

BOOK REVIEWS

Activists and the AIDS Business

Against the Odds. The Story of AIDS Drug Development, Politics and Profits. PETER S. ARNO and KARYN L. FEIDEN. HarperCollins, New York, 1992. xx, 314 pp. \$23.

On 21 May 1990, about 1000 demonstrators marched onto the campus of the National Institutes of Health to protest the lack of progress in AIDS research. Their frustration was captured in their chant: "Ten years, one billion dollars, one drug, big deal."

Against the Odds is the story of the people who fought to get drugs to treat AIDS and the often ambivalent responses of those involved in research, regulation, and production. Although much of the history is familiar to the scientific community, the authors offer an updated tale of a new breed of political activist. Peter Arno is a health economist with Montefiore Medical Center and Albert Einstein College of Medicine in New York. Karyn Feiden is a free-lance journalist, known for *Hope and Help for Chronic Fatigue Syndrome*. They ably depict the anger and frustration that swelled up to challenge the traditional pace of research and drug approval policy.

The stories of ACT-UP members illicitly barricading themselves in an office in Burroughs Wellcome headquarters and invading the New York Stock Exchange to protest the price of AZT are wonderfully told. Another telling episode is Terry Sutton's blockade of the Golden Gate Bridge during San Francisco's morning rush hour to protest overly strict exclusion criteria for clinical trials of foscarnet. Avoiding technical analysis, the authors write with a breeziness accessible to the general public. Scientists might be wise to see how things look from the perspective of people in the street.

The central question raised is whether patients are entitled to have access to drugs that offer some hope of ameliorating a virtually fatal disease, even if the safety and effectiveness of such drugs are unknown. In 1979, in *United States v. Rutherford*, the United States Supreme Court said no, finding that even dying cancer patients had no right to use laetrile because it was not approved by the Food and Drug Administration (FDA). The court was concerned that patients would be exploited by purveyors of nostrums, losing the chance for life that orthodox, approved drugs

offered, as well as their money. Not forgotten were the tragedies of the *caveat emptor* era. Reading the statute, the court held that the Food, Drug and Cosmetic Act "makes no special provision for drugs used to treat terminally ill patients."

Two years later AIDS was identified, and a new constituency arose to challenge the protectionist tradition. Where no approved cure exists, it was argued, the patient, not the government, should be free to choose what risks to take. Interestingly, as the authors point out, this was the argument used by the American Medical Association to oppose the 1962 Kefauver amendments to the Food, Drug and Cosmetic Act that required a drug to be effective (as well as safe) before it was licensed for marketing. The AMA lost that battle, but in the late 1980s the FDA began changing its rules to allow AIDS patients to use investigational drugs undergoing clinical trials and to import unapproved drugs from overseas for personal use. More important, the FDA began to speed up its drug approval process. The authors acknowledge that the changes had been advocated by the pharmaceutical industry and were supported by the Reagan administration, with then Vice-President Bush taking the lead. But they seem to believe that it was the AIDS activists that finally persuaded the FDA to act.

When no miracles emerged from the regulatory pipeline, the activists saw that output depended upon input and turned their attention to NIH researchers. They criticized most aspects of clinical trials, including randomization, eligibility criteria, outcome measures, and delay of publication of results until after peer review. Indeed, they challenged the nature of research as an elitist enterprise that sacrificed dying patients to unnecessarily rigid academic standards and personal career goals. The authors often seem to agree with this assessment, giving relatively little weight to counterarguments, such as the need to obtain accurate information to determine which drugs work and which do not. The focus here is on people with AIDS, too often called "desperate," and the need for life-saving treatment.

While scientists were painstakingly trying to decipher HIV, the AIDS community interpreted deliberation and arguments over scientific methods as fruitless delays and evidence of lack of concern for fellow

human beings. Many activists concluded that the scientific community had to be shocked into paying attention to AIDS. This is an unfortunate conclusion because it blames scientists for the inherent difficulty of their work and the lack of support from the highest levels of government.

The authors acknowledge that both the FDA and NIH sometimes have tried to speed up the process of drug approval, but mostly they find grinding bureaucracies mired in outdated habits and suspicious of laypeople. For example, they argue that NIAID's efforts to establish the AIDS Clinical Trial Group (to conduct coordinated trials of investigational AIDS drugs in human subjects) mismanaged and delayed the introduction of aerosolized pentamidine for several years. There is no question that anger is a rational response to the absence of a cure. Whether that absence is the fault of the research and regulatory communities is a closer question.

Whatever the answer, many people with HIV or AIDS sought therapies outside orthodox medical channels. Sometimes they were disappointed. This year several people with AIDS are suing a retired radiologist who touted his own unproven concoction of citrus extracts and ozone called Viroxin as a cure for AIDS, acne, arthritis, chicken pox, and diaper rash, among other afflictions. Injections cost \$300 a month and left some patients with lumps of dead tissue in their buttocks. The doctor, who pleaded guilty to distributing an unlicensed drug and surrendered his medical license, discouraged his AIDS patients from using licensed antiretroviral drugs like AZT. Thus, while some people with AIDS fight for the right to use any experimental medication, others resent being used as "experimental animals."

Whichever position they take, members of the AIDS community are willing to fight for their beliefs. *Against the Odds* argues that the power of the AIDS community will endure and provide a model for others. To the extent that AIDS brought people together to build networks of services and to persuade the FDA and the NIH to become more efficient, that model teaches a valuable lesson—one that has not been missed by victims of other diseases, such as cancer and Alzheimer's disease. The authors also describe changes they view as having been wrought by the AIDS community. Patients have earned a more respected place in the conduct of scientific research. Many scientists are receptive to their participation in designing clinical trials and parallel track. Objections to strict exclusionary criteria, especially those affecting women and intravenous drug users, are being taken more seriously. The community-based research efforts that harness local physicians to study patients in the community have gained a

measure of respectability. Patients may have access to investigational drugs for their own treatment outside clinical trials. The FDA has tried to expedite both testing and approval. All this has made the drug testing process more inclusionary and, arguably, more efficient and has shortened the time between the beginning of clinical trials and new drug approval.

But none of these changes proves that AIDS has revolutionized drug development. The fundamental goals and methods of both FDA and NIH remain essentially the same. And, unfortunately, there remains an element of tokenism in participation by people with AIDS in scientific endeavors. At the International Conference on AIDS held in July 1992 in Amsterdam, for example, most HIV-positive speakers were relegated to unenlightening sessions on policy, law, and ethics.

Arno and Feiden also believe that AIDS activism has made a difference in the pharmaceutical industry. They suggest that because ACT-UP took dramatic actions to protest high drug prices, drug companies are now careful not to price their drugs too high. But one could argue that the industry learned precisely the opposite lesson. When Burroughs Wellcome initially priced AZT at \$10,000 for an average year's supply and got away with it, the industry learned that it could charge whatever the market would bear. The more "desperate" the market, the higher the price. Lyphomed Inc. raised the price of injectable pentamidine as an orphan drug four times as the aerosolized version appeared more effective. Burroughs Wellcome's AZT price decrease, four days after ACT-UP's Wall Street demonstration, also coincided with developing challenges to its patent and threats of congressional hearings. The company might have learned then that a high starting price could later be reduced to garner good publicity and still leave the company with a handsome profit. AZT sales boosted the company's stock price enough that, in July 1992, about 30 percent of its stock was sold for more than \$4 billion. Income from the proceeds, reinvested by the nonprofit Wellcome Trust, should generate about \$187 million for medical research. So far, none of that research is expected to be directed at AIDS. The federal government, which helped develop AZT and subsidizes its purchase for Medicaid patients, has made a substantial financial contribution to British medical research.

It is difficult to find any dramatic change in industry practices yet. The industry has withstood repeated attacks on its prices without ever being forced to disclose its costs of research, development, or manufacturing, its pricing methods, or its profit margin. Since it is industry that ultimately decides whether or not to put new drugs on the market and at what price, it is unclear how the AIDS model

can affect long-term access to new drugs. All of the reforms in government research and regulation will count for naught if no new effective drugs are developed or people cannot afford the drugs that are produced.

The truth may be that very little has changed. What has changed are the expectations of the AIDS community. As the authors note, many activists grew up in an America with "confidence in the miracles of Western medicine." In the early 1980s, with vaccines against poliomyelitis, measles, and other infectious diseases, it was easy to believe that, given enough money and attention, modern science could cure virtually any disease. It took almost a decade of AIDS to shake that faith. Once lost, faith is difficult to restore. But a more realistic faith may result. The more sophisticated students of the AIDS epidemic now recognize that HIV is a nasty, complicated virus that will not yield its secrets easily. Government is no longer seen as the only obstacle to overcoming this dread disease. At the Amsterdam conference, Mark Harrington of ACT-UP asked the right question: "What is the point of streamlining access and approval when the result is merely to replace AZT" with "mediocre, toxic, expensive" drugs?

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Microstructure Revealed

Images of Materials. DAVID B. WILLIAMS, ALAN R. PELTON, and RONALD GRONSKY, Eds. Oxford University Press, New York, 1992. xiv, 379 pp., illus. \$75. From a symposium, Chicago, Sept. 1988.

The systematic analysis of microstructure in materials science began with the study of steels by H. C. Sorby of Sheffield in the 1860s. For decades thereafter, light microscopy was the exclusive means for microstructural analysis. The advent of the transmission electron microscope in the 1930s paved the way for an array of increasingly powerful techniques that use electrons or ion beams for "illumination."

The impact of these techniques can be understood through the remarkable improvements in spatial resolution. The resolution of light microscopy is limited by diffraction to half a wavelength, or about one quarter of a micrometer. In the electron- and ion-beam methods, this limitation is virtually eliminated by either re-

ducing the wavelength of the illuminating beam to sub-angstrom levels or reducing the size of the beam to submicrometer diameters. These methods have now progressed to what might be considered the ultimate resolution of microscopy—the ability to observe and identify individual atoms.

Images of Materials is an exceptional collection of 12 chapters describing several types and techniques of microscopy that are the basis of modern microstructural analysis in materials science. Although each of the topics covered is broad, the authors have generally provided complete introductions, with numerous examples showing the present state of the art. With their extensive references, the chapters also serve as a guide to further information on various aspects of each type of microscopy.

The chapters on transmission electron microscopy by Williams and Vecchio ("Electron diffraction images") and Gronsky ("Atomic-resolution imaging") are outstanding in that they are written and illustrated sufficiently clearly to be informative to the nonspecialist and are detailed enough to be a valuable reference for those experienced electron microscopists who wish to learn about these specialties. Williams and Vecchio's treatment of convergent-beam electron diffraction is particularly welcome as an introduction to the sometimes difficult-to-decipher technical literature on this topic. It describes the diffraction effects due to kinematical and dynamical scattering, which can be used to determine crystal point symmetry and space group from volumes of material as small as 10^{-14} cubic millimeter. Similarly, Gronsky's chapter clearly explains the principles of "phase-contrast" imaging and illustrates the need for image calculation in the interpretation of atomic-resolution micrographs.

All of the chapters are written in a clear style well suited to the nonexpert reader. Topics treated (besides those mentioned above) include light-optical, acoustic, scanning-ion, scanning-tunneling, and atom-probe field-ion microscopies, various specialties of scanning and transmission electron microscopy, and computer enhancement and analysis of micrographs.

A major strength of the book is that it is very well illustrated with excellent reproduction of the micrographs. The numerous images include 77 color plates. One stated goal of the editors is to celebrate "the beauty of the structure of materials that we use in our everyday life," and this book indeed provides a delightful view into the world of materials.

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