

Hart's juxtaposition of the experiences of the three groups of women illustrates the ways that reformers' biases influenced the services they developed. In their programs for African American women, for example, health officials chose to implement one of their first health demonstration projects focusing on congenital syphilis because of the pervasive belief that blacks were hypersexual and prone to syphilis. Efforts to get Italian immigrant women to accept the delivery of babies by physicians instead of midwives was driven by health reformers' view of these women as uniquely backward and ignorant. Although Hart finds much to criticize in the top-down approach of health reformers and their racial and class biases, she acknowledges the beneficial effects these programs sometimes had. She also argues for the rational and constructive nature of poor women's health behaviors and practices, which outsiders saw as benighted.

Hart weaves other strands into her central narrative. She describes the evolution of the professions of medicine, public health, nursing, and social work during this period, and the growing significance of statistical analyses conducted by insurance company actuaries such as Louis Dublin that provided an empirical basis and a justification (however flawed) for the programs that were undertaken.

The book's chief strengths are its comparative approach and the variety of primary sources Hart draws upon. In addition to the records of the Department of Health and the Association for Improving the Condition for the Poor, she has consulted patient records from clinics in the affected neighborhoods, the files of other charitable organizations, and census data, and she augments these with cultural and artistic products such as literary works, folklore, and music. She interprets all these sources with a discerning eye, careful to note their biases and limitations.

Building on seminal studies such as Alan Kraut's work on the history of the immigrant experience, Susan L. Smith's analysis of black women's health activism, and Evelyn M. Hammonds's examination of Progressive Era health demonstrations, Hart's book offers important insights into the gendered and racialized notions of health and citizenship that animated public health programs in the early decades of the twentieth century and the attitudes and beliefs of the women who experienced these efforts.

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**Lara V. Marks.** *The Lock and Key of Medicine: Monoclonal Antibodies and the Transformation of Healthcare.* New Haven, Yale University Press, 2015. xxv, 316 pp., illus., \$40.00.

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Forty years ago, in the summer of 1975, César Milstein and Georges Kohler first reported on the production of "monoclonal antibodies" (Mabs) in the lab. At the

time, Britain's National Research Development Corporation (responsible for patenting innovations arising from the Medical Research Council laboratories, wherein Milstein and Kohler worked) failed to "identify any immediate practical applications which could be pursued as a commercial venture" (27). In the summer of 2015, as I write this review, the Food and Drug Administration has just approved a new class of anti-cholesterol medications, PCSK9 inhibitors, Mabs targeted against a protein involved in cholesterol uptake. Technological marvels, the drugs are likewise potential budget-breaking blockbusters, estimated to be priced at \$7,000–\$12,000 per year and reported as quickly in the business literature as in the biomedical literature. How did Mabs get from point A to point B in the span of four decades? In this volume, Lara Marks examines the complex interplay of science and commerce in the making and remaking of magic bullets and their roles.

After a somewhat muddled prehistory of the search for immunological "magic bullets" (it should be noted that antipneumococcal antiserum-based pneumonia control programs were not initiated until the 1930s, rather than the 1920s, and that Macfarlane Burnet garnered the Nobel Prize in 1960 for his role in formulating immunological tolerance, rather than for the development of the clonal selection theory), Marks hits her stride thereafter, extending from the work of Alberto Cambrosio and Peter Keating. Research in support of the clonal selection theory in the 1960s had demonstrated that the immune system's antibody-secreting cellular lymphocytes were monospecific, i.e., that they secreted a single type of antibody generally coinciding with a particular antigen (the lock and key of the book's title). The diverse lymphocytes of immunized animals and humans generate a diverse population of antibodies, even to a single immunogenic challenge, with resulting immune sera historically falling short of pure, uniform magic bullets. But myelomas—cancerous lymphocytes unable to be turned off in nature—served as a model (and substrate) for researchers looking for antibodies of a single specificity; and by 1975, Milstein and Kohler were able to fuse myeloma cells with spleen cells taken from immunized mice to generate an immortal cell line (what would come to be termed a "hybridoma") capable of secreting Mabs against a known antigen.

In the modest, early days of Mabs, Milstein was personally sending out cell lines to researchers while wrestling with the difficult production of such novel biologicals. After a "hesitant start" (to use Marks's term), however, researchers on both sides of the Atlantic were imaginatively exploring their uses. At the bench, they quickly turned to identifying novel cell markers (perhaps most famously, the CD4 antigen on the surface of certain T cells), altering the very characterization of the immune and nervous systems in the process. While the dissection of the immune system would come to play a critical role in confronting the HIV epidemic, more immediately obvious clinical applications of Mabs were likewise apparent. These ranged from their use in purifying such similarly emerging biologicals as recombinant interferon, to their use in blood typing, in identifying (and standardizing the measurement of) novel tumor markers like PSA, CEA, and CA-125, and, as millions around the world would come to appreciate in the comfort of their home, in the measurement

of HCG and hence pregnancy determination. But the holy grail of magic bullets was their therapeutic use, and this entailed engineering difficulties of scaling up the production of such biologicals, as well as eventually rendering them less recognizable by the human immune system and hence less apt to cause unwanted side effects. From a modest beginning in 1986 with the approval of Orthoclone to prevent the rejection of kidney transplants, biotechnology start-ups, at times working with established firms, began from the late 1990s onward to generate the series of blockbuster Mabs—Remicaide (infliximab), Rituxan (rituximab), Herceptin (trastuzumab), Humira (adalimumab), etc.—that have transformed clinical practice (especially gastroenterology, oncology, and rheumatology) and yielded billions of dollars in revenue for their companies.

It is in tracing this relationship among the lab, clinic, and industry that Marks' book—bolstered by dozens of interviews and novel archival material—is most valuable. We see the humble beginnings of the monoclonal antibody industry in David Murray's long-forgotten Sera-lab, distributing cell lines (Milstein's, initially) to researchers by the late 1970s. We see the difficult decisions of start-ups like Centocor and Hybritech regarding what to invest in, how to engage the regulatory system, and whether to partner with existing pharmaceutical giants, all the while hoping to secure enough venture capital to bring their products to market. The origins and early years of such an industry (Sera-lab's advertisements had to remind purchasers to "remember that monoclonal means the same antibody against the same determinant every time," while Hybritech was started with a \$300,000 investment), just over the historical horizon, are all the more striking in the context of the massive monoclonal industry that would follow.

My primary critique is that while Marks briefly examines the high costs of contemporary therapeutic Mabs and the consequences—both scientifically and with respect to public health—of the multiplicity of patents pervading a technology initially considered unworthy of a patent, still more examination of the tension among the scientific, public health, and commercial aspects of the story is in order. Centocor's 60 percent profit margin in 1998 is reported (212) without any direct discussion of the consequent cost of such health products to consumers; rather, the admittedly fascinating fates of the biotechnology companies themselves tend to obscure the problematic financing and distribution of such blockbuster Mabs. This is likely not an issue that will go away soon. While the transformation of medicine ushered in by Mabs has indeed been a "quiet revolution" (to use Marks' term again), it generates more public attention and discussion all the time. We are fortunate, though, to have Marks' recounting to help us appreciate and engage with such a transformation.

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