MILESTONES in Urolithiasis

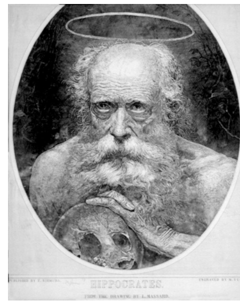
the William P. Didusch Center for Urologic History

Milestones in Urolithiasis

For millennia, depending on where they were located, urinary tract stones have been a pain in the back, flank, groin, or pelvis. From stones found in mummies, we know that stones were not uncommon in Egypt; we imagine the same about other countries, but for most civilizations, there exist no written records from thousands of years ago. There is increasing evidence that our prehistoric ancestors formed urolithiasis.

Stones usually form in the kidney and, if they are small enough, may travel down the ureter where they may get stuck at the outlet of the kidney or where the ureter crosses the large pelvic vessels or at the entry into the bladder. Once in the bladder, stones can either be passed spontaneously or continue to grow.

The history of urinary stone disease is fascinating. The writings of **Hippocrates** (460 – 370 BCE, Kos, Greece) mention stones in 24 passages. **Aristotle** (384 BC - 322 BCE) questioned "Why none of the animals but Man alone can become gravelly?" The fact that the *Hippocratic Oath* states "I will not cut upon the stone but leave this to practitioners of this art," clearly indicates that there were experts who removed bladder stones, despite the high mortality rate.



Hippocrates

National Library of Medicine

I swear by Apollo Physician and Asclepios and Hygeia and Panacea and all the gods and goddesses...that I will fulfill according to my ability and judgment this oath and covenant:

...I will not cut upon the stone but leave this to the practitioners of this art...

FOUNDING FATHERS OF STONE COMPOSITION AND FORMATION

In ancient times the Greeks and later the Romans attempted to prevent stones by figuring out how they were formed. **Galen** (130 – 200 CE) proposed:

> *The tough slime [in the kidneys] hardens by the heat of the kidneys and is baked to a stone. But the fire is indeed the cause, but that it does not act by its heat alone, but by drying and hardening the substance.*

Many physicians and other researchers worked to understand the composition and formation of stones in the urinary tract; in the Middle Ages in Europe, **Guido Lanfranchi** (c. 1250–1306), still believed stones grew from an imbalance of the four humors, stipulating that humans must have a certain balance of minerals and certain illnesses could cure them. He believed that kidneys have great natural heat which bakes the stone and that children, whose kidneys are less hot, form bladder stones.

National Library of Medicine

Johan van Beverwijck (1594-1647) used William Harvey's new concept of blood circulation to develop a hypothesis of stone formation that deviated from the Hippocratic and Galenic explanations, stating:

> *...the Stone is a hard body growing out of an earthy substance owing to inefficiency of the kidneys or bladder and, having hardened into a stony shape, causes very painful tension and obstruction.*

Today we know that supersaturation of the urine is a contributing factor to stone formation.

In the 1700s **Andreas S. Marggraf** (1709-1782) was the first person to note that there are different types of urinary stones based on composition.

Matthew Dobson (1732-1784) concluded that stone disease was more common in the "Cyder" districts and that hard water prevents rather than promotes the formation of stone disease. "This doctrine of the solution of calcareous earths, naturally suggested the idea of the solubility of the human calculus while yet in the bladder, by the regular and continued use of Fixed Air." He was trying to define the notion of supersaturation of solutes with an interaction of carbon dioxide. He did not know about the conversion by the kidney into bicarbonate ions and the buffering effects of citrate, but he was getting remarkably close to modern urine biochemistry.

Sampson Perry (1747 – 1823) stipulated that human calculi form in the kidney and are then conveyed to the bladder where they can grow and enlarge, causing trouble. Smaller concretions could also be passed. He stated:

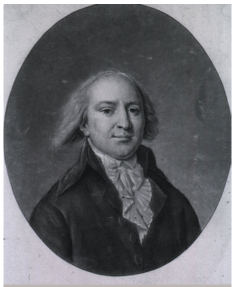
> *...human calculi are of very different degrees of density and cohesion; some being so loose and friable as to crumble to pieces between the fingers, while others have been taken from the body, of such a compact and flinty nature, as to strike fire in collision with steel...*
>
> *The Real Cause of the Stone*

Perry believed that the elemental particles that produce the stone separate from the blood in the tubules of the kidney, and he named them *primary particles of stone*. Once the primary particles are separated from the blood in the tubules of the kidney:

> *those primary particles so as to become a nucleus of the stone: for, from the second experiment of the same section we find, that when once a nucleus exists in the body, it collects by its attractive power, the particles about its surface, and thereby accumulates continually.*

Perry was getting to the modern notions of nucleation, fixed particle retention, and supersaturation.

Two schools of calculous chemistry arose in the face of war-torn Europe at the end of the Eighteenth century: one centered in England and the other in France. The English school of stone chemistry used early chemical methods to identify and categorize stones based upon the pioneering work of Reverend Stephen Hales (1677-1761) and Karl Wilhelm Scheele (1742-1786). William Hyde Wollaston (1766-1826) was followed by Alexander Marcet (1770-1822), Henry Bence Jones (1813-1873), William Prout (1785-1850) and Golding Bird (1814-1854). The French school started with Antoine-Laurent Lavoisier (1743-1794), Félix Vicq D'Azyr (1748-1794), Antoine F. Fourcroy (1755-1809) and Nicolas Louis Vauquelin (1763-1829). In a period of less than two decades, these unique individuals identified and named almost all of the culprits of stone-forming chemistry that are known today.



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Antoine F. Fourcroy (1755-1809) experimented upon a large number of urinary stones and wondered if uric acid was confined to humans and how uric acid affected urinary stone formation. In 1802, Fourcroy published his extensive research on stone disease. He identified twelve constituents in stones (seven of these in human stones) as follows: uric acid, ammonia urate, calcium phosphate, magnesium ammonium phosphate, calcium oxalate, and animal matter (gelatin) or combinations of these. He believed that uric acid was the most common substance in stones. His incidence of stone types concluded: 25% were predominately uric acid, 25% were calcium oxalate, and the rest were mixtures. These numbers are eerily similar to modern series.

Dr. Robert Peter

University of Kentuck Archives

At roughly the same time, **Dr. Robert Peter** (1805-1894) in Kentucky, working with two of the leading lithotomists in colonial America, analyzed the stones removed by lithotomy and mounted them on cardboard with date, name of patient, and stone composition using the chemistry and scheme developed by Wollaston and published by Golding Bird. His analyses were sought after, not only in Kentucky, but as far away as Philadelphia.

Human Bladder Stone,
Calcium Oxalate/Carbonate Apatite, 24mm

William P. Didusch Center for Urologic History,

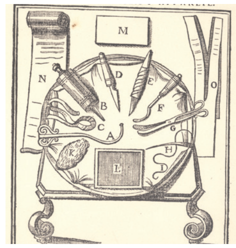
CUTTING FOR STONE: LITHOTOMY

For centuries the only operation for stones was performed on the bladder and almost always through the *perineum*, that area between the scrotum and anus in males or vagina and anus in females. This operation was performed in a similar fashion in Greece and India, and later in Rome, where we get the first detailed descriptions of the operation in the writings of **Aulus Cornelius Celsus** (c. 25 – 50 BCE). Though not a physician, Celsus described the *Apparatus Minor*, which used a small number of instruments. It was more than a millennia before the procedure was changed; in the early 1500s Francisco de Romanis and Mariano Santo developed and popularized the *Apparatus Major*, which called upon a number of newly-developed instruments, including a gorget, dilators, urethrotomes, scalpels and the grooved staff used to prove the presence of the stone and guide the cutting blade through the urethra, prostate and bladder neck into the bladder. This incision could then be enlarged at the bladder neck to allow grasping the stone with forceps, which came in different shapes and sizes. Most barber-surgeons who performed this operation could complete their work within 30 minutes.

Aulus Cornelius Celsus 1771

National Library of Medicine

Pierre Franco (1500 – 1573 CE) modified the procedure of Mariano Santo by adding a double-bladed knife used to cut the bottom and the top of the opening into the bladder. If the stone was too large to be extracted, a second operation was performed a few days later after the patient had recovered enough to tolerate the removal. These operations were done without anesthesia, though alcohol and somniferous herbs were given to make the patient drowsy. There were no antibiotics, and suture material, if used, was crude.

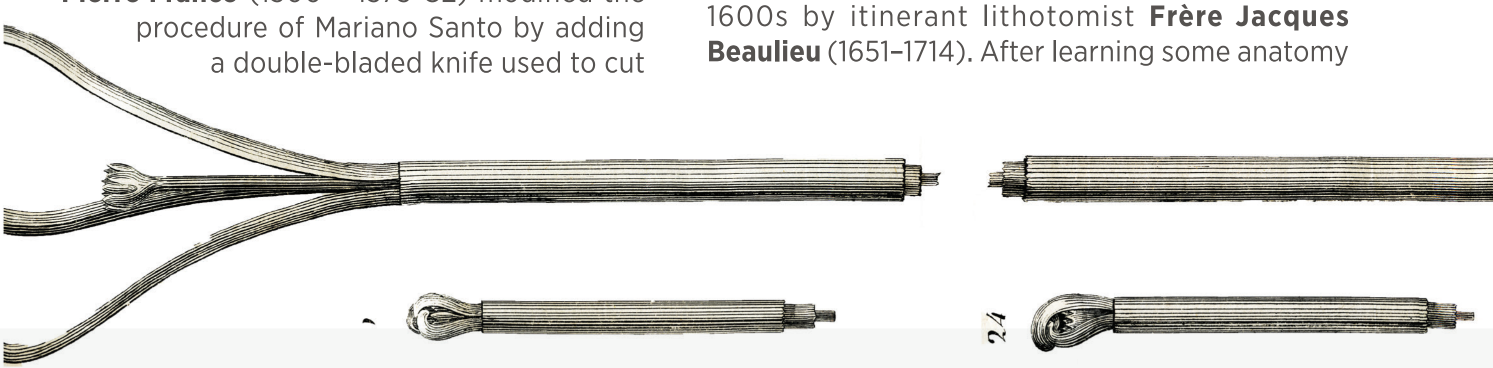


Early Lithotomy instruments, *Les Instruments de Chirurgie Urinaire, Octave Pasteau* 1914

William P. Didusch Center for Urologic History, donated by John Herman, MD

The *High Operation* or *suprapubic approach* was first documented in 1651 by Pierre Franco, who was unable to remove a large stone from a two-year-old child. As the parents begged him to continue, he performed the suprapubic incision to remove the stone but advised others not to do so. The suprapubic approach had several risks, the largest of which was cutting into the peritoneum unless the procedure was performed with a full bladder; cutting into the peritoneum frequently led to peritonitis, which usually ended with the patient's death.

William Cheselden (1688 –1752) also described this operation almost 100 years later but abandoned the procedure to perform the lateral perineal incision instead. This approach was developed in the late 1600s by itinerant lithotomist **Frère Jacques Beaulieu** (1651–1714). After learning some anatomy



Civiale lithotripteur *De La Lithotritie, Jean Civiale* 1827

William P. Didusch Center for Urologic History, donated by John Herman, MD in France, he modified the operation, continuing to use a grooved staff, and incised the prostate and bladder neck by cutting on the groove. It is said that Frère Jacques had operated on 5,000 patients when he died in 1714.

While these were improvements, a major shift in the philosophy of surgical intervention came with **Franz von Paula Gruithuisen's** (1774 – 1852) 1813 paper published in the *Journal of Medicine and Surgery* of a new method to break up a bladder stone. This paper detailed his instruments, which included a straight rod with an obturator that could be inserted into the bladder, followed by a loop to trap the stone, a drill to break up the stone and a spark electrode. His procedure was difficult, but the idea caught on quickly, and it was not long before Jean Civiale and Leroy d'Etoilles described their transurethral lithotomies by drilling the stone into smaller fragments. In essence, Gruithuisen could be considered an originator of minimally invasive surgery in urology, replacing a risky operation with a safer and more comfortable procedure, though others less well-known (Ammonius, Albucasis, Franco) also made contributions to the procedure.

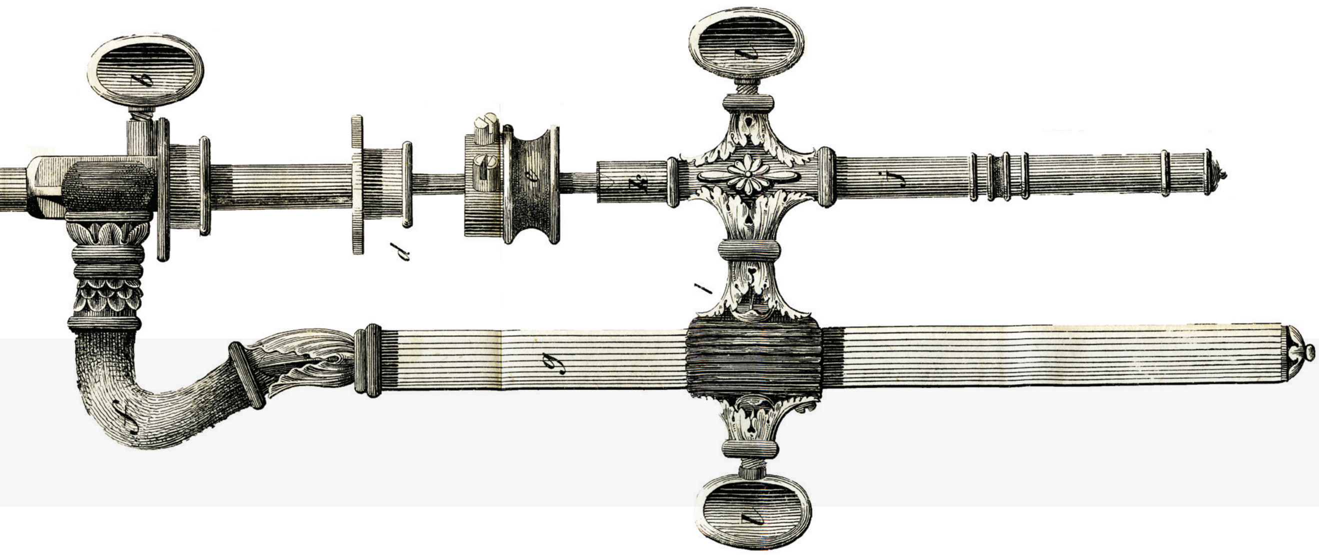
The first clinically *successful* drilling instrument was developed by **Jean Civiale** (1792 – 1867) and demonstrated in 1823. His long tubular instrument was inserted into the bladder, and three-pronged pincers were blindly advanced to grasp the stone. A bow-driven drill bit between the pincers fragmented the stone. Though Americans did not have good success with Civiale's technique, Civiale himself claimed a 3% mortality rate. He was closely followed by **Leroy d'Etoilles** (1798 – 1860) and **Baron L.S. Heurteloup** (1793-1864), who was the first to practice lithotrity in England. As with lithotomy, surgeons operated as quickly as they could; three minutes or less at one sitting was the standard limit at this time prior to anesthesia.

Frère Jacques de Beaulieu

Courtesy of Boerhaave Museum, Leiden, The Netherlands

"Lithotomy Position," *Traite de la Lithotomie, Francois Tolet* **1682**

William P. Didusch Center for Urologic History, donated by John Herman, MD



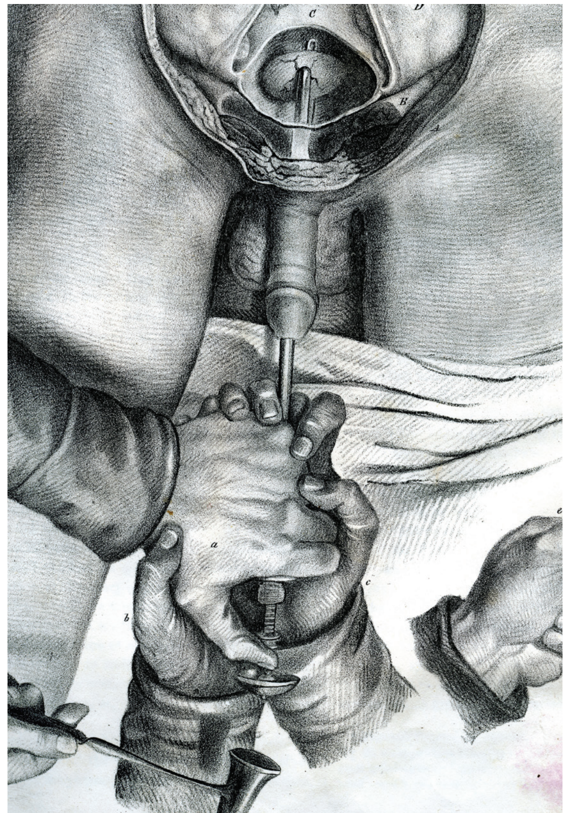
CRUSHING THE STONE

Percussion lithotrites - introduced by **Weiss** in 1830 and **Heurteloup** in 1831 - required two separate actions: the stone was caught between a stationary and a movable blade and then crushed by pounding on the movable blade. **Charriere**, an instrument maker in Paris, eventually developed a key that quickly closed the jaws - before the stone could escape – and applied enough pressure to crush the trapped stone. In 1850 **Sir Henry Thompson** (1820 – 1903) improved the mechanism with a cylindrical handle, a stronger shaft to crush larger stones, and a quick-release for the jaws. Henry Bigelow further improved the lithotrite and the method of evacuating the stone fragments.

National Library of Medicine

Henry Jacob Bigelow (1818 – 1890) graduated from Harvard College in 1837. Following in his physician father's footsteps, he went to medical school at Harvard and earned his degree in 1841. Like many American physicians desirous of expanding their medical knowledge, he went to Paris and then London to study for the next three years. Upon his return to Boston he began to practice, working at the Massachusetts General Hospital and the Harvard Medical School.

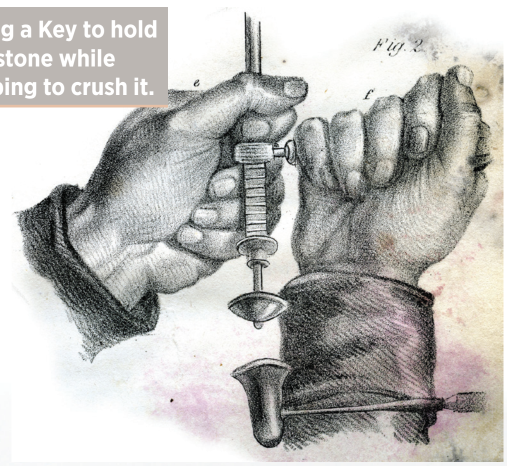
A surgeon with broad interests, Bigelow was also interested in urological operations, foremost among these the operation for the stone. Dissatisfied with the performance of available lithotriptors, he designed his own, with a larger size, stronger shaft, big jaws and, aided by an evacuation system that allowed swift removal of smaller fragments, leading him to publish his experience in 1878 under the title *Lithotrity by a Single Operation* in the *American Journal of Medical Sciences.*

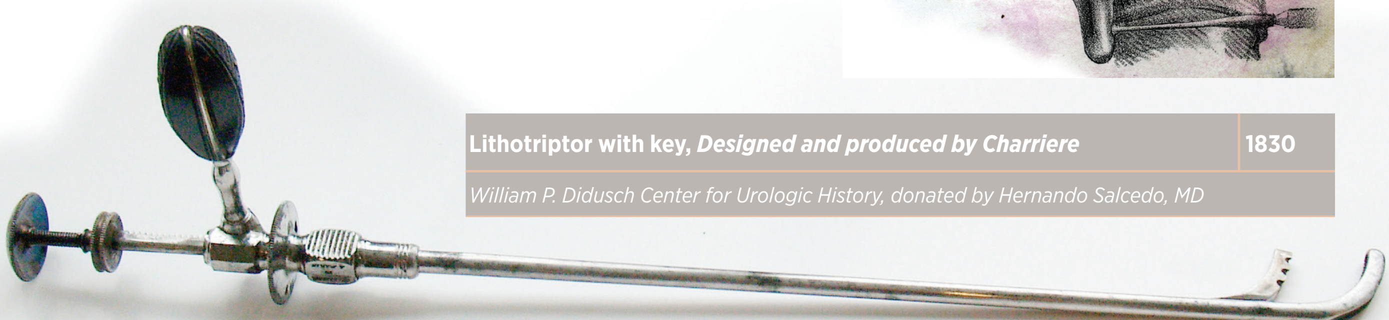


A Treatise on Operative Surgery, *Joseph Pancoast* | **1846**

William P. Didusch Center for Urologic History, donated by Christopher and Martha Campbell

Using a Key to hold the stone while tapping to crush it.





Lithotriptor with key, *Designed and produced by Charriere* | **1830**

William P. Didusch Center for Urologic History, donated by Hernando Salcedo, MD

Wilhelm Fabry or Fabricius Hildanus (1560 - 1634) was one of the most eminent barber-surgeons in Europe at the turn of the 17th century, though his significance as lithotomist is less recognized. A prolific writer, he wrote of his experience in practically each specialty of medicine in numerous monographs, and published a collection of 600 informative case reports.

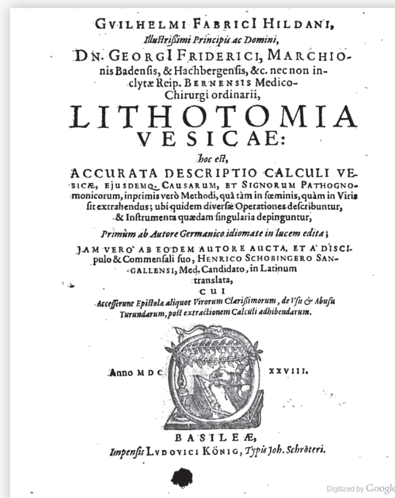
Fabry's book, *Lithotomia Vesicalis*, first published in 1626, includes 28 chapters that review all surgical techniques of "cutting on the stone," and addresses nearly all diagnostic and therapeutic aspects of urolithiasis. Regarding lithogenesis, Fabry subscribed to the classic Hippocratic and Galenic humour theory, maintaining that extreme heat transforms thick phlegm into stone material. He also considered the composition of drinking water and diet, and gave prophylactic advice. He wrote extensively on preparation of the patient for surgery, and refused to operate in "hopeless cases," as when the patient was debilitated or the stone too big. Lithotomy was only acceptable if the patient would otherwise die "within a few days."

Due to his profound knowledge of human anatomy and his studies of classical medical authorities, Wilhelm Fabry exemplifies the change from the experience-based *barber-surgeon* to the educated and scientific *operating physician*. He modified the surgical techniques of the **Apparatus Major** lithotomy, adding two sizes of "speculo-forceps" to the armamentarium, advised (like Franco) that lithotomy on larger stones be approached as a "two-stage" procedure, and emphasized transvaginal removal of big bladder stones in women.

In practice, Fabry was cautious and patient-oriented. He made high ethical and professional demands on himself and every lithotomist, and fought actively against quacks that "carelessly cut into the human body as butchers do in unreasonable animals." He emphasized the need to inform the patient and his relatives preoperatively about the complications and dangers of the surgery.

> *Hippocrates considers injuries of the bladder as deadly. But I have seen myself that some may recover.*
>
> *Fabricius Hildanus (1560 - 1634)*

Wilhelm Fabry was born in 1560 in Hilden, a small town near Düsseldorf, Germany. He attended school and learned classical languages before serving the well-known surgeon Vesal Cosmas Slotanus. Fabry became the official and beloved surgeon of Berne in 1615 until his death in 1634.


GVILHELMI FABRICI HILDANI,
Illustrißimi Principis ac Domini,
DN. GEORGI FRIDERICI, MARCHIO-
nis Badensis, & Hachbergensis, &c. nec non in-
clytæ Reip. BERNENSIS Medico-
Chirurgi ordinarii,

LITHOTOMIA
VESICAE:

hoc est,

ACCURATA DESCRIPTIO CALCULI VE-
SICÆ, EJUSDEMQ. CAUSARUM, ET SIGNORUM PATHOGNO-
monicorum, inprimis verò Methodi, quâ tàm in fœminis, quàm in Viris
sit extrahendus; ubi quidem diversæ Operationes describuntur,
& Instrumenta quædam singularia depinguntur,

Primùm ab Autore Germanico idiomate in lucem edita;

JAM VERO' AB EODEM AUTORE AUCTA, ET A' DISCI-
pulo & Commensali suo, HENRICO SCHOBINGERO SAN-
GALLENSI, Med. Candidato, in Latinum
translata,
CUI
Accesserunt Epistolæ aliquot Virorum Clarißimorum, de Vsu & Abusu Turundarum, post extractionem Calculi adhibendarum.

Anno MDC XXVIII.

BASILEÆ,
Impensis LUDOVICI KÖNIG, *Typis Joh. Schröteri.*

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***Lithotomia Vesicalis*, Willhelm Fabry** | **1626**

STONE DISEASE AND THE ROYAL PATIENTS

Napoleon III

Commons Wikimedia

Charles Louis Napoléon Bonaparte (1808 – 1873) was the only emperor of the Second French Empire. Louis-Napoléon was brought up in exile in Switzerland and Germany, and later in the U.S., where he spent time in New York. Elected president of the 2nd French Republic in 1848, he staged a coup d'état in 1851 and re-established the French Empire. Under his rule from 1848 to 1870, France underwent rapid economic growth.

In 1864 Napoleon suffered a urinary tract infection and was seen by eminent French physician **Baron Hippolite Felix Larrey** (1808 -1895) who wrote:

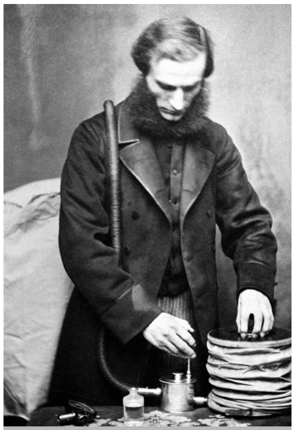
> *He felt in the night some accidents whose signs, well explained by himself, absolutely revealed for me, as they would have done for any other surgeon, the symptoms of a bladder stone.*

Two years later, following a catheterization, Doctor Guillon at Vichy, confirmed the diagnosis: stone.

Napoleon III was captured during the Franco-Prussian War in 1870; some of his biographers attribute his military loss at the battle of Sedan to his suffering from stones and colic. When the Germans released him in 1872, Napoleon III joined his wife and son in England.

Baron Félix Hippolyte Larrey

Wellcome Library, London



J. T. Clover with his chloroform apparatus.

Wellcome Library, London

On Dec. 15, 1872, suffering severely from his bladder stone, the emperor consulted **Sir Henry Thompson** (1820–1904), one of the most celebrated urologists in England who specialized in the removal of bladder stones, as well as Sir William Gull (1816–1890) and Sir James Paget (1814–1899).

On January 2, 1873, Thompson performed a lithotripsy to destroy the stone. The royal patient was anaesthetised by **Joseph T. Clover** (1825–1882), who developed the first stone evacuator. On January 6, a second lithotripsy followed. The Emperor died on January 9, 1873, not from the surgical procedure, as was proved by the post-mortem examination, but from uremia.

Although the story is well documented, several of Napoleon's biographies contain inconsistencies regarding his medical condition. The operation was widely discussed in the popular press at the time of Napoleon's death; the English surgeons and physicians defended themselves against French claims that they took less-than-optimal care of their prominent patient. In addition, both Thompson's lithotripsy and Clover's anaesthesia were novel medical techniques, and the practitioners hoped to publicize both techniques and their proficiency.

Leopold I, King of the Belgians.

Wellcome Library, London

On the other hand, **Henry Thompson** gained a great European reputation when he was asked to consult on **Leopold I**, King of the Belgians, who was visiting Queen Victoria when he developed bladder symptoms. The Queen's surgeon, Sir Benjamin Brodie, advised the King to return to Brussels and to consult with **Civiale**.

Thompson, who had trained with Civiale, concurred. In March of 1862, Civiale performed the first of three or four lithotrities with his *lithontripteur* over three months, but a larger stone was discovered; by December, the King's condition had deteriorated.

Thompson was called again to visit the King in Brussels. He had new instruments made and took his trusted anesthesiologist Dr. Clover to administer an inhalational agent to the King. They arrived at the Palace in Lieken on May 18, and the King allowed Thompson to sound his bladder. Thompson wrote his wife at this time

> *I slept only 1 ½ hours last night, between 5 and 6 a.m. I took too much coffee and couldn't sleep, and then I got thinking about my case and I got horribly anxious about it in the night. No one knows how anxious, but those who are placed in like circumstances.*

On June 1, 1863 Thompson sounded the King and discovered what he believed to be the stone. He arranged a second sitting for June 6th and crushed the stone with his new lithotrite:

> *We saw the King at nine. I injected the bladder with water at H.M.'s wish, having drawn off the urine. I then introduced very carefully the sound and turning to the left, instantly found the hard body. I struck it hard and got again the dull note...I withdrew the sound, introduced the lithotrite with plane blades and turned to the left. I found nothing, to the floor, found nothing but grazed it in the middle line first position and caught it by short diameter crushing it twice. My blades were full, I screwed home tight and withdrew them full with a good quantity of phosphatic debris. After waiting 15 minutes...I injected again at his wish, withdrawing first the water – no blood and introduced again the same lithotrite in the same position and with the same result. A good quantity is now removed. It is what would be an excellent result in any case. Slight trace of blood this time. Pain not much.*

A second sitting was undertaken about four days later, and the King made a rapid and improved recovery. Thompson returned from his 26-day stay in Brussels with a fee of 3,000 pounds. He returned one year later for a week's duration in follow-up and received another 1,000 pounds. It was a very good year for Thompson, as his textbook *Practical Lithotomy and Lithotrity* was also released. Thompson sent his old master, Jean Civiale, a note thanking him for all of his successes. Thompson was appointed *surgeon extraordinaire* to the King, a title that was maintained by his son, Leopold II, and was later knighted by Queen Victoria in 1867.

Sir Henry Thompson, by John Everett Millais | **1881**

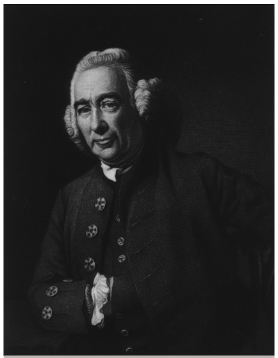
EARLY AMERICAN LITHOTOMY

Dr. John Clark, *by Augustine Clement.*

The Boston Medical Library in the Francis A. Countway Library of Medicine, Boston, MA.

The Pilgrims landed in Massachusetts in 1620, and by 1637, a **Dr. John Clark** (1598 – 1664) is documented in the records of Newbury, Massachusetts, exempting him of "...all publick rates for the town or the county so long as he shall remain with us and exercise his calling among us." Clark was born in the north of England and attended medical school in Edinburgh; according to a handwritten account written by his grandson in 1731, Clark "had from the college a diploma for a practitioner, and on his successful cutting several of the stone (sic) he had a separate diploma as to that faculty...."

Another early lithotomist on the eastern seaboard was **Silvester Gardiner** (1708 – 1786), a Rhode Island native, who began his apprenticeship in 1720 in Boston with Dr. John Gibbon. Gardiner's uncle financed most of the young man's nearly eight years of medical study in Paris and London. In Paris, Gardiner studied fracture treatment, amputations, and basic anatomy. In London, he spent most of his time with William Cheselden, where he learned to perform lithotomies using the lateral approach. Upon his return to Boston in 1731, he opened a shop called "Unicorn and Mortar" where he sold imported drugs, herbs, self-help and medical manuals.



Silvester Gardiner

National Library of Medicine

Ephraim McDowell

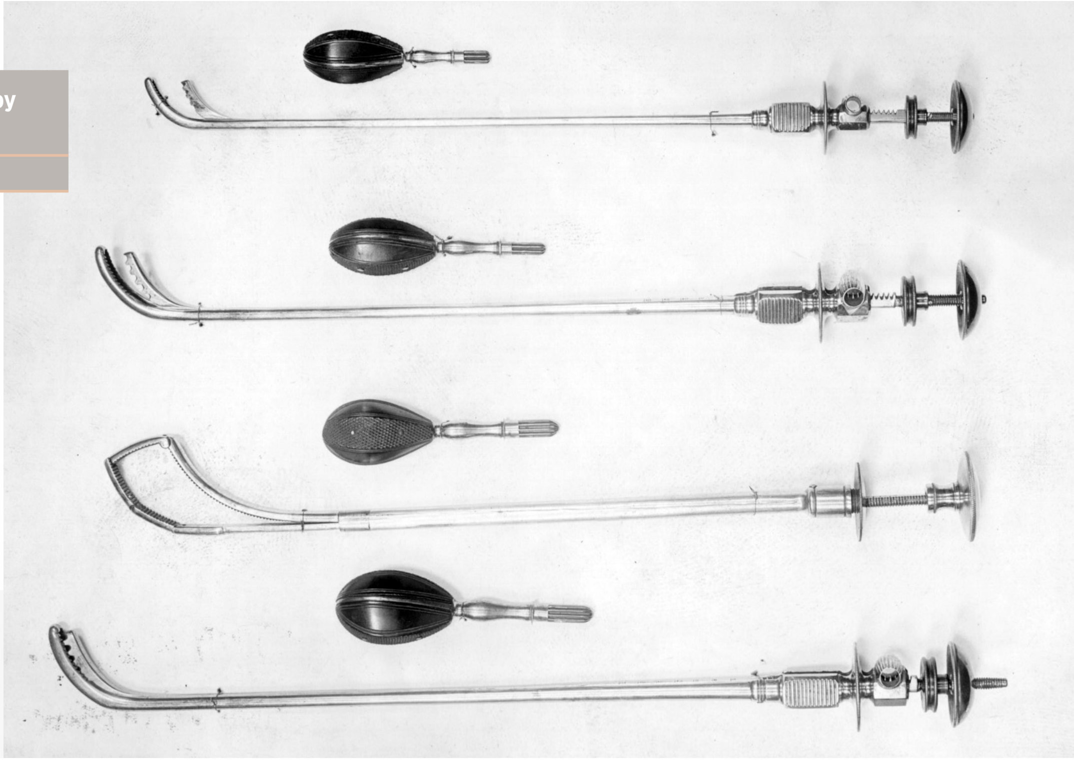
Courtesy of Erwin Rugendorff, MD

One notable Kentucky lithotomist was **Ephraim McDowell** (1771 –1830), who studied in Staunton, Virginia with Dr. Alexander Humphreys before apprenticing with a local physician. In 1793 Ephraim McDowell went to the University at Edinburgh to study under John Bell, who regularly lectured on "stone in the bladder." When Bell told his students that stones were frequently found in limestone country, McDowell became fascinated, recalling that Kentucky is limestone country. McDowell watched Bell operate for stones, usually successfully. Two years later McDowell returned to Danville and soon acquired an outstanding reputation as a skilled surgeon. Probably the best-known of McDowell's lithotomies was performed on James K. Polk in 1812, when Polk was 17 years old. Polk had suffered from a bladder stone since age 11, and the family decided to have the renowned surgeon, Philip Syng Physick perform the lithotomy. During the transport, however, James grew worse and they diverted to the closer surgeon, Ephraim McDowell. Polk recovered but was probably rendered sterile from the operation; he later became President of the United States in 1845.

Benjamin Winslow Dudley (1785-1870) apprenticed with a "well-known physician in the West," Dr. Ridgley, before deciding that he wanted to expand his knowledge by studying abroad. Unlike many of his peers who came from families with money, Dudley earned his own way to Europe by purchasing a small barge, loading it with produce, and floating down the Mississippi to New Orleans, where he sold his cargo and boat. He invested the money in flour, which he shipped to Gibraltar. He arrived there in 1810 and sold everything for profit, which allowed him to move to Paris. After about three years, Dudley moved on to London where he watched Sir Astley Cooper operate, worked for a time in a large London hospital, and, upon leaving, was elected a member of the Royal College of Surgeons.

In 1814, Dudley returned to Lexington and settled down to practice medicine. Though he practiced both medicine and surgery, Dudley became the leading lithotomist in the United States, operating on 225 patients and losing only three. He performed his first lithotomy in early 1817 in Paris, Kentucky, on a little boy, and the second on a man in November 1817 in Lexington, Kentucky. Dudley used a grooved sound, gorget, and a lithotome caché, as well as urethral dilators and urethral stone fragment extractors and the usual forceps. Dudley, like McDowell before him, used the lateral approach for his lithotomies but would not use any of the European lithotrites, stating that litholopaxy was not safe.

> *...when the calculus is either remarkable for its magnitude or hardness, when the bladder is ulcerated, inflamed or highly excitable, when the prostate gland is diseased, or the urethra contracted and inflamed, the instruments of Civiale are inadmissible with the safety of the patient.*
>
> *Benjamin W. Dudley, M.D.*



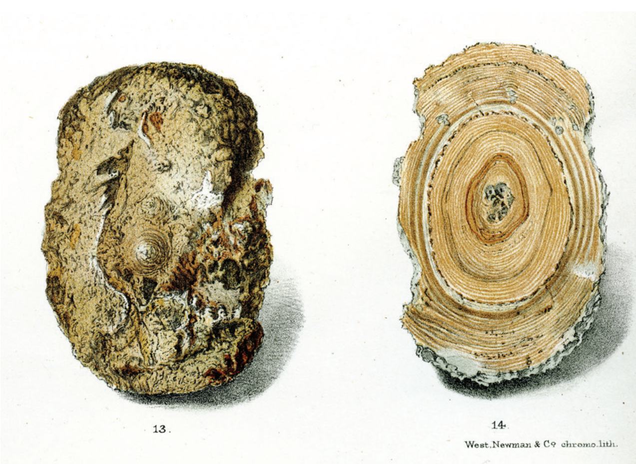
Lithotomy Instruments used by early American physicians

University of Kentucky Archives

DISSOLVING THE STONE

History is replete with attempts to create a universal remedy for the dissolution of stones in the urinary tract. No one has been able yet to accomplish this in a non-toxic fashion, though there are acids that can accomplish this mythical task with equally damaging capabilities on the bladder itself (nitric acid). Herb concoctions were used for hundreds of years, as well as a strange remedy by **Friar Giovanni Andrea** of the Order of the Jesuati Friars of Saint Jerome (Bruscia, Italy) that read:

> *Take the blood of a fox and its testicles and make this tepid and put it in the opening of the penis and also bathe under the testicles. Do this several times and the stone will be broken. Also give this blood to be drunk or make it into powder with warm white wine. By using these remedies repeatedly, the patient will soon be freed. Also, smear your fingers with this blood and rub it on the body: that is, on the pubes, on the kidneys, and under the testicles where the neck of the bladder is. Do all these things in one treatment: that is, the beverage, smearing the penis and the other rubbings. Do not live in a disorderly way and do not go out when you do this and very soon you will bring out the broken stone.*



Surfaces of a calculus that has undergone partial solution in the bladder. | **1888**

Atlas of Illustrations of Pathology, William P. Didusch Center for Urologic History

Andrea's *Libro de I Secreti e Ricelle* (*Book of Secret Remedies*) is full of exotic treatments for maladies ranging from bladder stones to hemorrhoids to the involuntary escape of sperm, and he was one of the early physicians to suggest that the reader experiment to discover the efficacy of his recommendations.

Since survival after a perineal lithotomy was always uncertain and the procedure itself quite painful, quacks in London had no problems hawking their stone-dissolving concoctions. In the early 18th century, the incidence of stone disease had become significant enough that a public outcry began to force those in public office to pay particular attention. The significance and prevalence of stone disease is clearly presented by the campaign to fund the £5,000 reward asked by Mrs. Joanna Stephens for her secret remedy for dissolving bladder stones. Mrs. Joanna Stephens from London submitted the best of several stone-dissolving remedies for examination and experimentation by a panel of experts. Four patients with documented bladder stones were chosen and received her concoction. Each patient passed stone fragments and exhibited copious white mucus in his urine; subjectively, each was greatly relieved. A repeat examination with probes showed that no further stones were present within the bladder. The review of Mrs. Stephens' remedy ended on March 5, 1740, and the panel awarded her the full £5000.

Robert Whytt

National Library of Medicine

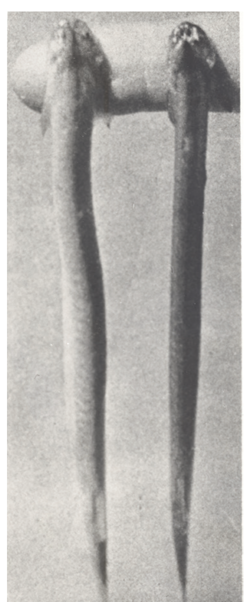
In response to Mrs. Stephens, **Robert Whytt** (1714 – 1767, Edinburgh) presented a paper in 1743 entitled, *On the Virtues of Lime-Water in the Cure of Stone*. Whytt thought that lime-water might be a better treatment and began to prescribe it to his stone patients by 1741. This may have been effective on uric acid stone formers, but further laboratory experiments led him to report that lime-water did not dissolve every stone.

David Hartley (1705 - 1757) met Joanna Stephens when he was 32 years old. After experimenting on himself with her stone remedy, Hartley wrote, "A View of the Present Evidence for and against Mrs. Stephens's Medicines as a Solvent for the Stone." He eventually died of the disease he thought her recipe had cured.

Wellcome Library, London

This ancient notion of restoring to solution the concretions that have precipitated seems reasonable with current chemical knowledge. Crowell had attempted to dissolve a cystine stone in a kidney by retrogradely lavaging mercurochrome every other day in 1924. Hellstrom also reported an attempt to dissolve an infectious-type stone using a 1% phosphoric acid, boric acid, and potassium permanganate to acidify the urine in his patient in 1938. The following year, Fuller Albright and his team at Massachusetts General Hospital tried to dissolve calcium phosphate bladder stones using isotonic citrate solutions. Knowing that natives in the Amazon basin use the juice of the *buitach apple* or *genipa american L* (with high citric acid levels) to kill a small parasitic catfish (Candiru) that penetrates the urethra of human bathers, E. Lin attempted to dissolve incrustation in the urinary bladder using this fruit solution in 1945.

The attempts to discover or create a solution to dissolve stones have not ceased. In 1959, Howard Suby created a solution of isotonic citrate, magnesium oxide and sodium carbonate that dissolved phosphatic stones in vivo. Initially the solution was called *Howard Suby's G solution*; it eventually was marketed as Renacidin®. This was effective at removing encrustations on catheters and a preferred treatment for struvite stones into the early 1960s. At that point, several deaths from the solution were reported, and the Food and Drug Administration banned its use in June of 1963. Subsequent work by many investigators has salvaged the use of Renacidin®. It is now useful in situations where infected stone fragments and rapid calcification of foreign bodies becomes a problem.



Candiru Catfish, from Lins, E E, *The solution of incrustations in the urinary bladder by a new method* **1945**

Journal of Urology

Buitach apple

STONES FORMING AROUND FOREIGN BODIES

There is a type of stone that forms not because of imbalances in the urine, but because of an indwelling foreign body within the bladder. Probably the earliest description of such a stone comes from **Giovanni Battista Morgagni** (1682-1771), who wrote his observations on a patient with stone disease:

> *a country girl…died in her fourteenth year. For having introduc'd a brass hair-bodkin, notwithstanding it was bent in the middle, very high into the urethra,…she was silent as to the true cause of the pains. For even the bodkin could not be extracted, by reason of a calculus that was form'd upon it. But the ureters, and the kidnies themselves, were in a very bad condition indeed.*

Today we still see unusual foreign bodies introduced into the bladder. Sometimes this is a fragment of a catheter; the tip broke off and a stone grew around it without the patient initially knowing that something was amiss. More commonly in times of war, stones form around a bullet or pieces of clothing dragged by the bullet that lodge in the bladder. *The Medical and Surgical History of the War of the Rebellion*, issued by the US Government after the Civil War, is a collection of all medical and surgical cases reported to the US Army. A few cases illustrate this problem.

Private T. Lindsay (HIPAA did not exist at that time and thus personal information is contained with each of the reported cases), Company F 69th Pennsylvania, Age 43, was wounded at Gettysburg, July 2, 1863 while in a kneeling position by a ball which, after passing through his canteen, entered his thigh. Surgeon James, USV, reported that Lindsay was treated at Camp Letterman from August 5 to November 5, 1863, for a gunshot wound penetrating the pelvis and was then transferred to Newton University Hospital in Baltimore, MD. Surgeon C.W. Jones, USV, reports that "a ball passed into the pelvic region, causing incontinence of urine and impairing the motions of the hip joint" and that the patient was discharged from service January 18, 1864. On his return home to Chester, PA, Lindsay suffered many of the symptoms of stone in the bladder, for which he was treated from time to time until February 1865 when an operation for strangulated hernia, the result of dyspnea, became necessary. On April 12, 1866, the operation of lithotomy was performed by Dr. J.L. Foreword when, most unexpectedly, an irregularly-shaped ball coated with a phosphatic deposit was removed from the bladder. The concretion and nucleus weighed 768 grains. The operation was successful. There was no pension record for the case, indicating that this soldier was functioning normally following his recovery.

There are numerous other cases that tell the same story. Usually following a gunshot wound, a patient was cared for at a field hospital, then at a larger institution, and was commonly discharged feeling quite well. It was 5 to 8 years before the patient presented with classic symptoms of a bladder stone: frequent bloody urination, pain – particularly on movement – and frequent urination with sudden stoppage of the flow in midstream.

Fig VII. Calculus of uric acid deposited on a piece of steel, apparently a stylet.
Atlas of Illustrations of Pathology, The New Sydenham Society
1888

William P. Didusch Center for Urologic History

Concretions formed around bullets in the bladder. ***The Medical and Surgical History of the War of the Rebellion*** **1888**

William P. Didusch Center for Urologic History

A table from *The Medical and Surgical History of the War of the Rebellion* presents 21 patients who underwent "lithotomy for extraction of projectiles of traumatic vesical calculi." Of these 21, three had a suprapubic approach - in those days very uncommon. Two of these patients died, though the cause of death was not listed. The remaining patients all underwent perineal lithotomy and, as far as we can tell from the records, did well.

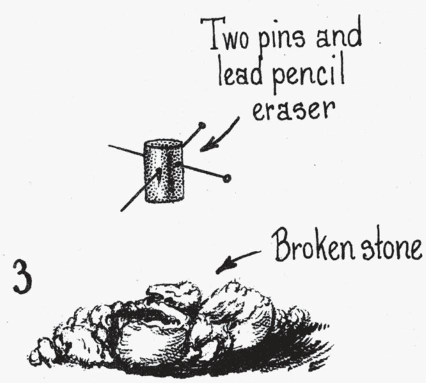
In **Wirt Dakin's** famous book of 1948, *Urological Oddities*, he lists 55 cases of foreign bodies in the bladder that led to stone formations: the most popular item seems to have been chewing gum (10 cases reported, with some indication that gum was used as birth control). Other objects forming the nucleus of bladder stones included: cloth, fishing line (and one sinker), hairpins, kidney bean, gold watch chain, arrowhead, glass swizzle sticks, pencils, and a wedding ring. Dakin also reported on several items lost in surgical operations that eventually became bladder stones (catheter pieces, bougie tip, gauze and sponges) as well as five cases of stones forming around bullets in the bladder.

Bladder stone formed around thermometer

Courtesy of Hank Parfitt, MD, Fayetteville Urology Associates

Urological Oddities, **Wirt Dakin, Illustration by William P. Didusch** **1948**

William P. Didusch Center for Urologic History



A girl, twenty years old, came into the office complaining of burning after voiding and pus in the urine. X-ray and cystoscopy demonstrated a stone about one inch in diameter, of extraordinarily hard consistency. The stone was removed suprapubically, and on the inside was an ordinary lead pencil eraser with two common pins at right angles to each other, piercing the eraser. How did this get into the bladder?

Ernest O. Nay, M.D.,
Terr Haute, IN

IMAGING THE STONE

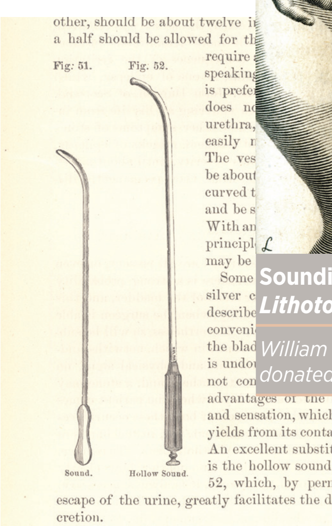
Diagnosis of stone disease before the advent of Wilhelm Conrad Röntgen was done by careful history and physical examination. The technique to identify a stone was called "sounding," as the specialist would pass an instrument (typically metal, though occasionally porcelain or glass) transurethrally in the person suspected of suffering stone disease and listen intently for the metallic "clink" associated with a stone. A skilled practitioner was capable of gathering information on the size and number of stones in the bladder.

The art of sounding was itself risky as noted by Samuel D. Gross in his 1876 *A Practical Treatise on the Diseases and Injuries of the Urinary Bladder*:

> *If it is important...to prepare the system for the operation of lithotomy, it is hardly less so, in my judgement, to prepare it for that of sounding. From neglect of this precaution, patients are often subjected to much suffering, and even to great risk. Indeed, there is reason to believe that life has been repeatedly sacrificed in this way. Bad consequences occasionally follow, even when the utmost care is taken.*

Sounding, *Traite de la Lithotomie, Francois Tolet* | **1682**

William P. Didusch Center for Urologic History, donated by John Herman, MD



A Practical Treatise on the Diseases and Injuries of the Urinary Bladder, Samuel D. Gross | **1876**

William P. Didusch Center for Urologic History, donated by the Martin Resnick family

Röntgen:

On November 8, 1895, **William Conrad Röntgen** (1845-1923) discovered a type of ray that penetrated certain substances, leaving an image of different densities behind. He exposed his wife's hand to the ray over a photographic plate and, after developing the photograph, noted the shadow image of the bones of her hand with the ring she was wearing.

John MacIntyre (1857-1928) in Edinburgh published his historical paper of the first clinical use of the new X-rays in a patient with stone disease on July 11, 1896. MacIntyre began, "During the past four months I have, at the request of several physicians and surgeons, tried to photograph some cases in which the presence of renal calculus was suggested by the symptoms present." He called the ability to visualize a stone "irradiability" and created a table to demonstrate X-rays abilities to image a stone in the order of their highest specific gravity, their greatest permeability to the rays, and their greatest density of shadow:

Specific Gravity	Permeability to X-Ray	Density of Shadow
Calcium oxalate	Biliary calculi	Calcium oxalate
Uric acid	Uric acid	Phosphates
Phosphates	Phosphates	Uric acid
Biliary calculi	Calcium oxalate	Biliary calculi

Edwin Hurry Fenwick's 1908 textbook, *The Value of Radiography in the Diagnosis and Treatment of Urinary Stone: A Study in Clinical and Operative Surgery* is the first real urologic treatise on imaging urolithiasis:

> *Two groups of professional workers are mainly concerned in a careful study of shadows cast by the Röntgen rays in the urinary tract- the operator and the radiographer. Both work independently and yet both are interdependent. The former cannot justly cast the responsibility of shadow deduction upon the latter, though he is dependent upon him for skill in shadow detection. The radiographer cannot be content with merely producing shadows: he must aspire to the knowledge of their causation, and to obtain this he must examine critically and learn from the work of the operator. Each must give: each take.*

There is no better opening paragraph to a new era of diagnosis than this. Fenwick outlined the course of the ureters clearly for the first time. He tried to quantify the location of *phleboliths* (calcified venous valves of the pelvis) which caused false positive radiographic evidence of ureteral stones. These patients could end up getting explored for ureteral stones and none were present. His book has eleven chapters and is richly illustrated by eighty x-ray plates. At this early phase of radiography, this textbook is amazing, and clearly points out the potential for changing the way stone patients are diagnosed.

Large Bladder Stone in Neuropathic Bladder Patient

"The restricted and ordinary meaning of sounding is, the introduction of an instrument through the urethra into the bladder, to obtain evidence, by the touch or hearing, of a calculus being present."

- John Green Crosse, 1835

MODERN STONE SURGERY

Aseptic surgery introduced by Lord Lister rapidly reduced the postoperative mortality and morbidity from wound infections. Upper tract disease was initially diagnosed with finely waxed catheters as demonstrated by Howard A. Kelly, then increasingly with X-rays, and finally with intravenous pyelograms that could accurately determine the size and location of the stone. But these massively successful methods did not all come at once. Following the availability of both general anesthesia and aseptic surgical technique, many patients underwent surgery for an upper tract stone that was never found. Surgery was now possible, and stone disease was ready to undergo an epiphany. No longer was colic to be suffered and endured, when surgery offered a now painless, and less risky method of delivering those suffering with stones. Aggressive surgeons were perhaps following the dictum of George Bernard Shaw, who said, "Chloroform has done a lot of mischief. It's enabled every fool to be a surgeon."

Ureterolithotomy:

Horace Winsbury-White (1889 - 1962) in his 1929 textbook, *Stone in the Urinary Tract*, devotes chapters seven through nine to the diagnosis and treatment of calculus in the ureter. He noted the percentage of stones presenting at different levels of the ureter as follows: lumbar 22%, iliac 7%, pelvic 51%, and intra-mural 17%. He, too, did not depend solely upon the radiograph but used Kelly's method of waxed catheter method. He wrote: "There are three alternatives in dealing with a ureteric calculus: the stone may be left to pass by natural means, its passage may be aided by transcystoscopic measures, or it may be removed by operation."

Open Renal Stone Surgery: Nephrolithotomy and Pyelolithotomy:

Howard Kelly

National Library of Medicine

Howard Kelly (1858 –1943), one of the founding fathers of gynecology, was a stunning surgeon with contributions in renal stone surgery: "The general rule may be safely laid down, always operate for fixed stones and for stones which cannot reasonably be expected to pass down and escape per *vias naturals*. Another valuable rule is always to operate when infection is present." He also discussed surgical options for the surgeon upon the kidney: "Whenever it can be done with safety, the stone in the pelvis of the kidney ought to be removed through the pelvis (pyelotomy) and not through the kidney tissue." He noted that the pyelotomy is simpler, less bloody, and "free from any mutilation."

J.E. Dees reported the use of fibrinogen coagulum to extract complex stones via pyelotomy in 1946. **William H. Boyce** (1918 - 2012), completed the revolution of open stone surgery by developing renal-sparing surgery for complex staghorn stones with intrarenal reconstruction and following the patients over many years.

William H. Boyce

William P. Didusch Center for Urologic History

Intracorporeal Lithotripsy:

Technology soon developed that would forever alter the management of bladder stones. Methods to destroy the stone by applied energy were investigated. Initially an electrical current alone was applied to stones, but this proved unsafe. Some of the first shock wave lithotripsy used microexplosives placed on a calculus to explode the stone; many social issues limited these methods.

There are four basic methods for intracorporeal lithotripsy: electrohydraulic, ultrasonic, ballistic and laser. While each modality has its advantages and disadvantages, laser lithotripsy is beginning to demonstrate a safety profile and broad spectrum of applicability to bring it to the forefront of the newer technologies for treating urolithiasis. Deployment of intracorporeal lithotripsy can be accomplished by a variety of routes using both flexible, semirigid and rigid endoscopes usually coupled with video-assisted imaging systems. These approaches are percutaneous nephroscopy (usually rigid endoscopes), percutaneous antegrade ureteroscopy, transurethral ureteroscopy and laparoscopic methods. The availability of smaller ureteroscopes allows more options via the transurethral approach.

Extracorporeal Lithotripsy:

A revolution in stone surgery came from aerospace research in the 1970s; a team including (among others) Professor E. Schmiedt, Christian Chaussy, Ferdinand Eisenberger and Bernd Forssman, produced and experimented with an extracorporeal shock wave lithotriptor. First *in situ* followed by *in vivo* in animals, culminated with Christian Chaussy treating the first human patient on February 20, 1980. High energy shock waves were produced outside of the body and focused upon the stone inside the human body. There are three types of extracorporeal shock wave lithotriptors. **Electrohydraulic lithotriptors**, in which the high energy shock wave is produced by a spark-gap electrode, were the first types used throughout the world. **Electromagnetic lithotriptors** create a shock wave by an electromagnetic coil and a metallic oscillating membrane; the shock wave is then focused, typically by an acoustic lens. **Piezoelectric lithotriptors** use a series of ceramic ultrasound elements arrayed within a reflector to generate and focus the shock wave.

Shock waves from the electrohydraulic and electromagnetic devices have been the most efficacious to date in producing the greatest stone-free rates coupled with the lowest retreatment rates. Stones have been successfully treated with shock wave lithotripsy in all locations within the urinary tract.

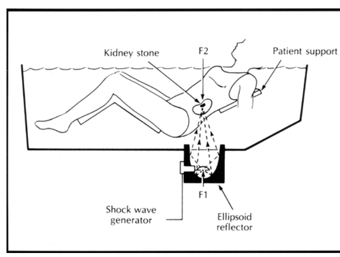


Diagram of ESWL

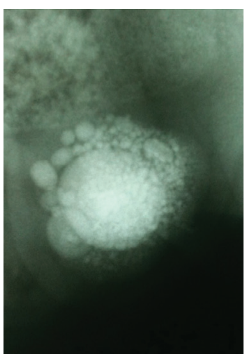
William P. Didusch Center for Urologic History

Chaussy, Eisenberger and Forssman at work on the shockwave lithotriptor

William P. Didusch Center for Urologic History

STONES IN ANIMALS

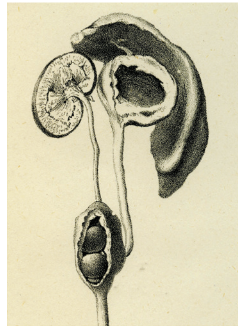
Though humans have struggled for centuries to overcome debilitating stone disease, animal stone disease is less discussed but no less fascinating. Stones have appeared in a broad range of species, including dogs, cats, livestock and even molluscs. Studying stones in animals is invaluable due to the similarities in calculus formation between humans and animals. These similarities allow insight into the treatment and prevention of stones, while advances in treatment for stones in humans have trickled down to pets and livestock. As the incidence of urolithiasis increases in humans – due to changes in diet, a more sedentary lifestyle and obesity – there is also a marked increase in stone disease in animals. While disease formation in most animals follows exactly the same mechanisms as in their human counterparts, commercial feed has been implicated as a prime culprit for this increasing trend of stone formation in domesticated animals.



Radiograph of dog bladder stone

Courtesy of Crawford Dog and Cat Hospital, Garden City Park, NY

Study of stone disease in animals includes artificial stone induction in rats and pigs, as well as naturally-formed stones in dogs and cats. Urolithiasis has been induced in rats through dietary supplements such as oxalic and uric acids, high dietary protein, or pyridoxine- (Vitamin B6) deficient diets. Animal models have also been used to study endogenous compounds that influence stone formation. In particular, the function of calcium crystallization inhibitor THP has been elucidated through a "knock-out" mouse that lacked THP. When fed a diet high in calcium and oxalate, these *knock-out* mice had increased renal calcium and oxalate crystals compared to normal mice.



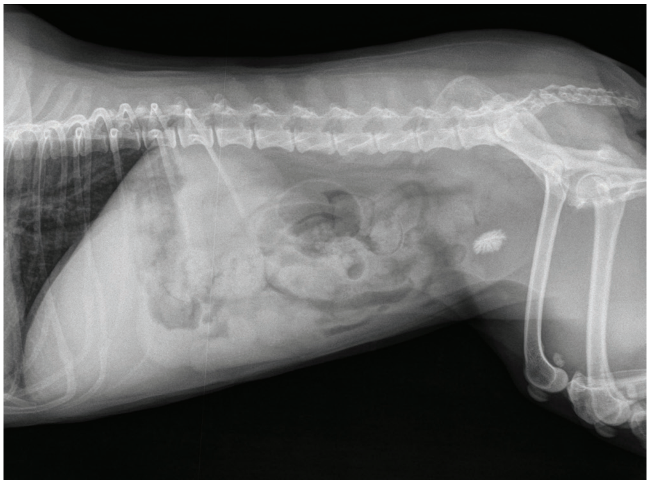
Spleen, both kidneys, bladder and urethra of a dog. Two large calculi fill the bladder.
Atlas of Illustrations of Pathology, The New Sydenham Society

1888

William P. Didusch Center for Urologic History

Naturally forming stones are most widely studied in dogs and cats. Many breeds of dogs such as Dalmatians (uric acid stone formers) have been shown to be more likely to develop stones, but stones are not isolated to just these breeds and have been reported in over 26 varieties of dogs. In fact, the root stock of all modern dog breeds, the gray wolf, also forms urolithiasis in the wild.

Kidney stones in pets entered the national spotlight in 2007 with the poisoning of thousands of pets from melamine contamination. *Melamine*

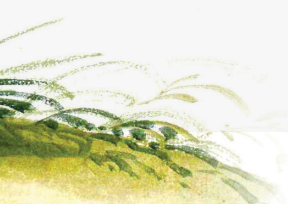


X-ray of dog bladder stone

Courtesy of Cherokee Trail Veterinary Hospital, Lexington, SC

is a nitrogen-containing compound that is used in Formica and plastics to increase durability and act as a flame retardant. Standard protein analysis of food measures the nitrogen content, so melamine can be added illegally to foods to falsely increase the measured protein content. Low doses of melamine alone have been shown to have no negative effects on overall health, but when combined with another non-toxic nitrogen-containing compound, cyanuric acid crystals form in the kidney with devastating consequences. In 2007, melamine contamination of wheat gluten caused the recall of more than 60 million containers of pet food manufactured by Menu Foods. Several cats became sick and died during quality control trials of the affected pet food, and Menu Foods began a voluntary recall of their products.

Studying stones in animals has allowed us to not only understand the process of stone formation, but also to understand the impact that unethical manufacturing can have on public health.



Caprine (goat)

Elephant

Canine

Stones courtesy of the G.V. Ling Urinary Stone Analysis Laboratory, University of California, Davis School of Veterinary Medicine

STONES IN PLANTS

Phytoliths are microscopic mineral deposits that form in the cells of many kinds of plants. Both calcium oxalate crystals and calcium carbonate cystoliths typically form inside specialized cells; these cells control where the mineral deposits form within the plant, as well as when and how they are synthesized and shaped.

Calcium oxalate crystals are very common in plants, though their function in plants is not clearly established. Some studies have indicated that they may serve to sequester excess calcium taken up into the plant from the soil. Other studies have demonstrated that these crystals may provide protection against chewing insects and other herbivores.

Cystoliths consist of calcium carbonate within a matrix of plant cell wall materials. They are typically not crystalline in plants, but there are some exceptions. Cystoliths are also not very common in plants. They form in only a few groups of plants in specialized cells called lithocysts, or “stone cells”. The shape of cystoliths varies among the plant groups that form them, but shape and distribution are consistent within species. The function of cystoliths has not been established. Some scientists have suggested that they may store CO_2. A recent study of *Ficus* leaf demonstrated that cystoliths directed light into the photosynthetic tissues of the leaf.

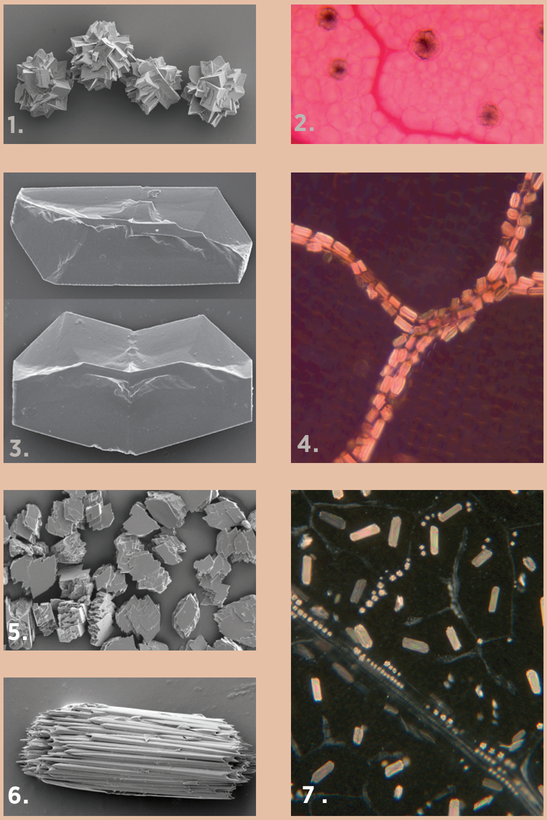
Christian Gottfried Ehrenberg (1795 -1876), a German scientist and a plant and animal microbiologist, conducted the earliest phytolith research. He observed siliceous bodies in soil samples sent to him from all over the world and called them “Phytolitharia” from the Greek meaning “plant stone,” and developed the first phytolith classification system.

Druses are spherical aggregates of multiple crystals that form around a central organic core, which is seen as a dark area inside the druses in 2.

Prismatic crystals resemble the shape of prisms. The crystals in bean are twinned crystals, that is, each unit is composed of two crystals. Distribution along the veins of the leaf protects the vital tissues that transport sugar from leaf-chewing or probing insects.

Raphides are needle-shaped crystals that form in bundles of hundreds to thousands of crystals in highly specialized cells. Raphides are present in some foods we eat, such as asparagus and pineapple, and in these foods they are not harmful. However, in some other plants, raphides are associated with bitter-tasting compounds that discourage animals from eating the plants or toxic compounds that can cause sickness or death in animals.

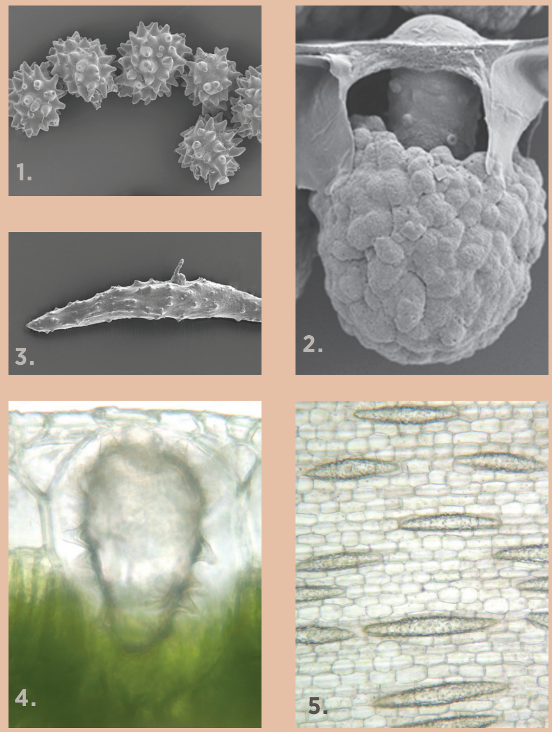
CALCIUM OXALATE CRYSTALS



1. Druses isolated from Schefflera leaves (SEM)
2. Druses in situ in specialized cells in Philodendron, cleared leaf stained with Safranin (LM brighfield)
3. Prismatic crystals isolated from Phaseolus, green bean (SEM)
4. Prismatic crystals in situ along veins in bean leaf, cleared leaf unstained (LM, crossed polarizers, enhanced with cellophane film)
5. Prismatic crystals isolated from Oxalis leaves (SEM)
6. Raphide bundle isolated from Vitis (grape) leaf (SEM)
7. Raphide bundles and druses in situ in grape leaf, cleared leaf unstained (LM, crossed polarizers)

Courtesy of Mary Alice Webb, Purdue University

CALCIUM CARBONATE "CYSTOLITHS"



1. Cystoliths isolated from ***Ficus*** (fig) leaf (SEM)
2. Cystolith isolated from ***Morus*** (mulberry) leaf, outside wall of epidermal cell still attached (SEM)
3. Cystolith isolated from ***Pilea*** (aluminum plant) leaf (SEM) with slender stalk that attaches body of cystolith to cell wall still attached
4. Cystolith in situ in specialized cell of ***Ficus*** leaf epidermis (LM, free hand section)
5. Cystoliths in situ in epidermis of ***Pilea*** stem, epidermal peel unstained (LM)

Courtesy of Mary Alice Webb, Purdue University

SPACE AND THE STONE: A GUIDE TO THE GALAXY

Outer space has always had a mysterious appeal to man; the planets and stars have been studied by scientists for thousands of years. But it has only been within the last century that human physiology and astronomy have intersected. As humans delve deeper into space, understanding the impact of zero gravity on different organ systems becomes crucial to maintain the health and safety of astronauts. Body fluid volumes, electrolyte levels, and bone and muscle are some of the many systems that experience significant changes as the body adapts to the weightless environment.

Early in the clinical literature of urolithiasis, it was documented that men who were bedridden were prone to kidney stones. In 1922, a physician reported on 20 cases of nephrolithiasis occurring in men following war wounds. Most of these patients were bedridden for prolonged periods of time. Researchers noted that recumbence appeared to be the critical problem associated with calcium stone formation, not the degree of trauma. It was eventually discovered that extended periods of bed rest led to a resorption of calcium from the bones and resulted in an increased risk of nephrolithiasis. These early researchers unknowingly discovered a model, specifically extended periods of bed rest, for zero gravity environments.

During short-term space missions, such as the Gemini, Apollo, and Space Shuttle flights, astronauts have been shown to be in a state of negative calcium balance where calcium and phosphate are lost from bone and excreted in the urine. Astronauts are also likely to become dehydrated following early flight space sickness and to experience decreased urinary volume and rising formation product. Urine specimens of male astronauts were collected before a mission, early in the mission, late in the mission, landing day, and a week after landing. Researchers found that urine output declined by 22-52% during spaceflight, and urine pH had a tendency toward increased acidity (lower pH), which eventually normalized. Urinary calcium levels increased for all members, and calcium excretion continued to increase during the flight.

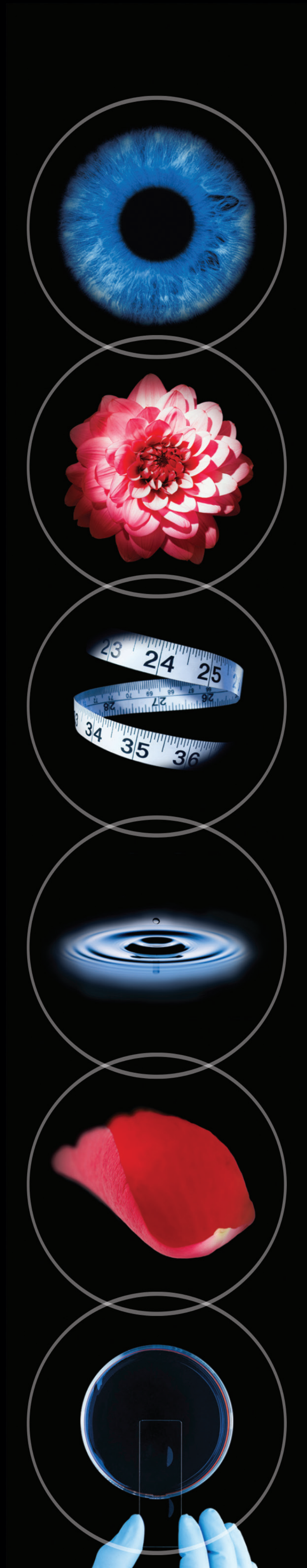
International Space Station

NASA

Stone disease represents a real risk to our humans in micro- or zero-gravity environments. The physiology behind this risk is well known but the cause not completely understood. Detailed data from 79 U.S. space missions, involving 219 person-flights and 175 astronauts, demonstrate 23 genitourinary problems (1.2% or 0.07 incidence per 7 days). In 2008, NASA scientists presented at the 2nd International Urolithiasis Research Symposium in Indianapolis, Indiana. The authors began:

> *U.S. spaceflight experience to date from early space vehicles (Mercury, Gemini, Apollo, Apollo-Soyuz) to Space Transportation Systems (STS-Shuttle) to long duration space platforms (Skylab, NASA-Mir, and International Space Station) cumulates to approximately 30,000 crew-days, >80 crew-years. On Shuttle missions from STS-1 to STS-108 (106 Shuttle flights) cumulating in 5496 flight days, 588 of 607 (97%) participating crew members experienced some medical symptoms.*

They went on to note that a whopping 74% of astronauts developed urinary symptoms. As mankind strives to gain access to the final frontier of outer space, health hazards must be studied and methods for adapting to these anticipated risks be found.



For more information on the history of stone disease, look for:

A Comprehensive History of Urolithiasis: No Stone Unturned
Michael Moran, M.D.
Elsevier Publishing, 2013

Fascination of Hidden Objects (in German)
Editors: Heiner Fangerau, Irmgard Müller
Steiner Publishing House, Stuttgart, 2013

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Text by

Rainer Engel, MD, *AUA Historian*

Michael Moran, MD, *Curator,*
William P. Didusch Center for Urologic History

Friedrich Moll, MD, *Curator, DGU*

Franz Josef Marx, MD, *Historian*

Mary Alice Webb, PhD, *Purdue University*

Hampton Addis, *University of Maryland Medical Student,*
WPD Center Summer intern

Designed by Jennifer Kennedy and Laura Farnen

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