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Unwrapping a Fragile Concept

Jason Karlawish
University of Pennsylvania, jason.karlawish@uphs.upenn.edu

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Unwrapping A Fragile Concept

BY JASON KARLAWISH

THE ALZHEIMER CONUNDRUM
by Margaret Lock
Princeton (NJ): Princeton University Press, 2014
328 pp., $29.95

In 2002 Margaret Lock, a medical anthropologist at McGill University in Montreal, Quebec, started work on a book about the social implications of genetic testing for complex diseases. She chose Alzheimer’s disease as her case study. Lock soon discovered that she had stepped into a far more complex and controversial situation than she had anticipated. “Among experts,” she observed, “the very category of AD [Alzheimer’s disease] was being subjected to questioning and possibly category fragmentation or reshuffling was in the air, making for a plethora of unknowns.”

Lock set out to explore these unknowns. She interviewed leading Alzheimer’s disease researchers, attended their conferences, and read their papers. She conducted ethnographic interviews with clinicians, patients, and their caregivers. The result is *The Alzheimer Conundrum*, an ambitious dissection of a vexing problem: Despite several decades of research, dementia remains a very real and devastating problem and the causes of the most common form--Alzheimer’s disease--remain elusive. Notably, the claim that the disease is distinct from aging is increasingly unstable. This conundrum has clear implications for what the United States should do to prevent Alzheimer’s disease.

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Although chapter and section titles such as “An Imperialism of Probabilities” and “Embodied Risk Made Visible” suggest an academic and jargon-filled science and technology study, *The Alzheimer Conundrum* is an engaging read that, while quite granular in its detail, is never dry.

The book begins with the basic premise that medical research proceeds according to a model of disease. The dominant disease model that Alzheimer’s researchers use defines disease as the effects of distinct entities, as in how the tuberculosis bacillus causes TB. In the case of diseases of the brain, this means that localized pathologies, or lesions, explain a patient’s symptoms, in the manner that a stroke in the motor cortex leads to corresponding limb weakness. In the particular case of Alzheimer’s disease, the pathology that has captured researchers’ attention is plaques of beta amyloid.

What follows is an overview of the twentieth-century history of Alzheimer’s disease that led to this consolidation of opinion around the amyloid cascade hypothesis. Subsequent chapters review how biomarker measures that are expanding the disease category into mildly impaired and even asymptomatic stages have also destabilized the tight link between pathology and disease. Lock goes on to examine the efforts of genome-wide association studies-- big data projects that, she argues, have expanded the facts about Alzheimer’s disease without concomitant progress in understanding its causes.

Lock clearly summarizes, synthesizes, and critiques the results from research in molecular biology, genetics, neuroimaging, and epidemiology. This work is supported by researchers’ candid and sometimes vivid reflections on the state of affairs. She is a keen observer of her subjects’ language and behaviors: how some have described those findings that do not fit their model as “junk,” “trash,” or “garbage,” and how others have stepped outside the lab as “rock stars of science,” performing “The Times They Are a-Changin’” with Aerosmith’s Joe Perry on Capitol Hill.

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Lock has discovered that the dominant concept of Alzheimer’s disease is in fact fragile. Plaque accumulation does not map onto a lesion-based disease model. Reducing the cause of Alzheimer’s disease to amyloid or other molecules ignores research showing that many older adults’ have brains filled with pathology, but they live disease-free lives. Alzheimer’s disease and aging are not distinct boxes in a periodic table; they are neighboring territories separated by man-made borders.

The book concludes with an ambitious summary of studies in epigenetics, genomics, and epidemiology whose results suggest that the many genes and molecules linked to Alzheimer’s disease are in a dynamic interaction with both their cellular and external environments. This, she argues, supports an alternative model of disease--an “entanglement theory”--that sees the aging brain and the world in a disrupted equilibrium, which, she argues, compels researchers to move from conceptualizing Alzheimer’s disease as caused by problems in the brain alone, to a problem of the person in their environmental, social, and political milieus.

The Alzheimer Conundrum arrives at an auspicious time. The United States has committed itself to preventing Alzheimer’s disease by 2025. This research supports partnerships among academics, the National Institutes of Health, and pharmaceutical companies whose goal is to discover targeted molecular diagnostics and therapeutics. Good data support these studies. *The Alzheimer Conundrum* suggests that efforts such as the Center for Disease Control’s Healthy Brain Initiative will increase our odds of success.

AUTHOR BIO

Jason Karlawish (jason.karlawish@uphs.upenn.edu) is a professor of medicine, medical ethics, and health policy at the University of Pennsylvania, in Philadelphia.