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Résumé de l'article

À la fin des années 1920, V. E. Henderson et son équipe de l'Université de Toronto découvrent les propriétés anesthésiques du cyclopropane. Pour diverses raisons, cependant, Henderson n'envisage pas le cyclopropane comme une technologie utile : pour lui, il s'agit seulement d'un gaz possédant incidemment des propriétés anesthésiques et non un potentiel instrument clinique, ce qui explique que le cyclopropane ne sera pas d'abord introduit en clinique dans les hôpitaux de Toronto. Aux États-Unis, par contraste, le clinicien Ralph M. Waters envisage bel et bien le cyclopropane comme une technologie médicale, en partie car cela supporte ses efforts de professionnalisation des anesthésistes dans les années 1930. Le présent article soutient l'idée qu'il est utile, sur le plan historique, de distinguer le cyclopropane comme gaz expérimental en laboratoire et le cyclopropane comme outil clinique. Une telle distinction met en lumière les dimensions sociales de la découverte scientifique, ainsi que la relation entre production scientifique et technologie médicale.

Envisioning Cyclopropane: Scientific Product or Medical Technology?¹

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Abstract: In the late 1920s, V.E. Henderson and his team at the University of Toronto discovered the anaesthetic properties of cyclopropane. For a number of reasons, Henderson did not envision cyclopropane as a useful technology: to him it was simply a gas that possessed anaesthetic properties, rather than a potential clinical product, and this explains why cyclopropane was not first introduced into Toronto hospitals. In contrast, the practicing anaesthesiologist Ralph M. Waters envisioned cyclopropane as a medical technology, partly because it could assist his effort to professionalize anaesthesiology in the 1930s. This paper argues that it is useful to make a historically-informed distinction between cyclopropane the experimental laboratory gas and cyclopropane the medical anaesthetic because such a distinction highlights the social dimensions of the process of scientific discovery and helps illuminate the relationship between scientific production and medical technology.

Résumé: À la fin des années 1920, V. E. Henderson et son équipe de l'Université de Toronto découvrent les propriétés anesthésiques du cyclopropane. Pour diverses raisons, cependant, Henderson n'envisage pas le cyclopropane comme une technologie utile : pour lui, il s'agit seulement d'un gaz possédant incidemment des propriétés anesthésiques et non un potentiel instrument clinique, ce qui explique que le cyclopropane ne sera pas d'abord introduit en clinique dans les hôpitaux de Toronto. Aux États-Unis, par contraste, le clinicien Ralph M. Waters envisage bel et bien le cyclopropane comme une technologie médicale, en partie car cela supporte ses efforts de professionnalisation des anesthésistes dans les années 1930. Le présent article soutient l'idée qu'il est utile, sur le plan historique, de distinguer le cyclopropane comme gaz expérimental en laboratoire et le cyclopropane comme outil clinique. Une telle distinction met en lumière les dimensions sociales de la découverte scientifique, ainsi que la relation entre production scientifique et technologie médicale.

1. I would like to thank Nikolai Kremontsov for suggesting cyclopropane as a research topic and for his comments on an early draft of this paper. I am grateful to Boaz Miller for pointing me toward some relevant secondary literature, as well as to *Scientia Canadensis'* two anonymous reviews for their comments and suggestions. This research was supported by the Social Sciences and Humanities Research Council.

In 1944, Professor Velyien Ewart Henderson of the University of Toronto received the prestigious Flavelle Medal for achievement in the medical sciences. The Royal Society of Canada, which awards this medal, praised Henderson for his outstanding contribution, submitting that “it is to him that we owe the important discovery of the anaesthetic properties of cyclopropane. This discovery, apart from its intrinsic scientific importance, is a very significant contribution to the efficiency of surgical medicine [...]”² Likely inadvertently, the Royal Society distinguished between the discovery of an anaesthetic and the discovery of “the anaesthetic properties” of a substance. Popular scientific and medical narratives, on the other hand, celebrate Henderson as the discoverer of the anaesthetic cyclopropane, despite the fact that he and his colleagues in Toronto did not introduce cyclopropane into medical practice, supposedly as a result of bad timing and bad fortune. Only several years later did the American anaesthesiologist Ralph Waters reconceptualise cyclopropane as a practical medical technology.

In this paper, I will argue that, for a number of reasons, Henderson did not in fact envision cyclopropane as a useful technology. To him cyclopropane was simply a gas that possessed anaesthetic properties, rather than a potential clinical product, and this explains why cyclopropane was not first introduced into Toronto hospitals. Historians have demonstrated that a particular scientific product can have different meanings in different contexts, such as the laboratory and the clinic. Christopher Lawrence, for example, has shown that Alfred Goodman Levy’s experiments illustrating the fatal impact that chloroform could have on the heart did not influence practicing anaesthesiologists for a long time, because they “were more synthetic in their approach” and “from their perspective, experiments illuminated only aspects of a clinical problem.”³ Similarly, Wai Chen has placed the discovery of penicillin in the context of Sir Almroth Wright’s laboratory, demonstrating that Alexander Fleming’s understanding of penicillin as a bacterial growth-inhibitor useful for vaccine research differed markedly from that of Howard Florey and Ernst Chain, who a few years later saw it as a potential therapeutic agent and turned penicillin into a mass-produced antibiotic drug.⁴ In a similar manner, factors intrinsic to the laboratory

2. The Royal Academy of Canada, “Flavelle Medal Award,” http://www.rsc.ca/awards_The_Flavelle_Medal_winner.php#TOC42, last accessed June 12, 2010.

3. Christopher Lawrence, “Experiment and Experience in Anesthesia: Alfred Goodman Levy and Chloroform Death, 1910-1960,” in *Medical Theory, Surgical Practice: Studies in the History of Surgery*, ed. Christopher Lawrence (London/New York: Routledge, 1992), 264.

4. Wai Chen, “The Laboratory as Business: Sir Almroth Wright’s Vaccine Programme and the Construction of Penicillin,” in *The Laboratory Revolution in Medicine*, eds. Andrew Cunningham and Perry Williams (Cambridge: Cambridge University Press, 1992), 245.

setting in which he worked circumscribed Henderson's conceptualization of cyclopropane as a gas that could inform research on the physiological effects of anaesthesia, rather than as a potential anaesthetic for use in the surgical theatre. In contrast, the practicing anaesthesiologist Ralph Waters, envisioned cyclopropane as a medical technology, partly because it could assist his effort to professionalize anaesthesiology in the 1930s.⁵

Social epistemologists have argued that, as Alan Gross put it, "discovery is not a historical event, but a retrospective social judgment,"⁶ and the history of cyclopropane illustrates this important distinction. Relying on archival material as well as published sources, I will analyze the knowledge-productive practices that contributed to Henderson's construction of cyclopropane in the 1920s and 1930s, as well as the narratives of discovery that were eventually generated. I conclude that it is useful to distinguish between cyclopropane the experimental laboratory gas and cyclopropane the medical anaesthetic, despite the fact that narratives of discovery do not differentiate between the two. This distinction is useful because it highlights the social dimensions of the process of scientific discovery and helps us to understand the relationship between scientific production and medical technology.

Anaesthesia in the 19th and 20th Centuries

The first anaesthetic widely used in surgery, ether, was introduced to a larger medical audience in 1846. On October 16 of that year, William T. G. Morton, who had been working with this substance in his private dental practice, gave a successful demonstration at the Massachusetts General Hospital. Morton etherized a patient who was just about to undergo surgery for the removal of a tumour of the jaw. The patient breathed in ether through an inhaler designed by Morton and subsequently reported no pain during the operation. The following year, the British physician Sir James Young Simpson discovered the anaesthetic properties of chloroform and immediately began to use it, both in general surgery and in his obstetrics practice. And finally, the third general anaesthetic in use during the 19th century was nitrous oxide, a gas that had been synthesized much earlier but which became widely introduced in medical practice only in 1868.⁷

5. This paper focuses principally on Henderson's research, discovery and conceptualization of cyclopropane. Although I explain Waters' circumstances and his contrasting vision for cyclopropane, this paper is not an exhaustive treatment of Waters' story.

6. Alan G. Gross, "Do disputes over priority tell us anything about science?," *Science in Context* 11, 2 (1998): 161.

7. For a general history of anesthesia, see Stephanie Snow, *Blessed Days of Anaesthesia: How Anaesthetics Changed the World* (Oxford: Oxford University Press, 2008); G.B.

As a consequence of the profound way in which anaesthesia eventually changed the practice of medicine, older histories of anaesthesia often portray the process through which various anaesthetics gained acceptance as self-evident and unproblematic. Historians have challenged this retrospective projection by emphasizing the complicated and socially determined process through which new medical technologies are adopted. Alison Winter, for example, has shown that the acceptance of ether in Victorian England hinged not so much on the substance's ability to relieve pain, but on its ability to induce suspended animation during surgery, as well as on the fact that it constituted a tool doctors could use in their fight against mesmeric anaesthesia, which was becoming popular at the time.⁸ Furthermore, although the dissemination of this new medical technology happened remarkably quickly, a large number of factors determined the specific ways in which anaesthesia was employed. According to historian Martin Pernick, 19th century American doctors followed a complicated calculus in deciding how to use anaesthesia: "the issue for them was not whether to use anaesthetics but when and to whom."⁹ The medical profession's understanding of suffering, as well as the notions of risk and benefit applied to individual patients, influenced a doctor's decision whether or not to use anaesthesia during a particular surgery. The local cultural context of medicine also determined the choice of anaesthetics and the techniques for delivering anaesthetics: in Britain chloroform was more popular than ether, whereas in the northern parts of the US the converse was true.¹⁰

Nineteenth-century physicians soon realized that the introduction of ether, chloroform, and nitrous oxide brought significant risks, including the risk of death. Chloroform, especially, although exceedingly popular in Britain, was blamed for a large number of deaths in the late 19th and early 20th centuries.¹¹ Apart from death, various serious side effects were also reported. In 1920, doctors described patients who had been etherized as "flaccid, cyanotic, pallid, or grey, with empty veins, weak peripheral

Rusham, R.S. Atkinson and N.J.H. Davies, *A Short History of Anaesthesia: The First 150 Years* (Boston: Butterworth-Heinemann, 1996); Barbara M. Duncum, *The Development of Inhalation Anaesthesia with Special Reference to the Years 1846-1900* (London: Wellcome Historical Medical Museum, 1947); Thomas Edward Keys, *The History of Surgical Anesthesia* (New York: Dover Publications, 1963).

8. A. Winter, "Ethereal Epidemic: Mesmerism and the Introduction of Inhalation Anaesthesia to Early Victorian London," *Social History of Medicine* 4, 1 (1991): 1.

9. Martin S. Pernick, *A Calculus of Suffering: Pain, Professionalism, and Anesthesia in Nineteenth-Century America* (New York: Columbia University Press, 1985), 5.

10. Stephanie J. Snow, *Operations Without Pain: The Practice and Science of Anaesthesia in Victorian Britain* (Basingstoke: Palgrave Macmillan, 2006), 66-68.

11. Snow, *Blessed Days of Anaesthesia*, 170-171.

pulses, and depressed respiration; it was one to three hours before consciousness returned, and this was followed by nausea, vomiting, and retching for some time afterwards.”¹²

In the early 20th century, the three 19th century anaesthetics continued to be the main agents in use. To these were added, in the 1920s, ethyl chloride and di-vinyl ether for short-term administration (they were toxic if administered for longer periods), as well as acetylene and ethylene, whose use, however, never became widespread, perhaps partly as a result of the fact that they were explosive and showed no clear advantage over the older anaesthetics in terms of side effects.¹³ Local and regional anaesthesia became well established in the 1920s, and various techniques (such as spinal anaesthesia), and compounds (such as procaine, stovaine, and cocaine) were introduced into practice.¹⁴ In the early 1930s, there were reports of experimental work with intravenous agents such as hexobarbitone and thiopentone,¹⁵ and in 1934, Ralph Waters published his clinical trials with cyclopropane.¹⁶ As I will describe later, just a few years after Waters’ report, cyclopropane became very popular in North America, though not in the UK. The subsequent introduction of muscle relaxants made surgery under anaesthesia more easily manageable, but it was not until after World War II, however, that halothane, the first “designer anaesthetic,” was created in a concerted effort that involved a close collaboration between anaesthesiologists, chemists and pharmacists employed by the British chemical company Imperial Chemical Industries. Halothane enjoyed a long and successful career as a general anaesthetic in the second half of the 20th century.¹⁷

Histories of anaesthesia have focused almost entirely on the 19th century, and much less is known about the complex social negotiations and local conditions that determined the introduction and choice of anaesthetics in different countries during the 20th century. Enormous social and political changes, ranging from world wars to medical specialization, characterized the period. The professionalization of anaesthesiology, for example, took

12. Y. Henderson, H.W. Haggard, and R.C. Coburn, “The Therapeutic Use of Carbon Dioxide after Ether Anesthesia and Operation,” *Journal of the American Medical Association* 74 (1920): 783-786, as cited in P.M. Drury, “Anaesthesia in the 1920s,” *British Journal of Anaesthesia* 80, 1 (1998): 96.

13. Drury, 97.

14. Ibid.

15. Richard Bodman, “Cyclopropane and the Development of Controlled Ventilation,” in *The History of Anaesthesia*, eds. R.S. Atkinson and T.B. Boulton (London: Parthenon Pub. Group, 1989), 216-221.

16. R.M. Waters and E.R. Schmidt, “Cyclopropane Anesthesia,” *Journal of the American Medical Association* 103, 13 (1934): 975.

17. Snow, *Blessed Days of Anaesthesia*, 184-187.

place in the 1930s and 1940s and surely had an impact on the fate of the various anaesthetics in use at the time.

The case of cyclopropane can begin to address this lacuna in historical scholarship. By the early 1920s, doctors were openly criticizing the shortcomings of ether, chloroform, and nitrous oxide (the latter used mostly in dentistry), and research proceeded in two directions: some projects were devoted to an active search for new anaesthetic agents, while others focused on the investigation of the toxic effects of the known anaesthetics. In the Department of Pharmacology at the University of Toronto, both kinds of research projects were being pursued post World War I.

Department of Pharmacology at University of Toronto's Faculty of Medicine

University of Toronto's medical school was established in 1843.¹⁸ After a brief period in which it did not offer instruction, the Faculty of Medicine was reopened in 1887, with twenty-nine staff members drawn both from the city's proprietary schools and from other departments within the University. As a result of the ever-increasing number of medical students, the school soon expanded its facilities. In 1913, the new building housing the Toronto General Hospital was opened, and its close physical proximity to the University and especially to the Faculty of Medicine reinforced the strong ties between these two institutions. The 1910 Flexner Report on medical education in the U.S. and Canada concluded that the University of Toronto's laboratory facilities were "among the best on the continent" and that "the school has recently perfected a very intimate relationship with the new Toronto General Hospital."¹⁹

V. E. Henderson returned to this well-equipped and prestigious institution in 1905, following his graduate studies in pharmacology and physiology with Hans Horst Meyer, the well-regarded chair of pharmacology at the University of Marburg in Germany whose research interests included anaesthesia.²⁰ Henderson, an Ontario native and graduate in arts and medicine from the University of Toronto, was first hired as a demonstrator in physiology and pharmacology.²¹ Three years

18. For a history of the medical school and the University of Toronto, see Martin L. Friedland, *The University of Toronto: A History* (Toronto: University of Toronto Press, 2002).

19. Abraham Flexner, *Medical Education in the United States and Canada* (New York: Carnegie Foundation for Higher Education, 1910), 323.

20. George Baehr, "In Memoriam: Hans Horst Meyer," *Bulletin of the New York Academy of Medicine* 16, 4 (1940): 260-261; R.L. Lipnick, "Hans Horst Meyer and the Lipoid Theory of Narcosis," *Trends in Pharmacological Sciences* 10, 7 (1989): 265.

21. Henderson's biographical information appears in various documents available at the University of Toronto Archives. For example, University of Toronto Archives (UTA),

later he was appointed lecturer in the Department of Pharmacology, and in 1910 he became associate professor. After nine years, he was named chair of the department, a position which he held until his sudden death from a heart attack in 1945. As the head of the department, Henderson's responsibility was to give lectures in pharmacology twice a week to medical students, to supervise the projects of other researchers who worked in the lab, and to conduct his own research. Henderson had received extensive training in physiology, and his first and most enduring research interest was the action of drugs on the intestines.

World War I put a hold on some research at the University of Toronto, since a significant number of professors were deployed abroad. Henderson himself enrolled as an infantry officer and served in France as medical officer for the 5th Canadian divisional artillery. After the war, the University continued to thrive. In 1920, the Faculty of Medicine received two important gifts. Sir John and Lady Eaton gave the University a gift of half a million dollars as an endowment for a chair in medicine, and around the same time the Rockefeller Foundation donated a million dollars to the Faculty of Medicine for establishing a chair in surgery and for other general expenditures within the school.²² Henderson resumed his research after the hiatus caused by the war, investigating the physiology of mammary glands and the pharmacological action of atropine.²³ In 1922, Dr. W. Easson Brown, an anaesthesiologist at the Toronto General Hospital who was interested in finding a new and better anaesthetic, came to Henderson's lab to experiment with ethylene. He found this gas to be an effective anaesthetic, and on March 10, 1923 Brown successfully tested ethylene on a former classmate who had recently become famous for the discovery of insulin – Frederick Banting.²⁴ Unfortunately, unbeknownst to Brown, two American researchers, Arno Luckhardt and Jay Carter, had been working with ethylene for a longer time, and their more thorough research was published virtually simultaneously with Brown's paper.²⁵ Over the next few years, Brown continued his

G.H.W. Lucas, B73-1012, "The Beginnings of Pharmacology in Canada," talk delivered in 1972; UTA, University of Toronto Department of Graduate Records, A1973-0026/147(27) and A1973-0026/244(33). See also, A.D. Welch, "Velyien Ewart Henderson 1877-1945," *Science* 104, 2700 (1946): 285.

22. Friedland, 281.

23. See the "University of Toronto President's Report 1919-1925."

24. Kim Turner cites Banting's daybook, March 10th, 1923. Kim Turner, *Cyclopropane, A Varsity Gift to Mankind*, unpublished pamphlet, <http://www.anesthesia.utoronto.ca/Assets/history/fndcyclopr.pdf>, last accessed May 24, 2009. Also reprinted in Robert J. Byrick, *A Commemorative History of the Department of Anaesthesia, University of Toronto* (Toronto: Dept. of Anaesthesia, University of Toronto, 2004).

25. William Easson Brown, "Preliminary Report Experiments with Ethylene as a General

investigation of anaesthetic gases by testing propylene, methane, and dimethyl-ether, and he also published three more papers on ethylene. Although Henderson did coauthor a paper on ethylene with Brown, his publications suggest that he was only marginally interested in anaesthesia in these early years.²⁶ Loyal to his long-time interest in the gut, he was busy investigating the action of atropine on the intestine and the urinary bladder, as well as intestinal peristalsis and the sensitivity of the small intestine to internal pressure.²⁷ By the mid 1920s, however, Henderson seems to have steered research in his laboratory away from the active search for a better anaesthetic to trying to understand the effects – especially the toxic effects – of known anaesthetics, such as nitrous oxide and propylene.²⁸ At the same time, another interesting change in research interests seems to have beset Henderson: he abandoned the gut and became focused on the respiratory system.²⁹ Thus, by the mid 1920s, just before cyclopropane became a topic of investigation in the department, Henderson's main research interests seem to have lain outside the topic of anaesthesia.

“Stumbling Upon” the Anaesthetic Properties of Cyclopropane

In 1927, Henderson hired a young chemist, George Lucas, to join the Department of Pharmacology. A native Ontarian, Lucas had graduated in 1923 from the University of Toronto with a PhD in chemistry and had worked for the next two years in Banting's lab.³⁰ His first tasks involved an investigation of the anaesthetic value of nitrous oxide under pressure, a study of the toxicity of bromine and chlorine containing anaesthetics, and an analysis of the toxic effects of propylene.³¹ In his past experiments

Anaesthetic,” *Canadian Medical Association Journal* 13, 3 (1923): 210; A.B. Luckhardt and Dean Lewis, “Clinical Experiences with Ethylene-Oxygen Anesthesia,” *Journal of the American Medical Association* 81, 22 (1923): 1851.

26. William Easson Brown and V.E. Henderson, “On Ethylene as an Anesthetic,” *Archives internationales de pharmacodynamie et de therapie* 28 (1923): 257.

27. See the “University of Toronto President's Report 1918-1925.”

28. W.E. Brown and V.E. Henderson, “Theory of Anesthesia and the Problem of Toxicity,” *Anesthesia & Analgesia* 6, 3 (1927): 141-145; V.E. Henderson, “Anaesthetic Toxicity,” *The Canadian Medical Association Journal* 17, 10 (1927): 1158-1162; G.H.W. Lucas, “Study of the Fate and Toxicity of Bromine and Chlorine Containing Anesthetics,” *Journal of Pharmacology & Experimental Therapy* 34, 2 (1928): 223-237.

29. V.E. Henderson and M.I. Sparks, “Recent Respiratory Stimulants,” *University of Toronto Medical Journal*, April 1927; V.E. Henderson and T.A. Sweet, “On the Respiratory Centre,” *American Journal of Physiology* 91, 1 (1929): 94.

30. Lucas seems to be proud of his “close association” with Banting, mentioning it often in autobiographical notes. See G.H.W. Lucas, “The Discovery of Cyclopropane,” *Anesthesia & Analgesia* 40, 1 (1961): 15.

31. Lucas, “Study of the Fate...,” 223-237; W.E. Brown, G.H.W. Lucas and V.E.

with propylene, a gas with known anaesthetic effects, Brown had noticed that when freshly prepared in the lab, propylene was a relatively potent anaesthetic (more potent than ethylene), but when it was liquefied and stored under pressure at room temperature in steel tanks, propylene became toxic, inducing nausea and cardiac irregularities. In 1928, Brown and Henderson asked Lucas to solve this mystery, and Lucas suggested that perhaps an isomer of propylene, cyclopropane, might be responsible for these toxic effects.³² Cyclopropane, a gaseous hydrocarbon, had been synthesized for the first time in 1882 by the Viennese chemist August von Freund (1835-1892).

Henderson encouraged Lucas to test his hypothesis. Lucas produced cyclopropane by reducing trimethylene bromide by zinc dust in the presence of alcohol and traces of water. The trimethylene, a difficult element to find, was bought from two German companies, Schuchart & Co. and Kodak Co. On November 22, 1928, Lucas prepared a sample of what he thought to be a very toxic gas. After diluting it with oxygen, he introduced the gas mixture to two kittens under a bell jar which contained a soda lime carbon dioxide absorber. Lucas expected the kittens to succumb to the toxicity of the gas, but to his surprise they immediately fell asleep, showing no abnormality in their respiration or muscular movement, and then quickly recovered once the bell jar was removed. Later in the day, a second trial produced the same effects, and Lucas concluded that he had stumbled upon the anaesthetic properties of cyclopropane.

In the months that followed, Lucas and Henderson conducted several experiments on kittens, cats, and rabbits in order to test physiological responses, side effects, and optimal concentrations. First, since the gas produced by the reduction of trimethylene bromide was not pure cyclopropane but contained propylene and another unknown gas, Lucas used potassium permanganate to absorb the propylene. Unable to extract the cyclopropane from the mixture with the unknown gas, Lucas had to show that the unknown gas was not contributing to anaesthesia, in order to ascribe the anaesthetic effect to cyclopropane. To this end, he removed the cyclopropane from the mixture by absorbing it with sulfuric acid and tested the unknown gas, which appeared to possess no anaesthetic properties.³³

Henderson, "Anesthetic Value of Nitrous Oxide Under Pressure," *Journal of Pharmacology & Experimental Therapy* 31, 4 (1927): 269-289.

32. Lucas, "The Discovery of Cyclopropane," 15. The following description of the experimental set-up is based on this source, as well as on G.H.W. Lucas and V.E. Henderson, "A New Anaesthetic Gas: Cyclopropane," *Canadian Medical Association Journal* 21, 2 (1929): 173.

33. Lucas and Henderson, "A New Anaesthetic Gas: Cyclopropane," 173.

After several other experiments, Lucas and Henderson concluded that cyclopropane was a very potent anaesthetic, requiring concentrations as low as twelve percent. Low concentrations of anaesthetics were very desirable, since more oxygen could be delivered to the patient. Furthermore, the wide range between the optimal concentration of cyclopropane and its fatal concentration – twelve percent to thirty percent – meant that there existed an ample margin of error and less opportunity for grave mistakes. Henderson and Lucas observed some toxic effects: in higher percentages cyclopropane caused a decrease in respiratory depth, a fall in blood pressure, and cardiac irregularities. Recovery, however, appeared to be short; apparently one cat “winked and moved its tongue in one minute, sat up, and walked about in three minutes. In five minutes [it] purred when petted.”³⁴

Having encountered this problem with propylene, Henderson and Lucas believed that the important test for their new gas was its behaviour when liquefied and stored under pressure. Most of the technology necessary for anaesthesia research had been designed and put together by the lab’s technical maverick – Alan Brock. According to Lucas, Brock was an unusually resourceful “machinist” whom Henderson had hired in 1919 to tend to the lab’s mechanical needs. For anaesthesia research Brock built a number of unique devices, including iron tanks with a glass face able to withstand a pressure of two atmospheres.³⁵ With the help of this technology, Lucas liquefied propylene by passing it through a glass coil immersed in liquid air, and then stored it into an iron tank at room temperature for a month. Subsequent experiments showed that the tanked cyclopropane did not behave like the tanked propylene. On the contrary, the gas appeared to be just as safe as it had been when freshly prepared, and Lucas and Henderson felt ready to take their research one step further: testing cyclopropane on humans. At this point, Brown, who had been away during these new developments, returned to the lab, and he was the one to administer the gas to the first volunteer, Henderson, who suffered no ill health following the anaesthesia.

Because he lived much longer than Henderson, Lucas was able to enjoy his cyclopropane fame longer, and was also able to give shape to cyclopropane’s history by publishing, in 1961, his personal

34. Lucas and Henderson, “A New Anaesthetic Gas: Cyclopropane,” 174.

35. UTA, George H.W. Lucas, B1973-1012, “The Beginnings of Pharmacology in Canada,” talk delivered December 1, 1972. Brock retired in 1964, after forty-five years of service. He died in 1971 after a long illness. Little is known about these behind-the-scenes laboratory technicians. For a history of laboratory workers in the Maritimes, see Peter L. Twohig, *Labour in the Laboratory: Medical Laboratory Workers in the Maritimes, 1900-1950* (Montreal: McGill-Queen’s University Press, 2005).

recollections.³⁶ Lucas contended that the discovery of the anaesthetic properties of cyclopropane could not have come at a worse time. According to him, at this time a number of deaths in Toronto hospitals were attributed to anaesthesia and were reported, in an exaggerated manner, in the newspapers. As a consequence, Lucas lamented, the head of the Anaesthesia Department at the Toronto General Hospital, Dr. Samuel Johnston, forbade the use of cyclopropane in the hospital, and thus no clinical trials were conducted in Toronto. But, according to Lucas, in the spirit of selflessness that becomes every scientist, Henderson encouraged his “close friend”³⁷ the American Ralph Milton Waters, the head of anaesthesia at the State of Wisconsin General Hospital in Madison, to pursue the clinical use of cyclopropane. Waters had been in the audience at the June 1929 meeting of the Canadian Medical Association in Montreal, where Henderson presented the cyclopropane paper that he had written with Lucas. Waters eventually ran the necessary clinical studies and introduced cyclopropane into clinical practice.

According to Lucas, “Dr. Waters made great strides in his researches and by 1933 [...] was able to give a preliminary clinical report [on cyclopropane as an anaesthetic agent], during the 12th Annual Congress of Anaesthetists at Chicago.”³⁸ By the late 1930s cyclopropane had become one of a handful of widely used anaesthetics in the United States and Canada. As early as 1937, the New Zealand doctor C. S. Williams observed on a trip through the US that “the gaseous anaesthetics, nitrous oxide and cyclopropane, were used almost universally.”³⁹ Cyclopropane’s popularity in North America remained virtually unchanged for the following three decades. Although it is not used anymore, as late as the 1980s cyclopropane was still employed periodically, especially in paediatric surgery and in surgery involving old and gravely ill patients.⁴⁰ However, cyclopropane did not fare as well in other countries, notably in

36. Lucas, “The Discovery of Cyclopropane,” 15.

37. *Ibid.*, 21. I have not come across evidence that suggests a close friendship (rather than a professional acquaintance) between Henderson and Waters, but clearly the idea of such a friendship suited Lucas’ story of comradeship in science. Turner, in his account of the discovery of cyclopropane, further reinforces this tradition, extolling “the unselfish collaboration between scientists and clinicians that continues to serve as an example to modern-day colleagues,” Turner, *Cyclopropane*, 85. Henderson and Waters had met each other (Waters was in the audience at the 1929 meeting of the Canadian Medical Association in Montreal when Henderson presented a preliminary study of cyclopropane), and they corresponded in the 1930s.

38. Lucas, “The Discovery of Cyclopropane,” 21.

39. C.S. Williams, “Cyclopropane: A New Anaesthetic Agent,” *New Zealand Medical Journal* 36 (1937): 193, as cited in Bodman, “Cyclopropane and the Development of Controlled Ventilation,” 216-221.

40. Rusham, Atkinson and Davies, *A Short History of Anaesthesia*, 46.

the United Kingdom. At the time, foreign doctors blamed the supposed conservatism of the British medical establishment for the evident reticence to employ the newer anaesthetics. “Their ingrained conservatism,” wrote one American doctor in 1938, “is such that they have fallen behind in the present forward surge of anaesthesia progress [...] they failed to accept ethylene [...] and are now just as staunchly refusing to try cyclopropane.”⁴¹ More research is needed to understand the dissimilar meanings that cyclopropane held in these different settings and the social factors that contributed to its level of popularity. It is clear, however, that the identity and the potential of cyclopropane were open to interpretation, and in what follows I will show the particular way in which this compound’s identity was envisioned by Henderson in Toronto in the late 1920s.

The Construction of Cyclopropane

Lucas’ 1961 narrative regresses conventionally to the familiar pattern of traditional stories of scientific discovery: serendipity, struggle for acceptance, bad luck, selfless sharing of scientific knowledge, and ultimately vindication and fame. Although such stories are appealing and serve the important social function of building a common identity among medical scientists, in this case it is very much a retrospective construction that neatly ties together a seemingly inevitable sequence of events while glossing over several problematic issues. Evidence from the late 1920s and 1930s paints a much more complicated story. Although fragmentary, this evidence suggests an alternative interpretation.

In his retrospective, Lucas blamed Dr. Samuel Johnston, the head of Anaesthesia at the Toronto General Hospital, for the failure to run clinical trials on cyclopropane in Toronto, citing Johnston’s wariness over media reports that blamed several patients’ deaths on anaesthesia. However, it is difficult to believe that the local media’s sensationalization of the deaths would have been the one insurmountable barrier preventing Henderson from introducing cyclopropane into clinical practice. At best, it would have been a minor barrier, considering the medical establishment’s exculpation of anaesthetics in the deaths, the timing of the deaths relative to the discovery of cyclopropane’s anaesthetic properties, and Henderson’s influential position in the Toronto medical circle.

In the span of six days in February 1930, four patients undergoing surgery died in Toronto hospitals. On February 19, James O. Buckley, a

41. W.L. Garth, “Some Observations of Anesthesia Abroad,” *Current Research in Anesthesia and Analgesia* 17, 5 (1938): 292-297, as cited in Bodman, “Cyclopropane and the Development of Controlled Ventilation,” 216-221.

prominent Toronto lawyer passed away during throat surgery.⁴² The man had suffered persistent bleeding prior to surgery, and due to his weakened condition he was only given half the usual amount of anaesthetic. A similar scenario, involving preexisting conditions, played out in the three other deaths. On February 21, forty year-old Myrtle Rodgers died during a routine appendectomy.⁴³ The autopsy revealed that her lungs showed a prior growth of fibrous tissue, which had made the lungs less permeable. An inquiry into this death absolved the anaesthesiologist and his anaesthetics of any culpability.⁴⁴ The media also blamed anaesthesia for the death, on the same day as Rodgers, of an elderly man who was undergoing surgery for an intestinal condition. And finally, the fourth casualty was a twenty-five month-old child severely ill with pneumonia.⁴⁵ Following media reports of these stories, some Torontonians apparently refused to undergo surgery for fear of dying under anaesthesia, and the Academy of Medicine blamed the adverse publicity and public hysteria for causing “needless woe” and contributing to unnecessary deaths.⁴⁶ The medical establishment, however, did not consider these deaths attributable to the anaesthetics that had been given, but rather to the patients’ preexisting conditions. Dr. Oskar Klotz of the University of Toronto, Department of Pathology and Bacteriology, presented a summary of his investigation into these deaths at the Eleventh Annual Congress of Anaesthetics in New York City.⁴⁷ He concluded that certain common ailments, such as influenza and pneumonia, scarred the lung and reduced its capacity to absorb oxygen. When such patients were put under anaesthesia, Klotz contended, the lung impairment reduced the patients’ capacity for oxidation, and they were more likely to die.

It is clear that these four deaths caused a local media storm, but it is equally clear that the medical profession did not consider these deaths to be unusual, given the severity of the patients’ illness. Media storms over anaesthetics were not a new phenomenon, and they were perceived

42. “Prominent Lawyer Passes in Hospital,” *The Globe*, February 20, 1930, 1, as cited in Turner, *Cyclopropane*, 77.

43. “Death Under Anesthetic Strikes Two in One Day In Hospital Operations,” *The Globe*, February 22, 1930, 1, as cited in Turner, *Cyclopropane*, 77-78.

44. “Jury Blames No One for the Death of Woman Under Anaesthetic – Pathological Condition of the Lungs Found to be Responsible – No Cause for Alarm,” *The Globe*, February 30, 1930, 1, as cited in Turner, *Cyclopropane*, 78.

45. Turner, *Cyclopropane*, 78.

46. “Adverse Publicity Claimed as Cause of Needless Woe – Academy of Medicine claims Fear of Anaesthesia Has Brought Deaths,” *The Toronto Star*, March 1, 1930, 1, as cited in Turner, *Cyclopropane*, 79. Fear of anesthesia and reports of deaths due to anesthesia were not unusual at the time. See “Death in Anesthesia Cause Ether Seizures,” *The New York Times*, August 21, 1929, 10.

47. “Way Found to Curb Operation Deaths,” *The New York Times*, October 18, 1932, 8.

differently in different cultural contexts. In 19th century Britain, for example, widespread newspaper reports of deaths due to chloroform did not diminish doctors' enthusiasm for this anaesthetic.⁴⁸ In the United States, on the other hand, fear of malpractice suits may be one reason why doctors preferred ether over chloroform – essentially choosing safety over ease of administration.⁴⁹ More research is needed to understand the Canadian context, but at the very least, as this example shows, the assumption that a local media storm would have such deep repercussions needs to be interrogated, rather than taken for granted. It is not a given that public opinion would necessarily have had a definitive effect on the viability of experimental trials with new anaesthetic gases like cyclopropane. Perhaps, following the media frenzy, Johnston needed more persuasion to consider clinical trials, but surely this would have constituted a minor barrier for someone as well connected as Henderson, if he believed that cyclopropane deserved to be introduced into clinical practice. On the contrary, one could imagine an enterprising researcher taking advantage of this situation by appealing to people's distrust of older anaesthetics to promote the discovery of a new and safer anaesthetic. This may have been especially true, given that oxygen absorption was believed to be a factor in the patients' deaths, and cyclopropane allowed the delivery of more oxygen.

Most importantly, nearly fifteen months elapsed from the day Lucas first observed the anaesthetic properties of the gas (November 22, 1928) to the day the first of the four deaths were reported in Toronto newspapers (February 20, 1930). Furthermore, Lucas and Henderson presented detailed data on cyclopropane at the June 1929 meeting of the Canadian Medical Association, ten months before the media storm. If Henderson were committed to introducing cyclopropane into clinical practice, he could have easily done so prior to February 1930. Thus, even if the media storm over the four deaths were a significant part of the story, one still has to explain the considerable time lag that occurred between the discovery of the anaesthetic properties of cyclopropane and the time of these deaths. Evidently, the reason why clinical trials did not take place in Toronto is much more complex.

Henderson had what appeared to be a well-equipped lab, and he worked in a Faculty of Medicine closely affiliated with a major and well-endowed hospital. He had a staff involved in anaesthesia research – indeed, one of his lab members also worked as an anaesthesiologist at the Toronto General Hospital. He had the authority and the connections, by virtue of his position as head of the department. He had powerful and influential friends such as Billy Bell, a former classmate of his who in the late 1920s

48. Snow, *Blessed Days of Anaesthesia*, 170-172.

49. Snow, *Operations Without Pain*, 196.

was the Deputy Minister of Health. Henderson and Bell had dinner regularly, and one night in March 1928, Henderson happily wrote to his wife that a dinner at Bell's house turned into "a great pow wow re[garding] Industrial med[icine]." ⁵⁰ Henderson also knew Frederick Banting, with whom he shared an intense dislike of J.J.R. MacLeod, the head of the Physiology Department. As Michael Bliss has shown, Banting felt very much in Henderson's debt, ever since Henderson gave Banting – in his destitute, pre-insulin times – lab space and a stipend. ⁵¹ Furthermore, as I have already mentioned, Banting had volunteered in 1923 to take Brown's anaesthetic ethylene; clearly he had proved a friend of the Department of Pharmacology. Ever since his discovery of insulin in 1922, Banting was treated as a Canadian hero, and at the Faculty of Medicine he wielded a lot of power by virtue of the capital insulin was continuously generating. It is therefore difficult to believe that any scientific product endorsed by Banting would not have been introduced into clinical practice, if only in a provisory manner. ⁵² In fact, the media would have almost certainly glorified cyclopropane, had Banting even mentioned it casually. However, with all these extraordinary resources at his fingertips, Henderson did not promote cyclopropane: there is no evidence to suggest that he asked his friend Banting to intercede on his behalf, or that he tried in any way to set up clinical trials. But Henderson chose not to take this course of action for a very good reason. He did not believe that cyclopropane was a useful anaesthetic, one worthy of introduction into clinical practice.

In retrospect, cyclopropane appears to be a significant discovery, an important anaesthetic that gained popularity and had a long career in the service of surgery. But in 1928 nobody could have predicted its future. To understand Henderson's attitude and his treatment of cyclopropane, one has to understand the way in which Henderson construed the potential of this gas in 1928, not years later when cyclopropane had gained acceptance as an effective anaesthetic. This is not to suggest that Henderson failed to

50. UTA, B1987-0024 001, Henderson Letters (1927-1928), V.E. Henderson to his wife, March 14th 1928.

51. Michael Bliss, *Banting: A Biography* (Toronto: McClelland and Stewart, 1984); Michael Bliss, *The Discovery of Insulin* (Toronto: McClelland and Stewart, 1982). Henderson and Banting got along very well; they were also united in a profound dislike of Macleod, the head of the Physiology Department in the Faculty of Medicine, in whose lab Banting discovered insulin, and who shared with Banting the Nobel Prize.

52. Lucas claimed that Banting also volunteered to inhale cyclopropane, but there is no corroborative evidence for this. Banting had noted in his daybook (March 10, 1923) when he volunteered to take ethylene, but according to Turner there is no note about cyclopropane five years later, Turner, *Cyclopropane*, 81. Furthermore, the accounts in local newspapers only mention Henderson's and Lucas' inhalation of cyclopropane, UTA, University of Toronto Department of Graduate Records, A1973-0026/147(27) and A1973-0026/244(33).

understand the importance and the potential of cyclopropane. On the contrary, acknowledging that cyclopropane had, initially, no intrinsic importance for anyone to passively stumble upon, I will show that cyclopropane as Henderson envisioned it in 1928 was simply a gas with anaesthetic properties, and not yet a useful clinical product.

As I have demonstrated, it is immediately apparent that Henderson was in no hurry to promote clinical trials at Toronto General. Archival records reveal that Henderson was not very committed to anaesthesia research around the time of Lucas' first cyclopropane experiment. It seems that between 1927 and 1928 Henderson expressed a desire to distance himself and his lab from anaesthesia research for a while. During that academic year, Henderson had sent his wife and younger son to France to study French. A prolific letter-writer, Henderson sent dozens of missives to his wife, describing domestic events, the latest gossip on campus, as well as activities at the laboratory. In a letter written on Wednesday, January 25th 1928, Henderson suggested that he wanted the laboratory to drop the work on anaesthesia for a time: "Lucas [...] is pressing for a new problem which will involve experimental and chemical work. It is a little hard to know just what it could be but we will try a new field and think for a time, and leave anaesthesia alone. Though perhaps we will come back to it." As for his own research, Henderson had been working with a colleague, Dr. T. A. Sweet, on the physiology of respiration, and he was so excited about this new research topic, that he mentioned his progress every two or three letters. "As for the work with Sweet," Henderson wrote, "it does seem a great mystery but I have little doubt that some day we will get closer to the bottom of it than anyone else has yet done."⁵³ In his letters, Henderson's excitement is palpable, and his disappointment, when experiments failed, is equally intense: it is clear that Henderson's imagination and energy were engaged in an entirely different direction.⁵⁴

53. UTA, B1987-0024 001, Henderson Letters (1927-1928), V.E. Henderson to his wife, January 25, 1928.

54. At around the same time, Henderson was also focused on trying to become the head of the Department of Physiology. J.J.R. MacLeod resigned in the spring of 1928, after a prolonged controversy about winning the Nobel Prize along with Banting. Henderson, who disliked MacLeod, tried to convince the President of the University to combine the Departments of Pharmacology, Therapeutics, and Physiology and to make him the head of this new combined department. "[I]t made me wonder whether I had better try to change Depts and he said yes he had thought of that. Well, when I [illegible] over the list of eligibles I do not know that they are likely to do much better. [...] If I had \$6000 I do not know that I have the ambition to take on the extra work of reorganizing that Dept. and making it a dept. of Physiology and not Biochemistry. [...] I hate to give or even contemplate giving up Pharmacol. and all the connections which it has developed and [illegible] the shingle up-stairs. What I would rather do were it possible is to become Director [?] of Physiol. Pharmacol. and bring in Victor Moorhouse from Winnipeg. Then

Nor does it seem that Henderson's enthusiasm for anaesthesia research came back after Lucas described the anaesthetic properties of cyclopropane. In 1929, Henderson wrote a short summary of the research that had been done in the 1928-1929 academic year in the Department of Pharmacology, a summary which was published in the President's annual report. "With the aid of Dr. Sweet," wrote Henderson, "I have carried on a series of very difficult experiments to determine the location and connection of the respiratory center."⁵⁵ The fact that this research on the respiratory center is mentioned first may indicate that Henderson believed it to be the most important research of the year. Only in the following paragraph did Henderson note that, "Dr. Lucas has isolated a new anaesthetic gas of high anaesthetic potency and having a low toxicity, which will enable several important problems in regard to anaesthesia to be undertaken in the future."⁵⁶ This is a very cautious description of cyclopropane; its future potential is articulated in a vague manner. At this point, Henderson appeared to be noncommittal about the value of this gas as a medical technology, pointing instead to future problems that could be explored. Similarly, in their 1929 report presented at the annual meeting of the Canadian Medical Association, Henderson and Lucas reported a number of toxic effects sustained by their animal subjects, as well as technical difficulties. They cautiously concluded that "we feel that this is to be regarded as a preliminary report only, and the conclusions we have drawn in regard to solubility and as to the anaesthetic qualities of the gas must be regarded as tentative only."⁵⁷ While a note of caution is perhaps conventional in such preliminary reports, this caveat appears particularly guarded. Nowhere in the paper did the University of Toronto researchers suggest that cyclopropane had the potential to enter clinical practice.

It is also significant that the lab's research agenda did not change dramatically after Lucas' discovery. If Henderson considered cyclopropane an important breakthrough, one would expect a flurry of activity and research on this subject in the department. The annual report of the President of the University of Toronto shows that in 1930 only Lucas continued to work on cyclopropane. Henderson was back to nitrous oxide: he and others in the lab were trying to understand why anaesthesia

if we can shift Taylor we could really make a good Dept. [...] I do not want to see another cocky overbearing foreigner in Physiol. No matter whether he is English or American." UTA, B1987-0024 001, Henderson Letters (1927-1928), V.E. Henderson to his wife, April 1st, 1928.

55. "University of Toronto President's Report 1928-1929," 38.

56. *Ibid.*, 38.

57. Lucas and Henderson, "A New Anaesthetic Gas: Cyclopropane," 175.

with nitrous oxide at an eighty percent concentration was accompanied by a profound state of anaemia.

In the spring of 1930, most likely having noticed that Henderson was not proceeding with clinical trials, Waters suggested in a letter to Henderson that “if you feel that this gas deserves further clinical trial than you are able to give it, we should be very glad, of course, to run a small series.”⁵⁸ Henderson responded that he could “see no possibility of really satisfactory clinical trials here” and that “we would be glad to see you try it, if you would care to do so, for anaesthesia.”⁵⁹ Henderson did not suggest any collaboration with Waters, but he gave the American anaesthesiologist permission to work with cyclopropane. On August 20th, 1930, Waters sent Henderson the clinical records of three patients to whom Waters had administered cyclopropane, and asked the Canadian doctor again for information regarding a discrepancy in cyclopropane concentration between his clinical observations and Henderson’s experimental results.⁶⁰ In a letter dated September 8, 1930, Henderson responded to Waters’ inquiry by explaining that “Our experiments with the human anaesthetics have not proceeded [sic] very far, owing to various delays and holidays. Consequently, we cannot give you very intelligent criticism on your findings.”⁶¹ Clearly, cyclopropane did not appear to have galvanized research in the lab, if “various delays and holidays” occurred. And even more remarkably, Henderson did not even share Waters’ letters with the principal cyclopropane researcher, Lucas, who only found out about this correspondence when he examined departmental records after Henderson’s death.⁶² The research on cyclopropane at the University of Toronto appears to have been neither focused nor systematic.

Taken together, all this evidence suggests that there was a lack of excitement and a failure to conduct significant further research on cyclopropane in Henderson’s laboratory immediately after the discovery of this gas’ anaesthetic properties. Only Lucas was entrusted with related research, but even this work was limited, since he had other research duties as well. Henderson noted in the President’s report for the academic year 1930-1931 that in addition to working on nitrous oxide, “Dr. Lucas

58. Cited in Betty J. Bamforth, “Cyclopropane Anesthesia: Its Introduction at Wisconsin,” in *Anaesthesia: Essays on its History*, eds. Joseph Ruprecht and al. (Berlin: Springer-Verlag, 1985), 272. The letter is not produced in its entirety, and the author did not include the exact date of this letter.

59. Ibid.

60. Ralph Waters to V.E. Henderson, August 20, 1930. Published as Figure 5A, 5B, 6A and 6B in Lucas, “The Discovery of Cyclopropane,” 15.

61. V.E. Henderson to Ralph Waters, September 8, 1930. Published as Figure 7 in Ibid.

62. Ibid., 21.

has also made some progress with the preparation and study of cyclopropane derivatives. This has proven a very difficult field of research.”⁶³ This field of research was so difficult that no publications resulted for either Lucas or Henderson. Evidently, the experiments produced no useful results, probably reinforcing Henderson’s belief that cyclopropane was not a worthy medical technology.

In 1931, the *New York Times* reported that at the Tenth Annual Congress of Anaesthetists – which was being held three years after the discovery of the anaesthetic properties of cyclopropane, and two years before Waters introduced it into clinical practice – Henderson gave a talk in which he expressed his hope that somewhere in the world, in some lab devoted to anaesthesia research, someone would soon find a great new anaesthetic, one that would combine all the qualities of the gases in use at the time, but without any of their shortcomings.⁶⁴ Evidently, Henderson did not think at the time that cyclopropane fit the bill, or else he would have mentioned its potential. By 1931 cyclopropane was clearly not a central research project in the Department of Pharmacology. Lucas was working on the absorption and medical use of iron, while Henderson was investigating the physiological mechanisms of saliva secretion. Henderson also continued to work on the physiology of respiration, a subject he would be partial to for the rest of his life. In 1932 and 1933, Lucas worked on the study of the movements of cilia and the effects of anaesthetics upon them, and Henderson began to be interested in spinal anaesthesia, publishing a first paper on this topic in 1932.⁶⁵

The lack of sustained research on cyclopropane, as well as the fact that clinical trials were not set up at Toronto General Hospital, can be explained by Henderson’s belief that cyclopropane had several very important limitations that undermined its value as an anaesthetic, in the clinical sense of the term. Apart from the difficulty with working with cyclopropane derivatives, Henderson was aware of a few other problems this gas posed. First, the production of cyclopropane was an extraordinarily costly process. In 1933, Henderson told a newspaper reporter that cyclopropane worked well, but was very pricey: “the chief component of cyclopropane is a chemical called trimethylene bromide, and this chemical is exceedingly expensive. For our experiments here, we practically bought out a supply from Germany, the only place we could get it.”⁶⁶ Henderson might have

63. “University of Toronto President’s Report 1930-1931,” 43.

64. “Anesthetist Hopes for a New Gas Soon,” *The New York Times*, October 15, 1931, 17.

65. “University of Toronto President’s Report 1930-1933.”

66. UTA, University of Toronto Department of Graduate Records, A1973-0026/147(27), The newspaper is not identified.

reasonably thought that the expense involved in producing this new gas would deter hospitals from wanting to adopt it as an anaesthetic.

Secondly, like ethylene, cyclopropane posed a fire threat: if not handled carefully it could easily explode. After Waters introduced it into medical practice, cyclopropane was indeed involved in some high-profile accidents. On April 17, 1940, for instance, a Canadian newspaper reported that a patient had recently died in New York due to the explosion of cyclopropane.⁶⁷ In the late 1940s and in the 1950s, the *New York Times* carried several stories about death or injury caused to patients due to the explosion of cyclopropane. Some of these patients, or their families, even sued the hospitals for negligence and were awarded significant damages.⁶⁸

Thirdly, the gas could potentially induce serious side effects. In 1938, at a time when cyclopropane was gaining popularity in hospitals across North America, a local Toronto newspaper cited Henderson's opinion that the perfect anaesthetic was still elusive; according to him, cyclopropane was not even close to perfection, since it caused cardiac irregularities, a problem he had noted in his experimental subjects in 1928.⁶⁹

In the late 1920s and early 1930s, on the topic of the latest and most exciting anaesthesia research, newspapers carried stories of spinal anaesthesia, epidural anaesthesia, and even enema anaesthesia, a German solution involving a bromine preparation introduced into the intestines through an enema.⁷⁰ A gas that was similar to ethylene could conceivably appear to be a relatively unexciting alternative. Both these gases' flammability, for example, was a serious concern that even worried Waters, as I will show shortly.

Historians who have written about medical innovation point out that "risk plays a key role in this process, since whether a medical novelty gets accepted or not is, in part, the result of a process of negotiating its potential benefits and dangers."⁷¹ This risk analysis may be even more important in the case of anaesthesia. Ian Burney, for example, has argued that in the 19th century risk assessment was seen as an objective way to

67. UTA, University of Toronto Department of Graduate Records, A1973-0026/147(27) "Co-Discoverers of Anaesthetic Report it Safe," *The Telegraph*, April 17, 1940.

68. See for instance, "Patient Badly Hurt By Anesthetic Blast," *The New York Times*, February 17, 1948, 27; "Hospital Death Case Won: Widow Gets \$23,000 Verdict in Anesthetic Explosion," *The New York Times*, June 14, 1952, 17.

69. UTA, University of Toronto Department of Graduate Records, A1973-0026/155(249) The newspaper is *The Star*.

70. "Way Found to Curb Operation Deaths," *The New York Times*, October 18, 1932, 8; "New Anesthetic Reported in Berlin," *The New York Times*, March 25, 1927, 7.

71. Thomas Schlich, "Risk and Medical Innovation, A Historical Perspective," in *The Risks of Medical Innovation: Risk Perception and Assessment in Historical Context*, eds. Thomas Schlich and Ulrich Trohler (London: Routledge, 2006), 2.

manage “the passions and anxieties provoked by anaesthesia,” essentially being “seen as a means for projecting rationally bounded actors onto this unstable scene of (potentially) irrational and ungovernable nerves.”⁷² Furthermore, different individuals, influenced by local conditions that include the setting in which they work, perform this cost-benefit calculus in different ways and may therefore reach different conclusions. Cyclopropane’s important limitations – its cost, its side effects, its flammability – most likely deterred Henderson from thinking of it as a viable future anaesthetic. The risk and cost-benefit analysis that Henderson conducted had a different outcome than Waters’.

Years after he introduced cyclopropane into clinical practice, Waters himself confessed that initially he had been bothered by very similar reservations. In a letter to Henderson, Waters described his initial excitement upon hearing Henderson’s talk on cyclopropane. However, soon thereafter,

It then became necessary to decide whether we would go into a thorough investigation with cyclopropane, and after careful thought at this time, I came to this conclusion. Organic chemistry had progressed a great deal in recent years. My attitude was that it would progress still further. [...] What we needed was a drug like nitrous oxide [which did not explode if carelessly handled] with simply a reasonable amount of added potency. My thought was that maybe some bright organic chemist would produce such a drug. I held off therefore with cyclopropane for a period of two years. [...] ⁷³

Cyclopropane had several advantages: its potency, the fact that it allowed an abundant use of oxygen, the ease of administration, and a relative lack of toxic effects. But these advantages had to be weighed against its negative features: its flammability, its cost, and a depression of breathing, potential cardiac arrhythmias and cardiac arrest.⁷⁴ Henderson’s thought process may not have been as consciously explicit as Waters’, or, alternatively, it may have involved an even more careful analysis of cyclopropane’s potential as a medical technology, but whatever the case, Henderson ultimately concluded that cyclopropane did not constitute a usable clinical product. Its features placed cyclopropane in an old category of anaesthetic gases like ethylene and propylene, a class of

72. Ian Burney, “Anaesthesia and the Evaluation of Surgical Risk in Mid-Nineteenth-Century Britain,” in *The Risks of Medical Innovation*, eds. Schlich and Trohler, 40.

73. Bamforth. “Cyclopropane Anesthesia,” 274. The author of this paper does not specify the date of the letter.

74. Philip Dudley Woodbridge, “A Technique for Staying out of Trouble while Using Cyclopropane,” *Anesthesia & Analgesia* 40, 1 (1961): 32. In the 1950s, the cause of the arrhythmias was determined to be inadequate ventilation and inadequate carbon dioxide elimination. See also, J.S. Denson, “Cyclopropane,” *International Anesthesiology Clinics* 1, 4 (1963): 1005.

anaesthetics that represented the past and not the future of anaesthesia. This conclusion, coupled with Henderson's diverging research interests at the time, explain the main reasons why cyclopropane was not introduced into clinical practice in Toronto. After expressing his initial doubts in his letter to Henderson, Waters concluded that "My impression now is [...] that cyclopropane has been a very, very great contribution to clinical anaesthesia."⁷⁵ Interestingly, Henderson and Waters weighed the various characteristics of cyclopropane, and eventually they ended up on opposite sides of the equation: Henderson saw cyclopropane as a gas that possessed anaesthetic properties, while Waters, despite his original reservations, eventually saw it as a useful medical technology.

Ralph M. Waters and the Professionalization of Anaesthesia

Ralph M. Waters worked in a very different environment and pursued very different professional goals than his Canadian colleague. In 1912, Waters obtained his MD from Western Reserve University in Cleveland. He first practiced in obstetrics and anaesthesia in Sioux City, Iowa and then moved to Kansas City in 1923, having decided to devote his professional life exclusively to anaesthesia. In 1927, he was offered the first chair of anaesthesiology in the world on the medical faculty at the University of Wisconsin. From this secure professional position, Waters began to coordinate a sustained effort to organize his medical specialty.⁷⁶ In the late 1920s and early 1930s in North America, specialization was reshaping the medical profession. Specialties such as neurosurgery, paediatrics, and anaesthesiology were establishing professional boundaries, were creating standardized procedures and curricula, and were trying to institute regulations and certification.⁷⁷ Waters was deeply involved in this process. He was on the board of directors of the American Board of Anaesthesiology from its very beginnings: the board was

75. Bamforth. "Cyclopropane Anesthesia," 274.

76. On Waters see Lucien E. Morris, Mark E. Schroeder and Mary Ellen Warner, *Ralph Milton Waters, M.D., Mentor to a Profession: Proceedings, the Ralph M. Waters International Symposium on Professionalism in Anesthesia, Madison, Wisconsin, 2002*. (Park Ridge: Wood Library-Museum of Anesthesiology, 2004); L.E. Morris, "The Continuing Influence of Ralph M. Waters on Education in Anesthesiology," in *Anaesthesia*, 33-35; Lucien E. Morris, "Ralph M. Waters (1883-1979)," in *The History of Anaesthesia*, 579-580; Leroy D. Vandam and Perry P. Volpito, *The Genesis of Contemporary American Anesthesiology* (Springfield: Thomas, 1982); Gwen Wilson and Lucien E. Morris, "'My Dear Dogfish' – A Correspondence between Ralph M. Waters (1887-1979) and Geoffrey Kaye (1903-1986)," in *The History of Anaesthesia*, eds. Atkinson and Boulton, 580-590.

77. On medical specialization see George Weisz, *Divide and Conquer: A Comparative History of Medical Specialization* (Oxford: Oxford University Press, 2006).

founded in 1937 and was recognized by the American Medical Association the following year. Over the course of the first decades of the 20th century, anaesthesia in the United States was most often administered by nurses, rather than by physicians, a practice Waters sought to change.⁷⁸

In the 1930s, Waters' department at the University of Wisconsin became "the Mecca of anaesthetics."⁷⁹ Waters argued that anaesthesiologists, not nurses, should be in charge of anaesthesia, and he emphasized the importance of education and training in the development of the profession. He taught a large number of doctors, not only from the US, but from all over the world. In 20 years, apart from numerous fellows and short-term visitors, 60 residents were educated in Waters' department, and many of them – like the Australian Geoffrey Kaye – subsequently imported Waters' techniques, curriculum, and ideas about professionalization to their own countries or to other American medical institutions.⁸⁰ One anaesthesiologist noted in 1985 that "a review of the professional genealogy of anaesthesiology reveals the startling fact that hundreds of academicians throughout the world and more than 80 departmental chairmen in medical schools in the United States alone have been of the Waters' lineage."⁸¹

Cyclopropane played a very important role in this process of professionalization of anaesthesia to which Waters was so deeply committed. In 1963, the Director of Anaesthesia at the Los Angeles County Hospital, J. S. Denson, remarked that "fortunately or unfortunately according to the individual's viewpoint, considerable skill is necessary in order to administer the drug safely and well."⁸² After cataloguing the great benefits but also the potential pitfalls of cyclopropane anaesthesia, which included the risk of explosion and the problem of cardiac arrhythmias, he concluded that "this drug is for the real pro, not the amateur."⁸³ Thus, cyclopropane was the perfect anaesthetic for the professional anaesthesiologist. Its administration required skill and training and careful monitoring of the patient; it could not be left to nurses or surgeons. Even though, as I have mentioned, Waters was aware of cyclopropane's drawbacks, at the beginning of the 1930s he seized upon this new anaesthetic and recruited it to play an active role in the institutionalization of anaesthesia. To a doctor who was hoping to overhaul the practice of

78. Snow, *Operations Without Pain*, 197.

79. Snow, *Blessed Days of Anaesthesia*, 178.

80. Morris, "Ralph M. Waters (1883-1979)," 579; Wilson and Morris, "'My Dear Dogfish'," 580-590.

81. L.E. Morris, "The Continuing Influence of Ralph M. Waters on Education in Anesthesiology," in *Anaesthesia*, 33.

82. Denson, "Cyclopropane," 1005.

83. *Ibid.*, 1032.

anaesthesia, to professionalize this medical specialty, and to increase the authority of anaesthesiologists, cyclopropane and the complexity of its administration offered an unparalleled professional boon.

After learning about cyclopropane in Montreal, at the June 1929 meeting of the Canadian Medical Association, Waters ordered a ten-gallon tank of the gas from a chemical company, and he anaesthetized his first patient on August 19, 1930. He had only tried it once, two days previously, on a wild “large shepherd dog.”⁸⁴ After using the gas on a few other patients, Waters ran out of cyclopropane, and had to wait until the spring of 1933 to purchase more from the manufacturer. In October 1933, Waters invited the members of the Anaesthetists Travel Club to watch a demonstration. One of the prominent anaesthesiologists who attended was Harold Griffith, who eventually introduced cyclopropane into practice in Canada.⁸⁵ It was in 1934 that Waters finally could report on 2000 administrations over the previous year, and he published a formal report in the *Journal of the American Medical Association*.⁸⁶

Unlike Henderson, Waters had a professional goal to sustain, as well as an ability to modify the necessary technology to make cyclopropane more acceptable as an anaesthetic. For example, he found a way to simultaneously reduce the precipitous cost of the anaesthetic and to improve the delivery technique. He used a device he had developed, a closed carbon dioxide absorption system which recycled the air the patient breathed, thus conserving anaesthetic.⁸⁷ By virtue of his position as an anaesthesiologist who was in close contact with colleagues, who trained future anaesthesiologists, and who was seeking increased authority for these doctors in the delivery of anaesthesia, Waters was able to foster and disseminate the use of cyclopropane. The professionalization of anaesthesia was thus an important social factor that contributed both to Waters’ conceptualization of cyclopropane as a potential medical technology and to the eventual success of this anaesthetic gas.

In October 1933, after Waters presented some of his preliminary data at the Congress of Anaesthetists in Chicago, the *New York Times* quoted Waters’ opinion that the new anaesthetic was “the ultimate in surgical aid.”⁸⁸ This assessment contrasts remarkably with the way cyclopropane was described by *Time* in September 1929. In a detailed report on the 13th

84. Vandam and Volpito, 59-61.

85. C. Ball and R.N. Westhorpe, “Cyclopropane,” *Anaesthesia and Intensive Care* 34, 6 (2006): 701-708. On Griffith, see Richard Bodman and Deirdre Gillies, *Harold Griffith: The Evolution of Modern Anaesthesia* (Toronto: Dundurn Press, 1992).

86. Waters and Schmidt, “Cyclopropane Anesthesia,” 975.

87. Ball and Westhorpe, “Cyclopropane,” 34.

88. “Declare New Gas Great Surgery Aid,” *The New York Times*, October 11, 1933, 11.

International Physiological Congress held at Harvard University, cyclopropane is sandwiched between gastric juice (“total loss of gastric juice causes death in five to eight days”) and a report on the eyes of hens (which “contain in the retina red, yellow and almost colorless green globules, which may be important in the undetermined mechanism of color vision”). Cyclopropane was briefly described as “a new gas [that] acts similarly to nitrous oxide (laughing gas) but has more satisfactory after effects. Recovery is rapid. The patient does not struggle. Respiration remains normal, the blood pressure almost so.”⁸⁹ Instead of being described as a dramatic innovation or discovery, cyclopropane is merely compared (favourably, but only mildly so) to an anaesthetic that had been around since the previous century. The difference between “the ultimate in surgical aid” and “more satisfactory after effects,” sums up the assessment that Waters and Henderson, respectively, made of this gas.

Cyclopropane thus seems to have undergone a dramatic makeover between the scientific laboratory and the hospital. Eventually, Lucas and others who began to write the history of cyclopropane once this gas gained a firm place in clinical practice, describe Henderson as the discoverer of the anaesthetic, in the clinical sense of the word, and ascribe the failure to set up clinical trials in Toronto to the media storm caused by the deaths of several surgical patients.⁹⁰ These narratives do not differentiate between the scientific artefact whose meaning was constructed in a particular way in the laboratory and the clinical product that was re-imagined before it was introduced into the hospital. As a consequence, the transition between the workbench and the operating table seems misleadingly unproblematic and predestined. Save for the vagaries of fortune, these writers suggest, cyclopropane would have become an anaesthetic in Toronto. In contrast to this position, I have argued that the transformation of a scientific product into a medical technology is not inevitable and self-evident. In the case of cyclopropane, this transition necessitated an overhaul and a re-construction of cyclopropane’s identity: Henderson and Waters envisioned its potential in markedly different ways in their respective professional contexts.

89. “Medicine: Physiological Congress,” *Time*, September 2, 1929.

90. Lucas, “The Discovery of Cyclopropane”; Turner, *Cyclopropane*; Bamforth, “Cyclopropane Anesthesia”; Rusham, Atkinson and Davies, *A Short History of Anaesthesia*; Griffith, “The Early Clinical Use of Cyclopropane,” 28; David A.E. Shephard and Kim Turner, *Preserving the Heritage of Canadian Anesthesiology, a Panorama of People, Ideas, Techniques and Events*, unpublished pamphlet http://www.cas.ca/public/archive_catalog/Archivesen.pdf, last accessed May 24, 2009.

Conclusion

Just as Fleming considered penicillin as a useful product in the laboratory to inhibit the growth of certain bacteria and thus to assist with vaccine research, whereas Florey and Chain saw it as a potential therapeutic agent, Henderson and Waters perceived cyclopropane in a different light.⁹¹ Although Henderson, as the head of the Pharmacology Department of the Faculty of Medicine, was in an excellent position to translate scientific research into medical technology, his identity as a laboratory scientist may have led him to conceptualize cyclopropane in an entirely different fashion from the manner in which Waters, a practicing anaesthesiologist deeply invested in the professionalization of his medical specialty, eventually understood this gas. Perhaps Henderson believed that the next generation of anaesthetics ought to have features that he could not reconcile with cyclopropane's characteristics, which placed it in the category of older anaesthetics like ethylene and propylene. Historical evidence hints to the cost of cyclopropane, as well as its flammability and potential side effects, as explanations for the fact that Henderson did not conceptualize and promote it as a novel medical technology.

In this paper, I have argued that it is useful to distinguish between the discovery of an anaesthetic and the discovery of the anaesthetic properties of a substance. This distinction is not trivial: it reveals important clues about the manner in which a discovery is conceptualized and can explain whether or not a scientific product eventually transitions into a medical technology. Historians, sociologists of science, and social epistemologists have repeatedly emphasized that scientists do not observe nature or make inevitable discoveries unproblematically, but rather interpret, construct models, and negotiate the meaning of data.⁹² Observation does not happen in a vacuum; it is constrained by theory and by a multiplicity of other knowledge-productive practices, from the choice of the experimental set-up to ideological commitments to aesthetic choices. Thus, what appears to be at first a subtle distinction allows us to understand why Henderson did not introduce cyclopropane into medical practice in Toronto, and why, despite later narratives that consider him the discoverer of the anaesthetic cyclopropane, he did not think of cyclopropane as a clinical product. Although he observed and described the anaesthetic properties of the gas, Henderson did not envision cyclopropane as a practical medical technology.

91. Chen, "The Laboratory as Business," 245.

92. For an excellent review of the literature, see Helen E. Longino, *The Fate of Knowledge* (Princeton: Princeton University Press, 2002), especially Chapter 5, 97-123.