History of Anaesthesia

John Snow and Research

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John Snow's leadership in epidemiology as well as anaesthesia resulted from his research as much as his clinical practice. In anaesthesia, Snow's research concerned the regulation of concentrations of volatile agents and the development of efficient inhalers; the uptake and elimination of volatile agents; stages of anaesthesia; carbon dioxide metabolism and rebreathing; and metabolism in anaesthesia and the theory of anaesthesia. In epidemiology, Snow investigated the relationship of water supplies to mortality in cholera during the London epidemic in 1854, which led him to formulate an original and valid theory of the transmission of cholera. Snow's research, which has received less attention than anecdotes concerning his career (e.g., his anaesthetizing Queen Victoria and urging removal of the handle of a contaminated water pump), was always directed towards solving specific problems. The significance of his research is evident in its leading not only to improvements in health care but also to the evolution of anaesthesia and epidemiology as professional disciplines.

John Snow (1813–1858) (Figure 1) achieved fame and leadership in two different fields – anaesthesia and epidemiology. A busy practitioner, his fame and leadership derive largely from the value of his research in these two disciplines. His research, however, is generally less well known than the highlights of his life and career (Table)[1–9] and those episodes in his life that are the stuff of legend rather than the substance of research. Thus he is remembered for administering chloroform to Queen Victoria (hence the term *à la reine*) rather than for carrying out research that laid the basis of understanding

FIGURE 1 John Snow.

of the nature of anaesthesia, and for urging the removal of the handle of a pump of a contaminated well in Broad Street, London (admittedly a symbolic act) rather than for conducting a complex epidemiological investigation of the cholera epidemic in London in 1854.

Snow's research is worth study for several reasons. First, his research advanced immeasurably the evolution of anaesthesia in its early years: he initiated its transformation from a rag-and-bottle craft to a specialty based on scientific knowledge. Likewise, as member of the London Epidemiological Society, he was one of a handful of

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TABLE Highlights of the life and career of John Snow (1815–1858)*

1813 (March 15)	Born, York, England
1827	Apprenticed to William Hardcastle, Newcastle-on-Tyne
1831	Attended cholera victims, Killingworth
1836	Walked to London, visiting Wales and Bath en route Student of anatomy at Hunterian School of Medicine
1837	Student at Westminster Hospital
1838	Passed examinations for MRCS and LSA Set up general practice in Soho, London
1843	Graduated MB, BS (London)
1844	Obtained higher degree of MD (London) Constructed ether inhaler
1846	Anaesthetist, St. George's Hospital and University College Hospital
1847	Published *On Ether*
1848	Constructed chloroform inhaler
1849	Published *On the Mode of Communication of Cholera*
1853	Anaesthetised Queen Victoria at birth of Prince Leopold
1854	Urged removal of handle of cholera-contaminated water pump in Broad (now Broadwick) Street London, and conducted classic epidemiologic investigation of the London epidemic.
1855	Published 2nd edition of monograph on cholera. Elected President, Medical Society of London
1857	Anaesthetised Queen Victoria at birth of Princess Beatrice
1858 (June 16)	Died, London *On Chloroform and Other Anaesthetics* published posthumously

*There are numerous accounts of Snow's life and work in the literature of anaesthesia, epidemiology and general practice. The biographic accounts are short sketches. The only contemporary accounts are those by B. W. Richardson,[1,2] on which many later accounts are based. Among other accounts are those by Griffith (1934),[3] Key (1946),[4] Bergman (1958),[5] Cartwright (1958),[6] Edwards (1959),[7] Brown (1964) and Thomas (1969).[9]

individuals in the mid-19th century who stressed the use of epidemiology as a valuable tool. Second, within a few months of the introduction of ether and then chloroform his research enabled him to clarify the nature of anaesthesia and to provide a rational basis for the safe administration of anaesthetic agents. Similarly, his research on cholera permitted him to elucidate its nature and the means of its transmission, so that the disease could be prevented – for in his day, when the bacterial cause was not known, it could not be treated specifically. And third, the methods he used to solve problems remain of interest today; they are not anachronisms.

This paper examines some aspects of Snow's research in order to assess its significance as part of his overall contributions to medicine. Most of his research was directed to solving problems related to anaesthesia and cholera, but some of his efforts were spent in studying unrelated topics that, while of much less importance, do illustrate the range and nature of his research. Considering his research also illuminates the personality of the man as well as his approach to research.

Snow's research in anaesthesia

Snow was interested in all aspects of anaesthesia as it existed in its first decade. Those on which he conducted research are principally the following: (1) respiratory physiology, asphyxia and resuscitation; (2) the regulation of concentrations of volatile anaesthetic agents and the development of efficient inhalers; (3) the clinical staging of depth of anaesthesia: (4) the uptake of volatile agents: (5) the elimination of volatile agents, carbon dioxide metabolism and rebreathing; and (6) metabolism in anaesthesia and his theory of anaesthesia.

Respiratory physiology, asphyxia and resuscitation

Snow opened his great text *On Chloroform and Other Anaesthetics: Their Action and Administration* with a revealing statement on inhalation:

> This process of inhaling smoke, as I first witnessed and in a gentleman connected with one of the eastern embassies to this metropolis, is very instructive, as showing that the lungs become emptied of their contents by three rather full expirations and inspirations. When this gentleman took the cigar from his mouth to speak, the smoke could be seen issuing thickly with each word till there was a momentary pause as he took a fresh inspiration, then the smoke could be seen issuing with each word as before, only not so thick, and after another inspiration, the smoke could be still perceived in the expired air, but in a very diluted state; but after a third inspiration, it could no longer be seen till he had resumed his cigar.[10]

Snow not only was observant but also understood a basic aspect of respiration. He understood the physiology of respiration long before he began his research into anaesthesia. Two topics that interested him in these early years (1837–1847) were the toxicity of carbon dioxide and asphyxia.

CARBON DIOXIDE TOXICITY

On December 1, 1838, at a meeting of the Westminster Medical Society, Snow asked Dr. Golding Bird to explain a statement he had made at the previous meeting. When Dr. Bird had said that from eight to ten per cent of carbonic acid in the atmosphere would be fatal to life, was he referring to an adulteration of the atmosphere by the addition of that quantity of carbonic acid, or the deterioration of the atmosphere by its decomposition, as by the burning of a charcoal stove? Snow pointed out that, in the latter case, the fatal effects of vitiated air would be attributed to the resulting deficiency of oxygen. According to the *London Medical Gazette*, Snow, in researching this question, "had mixed certain gases, and had respired with impunity as much as .40 of carbonic acid, when the proportion of oxygen was increased in an equal degree." These experiments led him to conclude that "the absence of oxygen, not the presence of carbonic acid, or any other gas, was the usual cause of death in cases of asphyxia from deteriorated atmosphere."[11]

This topic was debated in the Westminster Medical Society over the next few months. By the end of March 1839, however, Snow had become convinced that carbon dioxide exerted a deleterious effect "independent of the diminution of oxygen consequent on its inhalation." He described some experiments he had performed on small animals and birds designed to determine the effects of breathing "factitious" atmospheres consisting of different proportions of air, oxygen and carbon dioxide.[12]

Snow thought this topic "of great importance" and evidently preserved the records of his experiments, for it was seven years later when finally he published the results of these 18 experiments.[13] His work yielded two conclusions: first, that "5 or 6 per cent of carbonic acid cannot exist in the air without danger to life, and that less than half this amount will soon be fatal"; and, second, that "illness and subsequent death [occur] after removal from an atmosphere deteriorated by removal of part of its oxygen, whilst no carbonic acid was present." Snow, who was adept at chemistry and had been schooled in the country that had given birth to such eminent chemists as Robert Boyle, Henry Cavendish, Joseph Priestley, Humphrey Davy, Michael Faraday and John Dalton, paid particular attention to the absorption of carbon dioxide. He wrote that in some of these experiments "the small quantity of carbonic acid given off from the lungs of the [experimental] animal was absorbed by lime water." In discussing his results, Snow referred to the suggestion of a Professor Graham that the carbon dioxide remaining after explosion of fire-damp (i.e., chiefly methane) in coal mines be removed "by means of inhaling the air through a cushion filled with a mixture of slaked lime and powdered sulphate of soda." Snow remembered this suggestion when he came to conduct experiments on rebreathing in the context of anaesthesia four years later.[14]

ASPHYXIA AND RESUSCITATION

Asphyxia and resuscitation also prepared Snow's mind for his later work on anaesthesia. He discussed this topic first at a meeting of the Westminster Medical Society on October 16, 1841.[15] Much of his paper, which was published later in the year,[16] concerned asphyxia in the stillborn, but his discussion on respiration is interesting because it reflects his knowledge of respiratory physiology as it stood in the middle of the 19th century. The main object of the paper was a discussion of neonatal asphyxia, which, Snow related, affected "a large proportion" of the five per cent of infants who were delivered stillborn.

Snow's chief reason for discussing this topic was to describe an apparatus designed to resuscitate asphyxiated stillborn infants; his paper is of interest because it is his first formal paper and because it illustrates his interest in pursuing a research interest that proved relevant to his ready understanding of anaesthesia a little later. In 1838, Snow noted, a Mr. Read had demonstrated "a syringe for exhausting the lungs by the mouth, the nostrils in the mean time being held, when, on removing the pressure from the nostrils, the chest expanded again by the natural elasticity and resiliency of the ribs, muscles of respiration, and pulmonary tissue. . . ." This apparatus had evidently been designed for use in adults, but Snow wondered whether it could be adapted to the "restoration" of stillborn infants. However, what seemed to be "insurmountable difficulties" – the emptiness and lack of resiliency of neonatal lungs, for example – prevented Snow from following up this idea. But in 1841 he did ask Mr. Read to "make a little instrument on exactly the same plan, adapted to the size of new-born children." This was done, in the following form and operation:

> It consists of two syringes, one of which, by a tube adapted to the mouth, and closing it, withdraws air from the lungs, and the other syringe returns the same quantity of fresh air through a tube fitted to the nostrils. The two pistons are held in the same hand, and lifted up and pressed down together, the cylinders being fixed side by side, and each having two valves. When the pistons are raised, one cylinder becomes filled with air from the lungs, and the other with fresh air from the atmosphere, which can be warmed on its way by passing through a tube and metal coil placed in hot water. When the pistons are depressed, the latter cylinder is emptied into the lungs, and the

> air in the former is ejected into the atmosphere. In this way a constant current of air to and from the lungs is maintained, as in natural respiration.[16]

Concerning the actual use of the apparatus, Snow wrote in somewhat general and theoretical terms. There is no evidence of its ever being used in clinical practice.

His paper on asphyxia and other of his publications indicate that Snow was familiar with the use of tracheostomy and artificial ventilation in resuscitation, in both clinical and experimental settings. In his paper of 1841 he described experiments on a guinea pig that he had drowned. The animal died two minutes later. On opening the animal's chest he found that the heart was "perfectly still," apart from "a slight vermicular motion in the right auricle." He then divided the trachea and performed artificial respiration, after which the heart began to contract rhythmically again, though "blood was not expelled from the heart."

In other experiments, Snow performed tracheostomy and artificial respiration in cats and a rabbit "in order to see more precisely the action of the vapour of chloroform on the heart, when not sufficiently diluted."[17] He introduced chloroform into a jar, opened the trachea and tied a tube into it to enable the rabbit to breathe from a "bladder." When the animal regained consciousness, a second bladder, containing air and ten per cent chloroform vapour, was substituted for the first. The lungs and heart were then exposed and observed.

Although Snow himself never had occasion to resort to tracheostomy and artificial respiration, he did note that this technique was used by some of his contemporaries. He did so in reviewing 50 cases of cardiac arrest under chloroform anaesthesia that were drawn to his attention while analyzing deaths in association with chloroform anaesthesia.[18]

Snow's several references to the use of artificial respiration in asphyxia indicate that he was familiar with the techniques of resuscitation that had been advocated since the last quarter of the 18th century, most often for the drowned. These techniques included ventilation of the lungs by means of mouth-to-mouth ventilation, tracheal intubation or tracheostomy as well as manual compression of the chest and abdomen.[19] Others included stimulating the body by means of rubbing the skin of the limbs or trunk, introducing pungent vapours into the rectum and applying a galvanic current. Long before he began to practise anaesthesia Snow was familiar with the use of galvanism, though he pointed out that "the chief intention of electricity is to excite the respiratory movements; and this is fulfilled by an efficient artificial respiration."[16] Therefore it is not surprising that Snow, like others of his day, soon adopted the more appropriate of these resuscitative techniques to the treatment of cardiorespiratory cessation during anaesthesia.

The regulation of concentrations of volatile agents and the development of efficient inhalers

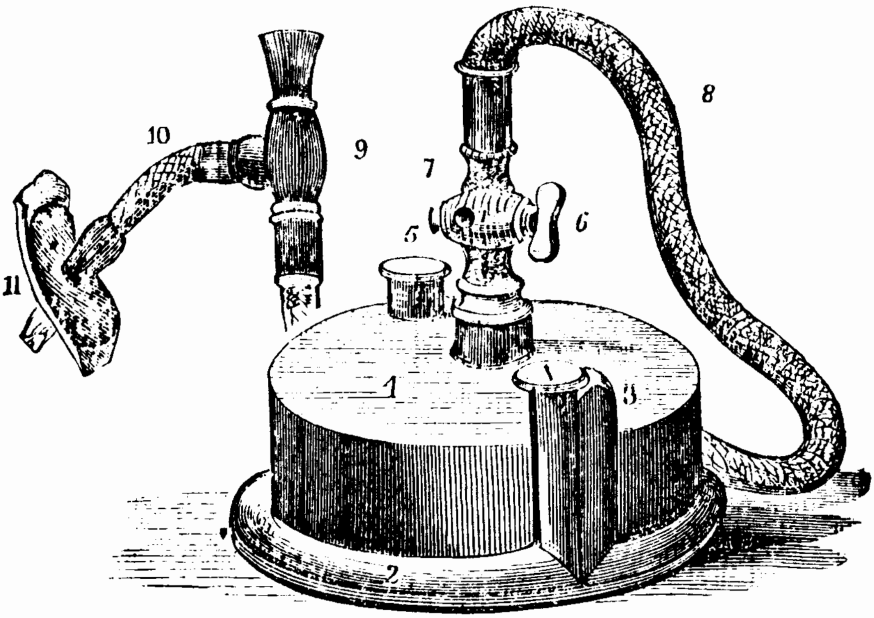
Less than a month after ether had been introduced into medical practice in England, Snow realized that the earliest anaesthetic inhalers were defective and unreliable.[20] These consisted of glass vessels containing sponge. He commented on these crude devices as follows:

> Both glass and sponge being very indifferent conductors of caloric, the interior of the inhalers became very much reduced in temperature, the evaporation of ether was very much checked, and the patient breathed air much colder than the freezing point of water, and containing very little of the vapour of ether. On this account, and through other defects in the inhalers, the patient was often very long in becoming insensible, and, in not a few cases, he did not become affected beyond a degree of excitement and inebriety.[21]

The earliest inhalers, instead of facilitating respiration, obstructed it. Respiration was obstructed by the sponges, the ether itself, valves that were too small and, particularly, breathing tubes that were too narrow. As Snow wrote of this mechanical problem, "there is reason to believe that, in many instances, this was the cause of failure, and that in others the insensibility, when produced, was partly due to asphyxia."[20]

But there was a second problem: "the medical practitioner," he wrote in March 1847, "ought to be acquainted with the strength of the various components . . . and . . . to be able to regulate their potency."[22] Many factors had to be considered with a compound like ether: its proportion in the air, its solubility and absorption in the blood, the balance between inhalation and exhalation of it, and the ambient temperature. Snow had concluded that "by regulating the temperature of the air whilst it is exposed to the ether, we should have the means of ascertaining and adjusting the quantity of vapour that will be contained in it . . . ." This was one of Snow's great contributions: he applied the results of his research on the vaporization of ether at different temperatures to the design of an inhaler so that the concentration that was being delivered at any one moment could be determined quite easily. (The accuracy of Snow's calculation is discussed in the Appendix.)

The practical import was obvious: since the early inhalers "did not allow of any regulation of temperature



1, Cap which unscrews to admit the air to
2, Metal pipe.
3, Entrance of ditto into
4, Spial chamber.
5, Star closing aperture for putting in or pouring out ether.
6, Two-way tap.
7, External opening of ditto.
8, Flexible tube.
9, Ebony tube, containing ball valves of cedar wood.
10, Portion of flexible tube to admit of change of position of
11, Mouth-piece, with soft cushion, &c.

FIGURE 2 Snow's prototype ether inhaler (March 1847).

but were always used at that of the apartment, whatever it might be, and this afforded no index to the quantity of vapour taken up . . .," what was needed was an inhaler designed to take the ambient temperature into account. Then anaesthetists would be able to "determine the proportion of ether to air, and by measuring the ether consumed in an operation, the quantity of air, as well as of vapour, breathed per minute, or throughout the inhalation . . . ." He then continued:

> All that was required to regulate the temperature of both the ether and the air, and, consequently, of the resulting mixture, was to bring them into proximity with substances having a good capacity for, and a good power of conducting, caloric. The first we have in water, and the second in the metals; therefore, by placing the ether in a metal vessel, and that vessel in a basin of water brought to the desired temperature by mixing cold and warm water together, the object was attained. Two or three pints of water supply the caloric abstracted in the evaporation of an ounce or two of ether without being much reduced in temperature; and, as the water never requires to be many degrees either above or below the heat of the apartment, its temperature is but little altered by the surrounding air during the short time of an operation.[22]

Snow brought a scientific approach to the administration of ether; he put it on a quantitative footing.

He extended quantification to the design of the inhaler itself. His first model (Figure 2), which he demonstrated to the Westminster Medical Society on January 23, 1847 took the form of "a round tin box, two inches [5 cm] deep and four or five inches [10 or 12.5 cm] in diameter." This was modified during the summer of 1847 to become the better known box-like inhaler, the size of a large octavo volume.[24] It consisted of two main portions (Figure 3). In one, a circular ether chamber six inches (15 cm) in diameter and one and a quarter inches (0.62 cm) in depth contained a spiral baffle plate soldered to the roof and extending to one-sixteenth of an inch (0.16 cm) of the floor. The other half held the water, at a temperature of 50

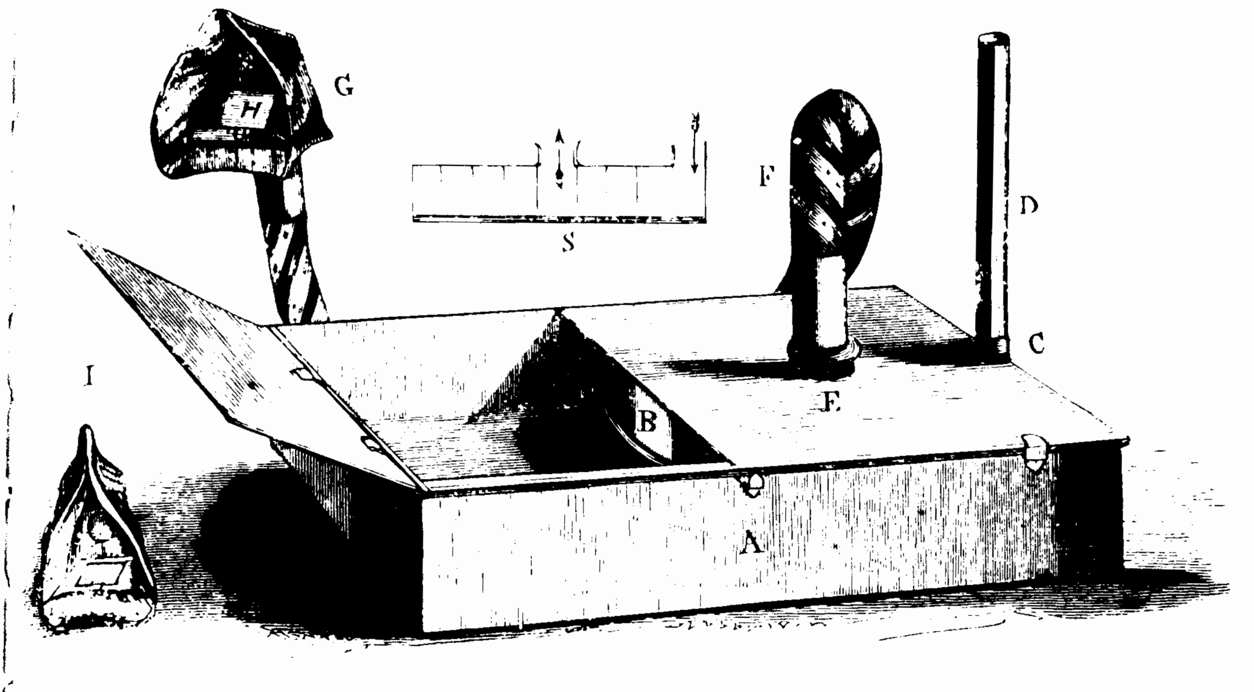


FIGURE 3 Snow's definitive ether inhaler, perfected during the summer of 1847.

to 60° F (10 to 15.5° C). A metal tube over the periphery of the ether chamber led to the facepiece. Snow gave much thought to the dimensions of his inhaler; "the dimensions of the ether chamber" he wrote, "are not a matter of indifference." The chamber had to be shallow enough to allow the air passing through it to be brought into contact with the surface of the ether, yet not so shallow as to induce, during vigorous inspiration, splashing of ether into the breathing tube. The calibre of the breathing tube was critical also: "it ought to be so capacious as to offer no impediment to the most rapid inspiration; and to meet this requirement it must be wider than the trachea, to compensate for the resistance arising from the friction of the air against the interior of the tube. It is, therefore, three-quarters of an inch [1.87 cm], in internal diameter."

As he had done with ether, Snow stressed the influence of the ambient temperature on the concentration of chloroform inhaled and performed experiments to determine the quantity of chloroform vapour that would be taken up by 100 ml of air at different temperatures.[25] Snow then wasted no time in designing an inhaler for the administration of chloroform.[26] This was smaller than the ether inhaler and more portable (Figure 4). It comprised two metal cylinders. On the upper surface of the inner one a perforated disc allowed air to pass into the cylinder, which served as an evaporating chamber. Inside the inner cylinder was screwed a frame with four stiff wires that supported two coils of "bibulous paper" (i.e., blotting paper), at the bottom of which four notches allowed air to become saturated with chloroform vapour and to pass upwards and onto the breathing tube. The space between the inner and the outer cylinder contained water, the temperature of which never exceeded 60° F (15.5° C).

Other types of apparatus for the administration of chloroform did not account for factors affecting vaporization, particularly variations in temperature, and Snow warned that ignoring the effect of the ambient temperature could mean that a high concentration might be unknowingly delivered by the anaesthetist. Snow pointed out that "if . . . a person inhales chloroform from a handerkerchief or an inhaler, in such a way that the air he breathes shall be half-saturated with the vapour, then supposing the temperature of the apartment, the handerchief, etc., to be 50° [10° C], the air he breathes will contain 4 per cent; but if the temperature be 70° [21.1° C], the air will contain 9.5 per cent of the vapour."[27] Snow was critical of the Scottish method of administering chloroform – an initial dose of "two or three drachms* spilt on the handkerchief or lint" and more added from time to time[28] – because the concentration of chloroform could not be regulated accurately.

Solving the fundamental problem of how to control the

*One fluid drachm (or dram) is equivalent to 3.698 ml.

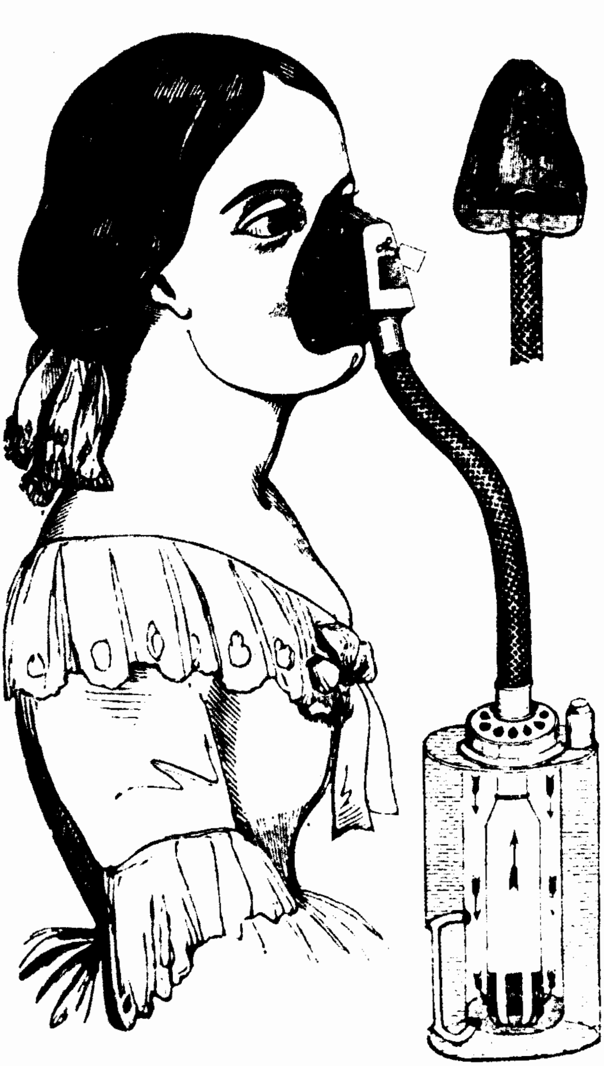


FIGURE 4 Snow's chloroform inhaler (February 1848).

depth of anaesthesia by regulating the concentrations of volatile agents was one of Snow's greatest contributions to the development of anaesthesia. He was the first to introduce *measurement* into what was in most hands a haphazard procedure, and his emphasis on the effects of the ambient temperature on vaporization of ether and chloroform set the pattern for the development of vaporizers later in the 19th century. At the same time, as he showed in administering chloroform *a la reine*, Snow was equally adept at administering anaesthesia using clinical rather than physical reference points.

The clinical staging of the depth of anaesthesia

Snow opened his monograph on ether by stating that "the point requiring most skill and care in the administration of the vapour of ether is, undoubtedly, to determine when it has been carried far enough."[29] Others besides Snow (e.g., Plomley in England and Flourens and Longet in France[30]) were interested in gauging the depth of anaesthesia by classifying the effects of ether into stages, or degrees, but Snow, characteristically, went further and supported his clinical observations and classification of the depth of anaesthesia into five degrees (i.e., stages) by experimental work also.

Much of his most important research on the depth of anaethesia Snow described from 1848 to 1851 in a series of 16 papers[31] – one of the classics of the literature of anaesthesia. In the first paper he wrote that he had "found a plan of determining more exactly the proportion of ether and of other volatile substances present in the blood in the different degrees of narcotism. It consists in ascertaining the most diluted mixture of vapour and of air that will suffice to produce any particular amount of narcotism . . . ." His plan was to ascertain the smallest quantity of vapour, in proportion to the air, that would produce a given effect. He intended to do this by weighing a small quantity of the volatile agent in a bottle and introducing a small animal or bird into a jar and waiting until the effects of the vapour no longer increased.

Over the years Snow performed no fewer than 79 experiments as part of his research "On Narcotism by the Inhalation of Vapours." From them he learned the effects of anaesthesia on animals and the concentrations of volatile agents in the blood that would produce different degrees of anaesthesia. From the results of these animal experiments he extrapolated the calculations to estimating volumes in the human body.[32] A current estimate was that the quantity of the blood averaged 30 pounds. This quantity would contain 26 pounds 5 ounces of serum, which would measure 410 fluid ounces. This being reduced to minims,* and multiplied by 0.0000614, gave 12 minims as the whole quantity in the blood. More than this was used in practice, Snow noted, because some of it reached no further than the upper airway. But he found that if he put 12 minims into a "bladder" and breathed it over and over again ("in the manner of taking nitrous oxide") it sufficed to induce anaesthesia to the second degree (in which "the mental functions are impaired, but not necessarily suspended"). To induce the third degree (in which surgical operations were best performed) about 18 minims would be absorbed; to induce the fourth degree (when the breathing is stertorous, the pupils dilated, and the muscles completely relaxed and the patient "perfectly insensible"), 24 minims; while to induce respiratory arrest (the fifth degree), about 36 minims would be absorbed.

*One minim, or 1/60 of a fluid drachm, is equivalent to 0.0616 ml.

Snow, therefore, quantified the degrees of anaesthetic depth. Although in practice he relied on the clinical signs, he knew from his research how much ether or chloroform he would require for an anaesthetic and how much a patient would have absorbed at a particular depth of anaesthesia.

The uptake of volatile agents

The efficacy of ether and chloroform was immediately welcomed, but it soon became clear that neither agent was ideal. So Snow began to search for the "perfect" anaesthetic. (He also sought a "perfect" local anaesthetic, including freezing mixtures, but the lack of success in this search led him to abandon it in order to concentrate on the search for a perfect narcotic vapour.[33]) As Richardson wrote, "his grand search was for a narcotic vapour which, having the physical properties and practicability of chloroform, should, in its physiological effects, resemble ether in not producing, by any accident of administration, paralysis of the heart"; he was looking for "an anaesthetic which might be inhaled with absolute safety, and which would destroy common sensation without destroying consciousness."[34] His studies performed from 1848 to 1851 were conducted with this in mind. Although he never found the perfect anaesthetic among the eight volatile agents he studied (ether, chloroform, ethyl nitrate, carbon disulphide, benzene, tribromomethane, ethyl bromide, and 1,2-dichloroethane), he did learn a very great deal about these substances and about the nature of anaesthesia.

Indeed, this research enabled him to formulate "Snow's rule." He wrote as follows:

> We find that the quantity of each substance in the blood, in corresponding degrees of narcotism, bears a certain proportion to what the blood would dissolve – a proportion that is almost exactly the same for all of them, with a slight exception in the case of benzin, which I believe is more apparent than real. The actual quantity of the different substances in the blood, however, differs widely; being influenced by their solubility. When the amount of saturation of the blood is the same, then it follows that the quantity of vapour required to produce the effect must increase with the solubility, and the effect produced by a given quantity must be in the inverse ratio of their solubility....[35]

He found that this rule held good for all the substances and, in addition, for carbon bichloride, ethyl iodide, ethyl oxide acetate, methyl oxide nitrate, pyroxilic spirit, acetone and alcohol. This "general law," Snow said, did not apply to all narcotics, but only those producing effects "analogous to what are produced by ether, and having . . . a similar mode of action." He went on to explain: "I am not able at present to define them better than by calling them, that group of narcotics whose strength is inversely as their solubility in water (and consequently in the blood)." He added that "in estimating their strength, when inhaled in the ordinary way, another element has to be taken into account, viz., their volatility; for that influences the quantity that would be inhaled." Interestingly, he arranged all the volatile substances he mentioned in two series: "in the first column, in the inverse order of their solubility, which is the direct order of their actual potency; and in the second column, in the order in which they stand after their volatility is taken into the account, which is the order of their potency when mixed with air till it is saturated at any constant temperature."

This series of studies did not include studies of another volatile agent, amylene. He conducted other experiments on this[36,37] and also on amyl chloride.[38] Amylene was associated with two deaths in Snow's hands – a most unusual occurrence and in contrast to his experience with chloroform, from which he himself never had a fatality directly resulting from its use in the entire decade of his experience with it.

Elimination of volatile agents, carbon dioxide metabolism and rebreathing

Snow was concerned with the "speedy subsidence" of the anaesthetic state as well as its onset. Having, in 1847, "ascertained that the vapour of ether was given out again from the lungs unchanged,"[39] he conducted experiments to determine whether preventing removal of volatile agents during exhalation would prolong their effects. Snow in fact formulated the concept of rebreathing in a closed circuit using the principle of carbon dioxide absorption; he did so 65 years before Dennis Jackson described his research into carbon dioxide absorption.[40]

Passages from a paper he wrote in 1850 provide the details of this research:

> I have assumed from the first that the speedy subsidence of the narcotism caused by chloroform and ether, in comparison with that from alcohol and other narcotics, depends on the volatility of the former substances, which allows of their ready exit by the expired air . . . . It was previously estimated, for instance, that twenty-four minims of chloroform are contained in the blood of an adult of average size in a state of very complete insensibility; this being about one-twenty-eighth part as much as the blood would dissolve. The inhalation being now discontinued,

> the fresh air which reaches the air cells will abstract from the blood nearly one-twenty-eighth part as much as it can hold in suspension at the temperature of 100° [38.°C] and as each hundred cubic inches of air when saturated at 100°, contains 43.3 cubic inches of vapour of chloroform, 43.3 ÷ 28 = 1.54 cubic inches, or 1.48 minims, will be the quantity removed by the first hundred cubic inches of air which reaches the air cells. It has been shown that about half the inspired air gets as far as the air-cells; and supposing the patient to be breathing 400 cubic inches in the minute, 200 cubic inches would act in the removal of the vapour. In this manner it would take two minutes and a half to reduce the quantity of chloroform from 24 to 18 minims . . . after which the effects would diminish more slowly . . . . It follows as a necessary consequence of this mode of excretion of a vapour that, if its exhalation by the breath could in any way be stopped, its narcotic effects ought to be much prolonged.[41]

Having formulated the hypothesis, Snow sought to test it. To do this he designed three experiments. They showed that "such is the case."

What Snow did was as follows. First, he introduced some 750 cubic inches of oxygen into an impermeable balloon attached to his ether inhaler. He put four ounces of "solution of potassa"* into the inhaler, to the other opening of which was attached a tube connected to a valveless face mask. After inhaling as much chloroform as he himself could take "without being rendered unconscious," he breathed the oxygen from and to the balloon and over the potash solution. This process of rebreathing he continued for ten minutes, "during which time the feeling of narcotism subsided very little." He noticed that the feeling of narcotism passed off "very slowly afterwards, about half an hour elapsing before it was quite gone." On a second occasion he used the same quantity of oxygen and potash solution but placed 15 minims of chloroform in the spiral inhaler, in a small glass vessel, which prevented its mixing with the potash. He breathed as in the first experiment and found that he could do so for 15 minutes; the effects of the chloroform were induced in the first three minutes, producing "narcotism" but not unconsciousness. He discontinued the experiment "on account of a feeling of want of breath"; the effects of the chloroform did not pass off for another half-hour. In the third experiment he used two and a half drachms of ether, finding that he could breathe the oxygen for 20 minutes.

*The active ingredient of this solution, as far as Snow was concerned, was potassium hydroxide.

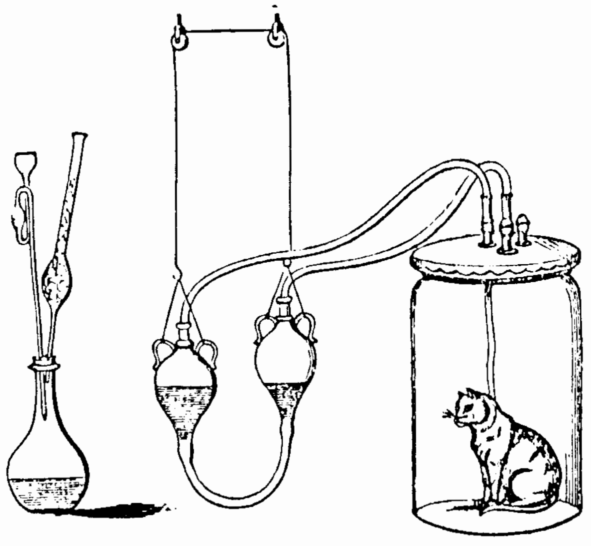


FIGURE 5 Apparatus used by Snow in 1851 to measure quantity of carbon dioxide excreted by animals during anesthesia. It was based on apparatus used by Regnault and Reiset in 1849 in their studies on respiration in animals.

He observed that "the effects of the small quantity of chloroform and ether inhaled in these experiments would have passed off in three or four minutes, if the exhaled vapour had been allowed to diffuse itself in the air in the usual way." He had shown that his hypothesis was sound. He did not, however, evidently put his idea into practice.

Remarkably, Snow was able to measure the amount of carbon dioxide exhaled before he breathed chloroform and while he breathed it. In experiment 67 of the narcotism series of studies, for example, he determined that 42 grains* of carbon dioxide were absorbed by the potash while he was breathing oxygen for ten minutes before he breathed the chloroform but just 33 grains of carbon dioxide after inhaling the chloroform.[42] He also found that the production of carbon dioxide was reduced from 4.20 to 3.30 grains.

Metabolism in anaesthesia and the theory of anaesthesia

The absorption of carbon dioxide to prolong the effects of ether and chloroform was only one aspect of Snow's overall interest in carbon dioxide excretion. This was a distinct phase of his research – "a separate branch of the inquiry into the action of narcotic vapours"[41] – and much of the concluding paper in his series "On Narcotism by the Inhalation of Vapours" in 1851[42] concerned his measure-

*One grain is equivalent to 0.065 gram.

ments of the amount of carbon dioxide excreted during anaesthesia. These experiments illustrate Snow's familiarity with respiratory anatomy and physiology[43] and his interest in the mechanism of anaesthesia.

The apparatus he used in these experiments (Figure 5) was based on that used by the two French respiratory physiologists, Regnault and Reiset.[44] In these experiments he placed a small animal (e.g., a dog or a cat) or a small bird (e.g., a pigeon) in a large glass jar that was covered with a lid containing three apertures. One aperture served for the introduction of ether or chloroform; the other two were connected by rubber tubing to the tops of two glass vessels, each of which was connected to the bottom of its fellow by a single piece of rubber tubing. In one phase of the experiment one of the vessels would be filled with an aqueous solution of potash; when full it would be raised, by a pulley, to a level higher than that of its fellow, which would then become filled with the potash solution. "As the tube from one of the potash vessels," Snow wrote, "is continuous with one which descends nearly to the bottom of the jar containing the animal . . . air is alternately withdrawn and returned to its upper and lower part. A constant circulation of air thus takes place, and the carbonic acid gas becomes absorbed soon after it is given off from the lungs."

Snow measured the carbon dioxide exhaled in the following way. He placed the "vitiated" potash solution in a flask and boiled it to expel the volatile agent. The flask, closed with a stopper through which passed a "safety tube" and a tube containing calcium chloride, was weighed, together with a bottle of sulphuric acid. Next, the acid was introduced through the safety tube into the potash solution. Carbon dioxide was expelled from the flask through the calcium chloride, its place being taken by air that passed into it through the other tube. After the flask had been cooled to the temperature at which it had previously been weighed, the flask was weighed again: the loss of weight showed that quantity of dry carbon dioxide expelled. "On deducting from this the small quantity known to have been contained in the solution of potassa employed, the remainder shows the quantity which has been absorbed by it during the experiment."

Ten experiments on animals constituted this phase of Snow's research. He found that the amount of carbon dioxide given off always decreased during their exposure to chloroform or ether. This was consistent with the findings in the experiments he had conducted on himself.

The results of these studies were of great significance to Snow in relation to his thinking about the mechanism of anaesthesia. The following excerpts from his 1851 paper reveal his concept of the mechanism, or theory, of anaesthesia:

> The diminution of the amount of carbonic acid gas excreted by the lungs under the influence of chloroform, ether, and alcohol, shows that the processes of oxidation going on in the body are lessened, for the amount of carbonic acid given off has a pretty close relation to the quantity of oxygen consumed.
>
> Chloroform, ether, and similar substances, when present in the blood in certain quantities, have the effect of limiting those combinations between the oxygen of the arterial blood and the tissues of the body which are essential to sensation, volition, and, in short, all the animal functions. The substances modify, and in larger quantities arrest, the animal functions, in the same way, and by the same power, that they modify by and arrest combustion, the slow oxidation of phosphorus, and other kinds of oxidation unconnected with the living body, when they are mixed in certain quantities with the atmospheric air.
>
> This explanation is probably applicable to the action of all narcotics whatever, but is here applied only in the class considered in these papers, namely the volatile narcotic substances not containing nitrogen, or those substances whose power was found to be in the inverse ratio of their solubility in water and the serum of the blood.[42]

Snow thought that this concept of the mechanism of anaesthesia was the best observation he had ever made.[45] Certainly it was important in his day, for some of Snow's contemporaries, in contrast to Snow, equated anaesthesia with asphyxia.[46] As early as February 1847 Snow showed that "asphyxia was a very different state from that produced by ether," for he had found that the effects of ether in air were no different from those of ether in oxygen.[47] Snow thought that his concept of anaesthesia would not be lost as "an historical truth"[48] – and it is by no means obvious that we have yet advanced far beyond Snow regarding a firm and clear understanding of the mechanism of anaesthesia. Faced with complex mechanisms that are difficult to understand and explain, we frequently resort to analogical expression – which is precisely what Snow did, as his friend Benjamin Ward Richardson told:

> Placing a taper, during one of our experiments, in a bottle through which chloroform was diffused, and watching the declining flame, he once said, "There, now, is all that occurs in narcotism; but to

> submit the candle to the action of the narcotic without extinguishing it altogether, you must neither expose it to much vapour at once, nor subject it to the vapour too long: and this is all you can provide against in submitting a man to the same influence. I could illustrate all the meaning of this great practical discovery on a farthing* candle, but I feel the experiment would be thought rather commonplace."[49]

The significance of Snow's researches in anaesthesia is profound. Snow charted waters that until then were completely uncharted. His work on inhalers set a precedent for the evolution of equipment that characterized the evolution of anaesthesia in England in the second half of the 19th century; it also provided a scientific basis for what was otherwise a crude craft. Delineating the clinical stages of anaesthesia set guideposts along the passage into and out of anaesthesia, which was otherwise unmarked. His concern with the uptake and elimination of anaesthetic agents presaged interest in the pharmacodynamics of volatile agents that came much, much later. In sum, Snow's researches in anaesthesia were the first pharmacological and physiological experiments in anaesthesia, and their significance is such that Richardson said of Snow's work that "what had been a mere accidental discovery was turned by the touch of the master into a veritable science."[50]

Snow's research on cholera

Ether and chloroform were tangible substances about which, in part due to Snow's efforts, there was, soon after their introduction as anaesthetics, a good deal of chemical knowledge and an increasing body of physiological understanding. The cholera vibrio, however, had neither been seen nor studied, and speculation rather than knowledge determined the action of physicians and public health authorities. Snow's research on cholera led to a new understanding of the disease and so of its prevention. With this new understanding, too, came an easing of some of society's fears about the disease and of some of the social tensions that the dread disease induced.[51] What Snow achieved in his epidemiological research on cholera was to construct a useful paradigm for the understanding of cholera. He helped to bring intellectual order out of emotional chaos.

Snow's approach to research on cholera was not dissimilar to his approach to research in anaesthesia. He began by making clinical observations; with these he formulated a hypothesis; to prove or disprove it he conducted what became a classic epidemiological investigation; a theory then resulted.

Snow's observations were based on his own experience, on the experiences of others and on extensive reading of the medical literature. The starting point was his own experience of cholera, gained in 1831 when, as an apprentice apothecary, he attended victims of cholera among miners in Killingworth, in the north of England. After seeing more of cholera in later years he came to make two important conclusions and an important deduction.[40] First, in contrast to most of his contemporaries, he concluded that cholera is a local affection of the alimentary canal and that it is communicated from one person to another. Next, 34 years before Koch demonstrated the existence of the cholera vibrio in 1883, Snow made an astute deduction based on his observations:

> . . . the disease must be caused by something which passes from the mucous membrane of the alimentary canal of one patient to that of the other, which it can only do by being swallowed; and as the disease grows in a community by what it feeds on, attacking a few people in a town first, and then becoming more prevalent, it is clear that the cholera poison must multiply itself by a kind of growth changing surrounding materials to its own nature like any other morbid poison; this increase is the case [sic] of the *materies morbi* of cholera taking place in the alimentary canal.[52]

Later, he emphasized that "the morbid matter of cholera having the property of reproducng its own kind, must necessarily have some sort of structure, *most likely that of a cell*"[53] (italics added).

Snow noticed that lack of personal hygiene and overcrowding were associated with cholera. But, Snow argued, "there is often a way open for it to extend itself more widely, and that is by the mixture of the cholera evacuations with the water used for drinking and culinary purposes, either by permeating the ground and getting into wells, or by running along channels and sewers into the rivers."[52]

Snow thus concluded that cholera was a water-borne infection. But, in the prevailing climate of thought that favoured a miasmatic rather than a contagious cause of cholera, if Snow was to convince anyone that he was correct, he had to prove the soundness of the theory that he had arrived at in the fall of 1848 and published first late in 1849.[54]

To put his theory to the test, Snow had to wait until 1854. In that year, London witnessed "the most terrible outbreak of cholera which ever occurred in this kingdom [of Great Britain]."[55] The epidemic centred on Broad

*A farthing, no longer in circulation in Great Britain, was worth one quarter of a penny.

FIGURE 6 "Spot" map constructed by Snow in 1854 to pinpoint the "epicentre" of cholera epidemic affecting the Golden Square and Broad Street area of Soho, London. (Each "spot" [bar] represents a death from cholera.)

(now Broadwick) Street (Figure 6). Snow, who practised in London, now made the most of his opportunity. Within a few weeks in the late summer of 1854 he conducted the two-phase investigation for which he is justly famous.

The first phase of the investigation comprised studies of the Broad Street epidemic. Snow soon concluded that the cause was contamination of the water pump in Broad Street: "there was no circumstance or agent common to the circumscribed locality in which this sudden increase of cholera occurred, and not extending beyond it, except the water of the . . . pump."[56] His opinion, now a conviction, led him to urge that the handle of the offending pump be removed. Although the epidemic had in fact begun to wane at that time, this legendary action was seen to be closely associated with the diminution of the number of cases of cholera. (The building that is at present located closest to the site of the pump is a "pub" known, ironically, for Snow was essentially a teetotaller, as "The John Snow." A plaque on the wall of the pub identifies the site as one of London's historic sites.[59])

The second phase of the investigation was much more far-reaching. In conducting it, Snow was at his most thorough, conscientious and single-minded. Wrote Snow, "I resolved to spare no exertion which might be necessary to ascertain the exact effect of the water supply on the progress of the epidemic."[57] He obtained the addresses of persons who had died of cholera in some districts in London where the water pipes, though carrying water supplies by two different companies, happened to be "intermingled" as they passed to their destinations. Then he checked the mortality rates associated with residence in the houses against the source of the water supplied to them. One source of supply originated in an unpolluted part of the river Thames; the other, in a polluted part. He did the bulk of this research largely single-handed; he explained this by saying, "I was desirous of making the investigation myself, in order that I might have the most satisfactory proof of the truth or fallacy of the doctrine which I had been advocating for five years."[58]

A remarkable feature of the investigation was its extent. It was an experiment "on the grandest scale":

> No fewer than three hundred thousand people of both sexes, of every age and occupation, and of every rank and station, from gentle folks down to the very poor, were divided into two groups without their choice, and, in most cases, without their knowledge; one group being supplied with water containing the sewage of London, and, amongst it, whatever might have come from the cholera patients, the other group having water quite free from such impurity.[60]

The essence of Snow's findings was this: in the first seven weeks of the epidemic, the mortality for persons living in the houses supplied with the polluted water was 8.5 times higher than for persons living in the houses supplied with the unpolluted water.[61] Later analysis of 21 subdistricts supported this: for the same period the mortality ratio averaged 7:1.[62]

Snow had done what no one else had done: quantitate the effect of cholera-contaminated water. Thereafter, the tide of opinion turned. One person who changed his mind about the value of Snow's work was Sir John Simon, the first Medical Officer of Health for the City of London, Medical Officer to the General Board of Health and Medical Officer of the Privy Council. Although for many years Simon never shared Snow's opinion that cholera was spread by water, he did come to write in 1890 this of Snow's concept: "though now more than 30 years old, [it] may probably still be counted the most important truth yet acquired by medical science for the prevention of epidemics of cholera."[63]

Although there were flaws in Snow's research,[64] it has deservedly been regarded as "a nearly perfect model" of epidemiological analysis and his argument as having "the permanence of a masterpiece."[65] (These flaws included the lack of proof that the Broad Street pump was actually contaminated, the absence of explanation for the rise and fall of the epidemic though the water supply had remained unchanged, the lack of information about the numbers of persons living in each of the houses in the various districts, use of a rather primitive chemical test to differentiate the two water supplies and the degree of elevation of land related to the water supply.[64]) His research on cholera, conducted on "the grandest scale," yielded results that, too, were of the grandest scale. Acceptance of Snow's theory meant that cholera could now be prevented, and, after 1866, cholera returned to Snow's own country no more. Snow's work came to benefit countless persons. Recognizing this, Henry Whitehead, formerly a coworker with Snow, praised Snow as being "as great a benefactor . . . to the human race . . . as appeared in the nineteenth century."[66]

Snow's research on other topics

Snow was licensed to practice medicine in 1838, at the age of 25, when he passed the examination of the Society of Apothecaries. A year earlier, when still a student, he had joined the Westminster Medical Society in London (later, the Medical Society of London), and regular attendance at its weekly meetings provided him with his postgraduate education. His participation in the Society's meetings enabled him to identify problems on which, interested as he was in research, he could cut his teeth. As he matured and as he worked towards his MD degree (obtained in 1844), the wide variety of topics discussed by the Society's members gave him much food for thought.

In the years before he concentrated on anaesthesia and cholera, Snow spoke on a number of topics at meetings of the Westminster Medical Society and he conducted research on some of them. In addition to neonatal asphyxia and carbon dioxide toxicity, the topics that interested Snow in his early years constituted a diverse group indeed: arsenic-containing candles;[67] injection of arsenious acid into cadavers;[69] postscarlatinal anasarca;[69] distortion of the chest and spine in children caused by enlargement of the abdomen;[70] the circulation in the capillary blood vessels;[71] inflammation;[72] lead carbonate poisoning;[75] haemorrhagic smallpox;[74] strangulation of the ileum;[75] and urinary calculi.[76] Later papers concerned inhalation of medicaments,[77] purpura haemorrhagica,[78] mortality in different occupations[79] and the adulteration of bread as a cause of rickets.[80] None of his research on these topics is of particular importance, yet it constitutes another facet of his work that impels one to conclude that Snow was a complete physician. These topics interested him as a general practitioner but they reveal him in our eyes as a physician who had broad interests in not only medical problems but social problems; as a physician who not only read widely but wrote on numerous topics of current interest; as a physician who was both curious and observant; and as a physician who was also a medical scientist with original ideas – ideas that, as his papers on environmental topics shared, are relevant today.

These aspects of Snow's interests are gems that add colour and variety to this remarkable physician's career. But, in the context of research, they also illustrate those traits in Snow's character that fitted him for research. He recognized a problem, sought ways of investigating it and then drew conclusions relating to current practice. Snow always wished to study a topic that interested him by doing the work himself, in part no doubt because he knew that the work would then be done thoroughly. As a medical student at the proprietary school of anatomy in Great Windmill Street in London (associated with the name of William Hunter[81]), he determined that the practice of using arsenious acid to preserve cadavers was indeed dangerous; he reported that he made "a careful examination" of the subject – a phrase that was characteristic of him then as it was later when he studied the London cholera epidemic of 1854.[46] He left no stone unturned.

Discussion

For John Snow, life was short but his art was long indeed. His life lasted only 45 years; his career as a physician, only two decades; his concern with the epidemiology of cholera, only 11 years; and his research in anaesthesia, but five years; yet in so short a career Snow conducted research that greatly expedited the evolution of two aspects of medicine. What is the significance of his research?

Snow's research has exerted its effect principally on the thinking and practice in the two fields of medicine that concerned him most – anaesthesia and epidemiology.

His research in anaesthesia was conducted during the first decade of this new discipline's development. The decade began with ether and chloroform being administered by means of crude equipment and by individuals who were not trained for the task; but it ended with these agents being accurately administered from relatively sophisticated equipment by, in England at least, physicians who derived from, and gave to, anaesthesia a rapidly developing sense of professionalism. The decade opened in the complete absence of theoretical and practical knowledge of anaesthesia; it closed with a considerable body of knowledge being available to those who administered anaesthesia. The decade started with anaesthesia regarded as a craft based on empirical techniques; it finished with anaesthesia, certainly in England, as a medical discipline founded on scientific knowledge and principles. Much of all this was largely the outcome of the work of one man – John Snow. He provided a paradigm for the understanding and practice of this new field of medical practice, even though it was some years before his influence was fully felt and appreciated.

In integrating research with clinical practice, Snow set an example for other 19th-century English anaesthetists to follow. But Snow himself was following the path taken in the late 18th century in England by a group of men who practised "pneumatic medicine" – Henry Cavendish, Joseph Priestley, James Watt, Josiah Wedgwood, Richard Pearson, Thomas Beddoes, and Humphrey Davy.[82] These men, familiar with the new chemistry that was directed to elucidating and making use of gases like oxygen, carbon dioxide, nitrous oxide and ether, stimulated an interest in chemistry and familiarity with crude inhalational equipment. Snow grew up when the work of these men was still relatively new. Snow, too, was only 13 years younger than Henry Hill Hickman, who was carrying out his experiments on carbon dioxide in the early 1820's,[83,84] when Snow had already set his sights on medicine as a career. Snow, of course, conducted his research after anaesthesia had finally been introduced into clinical practice, but he did so with a clear idea of the objectives of clinically oriented research, and it is because of this that his research gave direction to the new discipline of anaesthesia.

The most far-reaching influence of Snow's work in anaesthesia was its effect in professionalizing anaesthesia. This influence was summarized by Mushin in his John Snow Memorial Lecture for 1964 in the following terms:

> Snow was not the first or the last to have an inventive mind. Nor was he the first or last by accident of birth to live when a new door of knowledge is opened. He was, however, one of those rare men able to distinguish clearly between the value and importance of manual dexterity in medicine, however advanced it may be and however much application and development of skill it may need, and those intellectual processes of mind given to so few which can recognize the dependence of craft on continually expanding medical scientific knowledge. For without an appreciation of this, any manoeuvre performed by the hand is of no more significance or capable of true development than that of the simplest and most elemental man in prehistoric times.[85]

Part of the legacy of Snow's work, then, is the way anaesthesia began to evolve as a professional specialty.

Snow's work has exerted an influence partly through his writings. Although many of his publications were based on research, he wrote nothing without directing it to his fellow anaesthetists, so that they might be able to apply the results of his research in their everyday practice. Snow wrote a monograph on ether and a textbook on chloroform and other anaesthetics, together with many journal articles on anaesthesia-related subjects. Their volume and their quality placed Snow in an unrivalled position in his day as the doyen of English anaesthetists; his writings and his precepts profoundly influenced his fellow anaesthetists. The teachings embodied in his writings have also influenced the practice of anaesthetists who came long after him. His writings publicized a number of fundamental anaesthetic problems. It was Snow who formulated the rule relating solubility and potency; who pointed out the effect of temperature on vaporization of volatile agents; who conducted the first pharmacological experiments on the action of anaesthetic agents; who conceived the idea of carbon dioxide absorption in a closed-circuit apparatus; and who stressed the need to understand the physiochemical and physiological principles underlying the anaesthetic state and determining its safety. For Snow, research and clinical practice went hand in hand; but his research ultimately was the servant of clinical practice and so the resulting knowledge formed the matrix of anaesthesia. Each usage of a modern vaporizer, for example, is an unspoken testament to Snow's contributions to anaesthesia. The knowlege his research yielded entered the unwritten lore of anaesthesia, just as the knowledge of grammar enters the unwritten lore of speech yet is seldom overtly recognized for what it is.

Snow's research on cholera was designed to solve different problems from those of anaesthesia, but its influence too has been far-reaching. An immediate effect was to provide mid-Victorians with a sound paradigm for the understanding of cholera. The significance of his research lay in its originality; the reviewer of his critical work on cholera wrote of Snow's theory of the transmission of cholera that it presented "an entirely novel view of the mode in which it may become diffused."[86] Snow's view prevailed, and so countless thousands of people have unknowingly benefited, for Snow's research meant that they never contracted cholera.

Snow's research on cholera exerted an influence through his writings, too. Snow's epidemiological method has inspired epidemiologists, even up to the present day, and many current texts on epidemiology cite Snow's research on cholera as a model of epidemiological investigation. Although modern epidemiologists vary in the emphasis they place on Snow's work and in their interpretation of his work in relation to modern concepts of epidemiology,[87–90] a representative opinion is that "John Snow's contribution was to evolve an elegant, internally and externally consistent theory which concerned the mechanisms and processes involved in every aspect of the subject he had chosen to study."[88]

Finally, Snow's ideas, embodied in his writings, on cholera as on anaesthesia, continue to be of relevance. Snow is one of those figures who are historically significant because the ideas carry their meaning across the years. Kendall has suggested a test for the significance of ideas of historical figures: "read some of the papers of the great men of the past and see whether you do not come out with some new ideas bearing on your own work."[91] In this light, Snow's research is as significant in direct proportion to the number of those who have read his writings in the past, who read them today and who will read them in the future.

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Résumé

La direction de John Snow en épidémiologie et en anesthésie est le résultat de sa recherche ainsi que de sa pratique clinique. En anesthésie l'investigation de Snow était concernée par la concentration des agents volatiles et le développement des inhalateurs efficaces; l'admission et l'élimination des agents volatiles; les phases de l'anesthésie; le métabolisme d'anhydride carbonique et la respiration circulaire des gaz; le métabolisme en anesthésie et la théorie d'anesthésie. En épidémiologie, Snow a investigé la relation entre l'approvisionnement de l'eau et la moralité à Londres pendant l'épidémie de choléra en 1854, ce qui l'a aidé a formuler une théorie valide et originale sur la transmission du choléra. L'investigation de Snow a reçu moins d'attention que les anecdotes concernant sa carrière (par exemple, quand il a donné une anesthésie à la reine Victoria et aussi quand il a demandé d'enlever la poignée d'une pompe à eau), et il était toujours dirigé vers la solution de problèmes cliniques. La signification de son investigation est évidente dans sa direction, non seulement dans les soins de la santé mais aussi dans l'évolution de l'anesthésie et de l'épidémiologie comme disciplines professionelles.

Appendix

Accuracy of Snow's calculations on the volume of ether vapour taken up by 100 cubic inches of air at different temperatures.

In his major text *On Chloroform and Other Anaesthetics: Their Action and Administration*, Snow stated that at 40° F (4.4° C) 100 cubic inches of a saturated mixture of ether vapour and air would contain 27 cubic inches of ether vapour; he tabulated the proportional volumes at other temperatures also (pp. 347–48). To answer this question, the volume of ether vapour in 100 cubic inches of air at 40° F has been calculated using data from the *CRC Handbook of Chemistry and Physics* (67th edition, ed. R. C. Weast, Boca Raton, CRC Press, 1986), as follows:

1 Calculated vapour pressure of ether at 40° F (4.4° C) = 194.3 torr in a total atmosphere of 760 torr (1 standard atmosphere). This is 25.5 per cent of the pressure, or the partial pressure of the ether.

2 Amayat's law of partial volumes indicates that this vapour, if separable from the total volume, would occupy 25.5 per cent of the volume, or, in this case, 25.5 cubic inches of the 100 cubic inch basis.

This volume (25.5 cubic inches) differs very little from

Snow's calculated volume. The difference of 1.5 cubic inch can be explained on the basis that the ether Snow used was likely not to have been completely pure. He stated that its specific gravity was 0.735 at 60° F (15.5° C) and its boiling point, 98° F (36.8° C); today, the specific gravity of ether is put at 0.7138 gram per ml and the boiling point at 34.5° C.

Surprisingly, Snow, along with others, believed that chloroform contained two atoms, and that the atomic weight of carbon was six. These errors nullified each other, so that if Snow's own calculations were based on such beliefs no error resulted.