

SPECIAL ARTICLE

EXPERIMENT VERSUS AUTHORITY*

James Lind and Benjamin Rush

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IT is generally agreed today that the advent of the controlled clinical trial has been one of the most notable advances in modern medical practice. The type of trial that has evolved over the past 25 years is recognized as an essential part of the clinical evaluation of remedies.¹ There is increasing interest in evaluating the effects of surgical operations, as well as drugs, by the method of a controlled trial. It has become apparent that the only way to separate the effects of most types of therapy from those of patient selection is by a study in which patients are assigned at random to various modes of treatment. The general acceptance in recent years of the role of the statistical approach in clinical science is due in large measure to the work of Bradford Hill, who represents another example of the great debt that medicine owes to pioneers who were not physicians, such as Louis Pasteur, W. T. G. Morton and Florence Nightingale.

It is chastening to recall that the value of the controlled clinical trial was not generally accepted until almost the middle of the twentieth century. Yet as far back as the eighteenth century, two classic examples existed that demonstrated both the importance of proper controls and the dangers of neglecting them. James Lind and Benjamin Rush each described the treatment of an important disease of their day — namely, scurvy and yellow fever. Whereas Lind's work stands as an early model for the value of a controlled clinical experiment, that of Rush vividly illustrates the danger of authority and "revealed" concepts.

In his lifetime, Benjamin Rush (1745-1813) was by far the more famous physician of the two. A signer of the Declaration of Independence, he had a distinguished medical career, and was one of the best known physicians in the United States. His account of the terrible yellow-fever epidemic that afflicted Philadelphia in 1793 is well known.^{2,3} He decided, as a result of his experience in treating patients, that yellow fever must be treated by vigorous purging and copious bleeding. His methods are best described in his own words:

As soon as you are affected, (whether by *night* or day) with a pain in the head, or back, sickness at stomach, chills or fever; more especially, if those symptoms be accompanied by a redness, or faint yellowness in the eyes, take one of the powders in a little sugar and water, every six hours, until *they* produce four or five *large* evacuations

from the bowels — drink plentifully of water gruel, or barley water, or chicken water, or any other mild drink that is agreeable, to assist the operation of the physic. It will be proper to lie in bed while the medicine is operating; by which means a plentiful sweat will be more easily brought on. After the bowels are *thoroughly* cleansed, if the pulse be *full* or *tense*, eight or ten ounces of blood should be taken from the arm, and *more*, if the tension or fulness of the pulse should continue. Balm tea, toast and water, lemonade, tamarind water, weak camomile tea, or barley water should be drunk during this state of the disorder — and the bowels should be kept constantly opened, either by another powder, or by small doses of cremor tartar, or cooling salts, or by common opening glysters; but if the pulse should become *weak* and *low* after the bowels are cleansed, infusions of camomile and snake-root in water, elixir of vitriol, and laudanum; also wine and water, or wine, punch, and porter should be given, and the bark either in infusion in water or in substance, may be administered in the intermission of the fever. Blisters may likewise be applied to the sides, neck, or head in this state of disorder, and the lower limbs may be wrapped up in flannels wetted in hot vinegar or water.⁴

Of more importance than the details of Rush's treatment, which differed little from that of many eighteenth-century physicians, was his fervent approach to therapy. The following passage illustrates his convictions regarding the value of his treatment:

I began by drawing a small quantity at a time. The appearance of the blood, and its effects upon the system, satisfied me of its safety and efficacy. Never before did I experience such sublime joy as I now felt in contemplating the success of my remedies. It repaid me for all the toils and studies of my life. The conquest of this formidable disease, was not the effect of an accident, nor of the application of a single remedy; but, it was the triumph of a principle in medicine. The reader will not wonder at this joyful state of my mind when I add a short extract from my note book, dated the 10th. of September, "Thank God!" Out of one hundred patients, whom I have visited, or prescribed for, this day, I have lost none.⁴

Rush was utterly convinced that he was benefiting his patients, and the attacks of some doctors on his methods only made him more assertive. The proper treatment of yellow fever had been revealed, and the idea of putting his theories to any form of test does not seem to have occurred to him. Not only did he bleed and purge his patients, he treated himself with the same regimen when he in turn contracted the disease. What a tragic picture Benjamin Rush makes in that long, hot, Philadelphia summer of 1793! Staying behind when others had fled the city, heroically treating thousands of patients, while losing his sister and three of his apprentices from the disease, Rush presented in many ways the figure of the devoted physician struggling to cope with a dreadful epidemic. Yet,

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how misguided were his efforts in reality, how baneful his influence, and how dangerous his certainty!

The work of James Lind (1716-1794) makes an interesting contrast to that of Rush. Like Rush, Lind was an Edinburgh graduate, and at the time of his classic observations on the treatment of scurvy, he was an obscure surgeon in the Royal Navy. His *Treatise of the Scurvy*⁵ published in Edinburgh in 1753, ". . . through its presentation of the subject, with its devastating criticism of superstition and muddled thinking, its insistence on careful observation and controlled experiment, its rigid reliance on facts and its logical interpretation of them . . . became one of the great medical classics of all time."⁶ Lind's account of his experiment is as follows:

On the 20th of *May*, 1747, I took twelve patients in the scurvy, on board the *Salisbury* at sea. Their cases were as similar as I could have them. They all in general had putrid gums, the spots and lassitude, with weakness of their knees. They lay together in one place, being a proper apartment for the sick in the forehold; and had one diet common to all, *viz.* water-gruel sweetened with sugar in the morning; fresh mutton-broth often times for dinner; at other times puddings, boiled biscuit with sugar, etc.; and for supper, barley and raisins, rice and currants, sago and wine, or the like. Two of these were ordered each a quart of cyder a-day. Two others took twenty-five gutts of *elixir vitriol* three times a-day, upon an empty stomach; using a gargle strongly acidulated with it for their mouths. Two others took two spoonfuls of vinegar three times a-day, upon an empty stomach; having their gruels and their other food well acidulated with it, as also the gargle for their mouth. Two of the worst patients, with the tendons in the ham rigid, (a symptom none of the rest had), were put under a course of sea-water. Of this they drank half a pint every day, and sometimes more or less as it operated, by way of gentle physic. Two others had each two oranges and one lemon given them every day. These they eat with greediness, at different times, upon an empty stomach. They continued but six days under this course, having consumed the quantity that could be spared. The two remaining patients, took the bigness of a nutmeg three times a-day, of an electuary recommended by an hospital-surgeon, made of garlic, mustard-seed, *rad. raphan.* balsam of *Peru*, and gum myrrh; using for common drink, barley-water well acidulated with tamarinds; by a decoction of which, with the addition of *cremor tartar* they were gently purged three or four times during the course.

The consequence was, that the most sudden and visible good effects were perceived from the use of the oranges and lemons; one of those who had taken them, being at the end of six days fit for duty. The spots were not indeed at that time quite off his body, nor his gums sound; but without any other medicine, than a gargarism of *elixir vitriol*, he became quite healthy before we came into *Plymouth*, which was on the 16th. of *June*. The other was the best recovered of any in his condition; and being now deemed pretty well, was appointed nurse to the rest of the sick.⁵

The treatment of scurvy by oranges and lemons is well known to have been established by Lind. What is perhaps less well known is that Lind's treatise represents the first deliberately planned controlled therapeutic trial ever undertaken. As a result of his work, an order enjoining the use of fruit juice

throughout the Royal Navy was issued in 1795.⁷ The daily allowance of lemon juice (an ounce per man after the sixth week at sea) was just enough to prevent open scurvy. The word "limey" to describe an Englishman dates from the naval practice of this time. It is a sad commentary that it took 40 years for the result of Lind's work to be applied, even to sailors in the Royal Navy. It was well into the nineteenth century before measures to prevent scurvy were more generally applied. It has been said, however, that the application of Lind's teaching doubled the effective fighting force of the Navy at sea during the Napoleonic Wars.⁸

What Lind had the foresight to perceive, and what Rush so signally did not, was that the only way to evaluate a new remedy is to compare it *simultaneously* with other accepted remedies, in comparable patients. Admittedly, Lind's task was easier than Rush's, for a man-of-war at sea is obviously a more controllable environment than a panicked city. But Lind in effect admitted that he did not know how to treat scurvy, and therefore conducted an experiment. Rush *knew* how to treat yellow fever, and refused to consider that his methods might be mistaken. Lind was an unknown naval surgeon, and it took many years before the importance of his work was fully appreciated. In contrast, Rush was already a well known and respected physician, and his fame immediately attracted innumerable patients during the Philadelphia epidemic, all of whom were duly "bled and purged."

It might be thought that this footnote to medical history has little contemporary relevance. However, a perusal of current medical journals shows readily that over 200 years after Lind conducted his controlled trial "on board the *Salisbury* at sea," new remedies are still being evaluated without concurrent controls. There need be no division between clinical and scientific medicine if we are willing to admit our ignorance regarding therapeutic measures, and are prepared to test our hypotheses properly.⁹ Santayana's comment seems an appropriate conclusion: "Those who cannot remember the past are condemned to repeat it."

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