interested in the myriad and complex interrelationships between stress and health because technical jargon is avoided and it is easy to understand. *Contentment* magazine is indexed by EBSCO and archived online at [stress.org](http://stress.org). Information in this publication is carefully compiled to ensure accuracy.

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# BODY ELECTRIC

## Electroceuticals and the Future of Medicine

A documentary film to revolutionize the way we think about health and the human body.

The American Institute of Stress is an executive producer of Body Electric: Electroceuticals and the Future of Medicine, a documentary film aimed to revolutionize the way we think about health and the human body. This 68 minute movie, by British producer/director/writer Justin Smith, is available online and on DVD for purchase through AIS.



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# IF YOU'RE LOOKING FOR ANSWERS, YOU HAVE TO ASK THE RIGHT QUESTIONS.

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started

For so many Americans, “mysterious” problems ranging from mild to severe are caused by that scourge of modern life – stress. That realization is the first step toward healing, but it often raises many more questions that must be addressed. How is stress affecting my life? My relationships? My work? My happiness? What can I do to reduce or better cope with it? Our Stress Mastery Questionnaire – an easy and confidential online self-assessment that comes with our Stress Mastery Guide and Workbook – can help you find answers. And life-changing solutions.



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# Editor's Message

Stephanie Ross, PhD, MHD, HT, CNC, FAIS  
Editor



If you want to avoid stress, you've been born in the wrong era. Chronic stress has become epidemic in our society and creates chronic havoc on your body, including the immune system. In fact, according to one meta-analysis involving 300 studies, researchers found that chronic stress can actually damage your immune system.

How does stress get “under the skin” to influence immunity? Immune cells have receptor sites for neurotransmitters and hormones such as norepinephrine, epinephrine, and cortisol, which function to mobilize and transport immune cells, preparing the body to initiate an immune response if needed. Recent research shows that immune cells (e.g., lymphocytes) change their responsiveness to these neurotransmitters and hormones during stress. Immunological responses are biologically and energetically costly, and over time, chronic stress produces negative systemic changes both in immune trafficking and in target tissues.

The connection between stress and immune function may be mediated by specific health behaviors, psychosocial factors, or both. As an example, stress

has been linked to neuro-nutrient deficiencies, microbial and mitochondrial imbalances, poor sleep, and loneliness, which have each in turn been linked to increases in pro-inflammatory responses to stress.

Psychological stress has been connected to altered immune functioning

in many diseases. Stress induces chronic immune activation and altered health outcomes that resemble those seen in chronic inflammatory diseases such as rheumatoid arthritis (RA). Changes in immune function can lead to exacerbated symptoms of both physical and psychological illnesses. In irritable bowel syndrome, sustained cortisol activity during stress is associated with an increase in gastrointestinal symptoms and intestinal permeability. High levels of proinflammatory cytokines resulting from stress have been

implicated in schizophrenia. In addition, chronic stress has been shown to enhance risk for developing autoimmune disease. More recently, research has shown that immune system cell (gamma delta T-cells) changes in the gut are linked to stress-induced depression.

Finally, research into the effects of stress on inflammation in clinical

**The connection between stress and immune function may be mediated by specific health behaviors, psychosocial factors, or both.**

populations has demonstrated that stress exposure can increase the likelihood of developing disease, as well as exacerbating preexisting conditions. It is estimated that 95% of all illness is caused or worsened by stress. This fact serves as motivation for making positive lifestyle change that help to reduce stress, restore calm and renew quality of life.

The Fall issue of *Contentment* magazine focuses on the connection between stress and the immune system and offers outstanding contributions by the following contributing authors.

**Cynthia Ackrill, MD, PCC, FAIS** is a leader in the field of leveraging stress for optimal productivity, health, and happiness. With a background in primary care and advanced training in applied neuroscience, certification in wellness and leadership coaching, she combines the science of human performance with wisdom, humor, and heart to address the critical relationships between thinking styles, behavior choices, performance capacities, leadership effectiveness, health, joy, and deep career/life satisfaction. She served as editor of the American Institute of Stress *Contentment* magazine, is on the faculty of multiple leadership/coaching programs, and contributes widely to the media, including Katie Couric, CNN, Today Show and Huffington Post.

In her feature article, “The Immune System-Stress Connection – Use It to Thrive!” Dr. Ackrill reminds us to pay attention to the wisdom of the whole, the importance of connection,

communication, and the coordination of all systems, including the social systems and environment, to embrace the impressive powers our incredible minds and bodies to prevent disease, self-heal, and orient to health.

**Brandon LaGreca, LAc, MAcOM**, is a licensed acupuncturist in the state of Wisconsin and nationally certified in the practice of Oriental medicine. In 2015, Brandon was diagnosed with stage 4 non-Hodgkin’s lymphoma. He achieved full remission eight months later by following an integrative medicine protocol that included immunotherapy without the use of chemotherapy, radiation, or surgery. Brandon is a thought leader in the synthesis of traditional and functional medicine, having written numerous articles on the subject. He is the author of “*Cancer and EMF Radiation: How to Protect Yourself From the Silent Carcinogen of Electropollution*,” and “*Cancer, Stress & Mindset: Focusing the Mind to Empower Healing and Resilience*,” He shares his thoughts at Empowered Patient [Blog.com](http://Blog.com).

In his article, Brandon LaGreca, LAc, MAcOM puts forth an important question regarding the connection between cancer and stress, “does stress cause or promote cancer, and if so, can the stress response be influenced to prevent or help treat malignancy? He then proceeds to answer these questions by reviewing the science placed within the context of the many factors that contribute to cancer formation.

**Stephanie Maxine Ross PhD, MHD, HT, CNC, FAIS** is an internationally

recognized leader in Integrative Health. She served as the Founding Director of the Department of Complementary and Integrative Health at Drexel University, a pioneering program that partnered with the Andrew Weil Center for Integrative Medicine.

In her article, “Connecting the Gut Microbiota, Stress and the Immune System,” Dr. Ross details the importance of gut microbiota and its role in both health and disease, and highlights its involvement in metabolism, physiology, nutrition, and immune function. She provides an overview of the early life stages of microbiota development where the establishment of a healthy gut microbiota is believed to have profound consequences on the future well-being of the individual.

**Marcia Uddoh, MD (candidate), PhD, MPH, MS, MSW, FAIS** is a pioneer in stress research and management, specializing in neurology and cognition. Grounded in Christian ethics but welcoming individuals of all faiths, she is a graduate of Dr. Andrew Weil’s esteemed integrative health research internship program at the University of Arizona School of Medicine. Dr. Uddoh has dedicated her career to holistic approaches to stress management.

As the founder of Stress Vitals Institute LLC, she has developed innovative, evidence-based stress assessments and interventions. These are delivered through cutting-edge methods like visualization and heart rate variability (HRV), aiming to empower individuals, especially in low-income communities.

In her article, “Guided Imagery: An Evidence-Based Approach for Cancer Immune Function - Exploring the Potential of the Infinite Holistic Image Model,” Dr. Uddoh captures the benefits attributed to guided imagery for cancer patients and emphasizes the importance of considering the underlying disease process, which provides a better understanding of the mechanics and scientific basis of the process that is crucial to explore guided imagery, and the mechanism of the disease process. Dr. Uddoh details a conceptual model that would offer a more comprehensive overview of the entire narrative.

In closing, it is my hope and prayer that each of us find the strength, resilience and endurance to prevail during these most difficult times. Fill your hearts with love and appreciation for those who surround you, find courage in faith, and channel the worries, stress, and anxiety of uncertainty by being of service to others!

My best,

*Stephanie*

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# REDUCE YOUR STRESS.

## *Grow your happiness.*

Is stress dragging you down physically and emotionally? The comprehensive, online “Stress to Joy” program, taught by bestselling author and board-certified psychiatrist Rozina Lakhani, MD, MPH, FAIS, gives you the tools you need for a return to joyful living. Dr. Rozina shares her proven stress management techniques in a way that’s both practical and inspirational. The program includes a workbook with step-by-step guidance, and it takes just 15 minutes per day for about three weeks. Make this powerful investment in your health and happiness – and turn the corner from stress to joy.

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STARTED**





# The Immune System- Stress Connection – *Use It to Thrive!*

By Cynthia Ackrill, MD, PCC, FAIS

**M**ost of us grow up and move through our days not really thinking about our immune systems, or for that matter, the miraculous powers of our bodies and minds to repair themselves. We've all cut ourselves shaving or slicing and dicing. Sure, we wash it (the important part!), maybe slap on some antimicrobial goop and a Band-Aid, but that's not what does the healing — our bodies do that part. Almost immediately, a multitude of specialized cells swoop in to stop the bleeding, defend against any foreign substances, create a temporary barrier, and over the next few days build bridges to mesh the sides of the wound back together. It's an impressive orchestration of chemical signaling and cellular activity... until it isn't.

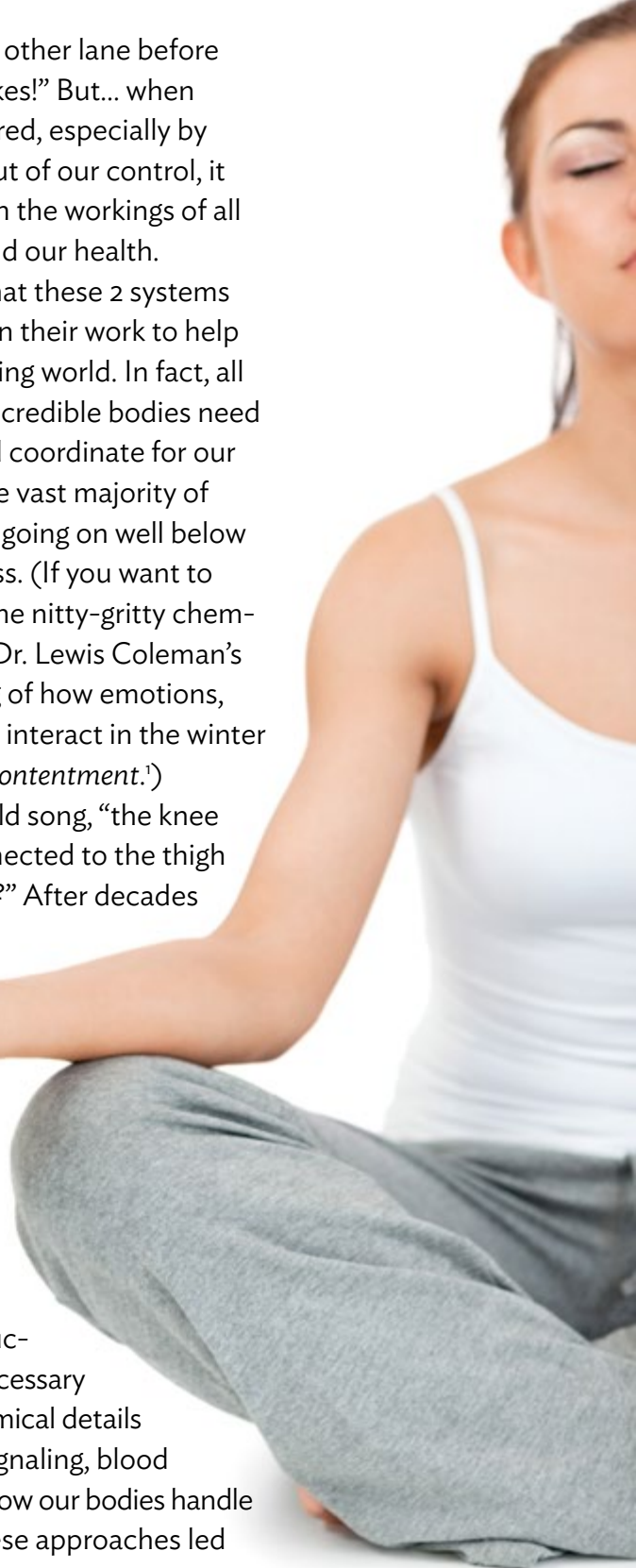
Like our immune system, our stress reaction system is also there to protect us from the dangers of the world. 24/7 the brain stays on high alert, scoping out any possible threats from escaped tigers to cars cutting us off to sneers on our partner's face. At any whiff of danger, the chemical cascade of the sympathetic nervous system is activated to make sure we are "ready" to defend ourselves — our hearts speed up, clotting cells gather, blood is sent to the large muscles of escape, even our senses are made more keen — all to help us fight or flee. This system is perfect for acute danger — we

wind up safely in the other lane before we can even say, "Yikes!" But... when it's chronically triggered, especially by thoughts or things out of our control, it can wreak havoc with the workings of all the other systems and our health.

It makes sense that these 2 systems are communicating in their work to help us survive a challenging world. In fact, all the systems of our incredible bodies need to communicate and coordinate for our well-being — and the vast majority of this full symphony is going on well below our level of awareness. (If you want to understand this on the nitty-gritty chemical level, check out Dr. Lewis Coleman's impressive rendering of how emotions, stress, and immunity interact in the winter 2021-2022 issue of *Contentment*.)

Remember the old song, "the knee bone's connected to the thigh bone...?" After decades

of medical advances, drilling down and separating out the workings of different parts of the body, it's time to reconnect to pieces. These reductionist paths were necessary to figure out the chemical details of things like nerve signaling, blood pressure regulation, how our bodies handle sodium, etc. And these approaches led



to advances in diagnosis and treatments we never thought possible — from cancer treatments to irradiating polio (almost?). But they also made it easy to lose track of several things:


1. The whole: the importance of the connection, communication, and coordination of all the parts and systems, including the social systems and environment. Each system can affect the workings of the others. And...
2. The powers our incredible minds and bodies have to prevent disease, self-heal, and orient to health.

It's time to pay attention to the wisdom of the whole and embrace the impressive powers we have to support our best functioning and overall health. We all know that when we are over-tired, we make more mistakes (our brains misfiring under stress). And we know that when we get run down, we are more prone to catching a cold from someone. On the flip side, when we are sick and our immune systems are working overtime, we don't handle stress as well. Now the science is catching up to our wisdom and giving us solid proof that we can make choices and create thought and behavior habits that help our minds and bodies thrive.

In my early days as a physician, I never really understood why so much of the practice of medicine focused on waiting for something to go wrong (like blood sugar too high) and then “treating” it. I have always been drawn to wanting to know more about how to make it go “right.” I was fascinated by how a person's mental state and attitude influenced their whole experience and often their outcomes.

I also learned (too much of it first-hand) about the interactions of stress and immunity. It's no secret that medical training is stressful. As an intern I was also struggling with infertility. Sadly, in a ‘just

*It's time to pay attention to the wisdom of the whole and embrace the impressive powers we have to support our best functioning and overall health.*

A woman with grey hair tied back is sitting on a light-colored couch. She is looking out a large window to her left, with her hands clasped together in a thoughtful pose. The background is a blurred view of greenery outside. The lighting is soft and natural, coming from the window.

*And we know  
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**I**t's been exciting to see more focus on "wellness" approaches, especially those such as functional medicine that emphasize the interactions of all the human health systems.



buck up' culture, I was shamed for stressing about it. (Can you say, "More stress?") Well, a couple of decades later, we now understand how stress can cause inflammation and how inflammation can interfere with fertility — duh! In fact, my poorly managed stress kept my immune system on overdrive until I am one of the 1 in 10 people dealing with autoimmune disease (a result of the immune system over-working to attack normal cells). And having an autoimmune issue is stressful. I've been forced to figure out the connections and employ all the tools I can to both handle stress more effectively and especially to embrace self-compassion along the way. (Yes, I am one of those people who learns to teach what they needed most!)

Recently, it's been exciting to see more focus on "wellness" approaches, especially those such as functional medicine that emphasize the interactions of all the human health systems. Thanks to Covid, it's also now much safer to openly discuss stress and learn effective ways to create less of it, leverage some of it for good, and learn practices to counter its negative effects. I'm thrilled people are finally realizing

that what we put in our bodies matters — that food can actually turn genes on or off! And, as exciting as this shift is, I also think we need to be very careful — the marketing and profits of the associated \$1.5 trillion (!!!) market can overwhelm or cloud both real science and wisdom.

So, what can you do?

1. Firstly, read *Contentment Magazine* regularly. I say that because yes, it is near and dear to my heart, but also because it's hard to sort out the deluge of information thrown at us daily: news that sensationalizes a tiny study about the "new, next best supplement" to relentless advertisements to the recommendations of well-meaning friends. We need to find resources we can trust to vet for real science. (Of course, there are many others.) Ask your doctor what to trust. Don't take in too much at once.
2. Brainstorm what areas of your life would benefit from some tweaking. Pick one that sounds not too hard to experiment with. Keep a light, compassionate heart as you do this — it's not about getting everything right, it's about slowly shifting to patterns that give you more ease and health.

3. Appreciate your wisdom more. What do you know works for you?
4. Keep an open mind and continue learning — we all need regular inspiration and motivation. Behavior change or creating new habits is not easy. We need regular “attention to our intention” to create new brain pathways to support the thought and behavior patterns we want for our best life. Consider hiring a coach to be on your team.

Humans were literally not designed to go it alone.

5. Build your toolbox of ways to best manage the challenges of life. Then practice them.
6. And don't forget to celebrate every little success... that helps your brain and your immune system do their best work!

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**Cynthia Ackrill** is a leader in the field of leveraging stress for optimal productivity, health, and happiness. With a background in primary care and advanced training in applied neuroscience (a look under the hood!), certification in wellness and leadership coaching, she combines the science of human performance with wisdom, humor, and heart to address the critical relationships between thinking styles, behavior choices, performance capacities, leadership effectiveness, health, joy, and deep career/life satisfaction. She served as editor of the American Institute of Stress Contentment magazine, is on the faculty of multiple leadership/coaching programs, and contributes widely to the media, including Katie Couric, CNN, Today Show and Huffington Post.



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# THE COST OF STRESS.

*The more we learn, the more vital our mission becomes.*

*The American Institute of Stress is the only organization in the world solely created and dedicated to study the science of stress and the advancement of innovative and scientifically based stress management techniques. AIS provides the latest evidence-based knowledge, research and management techniques for stress and stress-related disorders.*

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## Groundbreaking insights and approaches. World-changing mission.

Hans Selye, MD, PhD (1907-1982), is known as the father of stress research. In the 1920s, Selye coined the term “stress” in the context of explaining his pioneering research into



the signs and symptoms of disease curiously common in the majority of people who were ill, regardless of the diagnoses. Selye’s concept of stress was revolutionary then, and it has only grown in significance in the century since he

began his work. Founded in 1978 at Dr. Selye’s request, the American Institute of Stress (AIS) continues his legacy of advancing the understanding of stress and its enormous

impacts on health and well-being worldwide, both on an individual and societal level.

A forthcoming AIS initiative – called

**Engage. Empower. Educate.** – will leverage the latest research, tools and best practices for managing stress to make a difference in a world increasingly impacted by the effects of stress out of control. We hope you will consider supporting this critical outreach campaign.



[Click to view \*The American Institute of Stress Case Statement\*](#)



# A campaign to Engage. Empower. Educate.

The AIS campaign will support three key initiatives:

## Engage communities through public outreach



Improve the health and well-being of our communities and the world by serving as a nonprofit clearinghouse for information on all stress-related subjects.

The American Institute of Stress produces and disseminates a significant amount of evidence-based information, but there is a need to share this material with a wider audience in the U.S. and around the world.

Support for this initiative will provide funding to expand the organization's public outreach for its website and social media, documentary films, magazines, podcasts, blogs and courses.

## Empower professionals through best practices



Establish credentials, best practices, and standards of excellence for stress management and fostering intellectual discovery among scientists, healthcare professionals, medical practitioners and others in related fields.

AIS provides DAIS (Diplomate, AIS) and FAIS (Fellow, AIS) credentials for qualified healthcare professionals.

The AIS seal means a practitioner has training and experience in stress management and access to the latest stress research and techniques. It designates their practices as advanced treatment centers for stress-related illnesses.

Support for this initiative will provide funding to continually update best practices in the field.

## Educate all through the development and dissemination of evidence-based information



Develop and provide information, training and techniques for use in education, research, clinical care and the workplace. Some of the research-based information AIS develops and disseminates includes:

- Productions – *Mismatched: Your Brain Under Stress*, a six-part documentary featuring some of the world's leading experts on stress. Released in March 2021.
- Publications – *Contentment* magazine and *Combat Stress* magazine for service members, veterans and first responders.
- Podcasts, webinars and website resources – The free podcast series *Finding Contentment*



## The American Institute of Stress

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# The Stress- Cancer Connection

By Brandon LaGreca, LAc, MAcOM

**D**oes stress cause or promote cancer, and if so, can the stress response be influenced to prevent or help treat malignancy?

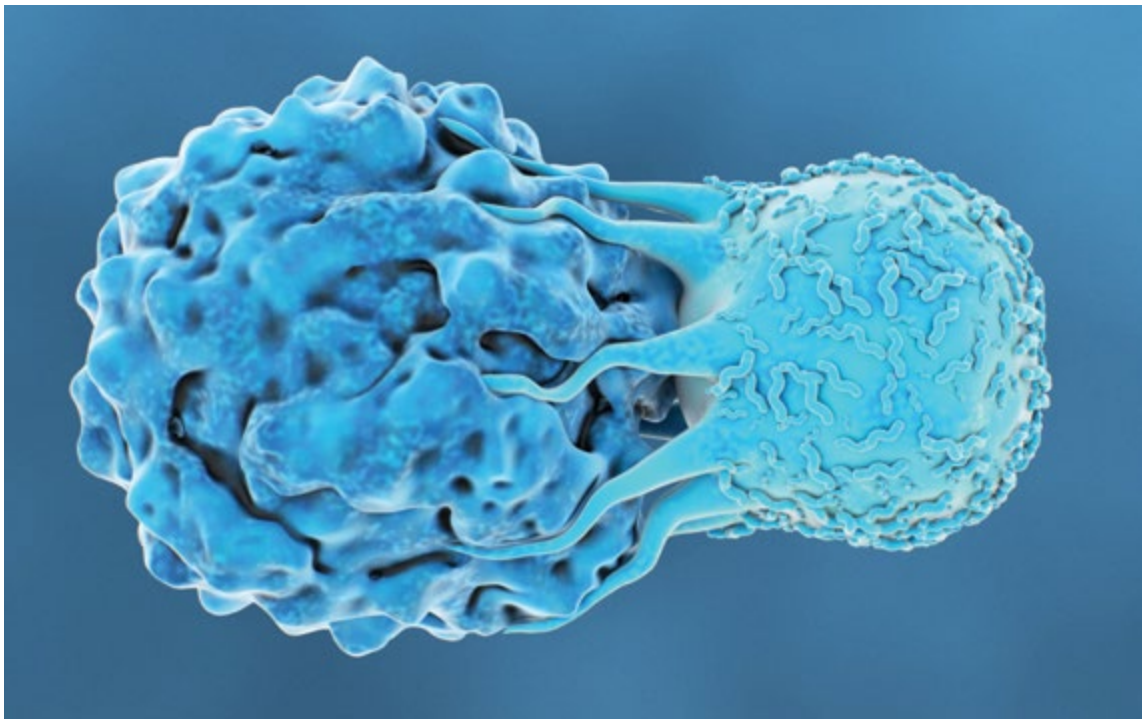
To answer these questions requires a firm grasp of the science placed within the context of the many factors that contribute to cancer formation.

The basic framework of stress physiology elucidates the likely mechanisms of the stress-cancer connection. The earliest indication came from Hans Selye, MD documenting atrophy in the thymus gland in stressed rats. The elevation of glucocorticoids is widely accepted as the dominant mechanism for this effect. Stress also suppresses activity of T lymphocytes and

natural killer cells, culminating in lowered immunity and increased tumor growth and development.<sup>1,2</sup>

Natural killer cells and T lymphocytes are two key players of cell-mediated immunity, the aspect of the immune system that patrols for and removes malignant cells. Of all the immune cell types, natural killer cells appear to be most significantly influenced by psychoneuro-immunology (PNI) factors. In addition, the PNI fallout from psychological stress is acknowledged to affect two additional aspects of carcinogenesis: DNA repair and regulation of apoptosis (programmed, healthy cell death that cancer cells circumnavigate).<sup>3</sup> Although cancer formation falls squarely on exposure to carcinogens, a suppressed immune system allows precancerous cells to grow unchecked.

**Natural killer cells and T lymphocytes are two key players of cell-mediated immunity, the aspect of the immune system that patrols for and removes malignant cells.**



**Chronic stress also undermines adherence to an anticancer lifestyle, leading to a vicious cycle of unhealthy choices.**

Biomedical research continues to explore the effect of stress on immunity. It was recently discovered that fragments of mitochondria (energy-generating organelles within the cytoplasm of cells) can be detected in the bloodstream following acute stress. This is called damage-associated molecular patterns, these mitochondrial fragments trigger immune and inflammatory pathways.<sup>4</sup>

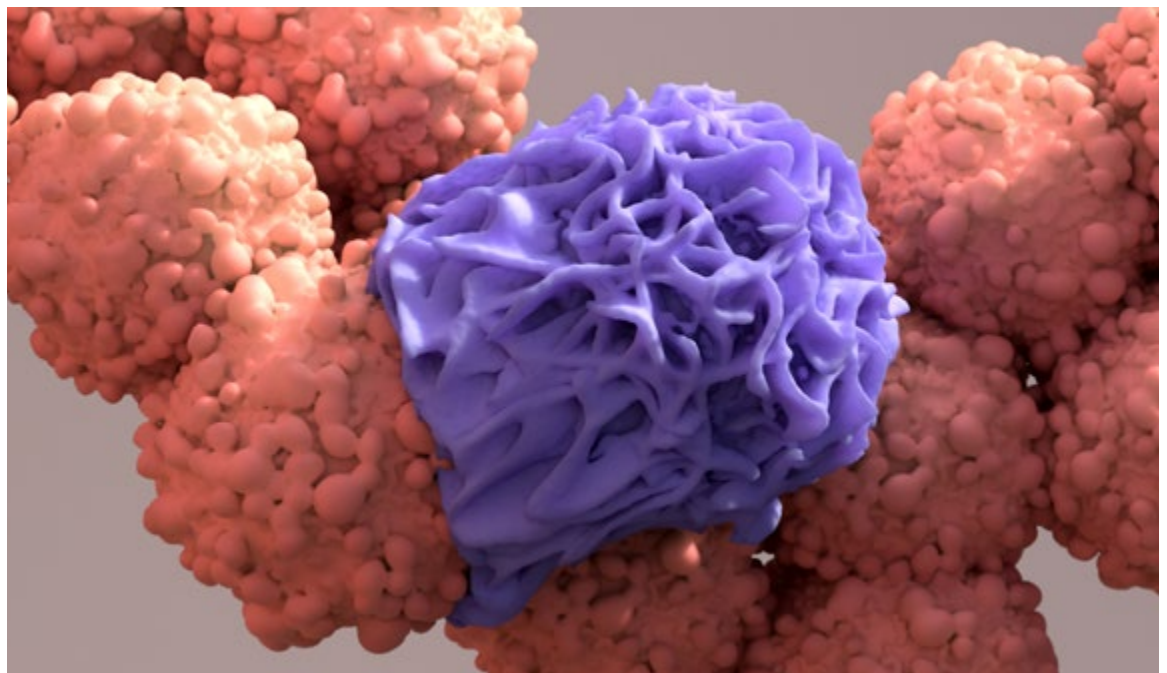
This is particularly concerning considering mitochondrial dysfunction is being studied as a major player in oncogenesis. Elevated glucocorticoids from chronic stress also aid angiogenesis, the process by which cancer cells increase blood supply to rapidly fuel their metabolism with glucose. Paired with the fact that glucocorticoids raise blood sugar (often a cancer cell's fuel of choice), these changes in the body's terrain represent yet another mechanism of how stress promotes a cancer microenvironment.<sup>5</sup>

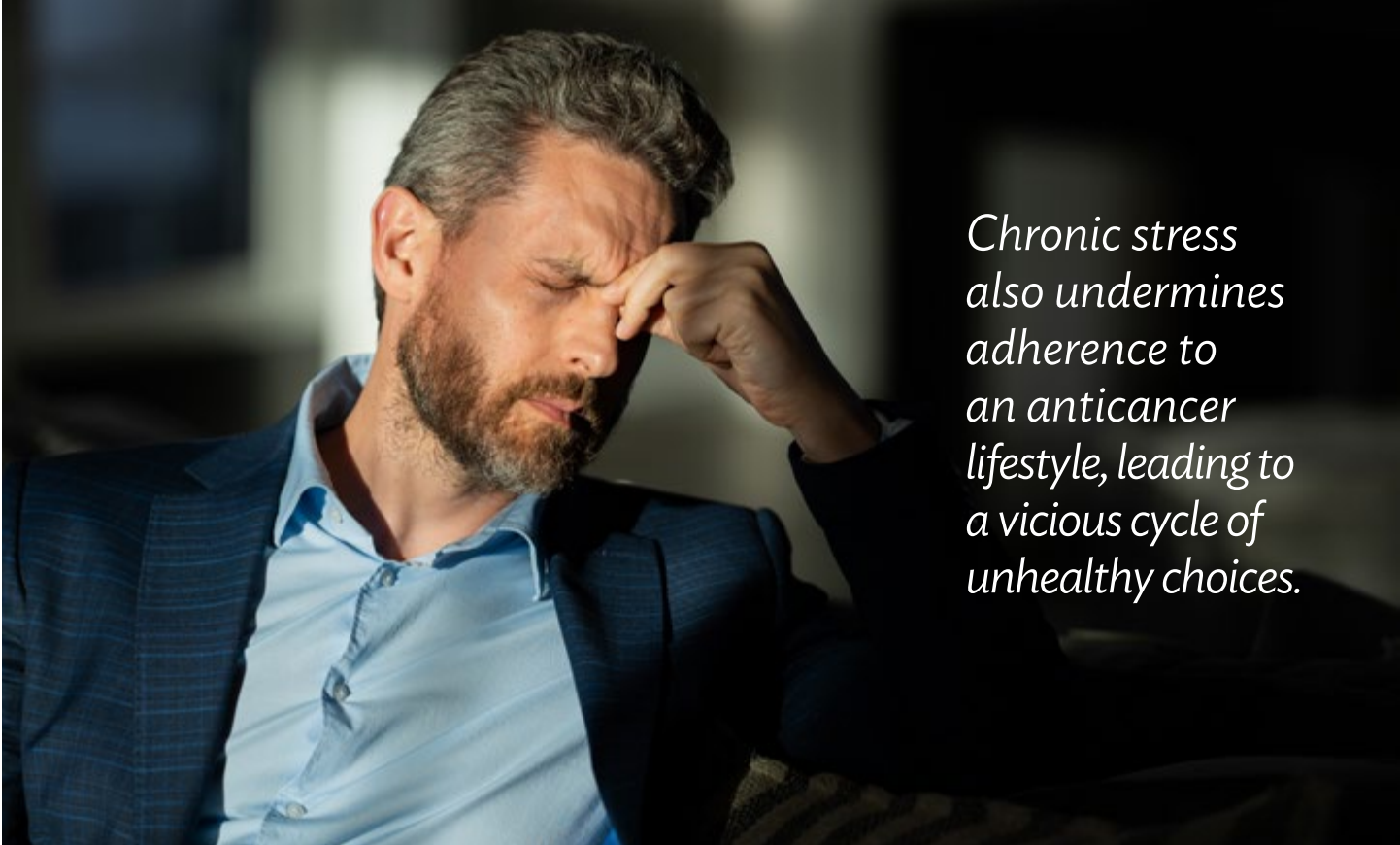
Pharmaceutical companies seek to leverage this aspect of tumor physiology by developing drug therapies targeting angiogenesis to slow the aggressiveness of certain cancers. Of course, a holistic

approach to cancer treatment would not rely on therapies to blunt angiogenesis without acknowledging the lifestyle factors that promote angiogenesis. If a bathtub is overflowing, it is wise to first turn off the faucet before unclogging the drain.

Systemic inflammation also ensues from chronic stress. Elevated expression of the inflammatory cytokine interleukin-6 (IL-6) can be detected in epithelial tumors, implicating IL-6 with tumor formation and disease progression.<sup>6</sup> The exact mechanism is unclear, and cytokine signaling can also have an antiapoptotic effect, yet elevated IL-6 can be observed in patients with different cancers and correlates with a poor prognosis. Whether these hallmarks of inflammation are the body's healing response to cancer or oncology treatment, or an underlying risk factor to cancer development remains to be seen.

Chronic stress also undermines adherence to an anticancer lifestyle, leading to a vicious cycle of unhealthy choices. When daily work and home stress become a deterrent to proper self-care, sleep quality and quantity are often affected. Prolonged





*Chronic stress also undermines adherence to an anticancer lifestyle, leading to a vicious cycle of unhealthy choices.*

stress also leads to destructive behaviors that are carcinogenic, such as cigarette smoking to alleviate anxiety.

Then a health crisis — a cancer diagnosis — hits, compounding stress exponentially. Stress may not have been the textbook carcinogen in this case, but by insidiously feeding several cancer contributors, stress should be considered a root cause of cancer development. The effect is incremental and indirect, but powerful.

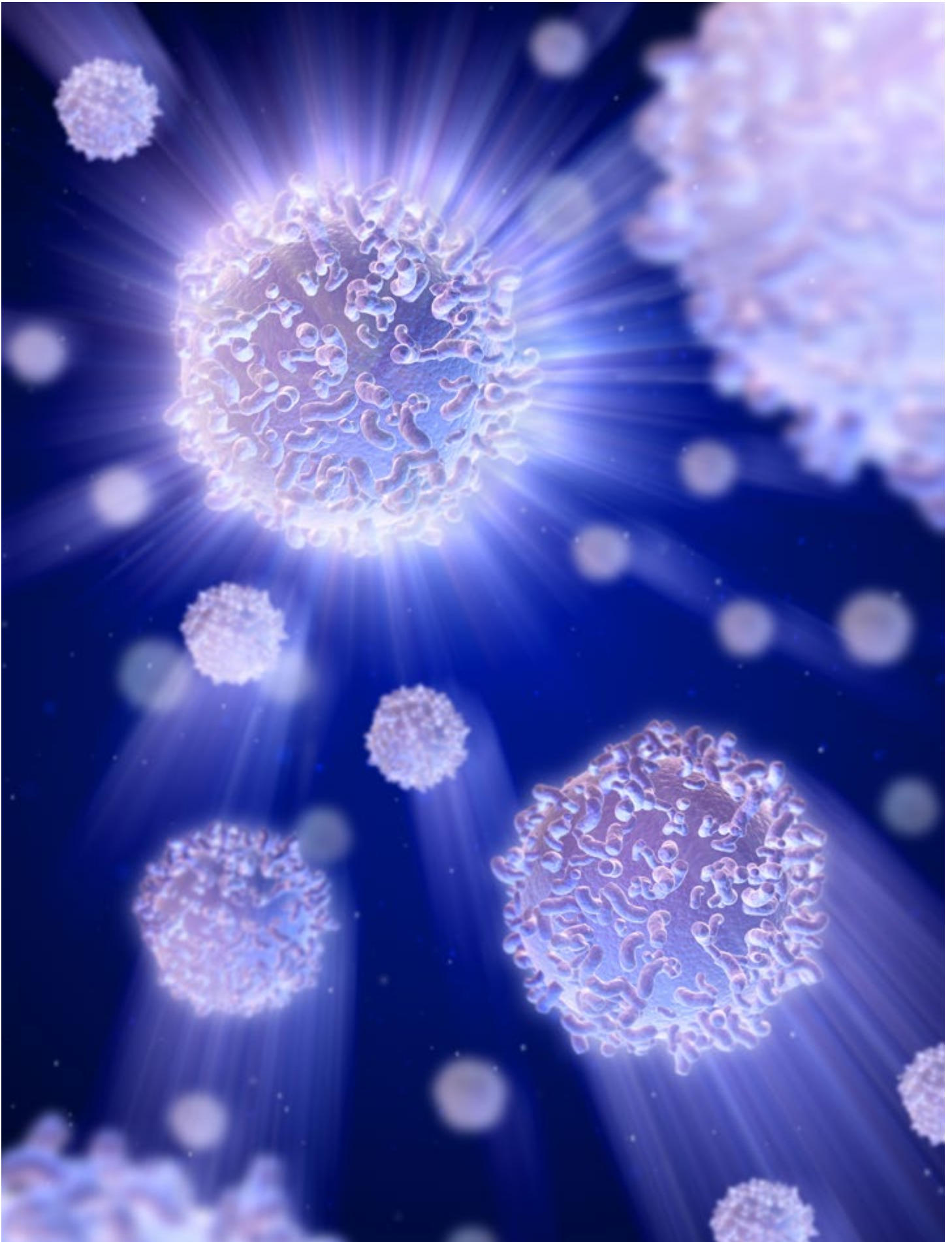
The effects of chronic stress and immune dysregulation are one line of evidence, but what about acute stress, activation of the sympathomedullary (SAM) pathway, and release of norepinephrine and epinephrine? Interestingly enough, pharmaceutical companies are well aware of this connection and are funding research to get beta-blocker drugs approved for cancer treatment and prevention based on their ability to antagonize norepinephrine and epinephrine receptors.<sup>7,8</sup>

To these clear mechanisms suggesting that acute and chronic stress promote

cancer progression can be added animal studies that show how controlled stress augments cancer formation. In one mouse model where tumors were induced by exposure to ionizing radiation, restraint stress was found to promote tumorigenesis through a loss of expression of a tumor-suppressor protein. Again, this effect is thought to be mediated by elevations in glucocorticoids (cortisol).<sup>9</sup>

Animal models also report several related mechanisms of cancer progression from stress, including increased angiogenesis via enhanced expression of growth factors.<sup>10</sup>

The case for cancer initiation in animal studies is less clear but suggestive of the ability of stressful conditions to jump-start latent malignancy that might not have manifested due to healthy immune surveillance. A number of stresses, including a breakdown in social order, create an immunocompetence sufficient to significantly increase tumor formation in mice when compared to unstressed controls.<sup>11,12</sup>



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## Epidemiological Evidence

**M**ice in lab experiments is one thing, but what about cancer initiation in humans from acute and chronic stress? A few lines of evidence suggest that elevated stress hormones can directly damage DNA and protect cancer cells from apoptosis (programmed cell death), a double whammy for tumorigenesis.<sup>13,14</sup>

A model of all these collective mechanisms — immune and metabolic dysregulation, inflammation, altered expression of tumor-suppressor proteins, DNA damage — opens the door for translation research to posit that stress may indeed underlie cancer formation.<sup>15</sup>

Of course, stress is only one of many carcinogens that people may be exposed to. Yet the weight of evidence clearly places stress as a significant promoter of cancer progression and influencer of cancer relapse, chemoresistance, angiogenesis, and metastasis.<sup>16,17,18</sup>

Biochemistry aside, a broader brushstroke reveals that psychosocial factors also influence cancer incidence and progression. Although the mechanism resides in the field of PNI, the precipitating cause may stem from big-picture psychosocial factors such as disruptions in a healthy diet, sleep, and exercise.<sup>19,20</sup>

In the same vein, depression and a lack of social support have been identified as risk factors for the development of cancer.<sup>21,22</sup>

Epidemiological studies in humans support this notion, with feelings of helplessness being associated with 160% more fatal cancers, losing an emotional relationship doubling the risk of breast cancer, and feeling alone when dealing with a trauma resulting in a 9 times greater risk of developing breast cancer.<sup>23,24,25</sup>

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## Research Controversy

**T**he evidence detailed here may not persuade a skeptic that stress should be classified as a textbook carcinogen. “Stress causes cancer” is a bold claim.

Stress unequivocally affects cancer progression in animal studies, but that is a difficult conclusion to scale to humans. For one, we’re a different species. Perhaps humans have evolved with better capacities to handle stress; the human higher brain affords some interesting stress-interrupting possibilities.

Another factor is that animal studies rely on tumors being artificially induced, typically from a single carcinogen or mutagenic virus. This is completely out of context with the environment in which human tumors develop, replete with multiple carcinogenic influences and cancer-promoting lifestyle factors.<sup>26</sup>

Most human studies are retrospective, looking back and attempting to correlate ongoing stress or a major trauma with cancer incidence. This level of evidence is vulnerable to confirmation bias and the shifting sands of human memory. The concern is that the reporting patient is more likely to associate stress with cancer development than someone who has not received such a devastating diagnosis.

Stress perception also plays a role. There is an inkling in the research literature that being stressed poses one risk and feeling stressed an additional one. The difference may seem subtle, but the perception that stress is damaging one’s health adds yet another layer to the problem, and humans are uniquely capable of feeling this. The catastrophizing human brain can elicit a stress response worse than what the stress stimulus itself would otherwise cause.<sup>27</sup>

Taken collectively, animal studies, mechanistic research, and

**B**iochemistry aside, a broader brushstroke reveals that psychosocial factors also influence cancer incidence and progression.

epidemiological surveys of psychosocial factors provide a framework for understanding the stress-cancer connection. How potent that influence is will be determined in time with further research into stress physiology and strategies to negate the negative effects of chronic stress.<sup>28</sup>

Science is a waiting game, but given the evidence presented here, it is up to the individual to determine how impactful stress is in their life and, if diagnosed with cancer, the degree that stress underlies the disease process you are positioning yourself to overcome.

**Disclosure Statement:** Portions of this article have been excerpted from Brandon's book, *Cancer, Stress & Mindset: Focusing the Mind to Empower Healing and Resilience*, available on his website [BrandonLaGreca.com](http://BrandonLaGreca.com) and through online retailers.

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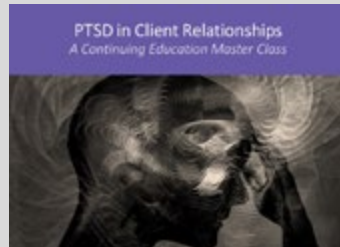
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# Connecting Gut Microbiota, Stress and the Immune System

By Stephanie Maxine Ross PhD, MHD, HT, CNC, FAIS

**T**he human body, including the gut, skin and other mucosal environments, is colonized by a tremendous number of micro-organisms, collectively termed the microbiome. The human gastrointestinal tract (GI, gut) is inhabited by a complex microbial ecosystem that consists of diverse microorganisms.<sup>1</sup> The gut microbiota consists predominantly of bacteria; however, it also contains protozoa, archaea, fungi, and viruses, which have coevolved with the human host. It is estimated that the human gut is colonized by 10 trillion to 100 trillion microbes, which encapsulate more than 3.3 million nonhuman genes, approximately 150 times more genetic material than the human genome itself.<sup>2</sup> These microbes are essential for health and have multiple, critical consequences for metabolic and physiological processes from early postnatal development, to nutrient processing, to immune system development, to normal health, brain function, and behavior.<sup>3-5</sup> Microbiota are considered part of the unconscious system that regulates behavior.<sup>6</sup> Research has shown that the GI microbiota has a major influence on cognitive function and basic behavioral patterns, stress, neuroinflammation, and the immune system.

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## **Microbiota-Gut-Brain Axis Evolutionary development in humans**

**T**here is a bidirectional communication that exists between the metabolically complex intestinal microbiota, the gut, and the brain.<sup>6-7</sup> The gut microbiota consists of a complex network called the microbiota-gut-brain axis that involves many organ systems, including the endocrine system, the immune system, and the autonomic, central, and enteric nervous systems, with the intestinal microbiota influencing these interactions.<sup>8</sup> The intestinal microbiota and its metabolites appear to modulate the peripheral and central nervous system, influencing brain function and development, whereas the brain affects GI activities, including motility, blood flow, secretions, and intestinal permeability, as well as microbiota composition and immunomodulation.<sup>9-10</sup> Over the past several years, the field of immunology has been revolutionized by the growing understanding of the fundamental role of the microbiota in the induction and function of the mammalian immune system.

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## **Microbiota-Immune System Connection Fetal microbiota ecosystem**

**F**etal development occurs in a sterile intrauterine environment. The colonization of bacteria in the intestines

**O**ver the past several years, the field of immunology has been revolutionized by the growing understanding of the fundamental role of the microbiota in the induction and function of the mammalian immune system.

**T**here are several variables that are known to affect the composition of infant gut microbiota, including the method of delivery, the manner of feeding, the duration of gestation, internal and external stressors, and the use of antibiotics and probiotics.

of the infant begins during birth when delivery exposes the infant to a complex microbiota, which is critical for maturation of the immune system.<sup>11</sup> It is in this early stage of life where the establishment of a healthy gut microbiota is believed to have profound consequences on the future well-being of the individual.<sup>12</sup> This initial phase of microbiota development is largely determined by the type of bacteria the infant is exposed to during the process of delivery and after the first few hours of life, with the maternal microbiome as its first inscription, through vagina, the anal area, and the skin.<sup>13</sup>

There are several variables that are known to affect the composition of infant gut microbiota, including the method of delivery, the manner of feeding, the duration of gestation, internal and external stressors, and the use of antibiotics and probiotics. The method of delivery has been shown to be the primary factor of a newborn's intestinal microbiota composition.<sup>14</sup> Vaginal deliveries provide infants higher numbers of beneficial *Lactobacillus*, *Bifidobacterium*, and *Bacteroides fragilis* and higher amounts of *Clostridium* microbiota, as compared with infants born through cesarean deliveries.<sup>15</sup> Present studies indicate that cesarean-born infants develop an intestinal microbiota with atypical short-term immune responses and an increased long-term risk of developing immune diseases.<sup>16</sup>

Dietary considerations are another significant factor that has a direct impact on establishing a healthy neonatal gut microbiota.<sup>13</sup> It is well established that breast-feeding offers the best source of nutrition for the growth and maturation of the infant intestinal microbiome.<sup>17</sup> Breast milk is composed of a complex mixture of oligosaccharides that are known

to stimulate the growth of beneficial bacteria such as *Bifidobacterium* that exerts a positive impact on the immune system while inhibits the binding of pathogenic bacteria.<sup>18</sup> Although breast milk feeding provides the best nutrition for the colonization of a beneficial microbiota, the transition to a healthy solid food source during weaning is essential for the development of a more complex, stable microbiota profile, characteristic of the adult GI tract.<sup>13</sup> It is during this transition period of weaning to a solid food diet where the most highly adapted *Bacteroidetes* and *Firmicutes* bacteria increase in numbers, laying the foundation for the adult gut microbiome.<sup>13</sup> Bacterial diversity continues to increase as the child ages, as a result of nutrition intake and environmental exposure, and after 1 year of age, a complex adult microbiome is established.<sup>19</sup>

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### **Adult microbiota ecosystem**

**T**he characteristic ecosystem found in the adult intestines includes the Bacteroidetes and Firmicutes phyla, *Proteobacteria*, and anaerobic bacteria such as *Bifidobacterium* species.<sup>20</sup>

Although the adult microflora is individual with specific variability in the enteric microbiota, it is the homeostasis within the microbiome that confers health benefits; an imbalance of beneficial bacteria can negatively impact the health and well-being of the individual.<sup>21</sup> It is clearly evident that the quality and balance of the microbiota differ markedly among those who age with good health and those whose health declines with age.<sup>21</sup>

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### **Microbiota in older adults**

**A**s the human organ systems undergo the process of aging, serious alterations in the composition of the gut



microbiota become increasingly apparent. Natural physiological changes, including digestive problems and decreased intestinal motility, can lead to an imbalanced dietary intake and malabsorption of nutrients, which ultimately compromise the intestinal microbiota composition in the older adults (>65 years of age).<sup>22</sup> Another process that negatively affects the homeostatic equilibrium of the gut microbiota in the older adults is a decline in functionality of the immune system (immunosenescence).

Furthermore, accompanying immunosenescence is a chronic, low-grade systemic inflammatory state that creates a favorable environment for the growth of pathobionts over symbiont bacteria.<sup>12</sup>

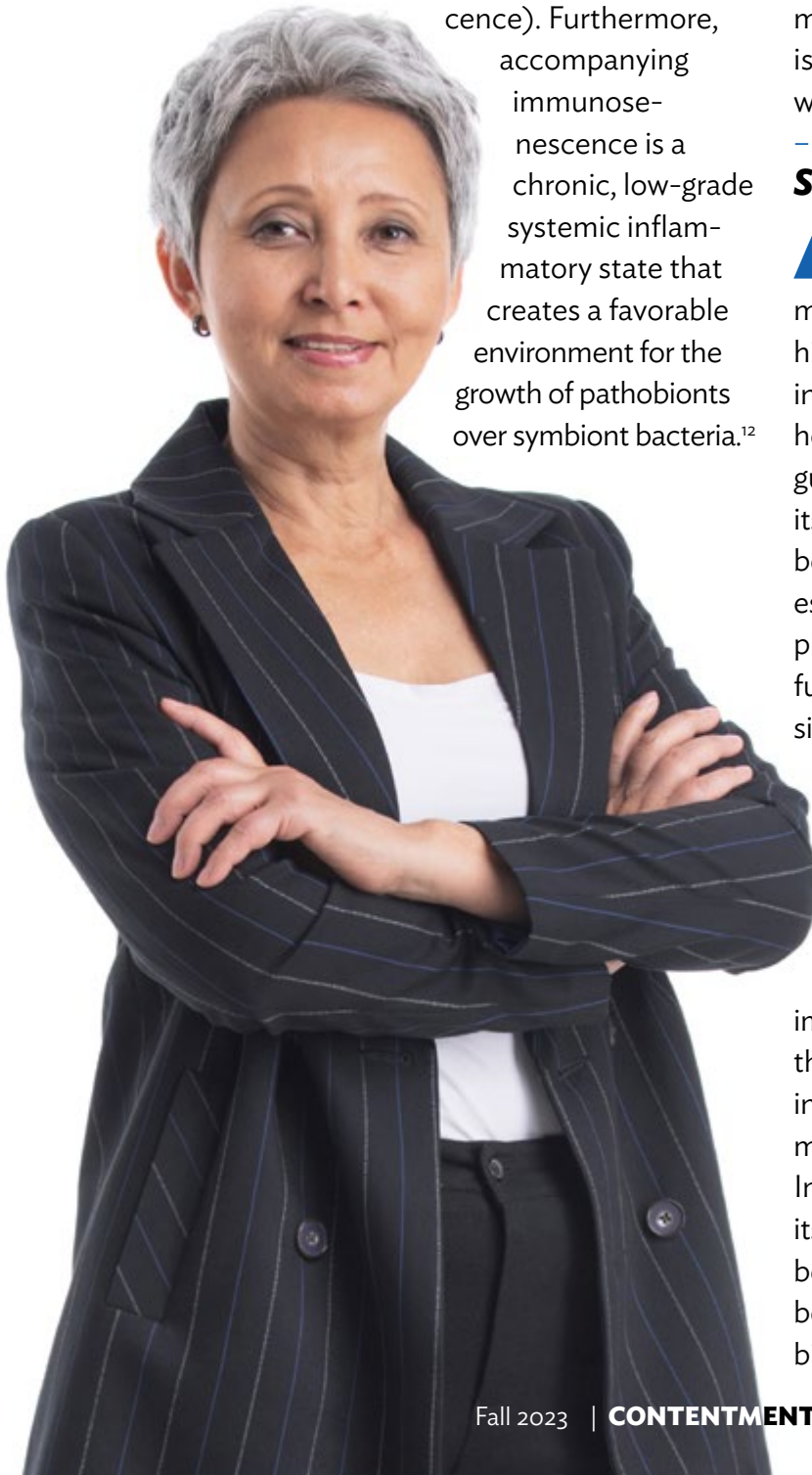
Although the composition of intestinal microbiota in the older adults is extremely variable among individuals, in general, the biodiversity is reduced, and the stability is compromised.<sup>23</sup> Studies indicate variations in gut microbiota composition among different nationalities that have been attributed to corresponding differences in lifestyle and characteristic diet types. All indications point to the fact that a healthy, diverse diet promotes a more diverse gut microbiota composition that, in turn, is greatly beneficial to the health and well-being of older adults.

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### Summary

**A** bidirectional signaling exists between the metabolically complex intestinal microbiota, the gut, and the brain. This highly complex connective system integrates immunological, neural, and hormonal signals between the microbiota-gut-brain axis. The GI microbiota and its role in both health and disease have been the focus of considerable research, establishing its involvement in metabolism, physiology, nutrition, and immune function. Alterations in the bidirectional signaling of the microbiota-gut-brain triad have been linked in the pathogenesis of brain-gut disorders, such as irritable bowel syndrome and inflammatory bowel disease, and the manifestation of obesity and type 2 diabetes.<sup>24</sup>

Recent studies have implicated an imbalance of normal gut microbiota in the pathology of several brain disorders including autism spectrum disorders,<sup>6</sup> mood disorders,<sup>6</sup> and immune function.<sup>24</sup> In addition, intestinal microbiota and its metabolites have been shown to be involved in modulating mood and behavior, stress responses, and brain biochemistry.



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**Dr. Stephanie Ross** is an internationally recognized leader in Integrative Health. She served as clinical professor and the founding Director of the Department of Complementary and Integrative Health at Drexel University, College of Nursing and Health Professions, a pioneering program that partnered with the Andrew Weil Center for Integrative Medicine. Prior to Drexel, she initiated the first course in phytomedicine at Temple University School of Medicine, where she taught medical students. In addition to her scholarly achievements, Dr. Ross is a skilled and dedicated Integrative Health Practitioner, who guides her patients in achieving optimal health and wellness, with emphasis on integrative stress solutions. Dr. Ross has garnered numerous awards, is listed in *Who's Who in Health Sciences*, and is a Fellow of the American Institute of Stress where she serves on the Executive Advisory Board and as Editor of *Contentment*, their peer-reviewed international publication.



Ross is extensively published with more than 97 articles featured in international peer-reviewed journals that are cited in the National Institute of Health's Library of Medicine (PubMed). Dr. Ross serves as the Associate Editor for the peer-reviewed international *Holistic Nursing Practice* journal. She is a sought after consultant on Workplace Stress and a keynote speaker at Corporations and Healthcare Systems.

Dr. Ross offers telehealth and on-site consultations. She works primarily with patients who are referred by healthcare providers, providing a supportive interprofessional healthcare team approach to maximize health and well-being.

# Guided Imagery: An Evidence-Based Approach for Cancer Immune Function – Exploring the Potential of Art Images





By Marcia Uddoh, MD (candidate), PhD, MPH, MS, MSW, FAIS

The good news about the benefits of guided imagery for cancer patients should consider the underlying disease process that led to its implementation.<sup>1</sup> This inclusion will allow for a better understanding of the mechanics and scientific basis of the process. Therefore, it is crucial to explore guided imagery and the mechanism of the disease process. To accomplish this, a conceptual model would be suitable as it offers a more comprehensive overview of the entire narrative.

### Introducing the Stress Vitals Cancer Image Model: A Multidisciplinary Approach

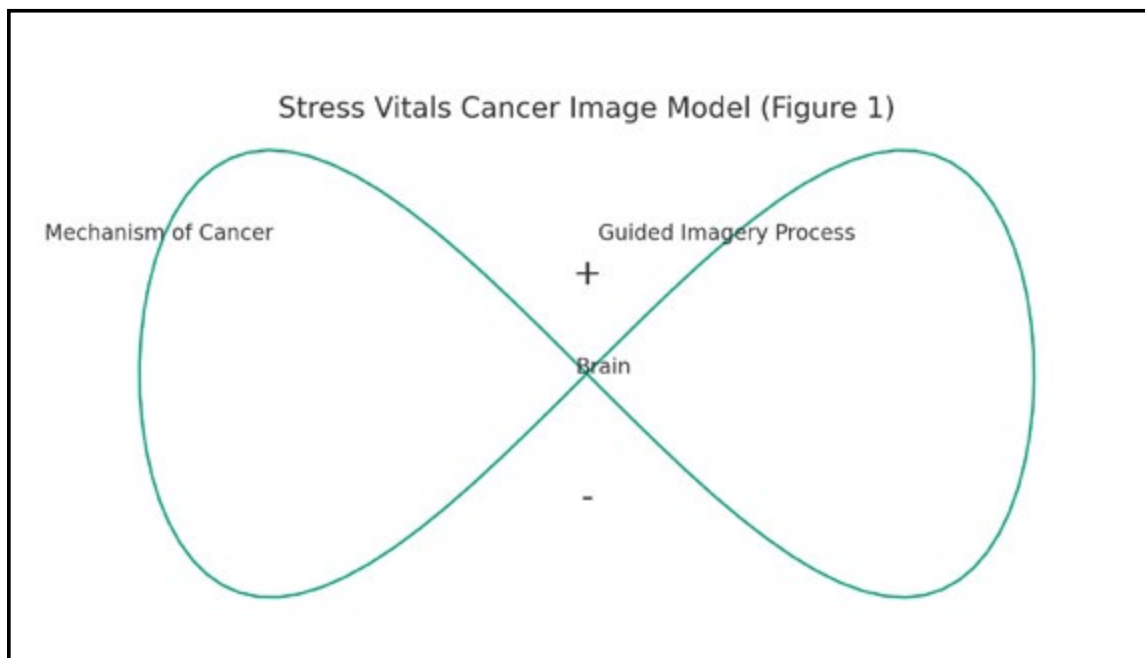
The Stress Vitals Cancer Image Model (SVCIM) is a conceptual framework

that can provide valuable insights to this discussion (see Figure 1). The model takes the form of an infinity sign, with one side representing the guided image process and the other representing the cancer mechanism. The center of the infinity loop is marked by a tension point, which represents stress. Stress is denoted by a positive sign (+), while the absence of stress is denoted by a negative sign (-).

Within the context of the model, the presence of stress within the cancer loop can be viewed with the progression of the disease. Similarly, the absence of stress can be considered within the guided imagery loop regarding relaxation.

The brain lies at the precise center of the model, marked by the crosshairs. The brain serves as the pivotal point from which either pathway can be initiated. This dual role is because the brain is connected to the disease process through stress and

**Guided imagery is a technique that involves the controlled visualization of goals, behaviors, and desired outcomes<sup>3</sup> (Giacobbi).**



**T**here are two main types of evaluation, enumerative and functional, that can assess the effectiveness of guided imagery from an immunological standpoint.<sup>8</sup>

the guided imagery process that leads to relaxation. Understanding the role of cognition in both pathways is crucial for a comprehensive discussion of this topic.

Various fields of study can classify and label the components of this conceptual framework differently. For this discussion, we will refer to the portion of the loop that visualizes the brain and its connection to cancer as "psychoneuroimmunology/cognitive theory." The portion that visualizes the brain and guided imagery will be referred to as "neuroaesthetics."

Guided imagery is a technique that involves the controlled visualization of goals, behaviors, and desired outcomes<sup>3</sup> (Giacobbi). On the other hand, neuroaesthetics is a relatively new field that gained prominence in the 1990s when Semir Zeki coined the term. Zeki, a professor at the University College of London, focused his research on aesthetic experiences.<sup>4</sup>

The inclusion of neuroaesthetics within the stress vitals cancer image model is appropriate because we aim to consider the aesthetic aspect and the expanded connection to psychological, aesthetics, biological mechanisms, and the human condition.<sup>4</sup>

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## **The Role of Psychoneuroimmunology in Stress-Induced Cancer Progression**

It is essential to define psychoneuroimmunology to understand better the role of immunity and stress in cancer. Psychoneuroimmunology is the study of how the brain, immune system, and behavior interact.<sup>5</sup> Within this field, the neuroendocrine system is a crucial mediator connecting stress to cancer. This system comprises the hypothalamus-pituitary-adrenal (HPA) axis and the sympathetic nervous system (SNS).<sup>6</sup> Stress triggers the release of three stress-related

hormones: epinephrine, norepinephrine, and glucocorticoids. In turn, these hormones activate cytokine secretion and molecular signaling pathways, which alter the tumor microenvironment (TME).<sup>6</sup> The TME, consisting of immune cells, blood vessels, stromal cells, and the extracellular matrix (ECM), varies depending on the type of tumor.<sup>7</sup> Rather than being a passive observer, the TME actively promotes cancer progression. In the early stages, the TME establishes a reciprocal relationship with cancer cells, enabling their survival, local invasion, and metastasis to other parts of the body.<sup>7</sup>

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## **The Science of Healing: Exploring Guided Imagery Through Multiple Lenses**

Guided imagery, also known as mental imagery or visualization, is an established intervention in integrative oncology. It has been extensively researched and has shown positive effects on the immune system.<sup>8</sup> Various terms have been used to describe guided imagery, but the one that aligns closely with our conceptual model is the one proposed by Green, Walters, Green, and Murphy. Their model considers cognition and perception relevant to the healing process.<sup>9</sup>

In their self-regulation theory, Green et al. consider how individuals process cognitive information and how it affects their behavior.<sup>9</sup> According to their conceptualization, the perception or image triggers an emotional response, which in turn elicits a biochemical response in the limbic, hypothalamic, and pituitary areas. This biochemical response can lead to physiological changes that individuals become aware of and respond to. Green et al. describe this process as a "cybernetic feedback loop."<sup>9</sup>

Another interpretation of guided

imagery is the cognitive theory, which suggests that changing negative thought patterns can decrease arousal in the autonomic nervous system (ANS).<sup>9</sup> Also, the psychoneuroimmunology paradigm proposes that guided imagery can downregulate the hypothalamic-pituitary axis, thereby reducing the stress response and promoting relaxation.<sup>9</sup>

Overall, guided imagery has been studied from various perspectives, including its effects on the immune system, cognitive processes, and the stress response. These different approaches provide insight into the mechanisms by which guided imagery can promote healing and well-being.

## Quantifying the Effects of Guided Imagery: An Immunological Perspective

There are two main types of evaluation, enumerative and functional, that can

assess the effectiveness of guided imagery from an immunological standpoint.<sup>8</sup>

Enumerative assessment focuses on counting the different components of the immune system, while functional assessment involves the conduction of various laboratory tests.<sup>8</sup> In this discussion, our main focus is on the components of the white blood cell population, such as granulocytes, NK cells, B-lymphocytes, T-lymphocytes, and monocytes.

Additionally, the population of antibodies in the blood, specifically immunoglobulins A, G, and M, is also of importance.<sup>8</sup>

One study examined the effects of guided imagery on immune cell counts, specifically white blood cells, neutrophils, and lymphocytes. The results showed that these counts decreased with the stages of relaxation experienced during the intervention.<sup>8</sup> Moreover, there was a noticeable reduction in stress levels.<sup>8</sup>

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*It is believed that an image can be used in guided imagery to induce healing on its own as long as it is capable of evoking vivid imagery.*





Another study implemented a psychoneuroimmunology-based intervention that incorporated guided imagery. The findings revealed increased immune markers, including CD8+ T cells, B cells, natural killer cells, serum immunoglobulin A, and immunoglobulin M.<sup>10</sup> Furthermore, a separate study with guided imagery observed an increase in NK cell cytotoxicity in the group that received the guided imagery intervention.<sup>11</sup> Specifically, when a comparison was made with the intervention group and the control group, the researchers discovered higher NK cell cytotoxicity at different effector cell-to-target cell ratios (E:T) (100:1, 50:1, and 25:1) ( $p < .01$  to  $p < .05$ ). Additionally, there was increased activation of IL-2 at different E:T ratios (100:1, 50:1, 25:1, and 12.5:1) ( $p < .01$  to  $p < .05$ ).<sup>11</sup>

**R**esearchers have discovered that the image alone can have a similar positive impact on the immune system.<sup>12</sup>

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## Images and Artwork in Guided Imagery: A Neuroaesthetic Perspective

**T**he connection between guided imagery and neuroaesthetics lies in the use of images or artworks as a foundational element in the process. It has been determined that images or artworks are an effective modality for guided imagery.<sup>8</sup> By incorporating neuroaesthetics, we can delve deeper into the interaction between these two fields and better understand the cognitive processes involved in images or artworks.<sup>8</sup>

It is believed that an image can be used in guided imagery to induce healing on its own as long as it is capable of evoking vivid imagery. Furthermore, researchers have discovered that the image alone can have a similar positive impact on the immune system.<sup>12</sup>

By exploring the relationship between Guided imagery and neuroaesthetics, we

can uncover valuable insights into how images and artworks can be utilized to enhance the healing process and positively influence the immune system.

## Incorporating Spiritual Themes in Guided Imagery: Implications for Future Studies

Our approach places a central focus on the image or artwork. The objective is to remove stress and promote relaxation, as stress is known to initiate the disease process. One potential thematic focus for the images/artworks is spirituality, which has been studied extensively with breast cancer survival.<sup>2</sup> Numerous studies have explored spiritually based interventions and their impact on psychoneuroimmunological (PNI) measurements.<sup>2</sup> Given that 92% of Americans believe in God or a higher power, and 56% consider religion very important in their lives, according to Pew Forum Research data,<sup>2</sup> incorporating spiritual images into our research seems plausible.

In conclusion, it is encouraging that guided imagery has emerged as an effective intervention in cancer treatment. By utilizing neuroaesthetics and images/artworks, we can further enhance the scientific exploration of this approach.

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### Acknowledgments

*This article's main text utilized Artificial Intelligence Support (AIS) by OpenAI for final sentence refinement. San Francisco, CA, USA.*

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