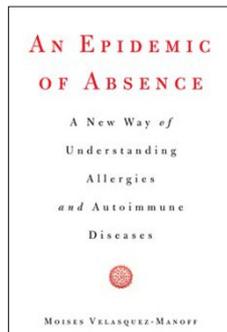


The hygiene hypothesis



An Epidemic of Absence: A New Way of Understanding Allergies and Autoimmune Diseases

Moises Velasquez-Manoff

Scribner, 2012

400 pp., hardcover, \$29.00

ISBN: 1439199388

Reviewed by Paul H Plotz

An Epidemic of Absence is a timely account of the hygiene hypothesis, and it delivers a rich lode of history, epidemiological data, immunological speculation and stories of human behavior. The author, Moises Velasquez-Manoff, was drawn to this subject by his near lifelong burdens of alopecia areata totalis, food allergies and asthma. I am slightly leery of researchers whose principal subject of interest is their own disease, but Velasquez-Manoff is a professional science writer, and the accounts of his own experiences in seeking to overcome his illnesses by self-infecting with helminths provide a compelling frame for his subject. Readers of this journal who have swallowed accounts of fecotherapy and read of respected medical centers carrying out studies of helminth therapy for multiple sclerosis and other diseases will be drawn into the fascinating body of knowledge and the theory that underlie this story.

Velasquez-Manoff describes how the epidemic—the new appearance or rapidly rising incidence of a variety of inflammatory, immune, allergic and autoimmune diseases—might be due to improved general hygiene and water purification; the growth of cities; the decline of family size; and other largely nineteenth-century epidemiological phenomena. The mechanism for this epidemic is postulated to be the removal, or, as in the title, “absence,” of many widespread familiar immunological stimuli, such as worms, which, until they were mostly eliminated from the environment, had been stimulating the regulatory T cells that have a braking effect on adaptive immunity. This tale is amusingly told, though with an unequal weighing of the evidence in which single patients’ stories are told more lovingly and at greater length than epidemiological or immunological observations. Velasquez-Manoff’s knowledge of the breadth of ways by which immune and inflammatory responses to infection are controlled appears incomplete, and his use of important terms such as ‘inflammation’ is quite loose. Some diseases and organisms are subject to deeper analysis: multiple sclerosis, asthma, inflammatory bowel disease, even autism, as well as several worms, *Mycobacterium tuberculosis*, *Helicobacter pylori* and the perennial favorite of immunologists, Epstein-Barr virus. These are

very good choices even when controversial. The historical accounts of the recognition of new diseases are especially well told, and the chapter epigraphs are splendid. Some of the speculation can at times be irritating as it may be based merely on personal histories. But this book can surely expose many readers to a wider view of the hottest topic in biological science, which is stimulating the most exciting observations and human experimentation in my medical lifetime.

Humankind’s exceptionalist view of its place in the world and the wider universe has been shaken by Lucretius’s atomic theory of matter; by Copernicus’s heliocentered solar system; by Darwin’s construction of the origin of species; by Freud’s recognition of the subconscious as a driver of sentient life; by Einstein’s insight into the construction of time and space; by the recognition that our genetic code is shared by essentially all living creatures; and by the discovery that mitochondrial DNA and some somatic DNA moved from microbes into our ancestral eukaryotic cells long ago. The realization that we cannot separate our existence from the microbial world that coats all our surfaces; that we depend on those commensals and recognize many aspects of our lives influenced by them; and that those commensals also depend on us is a huge idea that will forever alter our narcissistic isolation.

The idea that we each consist of a body determined by its own very slowly evolving, genetically encoded DNA is being overtaken by the concept that the body is a superorganism whose fuzzy boundaries, as we now conceive them, include zillions of rapidly dividing and evolving creatures on its internal and external surfaces. The interaction is alive, as bits of the commensals—viruses, microbes, worms and other parasitic forms and their macromolecules—explore and try to penetrate our imagined shield.

The residual narrow view of the role of our adaptive immune system—that it evolved to protect us higher creatures from outside attackers—is now recognized by most as obsolete. Adaptive immunity, with its random generation of variants by means of fragmented genes and their imperfect rejoinings, class switching and other clever devices, its promotion of useful variants and its rejection of useless or harmful variants, is an evolution-like pathway to compete with the faster evolution of microbial commensals. With the help of an early maternal boost, immunity allows us to adapt and evolve in response to our microbial part without a permanent genetic change. Above all, it is offered new to every human generation for establishing communication with the current commensal universe by receiving its messages and sending immune and inflammatory responses.

The daily flow of exciting new observations—epidemiological, molecular, behavioral—connected to this evolving view of the living universe is remarkable. Many of my colleagues are asking great questions about the ways in which changes in our microscopic fellow travelers affect us, or how we affect them. The possibilities seem vast, thrilling and also humbling: bounded not by a smooth, neat, sterile surface but by one that is hairy, flaky, mottled, wrinkled and itchy. Velasquez-Manoff provides an interesting and plausible perspective on this fascinating new world.

COMPETING FINANCIAL INTERESTS

The author declares no competing financial interests.

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