

# How Do We Know When a Medication Works?

**PRIOR TO THE 19TH CENTURY MEDICINE WAS A STAGNANT ART** punctuated occasionally by evidence-based insights. Certainly medicine brought comfort to its patients; but rarely were medicine's therapeutic interventions responsible for the cure.

Science demands, amongst other strictures, an atmosphere of complete objectivity and relentless skepticism. Consider the following 15th century scenario: A patient seeks help because of an array of symptoms. Certain interventions are then prescribed including medications, changes in lifestyle, perhaps even a surgical procedure. And after some days the patient declares himself better.

May this 15th century physician now claim that his efforts effected the cure? Perhaps, but had this same physician been consulted by another patient (same age, same gender, same symptoms) and rather than intervene the physician had adopted a prudent waiting attitude; and after a week, the patient was felt to be improved, indeed, as improved as the treated patient. This physician, proud of his innate honesty, now suspects that his course of treatment was at best irrelevant and that the first patient's recovery was ascribable to causes other than his efforts. But the realities of medicine, centuries ago, did not allow for planned clinical experiments. Each new patient was a mystery unto himself and it was not in the physician's thinking to undertake extensive field trials or question the centuries-old therapies that he had used.

Historians regard the 19th century as pivotal in the evolution of modern medicine. A number of forces conjoined during that century to propel the art of medicine into the domain of the sciences.

The 19th century beheld the development of a host of diagnostic instruments, many portable, allowing the physician to extract objective data defining the functioning of his patient's body. These instruments included the thermometer to measure body heat, blood pressure contrivances to determine the pressure within the patient's arteries, ophthalmoscopes and otoscopes to view the interior of the sense organs, stethoscopes to evaluate cardiac contractions and discern pulmonary functions; and by the opening decades of this past century, the employment of X-rays to disclose the pathological secrets of the body.

In parallel with these diagnostic advances came the clinical laboratory to inform the physician about the biochemical status of the patient's body fluids. And the pathologist, aided by the microscope, could now announce the nature and prognosis of tissues removed surgically.

Medical education had been essentially an apprenticeship experience until the 20th century. An eager student might work for years as a physician's assistant. And after an ill-defined interval, he might then begin his own independent practice perhaps after some qualifying examination conducted by a guild of practitioners. Apprenticeship standards were loose, baccalaureate and university-based medical education rare and state governmental control of medical licensure inconsistent.

And the problem of how to know whether a particular treatment was effective or whether the cure was merely lucky happenstance? Only when field trials were planned and undertaken could such questions be answered. And the 18th and 19th century witnessed a number of such deliberate experiments.

Consider the vexatious problem of scurvy, a mysterious disease that killed more sailors than the combined casualties of naval warfare. Many empiric remedies had been devised over the centuries but it required a British Navy physician, James Lind (1716–1794) to devise a test to determine, with confidence, that lime juice prevented scurvy. He maintained one shipload of sailors on their customary diet with no fresh vegetables; and another ship's company with the same limited diet but now supplemented by a daily dose of lime juice. Those receiving lime juice remained free of scurvy; and thus, the British Navy (the Limies) continued to rule the 18th and 19th century high seas.

The efficacy of the newly devised vaccine against smallpox was also questioned; and so a similar field test was begun in East Boston on May 31, 1802. A temporary hospital was erected on Noddle's Island housing 13 boys who had previously received the Jenner vaccine and two who had not. All were then deliberately exposed to smallpox pus and only the two unvaccinated boys developed smallpox. The vaccination procedure was declared a success by the supervising committee (headed by a local business man named Paul Revere.) The morality of deliberately exposing humans to a deadly pathogen was left for the physicians of future centuries to ponder upon.

The 19th century was the turning point for the profession of medicine, witnessing the development of effective vaccines against smallpox, rabies and other pestilences; the development of purposeful diagnostic instruments; the standardization of medical education; and the increasing employment of field tests to determine the efficacy of new therapies. The 20th century saw yet further advances in these components of rational medicine as well as the emergence of a parallel discipline called medical ethics to protect the rights of those humans volunteering for field tests.

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## Disclosure of Financial Interests

The author and his spouse/significant other have no financial interests to disclose.

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