Analyzing and labeling evolution in modern drug therapy

Jeremy Greene, Flurin Condrau, and Elizabeth Watkins (eds):
**Therapeutic revolutions: pharmaceuticals and social change in the
twentieth century. Chicago: University of Chicago Press, 2016, 321 pp,
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The eleven essays in *Therapeutic Revolutions* reexamine drug therapeutics in the twentieth century from a variety of historical perspectives and analytical approaches, to consider locations, populations, institutions, public health impact, and other areas. Their overall interest is to see what was really so revolutionary about that expansion of the inventory of drugs in this era, if indeed anything was. The chapters do more than acknowledge improvements in patient care and perhaps even an evolution in treatments. Still, the rather uniform conclusion, despite the traditional sense of a golden age marked by the triumphal march of chemotherapy, is that the classic vision of a twentieth-century revolution in therapeutics needs to be a bit more nuanced. That in itself of course is not new, as Charles Rosenberg's contribution to close the book reminds us. However, the way each contributor addresses the topic of therapeutic revolution is both fresh (though for many drawn from their previous work) and compelling.

Among the better crafted essays in the book is Scott Podolsky and Anne Kveim Lie's "Futures and Their Uses: Antibiotics and Therapeutic Revolutions," which addresses the revolution in antibiotics, but not necessarily the way that Henry Welch would have. Because of Welch and others, there were considerable expectations for antibiotics in the future. However, as industry continued to develop—and get approval for—fixed combinations of antibiotics of questionable merit, much less safety, a cadre of therapeutic reformers including Maxwell Finland pressed for more rational therapeutics. A massive National Academy of Sciences advisory appraisal

The views expressed here are those of the author, and not necessarily those of the FDA.

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of these and many other drugs gave rise to a post-Welch FDA that systematically removed such irrational combinations from the market. Also, antibiotic abandon started early in their history. The authors deftly portray the rise and impact of antibiotic resistance, leading, as the authors ironically point out, to efforts to incentivize industry to reignite the antibiotic pipeline.

In “Reconceiving the Pill: From Revolutionary Therapeutic to Lifestyle Drug,” Elizabeth Watkins explores the shift that the oral contraceptive made “from revolutionary to commonplace” (44). Tracking its quick rise to dominate the market in birth control, a tumbling of its popularity following the news of its association with blood clots, to a reemergence in the treatment of acne, menstrual interruption, and other uses, Watkins notes the industry’s decision to focus marketing more on the oral contraceptive’s value as a lifestyle product—like so many others on the market toward the century’s end.

Nicolas Henckes addresses the concept of a revolutionary role for neuroleptics such as chlorpromazine in “Magic Bullet in the Head? Psychiatric Revolutions and Their Aftermath,” where he interrogates the propagation of this concept by pharmaceutical companies, as well as the role of diagnostic standards and deinstitutionalization in psychiatric care. That the field itself was in a state of some turmoil, both among professionals and between practitioners and patients and their representatives, factored into the embrace or abandonment of neuroleptics. And the author is probably right that, “of all the therapeutic revolutions of the postwar era, the neuroleptic revolution was perhaps the most controversial, if not the most consequential” (87).

In “Revolutionary Markets? Approaching Therapeutic Innovation and Change through the Lens of West German IMS Health Data, 1959-1980,” Nils Kessel and Christian Bonah look in detail at drug market data. They start from a comment made by the eminent clinical pharmacologist Louis Lasagna about the revolutionary impact of antipsychotics, antihypertensives, and other mid-century developments that constituted a “veritable pharmacotherapeutic revolution” (97) to consider whether actual drug distribution supported this sense of revolutionary change. They make a strong argument that overall, well-established ‘legacy’ drugs made up a substantial proportion of prescription drugs dispensed and over-the-counter drugs purchased compared to revolutionary medicines, especially those used in psychopharmacology and in cardiovascular diseases.

Disease as the focus of alleged revolutionary therapeutic changes is the analytical approach used by Janina Kehr and Flurin Condrau in “Recurring Revolutions? Tuberculosis Treatments in the Era of Antibiotics.” That streptomycin’s discovery was met with “panic[ked] requests for the drug” (133) probably was not surprising considering the long- and short-term experiences with sanatoria and tuberculin, but even streptomycin had its limits, until coupled with isoniazid and PAS. The success of this regimen bred complacency in Europe and North America according to the authors, until the emergence of untreatable resistant forms developed, prompting long overdue attention and research support.

Jeremy Greene’s “Pharmaceutical Geographies: Mapping the Boundaries of the Therapeutic Revolution” investigates whether a therapeutic revolution is really revolutionary if its benefits are comparatively limited in space. This is applied both

locally and globally. Sen. Estes Kefauver's hearings clarified the former for the American public, while Walsh McDermott trumpeted how the rest of the world could and should benefit from therapeutic progress. In the wake of a 1979 meeting brokered by Sen. Edward Kennedy to provide key pharmaceuticals for developing countries, the World Health Organization moved to promote an essential medicines programs for developing nations, but implementation met several roadblocks. One could have expected more attention to be given to the President's Emergency Plan for AIDS Relief (PEPFAR), the program to provide antiretrovirals around the world, particularly in African nations. Nevertheless, Greene's point is well made and documented, that a therapeutic revolution is only as realistic as its ability to effect changes regardless of space.

Paul Farmer, Matthew Basilio, and Luke Messac revisit Thomas McKeown's take on the role of medical intervention and population health in "After McKeown: The Changing Roles of Biomedicine, Public Health, and Economic Growth in Mortality Declines." Their analysis includes consideration of how McKeown's ideas have fared considering the impact of such major public health measures as mass oral rehydration therapy and widespread provision of antiretroviral therapy. The problematical path of therapeutics in Botswana is among the developments traced by Julie Livingston in "Chemotherapy in the Shadow of Antiretrovirals: The Ambiguities of Hope as Seen in an African Cancer Ward." She focuses on the aftereffects of a long circuit that began with the marshaling of antibiotics to bring rampant tuberculosis under control in the 1970s, only to see the disease reignite with the HIV/AIDS crisis. And when antiretrovirals eventually helped reign in HIV, starting in the early 2000s, Botswana—with an adult HIV morbidity rate of 25 percent—witnessed an epidemic of virus-connected cancers, a consequence of suppressed immune systems.

Kristin Peterson's essay, "Volatility, Speculation, and Therapeutic Revolutions in Nigerian Drug Markets," expands on the issue of troublesome or nonexistent access to powerful new drugs, which other chapters address as well. Although, from the 1950s on, several large pharmaceutical manufacturers established a strong presence in Nigeria—a major distribution point for much of West and Central Africa—brand-name drugs dried up in the economic downturn of the 1980s. The end result was a market rife with counterfeits. Taking up this volume's theme, the author notes: "If there was any therapeutic revolution to be found in Nigerian drug markets in the aftermath of brand-name industry abandonment, it was innovation in new ways to fake drugs, and not the realization of new and much-needed therapeutics." (239)

In "Therapeutic Evolution or Revolution? Metaphors and Their Consequences," David S. Jones takes a much closer look at how evolution might be applied to the therapeutic developments of the twentieth century, borrowing from evolutionary biology analytical approaches such as niche, fitness, competition, taxonomy, and so on. This approach works better for some perspectives, but less so for others (such as "fitness"). Finally, Charles Rosenberg, whose work on therapeutic revolutions in the 1970s inspired this volume, reminds us that characterizing change involving therapeutics must take much more into account than new drugs, such as the various different choices that have an impact on health, and the economic pressures to prop up a firm's portfolio. Efficacy itself, he argues, is individualized and socialized, not

just a thing determined by a properly conducted randomized controlled clinical trial (RCT).

Therapeutic Revolutions sheds light on the many different ways that we can consider the drug-based therapeutic developments of the past. That the therapeutic armamentarium expanded substantially from about mid-century forward cannot be denied. But the issue in this volume is whether or not that expansion was revolutionary. As several essays point out, that depended on, for example, where you lived and the nature of a pharmaceutical's impact on disease. Also, it is worth knowing the extent to which these new medicines were actually taking the place of older drugs. It would have been helpful to learn more about how law and regulation have factored into this discussion, particularly given the risk–benefit calculus that is supposed to figure so prominently in allowing a medicine to be marketed. And had the timing been different, it would have been interesting to see some discussion of COVID-19, especially with respect to science, RCTs, and concerns about political expediency, although these questions no doubt will be fleshed out in many forthcoming volumes. From this one, the reader will take away valuable lessons on the many ways to look at and frame therapeutic change.

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