The management of renal stones in *Ratio medendi in nosocomio practico* (1773) of Anton De Haen (1704-1776)

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ABSTRACT
The purpose of this paper is to report the methods used and the experiments conducted by doctor Antonius De Haen mentioned in his masterpiece "*Ratio Medendi in Nosocomio Practico*" "*Medical skills in hospital practice*", to put his knowledge in the proper context of the time and explain his intuitions with the modern evidence in medical research. The book is written during his experience in the 18th century Viennese hospital, it contains numerous case histories and ranges widely over what must have been all the recognized clinical entities of the time.
Among the different topics covered, there is a chapter dedicated to "*Experimenta in calculosis et de calcula varia*" "Experiments in the calculosis and types of stones". In it there is a series of case studies of renal stones he followed that reveal the limits of the knowledge of the time. There is a punctual description of various consistencies and differences in the way of formation of the calculi and he frequently includes the results of his autopsies in his researches.
In fact, the author is asking himself how is possible that many men lead their lives, without the perception of the presence of the kidney stones, which often only appear post-mortem. Anton De Haen says in his script: "Nature itself provides insensibility to pain even before the resources of medical art, such as limewater or *Uva Ursi*". How *Uva Ursi* works is one of the unsolved question for the author, now we can finally explain how *Uva ursi* leaves and his nutrient have an antioxidant potential, how they attack the target bacterial cells, their quorum sensing communication systems and the direct antimicrobial growth-inhibitory activity and the safety of his use in the clinical practice.

KEYWORDS : Anton de Haen, 18th century, *Uva ursi*, kidney stones, hydroquinone.

Antonius De Haen

Antonius De Haen Gravenhage, (December 8, 1704 – Vienna, 5 September 1776) was a Dutch physician appointed as professor and first executive board director of the University of Vienna's medical clinic (Figure 1).

Figure 1

Antonius De Haen (1704 - 1776)

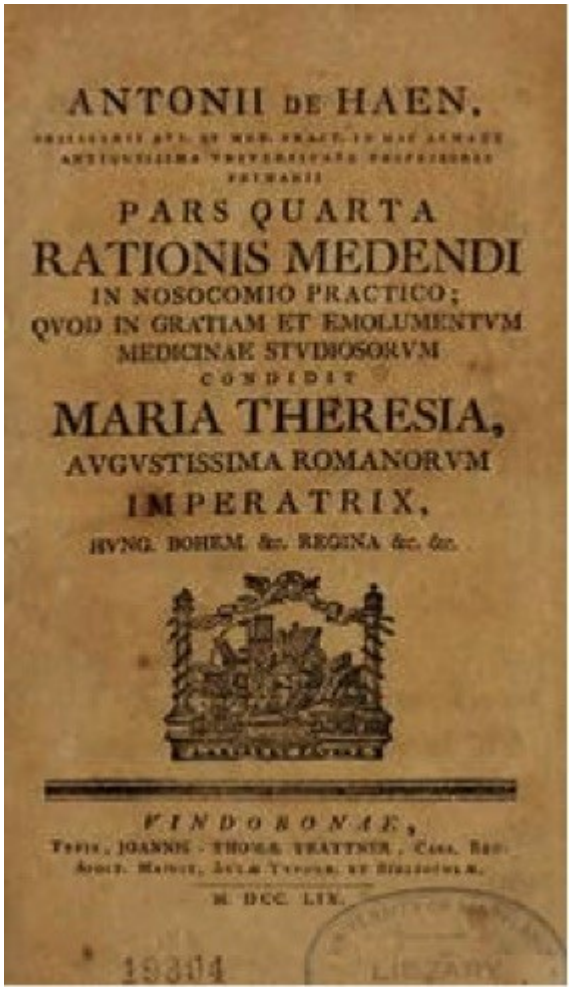
De Haen studied medicine in Leiden and qualified as a doctor in his hometown. He was brought by his former classmate Gerard van Swieten (7 may 1700 – 18 June 1772), the personal physician of Maria Theresia, from the Netherlands in 1754 to Vienna, there he became Professor of the First Medical Clinic of the University of Vienna in the Civil Hospital. He organized the Medical University after the model of his teacher Herman Boerhaave (31 December 1668 – 23 September 1738) away from the textbooks he was teaching medicine at the bedside of the patients. He insisted on detailed case histories and careful physical and laboratory examination before reaching a diagnosis and prescribing treatment (1).

He took over after the death of van Swieten his position as personal physician of Maria Theresia. He put great emphasis in the patient observation and explored the numerous forms of fevers and was one of the pioneers of using the thermometer, the temperature fluctuations and the pulse measurement to have a valuable indication of the severity of the illness. De Haen was one of the pioneers in the field of reanimation. During that period drowning was a major cause of death, which in the second half of the 18th century led to the creation of associations that sought to reanimate people in urban areas in Europe and North America after threatening drowning and cardiac arrest. In his work *Heilingsmethode,* litterally *"Methods of healing"*, De Haen introduced the method of ventilation for the human body with the knowledge of the anatomy and physiology he possessed on the human body. In addition to keeping track of detailed patient case descriptions, De Haen was in favor of post mortem examination to determine the cause of death and advance clinical knowledge.

His most famous written work is *Ratio Medendi in Nosocomio Practico* (Figure 2), in which he mentions his experience, during the 18th century, in the Viennese hospital and numerous patient casualties. This masterpiece dedicated to Empress Maria Theresa, its not just a guide to hospital practice as the title suggests but contains numerous case histories and ranges widely over what must have been all the recognized clinical entities of the time.

De Haen quotes widely from both ancient and contemporary authors and frequently includes the results of his autopsies.

Figure 2


ANTONII DE HAEN,

PARS QUARTA
RATIONIS MEDENDI
IN NOSOCOMIO PRACTICO;
QVOD IN GRATIAM ET EMOLUMENTVM
MEDICINAE STVDIOSORVM
CONDIDIT
MARIA THERESIA,
AVGVSTISSIMA ROMANORVM
IMPERATRIX,
HVNG. BOHEM. &c. REGINA &c. &c.

VINDOBONAE,

M. DCC. LIX.

Ratio Medendi in Nosocomio Practico, frontespice.

The treatment of Renal Stones in XVIII century

The XVIII century sees an improvement in the treatment of the renal calculi. Slowly the figure of the "travelling lithotomists", wandering barber-surgeons who traveled around Europe removing stones without any kind of anaesthetic, leave the place to professional figures with more expertise.

The original route of approach was through the perineum, first through the mid-line and later from the left side. The suprapubic or high operation started to be used in the early 18th century (2).

A great influence on the practice of lithotomy was given by the work of Jacques Beaulieu (1651-1714) who developed the method of "lateral lithotomy" (3).

Essentially it consisted of cutting the body of the prostate instead of dilating it, and cutting the bladder neck and some of the bladder wall. An incision was made on the left side of perineum medial to the ischial tuberosity and carried between the bulbar and ischiocavernosus muscles where a transverse incision was made through the body of the prostate, cutting the neck of the bladder. A sound in the urethra guided this supposedly less destructive entry into the bladder. After making an opening as big as the stone, a forceps was inserted through the wound to seize and remove it (4).

William Cheselden (19 October 1688 – 10 April 1752) (*Philosophical Transactions of the Royal Society of London,* 1722) and John Douglas (date of birth unknown – died 25 June 1743) (*Course of Anatomy, Chirurgical Operations, and Bandages*, 1719) were the first to realize that distended

bladder mowed upwards and therefore an extraperitoneal approach was possible. he started to use the 'apparatus major' procedure, but in 1722 he adopted the suprapubic approach, known as the 'haut appareil'. He had realized that the distended bladder moved upwards and therefore he could use an extraperitoneal approach. Eventually, dissatisfied with his results, he returned to the perineal approach that he later modified. He no longer distended the bladder with water, and introduced a grooved sound into the bladder, making his incision from below and upward "beginning near the place where the old operation ends, cutting down between the musculus accelerator urinae, and erector penis, and by the side of the intestinum rectum: I then feel for the staff, holding down the gut all the while with one or two fingers of my left hand, and cut upon it in that part of the urethra which lies beyond the corpora cavernosa urethrae, and in the prostate gland" (5, 6).
Herman Boerhaave (1668–1738) was one of the most important figures in 18th-century medicine. During the early 18th century the surgical approaches for lithotomy to treat lithiasis had very high risks of complications. In the face of the very common and dangerous complications, the doctors and surgeons actively sought all possible solutions short of surgery and left lithotomy as the last alternative. Boerhaave dedicated a chapter in his "*Institutiones Medicae*" "Medical Institutions" (1746) to the treatment of lithiasis of the urinary tract. His recommendations included an increase in liquid intake, a hot bath in order to induce vasodilation, and exercise. Using these methods, Boerhaave felt that stone removal should be achieved, perhaps reflecting both the status of surgery in the early 18th century and an appreciation of the risks of the surgical procedures available (7).

Boerhaave's opinion of lithotomy as a last resort when other approaches failed was "I think lithotomy is an act of pure faith" (8).

The history of urinary stones leads to the contribution of Anton De Haen and his accurate analysis of the knowledge of the time. He brings many witnesses, such as the studies of his colleague Dr. Heurn (date of birth and death unknown). De Haen, with big astonishment reported that Heurn collected after an autopsy 70 small kidney stones from the left kidney and 80 small kidney calculi from the right kidney, the surprise was that this patient wasn't suffering at all of symptomatic kidney stones manifestation.

Still De Haen brings the experience of Federico Cassio (date of birth and death unknown) and his patient that during his lifetime nourished, with no sign, a rough calculation that weighed 14 ounces (0.396 grams). The calculus did not obstruct the renal canal and the urine flowed without any hindrance.

He still mentions the colleague Antonio De Pozzi (date of birth and death unknown), this physician reports of a patient who had in both kidneys heavy calculi of 2 ounces and a patient who had two large 6 ounces calculi in the kidneys without any symptoms except the abundance of urine and an unbearable thirst, who found no respite with any drink.

De Haen still quotes the colleague John Crotone, who said that calculi often not only doesn't annoy much the patient and are almost silent, but even less when they are covered by lymph, in fact in this case they can only be identified post-mortem.

The author is asking himself how is possible that many men lead their lives, without the perception of the presence of the kidney stones, which often only appear post-mortem, after his autopsies.

Anton De Haen says in his script: "Nature itself provides insensibility to pain even before the resources of medical art, such as limewater or *Uva Ursi*".

The role of "*uva ursi*" for the therapy of renal calculi

Uva ursi, also knew as ursina grapes or bearberry, was an adjuvant both after lithotripsy therapy and as a treatment before an invasive intervention. The author reported several exacerbation of symptomatology and reformation of calculi after the suspension of the intake of ursina grape juice and a contraction of diuresis in the immediate subsequent period.

A prolonged use of ursina grain led to the objective data in the *matula* of a multitude of limestone. Uva ursi was also used as an alternative, palliative care for calculi particularly difficult to solve with litotrissia, in fact the efficacy was great to reduce the symptoms. Among clinical cases, it particularly relates to an 11-year-old child who was taken to the hospital for stranguria, which, as reported by parents, lasted for 4 years. They said that the urine came with drops of painful sorrows, fetid and with extreme effort and the child complained of urinary incontinence. Catheter exploration showed the presence of a calculus. In describing the clinical case, De Haen emphasizes the patient's unrest, typical of those with symptomatic calculi. He slammed his feet to the ground without respite, shouted disturbing the other patients. Twice a day he gave him a dracma of ursina grapes. The benefit was so effective that the pain was almost over and had a great benefit in not get drenched and in retaining urine, there was no symptom of the presence of the calculus. After spending a month, tired of staying in the hospital, he asked to go back to his father's house. For the first days he had no symptoms, in the following month, for his uncontrolled diet or for failing to take the medicine at right doses, the efficacy of the drug ceased. The pains and symptoms had a recurrence. The young man was admitted for a second time at the hospital with the indication of remove the calculus. While preparing for what was needed for surgery, De Haen insisted that the operation would be deferred until the effects of the previous treatment were reinforced three times a day: half a dracma of *uva ursi* was administered to him but the pain was still acute. He was given a painkiller with barley decoction and in less than three days the pain disappeared and the subject began to urinate in a very healthy way.

After 15 days, he came back home where he had been doing his regular daily activities for two months. Abandoning the care again and not respecting the medical dictates, he fell under the previous conditions.

For the third time he was hospitalized, the benefit was lower than the previous treatment and after a few days it was injected with flaxseed oil in the bladder, morning and evening, consequently symptomatology resolved without additional injections but only with maintenance therapy with powder of ursina grapes. After one year of treatment the patient remained asymptomatic and under periodic medical check-up.

The author shows still the case of a 9-year-old boy with strangulation, oliguria and unbearable pain. A catheter exploration had found a calculation that obstructed the bladder. In two months, the illness associated with the immune system was resolved with the use of ursina grapes. Oval calculation was then subsequently extracted by forceps from the surgeon. *Uva ursi* had also helped the patient in the post-operative course for onset of strangulation following a post-operative infection.

Still another patient referred abundant emission of blood with the urine a painful growing of the pain day after day, greatly worsening the quality of his life. Through the catheter exploration was found a large calculus. He suffered for 13 days of recurrent fever with high peaks and other lows. On the eleventh day, with the digital exploration, there was an evidence of a prolapse of the bladder, stranguria and fever with high temperature.

De Haen gave to the boy a decoction of barley mellitus for the fever, and for the pain linseed oil, injected twice a day and *Uva ursi* decoction.

The fever became lighter and only in daytime, after 14 days it ceased completely, and even the painful symptoms of the calculus were attenuated, the boy urinated normally and without pain.

The use of "*uva ursi*" in modern times

The *Uva ursi* mentioned by the authors is commonly known as Bear Berry or with the scientific name *Arctostaphylos uva-ursi*, from the greek word *artos* (bear) and stafulh (grape), from the family of Ericaceae.

The flowers are urn-shaped, red bright, pink or white and borne in small terminal clusters. The fruits are small 5-10 mm in diameter), round, smooth, berry-like drupe looking like a miniature red apple.

The main components of ursina – leaf leaves are phenolic glucosides (5-15%), represented by 6-10% of arbutin and methylbutin, whose aglicons are made up of hydroquinone and methylhydroquinone molecules. Other constituents include ursolic acid, tannic acid, gallic acid, *p*-coumaric acid, syringic acid, galloylarbutin, gallo-tannins, and flavonoids, notably glycosides of quercetin, kaempferol, and myricetin (9).

At intestinal level, arbutin is hydrolyzed to hydroquinone and glucose; After absorption, hydroquinone is predominantly conjugated to the liver, then released into the urine as glucuronide and sulphate. Bacteria in the bladder have the ability to deconquer hydroquinone from glucuronide; The active ingredient can then perform its antimicrobial action, which has proved useful in vitro against numerous bacterial strains commonly responsible for urogenital tract infections. Other phytocomplex components, such as tannins and piceoside metabolites, perform synergistic action with arbutin.

Hydroquinone has been shown to be effective in counteracting urinary infections and in vitro model infections sustained by various types of infective agents, such as *Staphylococcus aureus (10), Bacillus subtilis (11)*, *Mycobacterium tuberculosis (12) and other bacteria using the quorum sensing communication system.*

Hydroquinone in fact has three types of activity in combinations: direct antimicrobial growth-inhibitory activity, non-specific and specific pro-quorum sensing activities, anti-quorum sensing activity (13).

Under the recommended use conditions Uva ursi extract is a safe therapeutic option for treating lower urinary tract infections. There is no direct evidence, regarding human data, supporting the fact that free hydroquinone, content in the Uva ursi leafs, causes convulsion, hepatotoxicity, nephrotoxicity, or promotion of tumors in humans (14).

Conclusions

Anton De Haen in his masterpiece shows us all the perseverance, the intuition and the knowledge that a Physician should bring in the daily clinical practice, the bedside approach to the patient and the enthusiasm of discovering new weapons against the diseases that since the dawn of medicine practice plague the society.

Thanks to his experience, he kept on using ancient remedies previously discovered by the older fathers of medicine. Even if they didn't have the correctly explanation of how this methods worked and even he didin't have a clear clue about how Uva ursi was so relevant in the treatment the urinary diseases, his constancy rewarded him with awesome feedbacks from the scientific

community of the time and from his patients, reason why we still recognise the contribution and the value of his work nowadays, almost three-hundreds years later.
The input he gave to the research inspired recent scientists to keep on looking on the use of herbs in the treatment of urinary calculi and lower urinary tract infections. These studies we reported explain how Uva ursi leaves and his nutrient have an antioxidant potential, how they attack the target bacterial cells, their quorum sensing communication systems and the direct antimicrobial growth-inhibitory activity and the safety of his use in the clinical practice.

So after all these years we can partially answer to the questions that our eminent colleague asked himself. I trust that in the same way, many of the unexplained, important questions we have in the daily medicine practice and in the scientific research, could be solved with the same strong evidences that Anton De Haen didn't have the possibilities to enjoy.

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