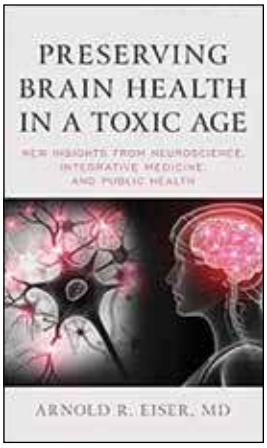
Book reviews

David A. Bennahum, MD, and Jack Coulehan, MD, Book Review Editors



Preserving Brain Health in a Toxic Age: New Insights from Neuroscience, Integrative Medicine, and Public Health

Arnold R. Eiser, MD
Rowman & Littlefield Publishers
October 11, 2021, 280 pages

Reviewed by David A. Bennahum, MD (AΩA, University of New Mexico School of Medicine, 1984, Faculty)

Arnold Eiser has written an interesting book filled with ideas and facts that includes 80 pages of references. The author first considers the evolution of the modern human brain as it was shaped by the environment and evolution, then by agriculture, writing, government, and universities, and since the modern age, beginning in the Renaissance, by science and global travel, industrialization, urbanization, climate change, and the Digital Age.

He states in his introduction that several themes will emerge in the ensuing chapters. He comments on nutrition as both causation and prevention. "The role of nutritional therapy has been seriously underutilized." [p3] The microbiome and the gut-brain connection have been under-researched and under-emphasized in medicine, and he therefore notes that, "the education of allopathic physicians has little focus on nutrition." [p3]

Eiser coins a new word "Evigrative" medicine as a subset of integrative medicine. It is a branch of medicine that derives knowledge from biochemical, genomic, and metabolic research, as well as from case studies. He suggests that not only mind-brain interactions are important, but that the brain interacts with other organs as well, and with the human microbiome. He is concerned that the thousands of industrial toxins in the environment, as well as the excessive use of medications such as acetaminophen, have long-term toxic effects. He is also concerned that digital violence, that which we see on our television screens has a toxic effect on brain neuroplasticity. This may well be true for children.

Beginning his review of the toxicities in the environment Eiser recalls the insight of John Snow that contaminated water was the cause of Cholera in 19th century London. The predominant theory prior to the work of Louis Pasteur was that miasmas caused many of what are now known as infectious diseases. The idea that bacteria or toxins could cause disease, until the discoveries of Pasteur and Lister, had been rejected. The author then explores the toxic environment in 13 chapters including neurotoxins, the human microbiome, food and the liver, the many facets of dementia, Alzheimer's, autism, chronic fatigue syndrome, stress and violence. He ends by contrasting allopathic and integrative medicine and offers a way forward to brain health.

This is all a most demanding and challenging series of ideas. The story of chronic traumatic encephalopathy (CTE) is well known. It was first discovered by a pathologist from Nigeria, Bennett Omalu, MD, working in Pittsburgh. Omalu coauthored a paper in 2005 that described CTE in a former Pittsburgh Steeler linebacker Mike Webster. The National Football League attempted to block Dr. Omalu's work. But, Dr. Ann McKee, a neuropathologist who was invited by Chris Nowinski, CEO of the Sports Legacy Institute, to examine the brain of Tom McHale who had played for the Green Bay Packers, discovered a buildup of tau, a toxic protein that forms neurofibrillary tangles in the brain. McKee later found that 90 of 94 NFL players examined had CTE. Injuries such as in boxing, cycling accidents, or soccer can lead to CTE, as happened to Muhammad Ali. Thus, one clear cause of chronic brain disease is recurrent injury.

The author mentions visiting Salzburg, Austria where both Mozart's wife and father are buried in the courtyard of the San Sebastian Monastery. There, he also found the grave of Paracelsus, the pseudonym of Phillipus Aureolus Theophrastus Bombastus von Hohenheim, the founder of toxicology in the 16th century. A controversial physician, mystic, and wanderer, Paracelsus was the first to have noticed that miner's lungs were damaged by their work. In his treatise, *On the Miner's Sickness and Other Diseases*, Paracelsus postulated that three elements—mercury, sulfur, and salt—contributed to all human disease. He also noted that the higher the dose the greater the poison. He stated that *solus dosis facit venenum*, (only the dose makes the poison).

Eiser notes that gastrointestinal dysfunction is extremely common in autistic children and that probiotics may be helpful in this group. Reminding the reader of the Mad Hatter in *Alice in Wonderland,* and the mercury vapors necessary to the making of felt for hats that caused a form of dementia, I was shocked to read that while the French Academy of Medicine described mercury as a cerebral toxin in 1869, hatmakers were not protected by law until

1898. In the United States, this process for the making of felts for hats with mercury vapor was permitted until 1941.

Eiser reminds us that dental amalgams can also be a source of mercury poisoning and toxic brain symptoms. He writes, "I believe that it is fair to say today that a variety of metal toxicities appear to be a factor or a cofactor in the development of Alzheimer's disease (AD)." p67

These chapters on toxins and the brain are simply fascinating as the author has a facility for holding the reader's attention while exhaustively examining each possible toxin.

In discussing AD Eiser remembers how shocked he and his wife were on reading about the great English author Iris Murdoch's decline into dementia, so well played by the actresses Kate Winslet and Dame Judi Dench in the film *Iris*. He writes:

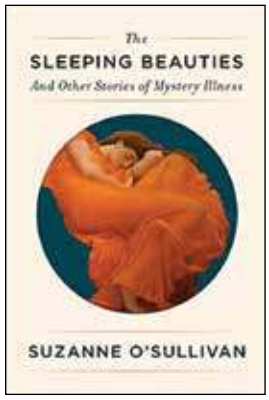
> Allopathic medicine and integrative medicine have taken different approaches to medical knowledge. Allopathic medicine with its focus on randomized prospective clinical trials (RCTs) of patentable drugs observes there is "no magic bullet," which goes without saying…Very highly regarded clinical researchers in this field have complained to me, off the record, that this standard for clinical practice guidelines does a disservice to many helpful interventions that are less amenable to RCTs. I am sympathetic to this concern.p77

The author writes that he was reluctant to write a chapter on autism, about which he at the time knew little, but, recognizing that it is a disorder that is increasingly recognized in the 21st century and that "moreover, as it affects our youngest and most vulnerable members of society, how we respond to this disorder is a measure of the worth of our society and culture. The continued rise of this disorder could likewise pose an existential threat to societal well-being and a hardship for countless families." p90

The approach that society takes to autism is influenced by both the effects of neurotoxicity and an emerging recognition that humans are neurodiverse. To aid in our understanding of what it means to be autistic, Eiser reminds us of the movie *Rainman*, the story of an autistic man, played by Dustin Hoffman and his selfish brother played by Tom Cruise. He also describes the life and accomplishments of the animal scientist Temple Grandin. Other than early intervention to acquire language and social skills there is little that is certain today. A wonderful resource is Steven Silberman's *Neuro Tribes: The Legacy of Autism and the Future of Neurodiversity*. A long list of toxins that may contribute to autism ranges from lead to endocrine disrupters like Bisphenol (BPA), to Perfluorinated hydrocarbons (PFCs). And, of course, genes must be part of the picture as well. The genetics of clinical syndromes cannot be understood without an understanding of epigenetics.

This is a fine book, engaging, searching, and deeply researched, but also written with a critical eye and a humanism that I found encouraging.

Dr. Bennahum is a member of *The Pharos* Editorial Board, and one of its Book Review Editors. He is Professor Emeritus of Internal Medicine, and Resident Scholar at the University of New Mexico's Institute for Ethics. His E-mail address is dbennahum@salud.unm.edu..



The Sleeping Beauties and Other Stories of Mystery Illness

Suzanne O'Sullivan
Pantheon, September 21, 2021
336 pages

Reviewed by Jack Coulehan, MD (ΑΩΑ, University of Pittsburgh, 1969)

In Sweden, hundreds of children lie unconscious for months or even years in their homes or hospitals. Full neurologic evaluation, including MRIs, EEGs, and other studies reveal no abnormalities. Their sleep-wake cycles remain intact, yet they are entirely catatonic, requiring feeding tubes and intensive nursing care. None of these children are Swedish. They are all immigrants from the Near East or former Soviet Republics, whose families are seeking permanent asylum in Sweden, a process that generally takes many months and may not be successful. Strikingly, if asylum is granted, the children gradually recover, although rehabilitation is lengthy and difficult. Neurologists have named this mysterious illness "resignation syndrome" and classified it a "functional neurological disorder." p4

Suzanne O'Sullivan, an Irish neurologist, set out in 2018 to study children suffering from resignation syndrome, a project that led to her to investigate other outbreaks of mysterious illness around the world. The result is her fascinating and eye-opening book, *The Sleeping Beauties and Other Stories of Mystery Illness*.

Resignation syndrome and the other functional neurological disorders discussed in this book differ from the

more traditional diagnoses of hysteria, or conversion disorder, which are applied primarily to individual persons. Instead, these conditions are communicable like infectious disease. They may spread acutely in epidemic fashion, or even become endemic in certain communities or cultures (i.e. culture-bound disease). According to O'Sullivan, they arise "from group interaction and, as such, (are) perhaps more appropriately, referred to as mass sociogenic illness," p257 often occurring in groups that have "a background of chronic tensions within a close knit community." p257

For example, *grisi siknis* is a functional neurologic disorder prevalent among the Miskito people of Nicaragua. It occurs almost exclusively in young girls and is characterized by convulsions and visual hallucinations of a dark, menacing figure, usually wearing a hat. While patients believe that *grisi sikness* is caused by an evil spirit, psychiatrists attribute it to the extreme sexual tensions experienced by adolescent girls in Miskito society. Acute *grisi sikness* is unresponsive to medical forms of treatment, and while many cases resolve, it sometimes becomes chronic. O'Sullivan notes that patients have access to modern hospitals, where complete neurologic and psychiatric evaluations are generally negative.

Communities often trace culture-bound syndromes of more recent origin to specific external factors that have impacted their town or region. For example, in the late 2000s, the government of Kazakhstan began to urge citizens to leave the city of Krasnogorsk after its coal mines had shut down. In 2010, sleeping sickness, a syndrome of vomiting, hallucinations, and bouts of hypersomnia appeared and quickly spread to more than 100 patients. The local people became convinced that poisoning by the government was the cause, even though medical work-ups, including toxicology, have always been negative.

Another example is a syndrome characterized by sudden collapse and convulsions among adolescent girls in northern Colombia. This illness first appeared in 2014 shortly after public health workers administered human papillomavirus (HPV) vaccine to high school students in the area. Originally, an outside physician visiting the area suggested there must be a link to the vaccine. An HPV etiology gained widespread acceptance, despite the fact that hundreds of millions of people around the world have been vaccinated without becoming ill. The syndrome "spread like wildfire," p193 and soon involved hundreds of girls. In some cases, symptoms resolved quickly, while in others, patients continue to be symptomatic for years. One woman reported to O'Sullivan, "I know it's still inside me," several years after her first episode.

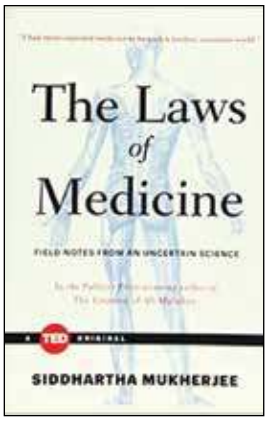
O'Sullivan notes, "there is a disconnect between the way mass psychogenic disease is defined and discussed by the small number of experts who study it and how it is understood outside those circles." p257 The public finds reports of such illnesses difficult to believe and generally assumes patients are malingering, or there is a hidden physical cause for their symptoms. In the United States, we tend to believe that mass sociogenic illness, if it exists at all, occurs only in backward cultures and not in our own enlightened society. Havana syndrome is a case in point. In 2016, a group of American diplomats in Cuba fell ill with a cluster of symptoms that included headache, earache, tinnitus, dizziness, visual disturbance, fatigue, and trouble concentrating. The first patient reported hearing a strange noise just before other symptoms began. Soon thereafter almost all the other patients recalled a similar experience. This noise was the stimulus for generating a powerful political narrative: Communist enemies were using some sort of advanced sonic weapon to cause brain injury among embassy staff. The narrative was strengthened when additional cases appeared among American diplomats in China.

Initially, researchers were reluctant to deny the sonic weapon story, yet since then no consistent brain abnormalities have been found, and extensive study has ruled-out the possibility of such a weapon. O'Sullivan believes that Havana syndrome is very likely "a mass sociogenic illness" occurring against "a background of chronic tensions within a close knit community." p257

The Sleeping Beauties is an illuminating book. It raises questions about a number of mysterious illnesses that are prevalent in the U.S. today. Consider, for example, chronic fatigue syndrome, fibromyalgia, and chronic Lyme disease. Consider also the multitude of chronic pain syndromes. Each of these illnesses is mysterious in the sense that its pathogenic mechanism remains unclear even after many years of study, and there is widespread disagreement about causation. While perhaps unlikely, is it possible that one or more of these syndromes is a mass sociogenic illness? And, if so, what does that mean?

You won't find the answer in *The Sleeping Beauties*, but it provokes the reader to ask the question.

Dr. Coulehan is a member of *The Pharos* Editorial Board, and one of its Book Review Editors. He is Emeritus Director of the Center for Medical Humanities, Compassionate Care, and Bioethics at Stony Brook University in New York. His E-mail address is john.coulehan@stonybrookmedicine.edu.



The Laws of Medicine: Field Notes from an Uncertain Science

Siddhartha Mukherjee
Simon & Schuster/TED;
First edition, October 13, 2015,
96 pages

Reviewed by Alan Jay Schwartz, MD, MSEd (AΩA, Lewis Katz School of Medicine at Temple University, 1972)

What to teach medical students, residents, fellows and clinical practitioners? How to become a master clinician? Easy questions to answer, right? Aren't the answers obvious?

Formal medical education is compartmentalized to teach the facts. Undergraduate medical education and graduate medical education curricula, formulated by consensus and monitored by the Association of American Medical Colleges, and the Accreditation Council for Graduate Medical Education outline the standardized algorithms to teach.

Is teaching clinical algorithms sufficient to provide sound diagnostic and treatment plans? The affirmative answer to this question reassures practitioners. Yes, evidenced-based facts guide treatment of patients. Yet there is a negative answer that baffles us. Baffled because clinical practice stares squarely at the face of incomplete information and unknowns. Despite learning a plethora of facts, clinicians are always making treatment decisions based on incomplete information. There is always one more piece of information to ferret out that may more firmly solidify the best prescription.

Siddhartha Mukherjee, author of *The Emperor of All Maladies: A Biography of Cancer,* in his more recent book, *The Laws of Medicine-Field Notes From an Uncertain Science* offers insights into why we are baffled, and advice on how to advance better patient care. "It's easy to make perfect decisions with perfect information," yet "Medicine asks you to make perfect decisions with imperfect [incomplete] information."[p4] We must teach medical students, residents, fellows and practitioners something more.

Mukherjee's *Laws of Medicine* are laws of uncertainty, imprecision, and incompleteness. *The Laws of Medicine* allude to clinical wisdom.

Law 1: A strong intuition is much more powerful than a weak test

Mukherjee reminds us that patient care is not an exact science; it is congested with incomplete information. We must rely on probability to ferret out a better clinical course. Teaching the facts devoid of the context of reality and probability will not facilitate diagnosis and treatment. When confronted with real patients and a hunch we can be more selective in ordering the additional test to gather a missing piece of information likely to reveal the patient's malady. Clinicians need to consider how diagnostics influence prior probability (prevalence, sensitivity, specificity, and predictive value) to arrive at a patient's most likely clinical diagnosis.

Law 1 begins with prior probability, a starting point in Bayes' Theorem (probability based on prior knowledge). This is not a strong intuition but reasoned assessment based on the patient's age, symptoms, known exposures, baseline prevalence of disease, and prior experience. We teach students, residents, and fellows how to have a reasoned assessment when we role model care individualized to each patient.

By teaching the concept of Bayes' Theorem, Mukherjee suggests we will expand medical acumen because we will consider prior knowledge. Mukherjee wants us to teach more than evidence, "Weigh evidence, make inferences, play with probability."[p29]

Law 2: Normals teach us rules, outliers teach us Laws

Mukherjee encourages us to reorient our thinking. Teach that the uncommon can be the key to understanding. Mukherjee's novel thought is, "Inliers create rules; outliers act as portals to understand deeper laws."[p53] He relates an example of the power of exploring outliers. David Solit, MD, a medical oncologist, and a laboratory scientist, investigates the effectiveness of cancer drugs. Solit studies large numbers of patients on new medications, many non-responders. His major focus is on single patient scenarios, the responders, the outliers. By asking why a drug has occasionally been highly effective and what was different about the responding patient, Solit has been able to fill in knowledge gaps and advance cancer chemotherapy.

Mukherjee's law chides us to think outside the box to expand our ability to provide more complete clinical care. Law 2 encourages teaching students and practitioners to fully consider both the most common clinical scenarios, and the unexpected aspects of a patient's story as we strive to fit each particular patient into more common yet incomplete diagnoses.

Law 3: For every perfect medical experiment there is…human bias

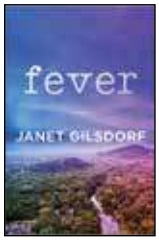
Mukherjee admonishes us to guard against bias. Voltaire said, "Doctors prescribe medicines of which they know little to cure diseases of which they know less in human beings of whom they know nothing."[p70] The pivotal word in this insight is know. To Voltaire's proclamation, Mukherjee responds, the discipline of medicine concerns the manipulation of knowledge under uncertainty. A striking example noted in the book is how Halsted's radical mastectomy surgery became standard practice for many years without accepting that there was little evidence to validate its effectiveness. "Sources of bias in Halsted's radical surgery; a powerful surgeon obsessed with innovation, a word that mutated in meaning, a generation of women forced to trust a physician's commands and a culture of perfection resistant to criticism."[p62] What more need be said about the negative power of bias?

The Laws of Medicine, is a succinct, explicitly stated, easy to read insightful essay. It advocates a more expansive way to conceptualize clinical medicine. In supporting the value of known facts, it champions additional consideration of how to apply the facts when a real patient is involved.

The Laws of Medicine is appropriate for varied audiences. For clinicians, it endorses an additional level of learning, i.e., mastering facts and pondering the most effective, efficient, and safe way to utilize medical knowledge for each individual patient. For teachers, it defines an additional student curriculum to expose. Incorporating the thought process of *The Laws of Medicine* into medical education and clinical practice will enable us to provide better care for patients in the face of the reality that we are always up against making consequential treatment decisions based on incomplete information.

Dr. Schwartz is retired adjunct professor, Department of Anesthesiology and Critical Care, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA. He is also Associate Editor and Editor, Review of Educational Materials for *Anesthesiology*. His E-mail address is ajschwartz@comcast.net.

More books by AΩA authors



Fever, a novel, by Janet Gilsdorf (AΩA, University of Michigan Medical School, 1999, Faculty); Beaufort Books, July 12, 2022, 300 pages.

Psychoanalytic Readings of Hawthorne's Romances: Narratives of Unconscious Crisis and Transformation, by David B. Diamond (AΩA, The Johns Hopkins University School of Medicine, 1969); Routledge, July 9, 2021; 192 pages.

When the Beast Comes For You: A Physician's Battle with Cancer, by John Martucci (AΩA, The Ohio State University College of Medicine); Eckhartz Press, April 26, 2022.

Learning the Art of Medicine – A Memoir, by Gordon Noel (AΩA, Uniformed Services University of the Health Sciences F. Edward Hébert School of Medicine, 1988, Faculty); Quimby House Press, March 15, 2021, 498 pages.