BOOKS: IMMUNOLOGY

Divergent Thinking About Self-Defense

Jonathan Howard

Despite their authors' radically different aspirations, the two approaches to immunology reviewed here have some interesting aspects in common. Both are intended for a broad range of readers and both are works of translation that aim to render their subject, one of the most complex and developed branches of modern biology, into different yet parallel languages. Irun Cohen, professor of immunology at the Weizmann Institute, Israel, has tried to abstract the field so that it can be mapped onto the conceptual structures of cognitive systems and information theory. In contrast, Cedric Mims, emeritus professor of microbiology at St. Guy's Hospital Medical School, London, has tried to simplify immunology so that it can be understood in the language of common speech. Where Cohen draws on the intuitions of a second abstruse discipline to make sense of his own, Mims calls on the everyday experience of the person in the street. Both authors, however, find themselves face to face with the same problem: what may one extract from such a rich brew as modern immunology and dare to represent in another medium as its essence?

Tending Adam's Garden
Evolving the Cognitive Immune Self
by Irun R. Cohen
Academic Press, San Diego, 2000. 286 pp. $49.95, £32.95. ISBN 0-12-178355-3.

The War Within Us
Everyman's Guide to Infection and Immunity
by Cedric Mims
Academic Press, San Diego, 2000. 288 pp. $39.95, $25.95. ISBN 0-12-498251-4.

Here the radically different purposes (and, indeed, skills) of the authors set the books off on divergent tracks. Cohen is judicious, almost to a fault, in stripping the subject bare of all detail extraneous to his elevated purpose. On the other hand, Mims bustles into it with a certain vague briskness, like a nurse in a hospital ward, dispensing packages of good advice (he is very severe on aerosols) and some unpleasant pills of real science whose occasional imprecision perhaps makes them more palatable. It may not be an important criticism—it may even not be a criticism at all—but I doubt very much whether an intelligent alien would recognize these two representations of immunology as depicting the same branch of natural knowledge.

It is, perhaps, unfair after all to force two such different books into such close company. Cohen's *Tending Adam's Garden* is without question a special book, an unusual achievement that makes special demands of attention both on its readers and its reviewers. The same cannot and should not be said of Mims's *The War Within Us*. Mims has written his book as plainly and simply as possible, and it is in this spirit that his account should be assessed. So let me break away from comparison and consider each of the books according to its own light.

Cohen does not want to teach us immunology; rather, he wishes to teach immunologists how to look at their world. Immunologists are interested in signals and in receptors, in individuality and in complexity. Thus, says Cohen, they had better be interested in information theory, evolution, and cognition because, by implication, these other fields have the expertise that immunology needs to understand its own business. By the same token, practitioners of these other fields may be interested in the extension of their conceptual framework to cover novel material.

Immunology is an odd science. The immune system is in a sense an add-on. Unlike cell replication, protein synthesis, or the maintenance of membrane polarity, and unlike the digestive tract, the muscles, or the brain, the immune system is dispensable. Even without an immune system, you could walk and talk, live and love. You could be as tall or as short, as ugly or as handsome as the rest of your genome determines. You could unplug the whole immune system and throw it away, and (for a time) nobody would notice any difference. Indeed, such a life would surely seem better: no asthma, no childhood diabetes, no multiple sclerosis, no graft rejection, none of the diseases caused by the immune system itself. (The proper understanding of these diseases is one of the goals of Cohen's book.) There is, however, a catch: such a tempting life would have to be led inside a sterile bag; otherwise, it would inexorably and quickly end through fatal infection. Death by infectious disease seems somehow banal. Nevertheless, to prevent it the immune system has evolved a complexity that has repeatedly earned it comparison with the brain. And unlike the rest of somatic physiology, immunology has now for a hundred years (since Paul Ehrlich's "side-chain" theory of antibody formation) lived in a conceptual world fizzing with large ideas, ideas of such status that they have twice earned their formulators Nobel Prizes.

In his book, Cohen does not develop a new theory of immunology; *Tending Adam's Garden* is a work of exposition and an attempt at cross-fertilization. It is full of insights and felicitous comparisons and analogies, which this reader found stimulating, memorable, and even occasionally moving. Oddly, for such a work, readers will repeatedly find themselves in almost personal touch with the author. We feel his intimate knowledge of the Talmud as a guide to right action, and we sense almost his physical presence as a man, a husband, and a father in the way he chooses to deliver his ideas. I don't want to quote specific examples from

Sovereign immunity. Pathology caused by immune responses accounts for much of the disease of tuberculosis. Thousands of English children suffering from scrofula (tuberculosis in the throat and neck) were brought to Charles II to be cured by his touch. Mims notes that the royal touch could have greatly boosted the sick child's morale and that those with such tuberculosis more often than not recover on their own.

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the book because taken out of context they will seem naïve or impertinent. But they are not, and they provide a leaven to this otherwise tough and demanding work.

There are some obvious problems with Cohen's book. As an immunologist, I am annoyed when the author reiterates that antibody-combining sites of high affinity are also of high specificity; the opposite is the general case, at least by my definition of specificity. But I would rather take such matters up personally with this humane and intelligent man. A more serious criticism is that Cohen's goal remains elusive. *Tending Adam's Garden* is full of interesting and suggestive notions that are expressed with enviable informality and clarity, but at the end, did I know what Cohen was really trying to do? Is there a falsifiable thesis? I do not think so. Cohen's remarkable book is an essay in interpretation, a personal exploration of possible contacts between disparate worlds. It is perhaps best seen as a manifesto for immunologists. The author is saying, try this way of looking and you will see our field very differently. Although I don't think Cohen has reformulated immunology, it is impossible not to admire the scale and scope of his insights.

These are not the right terms in which to judge or praise Mims's book. *The War Within Us* is a guide to infection and immunity for the general public. Its purpose is clear and also fulfilled. Unsurprisingly, considering Mims's own background, the infection aspects are presented better than the immunity. However, the facts of infectious disease are so breathtaking, so terrible, and so frightening that they have generated what amounts to a modern psychopathology of anxiety. Mims is really excellent here: calm, authoritative, and sensible. But beneath the calm lurks Mims's own more substantially grounded fear of the next great plague, whatever it may be, fuelled by global travel, population density, poverty, and stupidity. *The War Within Us* is an exciting book, despite Mims's ward-sister style. Who can fail to react to the knowledge that a Tanzanian coastal villager may receive 100,000 mosquito bites per year? Or to the affecting fact that Mims's own mother died of puerperal sepsis in 1930? Who is left unmoved by the colossal international effort of unselfish service that finally eliminated smallpox in 1974 and is now set to do the same with polio?

The public, as Mims stresses, is not of one mind over vaccination. For many common diseases, the consensus fails even before it reaches the public domain. I recently had personal experience of this when beginning a brief sabbatical in Paris from my home city of Cologne. To enter the French public school system, all children must be immunized against tuberculosis. On the other hand, in Germany no child is immunized against tuberculosis and a doctor who does so is not covered by malpractice insurance. Compare these two prosperous, adjacent, disease-conscious, public-spirited European countries: in France you must, in Germany you may not. Even here, with one of the oldest and trustiest of immunizations, we are still too close to the frontiers of knowledge to call the game. Those who are prepared to think for themselves on these complicated issues need a good book like Mims's to stimulate their intelligence.

BOOKS: PHYSICS

Explaining Time's Arrow

Jean Bricmont

Fortunato Depero's *Train Born from the Sun* (1924).

Here is a problem that has confused philosophers and physicists from the 19th century to the present. Our most common experience of the world is that time has a certain direction. We are born, grow old, and die; eggs break; liquids mix; and our offices tend to get more disordered—not the other way round. A quantitative characterization of such one-way behavior is encoded in the second law of thermodynamics: the entropy of isolated systems usually increases and never decreases. However, in our most basic and most successful scientific theories, time has no such direction. For any motion that produces these effects, there is another motion obeying the laws of microscopic-scale physics that produces the reversed effect. In other words, the fundamental physical laws are reversible. Although a satisfactory answer to this puzzling state of affairs was offered a long time ago by Ludwig Boltzmann, it is often misunderstood even by physicists. One of the goals of David Albert's *Time and Chance* is to explain Boltzmann's ideas in a very pedagogical manner.

Time and Chance
by David Z. Albert
Harvard University Press, Cambridge, MA, 2001. 186 pp. $29.95, £20.50. ISBN 0-674-00317-9.

In a nutshell, Boltzmann's solution goes as follows: First, we must distinguish between the microstate and the macrostate of a system. The microstate is rather familiar to physicists (in classical physics, for example, it is given by the coordinates and the velocities of all the particles of the system), whereas the macrostate is rather familiar to everybody else (it is composed of the observable regularities like the density, the average distribution of velocities, and similar macroscopic variables). It is easy to demonstrate that a given value of the macrostate corresponds to a very large number of microstates. The equilibrium value of the macrostate is defined as the one that corresponds to the largest number of microstates. And for systems composed of many particles, the difference between the largest number and all others is enormous. The "problem" of convergence to equilibrium is then simple to solve. If a system starts in a microstate corresponding to a nonequilibrium macrostate, it will very likely evolve toward a microstate corresponding to the equilibrium value of the macrostate, simply because there are so many more of the latter.

Objections were raised, even during Boltzmann's day (most notably by Poincaré and Zermelo), against this simple scheme, but they can be easily dealt with. However, the reversibility of the equations of motion leads immediately to a new worry: if physical systems are naturally expected to evolve toward equilibrium in the future, why don't they also do so in the past? We know that they don't, because we remember the past has having been more "ordered" (in the sense of being more out-of-equilibrium) than the present. But our explanation of the tendency of the entropy to increase in the future would lead us to expect the opposite. In other words, we are in the strange situation of being able to explain the future correctly, but not the past.

This puzzle is one of the main subjects discussed by Albert, a philosopher at

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