analgesia reduces chronic phantom limb pain intensity, prevalence, and frequency: A prospective, randomized, clinical trial. ANESTHESIOLOGY 2011; 114:1144–54
2. Bach S, Noreng MF, Tjéllden NU: Phantom limb pain in amputees during the first 12 months following limb amputation, after preoperative lumbar epidural blockade. Pain 1988; 33:297–301
3. Nikolajsen L, Ilkjaer S, Christensen JH, Krøner K, Jensen TS: Randomised trial of epidural bupivacaine and morphine in prevention of stump and phantom pain in lower-limb amputation. Lancet 1997; 350:1353–7

(Accepted for publication September 13, 2011.)

Humphry Davy

To the Editor:

Riegels and Richards stated that the goal of their article on Humphry Davy (1778–1829) was to demonstrate that Davy should be regarded as the "first anesthesiologist."[1] However, after consideration of a number of the facts regarding Davy, I believe that his experiments with nitrous oxide did not directly contribute to the development of modern inhalational anesthesia, and I would hesitate to anoint him as the "first anesthesiologist."

The idea of producing insensibility to facilitate surgical procedures is not new. Many ancient societies used soporific agents and nonpharmacological techniques to produce insensibility before surgical procedures. Sixteenth-century chickens may,[2] or may not have been,[3] the unwilling and pioneering recipients of diethyl ether at the hands of Paracelsus (1493–1541).

There is no doubt that Davy was a brilliant chemist. He was also young and reckless. He engaged in dangerous self-experimentation involving a variety of potentially toxic chemicals. Some of these trials could have resulted in his premature death, which would have deprived us of one of the most quoted sentences in the anesthesia literature. The quotation regarding the use of nitrous oxide for surgery is from the eighth page (page 556) of a 12-page conclusion of the fourth and final section of Davy's book on nitrous oxide.[4] Ironically, in some additional pages (pages 577–580) at the end of the book, Thomas Beddoes (1760–1808) has written a "Proposal for the preservation of accidental observations in Medicine."[4]

Davy inhaled nitrous oxide several times a day over a period of months, for "scientific" reasons, and possibly for "pleasure." Riegels and Richards did not discuss whether they considered if Davy had become addicted to nitrous oxide; this would be one of the earliest, if not the first, documented addiction to nitrous oxide.

Horace Wells (1815–1848) and William T. G. Morton (1819–1868) encountered distressing pain in most of their patients, and were motivated by the desire to reduce it. In addition, Morton also saw the prospect of financial benefit in alleviating pain.[5] Davy's apprenticeship with a surgeon-apothecary, John Borlase, may have led him to contemplate the advantages of nitrous oxide in surgery, but there is no evidence that he approached any surgeon to trial the agent.

Davy's failure to pursue clinical trials of nitrous oxide for surgery could be equated to the failure by Charles Thomas Jackson (1805–1880) to promote ether for surgical procedures. Jackson claimed in 1847 that he had thought of using ether to produce insensibility in 1842,[5] nearly 5 yr before Morton's first trial of ether. Jackson did not approach his surgical colleagues, and continued with his work in chemistry and geology. Unlike Davy, however, there was no contemporaneous documentation by Jackson of his initial thoughts on ether as an inhaled anesthetic agent.

Davy's description of the pleasurable effects of nitrous oxide was soon followed by other accounts of the inhalation of nitrous oxide, and increasing public interest in doing so. More than four decades separate Davy's research involving nitrous oxide and the first deliberate use, by Horace Wells, of nitrous oxide to produce insensibility. In that period, countless medical students and medical practitioners used nitrous oxide and ether for recreational purposes without considering them suitable for use during surgery. Davy experienced the analgesic effects of nitrous oxide and envisioned its potential use for surgery, but failed to follow up on it. There is no evidence that Davy's research contributed directly to the development of nitrous oxide as an anesthetic agent. His research involving nitrous oxide and other gases established him as major scientific figure, and may have contributed to his move away from medicine. Perhaps there were too many things for Davy to discover. The brilliant young scientist seems to have moved quickly from one discovery to another, and eventually away from medicine into chemistry.

Rajesh P. Haridas, M.B.Ch.B., F.A.N.Z.C.A., Mildura Private Hospital, Mildura, Victoria, Australia. rajesh.haridas@bigpond.com

References

1. Riegels N, Richards MJ: Humphry Davy: His life, works, and contribution to anesthesiology. ANESTHESIOLOGY 2011; 114: 1282–8
2. Keys TE: Paracelsus, 1493–1541. Anesth Analg 1972; 51:553
3. Gravenstein JS: Paracelsus and his contributions to anesthesia. ANESTHESIOLOGY 1965; 26:805–11
4. Davy H. Researches, Chemical and Philosophical; Chiefly Concerning Nitrous Oxide, or Dephlogisticated Nitrous Air, and Its Respiration. London: Printed for J. Johnson by Biggs and Cottle, Bristol, 1800
5. Wolfe RJ: Tarnished Idol: William Thomas Green Morton and the Introduction of Surgical Anesthesia: A Chronicle of the Ether Controversy. San Anselmo: Norman Publishing, 2001; pp 63, 137–8

(Accepted for publication September 29, 2011.)

In Reply:

Haridas rejects our assertion[1] that Humphry Davy might be considered the first anesthesiologist. Curiously, Haridas avoids any mention of Davy's groundbreaking experimental results, not only as they pertain to nitrous oxide, but also in the realm of respiratory physiology. He instead mounts an *ad hominem* attack on Davy for his youth and recklessness. If youth truly deserves our censure in connection with scientific discovery, then Haridas must broaden his denouncement. With respect to self-experimentation, undertaken, as Haridas observes, at considerable peril, Davy would doubtless hold himself guilty as charged; to Davy, science was exploration, and incidental threats to his personal safety were of little consequence. In this regard, we may perhaps compare Davy's experiments to those of August Bier and August Hildebrant in spinal anesthesia,[2] or of William Halstead in local anesthesia.[3] Halstead, as a consequence of his studies, struggled with and ultimately overcame cocaine addiction,[4] and Haridas, in turn, invites us to speculate whether Davy may have been addicted to nitrous oxide. Although Davy's pattern of daily nitrous oxide use during his time at the Bristol Pneumatic Institute suggests, at a minimum, a maladaptive pattern of behavior, there is no indication either from Davy's exhaustive notes, or from the many accounts of friends and colleagues, that Davy would have met modern criteria for substance dependence. There is, furthermore, no record of Davy having consumed nitrous oxide following his tenure in Bristol. Inexplicably, Haridas equates Davy's work with nitrous oxide to Charles Thomas Jackson's claims of priority with ether anesthesia, before abruptly conceding that Jackson never published experimental results pertaining to the anesthetic properties of ether.[5]

Haridas' critique ultimately appears to crystallize into one of pragmatism: Davy, he asserts, was a failure because he did not put nitrous oxide into practical use as an anesthetic. Haridas asks us to believe that Davy's body of work at the Pneumatic Institute has no intrinsic value: No matter that Davy conducted and published an unprecedented series of experiments on nitrous oxide and other inhaled gases, he did not "follow up." Haridas will have us stop there, but many, ourselves included, will continue to wonder why not only Davy, but also the innumerable readers of his work, did not follow up, or why not even Horace Wells' failed attempt to demonstrate nitrous oxide anesthesia did not provoke greater interest in the technique. Science does not exist in a vacuum, nor do its results always succeed, in the near term, on their merits; rather it is, and always has been, vulnerable to cultural context and a socially determined sense of possibility. Haridas chooses to evaluate Davy's work on strictly utilitarian grounds and concludes that it was a failure on this basis, in that it did not lead directly to the development of nitrous oxide anesthesia. We instead see in Davy's experiments the first systematic approach to the evaluation of several gases of immense practical significance to anesthesiology; it is this approach which, to our minds, defines the first practice of anesthesiology as a science, whereby we call Davy the first anesthesiologist.

Nicholas Riegels, M.D., Michael J. Richards, B.M., F.R.C.A.*
*University of Washington and Seattle Children's Hospital, Seattle, Washington. michael.richards@seattlechildrens.org

References

1. Riegels N, Richards MJ: Humphry Davy: His life, works, and contribution to anesthesiology. ANESTHESIOLOGY 2011; 114:1282–8
2. Bier A: Versuche uber Cocainisirung des Ruckenmarkes. (Experiments on the cocainization of the spinal cord) Deutsche Zeitschrift fur Chirurgie 1899; 51:361–9
3. Halstead WS: Practical comments on the use and abuse of cocaine, suggested by its invariably successful employment in more than a thousand minor surgical operations. NY State J Med 1885; 42:294–5
4. MacCallum WG: William Stewart Halsted, Surgeon. Baltimore: The Johns Hopkins Press; 1930
5. Fenster J: Ether Day: The Strange Tale of America's Greatest Medical Discovery and the Haunted Men Who Made It. New York: Harper Collins; 2001

(Accepted for publication September 29, 2011.)

Importance of Body Temperature and Clinical Data in Behavioral and Anesthesia Studies

To the Editor:
We have read with great interest the recent article "Anesthetic Ketamine Impairs Rats' Recall of Previous Information: The Nitric Oxide Synthase *N*-nitro-L-arginine Methylester Antagonizes this Ketamine-induced Recognition Memory Deficit,"[1] and we would like to address some comments. This study stresses that nitric oxide metabolism may modify the anesthetic effects of ketamine. Although this relation has been described previously, the approach using the *N*-nitro-L-arginine methylester (a nonselective nitric oxide synthase inhibitor) to influence the cognitive deficits induced by the posttraining administration of ketamine was interesting. Moreover, these effects were observed only when associated with a change in room temperature, suggesting that this change is a key factor in this study.

This article referred to the hypothermic properties of ketamine; however, hypothermia is usually induced in laboratory animals by anesthetics in general. Boultadakis and Pitsikas suggested that the effects of ketamine in cognition were dependent on the room temperature. Importantly, body temperature values for the tested animals were not shown in this study; instead, the authors forward the readers to a previous article, in which initial and 120-min postadministration temperatures in similar conditions were reported.[2] Although we agree that the body temperature values for animals tested in this study are probably within the same interval as those reported previously, we strongly disagree that these measures may be sufficient. Mild hypothermia values were observed at 120 min after anesthesia in the ketamine group kept at 21°C when animals were already recovered. However, it is highly probable that these values may have been lower during the anesthesia period. Therefore, body temperature curves throughout time should have been registered. The report of the body temperature curve would also dissipate the doubts about a potential hypothermic period in the