University of California, Davis

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The Art and Politics of Science (book review)

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venture into polemics on this topic; he simply tells vivid stories of our efforts to make sense out of natural variation. This is beautifully illustrated in his quote from Darwin: "The more I study nature, the more I am impressed with . . . the contrivances and beautiful adaptations slowly acquired" through natural selection, which "transcend in an incomparable degree the contrivances and adaptations which the most fertile imagination of the most imaginative man could suggest with unlimited time at his disposal."

Harry A. Fozzard

University of Chicago
hafozzar@uchicago.edu

The Art and Politics of Science.

By Harold Varmus. New York: Norton, 2009.
Pp. 315. $24.95.

In this autobiography and collection of essays, we learn how Harold Varmus created a life of consequence, enabled by his passions, a competitive streak, a certain quirky social deftness, a sixth sense for navigating political minefields, and a dose of chutzpah. Varmus readily admits that it was prizes (actually the Nobel Prize, although he also won the Lasker and many others) that opened doors for him to the halls of power. While the Nobel provides a public voice, it is the rare laureate who can parlay the media attention into a second career as the successful leader of a public institution and from there on to statesmanship. (Varmus was recently appointed co-chair of President Obama's Council of Advisors on Science and Technology.)

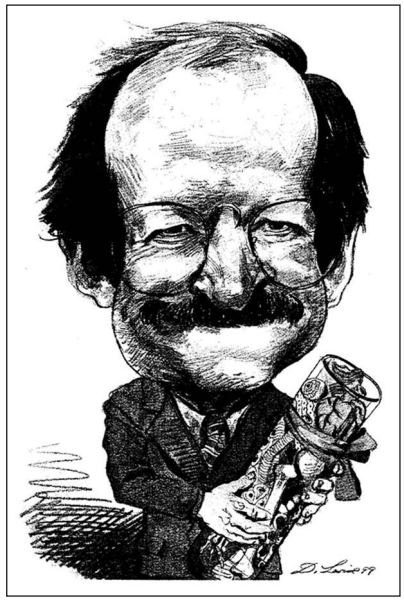
Arguably, ascending to positions of influence in science requires fluid communication skills and proficiency in the social realm as much as creativity in the laboratory. Varmus—who as an undergraduate at Amherst demonstrated a love for the novels of Shaw and Ibsen, served as editor-in-chief of the student newspaper and wrote a thesis on Dickens, and then spent a year in the Ph.D. program in English at Harvard—has easy facility with language. He enjoys lecturing and speaks widely on topics as varied as the genetic basis of cancer and global health. He has become one of the few public intellectuals of the 21st century to emerge from medical science, instead of from the ranks of social science, the arts, or literature.

Varmus also seems to thrive on community and collaboration. These personal qualities no doubt contributed to his success in the laboratory and his easy transition from cloistered University of California, San Francisco (UCSF) professor managing a small research group to visionary leader and public persona. His perspective on scientific teamwork is elaborated in a chapter on "Partnerships in

Science," which we learn from the acknowledgment was included at the suggestion of David Kessler (former FDA Commissioner and UCSF dean), who was apparently moved by Varmus's comments at a birthday celebration for his longtime collaborator J. Michael Bishop. Indeed, the type of collaboration that Bishop and Varmus had is rare in science. The two were drawn together because of common backgrounds and personalities (including a mutual love of words and language) and a shared vision about science. However, the situation is complicated. Varmus admits that during the 14 years he and Bishop shared a laboratory, they seldom discussed science with each other; their interactions mainly occurred during sessions with trainees. Varmus is frank in his disclosure that it was a sense of not being considered Bishop's equal that eventually drove them apart. Of course, ego is a prime motivator in science, and there must be a mechanism for its gratification even in team science. In any case, it was not only the feeling of subordination to Bishop that led Varmus to seek greener pastures. He admits that UCSF had become too comfortable, and he was frustrated by his lack of administrative responsibility.

After being passed over as director of the Whitehead Institute at the Massachusetts Institute of Technology, Varmus jumped at the opportunity to apply for the position of director of the National Institutes of Health (NIH), which he must have known would throw him into a political cauldron. The job became available during the transition to the Clinton administration. The NIH director at the time was Bernadine Healy, who Varmus notes was unpopular because of her "lack of laboratory experience, her corporate approach to 'strategic planning' for the NIH, her allegiance to the Bush-Quayle administration, and her own political ambitions." But it was her skirmishes with members of Congress that led to her tenure being cut short by the incoming administration of President Bill Clinton, a little over two years after she had assumed the director position.

Having been an intramural scientist at the NIH during the Varmus era, I experienced what seemed like a fresh breeze wafting over the campus when Varmus replaced the contentious Healy. A scientist of unquestioned credentials, Varmus was readily accepted as the proper role model for an institution that identifies with the academy and is uneasy in its location within the boundaries of a federal bureaucracy. Motivating and visionary scientific leaders rarely rise up in government. Most high-level managers are therefore recruited from the outside. In fact, Varmus was handpicked by Clinton's newly confirmed Health and Human Services secretary Donna Shalala to rejuvenate the NIH, which as former National Cancer Institute director Richard Klausner is reported to have said "needed a world-class scientist who could exemplify scientific excellence" (Fallows 1999). Facing the inertia of an institution that is comfortably supported by Congress but that does not easily tolerate change, and that offers swift retribution for the political faux pas, new recruits quickly abandon dreams of activism and invariably retreat to service as reliable custodians of the status quo. Given this familiar narrative, it was all the more breathtaking to see Varmus be-



A cartoon accompanying a profile of Varmus by James Fallows in the New Yorker. *The caption reads: "Clinton's greatest legacy may be Varmus's construction of a medical-industrial complex."*

Source: "The New Yorker." Reprinted with permission.

coming deeply engaged in the politically charged scientific issues of the day, such as the ethics of human embryonic stem-cell research, the failure of the developed world to address global health crises including the AIDS and malaria epidemics, and the controversy surrounding the race to sequence the human genome. Moreover, Varmus seemed to thrive and be nourished by this engagement, as if drawn along a path to self-realization. Years later he is still interested in and affected by these issues, as demonstrated by essays on stem cells, global health, and the human genome project that constitute the most successful chapters of this book. (The first half of the book attempts to explain the science of proto-oncogenes that led to the Nobel, but the historical account purportedly aimed at the lay reader is probably too technical for most and fails to successfully convey the unique contributions that Bishop and Varmus made which led to their being singled out for recognition.)

In turning outward at the NIH, Varmus showed himself to be a capable politician who was skillful, on the one hand, at militating Congressional support and, on the other, at proposing compromises to mollify radical political ideologies that would have caused the NIH to veer from its traditionally neutral stance. At the same time, Varmus seemed to relish being at the epicenter of power. He recounts an invitation to a small party at the White House, where he was greeted by Hillary Clinton as a "long-lost friend."

As NIH director, Varmus was serious about promoting excellent science and

creating a productive scientific enterprise. He recruited accomplished leaders from academia and revised the tenure track system for the review and promotion of intramural researchers so that it was closer to that used in elite research universities like UCSF. While moving intramural NIH (the large biomedical research institute mainly located on NIH's Bethesda, Maryland campus) to become more like UCSF, Varmus did little to encourage intramural NIH to differentiate itself. The NIH intramural research program has stable funding, exceptional core facilities, and a cadre of career scientists. Many observers have chided the NIH for failing to leverage its unique intramural resources to address high-risk, long-horizon projects that are not feasible in a university environment. Even today, intramural NIH, which consumes 10 or 11% of the NIH budget, struggles to define its relevance.

Along with a refreshing approach to science management and engagement in the larger societal issues of the day, Varmus paradoxically also brought a healthy relaxed atmosphere to the NIH campus. His tousled California style—thinning but longish hair, rumpled shirt, skewed tie (when he wore one), and slightly frayed jeans—seemed to set the right tone. Despite his informality, Varmus was a successful director in conventional terms. His good relations with Congress, especially with Representative John Porter and Senator Arlen Specter, the chairmen of the appropriations subcommittees, resulted in the initiation of a rapid acceleration in the growth of the NIH appropriation, from $10 billion to nearly $16 billion. Varmus was an effective advocate for basic research. At the same time, he succeeded in laying the plans for a new Clinical Research Center on the NIH campus and promoted clinical research support generally, believing that discoveries in the laboratory had matured to the point where they were ready for practical application.

Varmus chooses to touch only briefly on the nearly catastrophic unintended effects of a decision he made as NIH director that at the time must have seemed almost inconsequential. In an effort to reinvigorate the intramural research program, and in the belief that NIH was losing researchers to universities, he liberalized rules on outside activities so that NIH scientists were given the freedom to consult privately or speak on behalf of industry on the same terms as their colleagues in academia. This led to what were perceived as abuses, with many negative and damaging accounts in the press and a Congressional crackdown that embarrassed the subsequent NIH director. Eventually, a sweeping ban on outside consulting with pharmaceutical and biotechnology companies was imposed. The episode not only brought the NIH unwelcome publicity, but it was distracting and demoralizing to the research staff. Varmus is clearly bitter that he has been blamed for this debacle. He claims his decision was based on a recommendation of the Office of Government Ethics to ease excessive and unfair restrictions imposed by a prior NIH administration. Recriminations aside, we are left with the question: with the benefit of hindsight, should government scien-

tists (or medical school professors for that matter) be permitted outside consulting and, if so, under what terms? Varmus is mute.

Despite the meandering course of Varmus's career, we never believe for a moment that he is guided only by passion. There is ample evidence of thoughtful, at times agonizing, reflection on career strategy (as when he builds a "career decision mobile" in his college dormitory to help decide between graduate school in English, medical school, jobs in journalism, and fellowships in Japan or Norway). Still, what will certainly be his most enduring contribution as NIH director arose from a lightning strike of an idea that transformed him into what could have been branded a quixotic crusader—if it had not captured the public imagination. Thus, the final chapter in this book provides an heretofore untold account of how Varmus set in motion events that have deeply upset the staid world of biomedical publishing and resulted in easier access to the scientific record for researchers and the public.

Varmus wandered into the role of reformer through a chance conversation in 1998 with Patrick Brown, a former postdoctoral fellow, who opened his eyes to the possibilities provided by the Internet for facilitating the distribution of journal publications and enhancing communication among scientists. Once his passions took hold, Varmus penned an idealistic but impractical proposal, in which the NIH would completely reshape the 300-year-old system for science publishing by hosting reviewed and unreviewed journal articles on its Web site. This essay, unceremoniously posted on the NIH director's Web page, caused a firestorm of controversy. The public comments, still memorialized on the NIH Web site, document the enthusiastic support of scientists around the world and the horrified reactions of publishers (and a few scientists, most of whom had ties to professional societies that publish journals). Looking back a decade later, it seems that Varmus's grenade throwing from the NIH director's office will likely succeed in causing a real revolution. On December 26, 2008, Congress passed a bill mandating that all published research supported by funding from the NIH must be made freely accessible to the public on PubMed Central, the successor to Varmus's E-biomed. Moreover, Public Library of Science (PLoS), the publishing company that Varmus started out of frustration when journals refused to contribute their content to E-biomed, now coexists with traditional publishers, and the journals it publishes have achieved respect (although the long-term funding model is still not secure).

As the 20th century came to a close, Varmus ducked out of the political maelstrom to become, on January 1, 2000, head of the Memorial Sloan-Kettering Cancer Center in New York. Prior to his appointment, Varmus had publicly announced that he considered a six-year term to be an appropriate tenure for the NIH director—long enough to implement institutional changes, but not long enough to produce fatigue and a bureaucratic mindset. Varmus acknowledges that government jobs "grind you down" because of the "public exposure they

afford, and the incessant and inevitable conflicts." So perhaps it was fatigue or the wish to remain true to his word, or perhaps he was anticipating that the next president would make a change anyway. Still, there was much unfinished business to be done. It was bewildering for Varmus's tenure to end so abruptly—and the national science dialog may have been diminished because it did. The NIH director's post remained vacant for more than two years, as the Bush administration struggled to find a candidate who shared the White House line on embryonic stem-cell research. Nevertheless, the seeds that Varmus germinated began to mature. PubMed Central was launched in February 2000. In December 2002, PLoS announced it would begin publishing journals. The NIH budget continued to grow apace, in 2003 reaching the doubling promised by Congress five years before. And, construction on the new NIH Clinical Research Center was completed in 2004.

In the acknowledgments, we find that Constance Casey, Varmus's wife and a former newspaper editor, provides the following advice: "Keep them begging for more!" This book covers such a large swath of territory and, like Varmus himself, is so eclectic, that the reader is often unsatiated with respect to detail and motivation. Many of our questions may be answered if we are patient. It is unlikely that this will be the last memoir of the irrepressible Harold Varmus.

Michael A. Rogawski

University of California, Davis School of Medicine
rogawski@ucdavis.edu

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Birth Models That Work.

Edited by Robbie Davis-Floyd, Lesley Barclay, Betty-Anne Daviss, and Jan Tritten. Berkeley: Univ. of California Press, 2009. Pp. 496. $27.50 (paper).

Today in the United States, one third of all pregnant women do not give birth: their babies are cut out by an obstetrician/surgeon through major abdominal surgery—cesarean section. This means that of the 4 million births every year, there are over 1.2 million cesarean sections. The reported maternal mortality rate for the United States is 15 per 100,000 births (the actual rate is unquestionably higher). Since the maternal mortality for cesarean section is over double that for vaginal birth (Hall and Bewley 1999), 240 or 46% of the 520 annual reported maternal deaths are associated with cesarean section. No wonder the U.S. maternal mortality rate is higher than in over 30 other countries.