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Vol. 6, No. 10, October 2010 "Can You Handle the Truth?"

"The Progress of Experiment: Science and Therapeutic Reform in the United States: 1900-1990"

Harry M. Marks, 1997, 258 pages, Cambridge University Press, $34.99

Review by Norman M. Goldfarb

"The Progress of Experiment: Science and Therapeutic Reform in the United States: 1900-1990" explains the origins of clinical research in the United States and how it has evolved into an indispensible foundation for medical care. It also explains why the Food & Drug Administration controls the marketing and labeling of drugs but not how physicians prescribe them.

The book consists of nine chapters:

- Introduction
- A rational therapeutics
- Memories of underdevelopment: Therapeutic research in the United States, 1900-1935
- Playing it safe: The Federal Food, Drug and Cosmetic Act of 1938
- War and peace
- Managing chance: Statistics and therapeutic experiments, 1950-1960
- You gotta have heart
- Anatomy of a controversy: The University Group Diabetes Program study
- The dreams of reason: Retrospect and prospect

Prior to the 20th century, medical science was largely anecdotal. Two-hundred years ago, anatomy lectures still relied on the teachings of Galen, a remarkable scientist in the year 162, despite his belief that the heart operates through a sucking action and nerves consist of hollow tubes. Most medicinal treatments were placebos because they were simply ineffective, if not harmful. George Washington died after prominent physicians removed about 25% of his blood to treat pneumonia.

Medical reformers concluded that a more scientific approach was needed. Their theory was that physicians would improve their practices by relying on a growing body of scientific knowledge. This theory required two elements: First, that scientific knowledge could be created and, second, that practicing physicians would rely on it. Both of these elements proved to be more challenging than expected.

For example, "collective investigations" from about 1860 to 1950 compiled observations from numerous physicians in democratic attempts to answer medical questions. Unfortunately, it was impractical to draw many useful conclusions from the wide variety of data that was collected.

In 1906, the American Medical Association established the Council on Pharmacy and Chemistry to evaluate therapeutic claims by manufacturers. Laboratory and animal experiments provided fairly solid, but limited, data. Carefully designed human experiments were almost unknown, so the Council recruited expert clinical observers, each with his or her own series of clinical experiences…and opinions. The elite experts did not do much better than the democratic masses, for the simple reason that the data were inadequate.

It was not until the advent of multi-site, double-blinded, randomized clinical trials in the 1950s that clinical research gained its footing. The fundamental insight was that randomization made the statistics work and, with the help of double-blinding, minimized the role of investigator biases, intentional or otherwise. Previously, chance (randomization) had been thought of as the enemy of scientific progress because it confounded the logical progression from treatment to cure. Minimizing chance was considered a much better idea but inevitably introduced bias.

Randomization and double-blinding were not intuitive concepts for many physicians. “Biological complexity and clinical individuation were the stock-in-trade of specialists in chronic disease, whose authority rested on their claim to formulate complex, unquantifiable judgments about the myriad factors that determined why one patient responded to treatment and another did not.” Each patient is another step in the continuing process of experimentation that enables physicians to build their expertise. Closing one’s eyes (blinding) and drawing straws (randomization) is a very different approach.

Nevertheless, once randomized clinical trials were firmly established, the body of knowledge grew rapidly. The reformers’ first element was in place: scientific knowledge was being created. However, not all this knowledge proved useful to the medical practitioner. The problem has changed over the past 50 years from a shortage of scientific findings to an excess of often conflicting and confusing findings with unclear significance for the patient at hand. Nevertheless, standard therapies 20 years ago are now known to be useless or harmful. The physician may still have difficult choices to make, but the choices are generally better.

The reformers’ second element, that practicing physicians would rely on scientific knowledge, has been partially accomplished, but recent public policy debates about clinical practice guidelines make it clear that many physicians still trust their personal experience over scientific findings. Ask any pharmacist whether he or she ever fills prescriptions for obsolete medications.

The book is available in bookstores.

Reviewer

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