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Ptomaine Poisons as Clues to Chemical Neurotransmission

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Invoking the terms “nicotinic” and “muscarinic,” Sir Henry Dale named important biochemical components of the animal nervous system after vegetable alkaloids (Figure 1).^{1,2} The vegetable alkaloids, such as nicotine and muscarine, are bioactive amines that have evolved in the plant world to function, in many cases, as chemical weapons attacking the cholinergic nervous systems of insects. Indeed, the name muscarine indicates that the amine kills flies (genus *Musca*). Dale used many botanical defense molecules to help establish acetylcholine as a chemical neurotransmitter. A few others of his tools from plants included the well-known drugs atropine, physostigmine, and scopolamine. It is less appreciated that important “animal alkaloids” also facilitated the discovery of chemical neurotransmission.

Ptomaines

The animal alkaloids come not from fragrant tobacco leaves and brightly colored mushrooms. They come from putrid bile, rotten eggs, rancid meat, and decomposing brains. Named, as was apoptosis, from *ptoma*, a Greek word for corpse, they are the ptomaine poisons.³⁻⁷

Decomposing meat has long been known to contain poisons. Nineteenth-century chemists learned that putrefactive bacteria release large quantities of highly bioactive amines from nitrogen-containing decaying animal tissues. Some of the corpse-derived amines, such as putrescine and cadaverine, have vivid names. For Dale and other physiologists, three of the most important ptomaine poisons were histamine, tyramine, and a presciently named molecule called neurine.

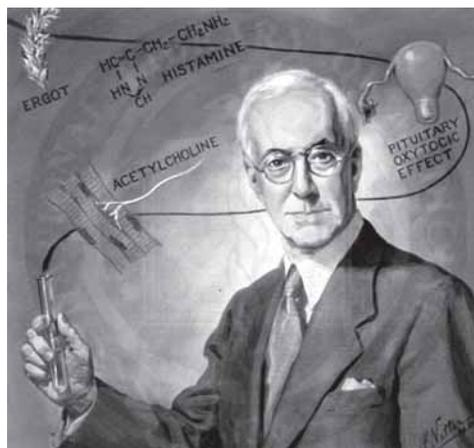


Fig. 1. English physician Henry Hallett Dale (1875-1968) shared with Otto Loewi the 1936 Nobel Prize in Physiology/Medicine for establishing acetylcholine as a chemical neurotransmitter (www.nobel.se). It was Dale who classified the acetylcholine receptors as nicotinic and muscarinic. He had broad interest in pharmacology, including that of anesthesia.^{1,2} He was knighted in 1932. Frank Netter did this portrait for a 1949 Armour Laboratories advertisement. The image is preserved by the U.S. National Library of Medicine.

Histamine and tyramine

Before his Nobel-garnering work on acetylcholine, Dale characterized the pharmacological properties of histamine (Figure 2).⁸ Histamine is now known to be one of the intrinsic neurotransmitters of the human brain. Dale started his histamine studies when the molecule was simply a long-known ptomaine, a bioactive product of tissue decay. The name histamine indicates that the ptomaine poison is an amine found as a tissue (*histos*) decomposition product. Histamine was long thought to be purely a

bacterial product responsible for some of the toxic consequences of bacterial infections. In 1927, Dale determined that histamine is normally present in uninfected mammalian tissues.⁹ In making that seminal observation, Dale contributed significantly to the eventual identification of histamine as a neurotransmitter.

Putrefactive bacteria synthesize histamine the same way that neurons (and mast cells) do. In one enzymatic step, they decarboxylate (remove the $-CO_2H$ acid group from) histidine, a common amino acid that is present in most proteins.¹⁰ Likewise, bacteria and neurons prepare tyramine; they decarboxylate the amino acid tyrosine into tyramine. Tyramine is the vasopressor formed by bacterial action in cheese (*tyros*). It is responsible for the hypertensive crisis that cheese can cause when hepatic monoamine oxidase is pharmacologically inhibited. Tyramine differs from norepinephrine in merely lacking two of the oxygen atoms of norepinephrine. Therefore, tyramine, the ptomaine, pointed strongly to norepinephrine, the neurotransmitter (Figure 2).

After neurine came bilineurine (renamed choline)

Dale's share of the 1936 Nobel Prize was for acetylcholine rather than for histamine or norepinephrine. The ptomaine poison for cholinergic receptors was called neurine (Figure 3).¹¹⁻¹³ The name neurine indicates that rotting brains are a rich source of this ptomaine.

Continued on page 36

History at the ASA Annual Meeting October 14-18, 2006, Chicago, IL

Forum on the History of Anesthesiology A Fellow's Story – What the WLM Fellowship Has Meant to Me

Monday, October 16, 2006
2:00 PM to 4:00 PM
McCormick Place, Room E353a

Moderator:

Douglas R. Bacon, M.D., M.A.
Professor of Anesthesiology and History of Medicine
Department of Anesthesiology
Mayo Clinic College of Medicine
Rochester, Minnesota

Anesthetic Risk: Gaining an Understanding via WLM Fellowship

David Brown, M.D.
Edward Rotan Distinguished Professor and Chair
MD Anderson Cancer Center, The University of Texas
Department of Anesthesiology and Pain Medicine
Houston, Texas

Facing the Future through the Lenses of the Past

Doris K. Cope, M.D.
Professor and Chief
Division of Pain Medicine
Department of Anesthesiology
University of Pittsburgh School of Medicine
Pittsburgh, Pennsylvania

Anesthesia Still Lives and Dies by the Airway: An Historical Review of the Oral Airway

Jonathan C. Berman, M.D.
Trustee, Wood Library-Museum of Anesthesiology
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Assistant Professor
Departments of Anesthesiology and Community Health and Epidemiology
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The Impact of the WLM Fellowship on My (Academic) Career

Babatunde Ogunnaike, M.D.
Associate Professor
Department of Anesthesiology and Pain Management
University of Texas Southwestern Medical Center
Dallas, Texas

The Evolution of Media in Anesthesia

Francis X. Whalen, M.D.
Assistant Professor
Department of Anesthesiology
Mayo Clinic College of Medicine
Rochester, Minnesota

Panel: Counterfactual History in Anesthesiology: What If?

Tuesday, October 17, 2006
2:00 PM to 4:00 PM
McCormick Place, Room E450a

Objectives: After attending this panel, the learner will understand the importance of singular events in the history of anesthesiology. By changing one fact, and constructing a "new" history around it, the listener will understand how the current structures and practices came to anesthesiology, which may influence current practice patterns.

Co-Moderator:

Douglas R. Bacon, M.D., M.A.
Professor of Anesthesiology and History of Medicine
Department of Anesthesiology
Mayo Clinic College of Medicine
Rochester, Minnesota

Co-Moderator:

Maurice S. Albin, M.D.
Professor of Anesthesiology
University of Alabama at Birmingham
Birmingham, Alabama

What if Humphrey Davy and Thomas Beddoes Had Followed Through on Their Observation and Used Nitrous Oxide for Surgical Anesthesia?

Amos J. Wright III, M.D.
Associate Professor of Anesthesiology
University of Alabama at Birmingham
Birmingham, Alabama

What if William Hammond was Not Chosen to Be Surgeon-General of the Union Armies during the Civil War?

Maurice S. Albin, M.D.

What if Gaston Labat had Not Left Paris in 1920?

Sandra L. Kopp, M.D.
Assistant Professor of Anesthesiology
Department of Anesthesiology
Mayo Clinic College of Medicine
Rochester, Minnesota

What Would Have Happened to Anesthesiology if There Hadn't Been a World War II?

David B. Waisel, M.D.
Assistant Professor of Anesthesia, Perioperative Medicine and Pain Medicine
Harvard Medical School
Children's Hospital of Boston
Boston, Massachusetts

From the Editor

The *Bulletin of Anesthesia History* has been in existence since December 1982 starting as a humble newsletter for the history community, described by Selma Calmes as "being put together on my kitchen table." Following Selma's nurturing of the *Anesthesia History Association Newsletter*, Ron Stephen took over as Chief Editor, frequenting Anesthesia history meetings requesting articles for publication and scouring the literature for suitable contributions to reprint. It was his idea to change the name to *Bulletin of Anesthesia History*, stressing original contributions and with his inspiration guiding us to take this publication to the next level. We instituted a peer review process, under the auspices of A.J. Wright, and also succeeded in listing the journal in several databases maintained by the U.S. National Library of Medicine including PubMed so that our articles would be widely accessible for medical literature searches.

As we go to print, Ron is now fading from us. His legacy to us is this *Bulletin* among many, many other contributions. He sought to bring the best of medical historical scholarship to the world and spent decades encouraging young scholars, myself included, to publish and present their research. It is most fitting that the Anesthesia History Association has named our initiative to enhance resident and fellow historical research the C. Ronald Stephen Resident Essay Award. Over the years, dozens of young scholars have been recognized by this award with the resultant essays published in this journal. The two things dear to Ron's heart: the quality of the *Bulletin* and the education of future anesthesiologists are thus advanced by this one award.

It is indeed fitting that we who have been inspired and mentored by Ron, as well as those who indirectly have benefited from his groundbreaking efforts, support the C. Ronald Stephen endowment of the AHA with all contributions going to fund the prize awards for the residents. We hope to make this an in perpetuity memorial to Ron, and at present have over half the money needed. Just today, I was notified that final tax exempt status has been granted to the Anesthesia History Association, due in no small part to Karen Bieterman, Librarian, Wood Library-Museum, so all contributions are now tax exempt. David Waisel, Treasurer of the AHA, is collecting the money and will pro-



vide donors with a tax exempt receipt for their contributions.

Please consider honoring Ron in one or more of three ways:

1. Involving yourself in historical scholarship that can be shared with your colleagues, present and those to come, by publishing in the *Bulletin of Anesthesia History*
2. Mentoring a young trainee in the "Family History" of our specialty
3. Contributing to the C. Ronald Stephen Endowment to fund the efforts of our residents

Contributions can be sent to:

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The *Bulletin*, formerly indexed in Histline, is now indexed in several databases maintained by the U.S. National Library of Medicine as follows:

1. Monographs: Old citations to historical monographs (including books, audiovisuals, serials, book chapters, and meeting papers) are now in LOCATORplus (<http://locatorplus.gov>), NLM's web-based online public access catalog, where they may be searched separately from now on, along with newly created citations.

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Ptomaine. . . Continued from Page 33

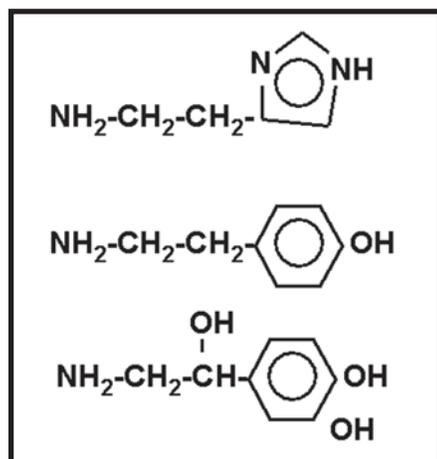


Fig. 2. Structural diagrams histamine, tyramine, and norepinephrine.

Neurine structurally resembles choline, and putrefactive bacteria synthesize neurine from choline-containing phospholipids. Most of the choline in brain tissue is not present as acetylcholine.¹⁴ Instead, most of the choline is present as a component of sphingomyelin, a phospholipid of myelin nerve sheaths. Sphingomyelin is wonderfully named after the Sphinx. That is, other than for its choline content, chemists found the complicated structure of the phospholipid from myelin to be enigmatic as the Sphinx.¹⁵

Neurine from rotten brains was one of the few alkaloids of the 19th century for which a complete chemical structure was established.¹¹ Since, like acetylcholine, neurine is a trimethylammonium compound, neurine pointed strongly to the possibility of a neurotransmitter bearing a trimethylammonium group.

Another clue was bilineurine, from bile. Named for brain neurine, bilineurine from bile also carries a trimethylammonium group. Bilineurine is derived from bile lecithin, which, like brain sphingomyelin, is a choline-containing phospholipid. Because of lack of aseptic conditions, bilineurine preparations were often contaminated with neurine molecules arising from bacterial action on the lecithin. So, bilineurine preparations showed some of the pharmacological properties of neurine. As it became clear that pure neurine was far more toxic than pure bilineurine, the "neur" was dropped from the name of the amine from bile. Since bile is *chole*, the preferred name for bilineurine became choline.¹⁶ An opinion of Hippocrates and Galen was therefore rephrased. The Greeks said that levels of bile (*chole*) control the mind and

body.¹⁷ Dale said the mind and body are prominently controlled by a molecule resembling bile choline.

Cholinergic actions of neurine

Neurine is a nicotinic antagonist.¹¹ By 1869, diverse quaternary amines were known to share the ability of neurine to weaken skeletal muscle.^{18,19}

Neurine also mimics muscarine. For instance, neurine and muscarine are both salivary stimulants.¹¹ Both agents arrest the heart in a mechanism blocked by atropine.¹¹ Thus, neurine and muscarine were both agonists at what Dale would later call the muscarinic receptor.

Unknown structure of muscarine (except for the trimethylammonium feature)

In all the years that Dale spoke of muscarinic receptors, he never knew the structure of the muscarine molecule (Figure 3). Chemists did not solve that puzzle until 1957.²⁰ However, 19th-century chemists did know that muscarine and choline were both trimethylammonium compounds. They knew because those quaternary amines undergo a reaction described by A.W. Hofmann, who is remembered by anesthesiologists today because of the chemistry of cisatracurium.²¹ The eponymous Hofmann Elimination split muscarine

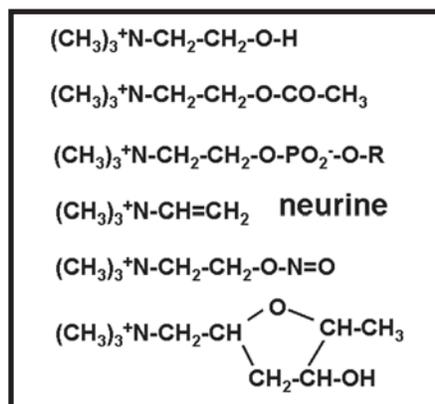


Fig. 3. Structural diagrams of choline, acetylcholine, choline phospholipid (as in lecithin or sphingomyelin), neurine, "artificial muscarine," and muscarine.

into trimethylamine and a structurally intractable product.²² Therefore, to Dale, muscarine was (CH₃)₃⁺N-R, with R yet to be identified.

Artificial synthesis of trimethylammonium analogs of muscarine includes synthesis of acetylcholine

Because neurine and muscarine were

trimethylammonium compounds, many chemists, including those working with Dale, synthesized a plethora of artificial muscarines.^{23,24} Dale's strongest "artificial muscarine" was a nitrite ester of choline (Figure 3). Had he examined that nitrovasodilator on endothelium-denuded vascular smooth muscle, he might have discovered the Endothelium-Derived Relaxing Factor a half-century ahead of schedule. Also remarkable, though we now view muscarine as an analog of acetylcholine, acetylcholine was chemically synthesized in 1894 as one of the many artificial analogs of muscarine.²⁵ In the 19th century, neurine and acetylcholine were viewed as mimics of muscarine. In the 20th century, Dale showed that neurine and muscarine are best considered to be mimics of acetylcholine.

Conclusion

Dale was interested in ptomaine poisons, and he knew the complete structure of the brain-derived trimethylammonium compound, neurine. The name neurine was certainly eye-catching. Surely neurine, as well as muscarine, steered Dale to acetylcholine.

In elucidating physiology with the aid of dreadful poisons, Dale solidified a prescient concept put forth by French physiologist Claude Bernard in 1864.²⁶ Examining curare, Bernard concluded the following.

"Poisons can be used as agents to destroy life or as means of curing diseases; but in addition to those two uses well-known to everyone, there is a third of particular interest to the physiologist. For him poison becomes an instrument to dissociate and analyze the most delicate phenomena of the living machine; and, by studying attentively the mechanism of death in various sorts of poisonings, he indirectly learns about the physiologic mechanism of life. This is the way in which I have long considered the action of toxic substances, and this is how I should like to discuss here the peculiar effects produced by some as yet little-known American [arrow] poisons."

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Careers in Anesthesiology, Volume IX. Park Ridge, IL: WLM, 2005. \$30 ISBN 1-889595-09-8.

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Introduction of Sevoflurane, The Final Achievement of Burnell R. Brown MD, PhD, FFARCS (1933 – 1995)*

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Acknowledgements: The authors gratefully acknowledge the assistance of Dr. Brown's family especially Helen Brown, and the staff of the Wood Library-Museum of Anesthesiology, Park Ridge, IL: Patrick Sim, Karen Bieterman, and Carole Siragusa.

Introduction

In a videotaped interview for the Wood library Museum, Burnell R. Brown MD, PhD, FFARCS, reflected on his career filled with many significant achievements. He felt that he had done five things of significance to society: promoting the use of alpha blockers in pheochromocytoma, founding and nourishing the department at the University of Arizona, working out the pathophysiology of halothane hepatotoxicity, editing the *Survey of Anesthesiology* and the textbook *General Anaesthesia*, Fifth Edition, and introducing sevoflurane to the US market.** The purpose of this essay is to describe Dr. Brown's role in the introduction of sevoflurane. This was his final achievement prior to his premature death at age 61 (August 8, 1995) from a highly anaplastic carcinoma of obscure origin. (Figure 1)

Inspiration to introduce a new agent

Burnell R Brown MD, PhD, FFARCS, was the founding chairman of the University of Arizona's Department of Anesthesiology, a post that he held from 1971 until his retirement in November 1994. He was born in Dallas, Texas, where he had his primary education. He took the MD degree at Tulane University in 1958, followed by a rotating internship and one year of anesthesiology at Parkland Memorial

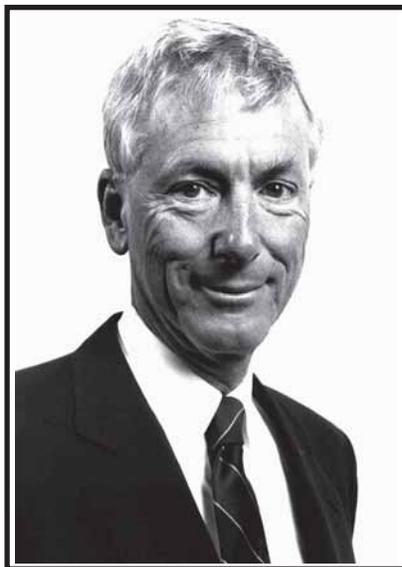


Fig. 1. Burnell R. Brown MD, PhD, FFARCS in 1994. Photo is from Helen Brown.

Hospital under Pepper Jenkins. He served in the U.S. Army Hospital, Munich, Germany. He returned to Dallas to finish his residency and to earn a PhD in pharmacology in 1969. His thesis was on the effects of five different inhalation agents on myocardial contractility.¹

During his years as a graduate student in pharmacology, he became fascinated by the possibility of introducing a new and useful drug to anesthetic practice. His fascination intensified when he met C. Ronald Stephen, (Figure 2) who had introduced halothane to the U.S. market in 1956 and who had joined the faculty at Southwestern in 1967 to become the director of anesthesiology at Children's Medical Center. Dr. Stephen invited Dr. Brown, who was also a part-time instructor in anesthesiology to participate in the phase three investigations of enflurane (in those days called Compound 347). Compound 347 was being considered as an alternative to halothane, which although extremely popular was increasingly being implicated as a hepatotoxin. Because Dr. Stephen was busy

setting up an anesthesia service in a newly built Children's Medical Center, he left much of the work of the investigation to his collaborators, Drs. Brown, Stanley and Botty. These three naturally developed an enthusiasm for the new drug and wanted the trials to go well, which they did for several patients. Their reports to Dr. Stephen and to the manufacturer were optimistic and enthusiastic until one day lightning struck. A patient developed convulsions under enflurane anesthesia.

When the first seizure occurred, the response was denial. Drs. Stanley, Botty and Brown examined every aspect of the patient's history, physical exam and laboratory work. They examined the anesthesia machine, the room temperature and every other possible explanation. Dr. Stephen joined them in the search and made suggestions of obscure etiologies of convulsions under anesthesia. They reported the convulsion to the manufacturer. The company's representatives were furi-



Fig. 2. Dr. C. Ronald Stephen was a professor at Southwestern Medical Center from 1967 to 1970 and inspired Dr. Brown's interest in new inhalation anesthetics. Photo is from departmental files.

*This essay is abstracted and modified from a comprehensive biography of Burnell R. Brown, which will be published in the *Careers Series* by the Wood Library Museum. **Burnell R. Brown MD, PhD, FFARCS, *Living History Interview with Adolph H. Giesecke and John Nunn*, Wood Library Museum, Park Ridge IL, May 1994.

ous. How could this happen? These dunces from Texas must have done something wrong. The patient must have hidden her history of seizure disorder. Then a second patient developed a similar seizure. In all, four of 142 patients developed seizures. Reluctantly, the company agreed to expand the investigation to include intra-operative electroencephalograms in the study patients.

In 1967, electroencephalograms were produced by a monstrous machine, which was not on wheels. Dr. Stephen invited the neurologist who had charge of the machine to participate in the study. Getting the machine to the operating room was a major production, requiring several days of planning and the help of the engineering department to devise and operate a hand truck to move the apparatus to the operating room. The project paid off and the seizures were found to occur when deep enflurane anesthesia, which caused respiratory depression, was combined with controlled ventilations leading to respiratory alkalosis. The combination of deep anesthesia and respiratory alkalosis caused the seizures. By keeping anesthesia light, controlled respirations could be added any time. Enflurane proved to be a valuable substitute for halothane when used with neuromuscular blockers and controlled respirations for all surgical procedures.² Dr. Stephen's inspiration remained with Dr. Brown for the next fifteen years.

The introduction of sevoflurane

Dr. Brown naturally became interested in sevoflurane when it was first described in 1975. His interest was further peaked when reports of the phase one trials were favorable. But work on the drug did not progress. Dr. Brown states in an editorial in 1992,³ "Sevoflurane received early investigative interest about the same time that isoflurane was in its last stages of development. On the surface, isoflurane had many salient features to recommend it over sevoflurane, a potential commercial as well as clinical rival." The salient features were that isoflurane was metabolized to a lesser extent than sevoflurane and that sevoflurane when exposed to soda lime with extreme heat decomposed to compound A. Dr. Brown continued, "It seemed quite logical at the time to shelve sevoflurane in favor of developing isoflurane. Sevoflurane remained dormant for years."

Eventually a Japanese pharmaceutical company became interested and questioned some of the condemning data regarding this drug. Additional research showed the degradation with soda lime occurs only at tem-

peratures higher than can be achieved in regular use and that the biotransformation does not result in either renal or hepatic damage. Also they found that sevoflurane has the advantage of rapid inhalation inductions, which were free of irritation. This advantage makes it valuable in pediatrics where inhalation inductions are common. Dr. Brown concluded in 1992 that, "The eventual role of this new/old anesthetic in our practice is a question for the future." When the company decided to push for approval in the USA, Dr. Brown became the drug's most energetic and vocal protagonist.

Dr. Brown and his team launched intensive investigations of the safety and biotransformation of sevoflurane in humans. They studied the metabolism of sevoflurane⁴ and the correlation with renal and hepatic function.⁵ They studied the breakdown of sevoflurane in soda lime in customary⁶ and low flow anesthesia.⁷ They studied hepatic blood flow and oxygenation under sevoflurane anesthesia.⁸ They compared sevoflurane with isoflurane in healthy patients.⁹ They studied its metabolism in obese patients compared to non-obese.¹⁰ They studied renal function after sevoflurane in rats¹¹ and after prolonged anesthesia in volunteers.¹²

Dr. Brown, himself, (Figure 3) volunteered to be a subject for the experiments. His confidence in the drug was complete but he had a tough time convincing his colleagues that he would make a suitable substitute for a paid "volunteer." Never-

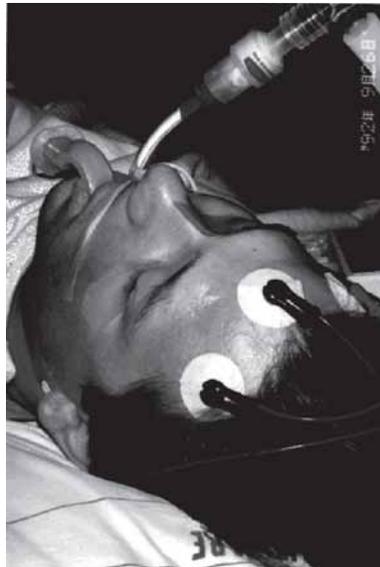


Fig. 3. Dr. Burnell Brown serves as the subject of an experiment on the biotransformation of sevoflurane on September 26, 1992. Photograph is from Helen Brown.

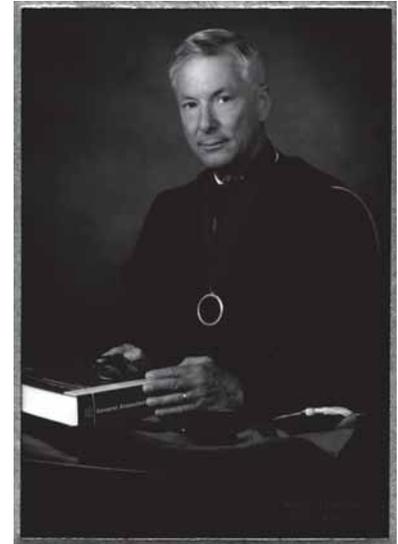


Fig. 4. Dr. Brown received many honors in recognition of his work but he was most proud of the Fellowship by election in the Faculty of Anaesthetists of the Royal College of Surgeons in 1988. He is shown here in his academic regalia with a copy of the textbook, *General Anaesthesia, Fifth Edition*, which he edited with Nunn and Utting. Photo is from Helen Brown.

theless, his persistence prevailed and he went through the experience with no sequelae.

The work was exhaustive, detailed and well documented. It demonstrated conclusively that even though sevoflurane was metabolized to a greater extent than isoflurane and occasionally resulted in fluoride concentrations higher than 50 mcg/L, it was not a threat to healthy renal function.¹³ However, the evidence failed to convince some who were fearful of a repetition of the nephrotoxicity of methoxyflurane. His thesis was sharply criticized by Drs. Tinker and Baker who referred to the "heavy biotransformation" of sevoflurane. Dr. Brown responded in another of his brilliant editorials where he called the putative nephrotoxic concentration of 50 mcg/L a shibboleth.¹⁴ Dr. Brown explained the difference between methoxyflurane, which is metabolized in the kidney to produce the critical concentration and sevoflurane, which is metabolized in the liver. He wrote "It is unfortunate that Tinker and Baker are prepared to pontificate with the statement that sevoflurane 'is a step backward,' a statement obviously made without access to the facts established with the clinical development of sevoflurane. I again pro-

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Sevoflurane. . . *Continued from Page 39*

pose that nephrotoxicity is agent-specific, occurring primarily because of intra-renal fluoride ion production, not primarily dependant on plasma fluoride ion concentration. It underscores the rule that medicine can never rest on its laurels, minds should remain open, vigilance should be maintained and new data should be continually sought."

His research and that of others consistently showed that sevoflurane was safe and had significant advantages over other inhalation anesthetics available at the time. In October 1994, he struggled to walk with a cane and the pain of his metastatic cancer was almost unbearable but he went to Washington one last time to give strong testimony to the FDA on the safety and utility of the drug. The effort was worth the pain. The FDA approved sevoflurane in 1995, only weeks before he died. He lived to see his dream become reality. He had helped to introduce a new and valuable inhalation anesthetic drug to the market.

So, turn on the sevoflurane, let your patient enjoy its advantages and reflect on the career of a great man, Burnell R. Brown MD, PhD, FFARCS. (Figure 4)

Summary

Burnell R. Brown MD, PhD, FFARCS, (1933-1995) included the introduction of sevoflurane into anesthetic practice as one of his most significant achievements. His studies of sevoflurane were comprehensive, detailed and well documented. Sevoflurane was approved by the FDA only weeks before his premature death at age 61. He was the founding chairman of the Department of Anesthesiology at the University of Arizona, Tucson. He was born in Dallas, Texas, and received the MD from Tulane University. 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 and take a PhD in pharmacology at Southwestern. 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. He was a superb clinician, scientist and teacher whose career is worthy of imitation by any ambitious young academic anesthesiologist.

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THE WOOD LIBRARY-MUSEUM

OF

ANESTHESIOLOGY

The American Society of Anesthesiologists: A Century of Challenges and Progress

Douglas R. Bacon, M.D., M.A.

Kathryn E. McGoldrick, M.D.

Mark J. Lema, M.D., Ph.D.

Editors

The history of ASA as told by the people who helped to shape it! Based upon the rich and extensive archives housed in the Wood Library-Museum, 21 authors tell their stories either as past participants or thoughtful historians, re-acting complicated historical issues and events in a present-day context. A clear departure from traditional history, this book may be read with ease and pleasure as individual essays or in its entirety, from its founding by an obscure group of nine in Long Island to the ultimate realization of a vibrant organization a century later. Readers will realize that the struggles and challenges, unique in different eras of the past, were the building blocks of success that spanned an entire century. This volume celebrates the centennial of an important professional organization by witnessing the pioneers' struggles to achieve what benefits all in American medicine today.



The American Society of Anesthesiologists: A Century of Challenges and Progress. Park Ridge, IL: WLM, 2005. \$55/Hardcover. ISBN 1-889595-15-2.

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AHA and HAS Meet at Mayo Clinic

by Selma H. Calmes, M.D.

The Department of Anesthesiology at the famous and historic Mayo Clinic in Rochester, Minnesota, hosted the summer meeting of the Anesthesia History Association, in conjunction with the History of Anaesthesia Society (UK), June 22-24, 2006. The meeting's theme was using history to teach professionalism; teaching professionalism is a new AGME requirement. Dr. Doug Bacon, head of the Section on History in the Department of Anesthesiology at Mayo Clinic, organized the meeting.

Plenary sessions covered important people and events in Mayo Clinic history. Topics included Dr. W.W. Mayo (father of the Mayo brothers Will and Charlie) and the beginning of the clinic, the history of the anesthesiology department and Dr. Will Mayo. This last talk was given at a luncheon at Dr. Will's lovely house, now called the Foundation House. The home is now used for various meetings. One plenary session, "Mississippi and the Mayo Brothers" by retired Mayo ophthalmologist and retinal surgeon, Dr. Dennis Robertson, was a particular hit. The Mississippi River is about 40 miles east of Rochester. The Mayo brothers each had their own steamboat and often enjoyed cruising on the river with their guests. Dr. Robertson reviewed the history of musical entertainments on steamboats and discussed how Dixieland jazz evolved in this setting. His talk had several interesting audio clips, and he also played his banjo. He has been a jazz musician for many years and still plays in a Dixieland band.

A lunch-time session by Dale Smith, Ph.D., (chair of history at the Uniformed Services University of the Health Sciences, Bethesda) and Dr. Bacon, suggested ways to use history to teach professionalism. The final plenary session reviewed the history of pain medicine at the Mayo Clinic.



The first and third prize winners of the 2005 AHA Resident Essay Contest (both from Baylor College of Medicine) presented their papers. (The second prize winner could not attend.) First prize winner, Christian Gonzales' paper was "Many men, three wars and one question: Foundations for the modern understanding of pain." Lori Conklin, third prize winner, presented



toxicity untangled" (Adolph Giesecke, Dallas). Raphael Ortega's (Brigham and Women's Hospital, Boston) paper reported on current efforts to restore the Ether Monument in Boston. Two papers on the clinic's first nurse anesthetists were presented by present Mayo Clinic CRNAs. Posters on CRNA history were also available for viewing on day two of the meeting. An exhibit in the History of Medicine Library recognized previous Mayo Clinic Librarian Tom Keys, who wrote the first definitive book on the history of anesthesia (*The History of Surgical Anesthesia*, 1945). This was prepared by Librarian Hilary Lane and Selma Calmes, who also gave a paper on how the book came to be written.

Tours of the Mayo Clinic were available. The downtown campus, where we met, is huge, beautiful and bustling with patients. The historic Plummer Building, where the history of medicine library is

located, is nicely integrated into the more modern facilities downtown, such as the new Gonda Building. The Plummer Building is worth exploring because of its splendid architectural detail and décor, with themes of medical and Mayo Clinic history. It opened in 1928 and was mostly designed by Dr. Henry S. Plummer (1874-1936), an early Clinic physician who also contributed a medical record system, the supporting statistical department and communication systems for patient information. Our meeting was held in the Gonda



"James Young Simpson: The voice of reason for the rights of women in labor 158 years later." Seventeen free papers were also presented. Subjects ranged from "A measure of gold: Hong Kong anesthesia at 50," (WLM librarian Patrick Sim) to "Burnell Brown, Halothane hepato-

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AHA... *Continued from Page 41*

Building, which has lovely meeting facilities. That location and the support of Mayo's CME section made for an excellent meeting. I spotted two baby grand pianos close to each other in the Gonda building and nearby was an exhibit on Rookwood Pottery and tile. (Rookwood tile was used extensively in the Plummer building.) These findings confirm that the arts are important to this institution.

Rochester's downtown consists of many hotels and shops for patients coming from long distances and their families. The lobby of the older Kahler Hotel, where I stayed, had a constant parade of patients with all kinds of disease. The hotel's TV channels included three Arabic language channels, including the notorious Aljazeera. Burka-clad women were often seen. From my hotel room, it was also possible to see an architectural feature of Rochester, a corn-cob shaped water tower. Corn was an important crop for the area in the past.

The Mayo Clinic is a unique and very successful American medical institution. To learn more about its history, see *Clapesattle, Helen. The Doctors Mayo. Minn: U. Minnesota Press, 1954, reprinted 1960.* To learn more about its famous anesthesia department see *Art to Science: Department of Anesthesiology, Mayo Clinic* by K. Rehder, P. Southorn and A. Sessler. Congratulations to all involved in putting on this excellent meeting!



Photographs courtesy of Dr. Selma Calmes, Dr. Martin Giesecke, and Judith Robins.



Lewis H. Wright Memorial Lecture: Alastair A. Spence, CBE, MD, FRCA, to Discuss “The Scottish Enlightenment: A Hotbed of Genius”*

by Susan A. Vassallo, M.D.

Chair

Lewis H. Wright Memorial Lecture Committee
Wood Library-Museum of Anesthesiology

The Lewis H. Wright Memorial Lecture is sponsored annually by the Wood Library-Museum of Anesthesiology (WLM) and honors its namesake, who was a pioneer in American anesthesiology. Dr. Wright was committed to enhancing the stature of anesthesiology as a clinical science and as an advanced medical specialty. He was a founding member of the WLM Board of Trustees and later served as its President Emeritus. In 1973, the New York State Society of Anesthesiologists endowed this lectureship to honor Dr. Wright, who died in 1974.

This year's distinguished speaker is Alastair A. Spence, C.B.E., M.D., F.R.C.A., Professor Emeritus, University of Edinburgh, and Past President of the Royal College of Anaesthetists, 1991-94.

Dr. Spence grew up along the Ayrshire Coast in Scotland; he came from a family of paper merchants based in nearby Glasgow. In 1960 he graduated from Glasgow University Medical School, one of the largest medical schools in the United Kingdom. Professor Spence earned cash on vacations as the official beach photographer at Ayr; his peak income was 6 pounds for a 6-day week, plus bonuses! While in medical school, Dr. Spence spent six months in the clinics of Dr. Ian Donald, (1910-1987), Regius Professor of Midwifery. The echo techniques used by the Royal Navy intrigued Dr. Donald, and he saw an application in medicine. To this day, Professor Spence is still proud to have witnessed some of the earliest obstetric ultrasound images.

Dr. Spence originally intended to pursue a career in medicine and neurology; the senior registrar in his medicine residency at Glasgow Royal Infirmary was a neurologist and Dr. Spence's role model.

**Lewis H. Wright Memorial Lecture: Alastair A. Spence, CBE, MD, FRCA, to Discuss “The Scottish Enlightenment: A Hotbed of Genius”, 2006 is reprinted with permission of the American Society of Anesthesiologists, 520 N. Northwest Highway, Park Ridge, Illinois 60068-2573.*



His change of heart was the result of both ambition and pragmatism. Dr. Spence recognized that training in medicine might not lead anywhere, as consultants' positions were limited. Anesthesiology was a burgeoning specialty with demand ahead of supply. He was appointed to the Fellowship of the Faculty of the Anaesthetists of the Royal College of Surgeons of England (F.F.A.R.C.S.) at the Western Infirmary, one of the leading teaching hospitals of Glasgow. This was a well-structured clinical training program with weekly departmental seminars. After clinical training, Dr. Spence received an 18-month research fellowship in the laboratory that investigated hyperbaric oxygen. The leading physiologists who visited this laboratory included John W. Severinghaus, M.D., and Hermann Rahn, M.D. (1912-1990), and Dr. Spence recalls this time as “a great opportunity to learn techniques of clinical measurement.”

John F. Nunn, M.D., Professor of Anesthesia at the University of Leeds and one of the premier anesthesiology academicians in the United Kingdom, also visited the Glasgow laboratory. In September 1966, Dr. Spence was recruited to Leeds where his research focused on postoperative pain, which was an extension of his Glasgow work on lung function. His query

was, “Which operations caused significant discomfort?” And his method was “to access by spirometry their effect on lung function.” He established a visible role on the ward, and in this capacity, was an early perioperative anesthesiologist. Dr. Spence observed that right paramedian incisions for gallbladder or peptic ulcer surgery were very painful, especially in the first 48 hours postoperatively. These patients had both reduced vital capacities and expiratory reserve volumes. From here he suggested using epidural anesthesia for 48 hours postoperatively after upper-abdominal surgery. A lucky break occurred when a senior doctor was admitted with bronchiectasis. He could not cough because of the pain. Dr. Spence placed an epidural catheter, and the doctor could cough. Dr. Spence “was king for a day!” He followed all of his epidural catheters for 48 hours and noted “bedside research often needs a heavy time commitment.”

He returned to Glasgow in 1969 as chair of the anesthesia department at the Western Campus. His Glasgow days were marked by his appointment in 1973 as editor of the *British Journal of Anaesthesia (BJA)*, a position he held until 1983. Under his guidance, the *BJA* became a well-respected academic publication and a financially profitable endeavor. In 1984, Dr. Spence assumed the chairmanship at the University of Edinburgh—a decision he never regretted. Edinburgh is the youngest of the four Scottish medical schools (Glasgow, St. Andrew's, Aberdeen), but Spence was able to recruit senior academic anesthesiologists.

Eventually he and his colleagues established Edinburgh as the premier Scottish center for clinical anesthesiology training and research. Professor Spence served as Chairman of the Department of Anaesthesia at Edinburgh at the Royal Infirmary of Edinburgh until 1998. His accomplishments in the advancement of Scottish medicine were recognized formally when he received the distinction of “Commander of the British Empire” in 1992.

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Along the way, Dr. Spence developed an interest in the Scottish Enlightenment, that period of creativity when brilliant minds moved Scotland forward in leaps and bounds. This intense movement produced contributions to science, philosophy, literature and art and also influenced the American and French Revolutions. The Enlightenment began around 1740 and was encapsulated by the poet and songwriter Robert Burns (1759-1796), who was born in Alloway, south of Ayr, the childhood town of Professor Spence. Burns was known as the "Bard of Scotland," and his ballads convey the hopes and dreams of the common man. During the Enlightenment, Adam Smith (1723-1790) gave us theories of economics, James Watt (1736-1819) engineered a better steam engine, David Hume (1711-1776) promoted moral philosophy, James Hutton (1726-1797) made discoveries in geology and Joseph Black (1728-1799) described the caloric theory of heat. The core theme of the Scottish Enlightenment was a belief that both science and the humanities were on equal ground; an enlightened man should embrace each discipline with fervor.

Edinburgh and Glasgow were the touchstones of medicine and surgery during the Enlightenment. In Glasgow the Gregory family led the way. In Edinburgh, the three Monroes (Primus, Secundus and Tertius) established a legacy by holding the Chair of Anatomy for 126 years. William Cullen (1710-1790) was a major force in chemistry and medicine. Professor Cullen held the chair of the Institute of Medicine and founded the Royal Medical Society of Edinburgh Society. Professor Cullen attracted the best minds from Europe and the United States. Our own Benjamin Franklin appreciated the success of the Edinburgh school; he sent William Shippen (1712-1801), physician and founder of the University of Pennsylvania, and John Morgan (1735-1789), a great innovator in American medical education, to work under William Cullen. Dr. Joseph Lister proposed the practice of antiseptics in 1865 while a surgeon at the Royal Infirmary of Glasgow, and he made his way to Edinburgh, as did James Young Simpson, M.D. (1811-1870), who introduced anesthesia for childbirth at the Royal Infirmary of Edinburgh. Charles Darwin (1809-1882) began graduate education at the medical school in Edinburgh. His father, grandfa-

ther and brother were all trained at the university and were physicians in the city. Darwin could not tolerate the anatomy sessions; he watched two operations without anesthesia and never returned to the surgical amphitheater.

For this year's lecture, Professor Alistair A. Spence will discuss "The Scottish Enlightenment: A Hotbed of Genius." In this talk, he will focus upon the achievements made in medicine and science. He will highlight the successes of the Scottish school and show how its leaders advanced the concept of a discrete disease state and a formal approach to its diagnosis.

The Wood Library-Museum is honored to have Professor Alastair A. Spence as the 2006 Lewis H. Wright Memorial Lecturer. His research in lung function and postoperative analgesia has helped us to improve strategies for surgical pain relief. Under his leadership at the University of Edinburgh and the Royal Infirmary of Edinburgh, scores of physicians received superb anesthesiology clinical training. We thank him for sharing his perspective on the Scottish Enlightenment and for illustrating again that science and history are inseparable.

YEAR 2008 LAUREATE OF THE HISTORY OF ANESTHESIA

Doris K. Cope, M.D., Chairman
www.asahq.org/wlm/

Nominations are invited for the person to be named the fourth Wood Library-Museum Laureate of the History of Anesthesia in the year 2008. Deadline for receipt of nominations is July 1, 2007.

This program, established in 1994, has as its purpose increased recognition of the richness and importance of the history of our specialty by recognizing the work of scholars who have made singular contributions to the field. The honor is awarded every four years by the WLM Laureate Committee to an individual who has a demonstrable record of contributing over the years outstanding, original materials related to the history of our specialty as reflected by articles published in peer-reviewed journals, and/or in monographs. The first Laureate, Dr. Gwenifer Wilson of Sydney, Australia was honored in 1996. The second Co-Laureates were Norman A. Bergman, M.D, F.R.C.A., and Thomas B. Boulton, M.D., Ch.B., F.R.C.A. in 2000. The third Laureate was Donald Caton, M.D. in 2004.

The Laureate Program is international. Nominations are sought by physicians, not just anesthesiologists, as well as medical historians from the international history community.

Additional information may be obtained by contacting the WLM Laureate Committee at the Wood Library-Museum, 520 N. Northwest Highway, Park Ridge, Illinois 60068-2573. Please see the WLM website - [/www.asahq.org/wlm/](http://www.asahq.org/wlm/) - for more information.

From the Literature

by A.J. Wright, M.L.S.

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Department of Anesthesiology
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Note: I have examined most of the items listed in this column. Books can be listed in this column more than once as new reviews appear. Older articles are included as I work through a large backlog of materials. Some listings are not directly related to anesthesia, pain or critical care; I interpret those categories very broadly. Some will concern individuals important in the history of the specialty [i.e., Harvey Cushing or William Halsted] who also achieved in other areas or widely-used equipment such as the stethoscope. I also include career profiles of living individuals. Non-English materials are so indicated. Columns for the past several years are available as "Recent Articles on Anesthesia History" on the Anesthesia History Association website at www.anes.uab.edu/anesthesia_history_association.htm. I urge readers to send me any citations, especially those not in English, that I may otherwise miss!

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This Month in Anesthesia History*

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1632 October 20: Christopher Wren is born in London. Around 1660 the English architect and astronomer began to experiment with the transfusion of blood between animals and intravenous injections into animals. An account of his work was published in the *Philosophical Transactions* of the Royal Society of London in 1665. Wren, the greatest English architect of his time who designed many of London's cathedrals, died in that city in February, 1723. A much earlier attempt at blood transfusion was described by Stefano Infessura [ca. 1435-1500], an anti-papist lawyer in Rome. According to Infessura's *Diary of the City of Rome*, when Pope Innocent VIII was on his deathbed, a Jewish physician

suggested infusing blood from three ten-year-old boys into the pontiff's veins. All three donors died and Innocent himself died on July 25, 1492. The *Catholic Encyclopedia* warns that Infessura's work is full of gossip and not to be trusted.

1708 October 16: Swiss scientist and writer Albrecht von Haller, father of experimental physiology, is born. He graduated from medical school in Leiden at age 19 and returned to Bern where he lectured on anatomy and wrote poetry. His research on the irritability or contractility of muscle tissue was published in 1732 as *A Dissertation on the Sensible and Irritable Parts of Animals*. In 1736 he was appointed professor of anatomy at the University of Gottingen's medical school, where he spent 17 years. In 1753 he returned again to Bern,

where he died in 1777. Haller published numerous other works, including bibliographies on anatomy, surgery, botany and medicine and a very popular collection of poems. A brief review of his life is available here.

1760 October 23: Japanese physician Hanaoka Seishu is born in Hirayama. In October 1805 Seishu performs an operation for breast cancer using "tsusensan" as an anesthetic. The research behind this event is portrayed in Sawako Ariyoshi's novel *The Doctor's Wife*. Seishu died on October 2, 1835.

1772 October 21: English poet Samuel Taylor Coleridge is born. In 1799 Coleridge participated in the nitrous oxide experiments being conducted by Dr.

*For the full calendar, go to www.anes.uab.edu

Thomas Beddoes and his research assistant Humphry Davy at the Pneumatic Institute in Clifton, just outside Bristol. Coleridge and other luminaries involved left written accounts published in Davy's great work on nitrous oxide which appeared in the summer of 1800. The enthusiasm for "laughing gas" inhalation by Coleridge, Davy, and fellow poet Robert Southey is depicted in the recent British film *Pandaemonium*.

1805 October 13: Japanese physician Hanaoka Seishu [1760-1835] performs an operation for breast cancer using "tsusensan" as an oral general anesthetic on a patient named Kan Aiya. The research behind this event is portrayed in Sawako Ariyoshi's novel *The Doctor's Wife*. [See also Ogata T. Seishu Hanaoka and his anaesthesiology and surgery. *Anaesthesia* 1973;28:645-652] Seishu left case records of more than 150 breast cancer patients.

1815 October 31: Humphry Davy patents the miner's safety lamp for use in coal mining. In addition to his classic work with nitrous oxide in 1799 and 1800, Davy isolated the metals potassium, sodium, barium, calcium, and magnesium. He also conducted early electric lighting experiments.

1835 October 2: Japanese physician Hanaoka Seishu dies. See entries above for 13 October 1805 and 23 October 1760.

1846 October 16: On this Friday morning, Boston dentist William Thomas Green Morton appeared in the operating theater of the Massachusetts General Hospital. Morton was running late, but surgeon John Collins Warren had not yet started the removal of a tumor from Gilbert Abbot's jaw. For about three minutes Abbot breathed ether vapor from Morton's simple apparatus-- which had been the source of his delay--and "sank into a state of insensibility," Warren noted later. The first public demonstration of ether anesthesia had begun and proved successful.

Abbot "did not experience pain at the time, although aware that the operation was proceeding," Warren wrote in his 1848 account of the event. The great surgeon is supposed to have declared, "Gentlemen, this is no humbug." The next day another MGH surgeon, George Hayward, removed a large tumor from a woman's arm while she was under the influence of the "Letheon," as Morton called it; for several weeks he did not reveal the nature of his anesthetic agent since he hoped to patent it. [Source: Keys

TE. *History of Surgical Anesthesia*. Huntington, New York: Krieger, 1978, pp27-29]

1846 October 17: At the Massachusetts General Hospital surgeon George Hayward removes a large tumor from the arm of a female patient anesthetized with ether. This operation is the second successful public demonstration of Morton's "Lethon."

1848 October 19: Samuel Guthrie, American chemist who discovered chloroform about the same time as Europeans Soubeiran and Justus Liebig, dies.

1849 October 7: American writer Edgar Allan Poe dies in Baltimore. Lesser-known among his works are three tales dealing with mesmerism, or what we now know as hypnotism. Mesmerism was developed in the late eighteenth-century by Viennese physician Franz Anton Mesmer [1734-1816] and for decades was associated with quackery. However, several physicians in the 1830s and 1840s in England and India used and promoted it as surgical pain relief until the introduction of ether by Morton. Poe's stories featuring mesmerism are "A Tale of the Ragged Mountains," "The Facts in the Case of M. Valdemar" and "Mesmerism Revelation." One recent history of mesmerism is Alison Winter's *Mesmerized: Powers of Mind in Victorian Britain* [1998]. Poe was born January 19, 1809.

1854 October 16: Irish writer Oscar Wilde is born in Dublin. The author of such iconic novels and plays as *The Picture of Dorian Gray* and *The Importance of Being Earnest*, Wilde today is also remembered for his pithy, often hilarious observations about human nature and behavior. His mother Jane was also a writer and his father William was a prominent physician whose vast professional achievements, like Oscar's, were tainted by scandal in his lifetime. [Defalque RJ, Wright AJ. Travers vs. Wilde and other: chloroform acquitted. *Bull Anesthesia History* 23(4): 1, 4-7, October 2005]. Father and son also had minor connections to the history of anesthesia. In his 1898 article "Consciousness under nitrous oxide," American philosopher William James quoted an anonymous letter widely believed to be written by Wilde. In it Wilde described the mystical insights he had during a dental anesthetic. "My God! I knew everything! A vast inrush of obvious and absolutely satisfying solutions to all possible problems overwhelmed my entire being, and an all embracing unification of hitherto contending and apparently diverse aspects of

truth took possession of my soul by force..." [See James W. *Consciousness under nitrous oxide*. *Psychol Rev* 5:194-196, 1898] Wilde died in Paris on November 30, 1900.

1881 October 15: English author Pelham Grenville Wodehouse is born in Surrey. As P. G. Wodehouse he published 96 humorous novels and collections of stories before his death on February 14, 1975. Many of the novels feature the wealthy Bertie Wooster and his valet Jeeves. One of his other novels, *Laughing Gas* (1936) tells the story of the Earl of Havershot, who exchanges identities with a child movie star after inhaling nitrous oxide in a dentist's office. Since 1936 the novel has been reprinted numerous times, translated into Italian, Japanese and Spanish, and remains in print today.

1883 October 9: Ralph M. Waters is born. Dr. Waters' achievements during a long career at the University of Wisconsin make him the father of academic anesthesia in the United States. Dr. Waters died in 1979. For more information see Lucien E. Morris, Mark E. Schroeder, Mary E. Warner, eds. *A Celebration of 75 Years Honoring Ralph Milton Waters, M.D., Mentor to a Profession*. Wood Library-Museum of Anesthesiology, 2004 [Proceedings of the Ralph M. Waters Symposium on Professionalism in Anesthesiology, Madison, Wisconsin, June 2002]

1888 October 17: American genius Thomas Alva Edison applies for his first patent for a device he calls a "Kinetoscope"--what we now know as a motion picture camera. Edison claimed that it would "do for the eye what the phonograph does for the ear." Work on the device by Edison's collaborator William K.L. Dickson had begun soon after the move the previous year into a new laboratory at West Orange, New Jersey. A prototype with the earliest film strips was demonstrated in May, 1891, and Edison's final patent filed in August of that year. Work on the Kinetoscope was completed in 1892. The following year Edison opened a motion picture studio and by 1894 was opening Kinetoscope viewing parlors in New York and other major cities. Competition from other companies led Edison into numerous legal battles, and by 1918 he had abandoned the motion picture business. However, one of his studio's early films, *Dr. Colton, or Dentist Scene*, has an important place in anesthesia history. This 1894 film was one of many "actualities" or

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short, non-fiction films made in the earliest period of motion pictures. A still from the film shows an elderly gentleman, apparently Gardner Quincy Colton, and others in either an actual or recreated dental procedure. If this is indeed Colton, who was born in 1814, he would have been 80 and the film made just four years before his death. In 1844 Colton had begun public nitrous oxide inhalation demonstrations in New England and toured the U.S. in subsequent years—he even came to Mobile, Alabama, in 1848! In 1863 he established the Colton Dental Association and began touring the U.S. and Europe to promote nitrous oxide anesthesia in dentistry. By 1894 Colton was perhaps the best known anesthetist in the world. And the brief film from Edison's studio is probably the first ever made of an anesthetic procedure. Edison died on October 18, 1931, in West Orange, New Jersey, age 84.

1894 October 7: American author and physician Oliver Wendell Holmes dies. In addition to his many other achievements, Holmes suggested to William Morton just weeks after Morton's October 1846 public demonstration in Boston that the mental state produced by ether inhalation be called "anaesthesia." The word is derived from an ancient Greek term meaning lack or loss of sensation and had been in circulation in English for over a century when Holmes suggested it be applied to Morton's technique.

1902 October 25: American author Frank Norris dies. In his novel *McTeague* [1899], Norris tells the story of a San Francisco dentist. Early in the novel *McTeague*

attacks one of his patients while she is under ether anesthesia.

1939 October 7: American neurosurgeon and medical historian Harvey Cushing dies. In 1894 Cushing and fellow Massachusetts General Hospital "house pup" Ernst Amory Codman [1869-1940] developed the first anesthetic record.

1947 October 13: In Britain, two patients, Albert Woolley and Cecil Roe, receive spinal anesthesia from the same anaesthetist, Dr. James M. Graham, for relatively minor surgical procedures, and both developed permanent, painful, spastic paraparesis. The men sued Dr. Graham and the Ministry of Health; the case finally went to trial in October, 1953, and lasted eleven days. The plaintiffs lost primarily due to testimony of Sir Robert Macintosh of Oxford University. Despite the outcome, the use of spinal anesthesia in the United Kingdom was retarded for the next 25 years. Details of the case can be found in Morgan M. The Woolley and Roe case. *Anaesthesia* 50:162-173, 1995.

1980 October: American Society of Post Anesthesia Nurses (ASPAN) is incorporated.

1990 October 21: Seven subspecialties admitted to the ASA House of Delegates.

1994 October 24: Twenty-cent U.S. stamp honoring Virginia Apgar is released at the annual meeting of the American Academy of Pediatrics in Dallas, Texas.

2001 October 11: Betty Jane Bamforth,

M.D., dies in Madison, Wisconsin. Dr. Bamforth received her M.D. degree from Boston University in 1947 and after an internship in Boston, finished a residency in anesthesiology at Wisconsin General Hospital in 1951. She was one of the last residents trained by Dr. Ralph Waters, the father of academic anesthesia and the first chair of the University of Wisconsin Anesthesiology Department. Dr. Bamforth spent three years at the University of Oklahoma, and then returned to Madison in 1954 and remained on the medical school faculty until her retirement in 1992. She served as acting chair of the department from 1969 until 1971, and was thus the first female chair of that department. She also served in various capacities in the medical school. Well-known for her writing and lecturing on anesthesia history, Dr. Bamforth delivered the ASA's Wright Memorial Lecture in 1982 and the Rovenstine Memorial Lecture in 1993. The Rovenstine Lecture is the most prestigious honor given by the ASA; she was the first woman to be so honored. Dr. Bamforth was born on January 20, 1923, in New Britain, Connecticut. [From Dr. Bamforth's obituary, *Wisconsin State Journal*, October 16, 2001]

2001 October 16: British medical historian Dr. Barbara M. Duncum dies. In 1947 Dr. Duncum published *The Development of Inhalation Anaesthesia*, which along with Thomas Keys' *The History of Surgical Anesthesia* is one of the major histories of the specialty. Her book was reprinted in 1994. Dr. Duncum was born February 22, 1910.

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