

# The hands of John Snow: clue to his untimely death?

A R Mawson

Department of Pediatrics,  
Division of Genetics and  
Epidemiology, University of  
Mississippi Medical Center,  
Jackson, Mississippi, USA

Correspondence to:  
Professor A R Mawson,  
Department of Pediatrics,  
Division of Genetics and  
Epidemiology, University of  
Mississippi Medical Center,  
2500 North State Street,  
Jackson, MS 39216 4505, USA;  
amawson@prevmmed.umsmed.  
edu

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## ABSTRACT

The accomplishments of John Snow (1813–1858), physician-epidemiologist, inventor and anaesthetist to Queen Victoria, are well documented, but the causes of his untimely death at age 45 remain conjectural. Snow suffered a paralysing stroke while working on his magnum opus, *On Chloroform and Other Anaesthetics*, and died a few days later on 16 June 1858. Snow had a history of renal problems associated with tuberculosis. He also experimented on himself with ether, chloroform and other agents over several years, but whether this prolonged self-experimentation contributed to his early death is uncertain. A photograph of Snow taken in 1857 shows that the fingers of his right hand were swollen. Could this be a clue to the cause of his death? The “modern” view is that Snow’s early tuberculosis and associated renal disease led to hypertension, chronic renal failure and stroke. The tuberculosis and renal involvement may have been worsened by vegetarianism and perhaps resulting vitamin D deficiency. However, the renal damage caused by tuberculosis is unlikely to have been progressive. Based on current evidence of renal toxicity associated with exposure to anaesthetic agents, it is perhaps more likely that extensive and prolonged self-experimentation with anaesthetics over a 9-year period led to Snow’s renal failure, swollen fingers and early death from stroke.

John Snow, MD (1813–1858) was a pioneering founder of anaesthesiology and epidemiology. Early in his medical career, already well known as an able clinician and scientist, Snow was invited to assist in delivering two of Queen Victoria’s children—Prince Leopold and Princess Beatrice—using chloroform, a substance he had carefully investigated through extensive experimentation on both animals and himself. He invented a mask and breathing apparatus for safely regulating the administration of anaesthetics. Above all, he conceived, tested and bravely promulgated the theory that cholera was transmitted by contaminated water, a view that contradicted the deeply entrenched position of the medical and public health authorities—that the disease was due to bad smells, otherwise known as noxious effluvia or “miasmata”. Although much has been written about Snow’s life and accomplishments, the causes of his untimely death at the age of 45 remain somewhat conjectural.

Snow was a bachelor who lived alone on Sackville Street in Soho, London. He appears to have suffered a paralysing stroke on Wednesday, 10 June 1858, falling off his chair while writing the concluding sentences of his book, *On Chloroform and Other Anaesthetics*. Snow told his housekeeper that he did not know what ailed him, but complained of chest pain and treated himself with ether. A more severe stroke the next day left him

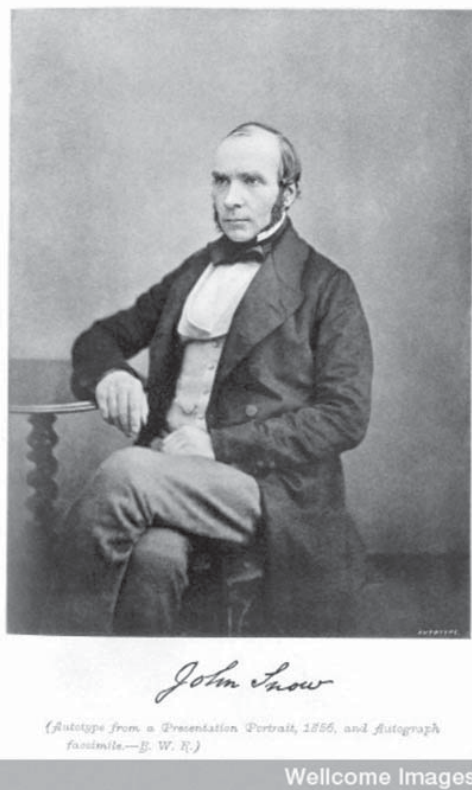
delirious and paralysed on his left side, and soon after he began vomiting blood. Lingered several more days, Snow died at 3 pm on 16 June, attended by his brother Thomas. He was buried at Brompton Cemetery.<sup>1,2</sup> At autopsy, his kidneys were found to be “shrunken, granular and encysted...” and there was “scar tissue from old bouts of tuberculosis”.<sup>1</sup>

Several theories have been proposed for Snow’s early death. His medical school friend, Joshua Parsons, attributed it to frequent fatigue due to vegetarianism. A second theory attributes his death to chronic illness resulting from an early bout of tuberculosis and acute renal failure. Thus Vinten-Johansen *et al*, in their comprehensive biography of Snow, wrote that, although “(r)egular exposure to a variety of toxins in his search for the perfect anaesthetic may have hastened his end, ... it is just as likely that his renal troubles had brought on the hypertension and stroke”.<sup>1</sup> Benjamin Richardson—another close friend, junior colleague and biographer—also believed that self-experimentation with anaesthetics had no bearing on Snow’s early death.<sup>2</sup> A third hypothesis is that of Ralph Frerichs,<sup>3</sup> who maintains an extensive website on Snow through the University of California, Los Angeles. According to Frerichs: “Likely of greater significance regarding his premature death at age 45 was his inappropriate use of anesthesia.... Snow did frequent experiments with anesthetic agents upon himself... and did not spare himself in investigating every possible substance that might be employed as an anesthetic. The pathologic effect of most of these agents was not known”.

## 150-YEAR-OLD PHOTO OFFERS CLUES

Reflecting on the chain of events leading to his death while examining a photograph of Snow taken in 1857, a year before his death (<http://www.ph.ucla.edu/epi/snowimage.html>) (fig 1), I noticed that the fingers of his right hand, particularly the exposed index finger, were somewhat swollen. Could this be a clue to the cause of Snow’s death?

The “modern” view is that Snow’s premature death from stroke was due to hypertension, which was caused and exacerbated by his early kidney disease.<sup>1,4</sup> As for the swollen fingers, chronic renal failure is associated with significantly increased hand volume and oedema as well as deterioration in hand function,<sup>5</sup> although whether Snow had difficulty in writing is unknown. Granted that Snow died from stroke and renal failure, the question at issue is the extent to which these were due to renal problems developing from early tuberculosis, as opposed to chronic renal failure brought on, years later, by self-experimentation with anaesthetics. The suggestion offered here is



**Figure 1** Dr John Snow in 1857, aged 44 (Source: John Snow, Photograph, 1857. Reproduced with permission from the Wellcome Library, London).

that prolonged exposure to anaesthetics through self-experimentation was indeed the proximate cause of his renal failure and early demise.

Richardson states that Snow's renal problems began in his early twenties as a sequel to tuberculosis and "symptoms of *Phthisis pulmonalis*", but he recovered after taking plenty of fresh air.<sup>2</sup> His medical school friend, Joshua Parsons, noted that Snow had been in poor health since his student days, and recalled him developing a fever and rapid pulse after minor injuries and often suffering from fatigue.<sup>1</sup> Tuberculosis affected his kidneys and, in the summer of 1845, a year after passing the examination for his MD degree, Snow "became unhinged for work, and ... was attacked with alarming and acute symptoms of renal disorder".<sup>2</sup> He was referred by Peter Marshall, a friend and physician, to Drs Richard Bright and William Prout, both of whom were noted authorities on diseases of the kidney. Snow was advised to take a brief holiday, to abandon his strict vegetarian diet and to take small quantities of wine; he complied, and thereafter his health reportedly improved.<sup>2</sup> He went to stay with Parsons in Somerset and recovered sufficiently to resume work.<sup>1</sup>

### EARLY TUBERCULOSIS

Snow developed a strict vegetarian diet at age 17 after reading John Frank Newton's *The Return to Nature: A Defence of the Vegetable Regimen* (1811).<sup>1</sup> This diet, and its associated vitamin D deficiency due to his abstention from eating butter, milk and eggs, may have contributed to the tuberculosis and renal disease that Snow experienced in his youth. Indeed, vegetarianism was an independent risk factor for tuberculosis in immigrant Asians

living in London, among whom vitamin D deficiency was common.<sup>6</sup> Reduced 25-OH-vitamin D levels compromise cell-mediated immunity and activate latent tuberculosis.<sup>7</sup> Another study found that, among predominantly vegetarian Asians in west London, those with undetectable serum 25-OH-vitamin D levels had an almost 10-fold increased risk of active tuberculosis.<sup>8</sup>

Tuberculosis, however, is an uncommon cause of progressive renal failure, but little information is available on the contribution of tuberculosis to the burden of renal disease.<sup>7</sup> The kidney is usually infected by haematogenous spread of bacilli from the lung, and renal tuberculosis is frequently bilateral. The bacilli tend to proliferate in the renal medulla, producing confluent epithelioid granulomata with caseous necrosis associated with vascular insufficiency of the papillae, leading to local tissue destruction. Scarring develops within the renal pelvis with calcification in 24% of cases.<sup>9</sup> These observations suggest that, while Snow's tuberculosis and perhaps vegetarianism and associated nutritional deficiency may have caused his acute renal problems, it is doubtful whether these led to renal failure and his fatal stroke at the age of 45. Could self-experimentation with anaesthetics have been a more likely cause?

### SELF-EXPERIMENTATION WITH ANAESTHETICS

Snow personally experimented with ether, chloroform, ethyl nitrate, carbon disulphide, benzene, bromoform, ethyl bromide and Dutch liquid (dichloroethane), and continued his self-experimentation for 9 years, from about 1845 to 1855. He developed a method for comparing new agents based on general principles of anaesthesia and narcosis. His goal was to identify a narcotic that had the properties and practical advantages of chloroform but was similar to ether in not causing cardiac arrest. He studied "narcotic symptoms, concentration, volatility, respiration time, and temperature",<sup>1</sup> and developed his anaesthetic inhaler and mouthpiece. Using his own inhaler, Snow would fasten the mouthpiece over his face, record the dose he was about to self-administer and then release the gas to determine its effect. Falling unconscious within seconds, he would awaken minutes later, check his stopwatch and carefully record the duration of unconsciousness.<sup>10</sup> In 1849, Snow published his classic article, "On fatal cases of inhalation of chloroform" in the *Edinburgh Medical and Surgical Journal* (Vol. 72, pp 75–87), and the brief first edition of his monograph, *On the Mode of Communication of Cholera* (London: Churchill).

Unlike his academic contemporary, Robert Glover, who was also an expert on anaesthetics but became addicted to and died from an overdose of chloroform,<sup>11</sup> there is no evidence that Snow's self-experimentation with anaesthetics and even alcohol was for any purpose than to explore a drug's anaesthetic properties or to study it as a potential treatment.<sup>1</sup> The invitation to Snow to administer chloroform at two of Queen Victoria's deliveries was a testament to the esteem in which he was held as a physician and scientist of high moral character and sound judgement.

Exposure to anaesthetic gases, including ether and chloroform, is now known to have numerous adverse health effects, causing severe damage to the kidney, central nervous system, reproductive organs and liver.<sup>12</sup> The kidney is a major target organ for chemical-induced toxicity. Microsomal cytochrome P450 monooxygenases play important roles in the biotransformation of numerous endogenous and xenobiotic anaesthetic compounds,<sup>13</sup> and several P450 isoforms are expressed in the kidney. Chloroform, a halogenated hydrocarbon, causes hepatic and renal damage in several species and is metabolically

activated through P450-dependent enzymes to phosgene, which reacts with cellular macromolecules to initiate tissue damage.<sup>14</sup> Recent animal studies have shown that renal P450 enzymes play an essential role in chloroform-induced renal toxicity.<sup>15</sup>

In summary, while Snow's early renal problems were due to tuberculosis, possibly worsened by vegetarianism and resulting vitamin D deficiency, it is unlikely that his tuberculosis-induced renal illness led to chronic renal failure. It is perhaps more likely that prolonged and extensive self-experimentation with a variety of anaesthetic agents over a 9-year period was responsible for this and for his swollen fingers, hypertension and death from stroke at the age of 45.

### IRONIES IN THE LIFE OF JOHN SNOW—EPIDEMIOLOGIST AND PUBLIC HEALTH ICON

The 1854 epidemic of cholera in Soho killed nearly 700 people within a few weeks and took place in the vicinity of a popular well, situated on what was formerly named Broad Street. Snow's initial investigations supported his hypothesis that contaminated water from the well was responsible for the epidemic. This realisation moved him to address the Board of Governors of St James Parish to plead for the removal of the pump handle. Although sceptical, the Board complied. The epidemic was already on the wane, partly because many local residents had left the area.<sup>16</sup> But the decision to remove the handle of the Broad Street pump famously contributed to shortening the epidemic and, indeed, prevented a second epidemic due to further contamination of the well water.<sup>10</sup> However, another 30 years elapsed before the infective bacterial agent, *Vibrio cholerae*, became widely known.<sup>17</sup> Removal of the pump handle was a turning point in contemporary public health, because it represented an intervention by a public health institution against an epidemic that, for the first time, was based on a scientifically sound theory of the disease.<sup>10</sup>

Every textbook of epidemiology recounts this event, which effectively protected the community of well users from cholera and from a death that often ensued within 24 hours of contracting it, and it has come to symbolise the public health approach to disease prevention. The widely held belief that atmospheric miasmata caused cholera even led to the official policy of diverting sewage from homes and neighbourhoods into the River Thames, the city's major source of drinking water, which thereby unwittingly contributed to epidemic cholera.

A tragic irony of Snow's early death is that, aside from self-experimentation with anaesthetics, he followed a regimen that would today be considered an ideal of preventive medicine and public health. In his teens in Yorkshire, he was impressed by the adverse effects of alcohol and became a teetotaler as well as helping to found the York Temperance Society. He also became a vegetarian. He took strenuous exercise and walked great distances throughout his life, engaging in extensive "shoe

leather epidemiology" during the cholera epidemics in London. He lived in Soho, in the heart of the neighbourhood ravaged by cholera, yet he himself was untouched by it. His early predilection for distilling his own drinking water and his unique understanding of the acute effects of anaesthetic gases may have spurred his insight that cholera was a waterborne disease rather than one induced by noxious odours. Snow was undoubtedly unaware, however, that the knowledge he was contributing to the science and practice of anaesthesia through prolonged self-experimentation was being gained at the expense of his health. We can only speculate on what Snow might have revealed and achieved in medicine and public health had his light in the scientific darkness not been so prematurely extinguished.

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