REPRINTS AND REFLECTIONS

The rise and fall of epidemiology, 1950–2000 A.D.* †

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In 1662 John Graunt, a London haberdasher, published his magnum opus, Natural and Political Observations... Made upon the Bills of Mortality, and thereby established the field of epidemiology. Graunt brought to light a diversity of facts about human life and disease that had not previously been appreciated. He was the first to notice that the number of births and deaths of males exceeded those of females (by the ratio of 14 to 13); he noticed, too, that despite their greater mortality, men had less morbidity than women. Graunt quantified for the first time the high mortality in children, noting that one-third died by the age of five. He documented that plague actually claimed many more deaths than had been ascribed to it, and he demonstrated that the frequency of rickets increased over the span of a few years from zero fatal cases to a level that indicated a serious epidemic.

Graunt’s profound observations quickly became the talk of educated London. Within weeks of the publication of his book, he was elected to the newly formed Royal Society. Unfortunately, his ascendency was brief; he contributed nothing further to epidemiology after the publication of his admirable book. In 1666, his haberdashery succumbed to the Fire of London leaving him destitute. Prejudice against him for his conversion to Roman Catholicism hindered his financial recovery, and he died in poverty and obscurity a few years later. Graunt’s personal fortunes proved to be an uncanny omen for the discipline that his work heralded.

Epidemiology originated in England because record keeping there provided both the means and the stimulus for monitoring statistics on death and illness. Graunt’s seminal work, however, was received as a curiosity; the rise of the new discipline was still 300 years away. For two centuries after Graunt there was no one who could be described as an epidemiologist. The first to follow Graunt’s initiative was William Farr, appointed in 1838 as Compiler of Abstracts to the General Register Office in England—a position that he retained for more than 40 years. Farr exhibited a keen insight into ‘dry’ mortality statistics; his work and that of a few other pioneering scientists formed the foundation for the epidemiology of the 20th century. It was a formidable science to practice because it depended totally on the availability of large, accurate bodies of data on the mortality and morbidity of human beings. If that obstacle was not enough to discourage a budding scientist, there was a further problem that the epidemiologic inferences built upon these collections of data suffered an extreme fragility inherent in their non-experimental origin.

Farr overcame these problems by systematizing the collection of mortality data and keeping his inferences cautious. He outlined the risks associated with various occupations while pointing out the fallacy of inferring anything about risk from data on age at death. He demonstrated the strong association between altitude and mortality from cholera, setting the stage for John Snow’s brilliant investigations of the role of water supply in the communication of cholera. These great strides served as an inspiration to 20th-century epidemiologists, but, like an echo of Graunt, the flowering of epidemiology in the 19th century was brief. After Farr, the field was again quiescent.

Substantial growth of the new discipline did not begin until the end of the Second World War, when the United States initiated many large studies designed to improve the health of its population. The community-intervention trials of fluoride supplementation in water, the Framingham Heart Study, and the largest formal experiment ever conducted with human beings, the field trial of the Salk vaccine, were part of a wave of epidemiologic fervour that followed the war. Adding to the momentum were the striking findings from the first studies linking cigarette smoking to lung cancer, culminating in the landmark report Smoking and Health, issued by the Surgeon General in 1964.2

The boom period for epidemiology, from 1950 until about 1980, was accompanied by all the signs of a nascent scientific discipline. Textbooks of epidemiology appeared for the first time, each quickly becoming outdated because of the rapid succession of theoretical advances in study design and analysis that were developed to overcome the inherent handicaps of non-experimental research. The early theoretical contributions were mostly from scientists who had been trained as statisticians; by 1970, however, epidemiologists were being trained as such at several universities, and soon the theoretical contributions flowed from those whose formal training was in the new discipline itself. The history of epidemiology during the 1970s and 1980s followed closely the paradigm of scientific revolution as Thomas Kuhn described it.3 Kuhn cited the remark of Max Planck that ‘a new scientific truth does not triumph by convincing its opponents and making them see the light, but rather because its opponents eventually die, and a new generation grows up that is familiar with it’.4 The emergence of epidemiologic theory was slowed by conflict between the older generation of physicians and statisticians on one hand and the newly trained epidemiologists on the other—a conflict that was resolved just as Planck’s dour complaint foretold.

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In its heyday during the 1970s, epidemiology was a word encountered frequently in public interchange. The national surge of interest in health, preventive medicine and environmental problems solidified public support for epidemiologic research. Many epidemiologic problems came under broad public scrutiny: the viral origin of some cancers, particularly hepatoma, the world’s most common cancer; estrogen-induced cancer of the endometrium; the health effects of exposure to low-level radiation; connections between diet and cardiovascular disease; hormonal drugs and their effects on offspring; reserpine and possible risks of breast cancer; vinyl chloride-induced angiosarcoma of the liver; Legionnaires’ disease; swine flu and Guillain-Barre syndrome; the identification of carcinogens in the workplace; the transmissibility of Hodgkin’s disease; and the carcinogenicity of non-nutritive sweeteners. Typically, these issues were clouded by sharp controversy, since many involved conflicts between business and consumer interests, and there were nearly always epidemiologists voicing opinions on both sides of each issue.

While the epidemiologists educated themselves, trained their successors, and earned attention for their research during the 1970s, the seeds of decline were germinating. A rising public sentiment for privacy, combined with an outcry in reaction to several medical experiments performed on prisoners or mentally handicapped persons who were not aware that they were subjects in medical studies, led to the initiation of institutional review boards. These boards served an important function by screening research proposals for considerations of privacy, ethics and protection of human rights. Their bureaucratic implementation, however, became a substantial cost of conducting epidemiologic research—more so than for other types of medical research. Because each institution had its own review board, any epidemiologic study that required recruiting subjects from more than one hospital had to be reviewed by each hospital. Even if all hospitals ultimately cooperated, the review process often delayed projects for 6–12 months. Each institution had its own application form, and often the review board of a large hospital would expect an investigator to attend a question-and-answer session on the study design. The degree of frustration that an epidemiologist faced was lamented by Prof. A.Z. Smith in reflecting on his important study of food additives and cancer, based on data from patients treated at 66 Boston-area hospitals: ‘One year of my career was invested in contacting hospitals, completing redundant forms about informed consent and privacy, assuring sceptical clinicians of the value of epidemiologic research such as mine, and writing letters repeatedly awakening slumbering administrators to the urgency of my request. It shocks me now to realize that I spent roughly 3% of my scientific career trying to get permission to conduct a single study, which in itself took only three years.’

The maze of regulation that appeared in the 1970s was accompanied by considerable misinterpretation by hospitals, health departments and other institutions—further hampering epidemiologic studies. For example, some hospitals refused to let a patient’s chart be examined without written consent from the patient. Since epidemiologic studies usually involve scanning dozens of charts to find one that matches the appropriate entry criteria for a study, these hospitals effectively blocked their participation in epidemiologic research. The validity of broad-based studies began to suffer as the participation of hospitals began to decline. Ironically, no government regulation ever required that a patient’s written consent be obtained before the chart could be examined for possible inclusion in an epidemiologic study. Some hospitals insisted on describing the hypothesis under evaluation to all subjects in full detail, thereby introducing an irremediable bias that negated the value of including such hospitals in interview studies.

The bureaucracy associated with the conduct of epidemiologic research increased with time. In 1980, five federal agencies represented by the Interagency Regulatory Liaison Group issued a set of guidelines for the conduct and reporting of epidemiologic research. The guidelines were drafted in consultation with only a few senior epidemiologists and emerged as obsolete rules that were naïve in regard to current theoretical advances. There was a resounding reaction among epidemiologists against promulgation of these guidelines, directed not so much at their mediocrity as against the intrusion of government into the planning and reporting of scientific research. The reaction was ignored; the guidelines were adopted, and within 10 years a slightly revised version was imposed as a standard criterion for evaluation by review groups for the National Institutes of Health. Although occasionally revised, these guidelines have never been concordant with epidemiologic theory more recent than 20 years old.

Academic positions in epidemiology became less attractive during the 1980s. A fledgling investigator could not reasonably expect to initiate and complete a single study before review for tenure. While academic salaries continued to slump, industry and government began to hire epidemiologists, as if both sides were recruiting for a coming regulatory war, which they were. As the academic base for the discipline shrank, epidemiologists were more often representing vested interests on one side or another of the ever-controversial issues. Their credentials as health lobbyists required an official sanction, and the once ignored American College of Epidemiology became the professional union. The College, which was spurned by the profession when it was organized in 1980 as a self-proclaimed accrediting body, used its entrance examination to restrict admission to its ranks. By 1990, certification by the College was regarded as instrumental for success in the courtrooms and hearing rooms where nearly all epidemiologic issues were decided.

Since 1990, fewer epidemiologic studies of scientific importance have been published each year. Governmental briefing papers, industry papers and commissioned critiques have accounted for the bulk of professional activity. The few original research papers that have been published have tended to be ecological studies based, like the work of Graunt and Farr, on routinely collected population statistics, along with a few small case-control studies from single institutions. Some enterprising closed-panel health plans have continued to support epidemiologic research on their own populations. Unfortunately, in the past decade several of these groups have terminated all research programs, probably in reaction to malpractice judgments awarded in favour of subscribers who received therapy that was subsequently found on epidemiologic follow-up to be questionable. Ignorance may not guarantee bliss, but it does offer protection against malpractice claims.
A scientific discipline that developed slowly and flourished briefly for several decades is now nearly gone, leaving behind some knowledge of disease prevention, a few controversial alarms, and a collection of techniques for assessing the health consequences of people’s actions. Among the legacies is the demise of major 20th-century epidemics attributable to tobacco, dietary fats and some carcinogens in the workplace and environment.

For many, however, epidemiology was an unpleasant science, providing frequent reminders that we are born into a dangerous world where no action is without some risk. Most of us have been persuaded to discard the belief that our modern world is a safe harbour, but now we shall have to muddle along with little specific knowledge of the risks we face. It is a small comfort, at least, that the methods devised by epidemiologists during the latter part of the 20th century will endure to serve some future generation with sufficient curiosity to apply them.

References

Commentary: Epidemiology still ascendant

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Though published in 1981, the footnote on the first page of ‘The Rise and Fall of Epidemiology’ indicates that it was a preprint of a talk ‘to be presented December 10, 2004, at the annual meeting of the John Graunt Literary Society, Harvard School of Public Health, Boston.’ Back in the 1970s, the facetiously named John Graunt Literary Society, or JGLS, met each Friday in the late afternoon at the Harvard epidemiology department to celebrate Graunt’s legacy with brewed beverages. Although the December date 23 years in the future at the time of publication was in fact a Friday, the ‘preprint’ implied that the JGLS was destined to evolve from a weekly beertfest into a yearly gathering of sober, serious speeches. In an essay that many readers took to be a cynical rant laden with gloomy predictions, this forecast for the JGLS was the gloomiest of all.

In fact the essay was not intended to predict the future of epidemiology, which I have always held to be bright. It was meant to be a warning about the growth of research bureaucracy and its effect on epidemiologic research. By 1980 administrative hurdles for epidemiologic research were growing at a worrisome pace. The essay mentions the travails of ‘Dr A. Z. Smith,’ who spent a full year trying to get permissions from 66 Boston-area hospitals to conduct a single study. The pseudonymous Dr Smith was actually my colleague Alan S. Morrison, who did spend that frustrating year getting permissions for a population-based case-control study of saccharin consumption and bladder cancer. The mounting burden was more than just administrative. Institutional Review Boards began telling epidemiologists that the specific objectives of their studies must be spelled out to participants in excruciating detail, making it impossible to avert recall bias in some interview-based studies. The government also introduced new roadblocks. At the time of writing, I was principal investigator for a peer-reviewed government funded contract to study hormonal exposure and birth defects. Approval came only after lengthy delay and in my case was conditional on numerous senseless changes that compromised the value of the information. All this transpired without the benefit of any dialogue.

From today’s perspective, the intrusion of review boards and government agencies into the research process may seem routine, and the complaints may seem to betray a naive