4.19 Cyclopropane Anesthesia: Its Introduction at Wisconsin

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Shortly after Ralph Milton Waters was appointed as Head of Anesthesia at the State of Wisconsin General Hospital in Madison, in 1927, he embarked on several laboratory investigations with members of the basic science faculty. These included evaluations of new drugs, mechanisms of anesthetic action, and methods of administration. Many efforts were made during the 1930s to find an anesthetic agent which would be more acceptable than the commonly used ethyl ether or the less potent gases, nitrous oxide and ethylene. Thus it was especially interesting to Waters, when in June 1929, at the meeting of the Canadian Medical Association in Montreal, he heard Prof. Velyien E. Henderson report the anesthetic properties of cyclopropane.

Professor Henderson, the Head of Pharmacology at the University of Toronto, and an anesthetist from Toronto General Hospital, Dr. W. Easson Brown, had been experimenting with propylene, but problems with toxic impurities led this investigation to be discontinued for a time. The chemist, George H. W. Lucas, who had joined Dr. Henderson’s department, suggested that cyclopropane, an isomer of propylene, might be the responsible contaminant. On 22 November 1928 he prepared enough of the gas to administer it to two small kittens in a bell jar. Lucas and Henderson were impressed with the resulting anesthesia and, realizing that cyclopropane was not the toxic impurity in the tanked propylene, conducted further investigations of the gas. They determined the concentrations needed for surgical anesthesia, the solubilities, and the explosive range. Dr. Brown anesthetized several of the staff, including both Lucas and Henderson. It seemed time to submit the agent to clinical trial.

However, as Lucas was later to report:

At this juncture our luck changed. Three anesthetic deaths occurred in Toronto in a relatively short period; there was much newspaper publicity about them. Dr. Brown, who had anasthetized several of us successfully in the laboratory, requested the privilege of administering cyclopropane, even for a short surgical procedure. A demonstration was arranged in our laboratory one evening, when Dr. Brown anaesthetized Dr. Frederick Banting before a group of Toronto anesthesiologists. Among the guests was the Head of the Department of Anaesthesia of the Toronto General Hospital. But because of the ethyl chloride deaths and the fear of any consequences should a fatality follow the administra-
tion of cyclopropane, Dr. Brown was forbidden to use this gas in the Hospital. We continued some experiments with commercial cyclopropane supplied in small tanks by E. R. Squibb & Sons Inc. Professor Henderson realized our position and encouraged his close friend, Dr. Ralph Waters, to use cyclopropane clinically" [1].

In the spring of 1930 Waters wrote to Henderson requesting reprints of papers on anesthesia and also said,

I should be greatly interested also in knowing what the latest developments are with the cyclopropane matter. 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; and as you know, our technique here lends itself readily to small quantities of gas, two or three gallons or four or five at the most, being sufficient for the conduct of an anesthesia”.

He was referring to his closed system of anesthesia with carbon dioxide absorption. (This and other letters quoted are in the Archives of the University of Wisconsin, Madison.)

Henderson responded,

We have recently tested on man, samples of cyclopropane furnished us by the Ohio Chemical Company, but see no possibility of really satisfactory clinical trials here. I have no doubt the Ohio people could furnish you with a good quality of cyclo and we would be glad to see you try it, if you would care to do so, for anaesthesia.

Waters admitted that he felt “some hesitancy” in asking the Ohio Chemical Company to supply samples of the gas because the hospital in Madison did not “habitually deal with the company.” However, on the same day he requested that they quote a price for a very small quantity of the gas. Records indicate that a cylinder containing 10 gallons of cyclopropane, at the cost of U.S. $ 5.00 for the tank and U.S. $ 16.00 for the contents, was shipped to Wisconsin General Hospital on 1 August 1930. Waters’ laboratory records note that on 17 August 1930.

A large shepherd dog (wild) was given (with no premedication and with the carbon dioxide absorber method) one part of cyclopropane and three parts of oxygen, beginning at 9:31½. Respiratory rate increased from 30 to 65; pupils dilated markedly and did not react to room light. Expiration was an extremely unusual jerky type during the induction. Complete loss of sensation and brain reflexes, together with conjunctival and corneal reflexes occurred in 1½ minutes. An unknown, but slight addition of oxygen then resulted in rather smooth, with apparent complete relaxation, respiration deep and slower and pupils contracted.

Waters stated:

From the above experiment, we will conclude that in this particular dog, surgical anesthesia could be maintained with responsible safety, with mixtures of cyclopropane and oxygen varying from fifteen percent up to fifty percent. We would also conclude that there is a reasonable margin of safety, at least on the table, in the use of this gas as an anesthetic agent, the circulatory system maintained long after respiratory depression and even arrest had occurred.

On the basis of the careful laboratory work of Lucas and Henderson and because of the small amount of cyclopropane available to him, Dr. Waters proceeded to anesthetize clinical subjects. On 20 August 1930, he wrote to Professor Henderson:

Being satisfied that I need not harm the patients, I have used the remainder of the tank for three complete clinical anesthesias. One simple appendectomy – thirty-five minutes, one inguinal hernia – forty minutes, and one fat lady (her tenth operation) for the removal of a gall bladder, previously drained, and the repair of an inguinal hernia, the latter operation lasting one hour and twenty-eight minutes. An attempt to use the tank again this morning gave me an induction, but during the insertion of the pharyngeal airway, the small amount of cyclopropane was lost so that the one dog anesthesia