

Birth of the clinical trial

Roy Porter

Quantification and the Quest for Medical Certainty. By J. Rosser Matthews. Princeton University Press: 1995. Pp. 195 \$39.50, £32.

Is medicine an art or a science? This was long a scholastic debate, with the weight of authority tending to come down in favour of the former — had not the very first of Hippocrates' aphorisms begun *ars longa vita brevis*? The issue was opened up again during the seventeenth-century scientific revolution, when progressive physicians attempted to develop iatromathematics. Yet such numerical medicine made but halting progress in a medical world dominated by clinicians whose prestige hinged on 'clinical judgement' grounded in vast but essentially personal wisdom.

As Dr Matthews recognizes in a perceptive book all the better for its brevity, while the relations between medicine and mathematics were long mooted, it was in the early nineteenth century that the balance finally tipped in favour of their marriage. A changing intellectual climate played its part. Auguste Comte's fashionable positivism offered a vision of a social science based on physical laws like any natural science, while Adolphe Quetelet was pioneering his challenging new statistical concept: average man. Objections that man could not be studied like molecules were pooh-pooed as antediluvian.

Within medicine proper, it was the French hospital environment that kindled the new fascination with quantification. Bursting with the expendable poor, the immense Paris hospitals became, in effect, great laboratories of the new scientific gaze created by pathological anatomy.

Reflecting the mathematician Poisson's notion of the 'law of large numbers' — an underwriting of probability theory — the physician Pierre Louis began systematically to tabulate medical events. Was bloodletting a beneficial therapy in diseases such as typhoid or pneumonitis? Don't rely on personal judgement, declared Louis, collect the data. He did, and found, contrary to orthodoxy, that patients subjected to venesection had a notably worse prognosis.

Louis's 'numerical method' inevitably sparked fierce controversy. Many clinicians, particularly the Montpellier professor Risueño d'Amador, turned on him with all the predictable (and not invalid) objections: no two cases are alike; reductionism ignores individual differences; clinical judgement is threatened by number-crunching. Matthews skilfully charts the disputes between Louis and his adversaries, and shows how ideas developed by Louis within pathology were later to lend

support to Claude Bernard's physiology. Bernard's aim of determining normal metabolic function implied significant assumptions about statistical probability and standard variation. He was in no doubt: "medicine is a science and not an art".

At a time when the tabulation of vital statistics was becoming routine in public health and state medicine, the Louis-Risueño d'Amador match was then, in effect, replayed on various national pitches, notably by Gustav Radicke and Karl Vierordt in Germany in the 1850s. In his most fascinating chapter, Matthews explores the joust in early twentieth-century Britain between the leading bacteriologist Almroth Wright and the pioneering biometricians Karl Pearson and Major Greenwood. In his own way Wright was a staunch progressive, full of faith in laboratory science, but when his immunological claims were challenged by statisticians he allowed himself to be manoeuvred into the fogeyish corner of declaring that he didn't understand them, but knew they must be misleading, and that he wanted nothing to do with them (similar things, one suspects, were being said about Cézanne and Schoenberg).

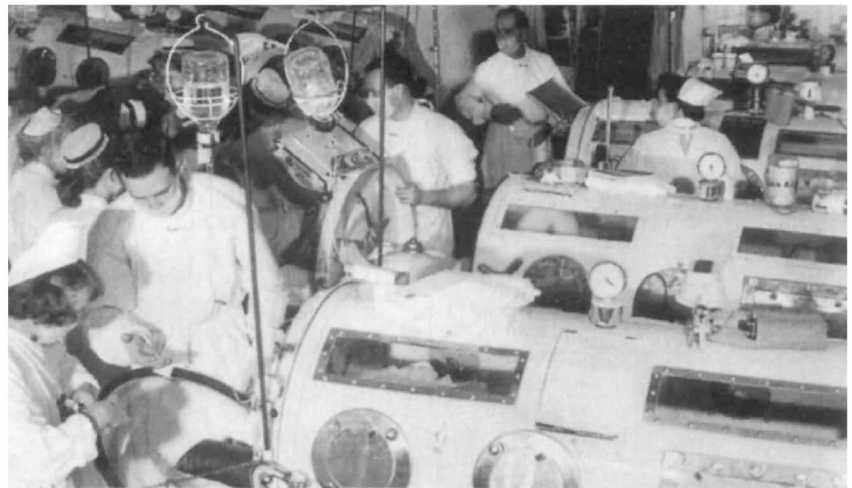
The Greenwood-Wright debate was an honourable draw, and resistance to medical quantification remained respectable at a time when fears were increasing that the triumph of scientific and technological

medicine was neglecting the sufferer and jeopardizing the doctor-patient relationship. Why, then, asks Matthews, after such a long history of reservations about the applicability of enumeration, did the clinical trials on streptomycin developed by Austin Bradford Hill in 1946 prove such an overwhelming success, finally converting the profession to a position about which it had so long remained divided? In part it was because the new clinical trials were conceptually watertight: the introduction of the double-blind element with proper controls really did, for the first time, make the numbers what they had always been claimed to be: reliably objective.

But another factor was at work, Matthews insists. With the marketing of ever more potent industrially produced drugs, and with shocking scandals such as thalidomide in the early 1960s, the public and the politicians were no longer disposed to accept 'clinical judgement' on the say-so of illustrious physicians. At long last the state required proof of the safety of medical procedures. Numbers offered a language that the politicians could trust.

This is a most illuminating study, which should be read alongside recent books by Theodore Porter, Ian Hacking and other historians who have analysed the assimilation of other aspects of the human condition within the growing 'empire of the probable'. If it is sobering to be reminded how readily in matters of life and death we relied, until so recently, on the personal judgement of fallible but often highly opinionated physicians, it should be of some comfort that today we are protected by rigorous clinical trials. □

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Iron lungs were — and for some they remain — life support systems for victims of poliomyelitis. This picture appears in *A Summer Plague: Polio and Its Survivors* by Tony Gould. The author, himself a survivor, provides a comprehensive account of the rise and fall of the epidemic. A compelling mix of clinical, scientific and political — as well as personal — perspectives. Yale University Press, £19.95.