BOOKS, TEACHING AND LEARNING

Disease of the kidney and of the urinary tract in De Medicina Methodica (Padua, 1611) of Prospero Alpini (1563-1616)

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Abstract

Aim: *The study was devised to understand the contribution to nephrology of De Medicina Methodica of Prospero Alpini published in 1511, at a time when the fame of the professor reached the azimuth.*

Method: *We have analyzed the contents of chapters devoted to nephrology in that book of Prospero Alpini and the novelties of his message.*

Results: *Prospero Alpini (1563-1616) taught at the University of Padua (1594-1616), at the same time of Galileo Galilei, Santorio Santorio, and Girolamo Fabrizi d'Acquapendente, when measurements (pulse, temperature, perspiration) were introduced into medicine. He was a travelling physician to whom we owe fundamental contributions to the use of urine to prognosticate life and death (De Praesagienda vita et morte aegrotantium libri septem (Venetiis, apud Haeredes Melchioris Sessae, 1601). As prefect of the Botanical Garden - the first ever and a model in the world - he could turn the study of simples into cures. De Medicina Methodica Libri Tredecim. Patavi, apud Franciscum Bolzettam, 1611. Ex typographia Laurentij Pasquali, is an in folio volume of XLVII + 424 pages, 54 lines per page), wherein Alpini aimed to rejuvenate antique medical Methodism. It "is a testimony of the interest of medicine philosophers of the modern era for the corpuscular and atomic ideas" (Nancy Siraisi).*
Methodists (2nd Century BC) refused anatomy and physiology as unique guidelines to the interpretations of diseases and gave importance to the development of a pharmacological science and alternative medicine. The book begins with a 3 page letter to Francis Maria della Rovere Duke of Montefeltro, and a 2 page letter to the readers.

We discuss the novelties of the chapters on renal colic (de dolore renum), hematuria (de sanguinis profluvium), pyuria, anuria (de urina suppressa) and its cure, polyuria (de urina profluvio), renal abscesses, hydrops and its treatment by skin incisions. We also analyze the chapter on kidney and bladder stones (Book X, Chapter XVIII, pp. 354-356) - a masterpiece of scholarly teaching - encompassing localization of stones, their formation and shape, renal colic and its irradiation according to the site and gender, the best antalgic position to pass stones, the use of laxatives, cathartics, warm baths, the plants to be used their preparation and quantity, the waters to be drank and their quantity (up to 15 pounds a day), the removal of bladder stones without surgery (methods learned in Cairo and described in Aegyptyan Medicine), and lithotomy and its feasibility even in old people.

Conclusion: *De Medicina Methodica was a modern monograph devoted to clinical medicine including urinary disease. The book reflected the polyhedral personality of the author, his experience as physician of the Republic of Venice at Cairo, and his capabilities as a director of the Botanical Garden of the University of Padua, a unique research centre in those times.*

Key words: anuria, De Medicina Methodica, diseases of the kidney and of the urinary tract, hematuria, Prospero Alpini, renal abscess, renal colic, stones, University of Padua

Background

In 1611 Prospero Alpini (Figure 1) - physician, reader and demonstrator in simples and prefect of the Botanic Garden at the University of Padua - published, in the printing house of Francesco Bolzetta, a book entitled *De medicina methodica libri tredecim*. The book had been announced by Alpini in 1601 in the preface of his masterpiece *De praesagienda vita et morti aegrotanti* / On prognosis of life and death.
In *De praesagienda* he announced:

"Itaque, optime Lector, hos interim legito, recte consulito, reliquos libros de aliis prognosis partibus conscriptos propediem expectato. Atque nostram fortasse Medicinam alias methodico modo informatam" / "Therefor excellent reader, in the meantime you read these books you will ponder attentively while waiting for my forthcoming books on the other parts of prognosis. Probably even our medicine will be differently inspired according to the methodic manner".

Still remains obscure the reasons why a prominent, busy academic scientist at the beginning of the 17th century informed the scientific community that he was going to study the Methodic School. Therefore a study has been devised with a threefold goal:

1. to assess the role of the Methodic School of Medicine
2. to understand why in the Galilean Padua, a scientist of international reputation, felt it necessary to work for 10 years on a medical school that expired in the course of the third century AD, and
3. to learn about the diseases of the kidney and urinary tract according to a school based on atoms, empty space and symptoms

The Methodic School of Medicine

The Methodic School of Medicine originated as a reaction to Hippocratic Medicine, against the theory of humors and the so called benevolent attitude of nature [1]. It had a lifespan of nearly 300 years, from the times of Mark Antony and Cleopatra to the death of Emperor Septimius Severus (235 AD). Its origins may be traced in Asclepiades of Bithynia. It was based on atomism and rooted in the work of Leucippus and Democritus of Abdera (5th century BC), Epicurus (341-270 BC), and of Heraclides of Pontus (390 BC-after 322 BC).

Health and disease depend on atoms, pores, and on movements of atoms. Atoms are round, smooth, small, breakable and have the capability to accrete and to enter into the body through respiration. Titus Lucretius Caro (died mid to late 50s BC) was its poet (*De natura rerum / On the nature of things*).

The school was founded by Themison of Laudicea, a pupil of Asclepiades. The adjective "me-

Figure 1.
Painting of Leandro da Ponte (Bassano), Oil on canvas—105.5x85.5 cm—Stuttgart, Staats Galerie.

thodic" means that the theory was based on a scientific method derived by atomism. Themison identified two states of the matter depending on the relaxation of pores (*status laxus)* and on their closure (*status strictus*). A third intermediary state (*status mixtus*), was also identified.

Leading physicians

Asclepiades (c.124-c70 BC) born at Prousias in Bithynia [1], the northwest region of Asia Minor, arrived in Rome around 100 BC. He was the first Hellenic physician to start medicine in Rome. Where he initially taught philosophy and later on practiced medicine. He adopted the Epicurean philosophy and rejected Hippocratic tenets.

"He suggested that the human body is composed of corpuscles made of atoms and void spaces. Diseases are caused by alteration of form, position and free flow of molecules. Thus he is appropriately credited of the introduction of molecular medicine" [2] (full text).

Asclepiades did not agree to wait for the power of nature to heal the patient and gave origin to a unifying theory for health and disease. The history of the patients - especially their symptoms - was the basic crucial elements. He introduced the concept of a therapy which had to be "immediate, comprehensive and pleasant (*cito, tuto et iucunde"*. With him physical exercises, gymnastics, hydrotherapy, walking, being in motion on carts, playing music and singing were the most important healing manoeuvres.

Asclepiades has been described as physician of "immense personal charm, with a brilliant mind... a messenger from heaven", although "some of his contemporaries and also late writers, notably Galen, counted him as a near charlatan" [3]. However he was appreciated by Aurelius Cornelius Celsus and listed among his patients Cicero, Lucius Crassus and Mark Antony.

For Asclepiades nature is not the healer: healing is a process mediated by physicians. Waiting for nature is just waiting for death. He rejected the humors as well as the importance of anatomy, and drove medicine into a new era, becoming the inspiration of a sect, one of a new school of the many flourishing in those days (Dogmatists, Empiricists, Pneumatists and Eclecticists). He based his art on a corpuscular theory made of continuously dividing atoms, continuously in motion. The theory did not contemplate gods, they were not needed.

For Asclepiades the duty of physicians was that of curing patients safely, as soon as possible and pleasantly "*Asclepiades officium medici esse dicit, ut tuto, ut celeriter, ut jucunde cure"*. Thus he prescribed baths, frictions, soothing medications, music, waters, enemas - but no purges - pleasant work, motion of any kind (in water, on hanging beds, boats, carriages and carts and on horses). Slow motion was the most healing since it favored sleep. In addition he allowed patients to drink wine.

Physicians help patients to acquire physical and mental health and to feel pleasure. He is considered as the father of clinical medicine, "a prominent figure in the history of medicine, as innovator and antidogmatic" [4]. According to Caeliua Aurelianus, he was credited to be the first to introduce the concept of acute and chronic disease.

Heat and cold were the product of the movement of atoms through pores, fever was a preternatural kind of heat arousing in all body parts, caused by obstruction and inflammation. Fever was caused by the blockage of atoms in the pores, due to the disproportion in size and shape between them and the pores. If the blockage is not removed fever is continuous. He is credited of the introduction of laryngectomy which was mentioned by Caelius Aurelianus as the *caduca atque temeraria Asclepiades invention* / the transient and daring discovery of Asclepiades.

Themison of Laodicea

These ideas of Asclepiades were furthered, after his death, by his pupil Themison of Laodicea who is considered the real founder of the school (50 BC). Themison abandoned the doctrine of the four humors that had dominated the Greek pathologic thinking for centuries.

Themison first posited the theory of "general states," or "communities" based on the principles of his master Asclepiades, who taught that the body was composed of atoms moving through pores" [5].

He developed a medicine based on contraction and relaxation of pores (*status strictus* and *status laxus*). An intermediate status (*status mixtus*) was also contemplated. In this system diseases were caused by constriction and relaxation of the pores as judged by evacuations, secretions, and feverishness of the sick. All other information was useless. The aim was that of building "on speculative grounds a mechanistic physiology" [1]. When the *status strictus* prevails there is heat, congestion, redness, thirst, when the *status laxus* prevails there is looseness, pallor, weak pulse. In the *status strictus* pores had to be relaxed by means of emollients, warm bath, walks, cradling and gymnastics. In the *status laxus* one needed cold water, tonics, stimulating drugs. In the intermediate status (*status mixtus)* physicians had the duty select each time the most appropriate means of cure. No drug was used to modify the ratio between humors. When pores were contracted Themison ordered a scanty diet, warm baths, poultices, humid air, bleeding. When pores were dilated he prescribed an increased food intake, cold baths, cold air and styptic medications to induce constriction [3].

Themison - defined by Pliny as *summus auctor* (supreme author) - identified in every disease four phases: onset, incremental stage, stable stage, and decline. He is credited for introducing the use of leeches for reducing local congestion, whereas bleeding was used for whole body relaxation.

He allowed wine, usually mixed with water in accurate proportions. In some instances salty water was used. For dropsy he prescribed walking quickly

for 12 stadiums (the Roman stadium was 185 m) before undergoing paracentesis (Caelius Aurelianus Chronicis I.III.c.7, c.8.) [6].

Thessalus of Tralles

Themison was followed by Thessalus of Tralles an ignorant yet very successful charlatan who met with great success. He lived in Rome between Nero and Trajan and prescribed whatever the patient wanted. For him disease affects the body as a whole, not its parts. Symptoms are the basis for treatment, the categorization of disease is useless. He did not prescribe evacuation or cupping.

Soranus of Ephesus

The third pillar of the Methodic School was Soranus of Ephesus (fl. c98-138 AD), the time of Trajan and Hadrian. A pupil of the Alexandrine School he investigated patients by palpation and percussion. He authored not less than 30 medical treatises, made the distinction of chronic from acute diseases [5] [7].

He spoke of disease as *"passio"* not as "*morbus"* [7] [7]. A great expert of leprosy, he developed his own original preparation which was quoted by Galen. He is also credited with the first description of a pediatric case of hydrophobia (rabies). He never allowed purges to avoid the risk of removing also good humors. He was an authority in obstetrics, gynecology and pediatrics, He described the breech presentation, the ligature of the umbilical cord and the gynecological chair. He wrote about genitals, and his anatomical knowledge was remarkable on the uterus, clitoris, and hymens.

Caelius Aurelianus

The last and very important member of the Methodic School was Caelius Aurelianus (5th Century AD) from Sicca Veneria in Numidia (nowadays Algeria). He is considered the most important medical writer after Galen. Albrecht von Haller defined him as "medicus et philosophus celeberrimus / very celebrated physician and philosopher". Caelius spoke of diseases with and without fever, *a capite ad calcem / from top to toe* and categorized diseases according to the status of pores that is *strictura* (contraction), *solution* (relaxation) and *complexio* (an intermediate status between contraction and relaxation).

He was the first to mention angina pectoris. According to Anne Dysert [5] "Caelius has left four extant texts, two of which are the translations *On Acute Diseases* and *On Chronic Diseases* from works of the same name by Soranus of Ephesus. His third extant work is fragments of a Latin translation of Soranus' *Gynaecia* and the fourth is his own original treatise entitled *Medicinales responsiones"*. "He unfortunately incorporated Soranus' theories into his own work, thus there are difficulties in identifying Soranus' contributions to his writings since we do not have the originals. Caelius was very hard with doctors using cupping, evacuations and other manoeuvres which are considered metasyncritic or capable of turning a diseased status into a healthy condition. He is only concerned with symptoms, he sticks firmly to them and escapes the temptation to deal with the causes of diseases, since symptoms guide therapy" [5].

Prospero Alpini and the quest for a revival of Methodic Medicine

Alpini aimed to revive the Methodic School and we are indebted to him "since he collected all historical documents inherent in the doctrine and its practical application with unsurpassable completeness" [8].

Prospero Alpini from Marostica (1553-1616), also known as Alpinus, was professor at the university of Padua in the years 1594-1616, reaching the peak of his career in 1603. In that year the Padua Studium bestowed on him a triple academic duty as reader and demonstrator in simples and prefect of the Botanic Garden. At that time he was also one of the most renowned and coveted physicians, being asked to consult even by Fabrici of Acquapendente (professor of surgery) and Alessandro Massaria (first chair of medicine) [9] [10] [11].

Alpini studied medicine at the university of Padua (1574-1578). In the years 1578-1579 he was community physician at Camposanpiero near Padua. Later on he worked in Cairo in Egypt as official physician of Giorgio Emo, Consul of Venice (1580-1584). In the years 1587-1590 he worked in Venice, Bassano and Genoa. In the last place he was the physician of Giovanni Andrea Doria, Prince of Melfi and Prefect of the fleet of Philip of Spain [9].

As the output of the work done in Cairo he published *De Medicina Aegyptiorum* (1591), *De balsamo dialogus* (1581, 1592) and *De Plantis Aegypty Liber* (1592). These books led to a call in 1594 from the University of Padua to become a reader in simples (a theoretical botany teaching). The call was followed by his advancement (1601) as first chair and by his nomination as prefect of the Botanic Garden (1603). Such duties were confirmed until his death (1616). Because of his expertise Charles Linneus dedicated to him the genus Alpinia (230 species of the ginger family, *Zizinberacaee*).

He authored *De praesagienda vita et morte aegrotantium libri septem* (a *quarto* volume, pages 8+163+16, printing house of the Heirs of Melchior Sessa, Venice 1601). The book is known as *De praesagienda / On prognosis).* At his death Alpini left various unpublished manuscripts among them *Prosperi Alpini Marosticensis de longitudinem et brevitate morborum libri duo / On disease of short and long duration, 2 books,* transcribed in 1967 [12]. In 2006 the Prospero Alpini Foundation was started with the publication of the first of a series of books on Prospero Alpini *(Alpiniana)* made of studies and texts [13] [14] [15].

Why in the Galilean Padua a treatise on Methodic Medicine?

De Medicina Methodica was published in 1611 as a *quarto* volume (30.5 cm in height) in the printing house of Francesco Bolzetta (*apud Franciscum Bolzettam*). It consists of XLVII+424 pages. In total 471 pages in black and red, each containing 51 lines.

The frontispiece (Figure 2, Figure 3) appears on page IV. The book is dedicated to Francesco Maria II Della Rovere, Count of Montefeltro, VI Duke of Urbino (pages V-VII), for his special interest in the dissemination of culture and his devotion to the development of the Library founded by Federico, Duke of Urbino. Alpini underlines that the Methodic Doctrine was unwisely abandoned, and its potential left unexplored and that he was unable to find an explanation for that. It is important to note that the dedication was signed in February 12, 1611 in the Garden of Simples in Padua, the institution Alpini was directing with great success, being the first of its kind worldwide.

On pages IX and X Alpini introduces the book to the reader. The book was written to recall

In the preface Alpini quotes many authorities including Galen, Paulus of Aegina, Asclepiades, Themison of Laudicea, Thessalus of Tralles, Aetius, Pliny, Soranus of Ephesus and Caelius Aurelianus. He therein also provides a concise synopsis on the methodic school which flourished between the advent of Marcus Antonius and the death of Emperor Septimius Severus (a timeline of nearly 300 years).

The index of chapters (*Index Omnium Capitum quae in toto opera continetur*) appears on pages XI-XVI. A general index (A to Y) follows (pages XVII-XLV). On page XLV one also finds the imprimatur of Friar Zacharias, Inquisitor of Padua, signed on May 14, 1610, as well as the imprimatur of Octavius Livellus for the Republic of Venice (May 21, 1610). The *Errata Corrige* is presented on pages XLVI and XLVII.

The book is structured in 13 books of various length, each of them is subdivided in chapters (Table 1).

In book no.1 Alpini deals with medicine in antiquity and the various medical schools and lists all known methodic physicians. Book no.2 discusses the peculiarity of the teachings of the Methodic sect which rejected the theory of humors. Book no.3 illustrates the practical usability of the teachings of the methodic school. Drugs, body exercises and the prophylaxis of venoms and animal venomous bites are discussed in book no.4. Fevers are illustrated in books no. 5 & 6 where the originality of the contribution of the Methodic school is also highlighted. Inflammation, suppurations and pains are discussed in books no.7, 8 and 9, apoplexy, stones, and icterus in book no.10, the healing means in book no.11. Diseases due to relaxation (ex *laxo*) are discussed in book 12, those of mixed origin (*mixti*) in book 13 which extensively deals with fevers, hemoptysis, cholera, diarrhea, liver diseases, gonorrhea. The book ends with a chapter on bleeding from genitals in women.

On the last page (424) one finds the imprimatur of Friar Zacharias Ravennas, Inquisitor of Padua (May 23, 1610) and that of the Republic of Venice (October 6,1610). It also reports on the place of printing (Padua), the printer (Lorenzo Pasquato) and year of printing (1611).

Kidney diseases in De Medicina Methodica

Table 2 outlines the passages dedicated to kidney and bladder diseases, some of which are translated below.

1. Drugs stimulating diuresis (*Urinam moventia*)

Book IV, 14, p. 130, lines 2-18

"Since they eliminate scanty urine and with a flow slower than usual (*Cum vero urina in ipsis pauca & tardius quam fuerit consueta reddatur)*, in order to preserve the symmetry of meatuses due to contraction (*adstrictum*), thus we must render his [patient's] constitution easier and more free, that can be achieved in part with foods and beverages and in part with the use of drugs stimulating diuresis. Among food very convenient are asparagus well cooked in water and seasoned with oil, vinegar and cinnamon, as well as fresh little stems of mallow and squash-tops well cooked in the same way, the roots of cumin, parsnip and parsley well done and ingested as a salad and also onion, garlic, and leek well done and ingested, all stimulating urination. Those who prefer raw herbs may use salads made in order to stimulate urine formation which are prepared with pennyroyal, water parsnip, cardamon, water-cress, wild rocket, celery, and marsh celery. Furthermore, the use of common horseradish roots, and the raw roots of radish eaten frequently, favor urination with efficacy. Turnip has the same properties, as well as the swede well done with fennel seeds which produce similar effect. Among drugs, very efficient is the decoction of fennel roots, parsley, celery (Smirnium olusatrum L.), Sysimbrium officinale L., minor cardamom, water-cress, adonis, marine eryngium, roots of Rubia tinctorum L., iris, cyperus, ginger, and similars made with water and given at a dose of six ounces...".

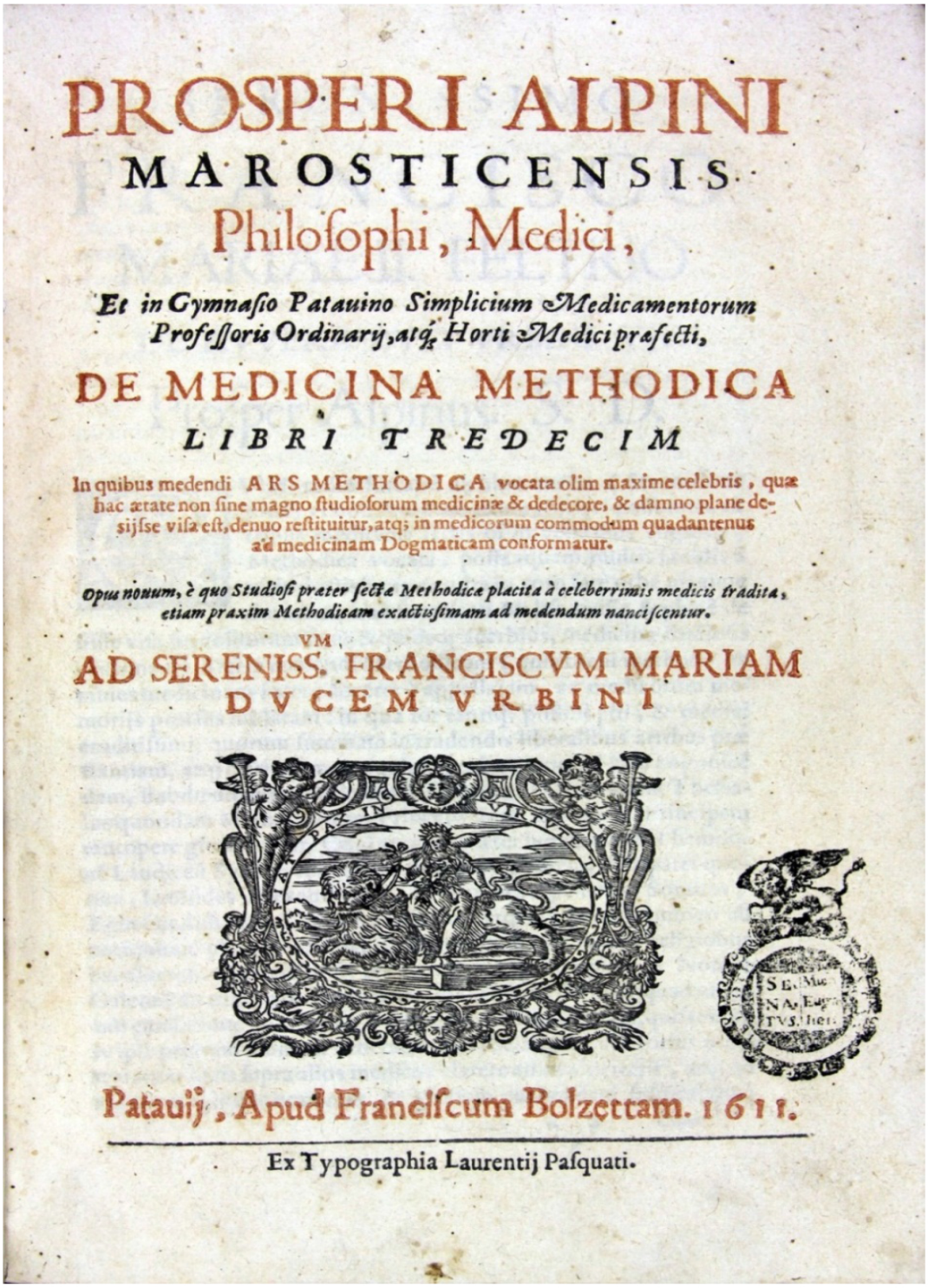
Book VI, 1, p. 177, lines 6 & 7.

"In the case the humor has an effect on urine (*si vero ad urinam humor inclinaverit*), which can be understood in presence of a more copious or acid urine, one should use drugs stimulating diuresis. Galen used to give decoction of..."

Book VI, 8, p. 204, lines 1-20

"We use internal and external drugs for urine suppression. Among internal drugs one gives nearly four ounces of the water oozeing from the roots of eryngium or broad beans, or from the adonis roots. One may also give two drachmas of rocket finely minced up in white wine. In the IV book we have written a lot on this topic and many others will follow in Book XI Among external drugs we list baths in moderately warmed fresh-water wherein one has boiled mallow, marshmallow, chamemelis, or stupes made with the same plants, and applied below on the pubes and on the whole abdomen; one can make ex-

tensive use of ointments with oil of sweet almonds or iris, oil of lily and much more of chamemelis, and that prepared from scorpions. Some fry leaves of pellitory in the pan with oil of chamemelis or of sweet almonds, or flowers of chamemelis and apply them warm. One shoud not condemn the use of seeds of melon, cucumber, marshmallow and of portulaca, since this juice can stimulate urine. However, one may learn more in Book XI. Sometime urine is accompanied by burning and pain, with great stress for patients which can be cured with warm decoction of either mallow or marshmallow or with fruits of vesicatory solanum (Solanum nigrum L.), four ounces before foods or of their drink in white sugar, oth-



PROSPERI ALPINI
MAROSTICENSIS
Philosophi, Medici,
Et in Gymnasio Patauino Simplicium Medicamentorum Professoris Ordinarij, atq; Horti Medici præfecti,
DE MEDICINA METHODICA
LIBRI TREDECIM
In quibus medendi ARS METHODICA vocata olim maxime celebris, quæ hac ætate non sine magno studiosorum medicinæ & dedecore, & damno plane desijsse visa est, denuo restituitur, atq; in medicorum commodum quadantenus ad medicinam Dogmaticam conformatur.
Opus nouum, è quo Studiosi præter sectæ Methodicæ placita à celeberrimis medicis tradita, etiam praxim Methodicam exactissimam ad medendum nanciscentur.
VM
AD SERENISS. FRANCISCVM MARIAM
DVCEM VRBINI
Patauij, Apud Franciscum Bolzettam. 1611.
Ex Typographia Laurentij Pasquati.

Figure 2.
De Medicina Methodica, First edition (1611). In folio, 299 mm x 203 mm - 424 pages.

erwise one may give decoction of fresh liquorice in white sugar. In the case there is at disposal the flower of cathartic cassia (also known as Abyssinian cassia, that with red cortex), that is appropriately preferred to all drugs in such diseases at a dose of 1 ounce plus half drachma of liquorice juice and white sugar, which gives to the patients the maximal benefits. However after taking into consideration the symptoms of fevers which are part of constricted affections, we still have to know and to treat symptoms to a relaxed (*ex laxo*) status".

2. Therapy of renal phlegmon (*De renum phlegmone sananda*)

Book VII, 19, pp. 241-243

"The inflammation of the kidney invades the major part of its substance and all that is therein contained, therefore vein, artery, nerve, caruncles and ureters which departing from the lower part of the kidney flow into the bladder. Bilateral lumbar pain is a symptom of the phlegmon. When both kidneys are affected by the inflammation, pain may be localized in one side when only one kidney is affected; pain

PROSPERI ALPINI

MAROSTICENSIS *Philosophi, Medici, & in Gymnasio* PATAVINO *Simplicium Medicamentorum Professoris Ordinarii, atque Horti Medici præfecti,*

DE

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LIBRI TREDECIM.

In quibus medendi ARS METHODICA vocata olim maxime celebris, quæ hac ætate non sine magno Studiosorum medicinæ & dedecore, & damno plane desiisse visa est, denuo restituitur, atque in Medicorum commodum quadantenus ad medicinam Dogmaticam conformatur.

Opus novum, è quo Studiosi præter sectæ Methodicæ placita à celeberrimis Medicis tradita, etiam praxim Methodicam exactissimam ad medendum nanciscentur.

EDITIO SECUNDA.

STRUCTA SUPER LAPIDEM QUI RUET ISTA DOMUS

LUGDUNI BATAVORUM,

Ex Officina BOUTESTEINIANA, 1719.

Figure 3.
De Medicina Methodica, Second Edition (1719). Quarto, 2000 mm x 160 mm; 765 pages

Table 1. Structure of De medicina methodica libri tredecim

Book	Chapters	Pages (nos.)
Introductory part		
I-III	Withe pages	3
IV	Frontispiece	1
VI-VIII	Dedication to Francisco Maria II della Rovere	3
IX, X	Dedication to the reader	2
XI-XVI	Index of all chapters	6
XVII-XLV*	General index	29
*XLV	Imprimatur	
XLI-XLVII	Errata corrige	2
1	XVII	43
2	XIII	31
3	XVIII	32
4	XX	34
5	IX	34
6	XI	34
7	XXIII	57
8	XIX	32
9	XIV	30
10	XX	44
11	XII	20
12	XIII	47
13*	XI	26

*at page 424 one finds Imprimatur of The Church and that of the Republic of Venice

may be localized in the lower abdomen, a pain which according to Aurelianus may be named "*clanium*", pain - Hippocrates says - is heavy when it affects the fleshy substance, whereas when the membranes covering the kidneys internally are affected, namely arteries, veins and ureters. Galen in Aphorisms says that pain is acute, the same happens when the phlegmon is great and compresses renal arteries, so one feels and observes a pulsation. The swelling is also felt with the compression of the inflamed kidney when the fleshy substance is the site of the phlegmon. In the same place one also feels a sensation of heat, there is little fever, mental alteration, difficulties in passing urine which is scarce in quantity, diluted, watery, free of suspended particles. However, by progression of the disease urine are thicker reddish, or - as some observe - of a putrid color, with a tendency to blackish, like wine, just due to blood coming out from small veins of the kidneys because of increased pressure, or because of their openings or - as Aurelianus says - because they are broken, mixed with urine, since urine is thick,

Table 2. Nephrology in De Medicina methodica

Book	Chapter	Page	Topic
III	XII	98-99	Drug administration through bladder
IV	XIV	130	Drugs stimulating diuresis
VI	I	177	Drugs stimulating diuresis
VI	VIII	204	Drugs stimulating diuresis
VII	XIX	241-243	Therapy of renal abscess
VII	XXIV	255	The incision of Andreas Laurentius* in hydrops
VII	XX	244-245	Therapy of bladder abscess
VIII	IX	267	Pyuria
VIII	XV	277	Theory of Andreas Laurentius* on the route of pus from chest to the kidneys
VIII	XVIV	286	Kidney ulcers
IX	XI	314-315	Kidney and bladder pains
X	XVII	354-356	Kidney and bladder stones
XI	X	375-376	Therapy of anuria
XII	XIII	406-408	Therapy of polyuria

André du Laurens, French anatomist, professor of anatomy at Montpellier, and later royal physician of Henri IV of France, author of Opera anatomica (1593) and Historia anatomica (1600) coined the term cauda equina.

reddish with a tendency to a black color. Sometime there is slight fever, however by progression of the disease it becomes violent and continuous, beginning with shivers, and associated with cold hands and feet. Later, it declines and may not even follow a typical pattern and be associated with transient mental alienation. Bilious vomiting may be present. When the disease deteriorates, all symptoms become heavier, patients have nausea vomit foods, the bowel is blocked and various problem affect the patient. If pus is formed, all symptoms are magnified, and irregular fevers may ensue with irregular shivers, increased pain, symptoms which - as expressed by Galen - "in any way you will be able to diagnose when a kidney is affected, if pain with shivers...".

"This disease is caused by a narrowing (*strictura*) of the kidneys caused by humors which obstruct the kidneys. They are usually preceded by frictions, blows, wounds, excessive intercourse, impetuous horse riding, excessive walking: all things predisposing kidneys to the phlegmon. The phlegmon is a very acute disease, since the veins going from liver to kidneys are inflamed at the same time. It must be added that sometimes anuria occurres which increases the severity of the phlegmon with impending death or concoction of the phlegmon into abscess, thus pus mixes with urine and sometimes with the putrid flesh of the kidneys. When the abscess is evacuated only a wound remains, which is long-lasting and nearly incurable. Therefore, a lot of attention must be paid since when a phlegmon is diagnosed, the humor must be ripened by means of evacuating drugs, and when the possibility still exists one should prevent its turning into pus. When pus is generated, one must act rapidly in order to eliminate it with urine, to prevent the ulcer, and in case it is present, it shall be dried. For this purpose, after a cathartic clyster (made with decoction of mallow... one shall drink up to three pounds of whey) thereafter an incision is made in the internal vein of the right elbow, followed by an incision on the vein of the malleolus...

I get back to what still lacks about the cure of inflamed kidneys. Therefore, having written about external drugs, I shall add that they shall be neither too hot, since these can move pus, nor very cold, since the disease blocks the passages internally and impedes relaxation, thus increasing in weak persons and extinguishes the inborn heat..."

Book VII, 20, pp. 244, lines 1-9

"Anyone expert in medicine knows that the bladder is frequently site of a phlegmon which in most cases is found within the muscle of the wall. Three pathognomonic specific signs have been described by the Greeks for this disease, and consist of a violent burning pain in the pubes, at the origin of the pudendum, in the hip bones, and buttocks; as well as hardening of the groin and of the pubes along with acute continuous fever. Other physicians add waking, dementia, bilious vomiting, difficult urination and sometimes anuria. This is a disease due to contraction (*passio stricturae*) and is the most burdensome disease of the bladder and is fatal and is more lethal when pain is very violent, fever is acute and coexists with hardening of the bladder in the pubic area, with block of the bowel and of urination".

3. Ache in the kidneys and in the bladder (*De dolore renum atque vesica*)

Book IX, 11, pp. 314 and 315 (lines 1-8)

"The ache in the kidneys is generally due either to stones or to a sour salty humor in a quantity capable of distension and of pungent quality, or by a blood clot, or by a swelling humor," or by viscid and slow mucus dried by the internal heat, which gives origin to stones / aut viscida lentaque pituita, quae a calore siccata calculus facit". Patients with renal disease (*nephritici*) are affected by a impairing pain in the kidneys which is felt like a post pushing with force in the same side whereas the testis below is aching. The thigh on the same side becomes insensible, the bowel is usually styptic and under the stimulus of a clyster causes emission of bilious feces and winds. Urine is usually scanty and rich in sediment. For us this is an indication that ache in the kidneys is due to stones "hisce signis dolorem in renibus à calculis fieri nobis indicator". However, when ache is caused by a blood clot, it is not only very violent but it manifests with severe symptoms, such a high fever, agitation, restlessness, anguish, which may cause unconsciousness and syncope. In the case pain is due to a thick and slow humor, there is tension and anuria. In case ache is due to an acidic, pungent and bitter humor, urine is colored. The same causes can induce bladder ache.

4. **Stones of the kidneys and of the bladder (*De renum vesicae calculis)***

X; 18, pp. 354-356)

The disease characterized by pain caused by stones is named lithiasis by Greeks and we call renal stones (*Renum affectum in quo à calculins homines vexantur, Graeci lithiasin, nostri renum calculum*). Aurelianus named it lithiasis. Pain tortures the affected persons. It depends on the presence of stones in one or both kidneys or in the ureters. Pain is peculiar, since it is intolerable and planted in the kidneys, like a perch driven into them. Furthermore pain is localized to the testis of the same side and also the thigh of the same side goes to sleep. The bowel is blocked at the beginning, however—sometimes but rarely— evacuation occurs. When the bowel is stimulated with clysters it discharges winds and bilious feces. Urine are scanty, sandy and rich in sediment. At a variance with pain on the colon patient with kidney stones localize it on the lower quadrant of the abdomen and irradiating to stomach, liver and spleen. In these persons the bowel is completely blocked and even winds do not pass. In bladder stones the pain is violent but the intensity is lower than that of kidney stones. Urine is uncooked, turbid, whitish and with a sandy sediment. Patients are affected by itching and pain on the genitals and urinate continuously (dripping). Sometimes urination is completely suppressed. Aurelianus probably provided the most accurate description of this disease. In fact he says that the disease follows the pain. [...].

Coming back we may say that lithiasis is a disease of contraction and its cure needs relaxant drugs, in order to prevent stone formation as well as to expel them before they become hard as a stone and cannot be broken so that no medicament will be able to expel them. However at present times the incision is so simple and safe, than even septuagenarians are relieved by the disease through the incision and may survive for many additional years in good health. However Egyptians, as we have seen personally, are able to remove the stones from the bladder - even when their size is that of the hazelnut or bigger - without incision from the urethral meatus. [...]. We have reported on this technique in *De medicina Aegyptiorum*. We will now discuss the methods to prevent the generation of stone in the kidneys and in the bladder, how to reduce their size and let them come out before final development, when their consistence is tophaceous, before they reach the consistence of a stone and are crumbly. For the reason among treatments is appropriate the use of blood-letting and oral drugs which act on the dense humor, wash the kidneys and the bladder thus alleviating the pain originating therein. [...].

5. Reinstatement of diuresis (*De urina suppressa restituenda*)

Book XI, 10, pp. 375-376

"There are 3 types of defects causing difficult exit of urine from bladder. The first is characterized by dripping, which means that urine comes out in drops, with pain. The Greek name this case strangury, the Methodists of trickling. In the second type urine comes out with difficulty. Greeks speak of dysuria, Methodists about difficult urination. In the third type urine is totally retained and no urine emission occurs and Greeks speak of ischuria, the Methodists of urine suppression.

The first type is due to acrimony, ulcers in the bladder, or to a pungent humor coming in the bladder from liver or pus originating in the liver or in the kidneys. It is really impossible to say if it is caused by bladder weakness due to mixture of humors or by obstruction of the urinary meatus because of a thick and viscous humor; or by a blood clot or by pus or by a caruncle or by a newly formed and retained stone. This is a serious disease and death may follow rapidly if one does not act immediately by inducing diuresis with drugs administered per os or applied externally or by introduction of a catheter which is carefully advanced and eased. Therefore, when urine is suppressed (when a disease is due to contraction (*ex strictu*), one shall use relaxing drugs internally or externally..." (a list of drugs follows).

6. How to reduce or eliminate the abundant urine discharge (polyuria) which the Greek name diabetes (*De urina profluvio quod Graeci diabetem appellant, tollendo, sive cohibendo*)

Book XII, 13, pp. 406-408:

"Although many authoritative Greek doctors have attributed to polyuria the weakness of the kidney because of a warm constitution due to acidic and salty humors in the kidney substance, thus suggesting that is a disease due to contraction (*ex strictu*), therefore it should not be cured as a disease *ex laxo* but as a mixed (*mixtus*) disease, meaning mixed with a disease *ex strictu*, that is an inflammatory disease, which is discussed in the last book. However, due to the fact that all doctors treat the disease with astringent drugs, which reduce the flow, it is appropriate to discuss and to explain the cure here. Although for the disease the use relaxing (*laxantia)* drugs has been suggested and particularly bleeding to remove a moderate quantity of blood, as well as purges and diaphoretics, I let the erudite doctors judge about the criteria followed in the prescriptions for a disease which is nearly *tubido* (sic!) obscure? There are also well learned doctors who do not agree to admit that polyuria is due to excessive heat in the kidneys or warm humors (as it was for the majority of ancient Greeks) absorbed in the kidney substance and thought that the disease was due to weakness and distension of mesenteric veins, especially by those originating in the liver, in the mouth, and in the kidneys. This is like *lienteria,* where food is unmodified due to weakness in the stomach and intestines, being the retentive strength lost; so that food comes down in the bowel and is own excreted? Thus, in polyuria the liquid part of urine, passing unmodified through the stomach, reaches - through the dilated mesenteric and liver veins - the kidneys in great quantity and is excreted. So, Galen was right when he compared *lienteria* to diabetes wherein beverages are excreted as introduced without any change. In fact, diabetes may not be caused by inflammation of the kidneys (as the majority of doctors think) since when kidneys are inflamed polyuria does not occur. Rather, we do not read in ancient medicine - those who wrote about inflammation of the kidneys - that polyuria was included among pathognomonic signs of inflammation of the kidneys. Furthermore, if the kidneys because of the high heat, were driven to attract exaggeratedly not only humors from veins, but (as all of them suspected) also those from the whole organism, in any inflammation of kidneys, they should behave similarly; this does not occur and is not seen in the course erysipelas when kidneys are heated maximally by extraordinary heat. Why one should be amazed if we ask that in presence of kidneys affected by a warm constitution - with salty and acidic humors - polyuria supervenes? In fact, it is more likely that this disease is due to relaxation of the kidneys veins and bladder. Once we had the chance to follow a case of polyuria in a sixty year old man, who only complained of polyuria and thirst but no heat and not ache in the kidneys. In fact, so intense heat within the kidneys would not remain undetected, and same would happen for the pain (which necessarily follows kidney inflammation) which was completely absent. Thus, it appears that thirst is not caused by inflammation but by the continuous watery urine emission through the bladder, which dehydrates the whole body and wastes it away. Thus polyuria cannot be ascribed to an inflammatory process in the kidneys, but to a relaxation (*laxitate*)

of the mesentery veins and of liver arriving to the kidneys and from these to the bladder. Therefore, we are facing a disease that is easily diagnosed because of the abundant urination and thirst and the peculiar aspect of the body which dehydrates and is wasted. The disease is long-lasting and fatal if one does not act properly with drugs from the very beginning. Being a disease by relaxation (l*axa*) and also facilitated by a relaxation (l*axa*), one should take into consideration astringent drugs (*adstrictoriis*). Also lifestyles will be of the astringent type (*adstrictoria*). Thus, one shall adopt cold and dry air, dense and solid foods, so that their liquid part - because of its density - in their passage through relaxed veins(*laxas*) do not easily flow-down into kidneys and bladder...

Discussion

The passages on the disease of the kidney and of the urinary tract attest the great capability of Prospero Alpini in describing the symptoms of each disease, including renal diseases, as described elsewhere [16] [17] [18] [19]. They also attest the unlimited knowledge in pharmaco-botanics [9] [11] [19].

The passages above have been translated into English for the first time. All chapters devoted to urinary disease herald the novelties introduced by Alpini in clinical practice on hematuria, anuria, polyuria, pyuria, kidney and bladder stones, abscesses as well as the effects of diarrhea. His therapy is innovative as it is rooted in the perfect knowledge of drugs, especially those of vegetable origin.

The description of the diseases expresses the medical knowledge of those times. Of course Alpini mastered the topic because of his long time interest and practice in the field which also reflected concepts expressed in previous papers like *Aegyptian medicine* and his extraordinary knowledge of medical plants..Obviously the use of the pathophysiological mechanism of the Methodist School does not change the diseases, their symptoms, clinical course and therapy, it only changes their interpretation.

De Medicina Methodica Alpini's time-consuming project

The publication of *De Medicina Methodica* had been announced by Alpini in 1601 in the preface of *De presagienda vita et morte aegrotanti.* It took ten years to complete it.

Why did Alpini decide to embark in such a time-consuming project of collecting, and commenting on the whole doctrine of the Methodic School? Why did Alpini consider the project so important that he felt it necessary to diffuse it in advance to the scientific community?

One should start by remembering that *De Medicina Methodica* was produced in a very creative time of the history of the Maritime Republic of Venice, the time when Galileo Galilei was professor at the university of Padua and with his presence fertilized the academic life as well as the social life of the city [17]. Alpini and Galilei knew each other, Galilei even used to attend the Alpini's annual inaugural lecture. That presence was a testimony that Galilei appreciated the work of the scientist who directed the botanical garden, a unique institution, the first ever in the world. The Padua Studium, which was supported economically by the Republic of Venice with two specific taxes - a citizenship tax (*broccatico*) plus a tax on any cart entering in the city - was at its maximum splendor. Some seven thousand students from abroad - mainly from Germany - registered every year, attracted by the curricula, the professors and the tolerant religious attitude of the city. Copernicus, Harvey and Pierre Dolet studied at the University of Padua where Vesal, Realdo Colombo, Fallopius, Girolamo Fabrici d' Acquapendente, Girolamo Mercuriale, Santorio Santorio, the rebel philosopher Pomponazzi, the philosopher Giacomo Zabarella and many other authorities taught [17].

In Padua science was even translated into practical applications, as happened when Galilei with the help of the glass workers in spring 1609 was able to produce a telescope which was shown to the Senate of the Republic) [17]. Padua also offered the proper environment for generating the new medicine. The university had established the anatomical theatre /*Theatrum Anatomicum)* which was in function since 1594 at Palazzo Bo, and the many Academies flourishing in the Republic of Venice played a stimulating role. For example at Palazzo Morosini used to meet all intellectuals arriving in Venice, at Sechini Palace in Padua the number of books and their quality increased day by day. In that Palace Galileo Galilei prepared his application for the university chair and even the material for his lessons [17] [20].

At Padua - under the Galilean influence - were developed the clinical thermometer and the *pulsilogium* (a stop clock to measure the pulse, following the principle of oscillation of the pendulum observed by Galilei in the Cathedral of Pisa), and body balance studies were started with weighing machine to measure perspiration by Santorio in the course of experiments in which also Galilei participated [17] [20] [21].

Medicine was at a cross point in those days, as in the time when the theory of humors had prevailed. However humors had failed, anyone could see the failure of the medical system based on humors. It was evident that it had been a mistake to let that method prevail. So Alpini decided to go back to a system which had simplified the approach to disease by rejecting humors and by making a very moderate use of anatomy. A system not based on speculations but based on physics (atoms and empty space) and deeply rooted in Leucippus, Democritus, Epicurus and Lucretius. Alpini foresaw a system not against metaphysics, but a system where metaphysics had a definite role, where speculation and conjectural did not prevail on the experiment. This seemed to hold great potential to generate a more comprehensive medical system. A doctrine based on *strictus* (a restriction to the movements of atoms, and generating heat) and on *laxus* (fluidic), generating secretions seemed to Alpini worth not only of revival but ca-

pable of fertilization through intellectual investments. However in Padua there was no lack of progression in medicine. Medicine entered into modernity, In Padua the transition from humors into physiology and anatomy generated a medicine based on measurements. It is important to stress that all the achievements occurred decades before the University of Padua created its own teaching hospital [22].

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