John Snow – Reductionist?

Dr. D. Zuck

Introduction

Apart from John Snow's *Case Books*, [1] from which it is possible to follow his clinical activities daily during the last ten years of his life, there is no direct evidence of his attitude to the events that were taking place around him, medical, scientific, cultural, or political. All the other records that he must have kept, of his experimental work, and perhaps of his thoughts and opinions, disappeared after his death. So Richardson's biographical essays give us no idea, for example, of how Snow would have reacted, had he lived eighteen months longer, to the publication of *The Origin of Species*; but examination of some of Snow's writings, and the opinions expressed in them, provides a clue to his philosophy of science. In particular, when one reads his contributions to the Westminster Medical Society, and the discussions that followed, one becomes aware very quickly that his mind functioned on a different wavelength from those of his fellow members, in that his knowledge of contemporary physiology, and his understanding of the implications of its findings for clinical medicine, was profounder, and that he was much readier to apply the basic sciences to the elucidation of physiological problems. This was emphatically brought home to me some years ago, when I read Raymond Fink's translation of Pirogoff's treatise on ether. [2]

Pirogoff is remembered today for his rectal ether technique, but the book contains also an account of his investigation of the mechanism of the action of ether, by experiments on conscious animals, mainly dogs. He applied ether to the peripheral nerves, the spinal cord, and the surface of the brain. He injected it into the carotid artery, the femoral artery, and the femoral vein;

and into the trachea, before and after section of the vagus nerves. All of which could be called typical nineteenth-century pharmacology, as practised by Magendie, Flourens, and Claude Bernard.

What is striking is the comparison with John Snow. Virtually all Snow's investigations, both clinical and anaesthetic, were chemical, and quantitative - not anatomical in the way that the classical pharmacologists of the 19th century investigated drug action. Snow researched inhaled concentrations and blood levels, and their relation to the depth of anaesthesia; in effect he set an agenda for an approach that was not taken up again until almost a century after his death. He had a propensity to look for general solutions to problems. For example, to distinguish between houses being supplied with water by the Lambeth Company, which drew it from a clean site thirty miles upstream, and the Southwark and Vauxhall, which took it from the tidal reaches of the Thames, he just measured the saline content;[3] and to estimate the blood level of ether at various depths of anaesthesia, it will be found, if his account is read carefully, that he did not do individual measurements. He evaluated the air-blood partition coefficient, and then calculated the blood content in each case from what his table of saturated vapour pressures told him was the concentration of ether in the mixture that he was administering. [4] Looking for a description of this approach, this attempt to reduce to a common denominator, I was led to the expression *reductionism*.

Reductionism

Reductionism is a word that can be applied to many activities in many ways, but here it is being used in a sense derived from a paragraph in Nagel's classic text on the philosophy of science, which is, that the methods of what he calls the modern natural sciences, are fully adequate to research the vital

processes of biology, and explain them in physicochemical terms - with the result that eventually the whole of biology would become simply a chapter of physics and chemistry. [5] So this enquiry is directed to ascertaining to what extent John Snow was prepared to use the methods of what we call the basic sciences to investigate physiological and pharmacological questions, and, more importantly, to accept the validity of the results without additional appeal to arcane mechanisms and mysterious indemonstrable forces.

We have become so used to the part played by the basic sciences in modern medicine that this must seem a stupid question, until we remember that from about 200 AD until little more than a century before Snow's birth, the received explanations of physiological phenomena were Galenic, or tinged with residual Galenism. Thus the veins possessed a blood-forming faculty, the arteries and the heart a pulsatile faculty, the muscles a contractile faculty, and the intestinal tract a digestive faculty. [6] According to Galen, the body had as many faculties as it had specific activities. End of physiology lesson!

Vitalism and Natural Theology

In Snow's time the prevailing philosophy was not Galenism but Vitalism. The concept of vitalism originated with Georg Stahl (1659-1734), and revolved around the idea that the body tended towards decay, but was protected from dissolution by the immortal soul, or anima. In the hands of Stahl's successors the anima was replaced by a vital principle, inherent in all living tissues, that counteracted the tendency to death. Vitalism was the accepted philosophy during the late eighteenth century. John Hunter, for example, was a confirmed vitalist; but vitalism then had little practical relevance. However, during the early nineteenth century the doctrine began to impinge on the physiological research of such notables as Magendie, and a

little later, Claude Bernard. The vitalistic belief was expressed in its clearest form by the influential French anatomist and physiologist, Xavier Bichat (1771-1802). He wrote that there is an immeasurable distance between the laws that govern the phenomena of the physical and the physiological sciences. "The laws of natural philosophy are constant and invariable ... whereas the vital functions are subject to numerous varieties ... baffle all calculations, and would require as many formulae as the cases that occur. In their phenomena nothing can be foreseen, foretold, or calculated." [7] It would be a mistake, he continued, to try to explain the phenomena of living bodies by the laws of inert bodies. A commentator added that, since the phenomena of life were different in kind, Newtonian Laws did not apply. So it is necessary to examine Snow's writings for his attitude to Vitalism.

Also there comes the problem of interpretation, because Snow's published opinions had to be expressed in terms acceptable to the religious beliefs of his colleagues, and vitalism allowed for the existence of the unknowable, the vital spark, the soul. The scientific revolution that began with Copernicus and Galileo, and culminated in Newton's definition of the laws of motion, and the extension of this mechanistic philosophy to living organisms, created problems for organized religion. On the Continent, Descartes' attempted resolution, by distinguishing between mankind and brutes and endowing only the first with a soul, was opposed by Spinoza's refusal to countenance that there could be any exceptions to the applications of the laws of nature. [8] In England the problem was resolved by a typically British compromise, *Natural Theology*, still alive and kicking under the name *Creationism,* or *Intelligent Design*: [9] God had constructed the universe, formulated the laws by which it worked, and set it going. The scientist's job was to find out what these laws were. The purpose of the Boyle Lectures of

the eighteenth century and the Bridgewater Treatises of the nineteenth was to reinforce this approach. [10] Darwin's reluctance to rock the boat is well known; and as Professor Potts has pointed out, even the great Richard Owen had to be careful when expressing his views in public. [11] The French revolution, and the concomitant anti-clericalism, had freed continental scientists from restraint, so that it was possible for the great Swedish chemist Berzelius (1779-1848), who was virtually the founder of biochemistry, to write: 'Life does not lie in any extraneous essence deposited in any organic or living body; its origin must be sought in the common fundamental forces of primal elements ... all that we explain with the words '*own vitality*' is entirely unexplained, and it is an illusion if they are given any other meaning than that of a still unknown mechanico-chemical process ...' and a little further he said: 'Unreasonable as it may seem ... our judgement, our memory, our reflections, as well as other functions of the brain, are organic, chemical processes, as much as, for instance, those of the intestines, the lungs, the glands ...' [12] But in the United Kingdom such freedom of expression was by no means the case. Hence, when reading Snow's writings some interpretation, some reading between the lines, may on occasion be necessary; but to go even as far as he did required some courage.

Contemporary Physiology

To understand Snow's position in relation to that of many of his contemporaries, it is helpful to review the considerable developments that had taken place during the previous half-century, and the contemporary problems and beliefs. Physiology, and the associated chemistry, had made great strides, especially since the 1820s. C. J. B. Williams, for example, who became the first specialist chest physician on the staff of University College Hospital, and

one of Joseph Clover's teachers, [13] gave vent to a complaint indicative of the speed with which knowledge was advancing, that became all too familiar to subsequent generations. "How often does it fall to the lot of the student of physiology to unlearn what he has been at pains to acquire!" Current problems included the source of body heat, the location of metabolic reactions, and the cause, if any, other than left ventricular contraction, of the return of blood through the capillaries and the veins to the heart; and Snow expressed opinions on all of them.

As we read the reports of discussions at the Westminster Medical Society, we become aware that the members can be divided into two populations, those fewer recent graduates who were contemporaneously up to date and knew the 'right' answers, and those older ones who didn't; and it has been noted that Snow generally started his communications with a review of the relevant contemporary physiology, no doubt for the benefit of the latter.[14] Here it is possible to consider four of Snow's publications only, from near the beginning, middle, and end of his clinical life, that illustrate his use of the basic sciences in the elucidation of questions of physiology.

Snow's Publications

The first dates from soon after Snow's qualification as surgeon-apothecary. On 7th November 1838 Mr John Goodman, MRCS, of Salford, addressed the Manchester Medical Society on the physiology of the mechanical action of the heart. [15] His paper, which ran to five full pages, was published in the *Lancet* on December 29th, and Snow's response, submitted on January 5th 1839, less than a year after he qualified, was published on 26th. [16] In summary, Goodman's thesis was that the bony chest wall, and the diaphragm, were sufficiently strong to resist the pressure of the atmosphere,

with the result that when the ventricles contract a small vacuum was left in the pericardium. This vacuum was the force that draws blood into the ventricles from the atria, which were then called the auricles, and since this was a passive effect there was no need for the auricular walls to contain any muscle fibres.

In his critique of this thesis, Snow started by pointing out that "the most delicate structures on earth bear the pressure of the atmosphere without detriment, as long as it is equal in all directions; a distended bladder, and bubbles blown in soap and water, bear it, because it is equal inside and out; but this is not what Mr. G. means with respect to the thorax." He continued, that "a thorax 10 inches deep and 30 inches in circumference (not a very large one), has 300 square inches of surface, and would have to resist a force of 4500 pounds, or more than two tons." In addition the diaphragm and the top of the thorax would have to resist half as much. "This would require thick walls of cast iron, instead of mere flesh and bone." He pointed out that in fact the atmospheric pressure was balanced inside and outside the thorax, and continued with as clear a description of the physics and mechanics of respiration as one could wish for. But the implied criticism of the the *Lancet* for publishing Mr Goodman's nonsense brought an unpleasant snub from Wakley several months later. [17]

The second example dates from January 1843, when Snow spoke at a meeting of the Westminster Medical Society about the circulation in the capillary blood vessels. [18] He discussed the exchanges that take place in the tissues, and postulated that what he called the attractions and repulsions that attend these exchanges also assist with impelling the blood to return to the heart. The background to this argument, very briefly, was contemporary doubt as to whether the cardiac impulse was sufficient in itself to effect the

complete circulation of blood, together with observations on the movement of fluid by osmosis, and a dispute about the location of the biochemical reactions that we now call tissue metabolism, which Lavoisier had placed in the lungs. As has been mentioned, a feature of most of Snow's contributions was that they started with a review of the relevant physiology, where appropriate. On this occasion Snow discussed both early and very recent researches in physical chemistry and comparative anatomy and physiology, and much of his arguments, from the ensuing discussion, must have been way over the heads of his audience. What did sting some of them was the following statement. 'I have nothing to advance concerning the intimate nature of the attractions and repulsions which accompany the changes of composition at the capillaries, and which tend to move the blood in a definite direction. I have carefully avoided such terms as chemical, electrical, and vital; both in order that I might not be misunderstood, and because I look upon chemical affinity, electricity, and vitality, rather as expressions which are useful to us in the infancy of science than as forces which have a separate and defined existence. Our ignorance, however, of the ultimate cause of these attractions is no argument against their existence; since we admit many laws in science of the causes of which we are ignorant.'

During the discussion of Snow's paper, which was reported in the *Lancet*, but not in the *London Medical Gazette*, exception was taken to his views both about vitalism and natural theology. [19] The conventional vitalist attitude was expressed by Dr. William Chowne, physician and lecturer on midwifery and medical jurisprudence, Charing Cross Hospital, a regular attender, who 'said he rather differed from Mr. Snow in his opinion respecting vitality; he considered that the vital principle was something definite and distinct from every other force, and he could in no respect agree with those

who consider that life merely arose from the structure and composition of matter.' Mr. H. J. Johnson (Assistant Surgeon, St. George's Hospital) said that 'he could not comprehend what was meant by these attractions or forces accompanying the changes which take place at the capillaries ... He was of the opinion that the arguments drawn from the lower classes of animals were scarcely valid, since nature often employs means in these animals which she afterwards leaves off when she had adopted more perfect ones ...' So Snow's tendency to reductionism was being resisted by the vitalist members of the Society, some of whom evidently were in ignorance of scientific developments, and by what one might call trial-and-error creationists, who did not share his confidence that physiological discoveries in the lower animals could be extrapolated to man.

The third example occurred in Snow's landmark paper of March 1847, which was published in the *Lancet* in two parts, on 19th and 26th.[20] During the first ten weeks of 1847 Snow, experimenting on animals and observing his patients during the administration of ether, laid down virtually all of the basic principles of inhalational anaesthesia. In particular, he established that during general anaesthesia the usage of oxygen in the body, and carbon dioxide output, are both reduced. In the second part of his March paper he observed that the depression of the central nervous system was progressive, consciousness being lost before the reflex reaction to pain, and also that a state of analgesia existed for a time while consciousness was being regained.[21] 'With respect to the psychological phenomena produced by ether, I have observed that consciousness seems to be lost before the sensibility to pain, and if an operation is commenced in this stage, the patient will flinch, and even utter cries, and give expressions of pain, but will not remember it, and will assert that he has felt none. Metaphysicians have distinguished

between sensibility and perception - between mere sensation and the consciousness and knowledge of that sensation, though the two functions have, as they supposed, always been combined. Ether seems to decompose mental phenomena as galvanism decomposes chemical compounds, allowing us to analyse them, and showing that the metaphysicians were right. During the recovery of the patient, consciousness, which first departed, generally returns first, and the curious phenomenon is witnessed of a patient talking, often quite rationally, about the most indifferent matters, whilst his body is being cut or stitched by the surgeon. I have never seen this insensibility to pain during the conscious state except where consciousness had been previously suspended.' He continued that he had intended to "make some remarks on the probable way in which ether acts in suspending sensibility," but had reserved them for a future communication, since he thought the article was long enough without them. This never appeared, but there is sufficient to indicate that Snow was implying a chemical basis for the psychological effects of general anaesthetics, hence, by implication, for consciousness itself.

The fourth, and most explicit example, dates from 1853, when, on the occasion of the 80th anniversary of its founding, Snow was elected to deliver the Oration by the Medical Society of London. The venue was the Thatched House Tavern, 85 St. James's Street, Piccadilly, a celebrated meeting place which had a large room suitable for public lectures. [22] Among the audience were some of the leaders of the profession, including Sir Benjamin Brodie. Snow used the Oration as the opportunity for promoting his theory that the morbid material that causes cholera is a living organism, and that it enters the body by ingestion, the commonest vehicle being water; and he spent the greater part of his time on this subject. But since the theory rested in part on

his ideas about the causative agent and its possible modus operandi, he had first to explain his ideas about the biochemical nature of the body. In the first ten pages of his oration we find the statement of these beliefs.[23]

Very briefly, he started with a discussion of the forces of attraction between molecules, at sensible distances, which is called gravity, and at what he calls insensible distances, very close together, which is chemical affinity. Then he went on to the phenomenon of counter-affinity, the ability of certain atoms to interfere between the affinity of one atom for another, and cited Thomas Graham's observations on the oxidation of phosphorus. This led him to combustion, and self-propagating reactions such as fermentation and putrefaction, all of which can have a beginning, given the requisite conditions, and an end, when they run out of fuel or air. In contrast to these spontaneously occurring self-limiting reactions, 'There are, however, changes of a more complicated nature - those to which plants and animals owe their development and continuance - that have never commenced anew within the experience of man.' Though they may for a time be suspended, as during hibernation, or in a seed, 'they start again at the exact point at which they ceased, and should the matter of the seed or egg have deviated into any foreign change, such as putrefaction, it is incapable of continuing the process in which it had previously been taking part. There is no distinct line of demarcation between vital processes and those which are not vital.' And he continued, reinforcing this view, '... all changes of composition, with their attendant phenomena, whether taking place within the living body or not, are alike the result of the attraction or affinity which exists among the ultimate atoms or molecules of matter.' [24] Then he made this remarkable statement: 'A species might diminish to one or two individuals without becoming extinct; and at the point at which new individuals commence, the molecular actions

are often confined to a minute quantity of substance. There is reason to believe, however, that this substance contains all the chief elementary and proximate principles of the mature being, as well as the power to communicate all those changes to suitable materials, by which they are assimilated, and made to form part of the individual.' It would be anachronistic to claim that Snow was describing RNA, but this, broadly speaking, was what he did.

So for John Snow, life consisted of a series of molecular reactions, that today we would in part call metabolism, that were continuous not only in the individual throughout his life, but throughout all living matter, and throughout all generations. By this statement he postulated a continuous line from the first particle of living matter to the present day. This claim for the continuity of life was essential for his theory of communicable diseases, because it denied the possibility of spontaneous generation. Some of his contemporaries believed that in certain circumstances it was possible for non-living entities to become living, and this was one aspect of the miasmic theory of epidemic diseases – categorised by Henle as miasmatic-contagious, which included cholera; [25] but Snow was having none of it.

He made it clear repeatedly that he was not a Vitalist. He believed that there is no essential difference between the chemical changes, or reactions, going on in the body, and those that can be replicated in the test tube. This view had been strongly influenced by the equivalence that he drew between Thomas Graham's observation that the oxidation of phosphorus in air was inhibited by certain vapours, including ethylene and ether, and his own demonstration that oxygen utilization and carbon dioxide output are reduced during ether anaesthesia. In both cases an oxidation reaction was being inhibited by an external agent. For Snow, the only difference between the vital

and the non-vital, was that as long as there is life, the molecular changes are continuous.

Having described the life-supporting purposes of these reactions, Snow turned to their reverse aspects. 'In addition to the series of continuous molecular changes having for their result the preservation of the individual and the species, there are others, occurring in living beings, that have an opposite tendency; they divert part of the substance of the individual from the actions which are natural to the species to another kind of action, in consequence of which this substance is employed in the multiplication and increase of the materies morbi of communicable diseases - an extensive group of maladies, each case of which is caused by some material that, as a general rule, has been produced in the system of another individual.' Snow was writing before Pasteur has commenced his bacteriological studies, and commentators have suggested that he was presciently describing pathogenic bacteria, but from the expression which commences *diverting part of the substance of the individual,* this suggests that he was envisaging something more like a virus; and in the light of his ideas about the nature of life, it is more rational and coherent to think of something that causes disease by subverting the normal processes, rather than to postulate an independently existing micro-organism, that is pathogenic for, in those days, no known reason.

Snow continued his argument against the miasma theory. After discussing the characteristics of communicable diseases, he went on, 'The material cause of every communicable disease resembles a species of living being in this, that both one and the other depend on, and in fact consist of, a series of continuous molecular changes, occurring in suitable materials. The organized matter, as we must presume it to be, which induces the symptoms

of a communicated disease ... possesses one great characteristic of plants and animals, - that of increasing and multiplying its own kind. ... No evident effects are produced at first by the reception of the material cause of any of these diseases. There is always a definite period, of longer or shorter duration, before the illness commences, which is called the period of incubation. As regards the materies morbi itself, is a period of something more than incubation; it is a period of reproduction.' This is different, he pointed out, from the behaviour of non-living poisons, which act very quickly, and an argument against miasmic and similar theories of communicable disease. The proponents of miasmic and similar theories had no serious suggestions about how they worked, but Snow was proposing a mechanism not just at the cellular but at the molecular level.

Snow made it clear repeatedly that he believed, like Berzelius, that there is no essential difference between the chemical changes, or reactions, going on in the body, and those that can be replicated in vitro; and almost echoing Berzelius, he described communication between individuals in these terms: 'The communication of certain molecular changes taking place in the brain ... extends collaterally in all directions, by means of vibrations in the air' (by which he meant sight and sound) '... if the brain is in a particular state of molecular action, from any object that excites fear or joy, it may cause a similar state of the brain in others of its species, by uttering a cry, or merely assuming a particular demeanour.' Even where the communication was by speech, or by writing, even across time, the essential mechanism was the same. So for John Snow, communication was just the replication, from one brain into another, of certain chemical states. One can hardly get more reductionist than that.

Richardson's Obituary

There is some oblique evidence from another quarter, of Snow's distance from the general run of his colleagues. When Richardson was writing his memoir of Snow, he, too, was constrained by the prevailing sentiment. He could hardly describe Snow as an agnostic, an atheist, or even, as he seems to imply, a Spinozan pantheist, in so many words. He had to wrap it up. So in the third version of his Memoir he said the following: 'Without any pretence, maintaining no connection with sect or party, he carried out a practical religion, independently of any hypothesis or abstruse profession, which few professors could approach. A child of nature, he knew no way of recognizing the Divine influence so purely as in silent and inexpressible admiration of those grand external phenomena which each moment convey, to men of his character, the direct impression of a Power all-present and revealing itself for ever.'[26] We may contrast this with the need felt by William Sharpey, Professor of Physiology at University College, London, in his address to the annual meeting of the British Medical Association in 1862, to placate the natural theologists, by suggesting that even Darwinism merely described the operation of a great natural cause that had been originally ordained by the Author of the Universe. [27] No such sentiment is to be found in John Snow's writings. There can be no doubt that he would have welcomed the publication of Darwin's *On the Origin of Species*. If he had lived longer, having completed his studies of anaesthetics and cholera, perhaps he would have applied his epidemiological skills to the science of genetics.

Conclusion

What I have tried to show in this paper is the enormous difference in mind-set between John Snow and the vast majority of his medical

contemporaries. Although we know today that some of his conclusions were erroneous, I hope it is not going over the top to suggest that in addition to his other virtues, he might be regarded as one of the first molecular biologists.

Acknowledgements

I am indebted to my friend Peter Vinten-Johansen, biographer of John Snow, [28] for many lively e-mail discussions and much illuminating advice; also to the librarians of the Royal Society of Medicine, and the Wellcome Library.

Endnotes

1. R. H. Ellis, ed. *The Case Books of John Snow* (London: Wellcome Institute, 1994).

2. N. Pirogoff, *Researches Practical and Physiological on Etherization,* translated by B. R. Fink (Park Ridge, Illinois: Wood Library-Museum, 1992).

3. It is true, as his critics pointed out, that the correctness of his results was aided by the seasonal height of the tides, but this does not negate the general point.

4. J. Snow, "On Narcotism by the Inhalation of Vapours," part 1, *London Medical Gazette* 41 (19 May 1848): 850-54. <http://johnsnow.matrix.msu.edu/work.php?id=15-78-6C>

5. E. Nagel, *The Structure of Science: Problems in the Logic of Scientific Explanation* (London: Routledge & Kegan Paul, 1968), 398.

6. R. E. Siegel, *Galen's System of Physiology and Medicine* (Basel: Karger, 1968), 183.

7. M. F. X. Bichat, *Anatomie Générale* (Paris, 1801); see also D. Zuck, "Anaesthesia and Physiology: the First Twenty Years," in *Proceedings of the History of Anaesthesia Society* 20 (1997): 75-90.

8. J. I Israel, *Radical Enlightenment: Philosophy and the Making of Modernity 1650-1750* (Oxford: Oxford University Press, 2001), 159-74.

9. *The Times* (September 28, 2005), p. 42, col. 6.

10. W. H. Brock, *From Protyl to Proton: William Prout and the Nature of Matter 1785-1850* (Bristol: Adam Hilger, 1985), 60-81.

11. W. T. W. Potts, "Sir Richard Owen," in *Proceedings of the History of Anaesthesia Society* 34 (2004): 28-34.

12. Cited in E. Nordenskiöld, *A History of Biology* (New York: Knopf, 1946), 272-73.

13. C. J. B. Williams, *Observations on the Changes Produced in the Blood in the Course of its Circulation* (London: Wilson, 1835).

14. D. Zuck, "John Snow on Paracentesis of the Thorax," in *Proceedings of the History of Anaesthesia Society* 30 (2002): 54-59. (Available at <http://www.histansoc.org.uk> – click on panel to enter site, click on Proceedings, and download the volume)

15. J. Goodman,"On the Physiology of the Mechanical Action of the Heart," *Lancet* 1 (29 December 1838): 515-19. (Available as a PDF, bundled with Snow's response at the URL in note #16.)

16. Snow, J. Mechanism of Respiration. *Lancet* 1 (26 January 1839): 653-55. (More readily available at <http://johnsnow.matrix.msu.edu/work.php?id=15-78-9> .

17. *Lancet* 2 (25 May 1839): 352. (<http://johnsnow.matrix.msu.edu/work.php?id=15-78-B>) It is an indication of the difference between Snow's and Wakley's mindsets, that the Editor of *The Lancet* could publish the following: 'The remarks of Mr. John Snow on a recent communication from M. H., on the physiology of respiration, have been received. We cannot help thinking that Mr. Snow might better employ himself in producing something, than in criticising the productions of others.

18. J. Snow, "On the Circulation in the Capillary Blood-Vessels," *London Medical Gazette* 31 (3 March 1843): 810-16. (<http://johnsnow.matrix.msu.edu/work.php?id=15-78-F>)

19. "Westminster Medical Society," *Lancet* 1 (1842-43): 693-95.

20. J. Snow, "On the Inhalation of the Vapour of Ether," part 1, *London Medical Gazette* 39 (19 March 1847): 499-502. <http://johnsnow.matrix.msu.edu/work.php?id=15-78-1B>

21. J. Snow, "On the Inhalation of the Vapour of Ether," part 2, *London Medical Gazette* (26 March 1847) 39, 539-42. <http://johnsnow.matrix.msu.edu/work.php?id=15-78-1B>

22. P. Cunningham, *Handbook of London (*London: John Murray, 1850), 492.

23. J. Snow, *On Continuous Molecular Changes, More Particularly in their Relation to Epidemic Diseases* (London: Churchill, 1853).

24. Although Snow's theory of communicable disease is not the principal subject of this paper, it may be pointed out that by distinguishing between fermentation and putrefaction and living processes, he was distancing himself from Farr's zymotic theory – see P. Vinten-Johansen, et al., *Cholera, Chloroform, and the Science of Medicine – a Life of John Snow* (New York: Oxford University Press, 2003), 181-85.

25. C. Singer and E. A. Underwood, *A Short History of Medicine* (Oxford: Clarendon Press, 1962), 729-30.

26. B. W. Richardson, "John Snow, M.D. – A Representative of Medical Science and Art of the Victorian Era," *The Asclepiad* 4 (1887): 274-300.

27. W. Sharpey, "Address in Physiology," *Lancet* 2 (1862): 182-88.

28. Vinten-Johansen, et al., *Cholera, Chloroform, and the Science of Medicine.*