The pacemaker story: A cold heart spin-off

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It is 1949. Visualize, if you will, Room 64 in the basement of the Banting Institute in Toronto — home of the cardiovascular surgical experimental laboratory. The room is 23 x 14 feet. A small, high window is below ground level. The adjoining Room 65 has recently been acquired.

This is stated very simply, but the process of acquiring extra space in an active university building requires a *tour de force*. To obtain space from someone in your own division is very difficult; from another division in the same department it is next to impossible; and to acquire space from another department is a meritorious accomplishment that has usually involved the dean of the faculty, at least two departmental heads, several committees, cajoling, entreaty, kindly offers, gifts, and even veiled threats. One must have several key people "on side". It is seldom successful as a single-handed operation. Room 65 was, in fact, an acquisition from another department. It was immediately converted into what we seriously called an operating room, though without the usual tiled wall and floors. It became the busiest large-animal laboratory in the university, and it still is. Animals were housed on the top floor.

To find Rooms 64 and 65, a visitor first proceeded down a stairway into a dimly lit basement with cement floor and brick walls. It was necessary to pick one's way carefully along the west corridor, which was (and still is) used as a storage area. Opening the door of Room 64 released the hum of activity of four to seven or eight busy people: two research fellows (John Callaghan and Ross Fleming), two technicians, a chemist, and assorted representatives from departments that were collaborating in the hypothermia and microcirculation research. To say that they were occupied is an understatement. They all felt that they were setting the stage for an explosion of knowledge and technology that would profoundly affect the whole practice of medicine.

Capillary circulation (microcirculation) was being observed through a microscope in a living animal. This was a new and exacting technique, hitherto viewed by only a few anatomists. It gets at the business end of the circulation, where all the action is. The hypothermia studies, we hoped, would allow direct-vision correction of heart defects, until now virtually unassailable. It was an awesomely fertile field.

The heart would cease to function at some point when the laboratory animal was cooled below 24°C. Why did the cold heart suddenly stop?

Dr. Callaghan was a flying doctor in the Arctic waiting for his appointment for surgical training. His plane had been forced down and it was lost in the snow of the barren lands for days. He finally received a letter advising him that he could start his training July 1, 1949. Now his first appointment was to be 1 year of research in the Banting Institute under a Dr. Bigelow. But he had wanted to do surgery, so he did not answer the letter. Finally a telegram arrived giving him 48 hours to reply. He arrived reluctantly, but within a few weeks he was inspired.

Microcirculation and hypothermia were initiated as two different research projects. Astoundingly, as work progressed it became apparent that they were closely interrelated. Cooling an animal below a certain body temperature produced some serious obstruction to flow in the capillary circulation.

The excitement of work in hypothermia was overshadowed by a great cloud of frustration. As noted earlier, the heart would cease to function (cardiac arrest) at some point when the laboratory animal was cooled below a body temperature of 24°C. And yet infant animals could be safely cooled and resuscitated from body temperatures near the freezing level (5°C). We were in a hurry to solve the problem so that we could study deep hypothermia. Why did the cold heart suddenly stop? We pondered, discussed, and read about the subject.

The heart stoppage or cardiac arrest was in two forms: cardiac standstill — a motionless heart; and ventricular fibrillation, where the auricles may still be beating, but the strong ventricles are ineffectively squirming. There had been 3 years' research with no answer.

One morning a standard experiment was planned. As I entered the laboratory, an anaesthetized dog was already being cooled in refrigeration blankets with ice bags. At a body temperature of 22°C with regular heart action and adequate blood pressure, the cooling was discontinued and the top blanket removed. After surgical preparation of the shaven skin, the chest was opened by a surgical incision. Cardiac arrest was not expected at 21°C in this particular animal. The pericardium was opened, exposing the normal pink heart beating slowly,

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This article is an excerpt from Dr. Bigelow's new book, "Cold Hearts", published last month by McClelland and Stewart Limited, Toronto. Due to space limitations we have eliminated the footnotes. Interested readers can refer to the book for these and for more of the story about the evolution of the modern pacemaker.

forcibly, and gracefully. We were now ready to make certain physiological observations regarding hypothermia, after which the pericardium and chest would be closed and the animal rewarmed.

Just as we were about to begin the tests the heart unexpectedly stopped. It lay quietly in standstill. Cardiac massage did not restart it. This meant that our experiment would have to be postponed for another day while we attempted to revive the animal.

I looked at the heart. It was quiet, cool, pink, and the muscle was firm. It was of normal appearance in all respects. What was wrong with the little rascal? Out of interest and in desperation, I gave the left ventricle a good poke with a probe I was holding. There was an immediate and sudden strong contraction that involved all chambers — then it returned to standstill. I did it again, with the same result. What an unexpected observation!

I poked it regularly every second. Lo and behold, it resembled a normal beating heart. Were these phony beats or real contractions expelling blood into the circulation? A technician acting as anaesthetist said, "Hey, I'm getting a blood pressure here." This meant that these were real contractions, that the heart was not only beating but forcibly expelling blood in a normal manner.

The heart had stopped while it appeared to be perfectly capable of continued function. An electrical impulse had the same effect as a poke. Perhaps all the cold heart needed was a pacemaker. What a fascinating idea! Perhaps we could keep the heart beating while we cooled the animal to deep hypothermia levels. We had read reports of research indicating that in laboratory animals, and presumably humans, nerve impulses were not conducted along the nerve below a body temperature of 9 or 10°C, while in hibernators conduction was not affected down to body temperatures of 2 or 3°C.

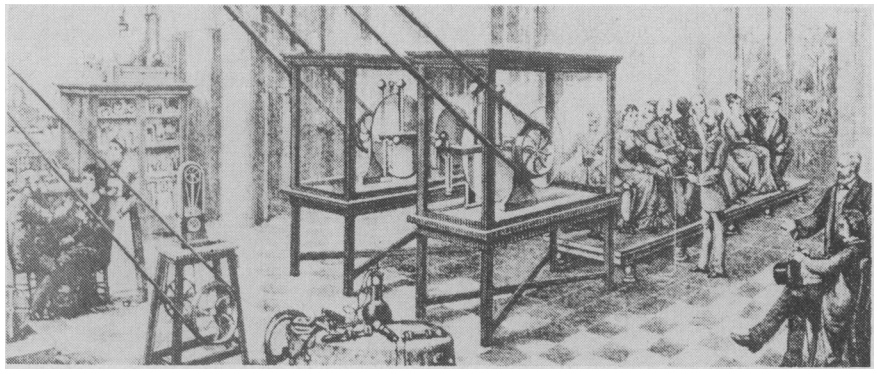
Our experimental animal was successfully resuscitated with manual cardiac massage while it was being rewarmed. The pericardium and chest were closed, and he recovered completely, little knowing that he had supported the germ of an idea that would lead to greater things. Soon after that experiment there were other opportunities to confirm our observations.

We had found a project to be pursued with vigour. John Callaghan and I, in an atmosphere of excitement and anticipation, sat in our dingy lab well into the night, and over many cups of coffee we discussed the prospects of an electric pacemaker for the heart. We agreed that:

- A pacemaker had unknown potential.
- We would enlist the best electrical engineering advice and create a stimulus that, as closely as possible, duplicated the electrical discharge in a normal heart.
- We were striving for excellence. We did not want an electrical discharge that would damage the nerve mechanism or muscle of the heart when used over a long period.
- We needed a stimulating electrode that would allow the chest to be closed, and would allow rewarming in a warm-water bath if necessary. This would involve a wire attached to the heart and coming out through the chest wall, or, preferably, an electrode passed down a vein into the heart. This latter prospect, if possible, was intriguing.

Callaghan would review the literature and I would take on the task of obtaining expert help. At the same time, our hypothermia research had turned to the problem of rewarming. We were in need of electrical engineering help to test the possibility of rapidly rewarming animals and, later, patients with a high-frequency diathermy machine. It would be more practical and aesthetically more acceptable than plunging them in warm water after surgery. Perhaps the same electrical engineer could help us with the proposed pacemaker.

With the rashness of youth, I obtained an interview with the head



A French clinic where patients were treated by the application of electrodes to the skin of the chest.

of the radio and electrical engineering division of the National Research Council in Ottawa, Dr. B.J. Ballard, who later became president of the NRC. I told my story and outlined with a modicum of dramatic licence the potential knowledge and practical benefits that might accrue from a study to develop a radio-frequency rewarming device and an electrical artificial pacemaker. We also needed an electrical defibrillator, so there would be lots to keep someone busy. To my great surprise, Dr. Ballard listened attentively and acted promptly. He must have possessed a remarkable intuitive sense, because I had little to recommend me as an investigator.

Dr. Ballard indicated that he had a man in his division who was busy studying the pasteurization of beer by radio-frequency rewarming. Apparently a brewery was supplying him with the raw material for his studies. I assumed without much effort that the brewery, to show their appreciation, would be supplying him with an adequate amount of the finished product as well. He sounded both imaginative and practical, and when Dr. Ballard offered us his part-time services we accepted enthusiastically, sight unseen.

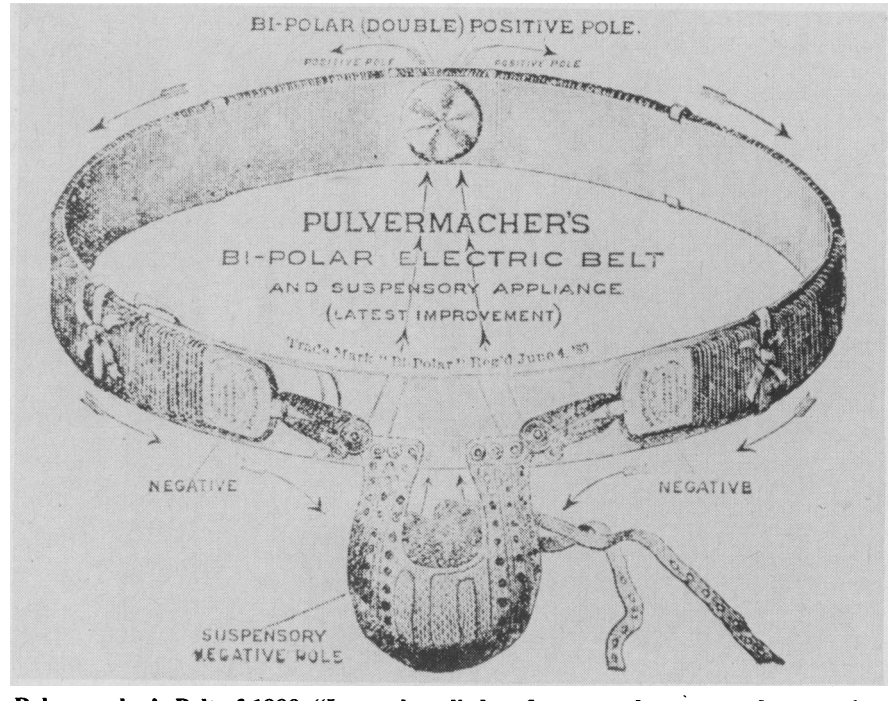
Accordingly, Jack Hopps, a brilliant electrical engineer, was assigned to our laboratory and given authority to travel back and forth from the National Research Council in Ottawa to our basement laboratory in the Banting Institute. He was a tall, thin, pleasant fellow — an ideal team man with the admirable combination of cheerfulness, expertise, and open-mindedness. On Hopps' arrival, a day with the zealous Callaghan won him totally to the cause.

Meanwhile, a review of the literature disclosed only one reference to a cardiac pacemaker. In 1932, an imaginative Dr. Hyman of New York had tested on guinea pigs a device he had constructed. Our original review has been extended to include references to a remarkable series of articles by Dr. David Schechter of New York, who thoroughly and dramatically has outlined the historical background of electrostimulation of the heart.

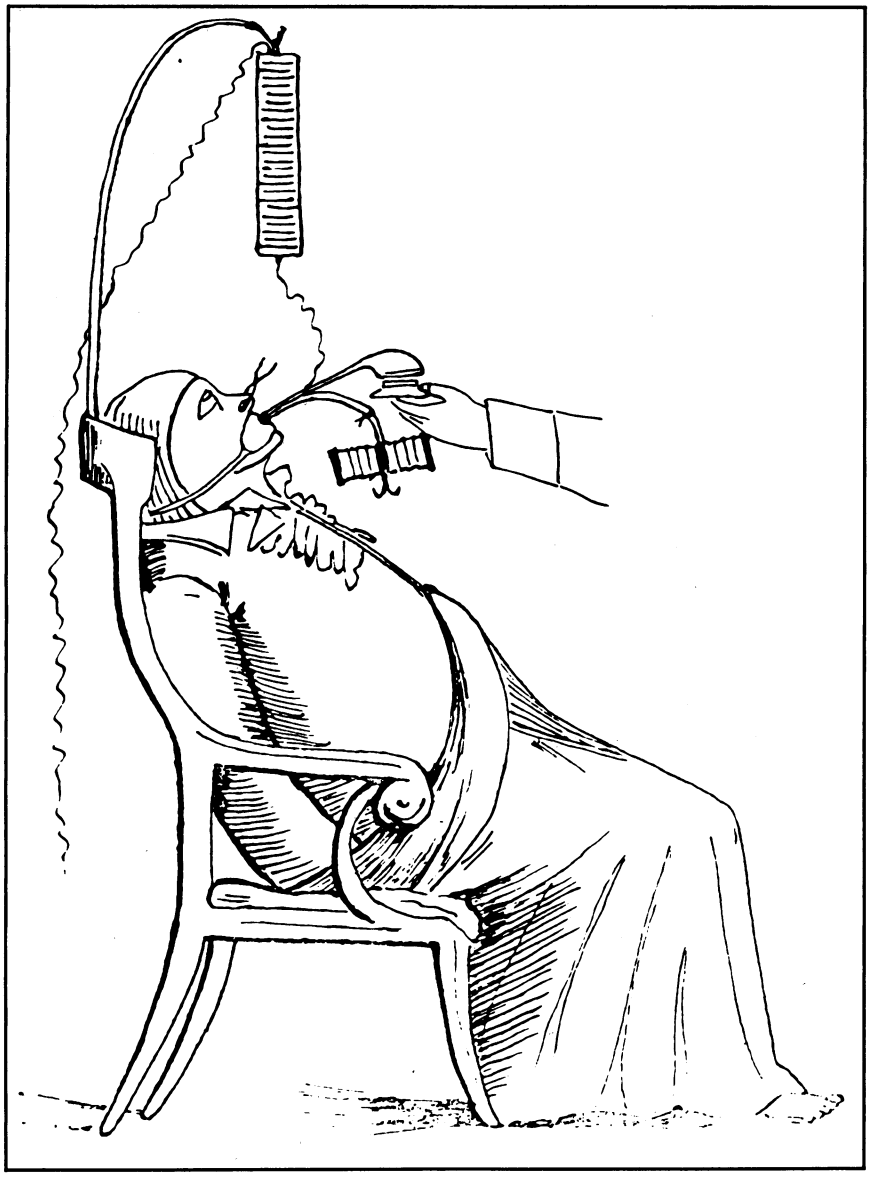
The study of static electricity goes back to Greek times. In the seventeenth and eighteenth centuries it was discovered how to store an electrical charge in a cylinder. A study of the properties and charges of electricity at rest (electrostatics) developed toward the end of that period. Remarkably enough, even at this embryonic stage, there were isolated reports of physicians testing the effect of an electrical discharge on the pulse rate.

It was not until 1800, with the work of Luigi Galvani and Volta, that it became feasible to pass a current of electricity along a conductor. This proved to be a fascinating phenomenon. During the 19th century it was thus only natural that this mysterious, freshly harnessed, but little understood source of energy would appeal to the imaginations of persons interested in health and disease. Electricity in many forms was used for every conceivable ailment. By the late 1800s there were elaborate devices that encompassed the whole body and devices that were designed to provide unknown benefits of electricity to special parts.

Patients with cardiovascular ailments were treated by having them stand in a solenoid cell charged with electricity. Its use was described: "the current . . . should be of great intensity . . . in order to obtain the best results . . . it should be strong enough to give a spark . . . 25 centimeters in length." In a French electrotherapy clinic, patients were treated by the application of electrodes to the skin of the chest. For



Pulvermacher's Belt of 1889: "It may be relied on for a complete cure and restoration to health and manly vigour . . . the only appliance of its kind . . ."



The reanimation chair of Dr. R. Reece of London, to restore life. A metal tube is thrust into the gullet. A wire coming from the suspended galvanic battery, "containing one hundred plates", is attached to the tube with the other electrode touching the body. The nostrils are clamped and air is pushed by a bellows into the pharynx. Various strong potions are administered. This represents an amazing attempt to use artificial respiration and transesphageal electrical cardiac stimulation over 100 years before knowledge and technology made this feasible.

this, patients could be fully clad, but in some instances they were relegated to a special electric bath in the nude. One of the most imaginative and I am sure popular electrical devices was Pulvermacher's bipolar electric belt of 1889, which, the supplier's brochure proclaimed, would cure "nervous and debilitated conditions of the generative organs". It promised to restore its user "to health and manly vigour" — what Schechter calls "an infra-cardiac pacemaker".

Along with devices to maintain and restore health, enterprising investigators looked to electricity to restore life to those who appeared ready to leave this world. An early try in this direction was the "reanimation chair" designed in 1824 by a truly remarkable man, Dr. R. Reece of London. This represented an amazing attempt to use artificial respiration and transesophageal electrical cardiac stimulation over 100 years before knowledge and technology made this feasible. Air was pushed by bellows into the larynx; a metal tube in the gullet contained "stimulating fluid"; one wire of a galvanic battery was fastened to the esophageal conduit while the other wire touched different parts of the body. I would think that this heroic treatment would be pretty decisive, one way or another.

Another simpler option for bringing life back to the body, although not at all attractive, was total electrification by a mouth-to-anus circuit. Electrodes made from different metals were inserted in each of these orifices and the attached wires were connected to produce a battery. The gentleman who first described this method of resuscitation tried it upon himself. He saw flashes of light, which he concluded was sufficient evidence that it was indeed effective. Medical historian David Schechter notes that there are no diagrams of this method available.

The knowledge of electrical currents after 1800 led to the discovery of electromagnetic induction of currents by Faraday in 1831. He designed the first generator. This set the stage for the massive explosion of knowledge of electrical phenomena that we enjoy today.

A milestone was the imaginative research of Dr. J. MacWilliams of London, whose animal experiments were a generation ahead of their time. He discarded galvanic and faradic currents in favour of a series of induction shocks. He felt that this was less likely to produce fatal "fibrillary" action of the heart. He apparently understood the difference between arrest of the heart due to cardiac standstill and ventricular fibrillation. Once again, repetitive stimulation was produced by a mechanical "make-and-break" device. In 1887, he temporarily stopped the hearts of animals by electrical stimulation of the vagus nerve in the neck and succeeded in reestablishing the heartbeat and improving the blood pressure by his electrical stimulation. The stimulation was applied both directly on the heart and over the heart on the chest wall.

The next milestone, 43 years later, was the work of Dr. A.S. Hyman. With the help of physiologists at his Beth David Hospital in New York, he developed a device he called a "pacemaker" that would produce sequential electric stimuli at 30, 60, and 120 times per minute. The hand crank wound up a spring that rotated a magneto. When the

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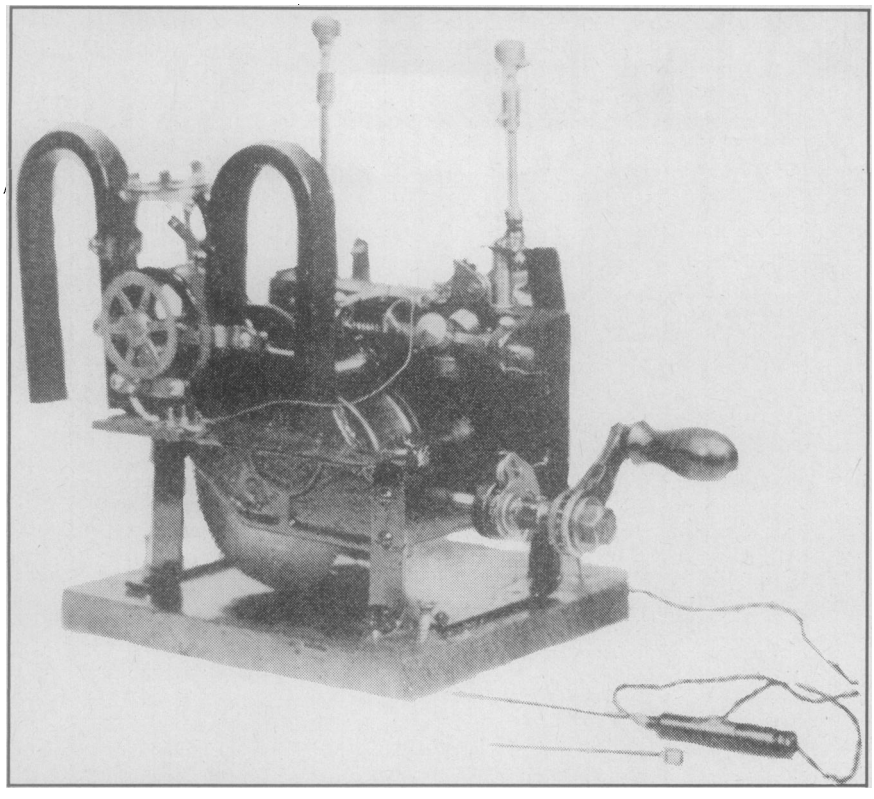


The electric pacemaker designed by Hyman in 1932. The handle was used for winding a spring motor, which in turn operated a magneto-generator. It would produce a current for 8 minutes. The stimulating electric current was conducted by a wire to a long stimulating needle that was thrust through the front of the chest until it was assessed that the tip had engaged the atrial wall of the heart. This was indeed an ingenious and courageous project.

spring became unwound, the pacemaker ceased functioning. This allowed it to operate for 8 minutes. In his article he described what appeared to be a high-frequency current, which is customarily used to heat tissues rather than stimulate them. There was no evidence of current control. He astutely observed that the stimulation was more effective when the two stimulating electrodes were in close proximity (bipolar).

Hyman experimented with guinea pigs and one dog. He produced cardiac standstill (arrest), confirmed with electrocardiogram, by asphyxiation. He used a long insulated needle mounted on a handle, which he inserted through the chest wall hopefully into the right auricle of the guinea pig's heart. His success rate was not stated. He demonstrated that the pacemaker could be inserted into the normal beating heart of a guinea pig, thus producing regular extra beats without causing the heart to stop.

He stated that it was used on patients but he did not report the experience. A degree of unreliability, maximum duration of 8 minutes, hemorrhage into the pericardium, and hostility against such an aggressive approach caused the technique to be abandoned. It was a great idea but it was not suitable for clinical use. There were no further reports of the construction or use of pacemakers for the heart from 1932 until our report in 1950.

It was apparent from this review of the literature that the field was wide open. In order to create a pacemaker where we knew the character of the electrical stimulus, a stimulating device (the Grass stimulator) was obtained. It delivered electrical current in periodic bursts of any desired wave form, duration, and frequency.

Following our initial experience, there were four other occasions in animal surgery where the heart arrested in standstill at a body temperature around 19–20°C with the chest open. Stimulating the surface of the heart restored the heart action. In the first two cases, when stimulation was stopped after 15 minutes the hearts reverted to standstill. They required cardiac massage. In two other experiments electric control of the heart for 10 and 30 minutes resulted in normal spontaneous heartbeats and recovery. This, no doubt, was due to unplanned rewarming.

Hopps and Callaghan, with the assistance of senior technicians Don Hughes and Ken Burly, began a careful and painstaking series of experiments: to assess the electrical activity on a normal heart; to determine comparable pulse characteristics that were most effective and safest; to decide on the best method of delivering a stimulus to the heart.

It became apparent that the electric stimulus applied to the heart must be of short duration. The electrical activity of what was called a "sine wave" or "square wave" form might persist into the late stage of heart contraction where the ventricle was in a sensitive state. This might precipitate a cardiac arrest. It was finally decided that a pulse wave with sharp rise and a 2-msec duration stimulated the normal p-wave on the electrocardiogram. The current should be low. With the heart exposed, the sinoauricular node (the area of the heart containing the natural pacemaker) could be stimulated using an electrode at the tip of an insulated rod. It was a single electrode with the other "dispersive" electrode on the chest wall.

To stimulate the heart without opening the chest, Hopps took a standard cardiac catheter and adapted it by passing a wire down the inside of the tube with a ring electrode mounted at the tip. This catheter electrode could be passed down a vein in the neck of a dog to be inside the heart and near the sinoauricular node. The second electrode was attached to the edge of the wound. It proved effective.

With great perception, he decided that having both electrodes in the one catheter would channel the electrical stimulation to the desired area and avoid muscle twitching caused by the second electrode. Would it work? He passed both wires down the catheter that attached to two small ring electrodes insulated from each other at the tip. It did work, and more effectively. This was the

first so-called "bipolar" catheter electrode to stimulate the lining of the heart. It is still used in pacemakers today.

Once the desired pulse features were determined, Hopps retired with the experimental data to his sophisticated electronics laboratory in the National Research Council in Ottawa. Assisted by the skilled technicians and equipment, he designed and built an efficient portable pacemaker unit incorporating the desired electrical features with a specialized circuit. It delivered what had been established as the ideal current and electrical pulse wave (monophasic or biphasic). It allowed dial control of heart rate and voltage. The unit was about 12 inches long and 7 inches high — the size of a mantel radio of that era. It was portable, but something that you didn't carry around with you.

It was a great day when Jack arrived back in the Banting laboratory with a big smile and carrying our first pacemaker unit carefully packaged. It was viewed with awe and pride. Here was a machine that could duplicate the electrical impulse that stimulated the heart to beat 40 million times a year. We all had a peek at the complicated circuitry and nodded gravely as Jack explained its function.

Setting ourselves the goal of duplicating the electrical impulse of a normal heart had meant many animal experiments and long hours of work. As one contemplated the future use of pacemakers for long periods of time, the goal appeared to have justified the effort. But what did we expect from a pacemaker?

- Our greatest hope was that by providing an artificial pacemaker for the heart, an experimental animal (and later a human) could be safely cooled to low body temperatures (deep hypothermia) and be rewarmed with no ill effect. This was based on our new theory that the heart stopped functioning below 20°C because the cardiac nerves were paralysed by the cold.
- If we did not succeed in achieving safe deep hypothermia, at least a heart that arrested in standstill during an operation with moderate hypothermia could be "paced" until the body was rewarmed sufficiently to allow return of normal heart action.
- Pacing the heart might improve its effectiveness and reduce the congestion that usually occurred at 20-24°C body temperature, thereby lessening the incidence of ventricular fibrillation.
- Its use in hearts at normal body temperature would have to be studied. This was a huge, unexplored continent.

In anticipation of the arrival of the pacemaker, the team had prepared an experiment with all hands on deck in our basement laboratory. A routine cooling procedure was carried out. A dog was anaesthetized and a tube was inserted into its trachea to control breathing. The electrocardiogram and blood pressure were recorded. The pacemaker electrode had been sterilized. Through a 1 inch incision in the animal's neck, the catheter was passed down a vein into the heart. When the stimulating tip was in the region of the sinoauricular node, there was evidence on the electrocardiogram to confirm its position. The blood pressure and heart rate were recorded by a fine pointer that produced a tracing on some smoked paper mounted on a rotating drum — a kymograph. This was 1950, before medical researchers had acquired some of the existing modern electronic techniques used by engineers.

The dog was cooled and all things proceeded without a hitch. At 21°C body temperature, the electrocardiogram showed changes we recognized as indicating that the heart was beginning to falter. It stopped at 20°C body temperature. The pacemaker was quickly switched on at a rate that was optimum for that body temperature. It immediately took control of the heart. The blood pressure and electrocardiogram improved.

There was a murmur and some cheerful expletives from the group huddled around watching the electrocardiogram and blood pressure. Cooling progressed without event: 19°C . . . 18°C . . . with a good, stable-appearing electrocardiogram. There were wary smiles exchanged among the watchers. Were we about to have the privilege of being the first to see safe deep hypothermia in an animal with the use of a pace-

maker? A body temperature of 17°C had just registered on the thermometer when suddenly the heart stopped. Changing the voltage current or position of the electrode had no effect. The pacemaker had failed us. It had reduced the lower limits of cooling by perhaps 2°C, but that was not enough to make it worthwhile. It did not solve our major problem.

This did not appear to be the answer to deep hypothermia. However, pacemaker research in hypothermia continued, and further experiments showed that the pacemaker could be used to improve the safety at moderate levels of hypothermia.

The next obvious step was to study the use of the pacemaker at normal body temperatures. Would the pacemaker produce expulsive beats if the heart stopped? We wanted dependable proof from well-controlled experiments using a physiological stimulus.

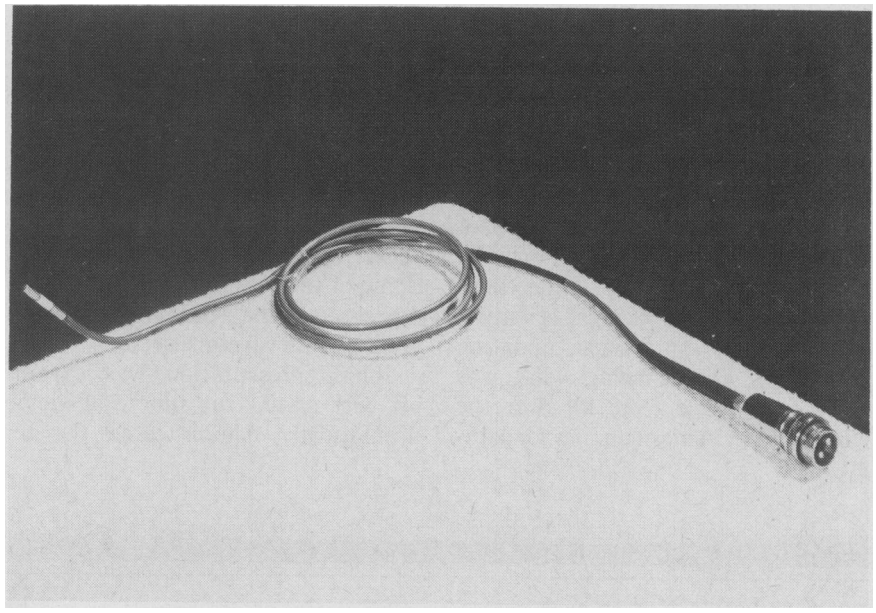
An unexpected problem was immediately encountered. How does one stop a heart? The situation had not been anticipated. An animal can be asphyxiated or chemically poisoned, producing cardiac arrest and death. This was not a reasonable solution. The heart would be damaged and attempts to restore such post-mortem hearts in animals and humans were seldom successful. Experimental surgical techniques to stop the heart or paralyse the sinoauricular node were not dependable in those days. How to stop a heart without damaging it? How to simulate the human condition where, in an otherwise healthy state, the heart slows or suddenly stops due to faulty impulse formation?

The literature indicated that turtle, rabbit, and dog hearts could be stopped temporarily by applying a continuous electric current (tetanizing) to the right vagus nerve in the neck. Callaghan tested all three animals and elected to use dogs and rabbits. It was fair to say that our past experience had not been extensive with turtles. The heart could be stopped for only about half a minute, but that was long enough to test the effectiveness of our pacemaker.

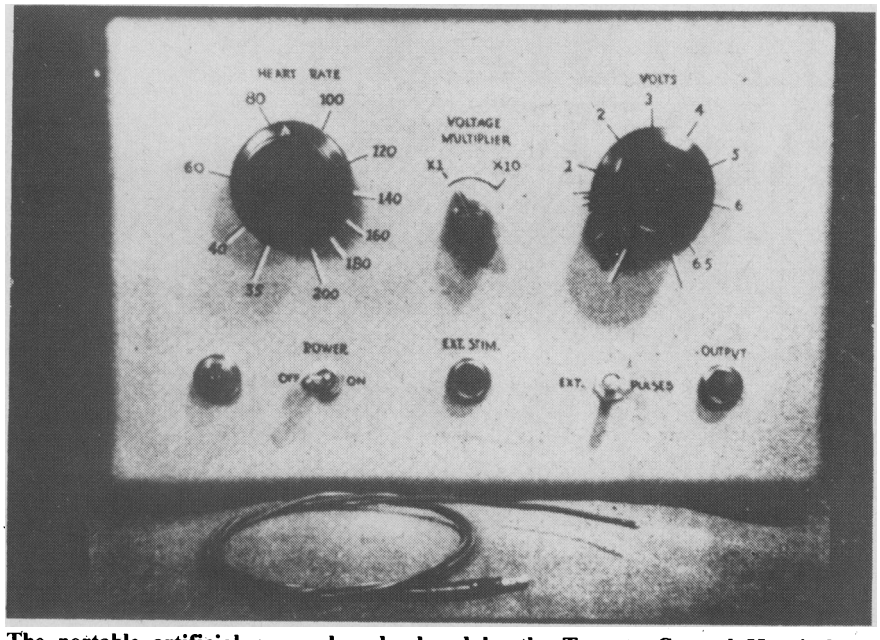
In the experiments the animals were anaesthetized. When the vagus nerve was exposed by a small incision in the neck and stimulated electrically, the heart stopped and the blood pressure fell precipitously. In each experiment the pacemaker would restore the heart beats and blood pressure during the arrest period.

During the course of these experiments the pacemaker was applied to the normal beating heart. A dog's normal heart rate is about 120 per minute. It was amazing to discover that the heart rate was effectively controlled by the pacemaker. It dominated the natural pacing mechanism. This finding was consistent. With a normal rate of 120, the pacemaker could regulate the heart action and increase the rate to 200 or lower it to 60 per minute. The blood pressure, interestingly enough, remained unchanged regardless of the heart rate, due to built-in reflexes.

Experiments during hypothermia



The intravenous catheter can conduct one (unipolar) or both (bipolar) stimulating wires. A bipolar electrode is shown where the two wire terminals are insulated from each other at the tip.



The portable artificial pacemaker developed by the Toronto General Hospital — National Research Council team. It is the first pacemaker for continuous human use with a controlled physiological electrical stimulus. It could start a stopped heart or control a beating heart, increasing or decreasing its rate as desired.

and at normal body temperature were duplicated using a bipolar stimulating electrode applied to the sinoauricular node; to the external surface of the exposed left ventricle; and, without opening the chest, by way of the intravenous electrode inside the heart at the level of the sinoauricular node.

All of these experiments were repeated many times with control studies and careful collection and analysis of data. Once again the heart rate and blood pressure were recorded on a smoked drum. To make doubly sure that we convinced the medical men and scientists who would hear this report, John Callaghan recorded key experiments by a motion picture, which still survives. In making an announcement to the medical world that a safe physiological pacemaker had been designed for human use, that could actually control the heart rate, the team had to be very sure of its ground.

Where should this be recorded? With the advice of Professor Robert Janes it was decided to send an abstract requesting a place on the program at the next meeting of the Annual Surgical Congress of the American College of Surgeons. This was and still is the largest meeting of surgeons in the world. What a relief it was when we were notified that our paper had been one of those selected for what is called the Surgical Forum. John was to make the presentation, and his name would appear first in our published report because he and Jack Hopps had done the lion's share of the work, particularly the normal body temperature studies.

We arrived in Boston on Oct. 22, 1950, and registered at our first "surgical congress". It was an enormously busy meeting with several amphitheatres and endless rows of scientific and commercial exhibits with crowds of viewers. Nine thousand surgeons and surgical scientists were meeting for 5 days, updating themselves and learning what was new. They came from all over the world. Many American and Canadian surgeons still use this meeting as an annual postgraduate course. We were pleased to discover that two Canadians had played an important role as founders of this great college in 1912; since 1920, six Canadians have been elected to the presidency, including W.E. Gallie for an unprecedented period of 5 years (1941–46) during the war.

The next day Callaghan and I were sitting near the front of a huge amphitheatre tensely waiting for his call to the podium. I glanced at him and thought: "This is quite a transformation for John, from the parka-clad flying Arctic doctor, within little more than a year, to addressing this large and distinguished scientific gathering." The meeting was beautifully managed. Each paper was exactly 10 minutes, and discussions were carefully controlled. Some of the 10-minute presentations represented the summary of many years of intensive research.

John's presentation was carried off with style. Our slide and movie dramatically demonstrated the re-

The combined stimulator-defibrillator, with a foot pedal to trip the single 200-volt defibrillating shock. Special electrodes were held on either side of the heart to conduct the electric current through the organ, and (A) an intravenous catheter electrode connected to the pacemaker.

markable ability of the pacemaker to control the heart. The daily congress newspaper noted that it was one of the scientific highlights of the day. We were sought out by newspaper reporters, who were naturally entertaining rather grandiose ideas as to the future use of such a contraption. William L. Laurence, the reigning dean of science writers, honoured us by selecting our paper as the subject for an article in *The New York Times*.

Then it was back to our Toronto laboratory and reality. We had reported the first pacemaker for continuous human use with a controlled physiological electrical stimulus that caused no injury to the heart muscle. The stimulated beats expelled blood. The electric stimuli from this unit could control a normal beating heart. Intravenous catheter electrodes, unipolar and bipolar, had been designed and used experimentally.

At the time of this report in 1950, Dr. Callaghan responded to five emergency calls from the operating room. Intracardiac catheter electrodes were rapidily passed through a vein in the arm or groin and connected to the pacemaker in an attempt to restore the function of a failing heart — without success. The cases were not suitable for pacing, but Callaghan decided years later that had he pushed the catheter just 2 inches further beyond the sinoauricular node and into the ventricle, he might have achieved a response.

We had no sooner returned from Boston than we received the first inquiry. A letter written one week after our presentation arrived from Paul Zoll, a cardiologist from Boston who expressed an interest in our pacemaker and said he was "most eager to get more information about the details of the stimulating apparatus". After an exchange of letters we finally supplied him with full details of the NRC circuit diagram. Soon after this he published an article reporting the interesting and successful use of a pacemaker ("stimulator") in two patients with a form of heart disease that had produced a failure of the natural pacemaker. The condition is called "heart block". It is characterized by periods when the heart rate would fall to a dangerous 20–40 beats per minute or stop altogether.

This was the first successful treatment of heart block with a pacemaker. His work drew the attention of the medical profession to the potential value of a pacemaker in treating heart disease. Zoll forgot to indicate in his articles the source of the electric circuit diagram that he used in his pacemaker. This was the first of many written inquiries that we received during the ensuing 3 to 4 years from centres around the world.

Our original pacemaker (the unit used by Zoll) was too large to carry about. There was limited interest among cardiologists in a form of treatment that required hospitalization and confinement to bed. Furthermore, Zoll had elected to use electrodes attached to the skin of the chest and the discomfort of the repeated electric shocks could be tolerated by the patient for only a few days at the most. Thus the treatment, although temporarily effective, was not attractive.

The 1950s saw the dawn of open-heart surgery. Surgeons were suddenly confronted with two major complications during and after these procedures: cardiac arrest and nerve conduction problems in the heart. Their proper management was often a key to the success of the procedure. Techniques of electric shock defibrillation for cardiac arrest developed during this era. A 200-v blast was used to shock the heart "to its senses" and start it beating properly. In 1951, Hopps and his NRC co-workers produced a combined stimulator-defibrillator.

To meet the problem of injury to the nerve conduction system that occasionally occurred during open-heart surgery, smaller portable pacing units operated by a battery were designed by Dr. Walton Lillehei and his team. They were still too large to be implanted under the skin. Such a unit, with one electrode attached to the heart and the other under the skin, had a valuable short-term use for a limited number of patients. Its use to avoid complications could be sustained only for periods up to 10 days or 2 weeks.

Thus, for 10 years the pacemaker was only used occasionally in a few centres to treat human disease. It literally sat on the shelf. Medical science had to wait while the transistor circuitry was being perfected. This was the breakthrough that allowed construction of a pacemaker so small that it could be implanted under the skin along with all the wires connecting it to the heart. Åke Senning of Stockholm was the first to accomplish this in 1959. It was the beginning of an explosion of knowledge that has produced the incredible era of pacemaking that we know today. ■