

THINK YOU'RE HAVING A BAD DAY?

Introduction

Bill Bigelow's legacy was already secure. In 1946, he conceptualized the idea of using hypothermia as an adjunct to open-heart surgery. In fact, he quickly became the foremost contributor to the development of inflow occlusion as a means of operating inside the heart. In 1949, during a routine dog experiment, he noticed that electrical contractions could be produced by touching the animal's heart with a surgical instrument. This unexpected observation led researchers at Toronto General Hospital to produce the first reliable external pacemaker. Indeed, Bigelow was recognized as a pioneer in cardiac surgery. (See Figure 1) So why then, in 1951, did he embark on the outlandish quest of unlocking the secrets of hibernation? Obviously, humans are warm-blooded homeotherms. True hibernators are poikilotherms – animals whose body temperature parallels their environment during winter months. Had Bigelow lost his mind? What good could possibly come from knowing how and why some animals hibernate? Bigelow's reasoning was sound. His colleague William Mustard worked across the street from him at the famed Hospital for Sick Children. On several occasions between 1951 and 1953, Bigelow had witnessed Mustard's technique of using monkey lungs for oxygenation during complex congenital repairs. In Bigelow's mind, extracorporeal circulation was just too dangerous and just too unpredictable. Instead, he imagined the prospect of combining hypothermia with hibernation – in effect, turning the patient into a poikilo-

therm. How spectacular would it be to safely extend the inflow occlusion time to over an hour, allowing the surgeon ample time to fix any defect! Bigelow's quest became a 10-year obsession. Initially, he surmised that animals such as the groundhog must possess some sort of chemical or hormone that induces the hibernating state. In time, Bigelow and his team would learn that Mother Nature guards her secrets very closely.

Groundhog Experiments

At his peak, Bigelow housed nearly 400 groundhogs at a custom-built farm north of Toronto. The first four years of his research focused on the groundhog's anatomy, with specific attention being directed at the hibernation gland. This gland, located near the groundhog's mediastinum adjacent to the

Kelly D. Hedlund,
MS, CCP

*The Michael E. DeBakey
Heart Institute*

Hays, Kansas

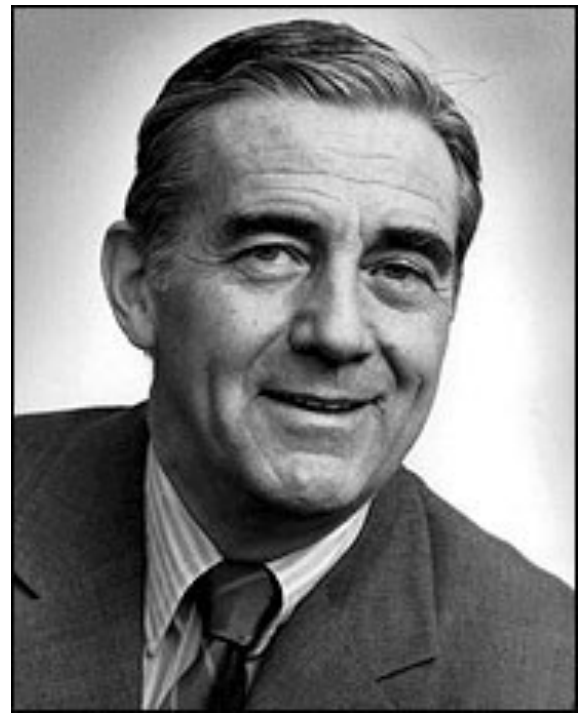


Figure 1. Dr. Wilfred G. Bigelow at the University of Toronto in 1965.

chest wall, appeared to reach maximum size just before the onset of hibernation. Furthermore, it contained streaks of brown fat. Bigelow was convinced that the secret hormone that triggered hibernation resided somewhere in this unusual brown fat. During the next four years, thousands of blood samples were obtained from hundreds of groundhogs in order to isolate the hibernating hormone. Over the years, Bigelow remained true to his goal – to discover the elusive hormone that would endow humans with the ability to withstand deep and prolonged hypothermia. Finally, after eight years of painstaking work, an extract was isolated. Unable to contain his excitement, Bigelow immediately named the chemical “Hibernin”. The final two-year phase of Bigelow’s research involved injecting Hibernin into small test animals such as rats or guinea pigs. Not only did they tolerate the injections, the animals withstood being cooled to body temperatures of 5°C. What excitement! The control animals could only be cooled to 14°C, below which they all died. Bigelow was so elated that he suspended his surgical practice, along with other members of his team. In addition, he sought a patent for his newly-discovered wonder drug. Remarkably, two human patients received Hibernin injections from Bigelow during this two-year period (1960-61). Both survived inflow occlusion and deep hypothermic repair of congenital defects. The recovery room nurses, however, reported that both patients acted drunk postoperatively.

The Grand Failure

Bigelow was ready to announce to the world his discovery. Several articles were written, with plans to submit them to various medical journals. One of the articles, targeted for a surgical journal, reported the first cases where Hibernin was used during human heart surgery. Bigelow would surely be on the list for a Nobel Prize! Unfortunately, just as he was about to go public Bigelow received a letter from the U.S. Patent Office. Bigelow’s hibernating hormone, Hibernin, that was destined to revolutionize heart surgery was already patented! To his dismay, Bigelow’s

extract was actually a plasticizer. Yup, a simple phthalate ring with two side chains invented twenty years earlier to maintain the pliability of plastic tubing. Bigelow called an emergency meeting. Were the blood specimens somehow contaminated? The evidence was irrefutable in specimen after specimen. The blood had obviously picked up some of the leached plasticizer as it coursed through the sampling tubing. Unbelievable! Ten years of work down the drain. Bigelow could only laugh at the absurdity of it all. Why then did the studies show repeatedly that the animals (and humans) receiving Hibernin tolerated hypothermia better? Amusingly, the key ingredient in the plasticizer was butyl alcohol. Once purified, this extract had the same effect as beverage (ethyl) alcohol. This explained the observation by the recovery room nurses. Furthermore, it was known from reports of accidental hypothermia that drunks falling asleep in the snow had survived remarkably low body temperatures. Bigelow chuckled at the irony, there was little else he could do.

Conclusion

Bigelow’s legacy is intact – he is the undisputed Father of Hypothermia. After a brilliant career he passed away in 2005 at the age of 92. Throughout his long life, he taught us a valuable lesson, his ability to laugh in the face of obvious disappointment. His story should remind us of an enduring adage, “*when you get knocked down, get up*”. Establishing a new scientific truth, even when using sound research, can be extremely difficult. Bigelow’s story reminds us of just how much we do not know and that a little laughter can be a good thing these days.

References

- Bigelow WG. *Cold Hearts: The Story of Hypothermia and the Pacemaker in Heart Surgery*. McClelland & Stewart Ltd. Toronto. 1984.
- Goor DA. *The Genius of C. Walton Lillehei and the True History of Open Heart Surgery*. Vantage Press Inc. New York. 2007.
- Shumacker HB. *The Evolution of Cardiac Surgery*. Indiana University Press. Indianapolis. 1992.