Anesthesia History Association

Medicine and the Civil War in Middle Tennessee

May 3-5, 2007
Scarritt-Bennett Conference Center
Nashville, Tennessee

SILVER ANNIVERSARY

25TH ANNUAL MEETING

Jointly sponsored by
the Vanderbilt School of Medicine Department of Anesthesiology
and the Anesthesia History Association
in conjunction with
the Tennessee Society of Anesthesiologists,
Tennessee Association of Nurse Anesthetists, and
the Middle Tennessee School of Nurse Anesthesia

Statement of Educational Need
The AHA is devoted to the proposition that accurate portrayal and dissemination of facts concerning triumphs and mistakes in the history of Medicine, in this case with emphasis on the practice of Anesthesiology, will prepare the recipients of this knowledge better to avoid pitfalls and pursue successful enterprises demonstrated by their predecessors. The habitual focus of AHA reports has been great individuals in the history of anesthesia and the accomplishments of these contributors. Reports frequently emphasize the practical problems of introducing new techniques and practices. Improvement in research techniques, application of new concepts, and lessons in the rewards of perseverance and enthusiasm will serve as inspiration and path guidance for currently active practitioners and academics.

Target Audience
This conference is designed for members of the Anesthesia History Association, historians, nurse anesthetists and physicians from other fields of practice.

Objectives
Upon completion of this program, participants should be able to:

- ***Identify historical incidents where the Profession of Anesthesiology has contributed to the improvement of the general practice of Medicine throughout the world, and derive implications for the present and future***

- ***Describe and discuss problems of medical logistics and medical practice in times of civil upheaval, war, or emergency, and appreciate lessons applicable to the present and future***

- ***Describe and discuss the knowledge and awareness of registrants of current scholarly activity applied to the history of Anesthesiology practice***

- ***Develop new or expanded teaching programs regarding Anesthesia History in their own institutions and medical practice communities***

Accreditation
This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of Vanderbilt School of Medicine Department of Anesthesiology and the Anesthesia History Association. Vanderbilt School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

Designation of Credit
Vanderbilt School of Medicine designates this educational activity for a maximum of 10.75 AMA PRA Category 1 Credit(s)™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Americans with Disabilities Act
It is the policy of Vanderbilt School of Medicine and the Trigeminal Neuralgia Association not to discriminate against any person on the basis of disabilities. If you feel you need services or auxiliary aids mentioned in this act in order to fully participate in this continuing education activity, please speak to someone at the registration desk for assistance.

Commercial Support
This educational activity received no commercial support.

Faculty

J. Antonio Aldrete, MD, MS	***Professor of Anesthesiology Emeritus***	***University of Alabama in Birmingham***
James Atkinson, MD, PhD	***Professor of Pathology***	***Vanderbilt School of Medicine***
Douglas Bacon, MD, MA	***Professor of Anesthesiology and History of Medicine***	***Mayo Clinic College of Medicine***
Selma Calmes, MD	***Clinical Professor of Anesthesiology***	***UCLA School of Medicine***
Thomas Cartwright	***CEO***	***Carter House Foundation***
Doris Cope, MD	***Professor of Anesthesiology and Vice Chairman of Pain Medicine***	***University of Pittsburgh School of Medicine***
David Currey	***Executive Director***	***Travelers Rest Plantation and Museum***
Ray Defalque, MD	***Professor of Anesthesia***	***University of Alabama at Birmingham***
Mary DeVasher, CRNA, MEd, MS, APN, ABD	***Vice President and Dean***	***Middle Tennessee School of Anesthesia***
Barrie Fairley	***Emeritus Professor***	***Stanford University***
John E. Forestner, MD	***Professor of Anesthesiology and Pain Management***	***University of Texas Southwestern Medical School***
Frank Freemon, MD, PhD	***Professor of Neurology Emeritus***	***Vanderbilt School of Medicine***
F. Andrew Gaffney, MD	***Associate Dean for Clinical Affairs***	***Vanderbilt School of Medicine***
Mark Haffey, CRNA, MSN, APN	***Immediate Past President***	***Tennessee Society of Nurse Anesthetists***
William Hammonds, MD, MPH	***Professor of Anesthesiology and Perioperative Medicine***	***Medical College of Georgia***
Allen Hayman, MD	***Fellow in Anesthesiology***	***Children's Hospital of Boston***
Michael Higgins, MD, MPH	***Professor and Chair of Anesthesiology***	***Vanderbilt School of Medicine***
Aimee Kakascik, DO	***Anesthesia Resident***	***University of Mississippi Medical Center***
Joseph Kreutz, MD	***Associate Professor of Anesthesiology***	***University of Vermont College of Medicine***
Mark. Mandabach, MD	***Assistant Professor of Anesthesiology***	***University of Alabama at Birmingham***
Janey McGee, MD	***Anesthesia Resident***	***University of North Carolina***
William McNiece, MD	***Associate Professor of Anesthesia***	***Indiana University School of Medicine***
S. Breanndan Moore, MD, FRCPI	***Professor of Laboratory Medicine***	***Mayo Clinic School of Medicine***

Nathaniel Nonoy, MD	***Clinical Fellow in Anaesthesia***	***Harvard Medical School***
Gregory Nuttall, MD	***Professor of Anesthesiology***	***Mayo Clinic College of Medicine***
Rafael Ortega, MD	***Associate Professor***	***Boston University Medical Center***
Jennifer Rabbits, MD	***Anesthesia Resident***	***Mayo Clinic College of Medicine***
Raymond Roy, MD, PhD	***Professor and Chair of Anesthesiology***	***Wake Forest University School of Medicine***
Mark Schroeder, MD	***Associate Professor of Anesthesiology***	***University of Wisconsin at Madison***
Alan Sessler, MD	***Professor of Anesthesiology Emeritus***	***Mayo Clinic College of Medicine***
John Shields, CRNA, MS	***Certified Registered Nurse Anesthetist***	***Vanderbilt University Medical Center***
Bradley Smith, MD	***Professor of Anesthesiology Emeritus***	***Vanderbilt School of Medicine***
Robert Strickland, MD	***Associate Professor of Anesthesiology***	***Wake Forest University School of Medicine***
Dina Velocci, CRNA, MS	***Certified Registered Nurse Anesthetist***	***Vanderbilt University Medical Center***
Dr. Adolfo Héctor Venturini	***Associate Honorary Investigator of History of the Medicine***	***University of Buenos Aires***
David Waisel, MD	***Assistant Professor of Anaesthesia***	***Harvard Medical School***
Dirk Wales	***CEO***	***Rainbow Productions***
David Wilkinson, MBBS, FRCA	***Consultant Anaesthetist***	***St. Bartholomew's Hospital***
Albert Woo, MD	***Resident in Anesthesiology***	***Boston University Medical Center***
A.J. Wright III, MLS	***Associate Professor***	***University of Alabama at Birmingham***
Jeffrey Zavaleta, MD	***Anesthesia Resident***	***University of Texas Southwestern Medical Center***
Gerald Zeitlin, MD, FRCA	***Instructor in Anesthesia, Retired***	***Harvard University School of Medicine***

Faculty Disclosure

It is the policy of Vanderbilt School of Medicine and the Trigeminal Neuralgia Association that participants in CME activities be made aware of any affiliation or financial interest that may affect the speaker's presentation(s). Each speaker has completed and signed a conflict of interest statement. The faculty members' relationships appear below.

The following planners and speakers indicated that they had no financial relationships to disclose:

J. Antonio Aldrete, MD, MS
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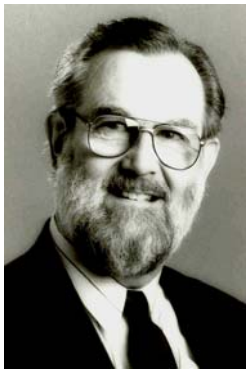
Albert Woo, MD
Amos J. Wright III, MLS
Jeffrey Zavaleta, MD
Gerald Zeitlin, MD, FRCA

The following speakers disclosed the following financial relationships:

Gregory Nuttall, MD	***Research Grant: Stryker, Bayer, Medafor***
Mark Schroeder, MD	***Consultant: Cardinal Health***
Bradley Smith, MD	***Consultant: Anesthesia Business Solutions***
	Speaker fee: Abbott Pharmaceuticals, Anesthesia Business Solutions, Baxter Pharmaceuticals
	Shareholder: Anesthesia Business Solution

Welcome to the Silver Anniversary Meeting of the Anesthesia History Association!



Douglas R. Bacon, M.D., M.S.
President
Anesthesia History Association

Bradley E. Smith, M.D.
Program Director
Silver Anniversary Annual Meeting

In 1982 and 1983 Dr. Selma Calmes, Dr. Rod Calverly, and approximately 45 others initiated the Anesthesia History Association. This effort has stimulated a continuing interest and growing appreciation for the accomplishments, toil, and legacy of those visionary pioneers, both distant and more recent, who have done so much to give the world the magnificent gift of pain relief, and who have shaped the modern practice of medicine in ways that would have been impossible without them.

In these 25 "silver" years members of our Association have published countless reports which enrich the medical and lay literature, have helped to preserve priceless artifacts precious to the understanding of medical development, and have nurtured our own, now highly respected, peer reviewed and recognized quarterly publication *Bulletin of Anesthesia History*.

Our Annual Meetings have become an enjoyable and productive opportunity for sharing our interests and delighting in the new discoveries of our colleagues. In addition, we typically exploit the historic resources of the locale in which we meet to broaden or general historic awareness.

This year, following that tradition, we plan to exploit the rich resources of Nashville, and our cosponsor host Vanderbilt University. Our speaker at the Annual Dinner on Thursday evening May 3rd will be the first physician into space, Dr Andrew Gaffney. In addition to his space medicine pursuits, Dr. Gaffney is a noted cardiologist, an expert on medical quality improvement, and a key leader in the Vanderbilt Medical Center administrative team.

Because Nashville has a strong Civil War heritage, there are many opportunities in and near Nashville to learn about Civil War medical practices and problems. We have obtained four highly knowledgeable experts on Civil War history and on medical problems of the period to share their knowledge of this period with us.

In addition, the "social program" will continue this theme, visiting battle sites and hospital sites of both the Battle of Franklin, Tennessee, and the Battle of Nashville, Tennessee. These battles mark the true "last gasp" of the Confederate States of America in that tragic conflict.

We have also organized an equally knowledgeable panel of experts who will explore the neglected utilization of visual materials in studying the history of anesthesia and pain relief.

The panel will be led by our unique fellow member of the AHA, Mr. Dirk Wales, who not only has been responsible for 80 productions related to the field of anesthesia, but was the first non-physician to be invited to be a member of the AHA Council.

Our "Free Paper" contributions this year are, as usual exciting and varied. From discussions of anesthesia in the Inca civilization, to the contributions of our friend Dr. Burnell Brown, each is more interesting than the next. Again this year we have excellent participation from Certified Registered Nurse Anesthetists.

Finally, we will be treated to hearing and seeing presentations of the three finalists in the C. Ronald Stephen Essay Award contest. The moderator will be the perennial organizer and chairperson of the Contest Committee, Dr. William D. Hammonds, who is now also the President of the Board of Directors of the Wood Library-Museum. In determining the winner, the panel of judges will consider presentation skills along with composition, accuracy of historic preparation, and significance of the subject matter

This year's program has been organized as an experiment to learn if a slightly shorter "away from home" time frame can still provide adequate time for the fellowship, learning opportunities, and relaxation that we have all come to expect from AHA meetings. Thus the total travel plus meeting experience can consume as little as three days. Your "feedback" will tell us if this experiment should be "deep sixed" or carried forward!

We speak for our colleague officers and the members of the AHA Council in thanking you for your attendance. Have a great time! Have a great learning experience!

President: Douglas R. Bacon, M.D., M.A.
Vice President: William D. Owens, M.D.
Secretary: Mark G. Mandabach, M.D.
Treasurer: David B. Waisel, M.D.
Councilor: N. Martin Giesecke, M.D.
Councilor: Mark E. Schroeder, M.D.
Councilor: Bradley E. Smith, M.D.
Councilor: Sandra L. Kopp, M.D.

A Brief History of the Anesthesia History Association

The First International Symposium on Modern Anesthesia History was held in Rotterdam in 1982. At that meeting, several members of the American Society of Anesthesiologists (ASA) discussed the possible organization of an anesthesia history society in the U.S. Following up on this, a group of 47 met on October 25, 1982, at the Annual Meeting of the American Society of Anesthesiologists (ASA). The meeting was chaired by Dr. Garth Huston, then Chairman of the Board of Trustees of the Wood Library-Museum of Anesthesiology (WLM). Various names for the new group were discussed. By January 1983, the name "Anesthesia History Association" (AHA) was agreed upon. Dr. Selma Calmes and Dr. Roderick Calverly are credited as co-founders of the AHA.

The "Inaugural Meeting" of the AHA was held on October 9, 1983. This, like the organizational meeting and all subsequent annual meetings of the AHA, was part of the program of the ASA Annual Meeting. Having begun under the aegis of the ASA, there was at first some confusion regarding the status of the AHA. However, the AHA soon established its own autonomy, and in October 2006 formally became a "501(3)c" corporation registered in Illinois.

The first issue of the *Anesthesia History Association Newsletter* was published in December 1982. It has remained in continuous publication, with an average of four issues per year (see the following list). In 1995, the WLM became co-publisher of the newsletter, a relationship that continues to the present. With the July 1995 issue, the name of the newsletter was changed to the *Bulletin of Anesthesia History*. In 1996, a cumulative index of the *AHA Newsletter* was published. Creation of the index was a joint project of the AHA, WLM, and ASA.

The AHA was a principal sponsor of the Third International Symposium on the History of Anesthesia. The meeting was held in Atlanta, Georgia, March 27-31, 1992. The theme of the symposium was the Crawford W. Long Sesquicentennial (the 150th anniversary of Dr. Long's use of ether vapor to produce surgical anesthesia). The AHA also co-sponsored the Bicentenary Meeting to mark Davy's Researches into Nitrous Oxide, held in Bristol, England, May 13-15, 1999.

Annual meetings are held in various parts of the United States, and a brief interim meeting and dinner is held annually during the ASA Annual Meeting. Annual meeting programs include plenary sessions devoted to targeted subject relative to anesthesia history or the teaching of history. "Free Papers" are devoted to historical events, trends, biography, etc related to medicine and to anesthesia. The most recent AHA meeting was a joint meeting with the History of Anaesthesia Society of the United Kingdom and was held at the Mayo Clinic College of Medicine in Rochester, Minnesota.

Membership averages 180 and attendance at the Annual Meetings varies from 30 to 75 registrants. The current President is Douglas R. Bacon, M.D., Professor of Anesthesiology and Medical History, Mayo Clinic College of Medicine, Rochester, Minnesota. The Immediate Past President is Doris K. Cope, M.D., Professor and Vice Chairman of Pain Medicine, Dept. of Anesthesiology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania.

A Very Brief History of Nashville

Nashville's history began more than 200 years ago. Long before the first guitar picker moved into town, the settlement of Nashborough-named after Revolutionary War hero Gen. Francis Nash-was being constructed as a fort on the west banks of the Cumberland River in 1779-80. Two groups of pioneer settlers, led by the founding fathers James Robertson and Colonel John Donelson, came by land and by water from Fort Patrick Henry in East Tennessee. James Robertson led a party of men on foot and horseback, arriving on Christmas Day 1779. John Donelson led a flotilla of approximately 30 flatboats, carrying the wives and children of the men who went with Robertson.

Traveling a thousand miles and surviving many hazards including Indian attacks, the Donelson party arrived on April 24, 1780,reuniting some 60 families. Col. Donelson's daughter Rachel would soon become the wife of Andrew Jackson, the nation's seventh president. Many things had changed within ten years of settlement. Nashborough underwent a name change and became Nashville. The first school was chartered-Davidson Academy, which remains operational today.Andrew Jackson arrived in town to serve as the public prosecutor. And Bob Renfroe opened the first tavern owned and operated by a freed African-Americans.

In 1796, Tennessee became the 16th state admitted to the Union. With the War of 1812, Tennessee earned its affectionate nickname of the "Volunteer State" by sending hundreds more soldiers to the war than was asked. In 1824 the music publishing industry took root with the publication of "Western Harmony", a book of hymns and instructions for singing. Andrew Jackson was elected the seventh president in 1828. He built his plantation, The Hermitage, for his beloved wife Rachel. The home and acreage remain today-one of the few presidential homes with a majority of the original furnishings on display.

Nashville was named the permanent capital of Tennessee in 1843, and one year later another Tennessean was elected president-James K.Polk. The year 1845 ushered in the construction of the state capitol building, designed by William Strickland, and the death of Andrew Jackson. Polk died in 1849, only a few years after Jackson's death, and was buried with his wife on the grounds of the State Capitol.

During the Civil War, African-AmericanNashvillians helped Union troops construct Fort Negley. The partially-restored fort which remains today overlooking downtown and open to the public. In a span of 25 years following the war, four colleges were founded including Vanderbilt University, Fisk University and Meharry Medical College. Nashville developed a third prominent nickname, the "Athens of the South."

The last decade of the 19th century proved to be an explosive one for many industries. The Ryman Auditorium was constructed originally as the Union Gospel Tabernacle, and today it's rated one of the top theaters in the country for performances. Joel Cheek developed the Maxwell House Coffee blend, still going strong 100 years later. The Tennessee Centennial Exposition was held in 1896 in Centennial Park and the Parthenon was constructed to honor the city's educational commitment as the "Athens of the South."

With the turn of the century came the city's first downtown skyscraper, the first African American owned bank-One Cent Savings Bank, the first movie theater and the first Model T Ford in Nashville.

The mid 1940s and early 1950s saw a new movement beginning in the music world. The Opry moved downtown to the Ryman and bestowed upon the Ryman its most affectionate nickname, "the Mother Church of Country Music."

Music Row, located on 16th and 17th Avenues South not far from downtown, began to take shape with the construction of recording studios and record labels. Castle Studio, Nashville's first recording studio, opened; Capitol Records became the first major company to locate its director of country music to Nashville; and the Country Music Association was founded. Soon the famous RCA Studio B opened it doors on Music Row and instantly became famous under the the management of Chet Atkins. Here the Nashville Sound was crafted and performers like Elvis, the Everly Brothers and Dolly Parton recorded their chart-topping hits. The Opry said good-bye to the Ryman in 1974 when it moved it its new home on the Gaylord Opryland complex.

Some Statistics about Nashville

Elevation: 550 feet at the lowest point; 1,100 feet at the highest point of the rim around the Nashville basin.

Nashville is the nation's city with the second largest land mass, totaling 533 square miles.

Metropolitan Statistical Area (MSA) is comprised of 10 counties: Cheatham, Davidson, Dickson, Maury, Montgomery, Robertson, Rutherford, Sumner, Williamson and Wilson.

Population: Nashville = 595,805; MSA = 1,541,659

Average Nashville Household Income: $55,598

Nashville Unemployment Rate: 3.9%

Industry breakdown:

- **Trade, Transportation & Utilities = 20.4%**
- **Education & Health Services = 13.7%**
- **Government = 13.1%**
- **Professional & Business Services = 12.1%**
- **Manufacturing = 11.5%**
- **Leisure & Hospitality = 10.4%**
- **Financial Activities = 6.5%**
- **Information = 2.9%**

Cost of Living: Nashville consistently ranks among the lowest for cost-of-living in comparable cities across the nation ranking more cost-efficient than Atlanta, Austin, Tampa and Richmond. The overall cost of living is 94.7% of the national average. All components (groceries, housing, utilities, etc.) of cost-of-living are typically below the national average.

Hospitality Industry*: More than 50,000 jobs are directly related to the hospitality industry.

(Condensed and edited from information supplied by the Nashville Convention and Visitor's Bureau-2007)

Introduction to Vanderbilt University Medical Center

Vanderbilt University Medical Center has built a strong reputation as a leader in medical education, research and patient care throughout the Southeast and the nation over the course of its 127-year history. The current Medical School class of 2007, selected from a pool of 3,741 applicants, represents 32 states and holds undergraduate degrees from 58 different colleges and universities. The School of Medicine placed 15th among 125 medical schools in US News & World Report's recent survey of "America's Best Graduate Schools."

Biomedical research at Vanderbilt has long been recognized for its contributions to the advancement of medicine. The School of Medicine claims two Nobel Laureates, Earl Sutherland, Jr. in 1971 for his discovery of the metabolic regulating compound "cyclic AMP," and Stanley Cohen in 1986 for his discovery with a colleague of epidermal growth factor. The Medical School's reputation for outstanding research is reflected in the amount of federal and private support it receives. Because of the creativity of the faculty, the School of Medicine consistently ranks in the top 20 out of 121 medical schools in the receipt of funding from the National Institute of Health. The Medical School has recently displayed a compound annual growth rate of 22.5% in NIH grant awards, the fastest growing program in the country. Support for competitive research grants from all external sources now exceeds $300 million annually.

Annually the Vanderbilt Clinic serves over 698,900 patient visits, and more than 33,800 patients are admitted to the Vanderbilt Hospital. (A substantial number of patients come from outside Tennessee.) Vanderbilt University Medical Center is ranked among the foremost programs in the nation by *U.S. News & World Report*'s "America's Best Hospitals" in nine of 12 major services ranked.

The Meharry-Vanderbilt Alliance was established to foster a diverse educational and scientific environment; this partnership has focused on clinical science training, academic support, biomedical research and training, health services initiatives and an institute for community health. Students from both campuses share cross cultural experiences through clerkships, residencies and fellowships benefiting student curricula and enhancing the academic support infrastructure of both institutions. Collaborative efforts in research and training have resulted in an aggregate of over $100 million in grants. This joint effort has created community health initiatives which are benefiting the underserved community and represents an interdisciplinary academic unit designed to create innovative paths for the provision of evidence-based health services to disadvantaged citizens.

Vanderbilt University and Vanderbilt Medical Center is the largest private employer in middle Tennessee and second largest in the state. Vanderbilt employs more than 18,500 and has an annual regional economic impact of approximately $4 billion, of which the Medical Center's impact totals over 2.7 billion. Vanderbilt provides more than $119 million each year in uncompensated and charity care to members of the community unable to pay for their own care. It is the largest provider in the region under the state's Medicaid program for the poor and uninsured.

Vanderbilt employees consistently lead all private universities in the country in support of the United Way and Combined Charities. The Medical Center leads one of the country's largest fundraising efforts for the American Heart Association. Annually Vanderbilt Medical Center typically receives more than $60 million in philanthropic gifts.

A Brief History of Vanderbilt University School of Medicine

The first diplomas issued by Vanderbilt University were to sixty-one Doctors of Medicine in February of 1875, because of shared classes and facilities with the Medical School of the University of Nashville. Thus, Vanderbilt offered a fully-organized and functioning medical school even before the traditional undergraduate campus was ready for classes in October of that year.

The arrangement continued for twenty more years, until Vanderbilt Medical School was reorganized. In the early days, the University of Nashville School of Medicine was owned and operated as a private property of the practicing physicians who composed the faculty and received the fees paid by students – a system typical of medical education in the United States at the time. After reorganization under the Vanderbilt Board in 1895, admission requirements were raised, the course was lengthened, and the system of instruction was changed to include laboratory work in the basic sciences.

The famous report of Abraham Flexner, published by the Carnegie Foundation in 1910 and afterward credited with revolutionizing medical education in America, singled out Vanderbilt as "the institution to which the responsibility for medical education in Tennessee should just now be left." Vanderbilt became one of only five schools in the "Old South" which were singled out by the Andrew Carnegie Foundation and from the (Rockefeller-financed) General Education Board. This continuing support enabled Vanderbilt to carry out the recommendations of the Flexner Report and the entire faculty and curriculum underwent an inspiring rebirth.

The reorganized school drew upon the best-trained scientists and teachers in the nation for its faculty. The full benefits of reorganization were realized in 1925 when the school moved from the old South Campus across town to the "new medical school building" (now incorporated into "Medical Center North and still very much in use). The school's new quarters were widely acclaimed as "the best arranged combination school and hospital to be found in the United States."

Anesthesia History Association
2007 Annual Meeting

May 3-5, 2007

Scarritt/Bennett Center
1008 19th Avenue South
Nashville, TN 37212-2126

Schedule

Thursday, May 3, 2007

1:00 PM – 6:00 PM	Meeting Registration *Main Foyer*
1:30 PM – 5:20 PM	Battle of Nashville Historical Sites Tour (optional)
5:30 PM – 6:30 PM	*Fondren 22* "An Introduction to Anesthesia History" **Bradley E. Smith, M.D.** Professor of Anesthesiology Emeritus Adjunct Professor of Clinical Anesthesiology Vanderbilt University Medical Center
7:15 PM – 9:15 PM	*International Room* AHA Banquet Keynote Speaker: **Professor F. Andrew Gaffney** Associate Dean for Clinical Affairs Vanderbilt University Medical Center

Friday, May 4, 2007

7:00 AM – 7:30 AM	*Susie Gray Dining Hall* Breakfast
7:30 AM – 7:45 AM	*Harambee Auditorium* Welcome and Announcements **Michael S. Higgins, M.D., M.P.H.** Chair, Department of Anesthesiology Professor of Anesthesiology, Surgery and Biomedical Informatics Executive Medical Director, Perioperative Services Vanderbilt University Medical Center
7:45 AM – 8:00 AM	**Douglas R. Bacon, M.D., M.A.** President, Anesthesia History Association Professor of Anesthesiology and History of Medicine Mayo Clinic College of Medicine
8:00 AM – 8:30 AM	Silver Anniversary Celebration Lecture "History of the Anesthesia History Association" **Selma H. Calmes, M.D.** Clinical Professor of Anesthesiology, UCLA School of Medicine Co-Founder and Past President

	Anesthesia History Association
8:30 AM – 9:30 AM	Panel: "Medicine, Anesthesia, and the Civil War in Middle Tennessee" Moderator: **Bradley E Smith, M.D.**
	"Civil War Medicine in the Union Armies" **Frank R. Freemon, M.D., Ph.D.** Professor of Neurology, Emeritus Vanderbilt University Medical Center Author, "Gangrene and Glory" Associated University Presses, London, Madison, Teaneck
	"Civil War Medicine in the Armies of the Confederacy" **James R. Atkinson, M.D., Ph.D.** Professor of Pathology Vanderbilt University Medical Center Board Member, Battle of Nashville Preservation Society
9:30 AM – 9:45 AM	Break: *Outside Harambee Auditorium*
9:30 AM – 9:45 AM	Viewing of Poster Presentations: *Outside Harambee Auditorium*
9:45 AM – 11:00 AM	Panel: "Medicine, Anesthesia, and the Civil War in Middle Tennessee" *(continued)*
	"The Tragedy of the Battle of Franklin, November 30, 1864" **Thomas Y. Cartwright** CEO, Carter House Foundation
	"The Last Decisive Battle of the Civil War: Nashville, December 15-16, 1864" **David D. Currey** Executive Director, Travelers Rest Plantation and Museum
11:00 AM – 12:10 PM	*Harambee Auditorium* 2007 C. Ronald Stephen Essay Contest Finalist Presentations
	Moderator: **William D. Hammonds, M.D., M.P.H.** Chair, C. Ronald Stephen Award Committee Professor, Anesthesiology and Perioperative Medicine Medical College of Georgia
	"Neonatal Pain: To Treat or Not to Treat?" **Janey P. McGee, M.D.** University of North Carolina School of Medicine
	"Halothane Hepatitis Solved: The Role of Burnell R. Brown MD, PhD" **Jeffrey R. Zavaleta, M.D.** University of Texas Southwestern Medical Center (Currently: University of Washington)
	"Opioids: A Social History" **Aimee Kakascik, D.O.** University of Mississippi Medical Center
12:10 PM – 1:10 PM	*Susie Gray Dining Hall*

	Luncheon
12:10 PM – 1:10 PM	*Susie Gray Dining Hall* AHA Council Meeting
1:10 PM – 1:30 PM	*Harambee Auditorium*
	"Are Greed and Villainy Inherited? The case of Dr. William James Morton and his father William T.G. Morton" **Gerald I. Zeitlin, M.D., F.R.C.A.** Instructor in Anesthesia, Retired Harvard University School of Medicine
	Panel: "The Visual History of Anesthesia" Moderator: **Dirk Wales** CEO, Rainbow Productions Initial Director, The Archive Film Task Force Former Council Member, Anesthesia History Association (longest tenured non-physician member of AHA)
	"Visual History of Anesthesia: Visual Media Are a Unique Resource for the Retrieval Retrieving and Teaching of Anesthesia History" **Dirk Wales**
	"Visual History of Anesthesia: The "Living History" Project of the Wood Library-Museum of Anesthesiology" **Alan A. Sessler, M.D.** Professor of Anesthesiology Emeritus Mayo Clinic College of Medicine President, Foundation for Anesthesia Education and Research (FAER).
	"The Use of Digital Media in Teaching Anesthesia History" **Rafael Ortega, M.D.** Associate Professor Vice-Chairman for Academic Affairs Department of Anesthesiology Boston University Medical Center Author: "Written in Granite" and **Albert Woo, M.D.** Resident Department of Anesthesiology Boston University Medical Center
3:30 PM – 3:45 PM	Break:O*utside Harambee Auditorium*
3:30 PM – 3:45 PM	Viewing of Poster Presentations: *Outside Harambee Auditorium)*
3:45 PM – 5:00 PM	(Concurrent Session) Free Papers
	Harambee Auditorium Moderator: **Mary E. DeVasher, CRNA MEd, MS** Vice President and Dean Middle Tennessee School of Anesthesia

3:45 PM – 4:05 PM	"Did The Incas Have A Form Of Anesthesia? A Conjecture" **Barrie Fairley, MB** Professor of Anesthesiology, Emeritus Stanford University
4:05 PM – 4:25 PM	"A Simplified Approach to the History of Anesthesia" **Adolph H. Giesecke M.D.** Professor of Anesthesiology and Pain Management, Emeritus University of Texas Southwestern Medical School Executive Director, CoAEMSP
4:25 PM – 4:45 PM	"Noel A. Gillespie and Albert Schweitzer" **Mark E. Schroeder, M.D.** Associate Professor Department of Anesthesiology University of Wisconsin at Madison
4:45 PM – 5:05 PM	"Dr. Victor Goldman 1903-1993: Close but No Cigar!" **David J. Wilkinson, M.B.B.S., F.R.C.A.** Consultant Anaesthetist Boyle Department of Anaesthesia St. Bartholomew's Hospital President, History of Anaesthesia Society (UK) 2002 Lewis H. Wright Memorial Lecturer
5:05 PM – 5:25 PM	"Untapped Sources for Anesthesia History" **A.J. Wright, M.L.S.** Associate Professor David H. Chestnut, M.D., Section on the History of Anesthesia Department of Anesthesiology University of Alabama at Birmingham
3:45 PM – 5:25 PM	(Concurrent Session) Free Papers *Fondren 22* Moderator**: William L. McNiece, M.D.** Associate Professor of Anesthesia Division of Pediatric Anesthesia Department of Anesthesia Indiana University School of Medicine
3:45 PM – 4:05 PM	"Frank Murphy, the Murphy Eye, and Mid-Century Anesthesia" **John E. Forestner, M.D.** Professor Department of Anesthesiology and Pain Management University of Texas Southwestern Medical School
4:05 PM – 4:25 PM	"Early Pediatric Regional Anesthesia: Contributions from Around the World" **Mark G. Mandabach, M.D.** Assistant Professor The David Hill Chestnut, M.D. Section on the History of Anesthesia Department of Anesthesiology University of Alabama at Birmingham

4:25 PM – 4:45 PM	"Blood Banking and Anesthesia: A "Natural" Convergence in the 1930s" **Jennifer A. Rabbitts, M.B.B.Ch.** Resident Department of Anesthesiology Mayo Clinic School of Medicine
4:45 PM – 5:05 PM	"The Role of the Education Process in the Development of Nurse Anesthesia" **Dina F. Velocci, C.R.N.A., M.S.** Vanderbilt University Medical Center Instructor, Middle Tennessee School of Anesthesia
5:05 PM – 5:25 PM	"Grading of Patients for Surgical Procedures: Evolution and Controversy" **Nathaniel P. Nonoy, M.D.** Clinical Fellow in Anaesthesia Departments of Anesthesiology Children's Hospital and Harvard Medical School
6:00 PM – 8:00 PM	Reception (Optional) *Nick and Rudy's Steakhouse* *204 21st AvenueSouth (300 yards from Scarritt/Bennett)*
8:00 PM –10:30 PM	****Reservations for 12 diners have been made at Nick and Rudy's Steakhouse to follow the reception. Dutch Treat. No sequestered dining room. Mix with the regular customers. Order from the excellent menu. Reservations through AHA are advised.****

Saturday, May 5, 2007

7:00 AM – 8:00 AM	*Susie Gray Dining Hall* Breakfast
7:30 AM – 9:30 AM	*Fondren 22* Free Papers Moderator: **Mark J. Haffey, CRNA, MSN, APN** Immediate Past President Tennessee Association of Nurse Anesthetists
7:30 AM – 7:50 AM	"The Introduction of Ether in Paris: New Findings on the Event and F.W. Fisher" **Ray J. Defalque, M.D.** Professor Department of Anesthesia University of Alabama at Birmingham
7:50 AM – 8:10 AM	"The Abajian Scales, The Untold History of John Abajian, Ed Brazell, and the University of Vermont's 1956 to 1959 Halothane Research" **Joseph M. Kreutz, M.D.** Associate Professor of Anesthesiology University of Vermont College of Medicine
8:10 AM – 8:30 AM	"Floyd T. Romberger, M.D. – Pioneering Indiana Anesthesiologist, Advocate for Physician Anesthesia and Organized Medicine" **William L. McNiece, M.D.**

	Associate Professor of Anesthesia Division of Pediatric Anesthesia Department of Anesthesia Indiana University School of Medicine
8:30 AM – 8:50 AM	"Who gave the first anesthesia in Argentina, a Brit -or- a Yankee?" **Dr. Adolfo Héctor Venturini** Associate Honorary Investigator Institute of History of the Medicine University of Buenos Aires
8:50 AM – 9:10 AM	"Pediatric Endotracheal Tubes Revisited" **Allen J. Hayman, M.D.** Fellow Dept. of Anesthesiology, Pain Medicine, and Perioperative Medicine Children's Hospital of Boston
9:10 AM – 9:30 AM	"Does Magnesium Produce Anesthesia? Truth or Illusion." **J. Antonio Aldrete, M.D., M.S.** Professor Emeritus Department of Anesthesiology University of Alabama in Birmingham
9:45 AM – 2:00 PM	Battle of Franklin Sites and Carter House Museum Tour (optional)
1:15 PM – 2:15 PM	Optional bus direct from Carter House to Nashville Airport departure gates ***(Arrival no later than 2:15 PM, barring crashes, mechanical failure, tornado, bolt of lightning from Thor, or other interferences.)*** ***[By reservation only!!]***

Civil War Medicine in the Union Armies

Frank R. Freemon, M.D., Ph.D.
Professor of Neurology, Emeritus
Vanderbilt University Medical Center
Author, "Gangrene and Glory"
Associated University Presses, London, Madison, Teaneck

The War Between the States was the great American Iliad, the massive blood letting that became a sacrifice to the founding of a new nation. Most historians claim that slavery was the cause of this war, but actually the differences in the economic systems of the northern and southern states only determined the fault line along which the confused states separated. The war concerned whether the United States was a single nation or a group of states with common interests. The modern European Union cannot decide if it is one nation with one system of laws or a group of independent states cooperating for economic purposes. Will it ever face armed conflict to decide this question?

The number of casualties staggered everyone. Previous wars with Britain and with Mexico gave no suggestion that the nation could bear such losses. The new weapon, the bullet that passed down a rifled barrel, went farther and hit harder than previous weapons. These new bullets, called minie balls, tore through flesh and splintered bones. A wound in the chest or abdomen was virtually always mortal. A serious limb wound led to amputation, the most frequent operation of the war.

The number of dead does not alarm modern readers because all participants, struck by a minie ball or spared, are now dead. Study of the suffering of the wounded brings home the horror of the war. The war was fought during the period between the discovery of anesthesia and the appreciation of bacteriology. No effort at asepsis or antisepsis was made. Anesthesia was almost always available, usually ether for the Union and chloroform for the Confederate surgeons. The medical authorities writing later referred to anesthesia as "the great blessing of the war."

Visual Media Treasures Available for Historical Research in the Archives of the Wood Library-Museum (WLM)

In addition to the better known books, periodicals, correspondence, and physical artifacts archived at the WLM are hundreds of pieces of visual and audio media historic information contained both in formal released productions and in unreleased professional, university, and in "home made" films, tapes, C-D's and DVD's. Much of this material is not yet formally cataloged, but a new project is in the planning stage to correct that deficit.

The following list describes the single largest collection of material in the visual history archives. In 2003 Rainbow International, Mr. Dirk Wales, C.E.O., donated these finished, commercial grade productions to the archives. They are available for study in the WLM, and in a few cases, on DVD format for study away from the WLM location.

Year of Production: 1974
Title of Production: Management of Ambulatory Surgery
Anesthesia Sub-Specialty: Outpatient
Participants/Medical Centers: Dr. Ed Brunner/Northwestern, Dr. Reed

Year of Production: 1975
Title of Production: Anesthesia: Inhaled or Injected? Part I
Anesthesia Sub-Specialty: General
Participants/Medical Centers: Drs. Edmund I. Eger II, Hornbein (U/Wash), Cascorbi (Wayne State) and Evan Fredrickson (Emory)

Title of Production: Anesthesia: Inhaled or Injected? Part II
Anesthesia Sub-Specialty: Continuation of General
Participants/Medical Centers: Drs. Edmund I. Eger II, Horbein (U/Wash), Cascorbi (Wayne State) and Fredrickson (Emory)

Year of Production: 1977-78
Title of Production: Dialogues I
Anesthesia Sub-Specialty: General
Participants/Medical Centers: Dr. Bruce Cullen (U.C. Irvine was Moderator with Drs. Bob Stoelting (Uni/Indiana), Joel Kaplan (Emory) Dick Maze (Stanford), Jack Michenfelder/ The Mayo Clinic

Title of Production: New Uses of Ethrane (slide show)
Anesthesia Sub-Specialty: General

Year of Production: 1979
Title of Production: Windows
Anesthesia Sub-Specialty: Teaching use of Ethrane to SRNA/CRNA
Participants/Medical Centers: Joyce Kelly (Kaiser Hospitals) and Susan Stoltzner (Johns-Hopkins), both CRNAs.

Title of Production: Ethrane Today
Anesthesia Sub-Specialty: Re-make of Ethrane Pharmacology film
Participants/Medical Centers: Dr. Harry Wollman (U/Penn) and Dr. Jack Nye (U/Penn)

Title of Production: State of the Art (post-production only for sales meeting)

Year of Production: 1980
Title of Production: Think Metabolism!
Anesthesia Sub-Specialty: Pharmacology

Participants / Medical Centers: Dr. Russell Van Dyke (The Mayo Clinic)

Title of Production: Dialogues II (#1193)
Anesthesia Sub-Specialty: General/mixed
Participants/Medical Centers: Rolling Moderator. Drs. John Tinker (Mayo Clinic), Bradley Smith (Vanderbilt), Burnell Brown (U/Arizona/Tucson) and a Malpractice Attorney from Cleveland

Title of Production: Disconnect!
Anesthesia Sub-Specialty: Machine/Practice: Awareness of Danger of Disconnection
Participants/Medical Centers: Dr. Jeffrey Cooper/MGH, Dr. Jim Philip/ Peter Bent Brigham Hospital

Title of Production: A Report on Forane
Anesthesia Sub-Specialty: Pharmacology

Title of Production: In Their Own Words (#1215)
Participants/Medical Centers: Drs. Bruce Cullen, Edmund I. Eger II, Tom Hornbein, et. al.

Year of Production: 1981
Title of Production: Forane Journal
Anesthesia Sub-Specialty: General
Participants/Medical Centers: This Journal was shot in ten cities, about 14 Institutions featuring about 21 Docs/CRNAs. Moderators were Drs. Edmund I. Eger II and Rick Siker (Mercy Hospital in Pittsburgh). The Centers: Toronto Sick Children; Pittsburgh Children; Mercy Hospital Pittsburgh; Brigham-Woman's Boston; Albert Einstein/NY; Mt. Sinai/NY; U/Penn-Phila; U/Maryland and Johns-Hopkins/Baltimore; Uni/Virgina-Charlottesburg; Uni/Missouri-Columbia; Parkland Hospital/Dallas; Uni/Utah-Salt Lake City; Bowman Gray/ Winston-Salem.

Title of Production: A Question of Pain
Participants/Medical Centers: Dr. John Bonica, University of Washington

Year of Production: 1982
Title of Production: Awakening
Anesthesia Sub-Specialty: Recovery Room Nurses
Participants/Medical Centers: Many RR Nurses all at Northwestern University/Chicago. No MDA involved.
Other Information: This film was the Premier showing at the First ASPAN Convention in 1982, St. Louis.

Title of Production: Point-of View (post-production only)
Anesthesia Sub-Specialty: Pediatrics
Participants/Medical Centers: Physicians from the Forane Journal (This material was shot along with the Forane Journal and edited for Pediatrics)

Title of Production: Dialogues IV- Series of short films
Anesthesia Sub-Specialty: C.A.D.
Participants / Medical Centers: Drs. Joel Kaplan and Cedric Prys-Roberts (Emory Clinic and Royal Infirmary in Bristol England)

Title of Production: Anesthesia for Uncommon Surgical Practices
Anesthesia Sub-Specialty: Liver Transplant, Kidney Transplant

Participants/Medical Centers: Anesthesia Team at U/Pitt/Presby at Medical College of Virginia, U/California at San Francisco at Mt. Sinai/New York

Title of Production: Perceptions
Anesthesia Sub-Specialty: Pharmacology
Participants/Medical Centers: Dr. Harry Wollman U/Penn

Title of Production: Liver Transplant Footage (#1253)
Participants/Medical Centers: Ohio Medical Center

Title of Production: Lab Elements (#1255)
Participants/Medical Centers: Ohio Medical Center

Title of Production: Systemic Toxicity
Anesthesia Sub-Specialty: General
Participants/Medical Centers: Dr. John J. Bonica; University of Washington

Year of Production: 1983
Title of Production: T.R.I.P., Techniques of Rapid Induction in Pediatrics
Anesthesia Sub-Specialty: Pediatrics
Participants/Medical Centers: Drs. William Wren/Sick Children's Hospital, Dublin Ireland and Noel Lawson/Texas Tech Medical Center, Lubbock, Texas

Title of Production: New Products Presentation (Slide Show)
Anesthesia Sub-Specialty: none

Title of Production: True-False
Anesthesia Sub-Specialty: Cardiac
Participants/Medical Centers: Dr. Robert Moreno/Oschner Clinic

Year of Production: 1984
Title of Production: A World of Difference
Anesthesia Sub-Specialty: Outpatient
Participants/Medical Centers: Drs. John Gordon/Omaha and Monte Lichitger/Miami

Title of Production: Toward a Better Anesthesia (US)
Anesthesia Sub-Specialty: General
Participants/Medical Centers: Drs. Alstair Spence/Glascow and Edmund I. Eger, II U/C SF moderators

Title of Production: Toward a Better Anesthesia (Forane Introduction Film/Europe)
Anesthesia Sub-Specialty: General
Participants/Medical Centers: Drs. Alstair Spence/Glascow and Edmund I. Eger II U/C SF moderators. European physicians from German Center in Muenster; Charlottenberg Hospital/Berlin; The Radcliffe Clinic (Oxford) England; Dr. Jan Cruel/Nimeggan Holland; and a pharmacologist speaking with Ross Terrell in Birmingham England.

Title of Production: T.R.I.P. (#1294)
Participants/Medical Centers: Ohio Medical Center

Year of Production: 1985
Title of Production: THE DEBATE (Inhaled versus Injected anesthesia)

Anesthesia Sub-Specialty: General
Participants/Medical Centers: Dr. Theodore Stanley debating Dr. Ron Miller with Dr. Nicolas Greene Moderating (Yale University)

Title of Production: Lifelines
Anesthesia Sub-Specialty: Geriatrics
Participants/Medical Centers: Dr. Ray Roy/Bowman Grey/Winston-Salem and Dr. David Watkins/Duke/Durham

Title of Production: New Product Demonstration
Anesthesia Sub-Specialty: General
Participants/Medical Centers: Physicians at Uni/Iowa and at Uni/Cal San Francisco

Title of Production: Patient Safety and Risk Management Program of ASA (1984-85)
Participants/Medical Centers: Dr. Ellison Pierce, et. al.

Title of Production: What to do after an Adverse Event (Script Only): For Patient Safety and Risk Management (Never Produced)
Participants/Medical Centers: ASA

Title of Production: Disconnect Revised Version for P.S. & R.M./ASA

Title of Production: Clinical Uses of Duramorph
Participants/Medical Centers: Dr. Shelia Cohen, et. al. (for Elkins-Sinn, Inc.)

Year of Production: 1986
Title of Production: Time to Comfortable Discharge
Anesthesia Sub-Specialty: Outpatient
Participants/Medical Centers: Dr. Jeff Apfelbaum/Uni/Penn, Dr. Otto Phillips record/Magee Women's/ Pittsburgh CNRA Nancy Gaskey/Western Penn Hospital/Pittsburgh

Year of Production: 1987-88
Title of Production: Anesthesia for the 1990's
Anesthesia Sub-Specialty: General
Participants/Medical Centers: Dr. John Ward Canada, Dr. John Tinker/Uni/Iowa

Title of Production: Small Steps: A Critical Skill
Anesthesia Sub-Specialty: Educational on Mask Induction
Participants/Medical Centers: Dr. William K. Hamilton

Year of Production: 1988
Title of Production: Competitive Edge

Title of Production: Anesthesia: The Strange Sleep
Other Information: Produced for the Museum of Science & Industry

Year of Production: 1989
Title of Production: Critical Issues In Cardiovascular Anesthesia
Anesthesia Sub-Specialty: Cardiovascular
Participants/Medical Centers: Dr. Earl Wyands (Canada), Drs. Tinker, Marin, Thomas (US) and Dr. Sabastian Reiz (Sweden)

Title of Production: Consumer Care, Consumer Anesthesia
Anesthesia Sub-Specialty: Outpatient

Participants/Medical Centers: Drs. Carl Battaglia (Texas Outpatient, Houston), Lou Freeman (Fresno Outpatient), Gary Silverman (Northwestern Suburban Outpatient/Chicago) and Drs. Ron Jones and Caroline X (Guy's Hospital/London)

Title of Production: Original DPP1 (Dr. Edmund I. Eger II's Uptake and Distribution Lecture)
Anesthesia Sub-Specialty: Pharmacology
Participants/Medical Centers: Dr. Edmund I. Eger II

Title of Production: Original DPE 2 (Applications of Uptake and Distribution)
Anesthesia Sub-Specialty: Applied Pharmacology
Participants/Medical Centers: Drs. Edmund I. Eger II and Dr. Doreen Wray (Cornell, NY)

Title of Production: Original DPP 3 (Inhalation Induction) (#1640)
Anesthesia Sub-Specialty: General Clinical Practice
Participants/Medical Centers: Drs. William K. Hamilton, Michael Roizen, Michael O'Conner (U/Chicago), Lance Lichtor (U/C), Steven Hall (Chicago Children's) and William Wren (Dublin, Ireland)

Title of Production: Mask Induction: A Critical Skill (#1572)
Participants/Medical Centers: Dr. William K. Hamilton

Title of Production: First Use of I-653
Participants/Medical Centers: Dr. Ron Jones and Dr. Mike Damask

Title of Production: T.R.I.P. Applications
Anesthesia Sub-Specialty: Pediatrics
Participants/Medical Centers: Drs. Noel Lawson (Uni/Texas/Galveston), Lance Lichtor (Uni/Chicago), Dr. Miles Dinner (Cornell, NY)

Year of Production: 1990
Title of Production: Original DPP 4 (Breath-by-Breath Monitoring)
Anesthesia Sub-Specialty: General
Participants/Medical Centers: Dr. Jim Philip. Brigham and Women's Hospital Boston

Title of Production: Balanced Anesthesia
Anesthesia Sub-Specialty: General
Participants/Medical Centers: Dr. James Brannon of Emory Clinic and Larry Levit of Hahnemann Medical Center/Philadelphia

Title of Production: Dr. Edmund I. Eger II's MAC Lecture
Anesthesia Sub-Specialty: Pharmacology/Clinical
Participants/Medical Centers: Dr. Edmund I. Eger II
Other Information: Note: This video was shot but never edited.

Title of Production: VideoJournal Anesthesia, Vol. One
Anesthesia Sub-Specialty: Community Hospitals
Participants/Medical Centers: Drs. Ron Miller, UCSF; George Lampe, Good Sam Hospital, San Jose; Jim Philip/Boston; Carl Hug, Emory Clinic Atlanta

Year of Production: 1991
Title of Production: VideoJournal Anesthesia, Volume Two
Anesthesia Sub-Specialty: Outpatient Cost
Participants/Medical Centers: Drs. Gary Silverman, NW Outpatient Chicago; David Edson, Community Practice Massachusetts

Title of Production: Awareness under Anesthesia
Anesthesia Sub-Specialty: General
Participants/Medical Centers: Dr. Peter Sebal, Emory and Dr. Hrnry Bennett, UC Davis

Title of Production: VideoJournal Anesthesia Volume Three
Anesthesia Sub-Specialty: General
Participants/Medical Centers: Dr. David Bevan Royal Infirmary. Montréal, Québec, Canada

Year of Production: 1992
Title of Production: The Pharmacology of Inhaled Agents, New DPP Series
Anesthesia Sub-Specialty: General
Participants/Medical Centers: Drs. John Kampine (Medical College of Wisconsin); Dr. Paul White (Southwest Medical Center); Dr. Dick Weiskopf (UC/SF); Edmund I. Eger, II and Dr. Ron Jones (St. Mary's Hospital London)

Title of Production: The Tec 6 Vaporizer
Anesthesia Sub-Specialty: General

Year of Production: 1992-3
Title of Production: The Suprane Experience Curve, Parts I & II
Anesthesia Sub-Specialty: General
Participants/Medical Centers: Dr. Sheila Gaughn (UC/San Diego), Dr. Robert Stoelting (Indiana University/Indianapolis), Dr. Melinda Baily (Medical University of South Carolina/Charleston), Dr. Robert Marino (Oschner Clinic), Dr. Marvin Palmore (Emory Clinic) Another physician from Oschner Clinic
Other Information: This box contains the original field Betacam tapes and VHS window dubs of those tapes. Approximately twenty hours of Anesthesiologists using Suprane for the first time and discussing their Experience then two months later.

Title of Production: The Suprane Experience Curve, Part II
Anesthesia Sub-Specialty: General
Participants/Medical Centers: Dr. Sheila Gaughn (UC/San Diego), Dr. Robert Stoelting (Indiana University/Indianapolis), Dr. Melinda Baily (Medical University of South Carolina/Charleston), Dr. Bob Marino (Oschner Clinic), Dr. Marvin Palmore (Emory Clinic). Another physician from Oschner Clinic.

Year of Production: 1993
Title of Production: Suprane Case History
Anesthesia Sub-Specialty: Cartoid Endarterectomy
Participants/Medical Centers: Dr. Rafeal Ortega/Boston

Title of Production: New Corporate Logo
Anesthesia Sub-Specialty: General

Title of Production: Wearing Masks
Anesthesia Sub-Specialty: Anesthesia Residents
Participants/Medical Centers: University of Washington; Wife of dead resident filmed in Denver Colorado
Other Information: This box contains the original Betacam field tapes & window dubs of those tapes. This program was made to advise spouses and families of all anesthesia residents of the potential for addiction problems in the specialty.

Year of Production: 1993-4

Title of Production:	**Brevibloc Case Studies, (Controlling Heart Rate and Blood Pressure in the Patient-at-Risk)**
Anesthesia Sub-Specialty:	**General**

Title of Production:	**Brevibloc Case Studies, Case 1**
Anesthesia Sub-Specialty:	**Orthopedics**
Participants/Medical Centers:	**Dr. Keith Lewis at the New England Deaconess Hospital/Boston**

Title of Production:	**Brevibloc Case Studies, Case 2**
Anesthesia Sub-Specialty:	**CABG**
Participants/Medical Centers:	**Dr John Ellis, University of Chicago.**

Year of Production: 1993-4

Title of Production:	**Brevibloc Case Studies, Case 3**
Anesthesia Sub-Specialty:	**Cartoid Endarterectomy**
Participants/Medical Centers:	**Dr. John Ellis, University of Chicago**

Title of Production:	**DPP 1 Uptake and Distribution of Inhaled Agents**
Anesthesia Sub-Specialty:	**General**
Participants/Medical Centers:	**Dr. Edmund I. Eger II (UC/SF) and residents and SRNAs of the University of Pittsburgh (Montefiore Hospital)**

Year of Production: 1994

Title of Production:	**VideoJournal Anesthesia, New Series, Volume One**
Anesthesia Sub-Specialty:	**General**
Participants/Medical Centers:	**Pharmacist Clark Lyda (U/Colorado), PACU Nurse Laurence Doyle Salinas (CA), Drs. William King (U/Texas, Galveston) Don Drury (Community Hospital, Florida), CRNA Karen Truver (Charleston), Guest appearance: Dr. Edmund I Eger II**

Title of Production:	**The Practice of Low Flow Anesthesia**
Participants/Medical Centers:	**Dr. William K. Hamilton; Dr. Reynolds Saunders; University of California, San Francisco and Mt. Sinai, Los Angeles**

The John W. Pender "Living History Project" Website

During the panel entitled "The Visual History of Anesthesia," Dr. Alan A. Sessler will describe the history of this wonderful and continuing project of the Wood Library-Museum (WLM). These interviews have recently been transferred to current DVD format discs and are available for purchase for viewing and study for a very nominal fee which has made them very practical for teaching, research, and pure enjoyment in your own living room!

To demonstrate the ease of locating this resource, and to provide an index of personalities already in the archive, a reproduction of the WLM website for this project follows.

New interviews are added every year. This year the Committee on "Living History of Anesthesia" of the WLM has added interviews with former ASA President John Neeld, Theodore (Ted) Smith, and John (Jack) Downes. During 2007 interviews are scheduled with former ASA Presidents, Norig Ellison, Eugene Sinclair, and Peter McDermot, and with Ty Smith, and Barrie Fairley.

Sample and enjoy!

The John W. Pender Collection of the Living History of Anesthesiology

Primarily interviews of anesthesiologists by anesthesiologists

Interviewee/Interviewer(s) Date

A

Adriani, John/Leroy D. Vandam (1977)
Albin, Maurice S./Douglas R. Bacon (2003)
Aldrete, J. Antonio/Maurice S. Albin (2004)
Allen, Charles R./Donald S. Prough (1994)
Ament, Richard/Elliott V. Miller (1987)
Anesthesiology Editors-in-Chief/Elliott V. Miller (1999)
Anesthesiology Editorial Panel II/Recollections & Perspectives (2000)
Artusio, Joseph F./Alan Van Poznak (1983)

B

Bause, George S./Charles Tandy (2005)
Bendixen, Henrik H./Elliott V. Miller (1988)
Remembering Henry K. Beecher, M.D. (1996)
Betcher, Albert M./Elliott V. Miller (1982)
Bird, Forest/Carter Ballinger
Bird, Harry H./Glenn Johnson (2005)
Bonica, John J./Thomas F. Hornbein (1978)
Brain, Archie / Rod K. Calverley (1993)
Bridenbaugh, Phillip O./David L. Brown (2002)
Briggs, Bernard D./M.T. Pepper Jenkins (1994)
Brown, Burnell/A.H. Giesecke, Jr., John Nunn (1994)
Brown, Eli M./Morris Brown (1999)
Buckley, Joseph J./William D. Owens (1990)

C

Calmes, Selma Harrison/Doris K. Cope (2004)
Caton, Donald/Elliott V. Miller (2005)
Churchill-Davidson, H.C./William Colvin (1967)
Clement, F.W. /Albert Faulconer (1977)
Coakley Charles S./Seymour Alpert (1984)
Collins, Vincent J./Ramez Salem (1996)
Conn, AW (Professor Emeritus)
Cullen, Stuart C./William K. Hamilton (1977)

D

Davis, David A./David Sabiston (1984)
Devloo, Robert/Roger White (2006 - Mayo Clinic Living History Series)
Didier, Edward Paul/Robert L. Lennon (2006 - Mayo Clinic Living History Series)
Dillon, John/ M.T. Pepper Jenkins (1990)
Ditzler, John W./John J. Leahy
Dornette, William/Ronald MacKenzie (2005 - Mayo Clinic Living History Series)
Dripps, Robert D./Drs. Prevoznik, Dumke, Eckenhoff, Vandam (1988)
Dumke, Paul R./Leroy D. Vandam (1985)

E

Eckenhoff, James E./Leroy D. Vandam (1988)
Eckenhoff, James/ Drs. Edward A. Brunner, Harry W. Linde (1982)

Eger, Edmond I., II/William K. Hamilton (1990)
Eggers, Jr., G.W.N./ Noel W. Lawson (1997)
Emerson, Jack/Alberto J. de Armendi (1993)
Emerson, John H./Henning Pontoppidan (1993)
Epstein, Burton/Bernard V. Wetchler (2003)
Epstein, Robert M./Longnecker D.E. (1995)
Etson, Benjamin E./Elliott V. Miller (1983)
Eversole, Urban/Elliott V. Miller (1980)

F

Fink, B. Raymond/Arthur S. Keats (1988)
Foldes, Francis F./E. S. Siker (1982)
Frumin, M. Jack/D. Robert Buechel (1991)

G

Giesecke, Adolph H./N. Martin Giesecke (2002)
Gilmartin, Tommy (1983)
Gilmartin, Tommy/William Wren (1983)
Gordh, Torsten/Nicholas Greene (1991)
Gordon, R. A. /Alan Conn (1979)
Gravenstein, Joachim S./Donald Caton (1997)
Greene, Nicholas M./Leroy D. Vandam (1985)
Griffith, Harold R./J. E. Wynands (1977)
Guedel, Arthur (Special Lecture)/ Roderick K. Calverley (1984)

H

Hale, Donald E./John W. Pender (1966)
Hamilton, William K./C. Philip Larson (1983)
Hand, Leo V./Elliott V. Miller (1988)
Harmel, M./Drs. Philip Bromage, Robert Virtue (1983)
Harmel, M./Philip Bromage, Robert Virtue (edited) (1983)
Harrison, G./ Prof. J. Lerman (1996)
Hornbein, Tom/Ted Egers (1994)
Harroun, Phyllis/with narr. by Fredrick Beckert, Carl Fisher (1946)
Hattox, John S./William K. Hamilton (1991)
Haugen, Frederick P./Burnell R. Brown (1982)
Helrich, Martin/E.S. Siker (1989)
Henschel, Ernst O./John P. Kampine (1979)
Hershey, S. G./Leroy D. Vandam (1987)
Hickman,Henry Hill/W.D.A. Smith (1987)
Hingson, Robert/Ralph Hingson (1989)
Hug, Carl C., Jr./William D. Hammonds (2004)

J

Jackson, Dennis E./Drs. Stetson, Striker, Felson (1981)
Jackson-Rees, Gordon/ (1979)
Jackson-Rees, Gordon/William Wren (1983)
Jacoby, Jay J./John McDonald (1989)
Jenkins, M. T. Pepper/Drs. A. H. Gieseke, Charles Tandy (1982)

K

Kaye, Geoffrey/John Paull (1984)
Keats, Arthur S./M.T. Pepper Jenkins (1988)
Keown, Kenneth K./Noel Lawson (1982)
Kinyon, Gilbert/Rod K. Calverley (1993)

Kitz, Richard J./Elliott V. Miller (1988)
Knight, Ralph/John W. Pender (1961)
Knoefel, Peter/Eugene H. Conner (1986)
Kornfield, Norman B./Howard S. Robbins (1992)

L

Lansdale, John , Esq./M. T. Pepper Jenkins (1982)
Leake, Chauncey D., Ph.D./William K. Hamilton (1976)
Leigh, Digby (1940's, 1962)
Little, David M., Jr. /Elliott V. Miller (1978)
Lundy, John S./John W. Pender (1966)

M

Macintosh, Sir Robert/James E. Eckenhoff (1983)
Magill, Sir Ivan/ (1944)
Marcus, Philip S. /Elliott V. Miller (1986)
Marin, Juan /J.S. Gravenstein (1992)
Marinko, William S./Elliott V. Miller (2002)
Martin, Stevens J./John W. Pender (1966)
Marx, Gertie F./M. Finster (1984)
McCuskey, Charles F./John W. Pender (1990)
McLeod, Enid Johnson/Charles E. Hope
Michenfelder, John D./Alan D. Sessler (1991)
Miller, Elliott V./Charles Tandy (1999)
Moore, Daniel C./Barrie Fairley (1978)
Morch E. Trier/Alon P. Winnie (1994)
Morris, Lucien E./Betty J. Bamforth (1981)
Mousel, Lloyd/ Seymour Alpert (1967)
Moyers, Jack/M.T. Pepper Jenkins (1990)
Mushin, William W. /Joseph Ruprecht (1982)

N

Neeld, John B. Jr./Bradley E. Smith (2006)
Neff, William B./J.W. Pender (1981)
Nunn, John F./John W. Severinghaus (1990)
Nunn, John F./R. Raymond Fink (1985)

O

Orkin, Louis R. /Howard L. Zauder (1988)

P

Papper, E. M./N. B. W. Craythorne (1979)
Parsloe, Carlos/Lucien Morris (1989)
Pauling, Linus/John Severinghaus (1991)
Pender, John W./Elliott V. Miller (1983)
Pender, John W./Elliott V. Miller (1996)
Pender, John W./Alan D. Sessler (1996)
Pierce, Ellison P., Jr.,/Elliott V. Miller (1983)
Pontoppidan, Henning/Elliott V. Miller (1992)
Priestley, Joseph/W.D.A. Smith (1978)

R

Reed, Wallace A. – An Interview with, History of the First Surgicenter (1993)
Reed, Wallace A. Hx of the First Surgicenter.
Revised version (1994)

Reed, Wallace A. Phoenix Surgicenter Employee Appreciation Day 1970-1995, Silver Anniversary (1995)
Revell, Daniel/Lucien Morris (1989)

S

Sadove, Max S./ Henry S. Havdala (1990)
Saidman, Lawrence J. (1997)
Secher, Ole/Jack Moyers (1992)
Seldon, T. Harry/B.B. Sankey (1978)
Sessler, Alan D./Mark A. Warner (2006 - Mayo Clinic Living History Series)
Severinghaus, John W./Thomas F. Hornbein (1988)
Siker, E.S./Bernard Wolfson (1984)
Sim, Patrick/Charles Tandy (2004)
Slocum, Harvey/James F. Arens (1983)
Smith, Robert M./Elliott V. Miller (1982)
Smith, Theodore C./Bradley E. Smith (2006)
Steinhaus, John E./Evan Frederickson (1983)
Stephen, C. Ronald/Warner Ahlgren, Edward R. Johnson (1983)
Stephenson, Betty P./James F Arens, Arthur S. Keats (2002)
Stoelting, V. K./William D. Owens (1985)
Stubbs, Donald H./Seymour Alpert (1993)
Sugioka, Kenneth/Kenneth J. Levin, Edward A. Yesrfleet (1983)

T

Tandy, Charles/ Elliott V. Miller (1995)
Tandy, Charles C. MD, Health Sciences Library Dedication (1999)
Tarrow, Arthur B./Jay Jacoby (1996)
Terrell, Ross, Ph.D./Alan Van Poznak (1998)
Travel Club/Canadian Members of Anesthetist's Travel Club (1986)
Travel Club/R. A. Gordon, Alan Conn (1979)

V

Vandam, Leroy D./Elliott V. Miller (1980)
VanPoznak, Alan/Kathryn McGoldrick (1998)
Virtue, Robert W./Philip R. Bromage (1982)
Volpitto, Perry P./Evan L. Frederickson (1981)

W

Waters, Ralph M./Perry P. Volpitto (1967)
Weiss, Jesse B./Elliott V. Miller (1985)
Wetchler, Bernard W./Erwin Lear (2000)
Woodbridge, Philip Dudley, Reminiscences of, with Morris J. Nicholson, John B. Stetson (1978?)
Wright, Lewis H. (1967)

Abstracts of Presentations

Does Magnesium Produce Anesthesia? Truth or Illusion.

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Magnesium has been used for therapeutic applications for over five centuries. These properties were noted in the Epsom waters in England; later promoted in Vittel, France. Many curative properties were attributed to this ion including treatment of high blood pressure, arrhythmias, nutritional deficits, and neurological disorders. However, its greater popularity has been as a purgative and as anti-inflammatory agent. From experiments by Claude Bernard, Meltzer and Auer produced depressant effects on the medulla oblongata of dogs.[1] They also administered it IV to three patients with questionable results as two of them moved and the third patient that received a larger dose stop breathing[2] Goodman and Gilman's[3] mentioned in their second edition (1955) that it was an anesthetic agent. In 1955, Pritchard[4] showed Mg's benefits in eclamptogenic toxemia, which he attributed to Mg's sedative and anticonvulsant actions.

In the 1960's several studies questioned these theories. First, Hilmy and Somjen[5] loaded rabbits with Mg++ and found that its uptake distributed mostly in muscle and only 8% in the brain. Typical of those days, Somjen and Hilmy infused each other, enough $MgSO_4$ to produce weakness with some respiratory difficulties; their plasma Mg at that time reach levels around 14mEqv/l; they however felt everything done to them and remembered it. The third author in this paper was C. R. Stephen[6] who resuscitated them both.

Subsequently, Aldrete, Barnes and Aikawa[7] injected awake dogs with $MgSO_4$ bolus of 1.0gm; noticing a "quasi anesthesia state" at plasma concentrations between 18 to 20mEqv/L; thereafter, CVS depression occurred gradually, reaching asystole at 23mEq/l. All the effects were promptly reversed with either $CaCl_2$, or neostigmine. These effects were attributed to muscle relaxation, along with cardiovascular and respiratory depression, rather than "anesthesia". Moreover, Giesecke, et. al.[8] noted that pregnant women having C-sections required less succinylcholine and d-tubocurarine than those patients not receiving Mg. In 1972, the fourth edition, of the pharmacology text, G&G felt that Mg was mostly a muscle relaxant and not an anesthetic.

References

1. **Meltzer SJ, Auer J. Physiological and pharmacological studies of Mg salts II. Toxicity of intravenous injections: in particular, effects upon the centres of the medulla oblongata. *Am J Physiol* 1906:17:387.**
2. **Peck CH, Meltzer SJ. Anesthesia in human beings by IV injection of $MgSO_4$. *JAMA* 1916:67:1131-4.**
3. **Goodman LS, Gilman A: Pharmacological basis of therapeutics.(eds) 2nd Ed 1955:813-7.**
4. **Pritchard JA.: The use of magnesium ion in the management of eclamptogenic toxemia. *Surg Gynec Obstet* 1955:100:131-9.**
5. **Hilmy M, Somjen GG. Distribution and tissue uptake of Mg related to its pharmacological effects. *Amer J Physiol* 1968:214:406-8.**
6. **Sonjen GG, Hilmy M, Sthepen CR: Failure to anesthetize human subjects by IV administration of $MgSO_4$. *J Pharmacol Exp Therap* 1966:154:652-7.**
7. **Aldrete JA, Barnes DR, Aikawa JK. Does Mg produce anesthesia? Effects of its administration on CVS and CNS. *Anesth Analg* 1968:47:428-33.**
8. **Giesecke AG, Morris RE, Stephen CR. On Mg, muscle relaxants, toxemic parturients and cats. *Anesth Analg* 1968:47:689-72.**
9. **Goodman LS, Gilman A. Pharmacological basis of therapeutics, (eds) 5th Edition, 1975:787-91.**

The Introduction of Ether in Paris: New Findings on the Event and F.W. Fisher

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I. New Findings on the Event and Controversies

In a letter[1] to the *Boston Medical and Surgical Journal*, F.W. Fisher, an American physician studying in Paris, wrote that in November 1846, shortly after receiving a letter from a "medical friend" and "medical instructer" (sic), announcing the introduction of ether in Boston, he asked Velpeau to let him administer ether for an operation. Velpeau refused. A few days later, accompanied by a friend, Dr Mason, he visited a Paris dentist to have a painful tooth extracted. He started inhaling ether but became violent and his friends stopped him. On December 15th, 1846, Jobert let him anesthetize a patient for excision of a lip cancer, using an inhaler similar to that of Boston. The anesthesia was only partially successful because his tumor prevented the patient from breathing through the mouth piece.

December 15th,1846 is generally considered to be the date of the first administration of ether in Europe, preceding by four days its use by Robinson for a dental extraction (December 19th) and by six days Liston's leg amputation (December 21st).

We have recently found new details and several controversies in that story.

1. **The first successful ether anesthesia in Europe (though not for surgery) occurred in London on November 11th, 1846.[2]**
2. **Velpeau and Fisher contradict each other on why Velpeau refused Fisher's offer.**
3. **Who was the medical "friend" and "instructer" (sic) remains unclear. Three candidates are: H.J. Bigelow, J.D. Fisher, and J. Ware. How and when the Boston letter reached Fisher can be inferred from several sources.**
4. **Dr. Mason, the friend who accompanied Fisher to the dentist, could not have been J. Mason Warren, as has been claimed. The dentist may have been C.S. Brewster, an American practitioner then popular in Paris.**
5. **Fisher's claim that his anesthesia was partially successful is an exaggeration. A witness[3] called it a failure and gave a different explanation for the fiasco. Jobert operated on an awake patient.**
6. **The inhaler used by Fisher on Jobert's patient was probably made at the Hôpital de St. Louis.**
7. **So far unnoticed is that a few days after the December 15th failure, Jobert, using Fisher's inhaler, operated on two patients under excellent ether anesthesia.[4]**
8. **The "friend" who sent Fisher a model of Morton's inhaler around mid-January, 1847 remains unknown.**
9. **The first use of ether in obstetrics is generally attributed to J.Y. Simpson on January 19th, 1847. A letter from Fisher[5] shows that ether was used by Paris obstetricians at the same time or even shortly before.**
10. **In 1894, two American physicians in Paris at the time gave a very different version of the introduction of ether in Paris and did not even mention Fisher.[6]**

II. Biographic Data on F.W. Fisher

Our search has revealed some new details (though still too few) on the mysterious Dr. Fisher:

1. **His birth on January 21st, 1821. Was it in New York City or in Massachusetts? The Fishers were a prominent Boston medical family.**
2. **His medical education at Harvard: dates, colleagues, teachers.**
3. **The date of his return to the U.S. in 1848.**
4. **His work as a police surgeon in New York City.**
5. **His 1855 marriage to Jennie Fairbank, a NYC socialite.**
6. **His enlistment in May, 1861 as a surgeon in the 83th Infantry Regiment of the NYC militia.**
7. **Fisher was the first physician to attend James Fisk, Jr., the robber baron who was shot in January, 1872 at the Grand Central Hotel where Fisher resided at the time. He was an expert witness at the assassin's trial.**
8. **Fisher died in New York City on January 20th, 1877, in mysterious circumstances, probably from an aconite overdose.**

Bibliography

1. **Fisher FW. The ether inhalation in Paris. *Boston Med Surg J* 1847;36:109-113.**
2. **Dawkins CM. The first public operation carried out under an anaesthetic in Europe. *Anaesthesia* 1947;2:51-61.**
3. **Gogue G. Aspiration de la vapeur d'ether sulfurique. Gaz Hopit Cviv Mil 1847;18:39-40.**
4. **Jobert A. Suite a la discussion sur les effets de l'ether sulfurique. *Bull Acad Med Paris* 12:314-317, 1846-7.**
5. **Fisher FW. Letter from Paris. Ethereal inhalation in insanity and obstetrics. *Boston Med Surg J* 1847;36:172-174.**
6. **C. The first administration of ether in Paris, and other reminiscences. *Boston Med Surg J* 1894;131:475.**

Did the Incas have a Form of Anesthesia? A Conjecture

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The Inca Empire of approximately six million people began in the region of Cuzco, Peru, in about 1200. It eventually encompassed 2,400 miles of the Andes, and lasted until 1532 when the conquistador Francisco Pizarro captured their king, *Atahualpa* at Cajamarca. We know that their *camascas or* medicine men practiced forms of surgery, and this paper will discuss the issue of whether they had a means of controlling the pain of their procedures.

The Incas did not have any written language. Any information that was left by them was told to the Spanish chroniclers who accompanied the conquistadors or followed soon after. In addition there are accounts by a few Incas who learned to read and write after the conquest, and recorded the information handed down in their families. These chronicles are therefore the primary sources for this history. They tell us little about surgery and almost nothing about pain relief, although Father Bernabé Cobo's *Historia del Nuevo Mundo* (History of the New World) describes thirteen herbs with central effects and these will be reviewed here. Thus, any statement about Inca 'anesthesia' will, at best, be a conjecture based on scattered information from the chronicles, ceramics, ethnobiology, osseous remains, and the observations of various anthropologists and medical historians in the subsequent years. There is no definitive published work on the subject.

Juan Betanzos was a Spaniard who married an Inca princess and spoke the Inca language, *Quechua*. He describes the nobles' lengthy coming-of-age ceremony, when they had their ears pierced with crude instruments to receive large ear plugs. They were given alcohol beforehand to make them unconscious, and various potent preparations of this *chicha* are mentioned in the chronicles. A French natural scientist, Francis de Castelnau, has described the use of *chicha* to perform female circumcisions on nine-to-ten year-old girls in the Peruvian highlands in the nineteenth century. There are also descriptions, in the chronicles and later, of unconsciousness produced by the use of *Datura Stramonium* (Jimsonweed/Angel's Trumpet/ Thorn Apple), which contains hyoscine and hyoscyamine, Also, Stevenson has reported the successful use of *Datura* in the nineteenth century by Zuñi Indians in New Mexico as an anesthetic for their operations. The components of this plant, which still grows in Peru, have been well studied and there are many instances of poisoning reported in the modern literature, that provide insight into the effects of large doses – essentially delirium and inappropriate behavior with death on rare occasions. The conflict between this toxicology information and the reports of *Datura*'s successful use as a pseudo-anesthetic has yet to be resolved.

Finally there is the *coca* plant which was rare in pre-Columbian times. The nobles controlled its use, and found that, when their workers sucked a wad of its leaves in their cheeks, they could work for long periods without food or drink. This habit became common after the conquest and ever since. We now know that when the leaves are mixed with an alkali, as was the custom, the juice then contains sufficient liberated cocaine to cause numbness of the tongue and throat, and it may have been used to produce local anesthesia in surgical and traumatic wounds,. We do know that they put *coca* leaves in wounds because of a perceived healing property and Bandalier reports seeing an associated anesthesia effect in the nineteenth century, although he doubts that the Indians understood its significance.

In summary, it is reasonable to conclude that the Incas used a potent preparation of *chicha* to produce unconsciousness for their surgery and that they also used *Datura* either in combination or alone to ablate the pain and produce amnesia. They probably used the juice of coca leaves to provide some degree of topical anesthesia.

Frank Murphy, the Murphy Eye, and Mid-Century Anesthesia

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Frank Murphy (1900-1972) is famous for first describing the second hole on the end of the endotracheal tube, commonly referred to as the Murphy eye. Most anesthesiologists know the eponym, but know nothing about the man. He wrote few scholarly publications, and left no collected papers, correspondence, or identifiable family. Reconstructing his career has been possible through information in the Wood Library Museum and the Mayo Clinic Archives, and by interviewing acquaintances and colleagues who are still alive.

He was born Francis John Murphy in 1900 in South Dakota, and was raised in Alberta, Canada. After graduating from university in Edmonton, he finished medical school at Magill University in Montreal, where he remained for two years of further training in anesthesia. Working at Montreal General Hospital and other private hospitals there, he had frequent contact with the well known Canadian anaesthetists C.S. Stewart, Wesley Bourne, and Harold Griffiths. After looking at several medical practice opportunities in both Canada and the United States, he finally settled in Detroit in the early 1930's, where he became chief of anesthesia at Harper Hospital. He knew McMechan, and was asked to comment on presentations at several yearly meetings of the I.A.R.S. during this period. Murphy's paper describing the side hole on the insufflation endotracheal tube was published in Anesthesia and Analgesia, McMechan's journal, in 1941.

Murphy was board certified in 1939 (certificate #60), and joined the American Society of Anesthetists in 1940. It is clear that he stayed in contact with his mentors in Montreal, who were all members of the famous Anesthetists' Travel Club, and this was most likely responsible for his election to the Travel Club as its 39th and last member, at the final meeting in November 1941, just before the start of the World War. He was later included as a charter member of the Academy of Anesthesiology, formed in 1952.

He left Detroit for active duty in the U.S. Navy in World War II, stationed in the Pacific theater, winding up as chief of anesthesia at the naval hospital at Pearl Harbor late in the war. After the war, rather than returning to Detroit, he was recruited by some navy colleagues to become chief of anesthesiology at the University of California Hospital in San Francisco, where he remained from 1946 to 1956. He resigned that position when the medical school decided to improve teaching and academic standards in his department, although economic factors may also have been involved in his removal. He moved to Billings, Montana, where he practiced until his death from a urologic malignancy in 1972.

Murphy contacted many people during his varied career, and interesting questions are raised about many aspects of his history, particularly concerning the end of his academic career in 1956. His major contribution, the Murphy eye, has evolved considerably since it was first described, and it is clear that he did not anticipate all its uses in his first publication.

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A Simplified Approach to the History of Anesthesia

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The history of anesthesia is a rich tapestry of thousands of details, some of which were important, some not so important, and some actually false. How can we simplify this mountain of detail into something that can be retained by the non-historian? The great teacher, Ron Stephen, was a master at reducing complex subjects to understandable essentials.

Dr. Stephen taught in 1967 that four sentinel events were epochal in that they were so important that they changed the behavior of doctors and patients forever and we never returned to the former way of doing things. Everything else is detail leading up to the sentinel event or refining and improving the product of the event. His four sentinel events were:

1. The epoch of inhalation anesthesia by Morton of Boston in 1846.
2. The epoch of regional anesthesia by Koller of Vienna in 1884.
3. The epoch of intravenous anesthesia by Lundy of Rochester MN in 1934.
4. The epoch of neuromuscular blockers by Griffith of Montreal in 1942.

Dr. Stephen acknowledged that Long gave ether anesthesia before Morton but did not publicize his discovery until after the technique had spread around the civilized world and brought relief to thousands of surgical patients. Likewise Dr. Stephen acknowledged that Inca shamans chewed coca leaves and spit the drug-laden saliva into painful wounds, but Koller's inspiration was to refine the use of cocaine for ophthalmic anesthesia and launch a new practice. Dr. Stephen acknowledged that intravenous barbiturates were given in Germany before Lundy's historic demonstration at the Mayo Clinic, but the German experiments did not catch on. Lundy's revelation ignited the world and changed our practice forever. Dr. Stephen further acknowledged that curare was used by native paleo-pharmacologists for centuries before Griffith introduced the drug, but the realized benefits of this family of drugs changed our practice forever.

Inspired by Dr. Stephen's teachings, I have added two more sentinel events, which were epochal in that they changed the behavior of anesthesiologists forever:

5. The epoch of balanced salt solutions in fluid therapy by Jenkins of Dallas in 1950.
6. The epoch of precision monitoring for patient safety by Pierce of Boston in 1986.

Before 1950 the patient had no intravenous started, received small amounts of D5W or received whole blood if bleeding was severe. Salt solutions were considered contraindicated. After Dr. Jenkins' recommendation, all patients now receive some salt solutions. Dr Pierce convinced the ASA to adopt minimum standards of monitoring in 1986. These standards eventually included ECG, NIBP, SPO2, end tidal CO2, O2, and anesthetic concentrations. The epoch of precision monitoring for patient safety had begun. Our practice was changed forever.

C. Ronald Stephen was Professor of Anesthesiology at University of Texas Southwestern Medical School from 1967 to 1971. Photograph is from the Wood Library-Museum.

Pediatric Endotracheal Tubes Revisited

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In March of 1953, Dr. Robert M. Smith (then chairman of the pediatric anesthesiology department at Children's Hospital Boston) published an article calling for improved intubation techniques to minimize the then high incidence of laryngeal irritation and tracheal edema following general endotracheal anesthesia in children.[1] This comparatively high incidence of morbidity and mortality in the pediatric population led to a general polarization among practitioners in the early 1950's. One group adopted the viewpoint that general endotracheal anesthesia should be avoided in the pediatric population. The second group felt that tracheitis was an unfortunate but unavoidable complication of pediatric endotracheal anesthesia which should not preclude its general use.[1] Using an admonition set forth by Gilles in 1951 that endotracheal anesthesia was too valuable a method to be jeopardized by abuse,[2] Smith made a plea to refine the methods of pediatric endotracheal anesthesia and incorporate special precautions that would eliminate those errors that might lead to the development of tracheal irritation.

In general, otorhinolaryngological surgeons were opposed to pediatric endotracheal anesthesia (except in a limited number of circumstances) while anesthesiologists favored the technique. Dr. Shirley Harold Baron (Division of Otolaryngology, Stanford University Medical School) opposed pediatric endotracheal anesthesia. While grudgingly admitting the merits of endotracheal anesthesia, he continually emphasized the disadvantages of the technique, especially in children, believing that both surgeons and anesthesiologists were becoming dangerously cavalier and complacent in employment of this technique. In a presentation before the 1950 meeting of the American Laryngological, Rhinological and Otological Society, Baron quoted the following statement made by Dr. Moss in 1930: "Ploughing up the pharynx with a laryngoscope in an attempt to dig out an epiglottis from a pool of blood and mucus is one of the least inspiring sights of modern anesthesia."[3] Baron later wrote, "It is difficult for us to understand why, in children, endotracheal anesthesia should be used for an adeno-tonsillectomy in any instance. Anesthetists have argued that they protect the patient's airway from the blood overflow that occurs in the hands of certain surgeons. This may be so in some instances but it does not seem reasonable that an endotracheal tube should be used as a substitute for good surgery."[4] While Baron conceded that certain institutions appear to have limited complications, he warned his fellow ORL surgeons to be guided by the facts of their own experiences and not be misled by "favorable statistics."

In attempting to save a technique that he thought vital to the advancement of pediatric anesthesia, Smith called on practitioners to modify their intubation equipment and techniques to minimize mechanical force trauma, chemical irritation, and contamination. Large, heavy laryngoscopes with too short or too wide blades and endotracheal tubes of excessive caliber invited "ploughing" of the pharynx and stretching or tearing of the vocal cords. He recommended using a long, narrow blade. He also emphasized the need for proper intubating conditions through a combination of adequate relaxation, proper head positioning (raising the head so that the neck is flexed to approximately 45 degrees), and prior recognition of anatomic abnormalities. Smith stressed proper securing of the endotracheal tube and the use of a more pliable polyvinyl tube to help reduce motion-associated trauma during the course of the anesthetic. To reduce the role of chemical irritation in pediatric tracheitis, Smith recommended rinsing endotracheal tubes to remove excess sterilizing solution and avoiding the use of lubricating ointments with anesthetic properties on endotracheal tubes. He found that dipping the endotracheal tube in water prior to insertion was usually more than adequate to help facilitate passage through the vocal cords. Smith also recognized the role

contamination played in development of post-intubation tracheitis and stressed proper hand hygiene prior to intubation.

In 1954,[5] Smith outlined the advantages and disadvantages of pediatric endotracheal intubation. Pediatric endotracheal intubation permitted control of the airway when the head is inaccessible to the anesthetist, control of ventilation in the open chest, ventilatory assistance in the prone position, prevention of aspiration of intestinal contents, blood and tissues, removal of a bulky apparatus from the surgical field, better relaxation for abdominal surgery, and provision for resuscitation. Smith also noted the disadvantages, which included reduction of the tracheal lumen by presence of the endotracheal tube, longer induction time, deeper plane of anesthesia required for maintenance, post-intubation hoarseness and cough, chipped or dislodged teeth, irritation and injury of the pharynx, glottis and trachea, hypoxia, spasm and reflex activity, disturbances associated with extubation, kinking of the endotracheal tube, mainstem intubation, aspiration of the endotracheal tube, and impeding the work of the surgeon.

References

1. **Smith RM. The prevention of tracheitis in children following endotracheal anesthesia. *Curr Res Anesth Analg* 1953 Mar-Apr;32(2):102-12.**
2. **Gilles J. Endotracheal methods; their use and abuse. *Curr Res Anesth Analg* 1951 Nov-Dec;30(6):343-7.**
3. **Moss MK. Endotracheal Anaesthesia. *Curr Res Anesth Analg* 1930;9:168-171.**
4. **Baron SH, Kohlmoos HW. Laryngeal sequelae of endotracheal anesthesia. *Ann Otol Rhinol Laryngol* 1951 Sep;60(3):767-92.**
5. **Smith RM. Indications for endotracheal intubation in pediatric anesthesia. *Curr Res Anesth Analg* 1954 Mar-Apr;33(2):107-14.**

Early Pediatric Regional Anesthesia: Contributions from Around the World

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Dr. Meredith Campbell (New York, NY) published the first report of pediatric caudal anesthesia in 1933.[1] Campbell utilized caudal anesthesia with 2% procaine for urological exams and minor procedures in boys 4 to 14 years of age. She claimed a 90% success rate with only minor complications.

The technique lay dormant for nearly 30 years before being rediscovered by Dr. Peter Spiegel in Rio de Janeiro, Brazil. Spiegel did not know of Campbell's work. In the 1960s, Dr. Philip Bromage had visited Rio; he and Dr. Armando Fortuna encouraged Spiegel to try caudal anesthesia for pediatric surgery. He was aware of the use of intramuscular thiopentone and began using that for perioperative sedation.[2] Spiegel published three articles between 1961 and 1965, two written in Portuguese and published in Brazil[3,4] and one written in English and published in the USA.[5] His first two papers (published in 1961 & 1962) were preliminary studies. His final paper was comprehensive and covered the period from November 1960 through July 1965. Four hundred twenty-five caudals were done. Infants and children up to fourteen years of age were included. In his earlier work, Spiegel used the following formula to determine the volume of local anesthetic injected: D=4+(C-15)/2, where D is the volume in ml injected and C is the distance in cm from the seventh cervical vertebra to the sacral hiatus. By the time of his 1965 publication, Spiegel determined lidocaine dosage by using a formula based on mg/kg: 5 mg/kg for perineal anesthesia, 7 ml/kg for T12 anesthesia and 10 mg/kg for T10 anesthesia. The following complications were cited: seven cases of systemic toxicity with one cardiac arrest requiring CPR, one accidental dural puncture, and frequent cases of hypotension (20% or greater drop from baseline). His success rate was 94-95%.

Dr. Italo Rodrigues was busy experimenting with pediatric regional anesthsesia during this same period. Rodgigues was a colleague of Spiegel and Fortuna and practiced in Rio. In 1959 he began using caudal and brachial plexus anesthesia for children, with over 250 cases reported. In 1964 he published his work on pediatric peridural anesthesia.[6] Thirty-six patients were included in the study. They ranged in age from four days to twelve years. Rodigues used lidocaine or mepivacaine (both with epinephrine) in concentrations ranging from 0.7% to 1.5%. No significant anesthetic complications were noted (and no total spinals), although four deaths occurred (none related to the anesthetic technique). Seven block failures were listed: in two cases, the block receded before the surgery was done, in the other five cases, three were incomplete blocks (the level was too low for the operation) and two were totally inadequate (one patient's block was determined to be paravertebral, not peridural and the other patient had an allergic reaction to the local anesthetic). Rodrigues advocated the use of peridural anesthesia for pediatric patients, even in high-risk patients and in those with previous complications from general anesthesia.

Dr. F. G. Ruston (Hamilton, Ontario, Canada) was another early proponent of pediatric regional anesthesia. Between 1954 and 1964 he published three articles on pediatric epidural anesthesia.[7-9] He often combined epidural and general anesthesia. Eighty cases were reported, with four caudal and 76 epidural blocks. Complications included two total spinals and one epidural hematoma (fatal).

Dr. Octavio Baquero and Dr. Fernando Vásques (Bogota, Columbia) reported their experience with pediatric caudal anesthesia in 1965.[10] One hundred cases were included in their study, but they had done over 300 caudals by the time that their paper went to press. The patients

were 68 boys and 32 girls, ranging in age from six days to fifteen years. They used Spiegel's dosing formula (D=4 +(C-15)/2). Their overall success rate was 87%. One patient had a seizure and was treated with oxygen and intravenous barbiturates. No adverse outcome occurred.

Dr. Armand Fortuna (Santos, SP, Brazil) made the next major contribution to pediatric caudal anesthesia in 1967.[11] One hundred seventy patients were included in his series. His success rate was 92-95%. Complications included: two seizures, two bloody taps, one case of restlessness/delirium, two cases of vomiting, two cases of transient apnea, and one inadvertent spinal block. Basic airway equipment and intravenous drugs were set up prior to performing the caudal blocks.

With the exception of Campbell's paper in 1933, the innovative research in pediatric regional anesthesia was begun in the 1960s. A significant portion of this work was done in Latin America and published in Spanish. Only one of Spiegel's three papers was published in English. Fortuna's paper was published in English and certainly did much to spread the knowledge of pediatric regional anesthesia to other parts of the world.

References

1. **Campbell MF. Caudal anesthesia in children. *Am J Urol* 1933;30:245-249.**
2. **Personal communication, Dr. Peter Spiegel.**
3. **Spiegel P, Carvalho AF, Faierchtein S. Anestesia peridural sacra em pacientes pediatricos. *Rev Bras Anest* 1961;11(Aug):139-155.**
4. **Spiegel P,Goncalves B. Anestesia peridural sacra em pacientes pediatricos. (II) *Rev Bras Anest* 1965;15(Oct-Dec):484-491.**
5. **Spiegel P. Caudal anesthesia in pediatric surgery; a preliminary report. *Cur Res Anesth Analg* 1962;41(2):218-221.**
6. **Rodrigues I. Anestesia peridural no paciente pediatrico. *Rev Bras Anest* 1964;14(April-June):116-130.**
7. **Ruston FG. Epidural anaesthesia in infants and children. *Can Anaes Soc J* 1954;1(1):37-44.**
8. **Ruston FG. Epidural anaesthesia in paediatric surgery. *Anesth Anal* 1957;36:76-82.**
9. **Ruston FG. Epidural anaesthesia in paediatric surgery: Present status in the Hamilton General Hospital. *Can Anaes Soc J* 1964;11(1);12-34.**
10. **Baquero PO, Vasques OF. Anesthesia caudal en pediatrica. *Rev Mex Anesth* 1965;24:101-117.**
11. **Fortuna A. Caudal anesthesia: A simple and safe technique in paediatric surgery. *Brit J Anaesth* 1967;39:165-170.**

Floyd T. Romberger, M.D. – Pioneering Indiana Anesthesiologist, Advocate for Physician Anesthesia and Organized Medicine

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Floyd Troutman Romberger, M.D., played an important role in the development of anesthesiology in Indiana. Born in 1887, Romberger was a native of Elizabethville, Pennsylvania; a town located about twenty-five miles north of Harrisburg. He obtained his medical degree from the University of Pennsylvania in 1909. Following graduation, he returned to Elizabethville, population about 1,000 residents, where he practiced general medicine as one of three physicians in town. He continued to practice in Elizabethville until World War One during which he saw eighteen months of service in the Army Medical Corp.

Soon after Romberger's return from WWI, he made the decision to move to Indiana. He obtained his Indiana license in 1920 and began a medical practice in West Lafayette, Indiana, population 3,830. Just across the Wabash River lay Lafayette, IN, population 22,456 with two hospitals. His initial listing in the American Medical Directory as an Indiana resident is from 1921 and indicates specialization in anesthesia. By way of comparison, Indianapolis at the time had a population of about 315,000. Only three physicians in Indianapolis indicated they were specializing in anesthesia, Arthur Guedel among them. By 1923, Romberger had become a member of the Associated Anesthetists of the United States and Canada, moved his practice to Lafayette, and declared himself a full-time anesthetist.

Romberger quickly became active in the Indiana State Medical Association (ISMA). In 1926, he became a member of the ISMA's Committee on Anesthesia and soon became the ISMA's Chair of the Committee on Postgraduate Study. In 1930, he began the first of thirteen years of service as a District Councilor ending with four years as Chairman of the Council. He also spent five years as an editor of the Journal of the ISMA. His involvement with the ISMA culminated in a year as President in 1947.

Romberger was convinced that the best route for anesthesia to travel for its "spiritual and professional growth" and its "just and lawful recognition" was through organized medicine.[1] He developed a plan for the formation of a Section of Anesthesia in the ISMA, which proved successful in October, 1934. Romberger served as the first Chairman of the Section. His Chairman's address at the Anesthesia Section's meeting on October 9, 1935, was titled "Organized Professional Anesthesia."

In addition to his contributions to organized medicine and anesthesia, Romberger was an active clinician and also contributed to the scientific understanding of anesthesia. He continued to practice anesthesia at both hospitals in Lafayette. This provided him the material to present a paper titled "Surgical Technique from a Study of 4000 Anesthesias" at the Third Annual Congress of Anesthetists in 1924, published the following year in Current Researches in *Anesthesia & Analgesia*. In March, 1947 his coauthored article, "Ten Thousand

Spinal Anesthesias: Five Thousand with Ephedrine Intrathecally–Random Comment," appeared in the *Journal of the ISMA*. That article was based on data collected on individual cards for cases done over nearly eighteen years.

Romberger fell ill in the fall of 1953 and died on New Year's Day, 1954. His thirty-three years of medical practice in Indiana saw major advances in anesthesiology as a recognized profession. Romberger played an important role in these advances.

1. **Romberger FT. History of Organized Anesthesia in Indiana *J Indiana State Med Assn* 1943;36:428-43.**

Grading of Patients for Surgical Procedures: Evolution and Controversy

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Nearly a century after the first ether anesthetic, the age of modern anesthesia was set to flourish. The 1940s represented a second revolution in medicine, from a mere art into a powerfully effective science.[1] The growth of the American Society of Anesthetists, the predecessor of the American Society of Anesthesiologists, reflected this dynamic change, and its members sought to distinguish themselves as an independent specialty, committed to the advancement of scientific research. One notable accomplishment was the ASA Physical Status Classification (ASA PS).

The purpose of the ASA PS was to study, examine, experiment and devise a system for the collection and tabulation of statistical data in anesthesia.[2] The authors specifically avoided the term operative risk, which may be of value in terms of prognosis, but useless from a statistical point of view. Through this taxonomy, they hoped to correlate the relationship between result, surgical procedure and preoperative condition, thereby promoting standardization of communication in research.

The original ASA PS had six categories. The first four referred to systemic disturbance, ranging from none to moderate, severe, and extreme. Five to ten clinical examples were given for each. Classes 5 and 6 were emergency categories and referred to emergencies from classes 1 and 2, and classes 3 and 4, respectively. A seventh class, containing the moribund patient expected to die in 24 hours, was later added.

Although it has undergone several changes, the original ASA PS shares many similarities with the one used today. Dripps proposed a revision in 1961,[3] reducing the number of categories from seven to five. In place of gradations of systemic disturbance, he used the terms healthy, mild, severe, and incapacitating disease. The modifier emergency replaced classes 5 and 6.

The strongest criticism of the ASA PS is that it has ironically developed into a measure of operative risk, perhaps because it is the only descriptor of overall preoperative condition consistently recorded. The largely retrospective studies that have shown correlation between surgical mortality and ASA PS have reinforced the idea that sicker patients are more likely to die.[4]

But as Owens argued, anesthesiologists should not confuse physical status and operative risk. Although studies have shown a correlation between the two, the relationship is largely surgery specific. Operative risk is different because of the surgery; the physical condition of the patient is the same.[5,6]

This has lead Lema to propose expanding the ASA PS into the realm of operative risk predictability. With the aid of computer modeling, prospective assignment of risk could be accomplished by considering not only preoperative status, but anesthetic technique, the nature of the operation, as well as surgical and anesthetic skill.[7]

The pioneers of the specialty demonstrated remarkable foresight in their publication of the ASA PS. Future adaptations, which might employ technology to more precisely quantify risk, will honor this tradition of innovation and growth.

1. **Kitz R. Anesthesia, 3rd Ed., Ed. RD Miller. 1990 p. 10.**
2. **Saklad M. Grading of patients for surgical procedures. *Anesthesiology* 1941;2:281-4.**

3. **Dripps R, Lamont A, Eckenhoff JE. The role of anesthesia in surgical mortality. *JAMA* 1961;178: 261–6.**
4. **Keats AS. THE ASA classification of physical status – a recapitulation. *Anesthesiology* 1978;49(4):233-6.**
5. **Owens WD, Felts JA, Spitznagel EL Jr. ASA physical status classifications: a study of consistency of ratings. *Anesthesiology* 1978;49(4):239-43.**
6. **Owens WD. American Society of Anesthesiologists Physical Status Classification System is not a risk classification system. *Anesthesiology* 2001;94(2):378.**
7. **Lema MJ. Using the ASA Physical Status Classification May Be Risky Business. *ASA Newsletter* 2002;66(9).**

Blood Banking and Anesthesia: A "Natural" Convergence in the 1930s

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In the early 1930s, transfusion of blood involved bringing of donors on site and directly transfusing blood from donor to recipient through a steel needle which was held in place for the duration of the transfusion. Placing the steel needle and keeping it in place requires great skill, especially in children. Anesthesiologists routinely placed this sort of intravenous access in the operating room and were already providing hospitalized patients with intravenous access in difficult cases.[1]

In 1933, Dr. Charles H. Mayo, recognizing the unique expertise and availability of the anesthesiologists, asked Dr. John Silas Lundy, the head of the anesthesiology section at the Mayo Clinic, to improve the Clinic's pediatric transfusion practice.[2] Lundy saw this as an opportunity for anesthesiologists to expand their practice and within a year the anesthesia section assumed responsibility for all transfusions at the Clinic. This led to a considerable increase in the number of transfusions, the majority of which were undertaken perioperatively.[1,3,4]

Lundy also realized the great need and opportunity for improvements in the rudimentary field of transfusion. In 1935, in order to overcome the barrier of patient to patient transfusion, Dr Lundy developed the practice of refrigerating blood for later administration. This was the first documented blood bank in Northern America.[2,5] He went on to invent a rapid infusing hand roller for the rapid administration of blood[6] and in 1938 he investigated the quick freezing of blood as a means to prolong shelf life of banked blood.[7] In 1942 Adams and Lundy suggested a hemoglobin transfusion "trigger" of 8 to 10 grams per deciliter for patients of poor surgical risk.[8]

Lundy kept detailed data and records of all transfusion performed at St. Marys Hospital, and soon gained a national reputation as an authority on transfusion and blood banking.[1,3,4]

References

1. **Lundy JS, Tovell RM. Annual report for 1934 of the section of anesthesia: Including data on blood transfusion. Proc. Staff Meet. *Mayo Clin* 1935;10:257–272.**
2. **Statement of Dr. John S. Lundy, Seattle, Washington to Dr. Waltman Walters Rochester, Minnesota, November 15 1967, obtained from the Mayo Historical Suite.**
3. **Lundy JS, Tovell RM, Tuohy EB. Annual report for 1935 of the section of anesthesia: Including data on blood transfusion. Proc. Staff Meet. *Mayo Clin* 1936;11:421–432.**
4. **Lundy JS, Tuohy EB, Adams RC. Annual report for 1936 of the section of anesthesia: Including data on blood transfusion. Proc. Staff Meet. *Mayo Clin* 1937;12:225-238.**
5. **Moore SB. A Brief History of the Early Years of Blood Transfusion at the Mayo Clinic: The First Blood Bank in the United States (1935). *Transfusion Medicine Reviews* 2005;19:241-245.**
6. **Lundy JS. Blood transfusion. *Surg Clin North Am* 1934;14:721–727.**
7. **Correspondence between Dr. JS Lundy and Mr. JC Hormel June 1938, obtained from the Mayo Historical Suite**
8. **Adams RC, Lundy JS. Anesthesia in cases of poor surgical risk. Some suggestions for decreasing the risk. *Surg Gynecol Obstet* 1942;64:1011–1019.**

Noel A. Gillespie and Albert Schweitzer

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For many years, a bust of Albert Schweitzer greeted patients and visitors to the Wisconsin General Hospital as they entered the lobby. The bust was a gift of Noel Gillespie in 1954 to recognize the great theologian, philosopher, musician and missionary doctor.

Noel Alexander Gillespie was a colleague of Dr. Ralph Waters at the University of Wisconsin beginning in 1939. He took responsibility for the annual Anesthesia Department statistical reports using the Hollerith punch card system, and authored the classic text entitled Endotracheal Anesthesia (1941).

Gillespie had more than a passing interest in Albert Schweitzer, having traveled to French Equatorial Africa with him in 1924 as his companion, secretary and English tutor. Schweitzer was returning to the mission hospital at Lambarene after an absence forced by the First World War. His wife, being in poor health, was not able to make the trip. On an English fundraising lecture-concert tour in 1922, Schweitzer met Gillespie's mother, Emily Rieder. They subsequently corresponded and the suggestion of Noel's accompanying Schweitzer must have been made. Schweitzer put the decision to the eighteen-year-old Oxford chemistry student in the early winter of 1923:

> **I am looking for a young man who will accompany me in Africa for six months as companion, secretary, and above all, as professor of English. We will leave the end of January. We will travel a month to the English Cameroons, and from there we will go to Lambarene. There you will help me to install the house and organize the hospital.**

Noel's decision was by way of a telegram to Schweitzer sent by his mother. A return letter gives travel plans and a wardrobe list including "three khaki outfits, three white, a black dinner jacket, one sun helmet…six soft cotton shirts which take perspiration well…." In late January came the final travel itinerary: meet in Paris for a February 18th departure from Bordeaux on the steamer *Orestes*.

Gillespie's letters to his mother begin off the Portuguese Coast with a description of the Marcoonist, dinner with the captain, and mention of a Viennese lady, "She apparently suffers, poor thing, very badly from seasickness…" Nearly a month later Noel writes, "…the fundamental difficulty with our lady passenger's health is that she is going to have a baby…." Two days later Schweitzer is called in for the delivery and Noel becomes the newborn's nurse.

After a stop in the Cameroons, Schweitzer and Gillespie board the *S. S. Europe*, sail across the equator, and reach Cape Lopez. A final two-day river trip brings them to Lambarene on Easter Sunday, April 20, 1924. Noel's letter of May 6 describes his first operation as assistant surgeon. He nearly collapsed at the sight of an injured hand combined with the heat and ether smell. During the next months he became proficient with the microscope and with intravenous injections. He traveled up the river and was struck with the incongruity of European civilization against the wildness of the primeval forest. Gillespie stayed with Schweitzer at Lambarene until July.

He returned home to England and his studies at Oxford where he entered medical school, undoubtedly influenced by his experiences in Africa. He later received a doctorate in medicine, writing the first Oxford University thesis on the topic of anesthesia.

References

1. **Noel A. Gillespie Papers, Wisconsin Historical Society, Madsion, WI.**
2. **Haygood WC. With Schweitzer in Lambarene: Noel Gillespie's Letters from Africa. *The Wisconsin Magazine of History* 1971;54(3):166-203.**

I Passed My First Test: The APGAR Test or, Dr. Apgar's Life in the US Postal Service Philately

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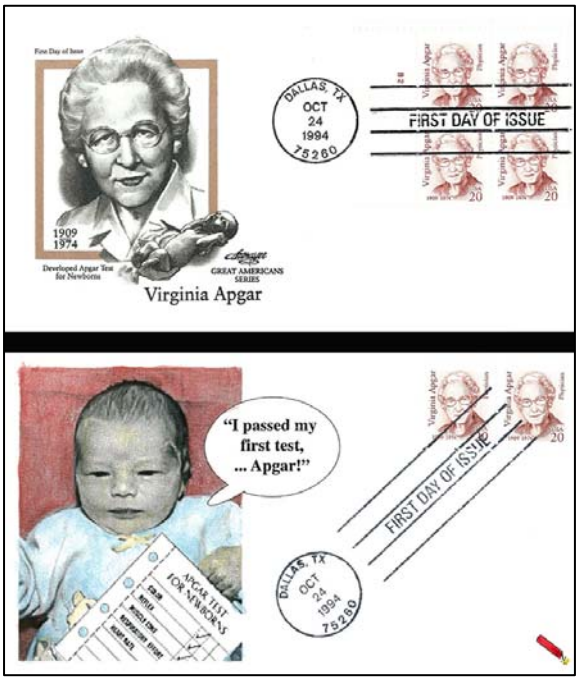
The Apgar Score is a universal assessment for neonatal well-being at one-minute and five-minutes after delivery. Many people are unaware that the originator of the APGAR Score was Virginia Apgar, M.D., an anesthesiologist. Also, she is the only American anesthesiologist to have a U.S. Postal Service (USPS) stamp and other philatelic items released in her honor. This abstract presentation briefly reviews her life and 15 of the USPS First Day Covers (FDCs) that commemorated this event on October 24, 1994 . FDCs are specially designed, commemorative envelopes that bear new stamps and are postmarked on the first day of release. Usually they are released from one location following a first day celebration ceremony.



Dr. Apgar was born June 7, 1909, in Westfield, NJ, the youngest of three children. An older brother died at age 3, and this may have influenced her interest in medicine. She graduated with an AB degree from Mount Holyoke College in 1929 and an MD degree from the College of Physicians and Surgeons, Columbia University, in 1933.

She was in a surgery internship with the famous Dr. Whipple when he encouraged her to go into anesthesiology, a specialty still in its early years. Her initial training occurred in New York City. This was followed by six months with Dr. Ralph Waters at the University of Wisconsin in 1937 and six months with Dr. Emory Rovenstine back in NYC at Bellevue Hospital.

From 1938-1959 she was at Columbia Presbyterian Medical Center as Director of the Division of Anesthesia. In 1949 she was appointed as Professor of Anesthesia, the first woman to be so honored at this institution.

Prompted by a conversation with a medical student, Dr. Apgar devised her scoring system for assessing the status of newborn infants that was first presented at a meeting in 1952 and published in 1953. In 1962 the acronym of APGAR (Appearance, Pulse, Grimace, Activity, Respiration) was applied to her newborn infant assessment.

In 1959 she obtained an MPH degree at Johns Hopkins University and became Professor of Pediatrics at Cornell University. She also joined the March of Dimes as head of the Division of Congenital Malformations until 1968. In 1961 she received the Distinguished Service Award from the ASA, and she has received many other awards. The American Academy of Pediatrics

has an annual Virginia Apgar Award for achievement in perinatal medicine. Also, she had a posthumous induction into the National Women's Hall of Fame in 1995.
She died on August 7, 1974, in her sleep. At that time she was senior vice president in charge of medical affairs with the March of Dimes.

Her hobbies included the construction of and playing stringed instruments, such as the violin and cello, and flying. In addition, and most pertinent to this display, was her great interest in stamp collecting. She was a life-time member of the American Philatelist Society, and it is reported that her collection numbered 50,000 stamps. This display shows fifteen different FDCs that were used to commemorate the introduction of the 20 cent Apgar stamp on October 24, 1994.

Chloroform Anesthesia Prior to Execution by Hanging in the 1800s

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The death penalty has been codified as punishment for specified criminal offenses since the incorporation of the United States as a nation. In the 1800s execution sites became limited to correctional facilities and several states abolished the death penalty. Of interest to anesthesiologists, attention occasionally focused on alleviation of the pain and suffering associated with the means of execution.

In 1848 G.W. Peck opined, "If we have the right to hang a man at noon-day on the 15th of September, then it follows that we have a right to give him CHLOROFORM at noon-day, and hang him immediately afterwards, while under its operation… By this means we avoid for him, not only the pain of the actual killing, but the agonizing instant of certain apprehension. The sponge is applied to his nostrils, and all that he is aware of is, that he sinks calmly (perforce) into a sleep, out of which he is to awaken on the other shore of the river of death; … it seems a shame to deprive a fellow-being of life, however necessary it may be to do so, and howsoever just his doom, by a mode which we instinctively desire to be delivered from, when we have another at our command. We surely ought to have more compassion for the worst of men than for a dog …"[1]

Beach discussed various modes of executions, especially hanging. He included the possible use of chloroform which "can be depended upon to cause speedy and probably painless death."[2]

Prompted by Beach's article, Thornton proposed that since "… it is quite generally known, I apprehend, how easy and painless a death can be produced by the use of this powerful agent (chloroform)," a deliberate anesthetic death should be substituted for the more "barbaric" hanging. He suggested medical experimentation on the chloroformed, condemned man, albeit under the auspices of a government appointed medical review board composed of "our most accomplished experts in comparative anatomy and savants in medicine." He continued, "… he shall be kept under the influence of the anaesthetic a sufficient length of time to insure the success of the experiment… and then the anaesthetic shall be pushed to the extreme, and so bring to a close the life which was condemned because it took a life."[3] Thus, the condemned would not be allowed to return to consciousness.

Bigelow, remarkably arguing that suffocation was painless, suggested that the condemned be rendered senseless by asphyxia prior to hanging. "I therefore suggest that the cap now always drawn over the head of the criminal be made of rubber or other impervious material, secured at the neck closely by a string or elastic, … I doubt whether the criminal would know even of the approach of insensibility. It must occur in a few minutes, however, much as if chloroform were introduced within the cap, and the drop could then be called upon to terminate the execution while the prisoner is unconscious. He would be confined exactly as now, or as in common anaesthesia where resistance is frequent, a medical attendant pronouncing upon the insensibility."[4]

We found no cases where either chloroform was administered or asphyxia produced prior to the actual hanging.

References

1. ***American Whig Review*** **1848;8:283-297.**
2. ***Medical Record*** **1886;30:89-90.**
3. ***Medical Record*** **1886;30:222-3.**
4. **Execution by Hanging, in Surgical Anaesthesia; addresses and other papers. (Boston: Little, Brown, and Company, 1900).**

Crawford Long, MD: Doctor's Day Celebration in US Postal Service Stamp

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The annual commemoration of Doctor's Day celebrates the first use of ether for surgical anesthesia on March 30, 1842, by Crawford Long, M.D. On April 8, 1940, the U.S. Postal Service (USPS) commemorated this event by issuing a stamp in Long's honor. This abstract reviews Long's life and shows fourteen different First Day Covers (FDCs) that celebrated this event. FDCs are specially designed, commemorative envelopes that bear new stamps and are postmarked on the first day of release. Usually they are released from one location (in this case Jefferson, GA) following a celebration ceremony.

Dr. Long was born on November 1, 1815, in Danielsville, GA. By the age of fourteen he was a student at Franklin Academy (later the University of Georgia), graduating with a Master of Arts at age 19. He taught school for one year at the Danielsville Academy and briefly "read medicine" with Dr. George R. Grant of Jefferson, GA. He attended medical school for one year at Transylvania University in Lexington, KY, transferred to the University of Pennsylvania and graduated in 1839. For 18 months he did hospital work in New York City, returning to Jefferson in 1841 and spent the remainder of his life in Georgia.

While a medical student and early in his tenure as a physician, Dr. Long participated in ether frolics, witnessing injuries and bruises that he and others sustained without memory of the events. He applied this observation to medicine, and on March 30, 1842, he administered ether to his friend James Venable for the excision of a cyst on his neck. Venable neither felt nor remembered anything, and he had a second neck cyst removed on June 6, again under the influence of inhaled ether.

In his rural, isolated location Long had occasion to use ether only a couple of times a year. Because many in Georgia negatively questioned the propriety of ether anesthesia, he delayed reporting his experiences until 1849, and then only after debate began about who had discovered ether anesthesia. After a thorough investigation it was found that Long was indeed the first, although not the most publicized, physician to administer ether anesthesia.

Two cases he described proved ether's benefits. In one patient he excised "three tumours the same day: the inhalation of ether was used only in the second operation, and was effectual in preventing pain, while the patient suffered severely from the extirpation of the other tumours."[1] When amputating two fingers the patient "was etherized during one amputation, and not during the other; he suffered from one operation, and was insensible during the other."[1] Dr. Long administered ether to his wife in 1847 to alleviate the pains of childbirth, the

same year that Simpson in Scotland is credited with the first obstetric anesthetic. Dr. Long died on June 16, 1878, after administering ether analgesia for childbirth.
The 14 FDCs in this presentation elucidate Dr. Long's importance to medicine and ultimately to our specialty.

Reference

1. Taylor FL. Crawford W. Long and the Discovery of Ether Anesthesia. New York: Paul B. Hoeber, Inc., 1928.

Who gave the first anesthesia in Argentina, a Brit -or- a Yankee?

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For over 150 years there has been controversy regarding who gave the first anesthesia in Argentina. In the 1840's the British Medical Dispensary (today British Hospital of Buenos Aires) developed a group that met annually before the Philanthropic Society that maintained the hospital, where diverse reports related with the functions of the Dispensary were presented. Days later, these reports appear in the newspaper, published in English *British Packet and Argentine News* that was published in Buenos Aires.

In the June 18, 1848 issue it was mentioned that Dr. John W. Mackenna, who was a surgeon at the hospital, presented a report claiming that he gave the first successful anesthetic with ether and subsequently the use of chloroform to a woman who had an osteotomy of the femur to repair a fracture that had healed badly (British Packet, July 8). However, Mackenna did not mention the date.

Currently, the British Hospital exhibits in the lobby of the main entrance, a brass plaque that reads: "In the British Hospital, Buenos Aires, in the year 1847, Dr. John McKenna performed the first operation under anaesthesia in Argentina."

In the same publication, but on the first page of the September 4, 1847 issue appeared an article titled "Vapour of ether" and as subtitle "To prevent pain in surgical operations." It went on to describe that the operation had been a correction of strabismus in a male patient of around 30 years of age who received a general anesthesia with ether. The anesthesist and surgeon was Dr. Tuksbury, as witness it listed Dr. Aubain. The intervention was realized successfully in Dr. Tuksbury's clinic located at the street of Peru, today in the San Telmo district of Buenos Aires.

John William Mackenna. (The brass plaque of British Hospital wrote "McKenna") Was born and was granted a doctorate in medicine in England. His diploma was validated in September of 1840 in Buenos Aires. He acted as surgeon in the British Medical Dispensary (British Hospital) of Buenos Aires between the years of 1844 and 1853, returning later to his country.

Jacob Merrill Tewksbury. (The newspaper wrote "Tuksbury") Was born on February 7, 1814, in Oxford, Maine, USA. He studied medicine with his father who was a physician, and attended the regular courses of the medical department of the Bowdoin College, graduating in medicine (MD) in 1836 at the age of 22. He worked in Oxford and Wiscasset. After practicing several years he left for Buenos Aires where he practiced as a medical doctor and dental surgeon. He applied the ether in his "clinic" and after married Emilia Ana Sutton (1830-1901) from Buenos Aires. On September 26, 1849, Tewksbury returned with its wife to San Francisco, California, attracted by the gold rush acquiring fame and wealth.

Teodoro Aubain. Born in 1814 in France, graduated as doctor in his native country. In 1842 he confirmed his title in Buenos Aires. He assisted Tewksbury in 1847 during the correction of a strabismus. A street in Buenos Aires has been named after him.

The controversy has been solved according to the sources mentioned the first anesthesia in Argentina, was administered by Dr. Jacob Merrill Tewksbury (U.S.A., 1814-1877), a medical doctor and dental surgeon from the USA. The operation was carried out in his clinic of

Buenos Aires during the last days of August of 1847. The anesthetic used was ether, administered to a man of about 30 years of age, for an operation of strabismus done by the same Tewksbury. Teodoro Aubain witnessed it and assisted. There were no anesthetic or surgical complications.

Dr. Victor Goldman 1903-1993: Close but No Cigar!

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Dr. Victor Goldman was the doyen of dental anaesthesia in the post war years in Central London. Hugely influential in his chosen field, he wrote one of the most popular textbooks fo anaesthesia which ran to four editions and designed a simple vaporiser that remained the one of choice for four decades in dental practice. His very high profile life somehow never translated into an influential political career within anaesthesia and he virtually disappeared following his retirement in the mid 1960s.

Goldman was born and educated in Birmingham and qualified from the Birmingham Medical School in 1927 and after a spell in general practice, during which time he started to specialise in anaesthesia, he moved down to London and became unofficially apprenticed to Ivan Magill. In 1935 he was appointed as a trainee to the Royal Free and Eastman Dental hospitals. It was in this latter post that he started using vinesthene and designed his own vaporiser for its administration. He passed his DA in 1936 and in the same year described a new laryngoscope. He was now able to take honorary consultant posts in a variety of London hospitals, earning his money through private practice.

Goldman was a great teacher and in 1938 he started a series of teaching courses that lasted beyond his retirement. Hundreds of anaesthetists from all over the world attended these teaching sessions which were both theoretical and intensely practical. He joined the army at the outbreak of the Second World War and was transferred to India in 1941 where he spent much of his time organising effective teaching for those in his command. He continued to publish and lecture during this time and then returned to London in 1947.

His book Aids to anaesthesia had been published just before he went away and subsequent revisions proved very popular. He had always taken a great interest in collecting data on patient safety and was a constant campaigner for greater transparency in the reporting of morbidity and mortality. When halothane was introduced in the mid 1950s, Goldman introduced his special vaporiser which proved to be one of the most popular simple draw-over vaporisers ever made. In the 1960s Goldman travelled the world on a series of lecture tours. He went to the USA, Canada, Sweden, Finland, Australia and the Far East, South America and South Africa. At each venue he was surrounded by those who had attended his courses or who knew of his writings. His publications continued right up to his retirement and he then developed into a reliable and thoughtful opinon in medico-legal cases.

He married twice but had no children and after his second wife's death in 1969 he became more reclusive although he still managed a paper in *Nature* when 66 years old. Following cataract surgery in the early 1970s his eye sight deteriorated rapidly until he became totally blind by 1985. He was made an Honorary Member of the Association of Anaesthetists of Great Britain and Ireland (AAGBI) in 1980. In 1984 an eponymous lecture was initiated by the Royal Free Hospital which was awarded biennially until 1995 when it fell into abeyance until it was restarted last year by the AAGBI.

Victor Goldman had a full and highly productive career in anaesthesia. He outlived his generation and on his death no obituary was written and his name began to be lost.

He is worthy of great recognition.

Are Greed and Villainy Inherited?
The Case of Dr. William James Morton and His Father William T.G. Morton

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Richard J. Wolfe, the former Curator of Rare Books at Harvard Medical School, has changed our opinion of William T.G. Morton's probity with the publication in 2001 of his book Tarnished Idol. In the opening chapters Wolfe meticulously documents Morton's travels and activities during the six year period before he settled into busy dental practice in Boston in 1844. Wolfe summarizes his findings thus: "Morton ……. (was) possessed of an unscrupulous character – indeed, perhaps even a criminal mind – that led him to lie, steal and commit gross misdeeds in order to achieve his goals which, all evidence indicates, was the pursuit of money, no matter how gained." Careful reading of Wolfe's book reveals a strong anti-Morton bias but there is no denying the evidence he presents about Morton's misdeeds in business. It is not unreasonable to assume that Morton's lifelong struggle with Dr. Charles Jackson to claim priority was also motivated by greed.

During a visit to William T.G. Morton's grave and monument in the Mount Auburn Cemetery, Cambridge, Massachusetts I observed that on the adjacent headstone for his son William James Morton, MD (1845 – 1920), there appears the following inscription under his dates and places of birth and death: DEVELOPED HIGH FREQUENCY CURRENT 1886. This struck me as a remarkable claim. I investigated this claim quite carefully and found that it was and is a lie.

This led me to study William James Morton's life and career in more detail. There is little in his career to contradict my findings that he was also a greedy villain. The only difference is that his behavior worsened as he got older and he was sent to jail for large scale fraud in his sixties. Although he achieved success and modest renown as a neurologist in New York City there are aspects of his life and career that parallel the most disreputable elements of his father's life. This raises the question: Is criminality an inherited trait or is it the result of the criminal's family environment?

I am not knowledgeable enough to answer this question and, so far, I have not consulted any criminal psychologists. The listener should judge for him or herself.

Nothing in this investigation should take away from the importance of the older Morton's public demonstration of the use of ether to abolish the agony of surgery.

Manuscripts

The Abajian Scales

The Untold History of John Abajian, Ed Brazell, and the University of Vermont's 1956 to 1959 Halothane Research

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From 1956 to 1959, the University of Vermont (UVM) Division of Anesthesiology was one of three centers in the United States studying the new anesthetic agent halothane. The publication of their results in an October 1959* JAMA *article, with an emphasis on precision vaporization using an innovative modification of the copper kettle, contributed to the acceptance of halothane into clinical practice. This article offers a behind-the-scenes look at the UVM halothane study – its origins, execution, conclusions, and aftermath – and the careers of UVM Anesthesia Division Chairman John Abajian, M.D., and his Director of Research, Edward Brazell, M.D.

Gino Dente, M.D., leans back in his favorite chair and thinks back to a conversation over a half century ago. "We had a student visiting us from England, and he mentioned a Dr. Raventos and asked if I had ever used halothane. Well, I told him that I had never even heard of it," recalls Dente, then a 39-year-old Assistant Professor of Anesthesiology at the University of Vermont (UVM). "That piqued my curiosity though, so I decided to write a letter to Dr. Raventos and ask him some questions, and a short time later he sent me two bottles of halothane. We had absolutely no idea how to use it. I gave one bottle to Ernie Mills at the DeGoesbriand (Bishop DeGoesbriand Hospital, Burlington), and kept one bottle for myself at the Fletcher (Mary Fletcher Hospital, Burlington) and we tried it."

So began UVM's halothane research study in November 1956. One of three centers in the United States studying the agent, by mid-1959 UVM anesthesiologists and CRNAs had performed over 5,000 halothane anesthetics and perfected its delivery with an innovative modification of the copper kettle. The publication of their experience in an October 1959 *JAMA* article, emphasizing the then-controversial importance of precision vaporization, contributed to the acceptance of halothane into clinical practice in the United States.[1]

"An unusual medical student: apparently, he knows everything."

Fig. 1. John Abajian in 1958

The driving force behind the halothane study, behind everything that went on in UVM's Anesthesia Division in the 1950's, was its controversial Chairman, "Big John" Abajian M.D. (Figure 1). He was a man with a keen intellect, innate curiosity, and boundless energy. He was also opinionated and volatile. "I don't keep my problems and frustrations bottled up inside," Abajian said. "Like a safety valve, I blow off steam easily. Maybe some of the patient souls around me get singed now and then, but it sure prevents ulcers!"[2]

The son of Armenian immigrants, Abajian was born and raised in Providence, Rhode Island, and attended Long Island University and New York College of Medicine. He was an undistinguished student whom his classmates

described as "an unusual medical student: apparently, he knows everything – at any rate, he always has a logical answer to the problems besetting us."[3] But one of his professors, James Gwathmey, M.D., took a liking to him and in December 1939, after graduation and a residency with Gwathmey, Abajian was named UVM's first Anesthesia Division Chairman. In his early years in Burlington he earned the respect of UVM surgeons for his use of innovative regional techniques, especially peridural anesthesia, a skill he learned from New Orleans surgeon Charlie Odom, M.D.

In 1942 Abajian enlisted in the Army. For unknown reasons, he was considered to be unqualified to immediately serve as an anesthetist and was assigned to train with Emery Rovenstine, M.D., in New York for a few months. Abajian was humiliated by the decision but made the best of it, learning from Rovenstine and enjoying the city nightlife with him, claiming later, "They wanted to punish me, but the only thing that suffered was our livers!"[4] Finally in early 1943, at the request of General George Patton's Surgery Consultant – Charlie Odom - Abajian, then only 30-years-old, was named the Consultant Anesthetist for the U.S. Third Army. He spent the war traveling between field hospitals in Europe, educating anesthetists and medical officers in regional anesthesia techniques and ultimately winning the Legion of Merit for his work.

Abajian returned to Burlington in 1946 and began building his Anesthesia Division, adding new faculty, establishing an anesthesia residency training program, and spending increasing amounts of time in his lab. Over the next ten years, he conducted research and published articles on a variety of topics including oximetry, curare, hypothermia, blood preservation, cardiac monitoring, and blood volume. It was considered solid but relatively obscure work. He organized the Vermont-New Hampshire Red Cross Blood Bank, the second of its kind in the country, and even started his own cable TV company. But Abajian's restless mind remained unsatisfied and he continued to search for a research project that would burnish his reputation.

"John said that halothane was just another damn chloroform."

John Mazuzan, M.D., knew Abajian better than any man alive. The two first met in the mid-1950s when Mazuzan was a medical student at UVM. In 1958 Mazuzan, then a Massachusetts General Hospital anesthesia resident, arranged a rotation in Burlington to work with Abajian and get a first-hand look at the new anesthetic agent he was hearing about. He must have made a good impression on Abajian during his stint at UVM – upon completion of his residency in August 1959, Abajian hired him and they soon became close friends.

Mazuzan recalls Abajian's initial opinion of halothane: "John said that halothane was just another damn chloroform and wouldn't have anything to do with it. But Gino conned him into trying it and he was blown away by how smooth it was!" The agent may have been smooth, but the anesthetics were not. "A couple of times we had trouble with it because it was a very potent anesthetic," says Dente in an understatement. As reported in the first presentation of the halothane study (at the October 1957 ASA "Work in Progress" program), "three cardiac arrests and frequent severe hypotension from overdosage of Fluothane" had been encountered in UVM's first hundred halothane anesthetics.[5]

"I had forgotten to ask Dr. Raventos for the instructions," jokes Dente. "Initially we tried to give it open-drop, like ether, and that was a mistake." Abajian, recognizing halothane's potential, pushed ahead anyway. He realized that control of the potent new agent with precision vaporization was the key to its safe use and searched for the right delivery system. Abajian thought that a semi-closed circuit with Lucien Morris' copper kettle might work, but no one knew how temperature fluctuations of the kettle would affect its output of halothane. He turned to his new Director of Anesthesiology Research for help.

"You know the Abajian scales, they're really the Brazell scales."

Fig. 2. Ed Brazell in 1958

Ed Brazell, M.D., was as different from Abajian as a person can be – he was introverted, cerebral, and patient (Figure 2). One of his hobbies was grinding telescope lenses. Born in Iron River, Michigan, Brazell was interested in a career in medicine while in high school, but got sidetracked after graduation, lured to Florida for thirteen dollars, a free bus ticket, and a chance to play trumpet in a band. Three years later, in 1941, he graduated from the University of Florida with a Physics degree and a Phi Beta Kappa key.

During World War II, Brazell worked on radar at the M.I.T. Radiation Laboratory and then in 1946, with government funding for military research drying up, migrated to California and spent two years as an electronics engineer in the Navy's new guided missile program.

At a meeting in New York in early 1948, Brazell made the acquaintance of another wartime radar researcher, Henry Abajian - John's brother. After a year working for John Abajian as a research assistant on a cardiac muscle project, he finally realized his dream and was accepted into UVM College of Medicine. "Ed was a genius, one of these oddball guys that John convinced to go to medical school," recalls Mazuzan. "He was an engineer too and John really liked engineers. John was a frustrated engineer himself." Not surprisingly, Abajian hired Brazell when he finished his anesthesia residency in July 1956 and named him Director of Anesthesiology Research (Figure 3).

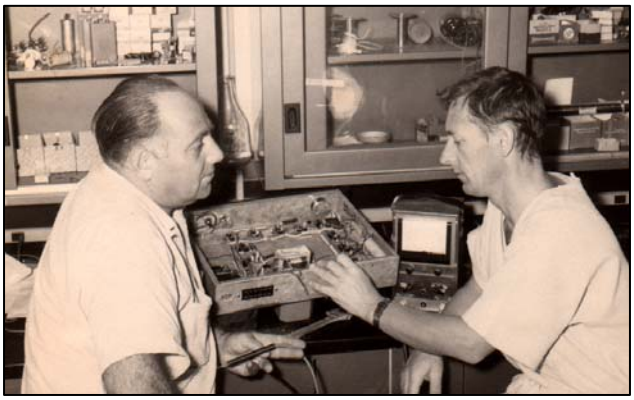

Fig. 3. John Abajian and Ed Brazell in their lab

Brazell put his physics and engineering background to work on the halothane project. In the laboratory, using a deceptively simple system with an oxygen flowmeter, copper kettle, and burette, he measured halothane gas volumes at different temperatures, and was thus able to predict exact halothane outputs and concentrations at various kettle flow rates (Figure 4).

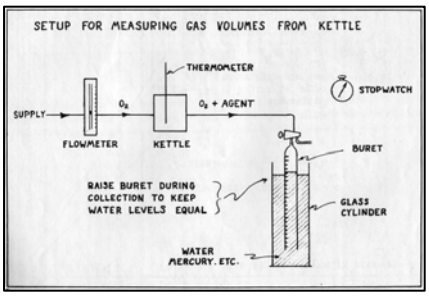

Fig. 4.

With an infrared spectrophotometer and the formulas he had derived, Brazell then measured the halothane and oxygen uptake of fifty patients and was able to control inspired halothane concentrations in a semi-closed circuit with a copper kettle to within 0.1% (Figure 5).

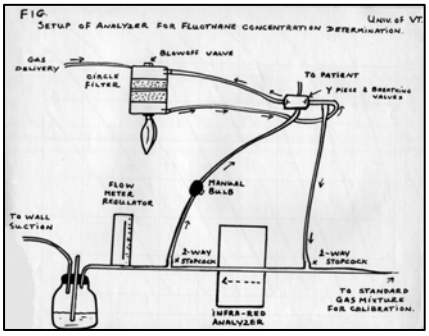

Fig. 5.

Finally, Brazell concocted a set of temperature-corrected flowmeter markings for the copper kettle, calibrated for halothane and based on a five liter total gas flow – what came to be known as the "Abajian scales" (Figure 6). It was a system so simple that even an anesthesiologist with no experience with the kettle could precisely control a halothane anesthetic. "You know the Abajian scales, they're really the Brazell scales," says Mazuzan. "Ed did most of the work on that and figured it out. It was pretty damned ingenious."

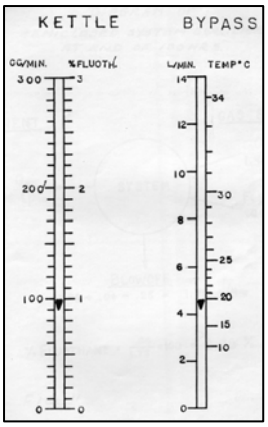

Fig. 6. The Abajian scales

"Fluothane … approaches the ideal anesthetic more closely than any of the agents previously and presently used for general anesthesia."

Abajian now had the precision vaporization system that he wanted and halothane became the standard anesthetic agent at UVM. From May 1957 through March 1958, 41% of all anesthetics in Burlington – virtually all the general anesthetics – were performed with a pure halothane-oxygen technique (Figure 7). "John didn't use Pentothal for induction and he didn't use nitrous oxide," remembers Mazuzan. "He wanted to test halothane in isolation, without other agents, which made some sense. John always contended that he did this because he wanted to see what halothane as an agent would do, could do, and could it be done safely?"

Fig. 7. CRNA Betty Wells administering halothane with a copper kettle in 1957

By March 1958, Abajian and his colleagues had given over 1,500 halothane anesthetics and presented their findings at the New England Assembly of Nurse Anesthetists.[6] In his lecture, Abajian stated, "Fluothane, with oxygen, in concentrations of 2% or less, approaches the ideal anesthetic more closely than any of the agents previously and presently used for general anesthesia… Fluothane anesthesia was safely administered to poor risk patients and patients of all ages for all types of surgery… No arrhythmias of any note were observed even with the routine use of epinephrine on neurosurgical cases… No alterations of kidney or liver function have been observed… Emergence from anesthesia was rapid and uneventful, with full consciousness and orientation returning in most patients within ten minutes… There was no problem of hypotension with carefully controlled administration… It cannot be overemphasized that it is vital for the concentration of Fluothane vapor to be known at all times and be adjustable within limits of 0.1%."

"John never invited him into the inner circle."

The halothane study began to wind down in the summer of 1959, with over 5,000 halothane anesthetics – some sources say 7,000 – performed at UVM by then. Ed Brazell wasn't there to see it. In November 1958 he left for Sutter Hospital in Sacramento, California, for reasons that are unclear to this day. "I don't know why Ed left, I really don't," says Dente. "I know there was a disagreement between him and John, there was some antagonism there, but it seemed none of my business."

Mazuzan is also unsure, but offers a clue: "I don't really know what happened. When I went back to Boston, Ed was in good stead, and all of a sudden a few months later I got a call saying that he had decided to go to California. But Ed was a young guy and John never invited him into the inner circle, never made him an offer to become a full partner. I don't know why."

It's possible that Brazell simply wanted to escape the brutal Vermont winters and have more opportunity to sail, one of his favorite pastimes. Whatever his motive, the move didn't work out well – two years after leaving Vermont, Brazell was diagnosed with acute leukemia. He died a few months later on July 16th, 1961, at age 43.

"Why don't you describe halothane as a wild stallion?"

In October 1959 John Abajian, Gino Dente, Ernie Mills, and Ed Brazell published their article "Experience with Halothane (Fluothane) in More Than Five Thousand Cases" in *JAMA* (Figure 8). Although more detailed than their earlier reports, their conclusions were not appreciably different than those of the 1958 lecture. Again they stated, "We want to emphasize that there is a definite need for precise knowledge of the exact concentration administered at all times. We place this safe value at 2%. However, it is possible that we may, in the future, revise this upward if experience permits." A discussion of delivery systems, emphasizing semi-closed circuits and including one of Ed Brazell's uptake diagrams (Figure 9), was included in the paper, as well as the statement "In order to deliver known concentrations of this agent, it is necessary to have special equipment and employ special techniques. A subsequent paper will deal with this aspect of the subject." But the promised article on the Abajian scales never appeared.

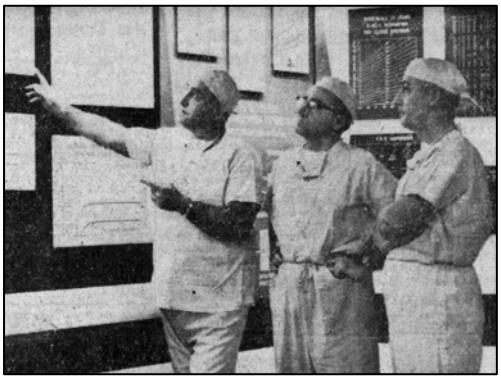

Fig. 8. John Abajian, Gino Dente, and Ernie Mills with the halothane exhibit in 1959

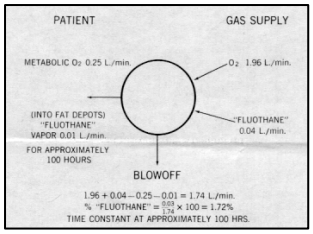

Fig. 9.

Abajian presented the halothane study at the 1959 ASA meeting in Miami, winning second prize for his scientific exhibit (Figure 10). Afterwards, he received numerous invitations to speak about the work and achieved minor celebrity status within the U.S. anesthesia community, but his emphasis on precision vaporization was controversial. "It was interesting how so many anesthesiologists objected to this idea of measuring what they're giving somebody," says Mazuzan. "A lot of people said the patient is the final arbiter of the dose. Well, that's true, but it doesn't mean that you shouldn't have a precise way of giving the dose. If you want to argue that, why don't you take all the markings off syringes! I told John, 'Why don't you describe halothane as a wild stallion? It's a beautiful horse running around out in the pasture, but it's wild. Once you get a harness on this horse, you can probably win the Kentucky Derby'."

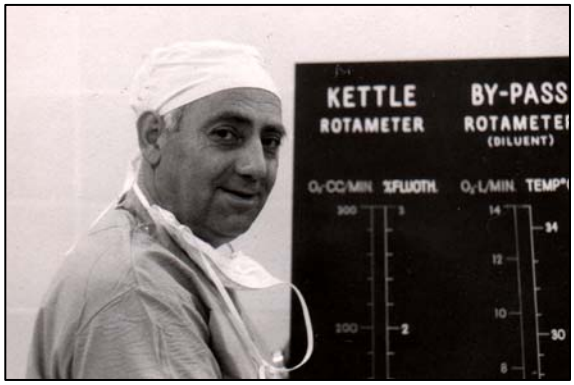

Fig. 10. John Abajian with the Abajian scales in 1959

Abajian's presentation style was also a problem. Mazuzan again: "His talk was a great talk. He was like some preacher going out on the stump. He was part showman, hidden amongst this great brainpower that he had. But John, as he often did, would carry things one step too far. He felt that some people objected to precision vaporization because they were afraid to learn a new agent and he would insult his audience." Mazuzan suggested that Abajian change the tone of his lecture, soften it, and incorporate a discussion of John Snow's work with chloroform over a century earlier. "John said, 'Well Mazu, I like that idea, using that history stuff'," says Mazuzan.

The biggest problem, though, was Abajian's contention that the copper kettle – with the Abajian scales, of course – was the most precise and thus safest halothane delivery system. By 1960 the Fluotec halothane vaporizer had been developed and the copper kettle was considered old-fashioned. "People bought Fluotecs," remembers Mazuzan. "John said it wasn't accurate and maybe he was right, at first, but the Fluotec gradually improved and

turned out to be a relatively inexpensive apparatus that you could add to any current equipment for a few hundred bucks."

"People may some day be flocking to UVM's College of Medicine to view a Fluothane Dome."

When halothane was released on the U.S. market, it was quickly accepted into clinical practice and Abajian's invitations to speak about the UVM halothane study dried up. He moved on to other projects, but the fire of ambition within him gradually died down and he spent the last years of his career playing the role of elder statesman and doing a few spinals in the cysto room at Mary Fletcher Hospital. Abajian retired in 1977 and was succeeded as Chairman of the UVM Division of Anesthesiology by his old friend and one-time protégé John Mazuzan. He died June 30th, 1996, a year after a stroke had silenced "Big John".

Ten years after his death, Abajian is primarily remembered for his halothane research, even though his other major accomplishments – the Third Army regional anesthesia training, VT-NH Red Cross Blood Bank, and UVM's anesthesia residency – had greater long-term impact. Abajian himself, in later years, didn't seem to consider the halothane study very important - in 1969 and 1995 interviews he barely mentioned it.[7,8] But the UVM halothane study is important. Halothane became the standard of care in the United States in part due to Abajian's (and Brazell's) work, and although the "Abajian scales" was a technological dead-end, the study's emphasis on precision vaporization foreshadowed the development of the sophisticated gas delivery systems and agent monitors used today.

Fifty years ago John Abajian saw the future but, as is often the case with visionaries, his view was a little hazy. In 1959 he said, only half-jokingly, "We may not be too far off base in predicting that Fluothane could supplant ether in eight to ten years. In fact, who knows but that people may some day be flocking to UVM's College of Medicine to view a Fluothane Dome, just as thousands of visitors each year have inspected the Ether Dome at the Massachusetts General Hospital in Boston."[9] Now that would be quite a sight.

References

1. **Abajian J, Brazell E, Dente G, Mills E. Experience with Halothane (Fluothane) in More Than Five Thousand Cases. *JAMA* 1959;171:535-540.**
2. **Meet Your Doctor: John Abajian, M.D. *Mary Fletcher Gazette* August 1958.**
3. **New York College of Medicine Yearbook 1937, 58.**
4. **Personal Communication, John Mazuzan, M.D.**
5. **Abajian J, Brazell E, Dente G, Mills E. Preliminary Clinical Appraisal of Fluothane (Abstract). *Anesthesiology* 1958;19:93.**
6. **Abajian J, Brazell E, Dente G, Mills E, Wells E. Fluothane: A Preliminary Clinical Appraisal. Presented at the New England Assembly of Nurse Anesthetists, March 24, 1958.**
7. **Interview of John Abajian, M.D., April 17, 1969, by Dr. Paul French, UVM College of Medicine Alumni Oral History Project, Bailey/Howe Library Special Collections, UVM.**
8. **Connor-Shapiro S. John Abajian, M.D. *UVM Anesthesia News* 1995;1:4-5.**
9. **Technique With New Anesthetic Brings Honors to City Doctors. *Burlington Free Press* December 29, 1959.**

The Role of the Education Process in the Development of Nurse Anesthesia

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The beginnings of anesthesia were known for the "occasional anesthetist," and the dedicated anesthesia care provider has evolved from medical student to nurse to anesthesia care team. The role of nurse anesthesia has evolved from untrained layperson to sisters to trained nurses. The last 100 years of nurse anesthesia has been marked by tremendous advances in both didactic and clinical education, as well as the proliferation of nurse anesthesia programs. Through the growth and refinement of these programs nurse anesthesia will continue to be a vital part of the surgical team.

The education process for a Certified Registered Nurse Anesthetist (C.R.N.A.) involves a master's degree as part of an advanced practice nursing program. The curriculum incorporates an extensive didactic program with a clinical practicum in a 24 to 36 month program, averaging 750 cases prior to graduation. Prior to beginning one of the 105 programs in the United States the nurse must first acquire at least twelve months experience in an intensive care unit. Around 1,500 C.R.N.A.'s graduate each year, and after graduation a certification examination must be completed with a minimum qualifying score of 450 prior to being allowed to practice. C.R.N.A.'s may practice under the direction of the surgeon (they are sole provider for 85% of anesthetics for America's 65 million people in rural areas[1]), or more conventionally they practice under the supervision of an anesthesiologist. Today approximately 27 million anesthetics are administered in the United States each year by 30,000 C.R.N.A.'s, and approximately 73% of those anesthetics are performed under the supervision of an anesthesiologist. The American Association of Nurse Anesthetists' 2002 Membership Survey reported that 40% of C.R.N.A.'s are employed as group employees, 33% are hospital employees, 13% are independent contractors, 6% are owners or partners in a practice, and 4% practice in the military or government.[2]

While at present the education process for C.R.N.A.'s is very organized and regulated, education of the early nurse anesthetists was hardly structured. At the time of the discovery of anesthesia, the nursing profession and schools of nursing were virtually nonexistent. The first nurses were male, as this type of duty was hardly befitting the Victorian image of the woman. Florence Nightingale is considered to have started nursing in the United States after training at Kaiserworth, Germany, at the Institute of the Protestant Deaconesses (circa 1836). She served in the Crimean War and with the horrific conditions in the hospitals wrote two separate books on the state of affairs with hospitals and nursing. She was credited with decreasing mortality rates in the British military hospital at Scutari in 1856 from 40% to 2%. She then started the first school of nursing in the United States (the Nightingale School and Home for Nursing) around 1860. Other nursing programs followed, with three nurses' training schools established in New York, New Haven and Boston in 1873. The American schools were "Nightingale" schools, modeled after her school at St. Thomas, and while the new nursing profession and women as caretakers was not initially universally accepted, physicians came to acknowledge nurses as capable of performing some very complex tasks.[3]

However, "nurse anesthesia" may actually predate the structured profession of nursing. When the Civil War broke out both armies' medical corps were unprepared for the degree of injuries, disease and infection rates, as well as the increased number of operations due to advanced weaponry. Nursing care was performed by lay people, such as poet Walt Whitman, author Louisa Mae Alcott, Red Cross founder Clara Barton and Mary Ann Bickerdyke, along with two thousand women in the North and South armies. Three million men fought in over 2,000 battles, and greater than 600,000 soldiers died.[4] Dr. W.T.G. Morton himself was very involved as one of the first military anesthetists,[5], at the Battle of Fredricksburg, December 13,

1862. However, due to the scope and magnitude of injury, the Civil War "etherizers" was untrained and could be anyone from a medical student to janitor. Among the first recognized "nurses" to administer anesthesia was Catherine S. Lawrence, who administered anesthesia for Civil War surgeons from 1861-1865.[6] In her memoirs she notes that she "administered chloroform to a fallen soldier" at the Second Battle of Bull Run. Another nurse ("Mrs. Harris") was implicated as performing anesthesia for Private Budlinger of the 76th Ohio Unit at Gettysburg,[7] as "more chloroform was added and reapplied by a nurse". While chloroform was the most popular agent as ether was flammable and surgery often involved the use of lanterns for lighting,[8] often a combination of alcohol, chloroform and ether (ACE) was used, and anesthesia mortality rates approached 5%. Of 8,900 documented cases using anesthesia, chloroform was the agent selected in 76.2% (6,784 cases), ether 14.7% (1,305 cases), and a combination of chloroform and ether 9.1% of the time.[9] Alcohol was used if excessive chloroform was used (it was considered to be a stimulant at the time). Wounded soldiers were triaged into one of three categories: mortally wounded, slightly wounded or operative cases. Most surgeries were amputations (much easier than exploring for the bullet, usually "Minie Ball" in a critically ill patient) and 95% involved some form of anesthesia, usually ether or chloroform.

After the Civil War, anesthesia continued to develop, but the etherizer remained the "occasional anesthetist". The administration of anesthesia was so poorly regulated that at age 16 Charles Mayo (co-founder of the Mayo Clinic) actually administered anesthesia for his father in the removal of a large ovarian tumor[10]. While the use of nurses as anesthetists or "etherizers" was happenstance at first, nurses were trained to perform anesthesia and became accepted anesthetists in the Franco-Prussian War in 1870[11]. Apparently "anesthetizers" would induce an anesthetic then move on to another patient, or would take over an anesthetic after the patient had been induced. This practice later drew harsh criticism, as anesthesia came under fire as a dangerous practice in the 1890's. The combination of untrained, inconsistent and inattentive anesthetizers spurred the American surgeons to develop a dedicated and committed anesthesia provider[12.]. Five key points were identified as requirements for a trained anesthetist: satisfaction with a subordinate role, anesthesia was the sole focus or interest, the position did not lend itself to acquiring the surgical technique or role, low wages were acceptable and the possession of skills to provide "smooth relaxation anesthesia". The catholic hospital sisters and the new professional nurses who graduated from Nightingale-patterned nursing schools were identified and sought by these surgeons to train as their sole anesthetist.

To this end, the first true nurse anesthetist is generally considered to have been Sister Mary Bernard, who practiced at St. Vincent's hospital in Erie, Pennsylvania. She entered the hospital in 1877 and took over the anesthesia practice in 1878, thus becoming the first nurse anesthetist in the United States.[7] Some fifty other Sisters also took up the work over the last two decades of the century,[12] but there was no real education process involved. At this time, there no incentive for physician providers to train in anesthesia, as often the "anesthetizer" was poorly compensated if even paid. The anesthetist was hardly considered to be a vital part of the surgical team, and for a standard procedure the "operator" received $100-200, and from this he would give the anesthetizer $5.00.[13]

To improve the quality of anesthesia care, in the 1880's the Franciscan sisters at St. John's hospital in Springfield, Illinois, began training hospital sisters as nurse anesthetists. These "nurse anesthetizers" migrated to other Midwestern hospitals to practice and meet the needs of the communities. In Rochester, Minnesota, the mother superior and Dr. William Mayo built St. Mary's hospital, and two nurses (Edith and Dinah Graham) directed and supervised the hospital's nursing and anesthesia services.[7] Dr. Mayo instructed the Grahams in their anesthesia duties, and Edith Graham eventually married Dr. Mayo. Her successor, Alice Magaw, took over the anesthesia administration duties, and became known as the "Mother of Anesthesia". Ms. Magaw's observations of anesthesia practice were published in various medical journals, including *Lancet*, *St. Paul Medical Journal*, Northwestern, and *Transactions*

of the Minnesota State Medical Association **from 1899-1906. Anesthesia at the Mayo Clinic was as well recognized as the Mayo Clinic's other successes, and these accomplishments led many nurses to specialize in the field and become anesthetists.[7] However, the education process was very much "on the job training" and no true academic process developed. To this point, the only formal education for nurse anesthetists involved a single chapter in Isabel Robb's nursing textbook in 1893 (**Nursing: Its Principles and Practices for Hospital and Private Use**), where it had a chapter entitled "The Administration of Anaesthetics." Soon, however, four post-graduate programs specializing in anesthesia were started at St. John's hospital in Springfield, Illinois (1912), New York Hospital in New York City (1912), Long Island College Hospital in Brooklyn, New York (1914) and St. Vincent's Hospital, Portland, Oregon (1909). Curriculum in these programs included anatomy and physiology, pharmacology and administration of common anesthetic agents.[7] Dr, George Crile chose Agatha Hodgkins, a Canadian nurse, to become his anesthetist in 1908 at Lakeside hospital. Crile and Hodgkins traveled to France together in 1914 and trained several English and French physicians and nurses in the art of anesthesia.**

The first recognized school of nurse anesthesia was founded in St. Vincent's hospital in Portland, Oregon, in 1909 by Agnes McGee, and consisted of courses in anatomy and physiology, pharmacology and common anesthetic techniques. Between 1912 and 1920, 19 schools opened, and the programs were approximately six months in length, and included programs at the Mayo Clinic, Johns Hopkins Hospital, Barnes Hospital, and Presbyterian Hospital. Physician residencies in anesthesia were not available, and so physicians often attending these programs to become skilled in this practice. One of these programs, Lakeside Hospital School of Anesthesia in Cleveland, Ohio, graduated six physicians, two dentists and eleven nurses in its first year. This program was six months in length, and the tuition was $50. During World War I, nurse anesthetists helped train the French and British physicians on how to provide anesthesia. Some nurse anesthetists became part of the medical school faculty, and participated in education of medical students in anesthesia practice. Agnes McGee taught third year medical students at the University of Oregon, while Alice Hunt was given the title of instructor in anesthesia at Yale University Medical Center in 1922 and held this title until 1947.

During World War II, the military had to train both nurses and physicians in anesthesia with 4-6 month programs, and by the end of the war it had prepared 2,000 nurse anesthetists. At that time, nurse anesthetists outnumbered physician anesthetists 17:1. However, the number of anesthesiology residencies increased dramatically, as the number of physician anesthetists increased from 285 in 1940 to 1,231 in 1949. Despite the increase in anesthesia residencies, and the large number of nurse anesthetists trained during World War II, a shortage of anesthesia providers existed during this time. After the Korean conflict, the American Association of Nurse Anesthetists (AANA) began its accreditation program for nurse anesthetist education, and in the 1960's the anesthesia shortage prompted the development of more nurse anesthesia programs. In the 1970's, nurse anesthesia education moved toward a baccalaureate framework, and by 1998, mandated a graduate degree.[15]

So what of nurse anesthesia education in Tennessee? There are currently five nurse anesthesia programs, including Union University in Jackson, Tennessee (2005), University of Tennessee College of Nursing, Anesthesia Focus, Memphis, Tennessee (1999), Erlanger Medical Center Nurse Anesthesia in Chattanooga (1995), the University of Tennessee at Knoxville, College of Nursing with Anesthesia Focus (1979), and the oldest school in the state, Middle Tennessee School of Anesthesia (1950). The school was started by Bernard Bowen, C.R.N.A., who came to Madison from Norwegian-American Hospital School of Anesthesia after graduating in 1947. Mr. Bowen started Madison Hospital School of Nurse Anesthesia after he noticed the shortage of qualified anesthesia personnel in the area. He had strong ties with the Madison Hospital, having been the first baby born at the Seventh Day Adventist hospital. The original class had two students, with two starting the 12 month program every three months. The program then expanded to an 18, 24, 27 then 28 month program. The original curriculum

consisted of 20 hours of pharmacology, 40 hours of anesthesia principles, 10 hours of respiratory physiology and a very heavy clinical component involving work in the hospital at Madison. Other hospitals initially included General Hospital and Vanderbilt University hospital in Nashville, Florida Sanitarium and Hospital in Orlando, Florida, Hinsdale Sanitarium and Masonic Hospital in Chicago, Illinois, and Charity Hospital in Shreveport, Louisiana. Along with establishing the Madison program, Mr. Bowen has served in every political capacity imaginable in nurse anesthesia including president of the Tennessee Association of Nurse Anesthetists and the American Association of Nurse Anesthetists. In the late 1970's, Mr. Bowen resigned as program director, and began doing locums tenens in the area before he retired in the 1980's (his anesthesia equipment was stolen and he considered it a sign that he needed to retire).

The current dean is Mary Elizabeth ("Ikey") DeVasher, who has directed the school since 1980 after Matt Faier and Stanley Sargent. During Ms. DeVasher's tenure the school enrollment has increased from twelve students to 72 students, the second largest school of nurse anesthesia in the country. While 60 nurse anesthesia programs closed down in the 1980's, the school continued to grow and adapt to the changing needs of accreditation and the anesthesia community. In 1994, after five years of preparation, the school was declared a master's program, the only free-standing, single purpose, regionally accredited anesthesia program in the country. The school now has a curriculum boasting 132 hours of pharmacology, 209 hours of physiology, 209 hours of principles of anesthesia, roughly 50 times the academic preparation of the 1909 Lakeside School of Anesthesia. In addition, there is 27 months of clinical experience involving 40-60 hours per week at 20 different affiliate hospitals and sites. The graduates have earned the highest board scores in the country, in large part due to faculty that teach both didactic and clinical, and a rigid selection process. The selection process for Middle Tennessee School of Anesthesia involves an open application process, and minimum criteria for acceptance includes 3.0 overall GPA, 3.0 science GPA, a bachelor's of science in a health related field, and at least one year's experience in an intensive care unit. Seventy-two students are selected from approximately 180 applicants, and last year's group averaged 2.2 years of intensive care unit practice with a GPA of 3.34.

The Council on Accreditation mandates at least 550 cases to graduate, the student nurse anesthetists averaged 1,003 cases each in 2006. Graduates from the class of 2006 took positions in eight states, and serve the practices in middle Tennessee in groups such as Anesthesia Medical Group (133 C.R.N.A.'s), Vanderbilt University Medical Center (66 C.R.N.A.'s) and Skyline Medical Center (20 C.R.N.A.'s). The graduates from MTSA have published case reports and original scientific articles in *Anesthesia and Analgesia*, *Journal of Cardiothoracic and Vascular Anesthesia* and the *Journal of the American Association of Nurse Anesthetists*. In addition, twelve of the graduates of the school either direct nurse anesthesia programs or are active academic faculty.

In summary, nurse anesthesia was born from quality of care issues, and through the evolution of its education process now is a very valuable member of the surgical team. From its humble beginnings the 105 nurse anesthesia programs will continue to contribute outstanding caregivers to meet the needs of society.

Bibliography

1. **Information for the Texas Association of Nurse Anesthetists, 2007.**
2. **Information from the American Association of Nurse Anesthetists, Park Ridge, Illinois, January 2007.**
3. **Starr P. The Social Transformation of American Medicine. New York, 1982. pp. 155**
4. **Kaufman HH. Treatment of head injuries in the American Civil War. *Journal of Neurosurgery* 1993:78:838-845.**
5. **Albin MS. William Thomas Green Morton as a military anesthetist during the Civil War. *Bulletin of Anesthesia History* 1996;14:23.**

6. **Lawrence CS. Autobiography: Sketch of Life and Labors of Miss Catherine S. Lawrence. Albany NY:James B. Lyon;1896:114.**
7. **Nagelhout JJ, Zaglaniczny KL. Nurse Anesthesia. Philadelphia, 2001, pp. 2, W.B. Saunders.**
8. **Dyer JF, Chesson MB. The Journal of a Civil War Surgeon. University of Nebraska Press, 2003.**
9. **Connor JTH. Chloroform and the Civil War. *Mil Med* 2004 Feb;169.**
10. **Byer D. Anesthetic administration by a juvenile: stories from a medical family. *Hist Anaesth Soc Proc* 2003;32:51-52.**
11. **Thatcher V. History of anesthesia with emphasis on the nurse specialist. Philadelphia, 1953, Lippincott.**
12. **Bankert M. Watchful Care: A History of America's Nurse Anesthetists. New York: Continuum, 1898, p. 50.**
13. **"Medical Societies," New York Academy of Medicine, Condensed from Phonographic Reports for the Medical and Surgical Reporter, *Hospital Practice* 1859 Dec 31;3(14)305. Galloway DH. The Anesthetizer as a Specialist. *The Philadelphia Medical Journal*, May 27, 1899, 1173.**
14. **Bernard Becker Medical Library Digital Collection. Women in health sciences. A brief note on nurse anesthetists. Washington University School of Medicine, St. Louis, Missouri. 2004.**
15. **Gunn IP. The history of nurse anesthesia education: highlights and influences. In Report of the National Commission on Nurse Anesthesia Education, Park Ridge, IL, 1990, American Association of Nurse Anesthetists, pp. 33-41.**

Untapped Sources for Anesthesia History

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Primary sources for anesthesia history research typically include such standards as professional medical books and journal articles and the surviving letters and other materials of departments and individuals. This presentation will describe some additional sources for such research: dissertations and theses, newspapers and popular magazines, and patents. These sources have always been available to the dedicated researcher and sometimes indexed in such print tools as Reader's Guide to Periodical Literature or indices of individual major newspapers such as the *New York Times* or *The Times, London*. Indeed, several articles have been published that used newspaper accounts as sources.[1-6] Today these sources are even more available via the combination of vast electronic databases and the Internet. Many of these databases are proprietary and thus require a subscription, fee-for-use or access [on site or remotely] to a library that subscribes, but an ever-increasing number of these resources are free for anyone to use.

What follows is a selection from the examples to be included in this presentation. My argument is that much useful information about anesthesia history can be found in these sources. Based on my own informal wanderings through newspapers, I suspect that crimes committed in the U.S. with chloroform have been much more numerous than previously believed. The easy availability of chloroform also seems to have made it a popular method of choice for suicides in the nineteenth and well into the twentieth centuries. Articles in newspapers and popular magazines can also provide information about public attitudes toward anesthesia and which anesthetic innovations have reached public awareness. Patents offer not only a window into practical aspects of equipment development and design, but also possible hints of "roads not taken." Doctoral dissertations and masters theses can provide a look at what aspects of anesthesia practice were important at academic medical centers in particular times and places.

1. Newspapers

1a. Colorado's Historic Newspaper Collection: www.cdpheritage.org/collection/chnc.cfm

"Effects of Chloroform" *Ft. Collins Weekly Courier* 14 December 1899.

"Dr. Osler has evidently changed his mind. No one hears of his asking anybody to pass him the chloroform" *Castle Rock Journal* 10 November 1905.

"Gem Bandits Get $500,000; Woman is Chloroformed Following New Year Party" *Creede Candle* 6 January 1923.

1b. New York *Times* Archive 1851-1980: www.nytimes.com/

"Nurse commits Suicide; Places Her Head in a Pan of Chloroform" 28 October 1901.

"Chloroform Thieves Led by a Doctor? Police Think some One with Medical Knowledge is Robbing East Site Flats; Whole Familes Drugged" 29 January 1908.

"Anaesthetics for Plants; Experiments Show That Ether and Chloroform Hasten Growth" 3 July 1910.

1c. *Washington Post* via Google News Archive: news.google.com/archivesearch

"Chloroformed By His Wife" 10 February 1886.

"Fatal Effects of Chloroform; Two Lady Patients Die While Under the Influence of the Drug" 17 February 1890.

"Masked Burglars Use Chloroform" 24 December 1899.

2. Popular Magazines

Time

"Will Ether Be Superceded?" [Luckhardt and Carter and ethylene] 17 March 1923.

"New Anesthetic" [Dr. Fredet of Paris, "sommifere"] 4 August 1924.

"Useful Poison" [Griffith and curare] 21 February 1944.

3. U.S. PATENTS via Google: www.google.com/patents

"Holder for Gas-Inhalers" US 340778, 8 January 1885

"Chloroform Dropper" US 859157, 27 June 1905

"Anesthesia Mask" US 955821, 13 October 1909

"Preparation of Cyclopropane" US 2261168, 30 April 1937

"Spinal Anesthetic Solution" US 2340425, 15 May 1940

4. Dissertations and Theses

Harvey, "Ether in Surgical Operations" University of Pennsylvania, 1851

Sackrider, "Ether and Chloroform" University of Michigan, 1856

Schneider, "Anaesthesia in Natural Labor" Female Medical College of Pennsylvania, 1879

Adams, "Intravenous Anesthesia" University of Minnesota, 1940

Lortie, "Doctors without Patients: the Anesthesiologist, a New Medical Specialist" University of Chicago, 1949

Soltero, "A Clinical Evaluation of Automatic Anesthesia" University of Minnesota, 1951

References

1. **Newson AJ. The contribution of newspapers and their advertisements to the history of colonial anaesthesia. *Anaesth Intensive Care*. 2006 Jun;34 Suppl 1:39-45.**
2. **Belicza B. [Ether and chloroform narcosis in the pages of Zagreb newspapers from 1847 to 1849] *Lijec Vjesn* 2000 Jan-Feb;122(1-2):32-9. Croatian.**

3. **Plotz J. [News of ether anesthesia in the local press in the 1847 in Bamburg] 449 -1 [How much blood flow is required by the myocardium?] *Anaesthesist* 1999 Jul;48(7):444-8. German.**
4. **Tammisto T, Tammisto C. Finland's first anaesthesia revealed by newspapers. *Acta Anaesthesiol Scand* 1999 Jan;43(1):97-9.**
5. **Franco A, Alvarez J, Cortes J, Rabanal S, Vidal MI, Barreiro JL. [Importance of the daily and political newspapers in Madrid on the introduction, popularization and awareness of anesthesia] *Rev Esp Anestesiol Reanim* 1994 Mar-Apr;41(2):100-8. Spanish.**
6. **Haddad FS. First newspaper announcements of the first public demonstration of ether anesthesia. *Middle East J Anesthesiol* 1992 Oct;11(6):583-5.**

C. Ronald Stephen Essay Award Finalists

Opioids: From the Assyrian Poppy Art to Modern Opiophobia; A Social History.

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"If men could learn from history, what lessons it might teach us! But passion and party blind our eyes, and the light which experience gives us is a lantern on the stern, which shines only on the waves behind us!"
–Samuel T. Coleridge, 18 December 1831, in T. Alsop, Recollections, 1836.

Introduction

The term opioid is a generic term used to designate those agents, whether natural or synthetic that combines with opioid receptors to produce physiologic effects and can be stereospecifically antagonized by naloxone (Jaffe and Martin, 1990, Eriator, 2000). Opioids include the commonly used medications like morphine, methadone, and meperidine, formerly referred to as "narcotics." The word "narcotic" originated from the Greek word for stupor or sleepiness, and it is increasingly used in a legal sense to describe medications associated with dependence, including opioids, cocaine and marijuana. The word narcotic is imprecise from the scientific point of view, especially with regards to pharmacological class and members. Opiate refers to drugs like codeine and morphine, whose origin is the opium poppy.

The word "opium" is derived from the Greek word for juice, in reference to the liquid that appears when the unripe poppy seed capsule is incised. Opium was the first clinical member of this group of medicine endowed salutary effects on pain and sorrow. These dual properties have been recognized since the dawn of civilization. (Crossland, 1970)

The evidence for use of opium dates back to the Assyrian "poppy" art from 4000 B.C. There are evidences of their use in studies of Egyptian, Greek and Persian cultures (Hawkes, 1992). With the dominance of misery and pain over mankind through the ages, it makes sense that opium was regarded as a God-sent gift. The Sumerians cultivated the poppy plants and isolated opium from the capsule of the seeds. They called opium "gil" (meaning joy), and the plant "hul gil" (meaning plant of joy) (Brownstein, 1993). In the odyssey, Homer (9th century B.C.), in probable reference to the opioid medication, wrote, "presently she cast a drug into the wine of which they drank to lull all pain and anger and bring forgetfulness of every sorrow." (Tainter, 1948) For about three thousand years, opium was used as a means of achieving sleep and dreams, and this is the origin of the phrase "pipe dreams." (Wall, 2000) Thomas Sydenham in 1680 wrote "among the remedies which it has pleased Almighty God to give to man to relieve his sufferings, none is so universal and so efficacious as opium." Goodman and Gilman, in the first edition of The Pharmacological Basis of Therapeutics (1941) wrote, "If it were necessary to restrict the choice of drugs to a very few, the great majority of physicians would place the opium alkaloids, particularly morphine, at the head of the list."

Early History: Though the use of opium has been in vogue before recorded time, the first authentic reference was in the writing of Theophrastus in the third century B.C. (Macht, 1915, Goodman and Gilman, 1941). He called opium "meconium," a synonym that persisted until recent times. Opium is also referred to in the Ebers papyri (about 1550, B.C.), and there were prescriptions for use of opium, including one by Isis for Ra's headache. (Bonica, 1990) There

are references to prescription for use to "prevent excessive crying of children" (Brownstein, 1993) and relief of pain during surgery.

Assyrian tablets of the seventh century, B.C., described the method for collecting opium. The unripe seed capsule of the poppy (papaver somniferum) is incised and a milky juice exudes and this solidifies in the air to give opium. The dried sap is scraped off the wound, usually by the next morning and powdered to make the opium. Discorides (first century A.D.) was apparently fully acquainted with the method for the collection and preparation of the syrup of opium, which he called "dia-kodion."

Galen described opium confections. These confections were quite popular in Rome , and were even hawked by shopkeepers and itinerant quacks. (Murphree, 1965) In the dark ages, knowledge of opium and other vestiges of the Graeco-Roman culture passed into the Arab world. The great Arab physician Avicenna (980-1037, A.D.) noted the use of opium for diarrhea, and is said to have died from a self-administered overdose. Through the Arab traders, opium was introduced to India and China around the ninth century.

In India, opium consumption was quite popular (Grossman, 1988), and it was used for several therapeutic conditions including dysentery and diarrhea. In the Rajputana province, it was used as a "drink of reconciliation and ordinary greeting." Later on, the Chinese imported opium from India. Initial use in China centered on treatment of dysentery. The practice of smoking opium in China began in the mid-seventeenth century after tobacco smoking was banned. (Brownstein, 1993) Smoking opium produced an effect that was used as a part of the social intercourse in the society. (Grossman, 1988) The problem of addiction to opium became very great. China became very concerned about the threat to health, morale and the economy and in 1820 issued an edict forbidding the entry of any vessel with opium on board. However the British traders in the early part of the 19th century viewed the opium trade as a mean of importing Chinese goods to Europe at a relatively cheap rate, and, in collaboration with their European allies, went to war to protect this interest. China lost Hong Kong after the first opium war (1840-1842). The second opium war (1857-1860) cost China her sovereignty and ensured an open door for the trade. (Porter, 1997) The opium wars solidified the hegemony of the opium trade. By 1906, it was estimated that 27% of adult males in China smoked opium. (Grossman, 1988)

Paracelsus (1493-1541, A.D.) carried opium in the pommel of his saddle, referring to it as the "stone of immortality." To him is accredited the compounding of tincture of opium which was called "laudanum" (meaning 'something to be praised'). (Goodman and Gilman, 1941) First prepared in the sixteenth century, it became very popular as an analgesic in the Victorian times. The uses of opium that are still valid today were fairly well understood at that time. Laudanum also provided a ready source of opium for the addict. The so-called opium eaters were usually laudanum drinkers. By the seventeenth century, the use of opium was widespread in Europe. Tinctures of laudanum were used in polite circles in London as a mild soporific. The educated class extensively dabbled in this usage. The influence of opium on Samuel Taylor Coleridge (1772-1834) is well known. He began using opium for medical reasons, but ended up suffering the horrors of addiction. (Porter, 1997) Also, Thomas de Quincey, in his Confessions of an Opium Eater stated, "Thou hast the keys of Paradise, oh just, Subtle, and mighty opium." The use of opium soared largely due to medical prescribing. The societal impact was also clearly evident at that time in London, where the opium dens were a constant feature of Victorian life. (Grossman, 1988) Since that time, opium has had a disgraceful image of misuse by social dropouts in the public arena.

Some practitioners expressed concerns that opium created dependency. By 1700, Dr. John Jones , a practitioner in London warned against "a long and lavish use." Samuel Crumpe noted that opium users when deprived even for a single day "became languid, dejected and uneasy." (Porter, 1997) Edward Levinstein (1831-1882) described morphine addiction in The Morbid Craving for Morphia. The withdrawal features including stomach cramps, diarrhea,

sleeplessness, nervousness, papillary dilatation and gooseflesh lead to the term "cold turkey."

The Nineteenth Centuy

At the beginning of the 19th century, two important developments opened up a new era of possibilities for the use and misuse of opioids. In 1805, Serturner, a little known pharmacist's assistant, described the isolation of a pure alkaloidal base from opium. His discovery was little known until 1816 when he wrote again, successfully calling attention to the isolated compound, which from his experiments he named morphine after the Greek god of dream. Discovery of other opioid alkaloids quickly followed. Codeine was isolated by Robiquet in 1832. Merck isolated papaverine in 1848. By the middle of the nineteenth century, the use of pure alkaloids rather than the crude opium preparations began to spread throughout the medical world. (Jaffe and Martin, 1990) Morphine paste was introduced locally using the point of a lancet, or the solutions were instilled in wounds.

The widespread adoption of the hypodermic syringe was another landmark event of the nineteenth century. Opiate and morphine were among the first drugs to be administered by the hypodermic syringe (Murphree, 1965), and the developments were regarded as "the greatest bon given to medicine since the discovery of chloroform." (Porter, 1997) Morphine was used for surgical procedures, post operative pain control as well as an adjunct to anesthesia. Claude Bernard investigated the use of morphine for premedicating experimental animals and observed that the amount of chloroform needed to produce anesthesia was reduced. (Brownstein, 1993) Florence Nightingale noted during her illness, "Nothing did me any good, but a curious little new fangled operation of putting opium under the skin which relieved one for 24 hours." (Porter, 1997) The American civil war (1861-1865) was the occasion for the first large-scale use of the hypodermic syringe. Patients were given syringes and taught how to dose themselves. The indiscriminate use of morphine turned many veterans into addicts. In fact, addiction for some time was known as "soldier's disease."

The Twentieth Century

It soon became clear that morphine was similar to opium in addiction potential. Attention was therefore turned towards the search for a safer medication without addicting properties. Wright produced diacetylmorphine in 1874 and it was marketed in 1898 under the name of heroin. Ironically, it was described as a safe preparation with many of the virtues and none of the dangers of morphine. It was also said to be free of addictive properties and was recommended even for the treatment of morphinism. This event was initially met with uncritical enthusiasm, which persisted for years despite the early warnings. Heroin abuse intensified after the Second World War and by mid twentieth century, intravenous abuse had reached epidemic proportions in the United States. (Joseph, Stancliff and Langrod, 2000)

In 1939, meperidine was serendipitously discovered while searching for a synthetic substitute for atropine. Meperidine was the first opioid with a structure far removed from that of morphine. Again it was initially thought to be non-addictive and it very soon became the most popular opiate analgesic in the United States. However, with clinical usage, the growing number of people addicted to this new medication soon convinced the Bureau of Narcotics of its addictive potential. (Synder, 1977)

In 1946, methadone was introduced, having been discovered while working with antispasmolytic compounds in Germany during the Second World War. This was the second compound with morphine-like pharmacological properties, though structurally unrelated to morphine. Paradoxically, the analgesic properties of methadone were not realized initially due to the high doses that were administered and the attendant intolerable side effects (Chen, 1948). The abstinence syndrome seen with methadone was different from that of the natural alkaloids, in that the onset was slower and its intensity was less. (Way, 1979, Browstein, 1993)

In 1949, Methadone was shown to be highly effective for withdrawing addicts from heroin. By 1950, oral methadone was established at U.S. Public Health Service hospitals for the treatment of opioids abstinence syndrome.

Nalorphine (N-allynormorphine) was produced in 1942 as the first opioid antagonist. Its development was a pharmacological milestone in the history of medicine. It was used as an antidote for the effects of morphine in the early 1950s. Interestingly in 1954, Lasagna and Beecher reported on the analgesic action of nalorphine in postoperative patients, despite its antagonist properties. However, it frequently produced anxiety and dysphoria, limiting its clinical analgesic applications. The discovery of its analgesic effects stimulated further research that culminated in the discovery of the "pure" antagonist, naloxone, the agonist-antagonist compounds like Pentazocine and butorphanol, and the partial agonist buprenorphine. (Way, 1979, Jaffe and Martin, 1990) Naloxone soon superseded nalorphine as the opioid antagonist of choice because of its potency. Naloxone also became the workhorse in the laboratory for determining the selectivity of opioids agonists.

Addiction was a great concern for scientists and members of the medical profession at the time. An idea of the general feeling about the use of opioids for pain control in the 1940s and 1950s may be obtained from the writings of the time. In an article published in *JAMA* in 1941 relating to the use of medications for terminal cancer pain, it was noted: "The use of narcotics in terminal cancer is to be condemned if it can possibly be avoided. Morphine and terminal cancer are in no way synonymous. Morphine use is an unpleasant experience to the majority of human subjects because of undesirable side effects. Dominant in the list of these unfortunate effects is addiction." (Lee, Jr., 1941)

With regards to control of cancer pain, the teaching in The Principles of Internal Medicine edited by Harrison et al. in 1950 was "Some physicians believe he should learn to endure pain, with the hope that it may lessen, rather than be put on narcotics with impression that it is hopeless and he might just as well be an addict." (Faull, 2000) Opiophobia is used to describe the irrational fear entertained by providers and lay public alike regarding the use of opioid medications for pain control. But this proscriptive view has gradually shifted. By 1983, regarding cancer pain control, the teaching in the tenth edition of The Principles of Internal Medicine edited by Harrison et al. was "Narcotic analgesics are the mainstay of therapy in malignant disease. Pain relief can be achieved in over 95% of patients, but narcotic use must be balanced against the undesirable side effects of sedation, constipation, tolerance, physical dependence and addiction." (Faull, 2000)

Conclusion

From the plant of joy of the ancient Sumerians to the irrational fears and enthusiasm of today, history clearly shows that the opioids have played major roles in the medical and social pilgrimage of the human civilization. Despite the significant progress in medicine and technology since the dawn of history, opioids still constitute the bedrock for relieving severe pain today. And despite the long period of hope and research, addiction remains an intrinsically linked part of their pharmacological and social roles.

References

1. **Bonica J. History of pain concepts and therapies. In: Bonica, J. (editor); The management of pain, Vol. 1., 2nd ed., Philadelphia, Lea and Febiger Publishers, 1990, Chapter 1, pp. 2-17.**
2. **Brownstein MJ. A brief history of opiates, opioid peptides, and opioid receptors. *Proc Natl Acad Sci USA* 1993 Jun 15;90(12):5391-3.**
3. **Chen KK. Pharmacology of methadone and related compounds. *Ann NY Acad Sci* 1948;51:83-97.**
4. **Crossland J. Analgesics. In: Lewis's Pharmacology. 4th edition, Edinburgh, Livingstone publ., 1970; Chap. 23, pp. 589-655.**

5. **Eriator I. Narcotic analgesics for chronic pain management. *Curr Rev Pain* 1998;2:193–2000.**
6. **Faull C. Influencing cancer pain management: Medical writing in the second half of the 20th century. In Proceedings of the 9th World Congress on Pain, Progress in Pain Research and management, Vol. 16, edited by M. Devor, M.C. Rowbotham, and Z. Wiesenfeld-Hallin, Seattle, IASP press, 2000; pp 35-40.**
7. **Goodman L and A Gilman. Morphine and other opium alkaloids. In: The Pharmacological Basis of Therapeutics, 1st ed., New York, Macmillan Publishers, 1941; Chapter 12, pp. 186-223.**
8. **Grossman A. Opioid peptides and pain. In: The history of the management of pain. Edited by Mann, R. D., Lancs, England, The Parthenon Pub. 1988; chapter 6; pp. 127-140.**
9. **Hawkes CH. Endorphins: the basis of pleasure? *J Neurol*, *Neurosurg Psychiatry* 1992;55(4):247-50.**
10. **Jaffe JH and Martin WR. Opioid analgesics and antagonists. In: Goodman and Gilman's The Pharmacological Basis of Therapeutics, 8th edition. Edited by Gilman, A.G., Rall, T. W., Nies, A. S. and Taylor , P., New York , Pergamon press, 1990; Chapter 21; pp. 485-532.**
11. **Joseph H, Stancliff S, Langrod J. Methadone maintenance treatment (MMT): a review of historical and clinical issues. *MT Sinai J Med* 2000;67(5-6):347–64.**
12. **Lasagna L, Beecher HK. The analgesic effectiveness of nalorphine and nalorphine-morphine combinations in man. *J Pharmacol Exp Ther* 1954;112(3):356–63.**
13. **Lee Jr LE. Medication in the control of pain in terminal cancer, with reference to the study of newer synthetic analgesics, *JAMA* 1941;116:216-219.**
14. **Macht DI. The history of opium and some of its preparations and alkaloids. *JAMA* 1915; 64: 477 - 481.**
15. **Murphree HB. Narcotic Analgesics 1: opium alkaloids. In: Drill's pharmacology in medicine, 3rd ed. Edited by Dipalma, J., New York , McGraw-Hill book Co. , 1965; Chapter 17, pp. 246-265.**
16. **Porter, R. Medicine, state and society. In: The greatest benefit to mankind, London, Harper Collins Pub., 1997; Chapter 20, pp. 628-667.**
17. **Synder SH. Opiate receptors and internal opiates. *Sci Am* 1977;236:44-56.**
18. **Tainter ML. Pain. *Ann NY Acad Sci* 1948;51:3-11.**
19. **Wall P. How treatment works. In: Pain: The science of suffering, New York, Columbia University press, 2000; chapter 8, pp. 107-124.**
20. **Way EL. Review and overview of four decades of opiate research. In: Loh, H. H. and Ross, D. H. (editors); Neurochemical mechanisms of opiates and endorphins (Adv. Biochem. Psychopharmacol. Vol. 20). Edited by Loh, H.H. and Ross, D.H., New York , Raven press, 1979; Pp 3-27.**

Neonatal Pain: To Treat or Not to Treat? That was the Question

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"I cannot help but wonder how such a situation came to develop… If I had been told by a physician, no matter how senior, that infants don't feel pain, I would never have believed it. What constitutes the difference between my reaction and that of the thousands of physicians who did believe it?"[1]

This comment was made by Jill Lawson who was the first recipient of an award created in 1996 by the American Pain Society to recognize advocacy in pediatric pain. The Jeffrey Lawson award is named after her son, who was born in 1985 at 25-26 weeks gestation and died at seven weeks of age, five weeks after cardiothoracic surgery to repair a patent ductus arteriosus. Jill Lawson was outraged after her son's death when she reviewed the surgical records and discovered that her son did not receive any analgesia during the procedure. He was administered only pancuronium for the surgery. She reports that his heart rate remained elevated for two days and the physicians told her the night after surgery that he was entering a catabolic shock and that his heart, kidneys, and liver were beginning to fail. His dependence on the ventilator increased and his intraventricular hemorrhage worsened. Jill Lawson feels that this was a pivotal time in his life. She later confronted the anesthesiologist regarding the lack of analgesia and was told, "it has never been shown that premature babies have pain."[2]

The theory that infants are incapable of experiencing pain was not proposed until the late 19th century. In fact, many of the most renowned thinkers throughout history believed that infants were hypersensitive to painful stimuli. Plato, in 400 BC, hypothesized that pain and pleasure were the result of an interaction of earth, fire, air, and water, with the soul housed in the body. Plato believed that at the beginning of life all these interactions were especially violent, so that for an infant all feeling was essentially painful.[3] The perspective that sensitivity to pain was, in part, determined by previous painful experiences was endorsed by many ancient writers. Hippocrates (460-370 B.C.) was a Greek physician on the island of Cos whose work and influence were of enormous importance in separating medicine from superstition. Using objective observations, he established the foundation of medicine as a branch of science. He is considered throughout history as the "Father of Medicine" and has been credited with the Hippocratic Oath. "The Aphorisms," one of his most renowned works, is a collection of his observations and deductions regarding medicine. In this collection he records: "Those who are used to bearing an accustomed pain, even if they be weak and old, bear it more easily than the young and strong who are unaccustomed."[3]

Felix Wurth, a 17th century physician in Basel and Zurich, wrote the first known book in western Europe to deal with pediatrics and surgery. The Children's Book, published in 1656, discussed issues dealing with the care of children and problems in pediatric surgery, primarily congenital and acquired orthopedic malformations. In his book he expressed the idea that the less mature the infant, the greater the degree of pain experienced:

> **If a new skin in old people be tender, what is it you think in a newborn Babe? Doth a small thing pain you so much on a finger, how painful is it then to a Child, which is tormented all the body over, which hath but a tender new grown flesh? If such a perfect Child is tormented so soon, what shall we think of a child that stayed not in the wombe its full time? Surely it is twice worse with him.[4]**

The theory that infants are incapable of experiencing pain was introduced in the late 19th century and continued through most of the 20th century. In 1872, Paul Flechsig, a scientist in Germany, conducted research in neuroanatomy and neuropathology that led to advancements in both fields. His early studies focused on myelogenesis of the spinal cord earning, as a result, the dorsal spinocerebellar tract to be called the "Flechsig's tract." Through the years he turned his attention to the myelogenesis of the brain hemispheres. He noted that the myelination of nerve fibers occurred at different rates during development and that in the newborn baby both myelinated and nonmyelinated fibers were present, with only myelinated fibers believed to be fully functional. He proposed that infants are not capable of feeling pain because their nerves are not completely myelinated.[5] However, in 1952, a French neurologist, Andre-Thomas, advocated caution regarding the exact function of the myelin sheath based on studies in young animals demonstrating that nonmyelinated fibers could be excited.[6]

Charles Darwin, in his work, The Expression of Emotions in Man and Animal, in 1872, postulated that children have no awareness of pain. He refused to believe that children's facial expressions, cries and tears, convulsive movement, and breathing changes reflected the sensory or emotional experience of pain. He thought they were just reflex actions, reinforced by habit. He went further to claim that expressions of pain in select groups including "animals, children, savages, and the insane" could under no circumstances imply the awareness of pain.[6]

Throughout the early 20th century common practice included performing surgery on infants and toddlers with no anesthesia. Max Thorek, 1880-1975, was a major figure in surgery who made contributions to several fields of study including plastic and reconstructive surgery. In his textbook, *Modern Surgical Technique,* in 1938, he described his view of adequate pediatric anesthesia: "Often no anesthesia is required. A sucker consisting of a sponge dipped in some sugar water will often suffice to calm a baby."[7] We now know that sucrose provides analgesia in infants less than two months, and the addition of sugar water did offer analgesia to the infants.

In 1917, psychologist Mary Blanton conducted a study at Johns Hopkins, recording infants' responses to blood draws and pinpricks on the wrist during sleep. She noted that infants reacted defensively and concluded, "the reflex and instinctive equipment of the child at birth is more complex and advanced than has hitherto been thought."[8,9] This challenged the currently accepted view that infants cannot experience pain, but did little to disprove the theory.

Myrtle McGraw was a psychologist from humble beginnings who devoted her academic life to infant and child development. She was born the fifth of seven children to an Alabama farmer and a seamstress. Her intellectual gifts were noted by a local lawyer who arranged for her to attend a boarding school while working to pay for her room and board. Through dedication and perseverance she obtained a Ph.D. in psychology. In 1941 at Columbia University and The Babies Hospital in New York, Dr. McGraw used pinpricks to reveal "progressive maturation of nerves." Seventy five infants were stimulated with a blunt sterile safety pin from birth to four years of age. Ten pinpricks were used in each area to ensure that the reactions were sufficiently intense. Responses "consisted of diffuse bodily movements accompanied by crying, and possibly a local reflex." After 2000 observations she concluded that a neonate in no way could localize or identify the source of a painful stimulation because the cortex was not sufficient developed.[10] She postulated that the ability to experience pain is not fully developed until age two. We now understand that, although infants may not be able to localize a painful stimulus, they are still fully capable of experiencing pain from noxious stimuli.

In 1968 surgeons L.I. Swafford, M.D., and D. Allen, M.D., contended that "pediatric patients seldom need medication for the relief of pain after general surgery. They tolerate discomfort

well. The child will say he does not feel well, or that he in uncomfortable or wants his parents, but often he will not relate this unhappiness to pain."[3] As late as 1982 Proctor and Gamble promoted Pampers to parents by providing Expecting Parents Information Kits, which included the statement: "You may be surprised to learn that circumcision will not be painful to your baby because at this early stage of development, the penis does not yet have functioning pain nerve endings."[6]

In 1987 a large number of hospitals were performing cardiothoracic and neurosurgical procedures on premature infants and neonates without any analgesia. Dr. Kanwaljeet "Sunny" Anand, a pediatrician with fellowship training in Pediatric Critical Care medicine has been a leader in research regarding neonatal pain. He authored or co-authored over 200 publications and was the recipient of many awards for his dedication to the study of neonatal pain, including the Jeffrey Lawson Award from the American Pain Society in 2000. A series of studies by Dr. Anand and colleagues at Oxford University from 1985-1987 addressed the issue of neonatal surgery without anesthesia and analgesia.[11,12,13] The research, consisting of precise measurements of infant reactions to surgery, proved that the babies experienced pain, needed and tolerated anesthesia well, and had metabolic and endocrine shock following operations without anesthesia. The research conducted by Dr. Anand, and the public outcry regarding Jeffrey Lawson, led to the rejection of the view that neonates are incapable of experiencing pain held throughout most of the 20th century.

Jill Lawson's outrage surrounding her son's death moved her to share Jeffrey's story with the popular press. She contacted over twenty organizations questioning the practice of operating on premature infants without analgesia. These organizations included the American Society of Anesthesiology, American Academy of Pediatrics, the American Civil Liberties Union, American Pain Society, and the National Committee for the Prevention of Child Abuse, among many others. Jill Lawson reports that one of her most disturbing experiences while investigating Jeffrey's lack of anesthesia and analgesia was the comment made by a senior staff neonatologist at the hospital during a meeting concerning Jeffrey's surgery. The neonatologist stated that what happened to her son didn't matter because he was a fetus. When she asked him how old someone had to be to feel pain, he placed the line of demarcation at about two years.[2] This was the age of pain perception that Myrtle McGraw concluded in her study conducted in 1941.

Due to Jill Lawson's efforts to ensure that other infants receive appropriate anesthesia and analgesia, a total of seventeen articles and television segments were generated in the mainstream and medical press. In June 1986, the *Journal of Birth* printed Jill Lawson's letter concerning surgery on infants without anesthesia, and in August 1986 the *Washington Post* printed a feature article, which was carried over the UPI wires and reprinted in several major cities newspapers. The article was then picked up by Cable News Network, which led to extensive coverage of the issue the week of October 17, 1986. The public outcry may have been the catalyst that led to the surge of research and discussion regarding neonatal pain and anesthesia practice. In 2001, Josep-Eladi Banos, M.D. Ph.D., from the University of Barcelona published An analysis of articles on neonatal pain published from 1965-1999. He found that few articles on neonatal pain were produced from 1965-1985, but the number of articles on this topic increased sharply after 1985. In his conclusion he states that "Pain in neonates was a neglected subject until the mid-1980s, and, currently, only a few countries seem interested in this type of pain."[14] The United States published almost forty percent of the articles on neonatal pain.

A number of unanswered questions regarding neonatal pain still exist, specifically in respect to the safest and most efficacious treatment regimens and long term implications of neonatal pain. Research in this population is difficult, and assessment of long term outcome is complex with multiple confounders. Thanks to advocates of pediatric pain, the pain that neonates and premature infants experience is now well established and deserves adequate recognition and treatment. The current debate is now centering on fetal pain. The research

conducted by Drs. Giannakoulopoulos, Gitau, and Fisk in separate clinical trials have demonstrated that fetuses as young as 18 weeks are capable of mounting a stress response to invasive procedures.[15,16,17] The question is whether the stress response, which consists of increase levels of beta endorphins and cortisol, proves that the fetus is capable of experiencing pain. The recent history of neonatal pain over the past thirty years is fascinating to review, and no doubt exists that in the next thirty years, the topic of fetal pain will be equally fascinating.

References

1. **Lawson J. Letter. *N Engl J Med* 1988 May:1198.**
2. **Lawson J. *Birth* 1988;13(2):36.**
3. **Unruh AM. Voices from the Past: Ancient Views of Pain in Childhood. *Clin J Pain* 1992 Sep;8(3):247-254.**
4. **Ruhrah J. Pediatrics of the Past. New York. Paul Hobner: 1925; 196-220.**
5. **Seror D, Szold A, Nissan S. Felix Wurtz: Surgeon and Pediatrician. *J Pediatr Surg* 1991 Oct;26(10):1152-5.**
6. **Cope DK. Neonatal Pain: The Evolution of an Idea. *ASA Newsletter* 1998 Sep;62(9).**
7. **Ruberg RL. Max Thorek: A Surgeon for all Seasons. *Clin Plast Surg* 1983 Oct;10(4):611-18.**
8. **Blanton MG. The Behavior of the Human Infant in the First 30 Days of Life. *Psychol Rev* 1917;24(6):456-483.**
9. **Chamberlain DB. "Babies Don't Feel Pain: A Century of Denial in Medicine" in Davis; Floyd R, Dumit J, (eds) (1998). Cyborg Babies: From Techno-Sex to Techno-Tots, New York and London: Routledge**
10. **McGraw M. Neural maturation as exemplified in the changing reactions of the infant to pin prick. *Child Dev* 1941;12(1):31-42.**
11. **Anand KJS, Aynsley-Green A. Metabolic and endocrine effects of surgical ligation of patent ductus arteriosus in the preterm neonate: Are there implications for further improvement in postoperative outcome?" *Mod Probl Paediatr* 1985;23:143-257.**
12. **Anand KJS. "Hormonal and metabolic functions of neonates and infants undergoing surgery. *Curr Opin Cardiol* 1986;1(5):681-9.**
13. **Anand KJ, Hickey PR. Pain and its effects in the human neonate and fetus. N *Engl J Med* 1987 Nov 19;317(21):1321-9.**
14. **Banos JE, Ruiz G, Guardiloa E. An analysis of articles on neonatal pain published from 1965 to 1999. *Pain Res Manage* 2001 Spring;6(1):45-50.**
15. **Giannokoulopoulos X, Sepulveda W, Kourtis P, Glover V, Fisk NM. Fetal plasma cortisol and beta-endorphin response to intrauterine needling. *Lancet* 1994Jul 9;344(8915):77-81.**
16. **Fisk NM, Gitau R, Teixeira JM, Giannakoulopoulos X, Cameron AD, Glover VA. Effect of direct fetal opiod analgesia on fetal hormonal and homodynamic stress response to intrauterine needling. *Anesthesiology* 2001 Oct; 95(4):828-35.**
17. **Gitau R, Fisk NM, Teixeira JM, Cameron AD, Glover V. Fetal hypothalamic-pituitary-adrenal stress responses to invasive procedures are independent of maternal responses. *J Clin Endocrinol Metab* 2001 Jan; 86(1):104-9.**

Halothane Hepatitis Solved,
A Scientific Odyssey of Burnell R. Brown MD, PhD, FFARCS (1933-1995)

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The author is indebted to his mentor, Adolph H. Giesecke, M.D., Emeritus Professor, Anesthesiology and Pain Management, U TX Southwestern Medical Center, to Helen Brown, to Jay Gandolfi, Ph.D., and to the staff of the Wood Library-Museum for their assistance in the preparation of this manuscript.

Introduction

An odyssey is defined as an extended wandering journey, like the one taken by Odysseus in the ten years following the Trojan War. The solution of the complex problem of halothane hepatitis was just this kind of journey. It required eighteen years of highly skilled, methodical, scientific research from widely dispersed investigators spanning oceans, and continents. It required revolutionary changes of previously held dogma relating to inhalation anesthetics. Burnell R. Brown, M.D., Ph.D., FFARCS (1933-1995), was always in the middle of it. He lent not only his own scientific brilliance, but also his unique literary abilities. Dr. Brown, in a videotaped interview for the Wood Library-Museum, said that solving the pathological mechanism of halothane hepatotoxicity was his most important scientific achievement.[1] This paper is a brief description of that journey.

Fig. 1. Dr. Burnell Brown at his desk with his friend and collaborator, Professor John Nunn in 1994. Photo is from Giesecke's files.

The odyssey begins

Our odyssey begins in 1956 because that is the year that halothane was introduced into the United States by C. Ronald Stephen, M.D., Professor and Chairman of Anesthesiology at Duke University. Halothane was a quantum leap in safety of anesthetic drugs. It was heralded as a true breakthrough because of its potency, lack of flammability, and general smoothness of administration. Animal studies at that time failed to demonstrate any hepatic injury.[2] Its introduction was quite rightly followed by an explosive increase in its clinical use. By the early 1960's it was the most commonly used anesthetic in the western nations.

Fig. 2. Dr. Ronald Stephen introduced halothane to the US market and served as inspiration to Dr Brown. In this picture taken in 1991, Dr. Stephen displays an FNS Vaporizer, a miniature vaporizer for halothane. Photo is from Giesecke's files.

In 1956, Burnell Brown was a sophomore medical student in Tulane University receiving his MD degree in 1958. He was born in 1933 in Dallas, Texas, where he took his primary and secondary education. He completed a rotating internship and a year of anesthesiology at Parkland Memorial Hospital under Pepper Jenkins before serving three years in the Army in Munich Germany. He returned to Parkland to complete his residency in 1965 and take a PhD in pharmacology at Southwestern under J. Richard Crout in 1969. He spent eighteen months at Peter Bent Brigham Hospital in Boston under Roy Vandam before becoming chairman of anesthesiology at University of Arizona in Tucson in 1972.

Fig. 3. Arial view of the University of Arizona Health Science Center in Tucson where Dr. Brown was chairman of anesthesiology from 1972 until he retired in 1994. Photo from University of Arizona Bioinformation Resources.

During this developmental period in Dr. Brown's life the dark side of halothane began to emerge. Anecdotal case reports of severe jaundice associated with fatal hepatic necrosis following anesthesia with halothane appeared. This condition was given the name "halothane hepatitis." By 1963, at least 350 putative cases of halothane hepatitis had been published. The incidence was estimated to be one case in 10,000 halothane anesthetics. This was based on presumed incidence of halothane anesthesia in populations from which anecdotal cases of halothane hepatitis were reported. Small-scale retrospective studies led to no resolution of the problem.[3] Anesthesiologists who dealt with the real advantages of the drug on a daily basis denied a cause-effect relationship and attributed these cases to viral hepatitis, which

was pandemic at the time. Internists and hepatologists were adamant about the cause/effect relationship and sounded an ever-increasing crescendo alarm. The controversy led to one of the largest epidemiological studies of all times, the National Halothane Study sponsored by the National Academy of Science.[4]

Dr. John Bunker, chairman of anesthesiology at Stanford University led the multidiscipline research group. Unfortunately, the massive study was inconclusive with regard to cause and effect. Halothane was not proven to be a cause of massive hepatic necrosis nor was it vindicated. Intrinsic problems prejudiced the results. The study was retrospective and non-randomized. Several of the participating institutions had already published case reports implicating halothane in postoperative jaundice.

In spite of the problems, several valid conclusions were possible. First, severe hepatic necrosis following halothane anesthesia was a rare occurrence, probably one in 30,000 anesthetics, rather than the one in 10,000 previously reported. Second, the histological appearance of halothane hepatitis could not be distinguished from viral hepatitis and some drug-induced forms of hepatitis. Third, the crude mortality rate following halothane was lower than the study as a whole and significantly lower than cyclopropane or ether. Rather than being a dangerous drug, halothane proved to be remarkably safe.

Most anesthesiologists were reassured by the results. After all, it was a massive study (over 200,000 anesthetics were included) and the finger of guilt did not land squarely on halothane. The feeling of comfort was not to last. Several risk factors were identified which predisposed patients to the possibility of halothane hepatitis. *Multiple exposures* were shown to be a risk factor suggesting an allergic or immunologic mechanism but no antibodies to halothane were ever found in animals or in humans. *Obesity* was shown to increase the incidence of elevated transaminase after halothane anesthesia but not the incidence of hepatic necrosis. *Age* was an important factor with 40 to 50 year olds at greatest risk and children exempt from halothane hepatitis. *Females* were affected twice as frequently as males. Some *related members* of families were affected suggesting that an inherited defect of drug metabolism may play a role.

The identification of risk factors profoundly influenced clinical practice but did little to establish an etiology of the hepatitis. Pediatric anesthesiologists continued to use halothane routinely in children. Anesthesiologists working with adult patients became very careful about repeated administrations, especially when the previous halothane anesthetic had been followed by unexplained fever or jaundice. Obese females between 40 and 50 years of age were excluded from halothane anesthesia. Some simply abandoned the routine use of halothane, reserving it for patients in whom it was specially indicated, such as severe asthmatics. In the late sixties, anesthesiologists grudgingly recognized the reality of biotransformation of inhaled anesthetics. Dr. Brown wrote an editorial, cleverly entitled "Minipigs, Microsomes, Metabolism and Maupassant."[5] The following is quoted directly from that editorial.

> **Only six years ago pharmacology students were taught categorically that, almost uniquely among drugs, inhalation anesthetics entered and left the lungs essentially unaltered by cohabitation with the body's biochemical machinery. Then in swift succession, several investigators determined this view of metabolic inertness of anesthetics was untenable. Van Dyke, Chenoweth and Van Poznak found that ether, methoxyflurane and halothane were metabolized to a considerable extent in animals, a finding documented and investigated further by Cohen and others. Rehder et al. determined the magnitude of halothane metabolism in man. This group of German investigators found that as much as 20 per cent of absorbed halothane was metabolized, a surprise indeed. Like the denouement of a de Maupassant short story, "O, ma pauvre Mathilde! Le mienne était fausse." (Oh, my poor Matilda, the truth that was mine has proved false.),**

Holaday and coworkers topped this by discovering that 50 per cent of absorbed methoxyflurane was converted to metabolic products in man!

Now a new avenue of research was opened. Dr. Brown wondered if the metabolites of halothane could be hepatotoxic. Biotransformation of a benign chemical to a toxic metabolite is well known. The hepatotoxicity of both chloroform and carbon tetrachloride, for example, depends on the cleavage of the carbon- chlorine bond by cytochromes P-450 to a trichloromethyl radical, which initiates a series of lipid peroxidation events resulting in subcellular membrane damage and hepato-cellular necrosis. Dr. Brown received a NIH, NIAMD grant for the study of drug-anesthetic interactions. Specifically, he wanted to study the effect of pretreatment with phenobarbital, which would induce cytochromes P-450, on the rate of metabolism of halothane. To assist in this work he recruited I. Glen Sipes, a toxicologist just beginning his career.

The major pathway for metabolism of halothane is oxidative leading to trifluroacetic acid and minor metabolites, such as trifluoroacetyl ethanolamine and N-acetyl-S- (2-bromo-2-chloro-1, 1-trifluoroacetyl)-l-cysteine. Attention was initially directed to these metabolites but none were found to be toxic or immunogenic. In fact, induction of the oxidative pathway by pre-treatment with phenobarbital, does not dispose laboratory rats to halothane hepatic necrosis as it does with chloroform or carbon tetrachloride.[6]

Fourteen years on the "wrong road"

Then the reductive metabolites of halothane were studied. Fluoride ion is cleaved from halothane and becomes a marker for the extent of reductive metabolism. The corresponding byproduct was 2-chlor-1, 1- difluorethylene. By 1980 a second reductive metabolite was found, 2-chlor-1, 1,1- trifluoroethane. Neither of these products was toxic per se, but the process of their formation produces radicals, which may bind covalently to liver macromolecules. Following this lead, Dr. Brown's laboratory produced an animal model for hepatic necrosis.[7] Animals were pretreated with phenobarbital to induce cytochromes P-450 and then the animals were anesthetized with halothane in a hypoxic environment. Under these circumstances centrilobular necrosis resulted in rats. Dr. Brown was convinced that this was the mechanism for halothane hepatitis in humans. He lectured and wrote widely about the toxicity of reductive metabolites of halothane. Finally, he admitted that this mechanism was not the proximate cause of halothane hepatitis in man because of the emergence of new evidence for an immunological mechanism.[8] The new evidence came from laboratories of the Kings College Hospital, London and National Institute of Health in Bethesda.

In London Vergani et al found an antibody to halothane-altered hepatocytes in patients with halothane hepatitis in 1980 and speculated on the importance saying, "It is possible that the presence of halothane in the cell membrane can expose hidden antigenic determinants. Alternatively, a reactive intermediate produced during oxidative or reductive metabolism may bind to cellular macromolecules including components of the endoplasmic reticulum and according to the membrane flow concept, it could then be transported to the cell surface and incorporated into the plasma membrane."[9]

Dienstag in an accompanying editorial stated that the data could be interpreted to show that the antibodies in the serum of the hepatitis patients could have been the result of the hepatic damage rather than the cause.[10] In a letter of rebuttal, Davis et al of King's College wrote, "Our view is that mild hepatic damage, seen in up to twenty percent of patients repeatedly anesthetized with halothane, may be a manifestation of direct toxic injury, whereas if the extremely rare severe lesion develops, an additional immune component may be involved. We have evidence that the antigen of the halothane-altered membrane is produced only when the oxidative pathway is activated."[11]

Their evidence, published in 1981 showed that "the expression of the antigen is associated with the oxidative metabolism of halothane, in contrast to other groups, which have shown that the reductive route is involved in the direct hepatotoxic reaction attributed to halothane."[12] One of the other groups to which the authors referred was McLain, Sipes and Brown,[7] who had demonstrated that halothane might be directly toxic to the liver of rats when the reductive pathway of halothane metabolism is stimulated.

At the NIH, Satoh, et. al. showed that antibodies to trifluoroaccetelyted protein are bound to the Cytochrome P450 unit that produced the metabolite. He did not speculate on the clinical significance of this finding and concluded, "Clearly more work is needed to elucidate the identity and origin of this plasma membrane-TFA adduct and to determine its relevance to halothane induced immunotoxicity."[13] The authors confirmed and extended this work in 1985, showing that the TFA binds with the lysine moiety and that when exposed to the antibody, the altered hepatocytes developed a linear granular appearance indicating membrane damage.[14] They conclude that "halothane metabolites do bind to the outer surface of the plasma membrane of hepatocytes and raise the possibility that sufficient amounts may be covalently bound to some membrane component to serve as an immunogen in some individuals. The rarity of the disease, thus, may not depend primarily on the activity of the enzymes that catalyze the formation of the reactive metabolite, but rather on the immunogenicity of the adduct and the variability of the immune mechanism in the human population."

At last, the right road

This story has all of the elements of a highly competitive race to the finish between three very competent laboratories. However, Dr. Brown felt that much more could be accomplished by collaboration than by competition and, in 1985, he arranged to take a sabbatical in England sponsored by the British National Research Council of which Prof. John Nunn was the Director. This sabbatical gave him an extended opportunity to brainstorm with the investigators at King's College. The cooperation paid off.

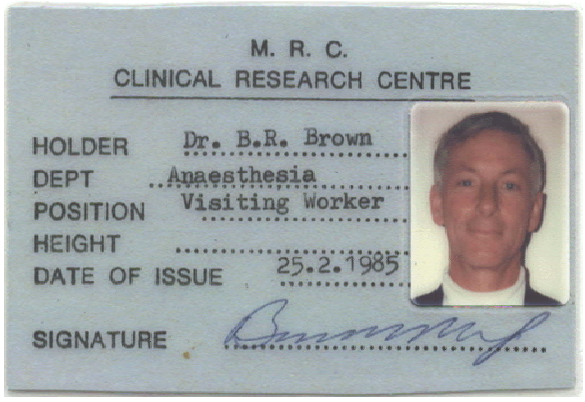

Fig. 4. The Clinical Research Center issued Dr. Burnell Brown's security badge during his sabbatical in 1985. Photo supplied by Helen Brown.

While he was in England, Dr. Brown's colleagues collaborated with the NIH group to publish a review of the evidence for an immunologic mechanism for hepatotoxicity in 1986.[15] They concluded that, "hepatotoxicity in animals is via bioactivation to reactive intermediates, however clinically, the hepatic injury mimics an immunologic hypersensitivity response." They further state that, "halothane exposure can produce in a laboratory animal and in humans an antibody against a covalently bound oxidative intermediate of halothane that has altered a host component into non-self immunogen."

However, a concise statement of the pathogenesis supported by laboratory and clinical evidence still had not been published and in 1987, Brown and Gandolfi still appeared to be on the "wrong road."[8] They were not alone. In April 1988, Gelman and Van Dyke published an editorial suggesting that reductive metabolism resulting from hepatic ischemia from

sympathetic over activity is the probable mechanism. They did not even mention the possibility of a role for the immune system.[16]

The definitive statement came in May 1988 as collaboration between the Arizona and British investigators. "Intracellular halothane is rapidly metabolized generating reactive metabolites that react with plasma membrane proteins to alter their antigenicity. Several populations of antibodies may be formed with specificities directed toward the hapten TFA. Antibodies may lyse any hepatocytes, which have altered membrane proteins. Thus, liver damage initiated by metabolite-mediated toxicity may be exacerbated during repeated exposure to halothane by immunologically mediated injury."[17] Eureka, after eighteen years of work the mechanism had been revealed.

In subsequent writings Dr. Brown was always careful to credit his collaborators with significant achievements leading to the solution of the puzzle. Dr. Brown concluded that halothane had two different effects on the liver. One was a transient elevation of hepatic enzymes, sometimes associated with mild and benign jaundice. He felt that the cause of this effect was an accumulation of the reductive metabolites of halothane associated with hypoxia or ischemia of the liver in the post anesthetic period. The second was a fulminate form of hepatic necrosis leading to hepatic failure and death in 25 to 30% of cases. This more severe manifestation was due to the oxidative metabolism of halothane to trifluoroacetyl chloride, the formation of a haptene from TFA and hepatocellular protein, the stimulation of an immune response to the abnormal protein, and on subsequent exposure death of the cell.[18] This careful work gained him and his colleagues recognition and awards throughout the world. The patho-physiologic mechanism of halothane hepatotoxicity was an important scientific revelation but its clinical importance had faded because, by 1988, anesthesiologists had largely switched to newer alternative drugs and halothane was rarely used.

Dr. Brown received many honors but he was most proud of the Fellowship by election in the Faculty of Anaesthetists of the Royal College of Surgeons of London in 1988. Dr. Brown died in August 1995 having lived a rich, full life. In addition to his monumental achievement in research, he had many interests outside of medicine and anesthesiology. He developed these interests to the same degree of excellence that he conducted scientific experiments and he proudly passed the knowledge and traits to his children and grandchildren. He was a remarkable man.

Summary

The revelation of the patho-physiological mechanism of halothane hepatitis was an odyssey of 18 years involving many researchers and laboratories on both sides of the Atlantic. Dr. Burnell Brown was always in the middle of it and was responsible for the definitive statement of the mechanism in 1988. Halothane undergoes oxidative metabolism in the liver to trifluoroacetic acid (TFA). TFA binds to membrane proteins in the cell wall. The combination TFA-protein is antigenic and promotes the production of antibodies. On subsequent exposure the antibodies attack the TFA-protein complex, the cell ruptures and dies. The revelation was a more important scientific than clinical achievement because by 1988 anesthesiologists had switched to alternative drugs. Dr. Brown considered the revelation of the pathophysiology of halothane hepatitis to be his most important scientific achievement. He lived a rich full life and died in 1995 at age 61.

References

1. **Burnell R. Brown MD, PhD, FFARCS, Living History Interview with Adolph H. Giesecke and John Nunn, Wood Library Museum, Park Ridge IL, May 1994.**
2. **Stephen CR, Margolis G, Fabian LW, Bourgeois-Gavardin M. Laboratory observations with Fluothane. *Anesthesiology* 1958;19:770-81.**

3. **Mushin WW, Rosen M, Bowen DJ, Campbell H. Halothane and liver dysfunction: a retrospective study. *Brit Med J* 1964;2:329-41.**
4. **Summary of the National Halothane Study: Possible association between halothane anesthesia and postoperative hepatic necrosis. Report by Subcommittee on the National Halothane Study of the Committee on Anesthesia, National Academy of Science. *JAMA* 1966;197:775- 88.**
5. **Brown BR. Minipigs, microsomes, metabolism and Maupassant, *Anesthesiology* 1971;34:217-8.**
6. **Brown BR, Sipes IG, Sagalyn AM. Mechanism of acute hepatic toxicity, chloroform, halothane and glutamine. *Anesthesiology* 1974;41:554-61.**
7. **McLain GE, Sipes IG, Brown BR. An animal model of halothane hepatotoxicity, roles of enzyme induction and hypoxia. *Anesthesiology* 1979;51:321-6.**
8. **Brown BR, Gandolfi AJ. Adverse effects of volatile agents. *Br J Anaesth* 1987;59:14-23.**
9. **Vergani D, Mieli-Vergani G, Alberti A, Neuberger J, Eddleston AL, Davis M, Williams R. Antibodies to the surface of halothane altered rabbit hepatocytes in patients with severe halothane hepatitis. *NEJM* 1980;303:66-71.**
10. **Dienstag JL. Halothane hepatitis, allergy or idiosyncrasy? *NEJM* 1981;303:102-4.**
11. **Davis M, Eddleston AL, Neuberger JM, Vergani D, Mieli-Vergani G, Williams R. Halothane hepatitis. *NEJM* 1980;303:1123.**
12. **Neuberger JM, Mieli-Vergani G, Tredger JM, Davis M, Williams R. Oxidative metabolism of halothane in the production of altered hepatocyte membrane antigens in acute halothane induced hepatic necrosis. *Gut* 1981;22: 669-72.**
13. **Satoh H, Gillette JR, Davies H, Schulick RD, Polh LR. Immunochemical evidence of trifluoroacetylated cytochrome P450 in the liver of halothane treated rats. *Mol Pharmacol* 1985;28:468-74.**
14. **Satoh H, Fukuda Y, Anderson DK, Ferrans VJ, Gillette JR, Pohl LR. Immunological studies on the mechanism of halothane-induced hepatotoxicity: immunochemical evidence of trifluoroacetlyated hepatocytes. *Pharmacol Exp Ther* 1985;233:857-62.**
15. **Callis AH, Brooks SD, Waters SJ, Lucas DO, Gandolfi AJ, Sipes IG. Evidence for a role of the immune system in the pathogenesis of halothane hepatitis. Chapter 38 in SH Roth & KW Miller. Molecular and Cellular Mechanisms of Anesthetic*s*. Plenum Medical Book Co., New York, 1986.**
16. **Gelman S, Van Dyke R. Mechanism of halothane-induced hepatotoxicity: another step in the long path. *Anesthesiology* 1988;68:479-82.**
17. **Hubbard AK, Roth TP, Gandolfi AJ, Brown BR, Webster NR, Nunn JF. Halothane hepatitis patients generate an antibody response towards covalently bound Halothane metabolite. *Anesthesiology* 1988;68:791-5.**
18. **Hubbard AK, Gandolfi AJ, Brown BR. Immunological basis of anesthetic-induced hepatotoxicity. *Anesthesiology* 1988;69:814-7.**

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