

## PERSPECTIVES

# Five Classic Articles in Public Health

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In this brief review, Dr. Jonathan Borak comments on five seminal papers that helped shape the fields of epidemiology and public health. These papers include Hill's criteria for inferring causality; the first proof of the multistage theory of cancer; the first evidence that subclinical lead exposures can cause neurobehavioral impairment in children; a simple yet robust study that had a major influence on setting current air pollution policies; and a landmark review of the general public's perception of risk in relation to actual public health hazard.

*Dr. Jonathan Borak is a Clinical Professor of Epidemiology and Public Health at the Yale School of Public Health, Clinical Professor of Internal Medicine at the Yale School of Medicine, and Director of the Yale Interdisciplinary Risk Assessment Forum. In this article, Dr. Borak provides his perspective on five publications that significantly influenced the study and practice of epidemiology and public health. This article is the first in a series that will identify and provide commentary on the top five seminal papers published in a field related to biology and medicine.*

A former student, a member of the *Yale Journal of Biology and Medicine's* Editorial Board, reminded me of a comment I made in class. I had described a particular assigned reading as "one of those classic articles" that should be read by everyone studying public health. Okay, he challenged me, what other "classic articles" were on my list? And so began the following: my short list of five articles that represent "must reading" for all students in public health.

First, note that I do not speak for public health in general, a field of great breadth of interest and activity, but only the narrower slice, including toxicology, risk assessment, and related interests. Also, I was principally concerned to identify articles that provide models of critical thinking, addressed issues of substantial public health importance, and served as stepping stones for subsequent research and the formulation of public health policy. I also wanted to include articles that were observational and opportunistic, i.e., based on real world observations and available data, not complex laboratory models.

My five choices below include: 1) a landmark presentation of criteria for inferring causality from observational data (Hill 1965); 2) a thought experiment based on the re-analysis of publicly available cancer mortality data, which shaped the fields of cancer biology and risk assessment (Armstrong & Doll, 1954); 3) an early study of the effects of lead exposure in school children (Needleman, 1979); 4) a study of the impact of air pollution on children's health, which was enabled by a fortuitous labor

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dispute that shuttered a polluting steel mill (Ransom & Pope, 1992); and, 5) a critical literature review of cognitive psychology research that shaped our understanding about how public health risks are perceived (Slovic, 1987).

**HILL AB. THE ENVIRONMENT AND DISEASE: ASSOCIATION OR CAUSATION? PROCEEDINGS OF THE ROYAL SOCIETY OF MEDICINE. 1965;58:295-300.**

Observational epidemiological studies can yield data that describe associations between environmental factors (e.g., dust) and health effects (e.g., lung disease), but not direct evidence of causation. However, it is our understanding of causation, rather than association, that is most likely to lead to appropriate public health action. In this landmark President's Address to the Royal Society of Medicine, Hill articulated nine common-sense criteria or "viewpoints" (e.g., strength of association; plausibility; consistency) that should be used to evaluate cause-and-effect hypotheses. None provides indisputable evidence and none is absolutely required, but together they lend substantial weight-of-evidence credibility to inferences of causation. The impact of this specific approach has been enormous. Reference to and reliance on these criteria have spread from the scientific community to the courtroom, where (for better or worse) the Hill viewpoints have become the standard by which the evidentiary merit of epidemiological studies is judged.

**ARMITRAGE P, DOLL R. THE AGE DISTRIBUTION OF CANCER AND A MULTI-STAGE THEORY OF CARCINOGENESIS. BRITISH JOURNAL OF CANCER. 1954;8:1-12. (REPRINTED IN INTERNATIONAL JOURNAL OF EPIDEMIOLOGY. 2004;33:1174-9).**

Understanding the mechanisms of carcinogenesis has posed a challenge to generations of scientists. Because today we describe those mechanisms using the concepts and tools

of contemporary cell biology, modern students may fail to appreciate how the foundations of those modern concepts derive from traditional epidemiology. In this 1954 re-analysis of age-related cancer death rates for adults in England and Wales, Peto and Doll demonstrated a nearly constant linear relationship between log transformed cancer mortality rates and age, thus indicating that the relationship between age and mortality rates was exponential, with a nearly constant power value across various types of cancer. From this, they inferred that cancers resulted from a sequence of independent "stages," with the rate of occurrence of one or more stages increasing with age. Thus developed the first "proof" of the multistage theory of cancer. Subsequent refinements incorporated the effects of specific exposures on occurrence rates, which led in turn to the "linearized multistage model of carcinogenesis," for years the default approach by which government agencies worldwide estimated the potency of carcinogens and thereby set public health exposure standards.

**NEEDLEMAN HL, ET AL. DEFICITS IN PSYCHOLOGIC AND CLASSROOM PERFORMANCE OF CHILDREN WITH ELEVATED DENTINE LEAD LEVELS. NEW ENGLAND JOURNAL OF MEDICINE. 1979;300:689-95.**

The neurotoxicity of high-dose lead exposure had been recognized since the Roman Empire. Until 1979, however, it remained uncertain whether exposures not associated with "obvious" toxicity caused adverse neurological effects. Two challenges to resolving the issue were lead's short half-life in blood (blood lead levels primarily reflect recent exposure) and the fact that most studies of more subtle neurotoxic effects mainly had included subjects with a history of overt lead poisoning or mental retardation. In this study, Needleman and colleagues measured lead levels in teeth (a stable measure of cumulative body burden) shed naturally by first- and second-grade students in Boston-area schools. Teachers collected the teeth and, without knowledge

of lead levels, rated the students' behavior. The findings were striking: Non-adaptive classroom behaviors increased in a dose-related manner, and the teachers' observations were confirmed by formal neuropsychological testing. It became clear that "subclinical" lead exposures could chronically impair neurobehavioral function and adversely impact school performance. Even more importantly, this study illuminated the enormous public health costs of what was otherwise viewed at that time as "acceptable" levels of lead exposure.

**RANSOM MR, POPE CA.  
ELEMENTARY SCHOOL ABSENCES  
AND PM<sub>10</sub> POLLUTION IN UTAH  
VALLEY. ENVIRONMENTAL  
RESEARCH. 1992;58:204-19.**

The public health implications of particulate air pollution are well recognized, but controversies continue over setting of exposure limits. One source of conflict has been the difficulty reconciling the results of classical toxicology with those of epidemiological time-series research; classical toxicology experiments rarely document adverse effects at the levels of exposure associated with such effects in time-series studies. Accordingly, some view time-series epidemiology as suspect. Ransom and Pope took advantage of an industrial quirk to more directly document the health effects of air contaminants in an area of Utah where particulate air pollution was historically dominated by emissions from a steel mill. Owing to a labor dispute, that mill was shut for 13 months, thus providing a "control" period to which pre- and post-closure public health measures could be compared. Two local school systems provided weekly and/or daily data on elementary school absences. After controlling for potentially confounding variables, a significant and robust association was found between PM<sub>10</sub> levels and absence rates, which persisted at levels below current air quality standards. The relative simplicity of this study and its intuitively reasonable findings had major influence on current air pollution policies.

**SLOVIC P. PERCEPTION OF RISK.  
SCIENCE. 1987;236:280-5.**

The promotion of public health and safety requires an understanding of how the "public" thinks about and responds to risks. However, research has repeatedly documented that "experts" and "lay persons" often differ significantly in their valuations of particular risks. Bridging that gap is essential for public health "experts" to effectively influence the risk perceptions and resulting behaviors of the "public." In this landmark review, Slovic summarized an array of social and cultural factors that lead the general public to perceive specific risks in seemingly inconsistent ways. Qualitative risk characteristics (e.g., "dreaded" or "involuntary" risks) can lead to risk valuations that differ markedly from corresponding actuarial risks. By contrast, risk valuations by experts generally ignore those characteristics, instead evaluating riskiness in quantitative terms such as morbidity and mortality rates. The key lesson here is that "riskiness" means more to people than "expected number of fatalities." To be effective, public health practitioners must understand the actuarial hazards of specific risks, while also empathizing with the non-quantitative (and often emotional) concerns of the general public.

**CONCLUSION**

Readers should note that each of these various authors wrote many excellent articles and books of importance to public health, while many other researchers made contributions at least as great as those listed above. Thus, my list is inherently arbitrary; the number of meritorious articles not included is enormous. But, to my thinking, these five are "classics" because of their substantial public health impact, their timeless relevance, and they illustrate the important contributions that public health students can make relying mainly on available data, astute observations, and a clever mind.