The Mystery of the Blue Death: A Case Study in Epidemiology and the History of Science

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Part I—Beginnings

John Snow was born in 1813 in York, England, one of 10 children of a working-class family. They lived in a poor neighborhood near the River Ouse, which would sometimes overflow, flooding the family home. Snow obtained a scholarship to a local school to learn to read and write and, with some extra money his parents managed to provide, to learn arithmetic. Snow's wealthy and well-connected uncle, Charles Empson, arranged an apprenticeship for his nephew with a surgeon-apothecary, one of the two types of health care providers in 19th-century London. Physicians were graduates of the medical programs at Oxford or Cambridge while surgeon-apothecaries went through a longer apprenticeship, attending classes part-time at smaller medical schools. John Snow moved to Newcastle at the age of 14 to apprentice with William Hardcastle, dividing his time between classes and assisting Hardcastle with routine tasks. He stayed several years. It was in Newcastle, near the end of Snow's apprenticeship, that he first encountered Asiatic cholera as it arrived in England in 1831.

In his medical studies, Snow learned the prevailing humoral model of disease, which held that health depended on the balance of four humors: blood, phlegm, black bile, and yellow bile. The tools of the surgeon-apothecary were very limited, consisting of bleeding with leeches as well as the use of purgatives and emetics to balance the humors. Cholera was treated in various ways depending on how physicians interpreted the humoral imbalance. Sometimes they recommended soup or thin gruel. Often, they prescribed the use of purgatives to cause diarrhea and emetics to cause vomiting, believing that these would help the body achieve a balance among the humors. During the 1831 cholera outbreak, Hardcastle sent Snow, then only 19, to the Killingworth Colliery, a coal mine, to treat the cholera outbreak there. In the coal mines of 19th-century England, women, children, and men worked 12-hour shifts under extremely unsanitary conditions. In the village where the mine was located, 330 of the 550 residents were stricken with cholera, and 65 died. Snow worked tirelessly caring for the ill, but could do little to help.

On his own, away from his mentor, Snow had the opportunity to think about the cholera outbreak, and his later work suggests that this is where he first began to doubt the conventional medical wisdom about the cause of cholera. Some biographers have suggested that this may have played a role in his decision to leave Newcastle for London and pursue further medical studies there.

Sanitation and Victorian London

London in the middle of the 19th century contained 2.5 million people, housed in 30 square miles, a population density greater than present-day Manhattan. During the Industrial Revolution, thousands of people moved from the countryside to London to take factory jobs, working long hours for little pay. Many people also lacked formal employment, and worked as day laborers for very low wages, or were self-employed, including many in the recycling trades. Nearly 100,000 people earned a living by collecting and reselling bone, rags, bits of copper, lumps of coal, human and animal wastes, and other salvageable materials.

Mid-19th-century London was crowded and dirty. Sanitation was generally poor, as the city lacked a sewer system except for draining rainwater. Cesspools were used to collect used water from washing, and human excreta were collected in pit latrines. Both often overflowed, and some buildings had several feet of accumulated waste in basements or courtyards.

Because of the problems of waste disposal, few Londoners had a source of drinking water uncontaminated by human sewage. At that time, a total of nine different water companies supplied Londoners with water, obtained from either shallow wells or the Thames River. In general, neighborhoods south of the Thames obtained water from the river, whereas neighborhoods north of the Thames had a wider range of sources. Some of the companies servicing these neighborhoods obtained their water farther upstream than others. Though only rain water was supposed to be in the sewer system, often human waste also wound up in the river. Accordingly, water companies that had their intake pipes farther downstream were more likely to obtain water contaminated with human waste.

According to the medical orthodoxy of the time, cholera was an example of an epidemic disease, a category of diseases thought to be explained by exposure to a toxic gas or miasma. The name malaria comes from the Italian meaning "bad air," reflecting this belief. The gases were believed to result from the fermentation of organic material. The sanitarian movement, early promoters of public health, focused on reducing miasmas by calling for the removal of the cesspools and piles of composting feces. They planned to build the network of sewer pipes that would carry wastes out to the Thames. One early proponent of public health, Edwin Chadwick, declared that, "All smell is disease." Chadwick sought to have sewers constructed for waste disposal in the river in order to rid communities of overflowing pit latrines. His plan also called for moving the water intake pipes upstream, but not until after the system of sewer pipes was constructed. Thus, although Chadwick was a leader in declaring that health can be addressed through infrastructure at the community level, his focus on the miasma model as the cause of disease may have led to the deaths of many Londoners from waterborne diseases resulting from drinking contaminated water.

John Snow and the Origins of Anesthesiology

After John Snow's initial experience with cholera in 1831, there were no further cholera outbreaks in England until 1847. In the meantime, John Snow went to London for further medical studies, probably again with the financial assistance of his uncle. After he finished his studies, he practiced surgery in a London hospital. At that time, surgery was done without anesthesia. Snow read the account of the first use of anesthesia in Boston, and saw the first demonstration of a surgical procedure employing anesthesia in England. He immediately realized the value of general anesthesia, although he recognized a critical problem with the procedure as demonstrated: the lack of precise control over the dosage of the anesthetic. Snow immediately set out to develop devices for administering gases as well as for measuring and controlling dosages, which he succeeded in doing very quickly. Snow had not been a particularly successful surgeon, but went on to develop one of the very first anesthesiology practices. This led to greater financial success as he cultivated a wealthier clientele, eventually including Queen Victoria, who sought relief from the discomfort of childbirth.

As his anesthesiology practice grew, John Snow continued to do research in a lab he had built in his home. In addition to designing gauges for controlling dosages of gases and masks for precise delivery of the drugs, he experimented with different drugs using a variety of animal models, carefully recording dosages and effects. As a result of his very extensive studies of anesthetics, he began to question conventional wisdom about miasmas, as epidemics did not seem consistent with what he had learned about toxic gases.

Questions

1. Models are analogies that allow us to clarify hypotheses—proposed explanations of relationships between causes and effects. What roles do models play in testing hypotheses?
2. What did the humoral model of disease propose as the cause for cholera?
3. What did the miasma model of disease propose as the cause for cholera?
4. Unlike Snow's later work on cholera, his research on anesthesia was experimental in nature. What general skills of experimental design were necessary to plan effective experiments to test dosage measuring and delivery systems for anesthesia, or to investigate the properties and effects of different drugs?
5. Why are experiments considered strong tests of hypotheses?

Part II—The Mystery of the Blue Death

Cholera returned to London in 1847 and rapidly spread through some neighborhoods causing numerous deaths and widespread fear. John Snow began to turn his attention to investigating the outbreak, seeing fewer patients in order to make time for his research. Having spent a great deal of time studying gases for anesthesiology, Snow recognized that the patterns of cholera cases were inconsistent with the patterns one would expect if people were being poisoned by a toxic gas; he reasoned that it was unlikely that a toxic gas would kill some members of a household and not others. Snow had no way of inducing cholera in an animal model, and he realized that studies of cholera would have to take a very different form.

The symptoms that cholera patients presented also seemed to Snow to be inconsistent with exposure to a toxic gas. Often called "blue cholera" or "the blue death," cholera usually caused death by respiratory failure, giving the skin a bluish tinge. To most of Snow's contemporaries, this observation seemed consistent with the miasma model, but Snow thought that the initial gastrointestinal symptoms might be more significant, and suspected that the causative agent was ingested rather than inhaled. He wondered about the "animalcules" identified by early microscopists, although the prevailing scientific wisdom was that these were harmless. He became particularly interested in the possibility that cholera was transmitted in water. He confided in some of his friends from the medical society about his suspicions. They were skeptical, and he resolved to collect additional data.

Snow recognized that an experimental test of his hypothesis was not possible, and began to look for other ways of testing his theory. He began to comb through all of the available records of cholera outbreaks in England to search for patterns. In studying an outbreak in an affluent neighborhood, he found that cesspools that should have contained only water from washing contained partially digested food. He hypothesized that the cesspools were contaminated with human feces, and somehow this contamination was spread to drinking water.

In 1849, Snow published a monograph entitled, "On the mode of communication of cholera." It was poorly received, with negative reviews in the *Lancet* and the *London Medical Gazette*. However, a reviewer in the latter journal made a helpful suggestion in terms of what evidence would be compelling: the crucial natural experiment *would* be to find people living side by side with lifestyles similar in all respects except for the water source.

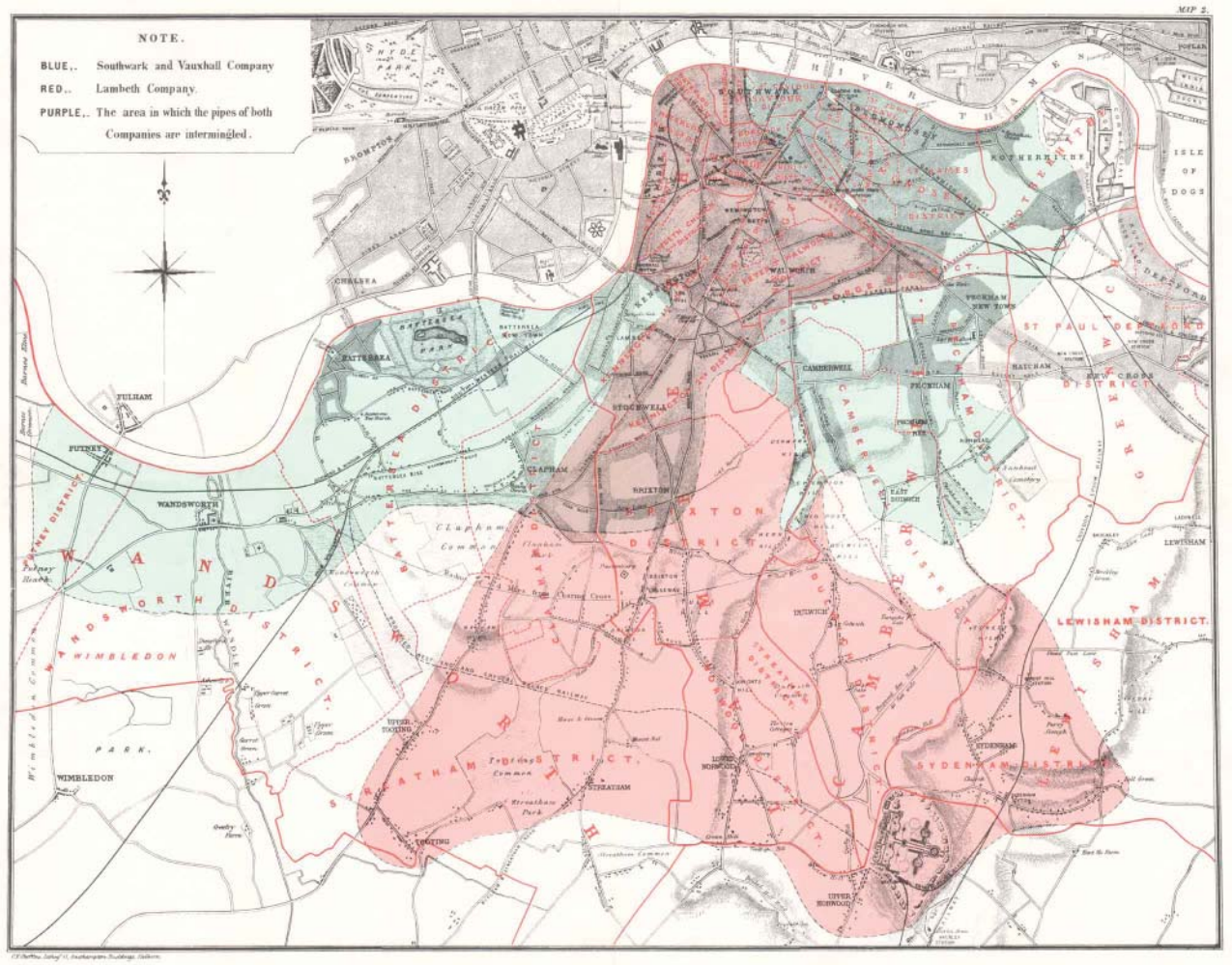
Questions

1. What causes cholera, and how is it transmitted?
2. Why weren't Snow's ideas about cholera accepted at this early date?
3. Explain why cholera outbreaks are more consistent with contamination of water than air.
4. Given that cholera outbreaks are more consistent with contamination of water than air, why did the miasma model persist?
5. How did Snow's experimental research on anesthesia help him design a new model for the cause of cholera?
6. Why would evidence of cholera in people living side by side, differing only in water supply, provide critical evidence?
7. When was the germ theory of disease proposed, and on what basis?

Part III—Solving the Mystery of the Blue Death

After Snow's monograph was rejected, he sought ways of strengthening his argument by carrying out the crucial experiment sought by the *Medical Gazette's* reviewer. He went door to door interviewing families of cholera victims. He also interviewed physicians who had treated cholera patients. In addition, he looked at the geographic distribution of other cholera outbreaks in England as compared to the drinking water sources.

Figure 1. "The Grand Experiment," 1854



Credit: Map courtesy of The John Snow Site, created by Ralph R. Frerichs, Department of Epidemiology, School of Public Health, UCLA. High resolution versions of this map suitable for printing are available at http://www.ph.ucla.edu/epi/snow/highressnowmap.html.

At the same time that Snow was beginning to consider questions of public health, so was William Farr, a contemporary of Snow's. Farr kept records of births and deaths for the city of London. He encouraged physicians to write down the cause of death, and began looking for patterns. Although a miasmatist, Farr, in response to Snow's inquiries, agreed to keep records of the water companies used by each neighborhood along with cholera deaths.

Snow began marking cholera deaths on city maps, and patterns began to emerge. One of the first patterns he noticed was in the mortality statistics from prisons and insane asylums. Residents of those institutions were not able to leave, and were forced to use the same water source. He found that they often had mortality

rates that were either higher or lower than those of the surrounding communities. From this, he concluded that he might be able to make a comparison of cholera rates in people with different water supplies. He soon realized that during the period when some water companies were moving their intake pipes upstream and others were not, there would be an opportunity to distinguish between the miasma model and his own hypothesis of water-borne transmission.

Snow pored over the maps of the city, initially trying to find areas served by a single water company. He was unsuccessful in finding such a neighborhood from the maps, but soon he recognized that neighborhoods in which two water companies were competing might be more valuable. There, neighbors would breathe the same air and would resemble each other more in variables other than water source.

Snow began to go door to door asking people about their water source. He found that often people did not know, so he sought a way to verify the source. He recognized that the tidal flow in the Thames held the key, with water obtained in London having a far higher salt content than water from sources upstream. He began taking water samples and testing them to determine the salt concentration, and thereby identifying the water company and the location of the source along the Thames. By then, it was winter and cholera had subsided for another year.

Questions

1. Why was it useful to be able to verify the source of the water?
2. Why would a neighborhood served by two different water companies be more useful for testing Snow's hypothesis than two neighborhoods each with their own source?
3. Epidemiologists often draw causal webs to illustrate the interrelationships among biological, social, and environmental variables that contribute to disease outbreaks. Based on what you have learned so far, what variables should be included in a causal web for cholera?
4. Snow considered his conclusions about cholera to be inferences from observations whereas the reviewer from the medical journal considered these to be conjectures. What is the difference between inference and conjecture?

Part IV—The Broad Street Pump

Late in the summer of 1854, cholera broke out once again, with a cluster of cases in the vicinity of Broad Street. This was a neighborhood that Snow knew well, having lived there for several years when he first arrived in London. By knocking on doors, Snow determined that all of the cases of cholera involved people who obtained their water from the Broad Street pump. Most of the victims lived closest to this pump; among those who did not were children who went to a school on Broad Street near the pump and a handful of people who preferred the taste of the water of the Broad Street pump to that of water from other pumps nearer their homes.

At that time, the local parish, St. James Church, was responsible for taking care of poor families in the neighborhood. A Parish Board was responsible for making decisions on how to provide charitable assistance. Snow went to the Board and made his case, arguing that the handle on the pump should be removed to prevent further cases of cholera. Although those on the board were skeptical, they decided that Snow's proposal would do no harm, and the handle was removed. Cases of cholera dropped.

Reverend Henry Whitehead, the minister of St. James Church, was skeptical of Snow's explanation and saw a critical flaw in Snow's work. Snow had focused on interviewing those households affected by the epidemic. As the parish priest, he had ministered to the sick and dying during the epidemic. Whitehead decided to interview people in households in which no one died from cholera. Much to his chagrin, he found that households using the Broad Street pump were nine times more likely to have cholera victims than those not using it. Through his careful interviewing, Whitehead also succeeded in identifying an earlier case, an infant living in a house a few feet from the Broad Street pump who died from diarrhea two days before the cholera outbreak was officially recognized.

Although Whitehead had initially sought to criticize Snow's work, the two became allies. Together, Whitehead and Snow asked the Board of Public Health to excavate the area around the pump. There, they found that water from the cesspool under the building where the first infant victim died was seeping out and into the water from the pump. On further inquiry, they learned that the baby's mother had washed the soiled diapers of her sick infant in the basement of her building, dumping the water in the cesspool.

Although many continued to reject Snow's explanation, some began to give it grudging acceptance, often without acknowledging his contribution. Snow's vindication came at a meeting of the Medical Society where a member stood up after such a presentation insisting that Snow be given credit. Sadly, not long after this, Snow suffered a series of strokes, dying at the age of 45.

The following summer, a drought compounded the problems of contamination of the Thames, resulting in pollution so severe that it was called the Great Stink. Members of Parliament were forced to meet in a remote location because of the stench, where they voted to initiate a vast construction project to move the sewer pipes far downstream. After the construction of the new sewer system, there were no more cholera outbreaks in England.

Questions

1. The basic questions of epidemiology focus on time and place: why here and why now. What are the answers to these questions for the Broad Street outbreak?
2. Epidemiology relies on non-experimental tests of hypotheses. What was Snow's hypothesis and how did he test it?
3. How did Whitehead improve on Snow's test of this hypothesis?
4. What is the difference between correlation and causation?

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