

Second Thoughts

WHICH JOHN SNOW SHOULD SET THE EXAMPLE FOR CLINICAL EPIDEMIOLOGY?

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John Snow's **On the Mode of Communication of Cholera** is a book known by every epidemiologist—at least by title [1]. Most believe that it is the archetype of epidemiologic research, in that our science arrives at very important medical discoveries without any recourse to biologic mechanisms [2]. Usually the story is recounted more or less the following way, even in the most recent textbooks [3-7]. The city of London experienced cholera epidemics in 1853 and 1854, two of the last epidemics of a whole series. These epidemics were investigated by Dr John Snow. This doctor, so it is told, tracked the distribution of the epidemic over the city, and by the drawing of maps upon which epidemic foci were indicated, he concluded that the distribution of cholera correlated with the drinking water supplies for the diverse parts of the city. Districts where water was provided by one company, had been spared; districts where another held a virtual monopoly became disaster areas. In this way, it is said, John Snow succeeded in intervening causally to halt the cholera epidemic without the benefit of our modern microbiological knowledge—several decades even before Robert Koch isolated the real cause, *Vibrio cholerae*. Thus, John Snow could accomplish grace to the methods of epidemiology.

This magnificent story about the way in which epidemiology proceeds, has been told and retold dozens of times, even though simple reading of the original works by John Snow shows that it does not hold [8]. John Snow was a practising physician, who stood at the forefront of medicine of his time. In the history of

medicine he is equally famous for his research into the cholera epidemic as for his work on the scientific basis of anesthetics [9]. The observations which we summarized above were published in his book **On the Mode of Communication of Cholera** in 1855. Few realize, however, that this famous and oft reprinted book was a *second* edition. The first edition was a short essay which was also published in the **London Medical Gazette** in 1849, 5 years *before* the famous cholera epidemics of 1853 and 1854 [13]. In his first writings, John Snow already proposed exactly the same theory which he upheld *after* his epidemiological observations, namely that cholera was transmitted from human to human by a living contagious agent which was able to multiply itself. John Snow was already a convinced contagionist before he started his epidemiologic studies [8].

This knowledge leads to several second thoughts: on the strength of specifying a research hypothesis beforehand; on the basis of John Snow's conviction; and on this famous epidemiologic method. Our first "second thought", the *a priori* specification of a research hypothesis, was common knowledge among his contemporaries. His friend and biographer, Richardson, puts it this way [10]:

"He argued in his own mind that the poison of cholera must be a poison acting on the alimentary canal by being brought into direct contact with the alimentary mucous surface, and not by the inhalation of any effluvium. In all known diseases, so he reasoned, in which the blood is poisoned in the first instance, there are developed certain general symptoms, such as rigors, headaches, and quickened pulse; and these symptoms all precede any local demonstration of disease. But in cholera this

rule is broken; the symptoms are primarily seated in the alimentary canal, and all the after-symptoms of a general kind are the results of the flux from the canal. His inference from this was, that the poison of cholera is taken direct into the canal by the mouth. This view led him to consider the media through which the poison is conveyed, and the nature of the poison itself."

Somewhat more recently the great infectious disease epidemiologist W. H. Frost, in an introduction to the 1936 reprint of John Snow's work, stated [11]:

"It has seemed unnecessary to reproduce the first paper in this volume, since it is included, for the most part in identical or slightly revised language, in the second edition; but it is important to remember that when Snow undertook his personal investigations in the epidemic of 1854 he already had in mind a definite and well matured theory which he was eager to put to the rigid test which the intermingling of two water supplies made possible."

John Snow was a man of his time, who had chosen his position in the debates between proponents of the miasma theory, the theory of poisoned air, emanating from rotting organic material, and the contagionists, who believed in living germs that could be transmitted between humans [8]. His story begins with a number of clinical observations. He had witnessed how children, who occupied the same bed in a hospice for the poor transmitted the cholera to each other, after having slept in each other's dirty linen. He had painstakingly researched incubation periods: he had witnessed how one person from an epidemic area could transmit the disease to another region; how the colera poison apparently could be present in minute quantities in drinking water to replicate itself in humans and distribute itself in large quantities. These were descriptions of single cases or small series, far removed from epidemiologic methods.

Snow reasoned exceedingly physiologically [12]. He described how patients dehydrated, urine production ceased, and how the disease ended in a circulatory collapse. To him this was caused by the active withdrawal of body fluids from the intestines that normally have a resorption function.

For this active withdrawal, some living agent is necessary, he inferred. Snow looked for this organism. He did not only draw maps and determine numerators, he also investigated the water, both chemically and microscopically.

The image of John Snow, which arises from this short historical excursion, is different from the one usually recognized in modern epidemiology.

In setting this historical example straight, we face important consequences. Which John Snow is to offer the paradigm for modern epidemiology, especially for its clinical variety? The imaginary one who came to causal conclusions merely by numerical observations, or the real one, who was a physician who had fixed his mind on a theory of disease causation? The idea that a "black-box" approach is the real strength of the epidemiologic method has been defended by many, most vocally by Peto [2]. The imaginary John Snow seems to offer support for this paradigm; the real one does not. Maybe, we should stick to the real John Snow as the prototype of the clinical and epidemiologic investigator. It might be time to tell our students not only about his 1855 writings, but to draw their attention equally to his clinical and physiological observations and his theorizing in the 1849 papers.

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