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BOOK REVIEW

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Taking aim at Pharma

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Marcia Angell earned her credibility as an articulate and principled critic of medical research during her two decades as editor of the *New England Journal of Medicine* and since. She is not a stranger to supporting unpopular or controversial issues when she believes they are warranted by the data. Her recent publication is clear evidence of her tenacity.

Angell is deeply troubled by the current state of the pharmaceutical industry. Her latest book, *The Truth About the Drug Companies: How They Deceive Us and What to Do About It*, is a stinging indictment of virtually all aspects of 'big pharma.' She accuses the industry of a multitude of sins. In particular, she claims that the pharmaceutical industry manipulates clinical trials and corrupts physicians, politicians and regulators; is anticompetitive and uses deceptive marketing; is not innovative, with most discoveries coming prepackaged through federally funded research; controls and manipulates drug prices, charging whatever the market will bear through anticompetitive behavior; is causing health care costs to spiral upward; and is amongst the most profitable of industries because it develops low-risk 'me too' drugs.

Her book portrays the pharmaceutical industry as a major contributor to our health care dilemma. Indeed, the pharmaceutical industry is facing increasing criticism and financial threats. Developing the blockbuster drugs on which the industry depends for survival is difficult, risky and costly, and Wall Street is unforgiving. Drug costs are rising, and those rising costs are increasingly shifted to the consumer. Political pressures are mounting to control prices and to

minimize pricing disparities between the United States and international markets. The recall of Vioxx, the impounding of the influenza vaccine and the recent disturbing disclosures concerning the withholding of information from clinical trials lend weight to more general concerns about the health of the pharmaceutical industry. What's more, big pharma will face increasing pressure from smaller, more nimble virtual pharmaceutical companies that, with much lower expenses and risks, are capable of bringing selective drugs to market. Nonetheless, when one compares the therapeutic armamentarium today to what was available when I was a medical resident in the late 1960s, one recognizes revolutionary improvements in the treatment of human disease. Many of these advances have come from the pharmaceutical industry. But what about Angell's specific charges? Virtually all have been vigorously contested by the industry's lobby group PhRMA and in two recent articles (*The New Yorker* **80**, 86–91; 2004; Tech Central Station, www.techcentralstation.com/090104F.html).

Angell, however, provides an important perspective, and I strongly agree with her in a number of key areas. I am deeply concerned about the manipulation of clinical trials and the inscrutable relationship between pharma and the for-profit clinical trial industry when it leads to withholding of clinical trial information. I believe there needs to be far greater transparency of clinical trial data. I also agree that the relationship between pharmaceutical marketing and the medical profession needs to be curtailed. Too many physicians rely on pharmaceutical marketing rather than unbiased sources of evidence for their selection of therapeutics and direct-to-consumer advertising has increased the pressure on physicians to compromise. Also, Angell points out several examples of big pharma's unconscionable abuse of patent expirations through marketing and legal manipulation. Physicians should be offended by this abuse and should not write prescriptions for expensive drugs that are no better than generics or over-the-counter equivalents.

Nonetheless, I differ from many of Angell's conclusions. Her anger about the industry's power and influence, in my view, obscures her recognition of significant contributions made by the pharmaceutical industry. For example, she condemns the lack of innovation by big pharma, but she seems not to understand the role of basic research discovery in the actual development of therapeutics. Discovery research creates 'possibilities' for the development of therapeutics, but not therapeutics *per se*. When I was involved in therapeutic development at Genentech in the late 1980s, we evaluated hundreds of exciting discoveries that had therapeutic potential. Even so, the company could develop only a handful of these at any given time because of the costs and lengthy process. Therefore, the choices made and the strategies used were critical to the development of important therapeutics. Competing biotechnology firms had similar choices of discoveries, but most of these companies failed because they did not choose the right ones or could not develop them into useful therapeutics. Drug development certainly requires innovation and is associated with great commercial risks.

I also disagree with Angell's criticism of the synergistic relationship between federally funded academic research and the pharmaceutical industry. Academic institutions are good at discovery research but are not prepared to develop drugs, nor should they be. Furthermore, I do not agree with Angell's criticisms of the US Food and Drug Administration (FDA) as being "big pharma's handmaiden." She criticizes comments from the FDA's leadership supporting the agency's responsibility to facilitate drug development. Her book implies that the only role of the FDA is to protect against dangerous drugs. They must of course do this. To serve the public, however, they must also facilitate the continued flow of useful new therapeutics. Angell also contends that the focus of the pharmaceutical industry is on the bottom line alone, and thus it cannot be trusted. Certainly, any public business is responsible to its shareholders. Enlightened corporations, however, understand that the best way to ensure a positive bottom line over the long run is to deliver important products that serve the public's needs. Certainly, oversight needs to be rigorous. Nonetheless, I do not agree that big industry is necessarily a dark force, incapable of supporting the public good. In my career, largely in academic medicine, I have had the opportunity to work in industry and closely with it. In both arenas, I have been impressed with the quality and commitment of most of the individuals with whom I have worked. Indeed, the focus I have seen in both has been on doing important things to improve health.

Angell's book proposes to "save the pharmaceutical industry" by enhancing drug innovation, strengthening the FDA, improving oversight of clinical trials, increasing competition, diminishing pharma's influence on government, and rationalizing drug prices. The goals are laudable, but some are impractical and others, if implemented, would do the reverse of what she intends by stifling innovation and competition. For example, Angell proposes a governmental entity for "overseeing and administering" clinical trials, which would be performed by academicians under contract. Having overseen a major academic medical center with the nation's largest academic clinical research institute, I can attest that this is an unworkable proposal and, if implemented, would grind drug development to a halt. Industry could not afford to develop drugs, then wait for an academic peer review process to give them access to a queue for clinical trials. Moreover, there is an insufficient clinical trial infrastructure in academic institutions to support the volume of clinical trials needed. She also voices a disdain of 'me too' drugs that is, in my view, overly simplistic. Continued development of antibiotics, adrenergic receptor inhibitors, calcium channel blockers and statins has markedly improved such pharmaceuticals since the initial agents were approved. Moreover, similar drugs are often in development by multiple companies at the same time. Drug development would spin into chaos if the first to market prevented the entry of others that are close behind.

I have tried to understand why Angell and I hold divergent views on important aspects of the pharmaceutical industry, given my deep

respect of her critical mind. The basic difference may be in whether one thinks about the pharmaceutical industry as an appropriate business or as a public utility that should be run by government for the common good. I think Angell supports the latter, whereas I favor the former with the obvious conditions of transparency and oversight. Angell's recommendations for change depend on the view that innovation, risk taking, drive and financial investment will continue unabated in a governmentally run system with highly regulated financial reward. I do not support this concept. Although I agree with many of her concerns, some of her solutions are unworkable.

Angell's book portrays big pharma as the enemy in our health care system. Rather, I agree with Pogo's famous assessment "I have seen the enemy and it is us." Our health care system is in shambles and in danger of collapse. It is inefficient, uncoordinated, inequitable and unaffordable. What is worse, we are capable of doing so much better with the resources at hand. The medical profession, government, the insurers, the public and pharma share in the blame for allowing a system that rewards irrational reimbursement rather than promoting health and preventing disease. This country needs constructive reform of our entire health care system wherein pharma is one part. Now that the election is over, hopefully health care reform will be a high priority, with the aim of enabling more cost-effective approaches, including personalized preventative care. Dr. Angell has written an important book that helps set the stage for a greater debate, but the reader is encouraged to maintain a critical eye.