

## Obituary: Richard Doll

Sir Richard Doll died earlier this year at age 92. The most celebrated epidemiologist of the 20th century, Doll is best known for his work on smoking and lung cancer, but there was so much more to his career.

His father was a general practitioner in London, and it was from St. Thomas's that Doll himself graduated in Medicine in 1937. Even as a student, he showed his interest in epidemiologic and statistical tools, publishing on the need for proper analysis and statistical testing in population studies of disease.

Later, Doll served in the Royal Medical Corps in France and the Middle East throughout the Second World War. He began his research career at the Middlesex Hospital, studying occupational factors in the development of peptic ulceration. He married Dr. Joan Faulkner around this time, and it was she who had been instrumental in his getting the position at the Middlesex.

In 1945, he began his collaboration with Austin Bradford Hill, and, together, they labored gloriously to establish better ways of doing epidemiology. It was chronic disease epidemiology, and particularly cancer epidemiology, that most benefited from this collaboration and from Doll's later work with Richard Peto.

**Tobacco.** The rising rate of lung cancer in a number of countries at the beginning of the 20th century was probably first noted by Duguid in 1927. Air pollution was a favored causal candidate for this increase but damp climate, dust and particulate matter, tarring of roads, vehicle exhaust, and the influenza epidemic of 1918 all soon had champions. Hoffman stated in 1929, "There is no definite evidence that smoking habits are a direct contributory cause toward malignant growths in the lungs," although he later changed his mind based on clinical data. Others accumulated clinical lung cancer series, but an association with smoking was still debated throughout the 1940s, with no study in the literature making the crucial comparison of the tobacco-smoking habits of those with and without lung cancer.

In 1950, three appropriately designed studies were published, two in the United States led by Ernst Wynder and Morton Levin and one by Richard Doll and Austin Bradford Hill in the United Kingdom. Each study reported that there were proportionately more smokers among the lung cancer cases than among the unaffected. Doll continued to make original use of analytic epidemiologic methods to determine the effects of tobacco smoke on human health. These observational studies were simple but sophisticated and rigorous. Following the 1950 case-control study, Doll and Hill established and followed a cohort of British doctors who had responded to a questionnaire regarding their smoking history. This seminal work moved the field from the few earlier anecdotal reports to a body of data sufficient to identify tobacco as a human health hazard with a certainty near to that obtained from experimental clinical trials. Doll's studies identified the protean pathologic effects of tobacco smoking, especially respiratory cancer and coronary heart disease; they also provided quantitative estimates of the relationships between amount and duration of smoking and the magnitudes of the health risks. The study of changes in disease rates after smoking cessation, compared with continuing smokers, continue to provide key information for disease control in a world where tobacco smoking constitutes the major single preventable cause of morbidity and mortality.

The studies by Doll are bold and original science. They represent an important part of the foundation of modern population-based chronic disease research. By the early 1960s, they constituted adequate evidence for public health action to reduce tobacco smoking; in 1964, the U.S. Surgeon General's first report on the adverse health consequences of tobacco was published. Today, they continue to remind us how carefully crafted observational studies can advance scientific knowledge regarding social and health issues that are not amenable to experimentation on human populations.

**Asbestos.** By the early 1930s, work in the asbestos products industry in Britain was known to increase the risk of a sometimes fatal nonmalignant pulmonary disease, termed asbestosis. However, in the ensuing two decades, although there were case reports of lung cancer and other malignancies arising in asbestos workers, no formal epidemiologic studies were conducted to document whether these reports were indicative of an etiologic connection or were merely a coincidence. The results of Richard Doll's cohort study of British asbestos workers, published in 1955, reoriented the entire field. Doll employed a study design that was rare at the time but state of the art even today: a comparison of the mortality experience of a group of workers in a large factory (in which asbestos products were made) during the prior three decades with that of the population in general, taking into account potential demographic differences between the groups. He identified a 14-fold increase in lung cancer mortality in these workers. This study provided convincing evidence that the health hazards associated with heavy asbestos exposure were not confined to asbestosis and stimulated research in other parts of the world to examine cancer occurrence in persons exposed to asbestos in other settings (e.g., in miners and insulation workers). The results of these latter studies, positive not only for lung cancer but also for mesothelioma, when combined with those of Doll, led to changes in workplace exposures that ultimately have prevented thousands of cases of cancer that would have occurred in the absence of this research.

Richard Doll's work in the area of asbestos and cancer did not end in 1955. In 1985, he and Julian Peto published an authoritative review of the subject, examining the complex issues that had intensely practical implications relating cancer risk to dose, recency of exposure, and type of asbestos fiber. This work proved to be an invaluable resource to persons charged with making regulatory decisions and no less to other investigators in prioritizing their own research efforts in this field.

Doll contributed to our understanding of other diseases too, showing, as noted above, that smoking caused cardiovascular deaths and that the bland diet prescribed for peptic ulcers was useless. He regarded his work on radiation and leukemia as his second most important contribution. He identified the lung cancer risk associated with indoor exposure to radon and, in the late 1990s, showed that a vitamin D supplement reduced the risk of fractures in the elderly.

Doll had a patrician air but a wonderful sense of humor. He had a prodigious memory. He remained productive and in good health to the time of his death.

William Richard Shaboe Doll, the greatest epidemiologist of our time: born October 28, 1912; died July 24, 2005.