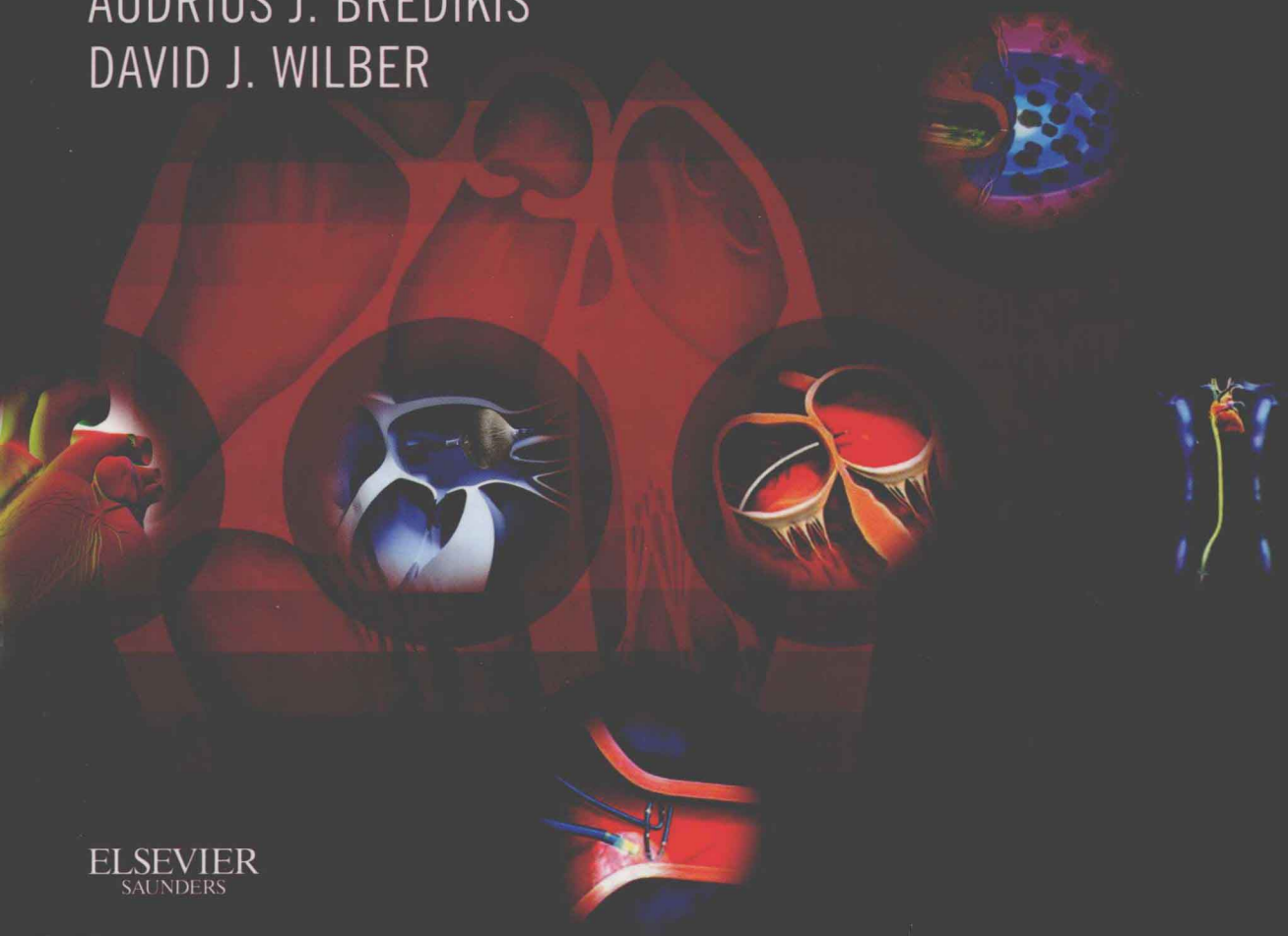


# CRYOABLATION OF CARDIAC ARRHYTHMIAS

AUDRIUS J. BREDIKIS  
DAVID J. WILBER





# Cryoablation of Cardiac Arrhythmias

**Audrius J. Bredikis, MD, FACC**

Cardiac Electrophysiology  
Holmes Regional Medical Center  
Melbourne, Florida  
Clinical Associate Professor of Medicine  
University of Central Florida



**David J. Wilber, MD, FAHA, FACC**

George M. Eisenberg Professor of Cardiovascular Sciences  
Director, Cardiovascular Institute  
Director, Division of Cardiology  
Medical Director, Electrophysiology Laboratory  
Loyola University Medical Center  
Maywood, Illinois

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CRYOABLATION OF CARDIAC ARRHYTHMIAS

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*To my father and mentor, Jurgis Bredikis; my mother, Danute; my wife, Egle; and children, Jurgis and Audre*

—A.B.

# Contributors

**Bernard Albat, MD, PhD**

Department of Cardiovascular Surgery  
Arnaud de Villeneuve Hospital  
Centre Hospitalier Régional Universitaire  
Montpellier, France

**Jesús Almendral, MD, PhD**

Head, Cardiac Electrophysiology Laboratory  
Grupo Hospital de Madrid  
Universidad CEU-San Pablo  
Madrid, Spain

**Robert Anders, MD**

Rush Presbyterian-St. Luke's Medical Center  
Chicago, Illinois

**Peter S. Andrew, MD, PhD**

ATLAS Medical Research Inc  
Edmonton, Alberta, Canada

**Mauricio S. Arruda, MD**

Director of Electrophysiology Section  
University Hospitals Harrington-McLaughlin Heart  
& Vascular Institute  
Case Western Reserve University School of  
Medicine  
Cleveland, Ohio

**Samuel J. Asirvatham, MD, FACC, FHRS**

Division of Cardiovascular Diseases  
Department of Internal Medicine  
Division of Pediatric Cardiology  
Department of Pediatric and Adolescent Medicine  
Mayo Clinic  
Rochester, Minnesota

**Felipe Atienza, MD, PhD**

Electrophysiology Laboratory  
Cardiology Department  
Hospital General Universitario Gregorio Marañón  
Madrid, Spain

**Koji Azegami, MD**

Yokohama City Mintao Red Cross Hospital  
Yokohama, Japan

**Alex Babkin, PhD**

Cryodynamics, LLC  
Albuquerque, New Mexico

**Alessandro Barbone, MD**

Division of Cardiac Surgery  
Istituto Clinico Humanitas  
Rozzano, Milano, Italy

**John G. Baust, PhD**

Binghamton University  
Institute of Biomedical Technology and Department  
of Biological Sciences  
Department of Biological Sciences and Institute  
of Biomedical Technology  
State University of New York  
Binghamton, New York

**John M. Baust, PhD**

CPSI Biotech  
Owego, New York

**Audrius J. Bredikis, MD, FACC**

Cardiac Electrophysiology  
Holmes Regional Medical Center  
Melbourne, Florida  
Clinical Associate Professor of Medicine  
University of Central Florida

**Bryan Cannon, MD**

Department of Pediatrics  
Mayo Clinic  
Rochester, Minnesota

**Victoria Carr-Brendel, PhD**

Vice President, Research and Development  
Boston Scientific  
Electrophysiology  
San Jose, California



**Kevin Christensen, BA**

Mayo School of Health Sciences  
Mayo Clinic  
Rochester, Minnesota

**Roland G. Demaria, MD, PhD**

Department of Cardiovascular Surgery  
Arnaud de Villeneuve Hospital  
Centre Hospitalier Régional Universitaire  
Montpellier, France

**Marc Dubuc, MD**

Electrophysiology Service  
Montreal Heart Institute  
University of Montreal  
Montreal, Quebec, Canada

**Damir Erkapic, MD**

Department of Cardiology  
Kerckhoff-Klinik  
Bad Nauheim, Germany

**Frédéric Franceschi, MD**

Electrophysiology Service  
Montreal Heart Institute  
University of Montreal  
Montreal, Quebec, Canada

**Jean-Marc Frapier, MD, PhD**

Department of Cardiovascular Surgery  
Arnaud de Villeneuve Hospital  
Centre Hospitalier Régional Universitaire  
Montpellier, France

**Andrew A. Gage, MD**

Professor of Surgery Emeritus  
School of Medicine & Biomedical Sciences  
State University of New York at Buffalo  
Buffalo, New York

**Fiorenzo Gaita, MD**

Division of Cardiology  
Cardinal Massaia Hospital  
University of Turin  
Torino, Italy

**Roberto Gallotti, MD**

Division of Cardiac Surgery  
Istituto Clinico Humanitas  
Rozzano, Milano, Italy

**Joann Heberer, MS**

Director, Research and Development  
Boston Scientific, Inc.  
Electrophysiology  
San Jose, California

**Atsushi Ikeda, MD, PhD**

Research Associate, Heart Rhythm Institute,  
University of Oklahoma Health Sciences Center  
Oklahoma City, Oklahoma

**Warren M. Jackman, MD**

George Lynn Cross Research Professor Emeritus  
of Medicine  
Co-Founder and Senior Advisor of the Heart  
Rhythm Institute  
University of Oklahoma Health Sciences Center  
Oklahoma City, Oklahoma

**Luc Jordaens, MD, PhD**

Departments of Clinical Electrophysiology  
and Experimental Cardiology  
Erasmus MC  
Rotterdam, The Netherlands

**Abdallah Kamouh, MD**

Case Western Reserve University  
University Hospitals of Cleveland  
Cleveland, Ohio

**Paul Khairy, MD, PhD**

Electrophysiology Service  
Montreal Heart Institute  
University of Montreal  
Montreal, Quebec, Canada

**Geert P. Kimman, MD, PhD**

Departments of Clinical Electrophysiology  
and Experimental Cardiology  
Erasmus MC  
Rotterdam, The Netherlands

**Paul Knops, Ing B**

Departments of Clinical Electrophysiology  
and Experimental Cardiology  
Erasmus MC  
Rotterdam, The Netherlands

**Malte Kuniss, MD**

Department of Cardiology  
Kerckhoff-Klinik  
Bad Nauheim, Germany

**Nirusha Lachman, PhD**

Department of Anatomy  
Mayo Clinic  
Rochester, Minnesota

**Dorothy J. Ladewig, BS**

Division of Cardiovascular Diseases  
Department of Internal Medicine  
Mayo Clinic  
Rochester, Minnesota

**Jean-Pierre Lalonde, BS**

Bachelor of Mechanical Engineering  
Medtronic CryoCath LP  
Kirkland, Quebec, Canada

**Peter J. Littrup, MD**

Karmanos Cancer Institute  
Detroit, Michigan

**Daniel L. Lustgarten, MD, PhD**

Associate Professor  
The University of Vermont School of Medicine  
Department of Medicine  
Fletcher Allen Health Care  
Burlington, Vermont

**Guillaume Maxant, MD**

Department of Cardiovascular Surgery  
Arnaud de Villeneuve Hospital  
Centre Hospitalier Régional Universitaire  
Montpellier, France

**Jennifer A. Mears, BS**

Division of Cardiovascular Diseases  
Department of Internal Medicine  
Mayo Clinic  
Rochester, Minnesota

**Teresa Mihalik, BS, MS**

Bachelor of Mechanical Engineering, Masters  
of Engineering  
Medtronic CryoCath LP  
Kirkland, Quebec, Canada

**Antonio Montefusco, MD**

Division of Cardiology  
Cardinal Massaia Hospital  
University of Turin  
Torino, Italy

**Annibale S. Montenero, MD, FESC,  
FHRS, FAHA**

Chairman, Cardiology Department and Arrhythmia  
Center  
MultiMedica General Hospital  
Milan, Italy

**Mirdavron M. Mukaddirov, MD, PhD**

V. Vakhidov Research Centre of Surgery  
Tashkent, Uzbekistan

**Hiroshi Nakagawa, MD, PhD**

Professor of Medicine  
Director of Clinical Catheter Ablation Program  
Director of Translational Electrophysiology  
Associate Director of Heart Rhythm Institute  
University of Oklahoma Health Sciences Center  
Oklahoma City, Oklahoma

**Thomas Neumann, MD**

Department of Cardiology  
Kerckhoff-Klinik  
Bad Nauheim, Germany

**Jacopo Perversi, MD**

Division of Cardiology  
Cardinal Massaia Hospital  
University of Turin  
Torino, Italy

**Jan V. Pitha, MD, PhD**

Professor of Pathology  
Department of Pathology  
Veterans Administration Medical Center  
University of Oklahoma Health Sciences Center  
Oklahoma City, Oklahoma

**Heinz F. Pitschner, MD**

Deputy Director, Department of Cardiology  
Head, Department of Electrophysiology  
Kerckhoff-Klinik  
Bad Nauheim, Germany

**John Roshan, MD**

Division of Cardiovascular Diseases  
Christian Medical College  
Vellore, India

**Philippe Rouviere, MD**

Department of Cardiovascular Surgery  
Arnaud de Villeneuve Hospital  
Centre Hospitalier Régional Universitaire  
Montpellier, France

**Bruno Schwagten, MD**

Departments of Clinical Electrophysiology  
and Experimental Cardiology  
Erasmus MC  
Rotterdam, The Netherlands

**Tushar Sharma, MD**

Research Fellow, Heart Rhythm Institute,  
University of Oklahoma Health Sciences Center  
Oklahoma City, Oklahoma

**Jeffrey Silver, BA**

Medtronic CryoCath LP  
Kirkland, Quebec, Canada

**Kristi K. Snyder, PhD**

CPSI Biotech  
Owego, New York

**Chung-Wah Siu, MBBS**

Cardiology Division  
Department of Medicine  
The University of Hong Kong  
Queen Mary Hospital  
Hong Kong, China

**Hung-Fat Tse, MBBS, MD, PhD**

Cardiology Division  
Department of Medicine  
The University of Hong Kong  
Queen Mary Hospital  
Hong Kong, China

**Heleen M. M. van Beusekom, PhD**

Departments of Clinical Electrophysiology  
and Experimental Cardiology  
Erasmus MC  
Rotterdam, The Netherlands

**Elza van Deel, BSc**

Departments of Clinical Electrophysiology  
and Experimental Cardiology  
Erasmus MC  
Rotterdam, The Netherlands

**Wim van der Giessen, MD, PhD**

Departments of Clinical Electrophysiology  
and Experimental Cardiology  
Erasmus MC  
Rotterdam, The Netherlands

**Zhong Wang, MD**

Loyola University  
Chicago, Illinois

**David J. Wilber, MD, FAHA, FACC**

George M. Eisenberg Professor of Cardiovascular  
Sciences  
Director, Cardiovascular Institute  
Director, Division of Cardiology  
Medical Director, Electrophysiology Laboratory  
Loyola University Medical Center  
Maywood, Illinois

**Dan Wittenberger, BS**

Bachelor of Engineering  
Medtronic CryoCath LP  
Kirkland, Quebec, Canada





# Preface

The purpose of this text is to provide a comprehensive resource on cryoablation, including tissue effects, cryotechnology, and clinical applications.

Cryoablation has unique properties that are very different from other energy sources used for ablation of cardiac or other tissues. Because freezing has minimal effects on elastic collagen structures and has less-detrimental effects on local microcirculation, tissue “architecture” remains preserved to some extent and tissues also heal better. This decreases the risk for stricture formation, stenosis, and ulceration of ablated areas. These features of cryoablation are especially useful when lesions have to be placed in close proximity to important cardiac structures such as the His bundle, pulmonary veins, coronary arteries, esophagus, and phrenic nerve.

Despite all these attractive features, cryoablation is underutilized because the more complex catheter design decreases maneuverability and the cryocatheters that are currently commercially available operate at  $-80^{\circ}\text{C}$ , requiring longer application times.

Recently developed balloon-based cryotechnology, as well as the availability of “colder” technologies utilizing critical nitrogen, super-critical nitrogen ( $-180^{\circ}\text{C}$  to  $-196^{\circ}\text{C}$ ), and other agents, has the potential to overcome these limitations and increase utilization of cryoablation in electrophysiology laboratories. Further development of these technologies will be extremely useful for ablation of ventricular tachycardia and for septal ablation in hypertrophic cardiomyopathy.

Audrius J. Bredikis, MD, FACC  
David J. Wilber, MD, FAHA, FACC



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Section I

# **Fundamental Aspects of Cryoablation**







## Chapter 1

# History of Cardiac Cryosurgery and Cryoablation

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*Daniel L. Lustgarten, MD, PhD*

### KEY POINTS

- The concept of using cryoenergy to treat medical illness has been present since the dawn of recorded history.
  - Specific application of cryoenergy as a therapeutic modality depended on practical application of the Joule-Thomson effect.
  - Invasive application of cryotherapy in the heart lagged behind other disciplines because of the relatively recent appreciation of the role of ablating abnormal cardiac substrate to treat arrhythmias.
  - The history of cardiac cryotherapy reflects progressively less invasive and more specialized delivery systems.
-

Robert Slama and colleagues<sup>1</sup> in Paris reported on surgical ablation of the atrioventricular (AV) node in patients with drug-refractory atrial arrhythmias in 1967. Subsequently, Will Sealy<sup>2</sup> at Duke University described successful surgical interruption of a right lateral accessory pathway in a 32-year-old fisherman with Wolff-Parkinson-White syndrome. These publications represent the birth of interventional electrophysiology, providing proof of concept that arrhythmias could be cured or alleviated by destroying cardiac tissue requisite for their clinical manifestation. Soon surgeons, in collaboration with their electrophysiologist colleagues, extended these findings to the management of supraventricular arrhythmias and ventricular tachyarrhythmias. However, incisional approaches to treating arrhythmias required open-heart surgery, typically requiring cardiopulmonary bypass, associated with significant morbidity and mortality.<sup>2,3</sup> The use of surgical electrocautery, formalin injection, and tissue ligation were all associated with disruption of the normal tricuspid valvular apparatus, ventriculoseptal defects, and injury to the aortic sinuses.<sup>4</sup> Therefore, from the inception of arrhythmia surgery, the search for less invasive approaches and ablative modalities was ongoing.

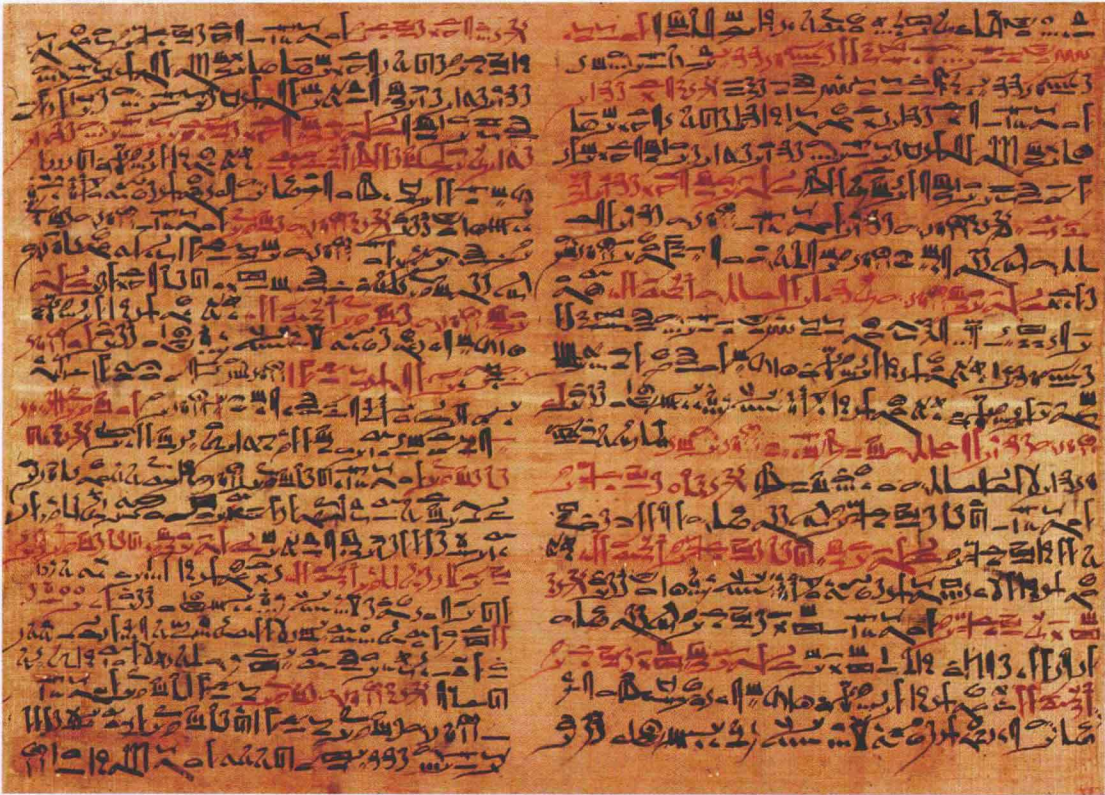
Although cryoablative approaches were studied during these early years of interventional electrophysiology, radiofrequency became the dominant ablative energy source because of the relative simplicity of radiofrequency-based catheter systems and the discrete targets of arrhythmias being treated. However, the extensive lesion sets associated with atrial fibrillation ablation and substrate-based ablation for scar-mediated ventricular tachycardia (VT) make cryoablation an attractive alternative to heat-based modalities, in that cryoablation may be less likely to cause collateral damage. The feasibility of using cryoablation for this purpose entered the practical realm with the realization that the Joule-Thomson effect could be applied to intravascular catheters to deliver ablative levels of cold energy. This chapter reviews the history of this technologic leap with a view toward providing perspective on the present and future roles of cryoablation in arrhythmia management, which is the topic of the ensuing chapters.

## JOULE-THOMSON EFFECT

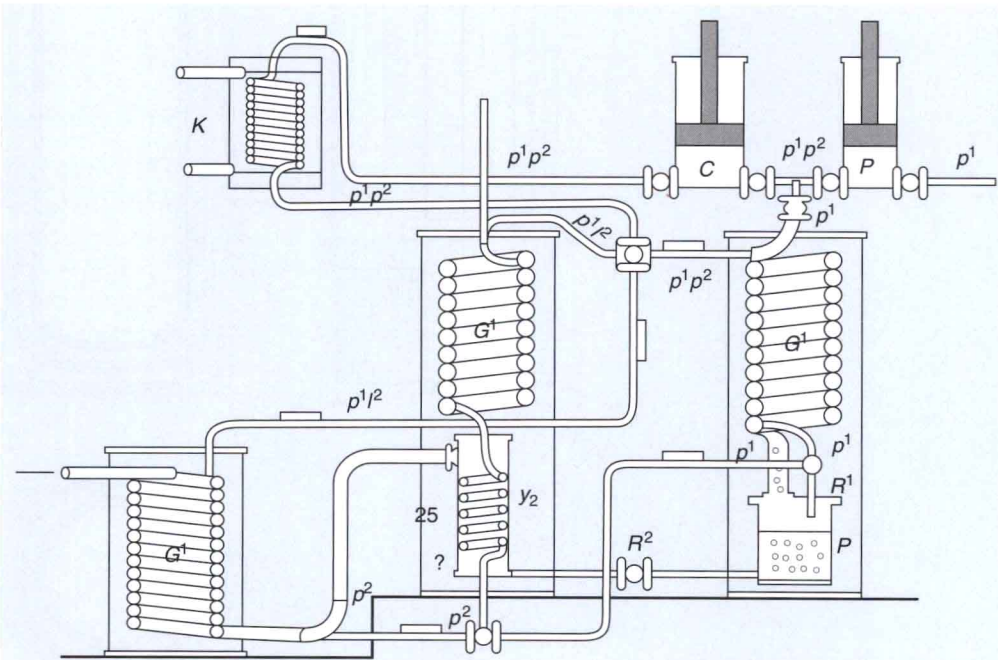
Intravenous catheter-delivered cryoenergy—that is, cold enough to destroy cardiac tissue—was made possible by the practical application of the Joule-Thomson effect, and it represents a fascinating chapter in the history of medicine. The alleviating effects of cryotherapy were appreciated at the dawn of medical history, with reference to the use of cold to treat battlefield injuries present in the oldest known medical document, the Edwin Smith papyrus (Figure 1–1). Writings attributed to Imhotep and his pupils (2600 BC) were discovered on papyrus that was purchased in Luxor in 1862 by Egyptologist Edwin Smith.<sup>5</sup> These writings specify the ingredients of cold compresses (figs, honey, and grease) to be applied to battle injuries. However, the notion that cold energy could be used to destroy diseased tissue required the ability to harness and deliver cryoenergy at extremes of cold far exceeding those of compresses, a notion that would take nearly four millennia to manifest.

During the Industrial Revolution, two major innovations occurred that ultimately set the stage for the modern conception of cryotherapy and ultimately cryocatheter-mediated mapping and ablation. One was the discovery and production of powerful refrigerants. In 1853, James Prescott Joule and Henry Thomson reported that the temperature of a real gas would vary depending on the initial temperature and pressure with expansion at constant enthalpy. Allowing compressed gas to rapidly expand below the gas's inversion temperature resulted in dramatic cooling caused by loss of kinetic energy. Carl Paul Gottfried von Linde (1842–1934) capitalized on the Joule-Thomson effect to make the first commercially viable refrigerant.<sup>6</sup> Von Linde developed vapor-compression refrigeration machines, the first iteration of which used dimethyl ether as the refrigerant. His apparatus for the liquefaction of air combined the cooling effect achieved by allowing a compressed gas to expand with a countercurrent heat exchange technique that used the cold air produced by expansion to chill ambient air entering the apparatus (Figure 1–2). This gradually cooled the apparatus and air within it to the point of liquefaction.





■ Figure 1-1 Part of the Edwin Smith papyrus containing teachings attributed to Imhotep.

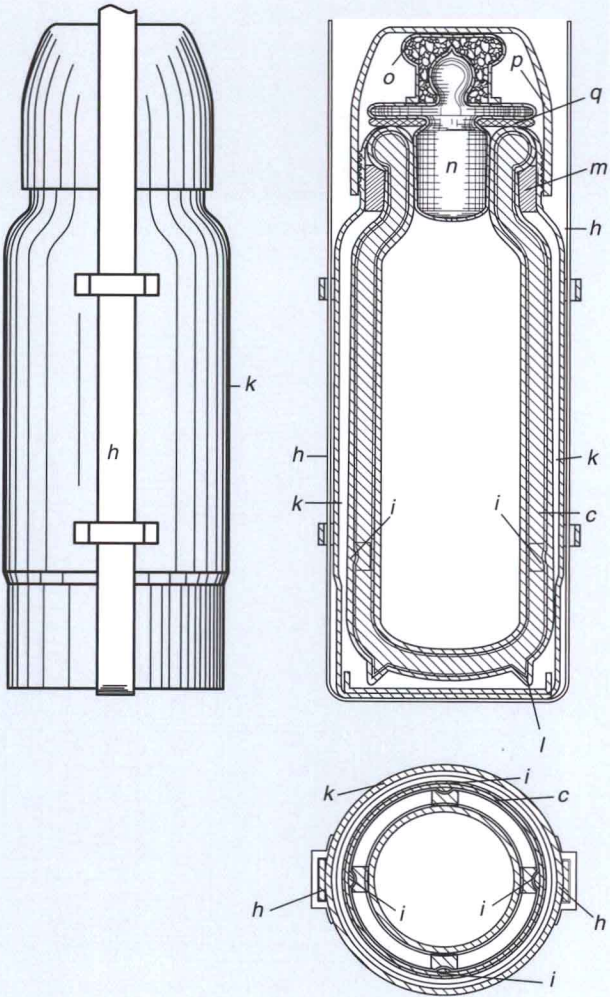


■ Figure 1-2 Von Linde's original patent design.

A system was needed that would allow the storage and transfer of frozen liquefied gases, for refrigerants to be applied medically. This second major innovation came in the form of the vacuum flask invented in 1892 by the Scottish physicist and chemist James Dewar (1842–1923).<sup>7</sup> The thermos consists of a vessel within a vessel separated by a vacuum, the latter preventing heat transfer by conduction or convection, with radiant heat loss being minimized with the use of silver-lined glass. The Dewar flask enabled storage, transfer, and ready access to fluids at temperatures less than  $-180^{\circ}\text{C}$ , setting the stage for the medical application of cryogenics. An example of an early patented version of a Dewar flask submitted by Reinhold Burger to the U.S.

Patent Office in 1907 is shown in Figure 1–3. With these innovations in place, it was now possible for medical scientists to test the effects of extreme cold on biological tissues.

In the first half of the 20th century, liquid refrigerants were used to destroy tumors and skin lesions by surface application. Refrigerants were applied at temperatures less than  $-70^{\circ}\text{C}$  to achieve cell death. In 1961, a handheld cryoprobe that would permit surgical application of cryoenergy was invented through collaboration between the renowned New York City neurosurgeon Irving Cooper, and Arnold Lee, an engineer from the Linde division of Union Carbide Corporation.<sup>8</sup> The handheld cryoprobe design is, in essence, a marriage between the concept of



■ Figure 1–3 An early Dewar flask patent.