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Research Article

A Brief Historical Survey of Nephrology (From the Most Ancient Civilizations to Hippocrates (460-390 B.C.) and From Hippocrates to Bowman (1816-1892)

Musitelli S[1]* and Bertozzi MA[2]

[1]*Expert of the history Office of the E.A.U. (European Association of Urology), Italy*

[2]*Head of the complex operative Department of Andrology at the Azienda Ospedaliera Universitaria Pisana, Italy*

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***Corresponding author**

Musitelli S, Department of Andrology and Sexology, University of Pavia, Italy, Tel: 39 029053748; Email: sergiomusitelli@libero.it

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Abstract

After a brief survey of the lack of any knowledge of the anatomophysiology of the genito-urinary apparatus in the most ancient civilizations and cultures: Mesopotamia, Egypt, China, India, Persia, the 5th-4th century of Greece with Hippocrates (c.469-c.399 B.C.), the authors deal with the first attempt at a scientific approach to the topic, which may be found- although with mistakes - in Aristotle's (384-322 B. C.) treatises. After him Cornelius Celsus (1st century B.C-1st century A.D.) dealt with the kidneys in the briefest chapter 1, 5-10 of the 4th book of his De medicina, in which one cannot find anything original. Galen (129 c. -199 c.) developed and improved Hippocrates' and Aristotle's statements - their mistakes included - and his description and theories about uropoiesis lasted till the 15th century. The founder of the "new kidney" - so to say - was Berengarius of Carpi (1470 - 1531), whose exceptionally original anatomical procedure, and acute observations and descriptions Andreas Vesalius (1514 - 1564) ignored, as well as he ignored the nearly perfect Gabriele Falloppio's (1523-1562) observations and descriptions and erroneously transferred the description of the scarified unipapillary kidney of a dog to the human pluripapillary kidney, mistaking the arcuate vessels for the calyces perfectly described by Falloppio.

Introduction

Before Hippocrates

Not even the faintest description of the anatomo-physiological structure of the kidney can be found either in the medical texts of the ancient Mesopotamia, or in those of the Ancient Egypt, or in those of the most ancient Persian, Chinese and Indian cultures. Indeed in some Assyrian and Babylonian tablets, in the ancient Egyptian medical papyruses, in some of the most ancient passages of the Avesta (the sacred book of ancient Persia), in the surely archaic passages of the Indian medical collection called Ayurveda (about the 5th century B.C.), in the most ancient Chinese medical treatise called Huang Ti Nei Ching su Wên (The canon of internal Medicine of the Yellow Emperor) (about 1000 B.C. if not more than 2000 years B.C.), as well as in the Indian medical treatises preserved with the names of Suçruta[4] and Caraka[5](2nd century A.D.) - the Suçrutasamhita (Suçruta's path) and Carakasamhita (Caraka's path) - one can find a lot of more or less correct and more or less ample descriptions of diseases of the urinary apparatus, this is true, but no allusion to the anatomical structure of the kidney can be found in any of these medical texts.

From Hippocrates to Galen

Although not only urological diseases (like "strangury", "dysuria" and "anuria", bladder and kidney stones) but even uroscopy are quoted in the works of the "Corpus hippocraticum" and although there is a brief, but very interesting treatise "On the heart", nevertheless nothing at all can be found about the anatomo-physiology of the kidney, so that we must conclude that the authors of the hippocratic collection did know nothing about it. But they surely knew that urine reached the kidney together with blood, was someway filtered by the kidneys and reached the bladder through the ureters to be expelled through the urethra. As to the function of urine the authors of the Corpus hippocraticum thought that the "watery humour" which composed urine had the main task of thinning out the blood so that it could flow more easily through the blood vessels (they didn't know any difference between veins and arteries and therefore had not even the faintest idea of blood circulation) and reach more quickly and freely every part of the living body. Once its function was no more necessary, urine became dangerous and therefore was expelled thanks to the kidneys, the ureters, the urinary bladder and the urethra. This opinion lasted at least until the XVII century.

The first author who described the anatomical structure of the kidney was Aristotle (384- 322 B. C.). He didn't still know the difference between veins and arteries, but observed that

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blood reached the kidney via the renal vein and artery and as neither blood nor blood clots could be found into the pelvis even in "post mortem" autopsies, he concluded that no blood reaches it. Urine derived from blood and accumulated into the pelvis to flow to the bladder thorough the ureters.

Apart from these correct observations and descriptions, he made three fundamental mistakes. He maintained:

1. That the right kidney was higher than the left, surely owing to having dissected cattle and Rhesus monkeys, in which the right kidney is really higher than the left. However it may be, Aristotle's mistake was erroneously confirmed by Galen and lasted until the XVI century.
2. That the human kidney is multilobate, most probably because he observed either foetal or bovine kidneys and referred their structure to the human kidney. As a consequence he maintained that the treatment of kidney diseases is much more difficult in man, because the structure itself of the part forces the physician to treat many kidneys at the same time.
3. That only the animals with bladder had also the kidneys and therefore birds could not have any kidney because they have no bladder and this erroneous opinion too lasted until the XVIII century [1].

After Aristotle, no description of the renal structure can be found until Aulus Cornelius Celsus (1st century B.C.-1st century A.D.).

This doesn't mean that the great anatomists of Alexandria, Herophilus and Erasistratus (3rd century B. C.), did not study it. They surely did, first of all because they studied not only the movements of the blood and the anatomical structure of the heart and discovered and described perfectly the atrioventricular valves, but also the genito-urinary apparatus and discovered the spermatic ampullae, the spermatic vesicles and the prostate gland; therefore it is absurd to suppose they didn't study and describe also the anatomical structure of the kidneys; second because as they gave a

"mechanical" interpretation of uropoiesis, they could only hypothesize it on the basis of surely as careful as skilful autopsies. Although unfortunately none of their works has been preserved, nevertheless we can know something about their knowledge of the anatomical structure of the kidney and their theories about uropoiesis from Celsus' De medicina (IV, 1, 5) and Galen's (129 c.- 199 c.) On the natural faculties (I, 15, K., II, 57 ff.)[6].

Celsus tells us that "the kidneys are separated and opposed each other; they adhere to the loins above the hips, being concave on the surface adhering to the hips, on the other surface convex: they are both vascular, have ventricles and are covered by coats...Again from the kidneys, two veins, white in colour, lead to the bladder; the Greeks call them "ureters", because they believe that through them the urine descending drops into the bladder".

Celsus surely derived his description not from autopsy, but from the Alexandrian authors and we can conclude that they knew the correct shape and the fibrous tunic of the kidneys, the pelvis and the calyces. As to the uropoiesis, Celsus' words "they [the Greeks] believe that urine descends through them [the ureters] and drops into the bladder" seem alluding to Asclepiades of Prusa's (40 B.C.) theory, which he surely adopted through Themison of Laodicea (1st century B. C.): to this strange author the kidneys were an absolutely useless part because urine transuded directly from the bowels and gathered into the bladder to be discharged through the urethra. As Celsus says "the Greeks believe", the legitimate suspicion arises that he is referring just to Asclepiades, who was not a Greek, but was born in Bithynia, on the southern coast of the Black Sea.

Galen, in his turn, engaged in controversy not only against Asclepiades and Themison (whom he literally ridiculed as absolutely ignorant of both anatomy and physiology of the kidneys)[7] but also and chiefly, against Herophilus and Erasistratus and their "mechanical" interpretation of uropoiesis. To them it was nothing but a passive "filtration" performed by the kidneys, the thick and hard substance of which received blood mixed with urine and separated the useless "watery humour" that accumulated into the pelvis to reach the bladder through the ureters. So (as Galen maintains) the matter of the kidneys was to them something like the wicker baskets used to make cheese: the whey (like urine) dropped through the network of the basket, while the thicker part (like pure blood) could not pass through the little holes of the basket and was kept there to become cheese. Obviously blood didn't remain into the substance of the kidney, but flowed back through the veins when purified of all the now useless humours.

Galen - like the great Alexandrian anatomists- was aware of the difference between veins and arteries, but had not even the faintest idea of blood circulation. He thought, like Hippocrates, that a certain quantity of humours was mixed with venous blood in order to make it more fluid and facilitate its flowing through the veins. Blood was attracted from the renal vein by the substance of the kidneys but did not reach the pelvis: The "superfluities" that blood carried with itself were separated from blood by the renal substance, dropped into the pelvis through the invisible pores of a "panniculus", that's to say a close network of arterial and venous capillaries covering the internal wall of the pelvis, accumulated into it and flowed to the bladder through the ureters. This being the fact, the kidneys were not at all a simple "filtering" and passive organ to him and uropoiesis wasn't at all a mechanical operation: it was the final result of the co-operation of the "attractive virtue" (the kidneys attracted blood mixed with "superfluities"), the "retentive virtue" (the kidneys restrained the "watery humour"), the "transformative virtue" (the kidneys transformed the mass of "superfluities" into urine) and the "expulsive virtue" (the kidneys expelled urine with the aid of the "attractive virtue" of the ureters). Galen's theory triumphed, together with "Galenism" in general, until the XVII century, that's to say until the "Galilean scientific revolution".

However, in spite of his "qualitative" and therefore "animistic" and "finalistic" interpretation of every anatomo-physiological phenomenon, Galen never described any "filtering membrane" dividing the pelvis into two cavities, that's to say he never described the "filter-kidney" that Vesalius (1514 - 1564) ridiculed with both his words and his figure. And this may easily be confirmed by the late and anonymous author of the brief treatise On diagnosis and cure of the diseases of the kidneys (K., XIX, 643 ff.), who surely wrote the work around the 5th century A. D. and described the famous "panniculus" as a network of venous and arterial capillaries covering the internal wall of the pelvis (like Galen) and the calyces (like Celsus and maintained correctly that stones form just into them. Obviously he confined himself to summarizing what he found in Galen's great treatises, most probably only for practical use.

The Middle Ages

No other description of the anatomo-physiology of the kidney may be found in any of the works of Greek, Latin and Arabian authors after the above quoted pseudo-galenic brief treatise, until Copho the Jounger's (1110) Anatomia porci and the Demonstratio anatomica (preserved by the code Q2 of the Maria Maddalena Library of Breslaw)[8] the anonymous author of which was surely contemporary with Copho, because he polemizes against him. Notwithstanding that both the works are based on autopsy of a pig (as usually was done during the Middle Ages) nothing new can be found about the anatomo physiology of the kidney and only one particular is worthy mentioning: the two authors describe correctly the pelvis, the calyces and the ureters; both the authors maintain that stones form into the calyces, but neither Copho, nor his anonymous opponent allude to any "filtering membrane" dividing the pelvis into two cavities!

The same description and the same statements may be found in the chapter entitled On anatomy of the vena cava and the emulgent veins of the kidneys of Mondino de' Liuzzi (or "Liucci")'s (1270 c. - 1326) famous Anothomia (sic!) (first edition printed in Padua in 1475) where the author does nothing but repeat the "galenic" anatomo-physiology on the basis of very few autopsies of human corpses (perhaps only two female corpses in 1315). As for the kidneys, he too doesn't mention any "filtering membrane", but confines himself to describing the galenic "panniculus" covering the internal cavity of the kidney, through which the urine drops into the pelvis to reach the bladder through the ureters and be discharged through the urethra. As for the urine that "drops downwards"-as Mundinus writes - one must have present that these words do not allude to any "filtering membrane" that separates the pelvis into two different cavities, one higher and the other lower. In fact the lowest point with respect to all the points of either a sphere or of any other cavity is its centre to all the ancient scientists! This is why the Earth lies to them in the lowest point of the concentric spheres of the Universe, i.e. just in their centre and the Devil, the fiercest enemy of the Lord, is driven in the lowest point of the entire Universe: the centre of the spherical Earth, i.e. the "centre of the centre" of the Universe, the farthest point from the Lord.

But the clearest proof that no medieval author ever thought of a "filtering membrane" dividing the pelvis into two cavities can be found in Henri de Mondeville's Surgery (cfr. First treatise, chapter 9). The very important passage reads as follows: "The human and the cow kidneys are similar, that's to say that they are gnarled as if they were composed of many kidneys, have a lot of inlets [obviously the calyces!] and therefore the diseases of the kidneys can be treated with much more difficult than those of the other parts. Moreover, the substance of the kidneys is harder than that of all the other parts of the body". No doubt, Henri is partly deriving from Aristotle, but the description of the renal pelvis is, generally speaking, sufficiently correct and, most of all, there is no mention of any "filtering membrane". On the contrary, there is a clear description of the renal calyces!

Gabriele Zerbi (1445- 1505) gave the same description of the anatomy of the kidneys and he too didn't speak at all of any "filtering membrane", but described - like Galen had done - the "panniculus" covering the internal wall of the pelvis in his Liber anathomiae corporis humani et singulorum membrorum illius (Book on the anatomy of the human body and each part of it) (Venice, 1502) (cfr. p. 34r, b ff.).

The first author who misunderstood both Galen and the following authors and supposed they were speaking about a "filering membrane" dividing the pelvis into two cavities was Giammatteo Ferrari da Gradi (1472). In the paragraph Anothomia (sic!) renum (Anatomy of the kidneys) of the chapter De difficultate urinae (On difficulty of urinating) of his Practica medicinae (Practice of medicine) (Milan, 1472), [but the original title was Pars prima Commentarij In Nonum Almansoris Cum Ampliacionibus et Addicionibus Materierum per Magistrum Johannem Matheum Ex Ferrariis De gradi Mediolanensem (First part of the commentary on Alamansor's Ninth Book[9] with improvements and additions of medical matters by the Milanese Master John Mathew Ferrari of Gradi)] he clearly maintains that "as appears from experience, no transverse filtering membrane that generally the authors write about, can be found into the internal cavity of the kidney". He is surely right, this is true, but nobody of his predecessors had ever described such a "filtering membrane" and he was he who misunderstood the meaning of the "panniculus" described by Galen and by all the following authors, Zerbi included and supposed they were describing just the "transverse filtering membrane" that he could not find in the pelvis as nobody had ever found and described!

And this misunderstanding - as we shall see - was inherited by Vesalius, who conceitedly claimed to be the first to give a correct description of the real anatomical structure of the human kidney... and described, instead, the unipapillary kidney of a dog, moreover understanding nothing at all even of what he was observing!

The First Step

He who really renewed the studies and laid the foundations of the modern knowledge of the anatomo-physiology of the kidney was Berengarius Jacopus of Carpi (1470 - 1531). He described his discoveries in Carpi commentaria cum amplissimis additionibus super Anatomia Mundini una cum textu eiusdem in pristinum et verum nitorem redacto (Carpi's commentaries on Mundinus' Anatomy, with very ample additions and the text of the work brought back to its former and true correctness) (Bologna, 1521). He injected water into the kidney through the "vena emulgens" (the renal vein) and observed that the liquid didn't flow directly into the pelvis, but accumulated into the substance of the kidney. Then he incised the surface of the kidney and observed that the accumulated liquid spurted from the incision. At this point he injected water into another kidney (most likely a pig's kidney), dissected it not from the convex, as had always been done, but from the concave side and discovered the "papillae like female nipples" through which the injected water percolated into the pelvis like milk does through the nipples of the female breast (Figure 1).

But it is worth quoting just the most astonishing passage of his treatise (pages CLXXVIv-CLXXXr). It reads as follows: "I wanted to see in the greatest detail the anatomical structure of the human kidney as well as the kidney of a pig and had recourse to the following anatomical procedure: I took the kidneys and inserted a syringe

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Figure 1: The renal "*papillae*" emphasized in the kidney of a pig with the same procedure of Berengarius of Carpi.

full of hot water into the emulgent vein and pushed it strongly in order to realize if the water penetrated till the ureter and observed that this did not occur. Indeed the kidney was filled with water and swelled. After having observed this fact, I made a little incision on the external surface o the same kidney and injected again hot water with the syringe through the emulgent vein in order to fill better both the renal ducts and the renal veins. At this point I succeeded in observing that the water I had injected with the syringe was flowing out of the incision I had made on the external surface of the kidney. After having observed this result of my experiment, I incised the ureter longitudinally till the inner cavity of the kidney and observed that the ureter widens in the inner part of the kidney and forms a sort of cavity, into which stones form in my opinion. After having bared this part and having incised the ureter, I inserted again the syringe into the emulgent vein of the same kidney I had opened and incised and observed that a much greater amount of water flowed out of the incised substance of the kidney and through the inner part of the ureter than through the convex surface of the kidney. Indeed in that cavity formed by the ureter there are well circumscribed fleshy grains that look like female nipples but are littler and I observed that the

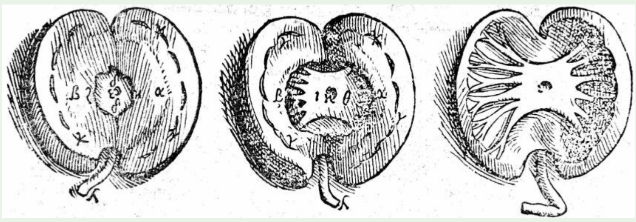
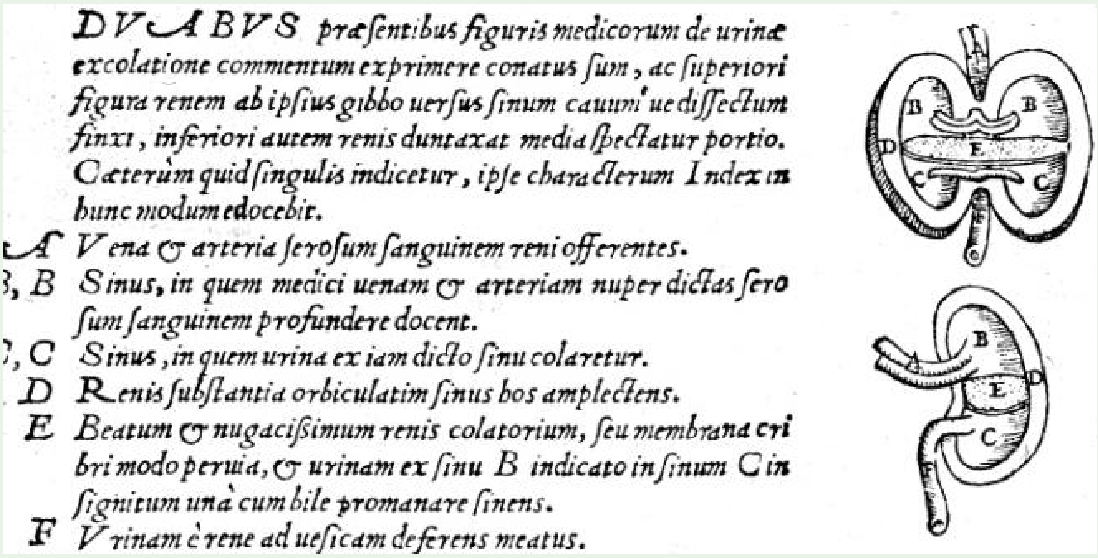


Figure 3: Vesalius' three figures illustrating the dissected monopapillary kidney of a dog.

water I had previously injected with the syringe through the emulgent vein flowed out just around these fleshy grains. At this point I wanted to realize as carefully as possible through which way the previously injected water flowed out and passed from the vein to the ureter and observed that the emulgent big vein divides into ever subtler veins, that the subtlest ones ran towards the external surface of the kidney and that some of them ran towards the ureter, i.e. towards the fleshy grains that look like female nipples. And I also observed that these subtlest veins end around these fleshy grains and bring the urinary liquid to the above mentioned cavity formed by the ureter. The fleshy and nipple-like grains I described above have their base where the branches of the emulgent vein end, whilst their cusp faces the ureter, whose substance is tendinous and the part, which faces the cusp of the nipple-like grains, is rather wide in order - I suppose - to prevent it from clogging up. Moreover I supposed that the urine oozed from the nipple-like grains into the cavity formed by the ureter like the milk oozes from the female nipples. However I could not succeed in observing this particular".

Berengarius' observations were confirmed by Niccolò Massa (1499 - 1569) in his Anatomiae liber introductorius (Introductory book of anatomy) (Venice, 1536), but both these authors and their fundamental discoveries were strangely ignored by Andreas Vesalius who ridiculed in the text, in the figure and in its captions the idea of a "panniculus" spreading out at the middle of the pelvis like a filter (cfr. De humani corporis fabriuca libri septem, Basel, 1543, V, X, pp.



DVABVS præsentibus figuris medicorum de urinæ excolatione commentum exprimere conatus sum, ac superiori figura renem ab ipsius gibbo uersus sinum cauum'ue dissectum finxi, inferiori autem renis duntaxat media spectatur portio. Cæterùm quid singulis indicetur, ipse characterum Index in hunc modum edocebit.

A Vena & arteria serosum sanguinem reni offerentes.

, B Sinus, in quem medici uenam & arteriam nuper dictas serosum sanguinem profundere docent.

, C Sinus, in quem urina ex iam dicto sinu colaretur.

D Renis substantia orbiculatim sinus hos amplectens.

E Beatum & nugacissimum renis colatorium, seu membrana cribri modo peruia, & urinam ex sinu B indicato in sinum C insignitum unà cum bile promanare sinens.

F Vrinam è rene ad uesicam deferens meatus.

Figure 2: The "*filtering membrane*" ridiculed by Vesalius.

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514 - 517) [2] (Figure 2), without taking pains to ascertain whether Ferrari's statement about the former anatomists was correct!

Moreover Vesalius made three great mistakes:

1. He still maintained (like Aristotle and Galen and all the following authors) that the right kidney was higher than the left. In this case too he was not at all so independent from Galen's authority as many scholars maintain: many of his anatomical descriptions repeat exactly Galen's ones and even his mistakes, as is the case of the anatomy of the eye, of the tongue, of the larynx and of the blood vessels and all his physiology, that of the kidneys included, is strictly galenic.
2. He dissected the unipapillary kidney of a dog, and cut and abraded the only papilla, without being aware of what he was doing, only because he ignored Berengarius' discovery of the "papillae". Should he have known Berengarius' work, he surely could understand that he was abrading just a "papilla"! Moreover he conferred the resulting structure to the human kidney (Figures 3 and 4), though Berengarius had already described it as pluripapillary[10].
3. He carried on a controversy against Gabriele Falloppio (1523 - 1562) owing to his misunderstanding of Fallopio's description of the calyces. He made the great mistake of taking the arcuate vessels he had observed in the unipapillary kidney of a dog for the calyces observed and described by Falloppio in the human kidney [3-8].

Nevertheless, there is no doubt that his work gave an impulse to the renewal of the studies of anatomy in general and of the anatomy of the kidney in particular and that his book (like Copernicus' (1473 - 1543) De revolutionibus orbium coelestium, published in the same year in Nuremberg) was much more determining than the work and the discoveries of Berengarius, although they were really exceptional.

Realdo Colombo (1516 - 1559) improved the study and the knowledge of the anatomo-physiology of the kidney with his De re anatomica libri XV (Fifteen books on anatomy) (Venice, 1559). The first clear description of the lesser blood circulation is his fundamental contribution to anatomo-physiology in general, but also his contributions to the knowledge of the renal anatomy are exceptionally important. First of all he and not Bartolomeo Eustachi (1510 - 1574) -as many historians of Urology write - was the first to liken the shape of the kidney to a bean[11] ; second he was the first to maintain against Aristotle and Galen and even Vesalius, that the right kidney is lower than the left, writing bravely (cfr. XI, 9): "It is amusing indeed to observe what a great to do was made by Galen so anxiously attempting at discovering why nature placed the right kidney higher than the left. But there is no doubt that our poor simple-minded Galen...made a useless inquiry...because what he maintains appears clearly and immediately to be false, if only one observes the human anatomy" and this correct statement (like the description of the lesser blood circulation) was confirmed by his disciple Juan Valverde de Hamusco (1515/20 - 1582).

Figure 4: The authors obtained the same results illustrated by Vesalius (Figure 3) by dissecting and scarifying the monopapillary kidney of a kid.

After Realdo Colombo a much greater contribution to the knowledge of the renal anatomy was given by Gabriele Falloppio (1523 - 1562), who, in spite of his deference and admiration for Vesalius, whom he always calls "divinus Vesalius" (divine Vesalius), maintained that his "master" (although he never attended any of Vesalius' lectures!) had made some great mistakes, chiefly as regards the structure of the human kidney (cfr. Observationes anatomicae, Anatomical observations, Venice, 1561, pp. 179 - 182). By dissecting from the concave part - like Berengarius - human and not canine kidneys, Falloppio gave a more exhaustive description of the papillae, already discovered and described by Berengarius and discovered and described perfectly the calyces, which Celsus had only vaguely mentioned, but which Vesalius could not observe because he had cut and abraded the only papilla of his canine kidney! This is why - as said above - he could not understand Falloppio's description and took the arcuate vessels for the calyces. Falloppio is also awarded the discovery of the seminal vesicles, which Vesalius didn't observe, but they had been already discovered and described by Herophilus and Galen. However, Falloppio could not know the Galenic passages as they were in the second part of the great treatise Anatomicae administrationes (Anatomical procedures) (book XII, chapter 7 ff.) which were preserved only in an Arabian translation that was only discovered and published at the end of the XIX century. At any rate, he thought the seminal vesicles to be nothing but sperm reservoirs.

The "Columbus of the New Kidney"

Bartolomeo Eustachi (1510 c - 1574) must rightly be considered as the "Columbus of the new kidney" thanks to his fundamental Libellus de renibus (Booklet on the kidneys) published in Venice in 1563 [9]. He too realised that the right kidney was lower than the

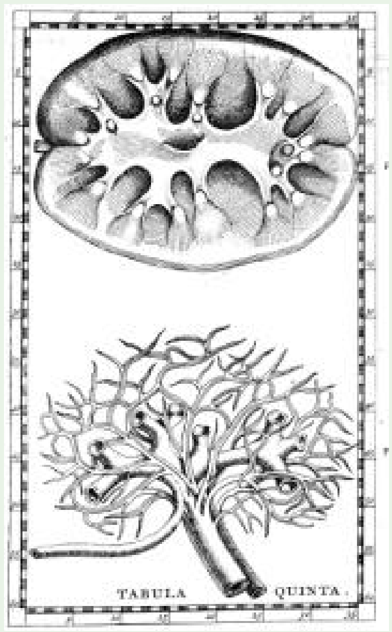

Figure 5: Eustachi's illustrations of the human kidney (above) and its vascular network (below).

left and discovered the adrenal capsules. He studied and described (like Berengarius of Carpi and Gabriele Falloppio) the pluripapillary human kidney and succeeded in observing (by vascular injections, scarification and insufflation to the point of lacerating the fibrous tunic) the vascular tree of the kidney, its terminal arches and the uriniferous tubules in the medullar substance (Figure 5).

Figure 5: Eustachi's illustrations of the human kidney (above) and its vascular network (below).

but he wrongly interpreted them as "furrows incised in the renal substance by urine". He too observed the "papillae" and confirmed Berengarius' description, but saw also their pores that had escaped Berengarius. Moreover he described correctly the funnel-shaped opening of the ureter and was the first to suppose that urine originated from arterial and not from venous blood, as had been maintained since Hippocrates up to this time. He brought the study of the anatomical structure of the kidney to the extreme limits visible by the naked eye, so that Marcello Malpighi (1628 - 1694) could rightly write that "If Eustachi could use not only the knife and injections of liquids (to which he had recourse only to study the structure of the kidney), but also a microscope, no doubt he dissuaded the following anatomists from continuing to study anatomy" (cfr. the letter to Giovanni Fantoni, that Giovanni Maria Lancisi (1654 -1720) prefixed to the edition of Eustachi's Anatomical plates, Rome, 1714).

André du Laurens († 1609), Caspar Bauhin (1560- 1624), Johann Vesling (1598 - 1649), Thomas Bartholin (1616 - 1680) and Jean Riolan (1580 -1657) followed in Falloppio's and Eustachi's footsteps, without giving any further original contribution to the knowledge of the renal anatomy, only one of Caspar Bartholin's (1655-1738) Icones aliquot ex libro Naturae, praeter communem anatomicorum sententiam, desumptate (Some images derived from the book of Nature besides the common opinion of the anatomists) excepted. This figure (which the author inserted in his Institutiones anatomicae (Anatomical institutions), in Theatrum anatomicum (Basel, 1592) and in Vivae imagines (Living images) (Basel, 1640) (Figure 6).

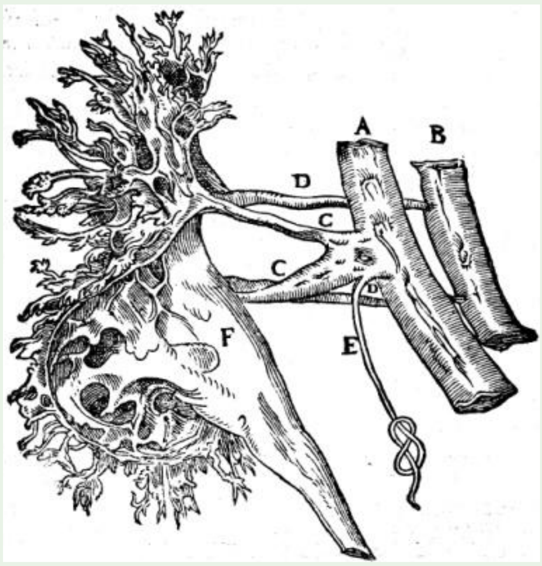

Figure 6: Caspar Bartholin's illustration of the vascular network of a kidney, emphasized by scarifying the renal parenchyma.

Represents the vascular skeleton of the kidney someway more realistically than Eustachi's plate, but Bartholin didn't add anything new to what he found in his predecessor's Libellus de renibus, of which he copied even the captions!

The "Galilean Revolution" and the Foundation of the "Iatromechanical" and "Iatrochemical" Schools

When Poggio Bracciolini (1380 - 1419) discovered, in 1417, Lucretiu's (1st century B. C.) poem De rerum natura (On nature), which brought to light the genuine theories of Epicurus (343- 270 B. C.) - although partially revised and corrected by the Roman poet - "atomism" spread rapidly through European science and the Universe began to be considered as an enormous "machina", composed of numberless little "machinulae" invisible to the naked eye. The problem of discovering these "machinulae" hypothesised by Francis Bacon's (1561-1626) "mechanismus latens" (latent mechanism) resulted in:

1. Marco Aurelio Severino's (1580-1656) interpretation of "anatomy" as "an' átoma" (dissection to the atoms), or "resolutio vel quasi reiterata sectio adusque invisibilia" (dissolution or nearly a repeated dissection until the indivisible parts), instead of "anà tomé" (cutting across/dissection), an opinion he advocated in his fundamental treatise Zootomia democritea (Democritean [that's to say "atomic"] zootomy), published in Nuremberg in 1645.

2. The "Galilean scientific revolution": the "qualitative" and therefore "animistic" and "finalistic" perception of the phenomena was replaced by a "quantitative", and therefore "mechanical" and "determinist" interpretation and by "experiment"; in other words, the Hippocratic "observatio et ratio" (the observation of a phenomenon and the rational evaluation of it) was replaced by the "experiment". For instance, a stone falls not because it is "animated" by the "virtue of falling" that leads it to attain its "end", i. e., "down", but because "it can do nothing else but fall" since its motion is determined "mechanically" by the product of its mass and that of the earth divided by the square distance between them, and what is at first no more than a "mathematical hypothesis", i. e., strictly "quantitative", is later confirmed by the "experiment". As has been said, the universe is an enormous "machine" and its bodies, heavenly or otherwise, are merely little "machines" (= "machinulae") inserted "mechanically" into the "universal machine".

3. The foundation of the "Iatromechanical School", which was the result of the transplantation of this new and revolutionary concept into the anatomo-physiological field by Giovanni Alfonso Borelli (1608 - 1679). The "Iatromechanical school" was soon joined, first in polemical opposition, then as a close ally, by the "Iatrochemical school", founded by Johan Baptist van Helmont (1577 -1644) in whose theory the same "mechanical" definition of physiological phenomena demolished the "humours" of the centuries-old previous doctrine (inaugurated by the authors of the Corpus hippocraticum and inherited by the subsequent centuries on Galen's authority), interpreting them as "substances" that react "chemically" and therefore "mechanically" between one another.

4. The discovery of blood circulation by William Harvey (1578 - 1657).

Citation: Musitelli S and Bertozzi MA. A Brief Historical Survey of Nephrology (From the Most Ancient Civilizations to Hippocrates (460-390 B.C.) and From Hippocrates to Bowman (1816-1892)[1]. J Nephrol Kidney Dis. 2017; 1(3): 1009.
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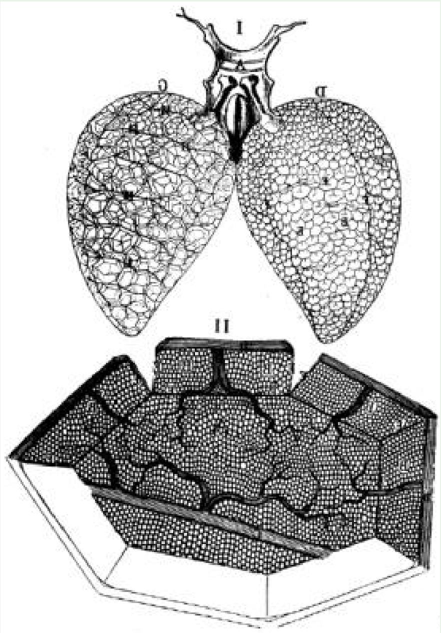

Figure 7: Malpighi's illustration of the anastomotic network of arterial and venous capillaries in the lungs of a frog.

5. The invention of the microscope and the birth of "microscopic anatomy" founded by Marcello Malpighi's (1628 - 1694) astonishing genius.

The Triumph of the Microscope and the "Natural Microscope"

The first achievements obtained by the use of the microscope (first "simple microscopes", that's to say simple magnifying glasses, like those used by Antony van Leeuwenhoeck (1632- 1723), then "composed microscopes", like those used by Marcello Malpighi) suggested that Nature itself gave "natural magnifications" of invisible structures. For example, a bluebottle was thought to be a "natural magnification" of a midge. This is what Johann Conrad Brunner (1653 - 1727) called "microscopium naturae" (natural microscope) and suggested to Claudius Aubry (17^{th} century) that the testicle of a wild boar was the natural magnification of the human testicle. A further development of this idea was that the microscope made it possible to discover structures that were invisible in the most complex animals, such as mammals, through the simpler structures (and therefore naturally magnified) in inferior animals, such as frogs and insects, by the observation of which the invisible ones in most complex animals could be discovered. A marvellous example is the discovery by Marcello Malpighi of the arterio-venous anastomosis in the human lungs through the study of the simpler lungs of frogs (Figure 7).

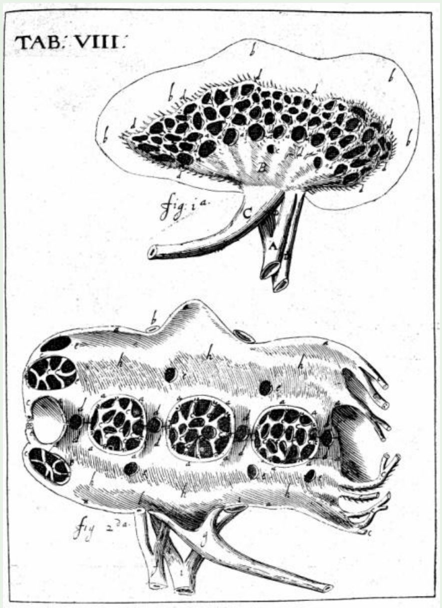

Figure 8: plate VIII of Highmore's treatise.

Microscopical Anatomy and Blood Circulation

The first attempt at linking microscopical observation, blood circulation and mechanic interpretation of the anatomo-physiology of the kidney was made by Nathanael Highmore (1613 - 1684). In his fundamental treatise Corporis humani disquisitio Anatomica in qua sanguinis circulationem in quavis Corporis parte, plurimis typis novis ac aenigmatum Medicorum succincta dilucidatione prosequutus est... Nathanael Highmorus (Anatomical dissertation in which Nathanael Highmore has followed the blood circulation in every part of the human body with many new plates and a concise explanation of the enigmas of physicians) published in La Haye in 1651 he described for the first time the structure of the vascular network at the limit between the medullar and the cortical substance (the arcuate vessels) (Figures 8 and 9).

On the basis of blood circulation, he maintained that this network was formed by an anastomosis between venous and arterial capillaries and partly paved the way for Lorenzo Bellini (1608 - 1679).

The Discovery of the "Ductus Belliniani"

In 1662 Giovanni Alfonso Borelli incited his young disciple Lorenzo Bellini to publish the results of his research on the structure of the kidney. Bellini published his fundamental Exercitatio

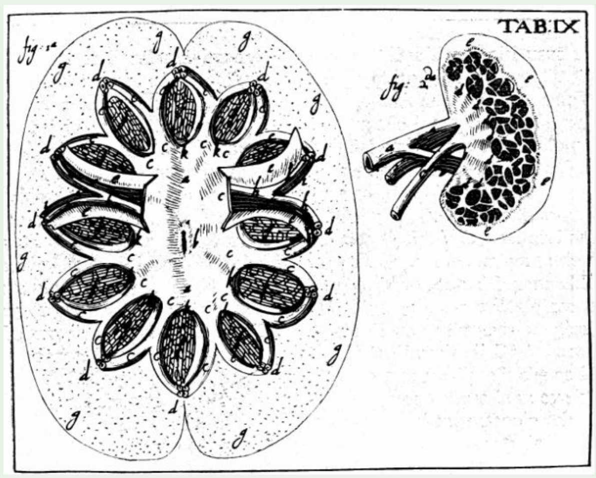

Figure 9: plate IX of Highmore's treatise.

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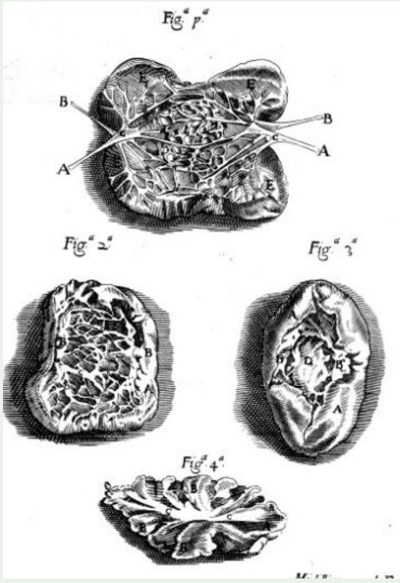

Figure 10: First Bellini's plate.

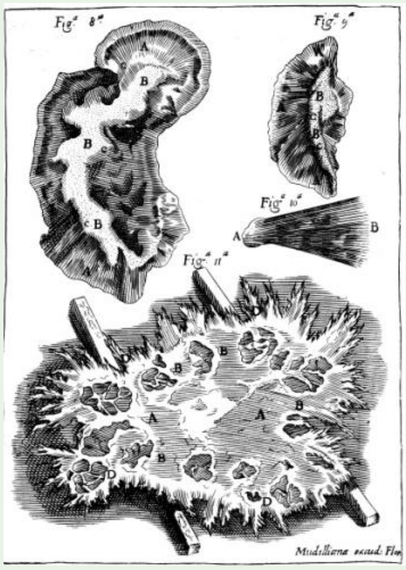

Figure 12: Third plate.

anatomica de structura et usu renum (Anatomical essay on the renal structure and function) (Florence, 1662), which paved the way definitively for Marcello Malpighi. The work is divided into three parts. In the first, Bellini reviews the former theories from Galen to Highmore, but he deceitfully makes no mention of his two greatest predecessors, Berengarius of Carpi and Bartolomeo Eustachi. In the second, he examines critically the former doctrines (chiefly Vesalius' and Falloppio's ones), while in the third he exposes and illustrates with 11 figures in three plates the results of his personal research (Figures 10- 12).

Bellini started from the arcuate vessels' network discovered by Nathanael Highmore, but didn't interpret them as arteriovenous anastomoses. This was because he had discovered straight capillary vessels branching from the arches of the highmorian network. These straight capillaries crossed the cortical substance, reached the renal surface and were the interlobular vessels that Bellini emphasised both by abrading the cortical substance and injecting coloured water, either through the emulgent vein or the emulgent artery. This way he could discover the "sinuli vermiculares et tortuosi" (vermicular and tortuous little sinuses), which formed a network on the renal surface. Therefore the renal substance was to him an "infinitorum sui generis vasorum aggregatum" (an aggregate of numberless and peculiar vessels), i.e. the so-called "ductus belliniani", which are continuous from the surface of the kidney to the cavity of the pelvis.

The discovery of the "ductus belliniani" inaugurated a new phase of the history of the renal structure, which culminated with Marcello Malpighi's discoveries.

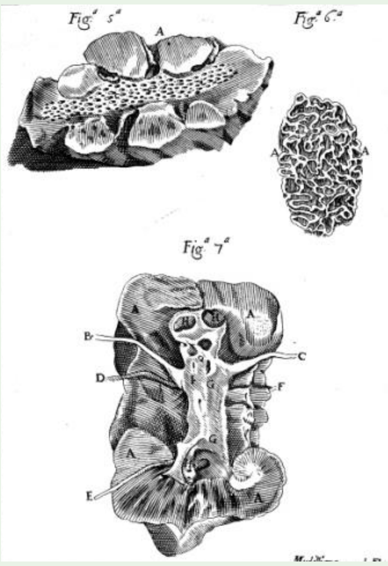

Figure 11: second s plate.

Figure 13: A "glandula miliaris" (millet like gland) drawn by Malpighi himself: the subtle tract at right is a capillary nerve.

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As to the mechanism of uropoiesis, Bellini explained it having recourse to the phenomenon of "capillarity", which had recently been discovered by his great master Giovanni Alfonso Borelli, who had also hinted at the so-called "Jurin's low", when he observed that the raising and lowering of a liquid in a tube depends on the nature of the liquid and the diameter of the tube where the meniscus forms.

Another of the fundamental contributions of Bellini is also worthy of particular mention: he was the first to allude to urodynamics in his De urinis et pulsibus quantum ad artem medicam pertinent (On urine and pulses in relation with the Art of Medicine) published in Bologna in 1683.

The Discovery of the "Malpighian Corpuscles"

As has been said, Marcello Malpighi was the founder of the modern microscopical anatomy. He deserves a prominent position in the history of general, as well as urological anatomo-physiology because he discovered:

1. The arteriovenous anastomoses by observing frog lungs, which were to him a "microscopium naturae" (natural microscope). He described his fundamental observations and discoveries in two letters De pulmonibus (On the lungs) addressed to his great master Giovanni Alfonso Borelli and published in Bologna in 1661. With this discovery Malpighi gave the final and unquestionable proof of blood circulation;

2. The real structure of the uriniferous canaliculi and the so-called "Malpighian corpuscles", which he was able to emphasise by injecting a solution of Indian ink and alcohol into the renal artery and described in his fundamental De renibus (On the kidneys), published in Bologna in 1666 in the collection De viscerum structura (On the structure of the organs), which contains also his treatises De hepate (On the liver), De cerebri cortice (On the cerebral cortex) and De liene (On the spleen). With the discovery of the corpuscles named after him, Malpighi started the final elucidation of the nephron, although the "corpuscles" were to him glandular follicles embraced by a network of arteriovenous capillaries, and changing into an excretory duct that he correctly described as winding in the first tract and then straight till the papilla, against Bellini, who thought the excretory ducts to be straight from the beginning to the end (Figures 13-15).

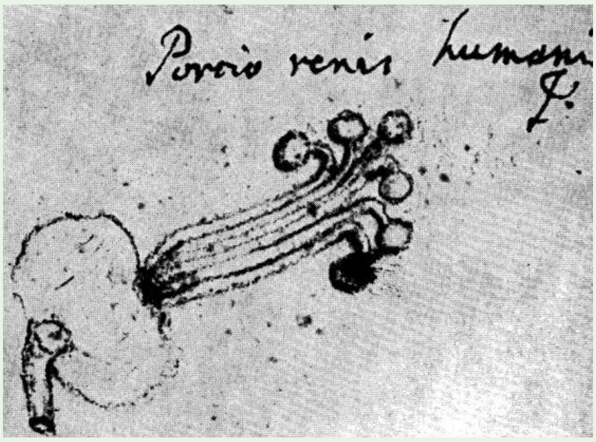

Figure 14: A "portion of the human kidney" drawn by Malpighi himself.

The last chapter of the treatise (the 6th) deals with the physiology of uropoiesis and is surely not as brilliant as the first five. According to Malpighi the infinitesimal parts (the "atoms" postulated by Francis Bacon, Galileo Galilei and Marco Aurelio Severino) of the substances that form urine have the same shape of the infinitesimal pores of both the arterial capillaries and the follicle, so that they can pass from the arteries to the follicle, flow through the excretory duct to the pelvis to be discharged through the ureters into the bladder and then eliminated through the urethra. These being the facts, Malpighi's theory of uropoiesis seems to go back to Galen (to whom too urine was filtered through the invisible pores of the arteriovenous network he called "panniculus") and to confine itself to transferring the "filtration" from the wall of the pelvis to the inner substance of the kidney!

The "Malpighian Corpuscles" Are Not Follicles but Balls of Blood Vessels

Frederik Ruysch (1638 - 1731) described and illustrated with marvellous plates the same reports of Highmore, Bellini and Malpighi on the renal structure (cfr. Thesaurus anatomicus, Treasure of anatomy, III, VI and X, Amsterdam, 1724), which he emphasised with coloured wax injections (Figure 11). Nevertheless, he was in contradiction to Malpighi about the real nature and structure of the "Malpighian corpuscles" and the mechanism of uropoiesis. He maintained correctly that the "corpuscles" discovered by Malpighi were not follicles embraced by arterio-venous capillaries and endowed with nerve ends and particular ducts, but instead a ball of capillary blood vessels (arteries and veins), that's to say "glomeruli" (that in Latin means just "little balls") that favoured the separation of the humours (urine) and changed directly into the excretory duct (Figure 16).

With his extraordinary observations and discoveries, Ruysch paved the way for all the subsequent studies on the inner anatomical structure of the kidney and the physiology of uropoiesis.

The First Chemical Analysis of Urine

Hermann Boerhaave (1658 - 738) tried to reconcile Ruysch's and Malpighi's theories on the nature and structure of the "Malpighian

Figure 15: The "*Malpighian corpuscles*" emphasized in the kidney of a kid by injecting a mixture of Indian ink and alcohol through the renal artery as Malpighi did. They appear just as he described them: "*like apples hung on a tree*".

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corpuscles" and the physiology of uropoiesis. At the beginning he was a follower of Hippocrates, but soon adhered to both the "Iatromechanical" and "Iatrochemical" schools. In his main work, Institutiones medicinales (Medical institutions) (Leiden, 1708), he maintained that nothing can be in urine that was not previously in blood, indeed an idea that had been already advocated by Aristotle and Galen, but that Boerhaave succeeded in demonstrating on the basis of his chemical studies. After having examined urine chemically - following the way paved by Paracelsus (1493 -1541) and van Helmont and agreeing with Bellini - he could realise that urine consisted of water derived from the blood in the proportion of 9 parts out of 20 and that it also contained a slightly alkaline but very acrid and volatile salt, decomposed and friable, unstable and volatile earth, sea salt and another salt, very similar to ammoniac salt. But he deserves a particular mention for the theory of uropoiesis, which he exposed in another fundamental work, the Institutiones medicae in usus annuae exercitationis domesticos, digestae ab Hermanno Boehraave (Medical institutions for home uses of annual exercise, put in order by Hermann Boehraave) (Leiden, 1713). In §. 353, De oeconomia animalis (On the economy of the animal) (p. 140 ff.), he maintained against Ruysch that both the "Malpighian corpuscles" as described by Malpighi, and the direct communication between blood capillary vessels and uriniferous tubules - advocated by Ruysch - were present in the renal substance and that urine was secreted by both. He also dealt with urological pathology and described erosions of the urethral mucosa and the localisation of infections in the "glands of Littre" in cases of venereal diseases. As to haematuria, he maintained that it could occur as a particular vicarious bleeding when menstrual blood or bleeding from haemorrhoids was suppressed.

The Discovery of "Bertin's Columns"

Bellini's, Malpighi's and Ruysch's researches and discoveries were improved by Exupère Joseph Bertin (1712- 1781) who studied both the anatomo-physiology of respiration and speech - engaging a controversy with Antoine Ferrein (1693 - 1769) -and the renal structure. He discovered the portions of the cortex passing between the pyramids, that's to say the so-called "Bertin's columns", which he described and illustrated in the essay Mémoirs pour servir à l'histoire des reins, published in Mémoirs de l'Académie des Sciences (Paris, 1744). According to him, the renal structure was made up of a major stratum (the "clear stria" discovered by him) and a lesser stratum. The major one consisted of convoluted tubules, in which - like in the parotid - the glandular function occurred, with secretion of the majority of the fluid of the urine. The lesser stratum consisted to him of very convoluted blood capillaries, which changed directly - as Ruysch had maintained - into major uriniferous tubules and had the function of secreting the bulkier part of the urine (Figure 17).

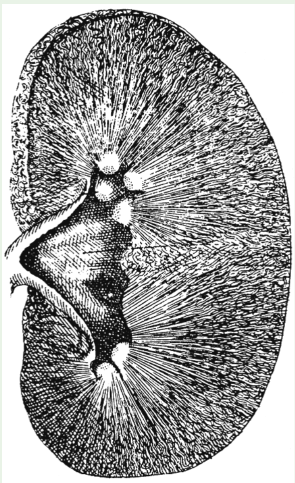

Figure 16: Ruysch's injected and dissected human kidney.

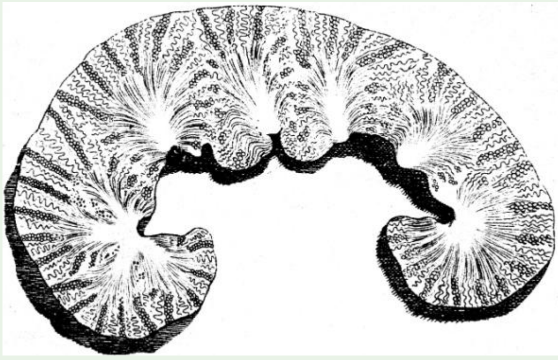

Figure 17: Bertin's illustration of the two "strata" of the kidney substance.

The Discovery of "Ferrein's Pyramids"

Notwithstanding his controversy with Bertin on the anatomo-physiology of respiration and speech, Antoine Ferrein prosecuted and improved his adversary's studies on the structure of the kidneys. He had began studying Theology, but turned to Medicine after having read Giovanni Alfonso Borelli's fundamental tratise De motu animalium (On the movement of animals) (Rome, 1680 - 1681), which was the real "Bible" of the "Iatromechanical school" for many decades. He devoted himself in particular to the study of the uriniferous tubules and discovered the radial striations going out from the medullar into the cortical substance (then called "Ferrein's pyramids" after him) (Figure 18).

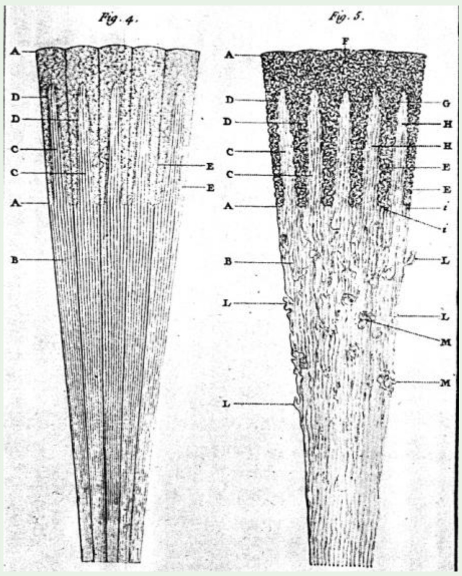

Figure 18: Ferrein's pyramids.

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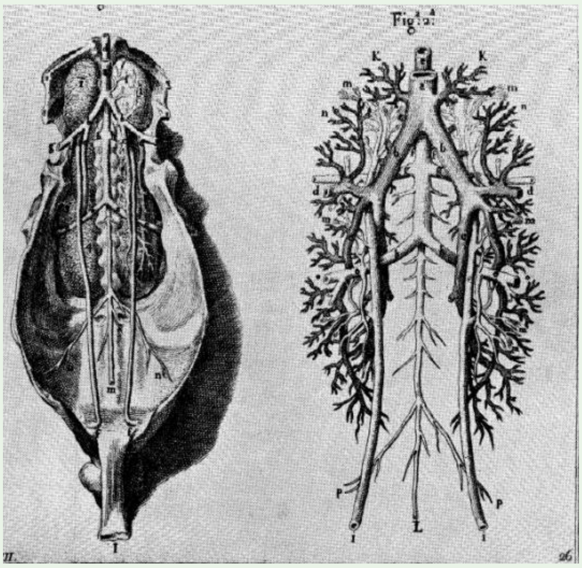

Figure 19: Galvani's illustration of the kidneys of a cock: (left.) the position of the kidneys; (right): division and distribution of both the emulgent ducts and the ureters.

However, he maintained that the kidney had glandular structure and function, that it was absolutely aglomerular and assigned the emunctory function to the "white cortical tubules", into the walls of which the thinnest blood vessels penetrated. Ferrein exposed his discoveries and theories in a fundamental article entitled Sur la structure des viscères nommés glanduleux et particulièrement sur celle des reins et du foie, published at p. 489 ff. of Histoire des Sciences, Année 1749 (Paris, 1753), in which he also described the ureters of birds 18 years before Luigi Galvani (1737 - 1798).

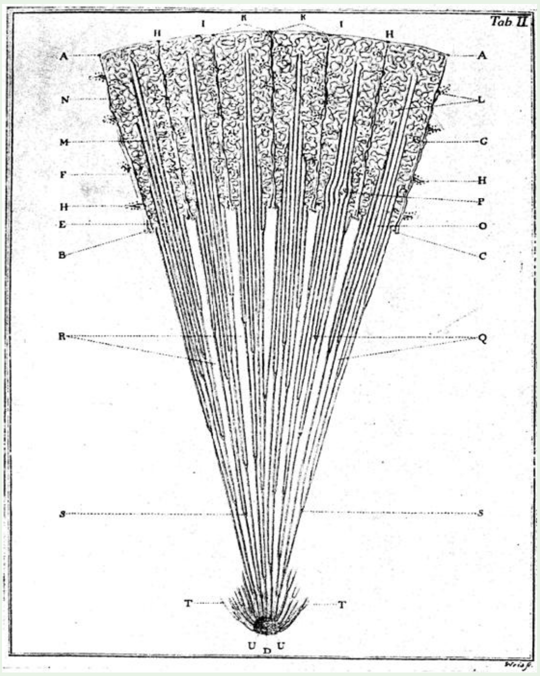

Figure 20: Schumlansky's convoluted tubules and collecting ducts.

The Kidneys of the Birds

As has been said at the beginning, according to Aristotle only the animals with bladder had also the kidneys and therefore birds could not have any kidney because they have no bladder. Luigi Galvani is worth mentioning in the History of Urology just for his contribution De renibus atque ureteribus volatilium (On the kidneys and ureters of the birds), published in Bologna in 1767 (cfr. De Bononiensi Scientiarum et Artium Instituto atque Academia Commentarii [Commentaries of the Institute and Academy of Sciences and Arts of Bologna], Bologna, 1767, V/2, pp. 500 - 508). In this short, but exceptionally important work Galvani described and illustrated both the kidneys and the ureters of birds (Figure 19), which he thought nobody had observed before him. In fact, both Marcello Malpighi and Antoine Ferrein had already studied the structures described by Galvani.

Notwithstanding that, his work is surely more complete and more exact than those of his predecessors and also more important chiefly because on the one hand he confirmed and proved Ruysch's opinion on the continuity between arterious vessels and excretory ducts; on the other hand, and just for this reason, he paved finally the way for Emil Huschke (1797 - 1858), Johannes Müller (1801 - 1858) and William Bowman (1816 - 1892).

Medullar Ducts, Convoluted Tubules and Glomerulus

Both birth and death dates of the Russian Alexander Schumlansky are unknown. He lived and was active between the 18th and the 19th century and studied in Strassbourg where he graduated in 1783 with a thesis entitled De structura renum (On the structure of the kidneys), which was edited by G. C. Wurtz in Strassbourg in 1788 with the title De structura renum tractatus physiologico-anatomicus (Physiological and anatomical treatise on the structure of the kidneys). In this fundamental work - in which he changed "Malpighian corpuscle" into "glomerulus" - Schumlansky maintained that the medullar ducts and the convoluted tubules were continuous and each convoluted tubule ended with a glomerulus. The convoluted tubules differed from the collecting ducts only in that they were convoluted in order to slow down the flow of urine, which was secreted by the glomerules and carried to the renal papilla by the collecting ducts (Figure 20).

With this exceptionally important research he paid homage to the genius of Marcello Malpighi and paved the way for William Bowman.

K. Wilhelm Eysenhardt - whose birth and death dates are unknown, but who worked at the Anatomical Institute directed by Karl Asmund Rudolphi (1771 - 1832) -continued and improved

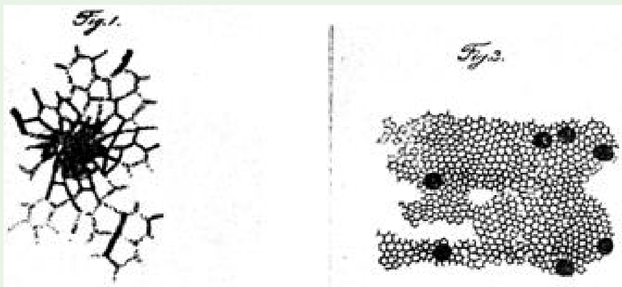

Figure 21: Figure 1 and Figure 3 of Eysenhardt's *De structura Renum Observationes Microscopicae.*

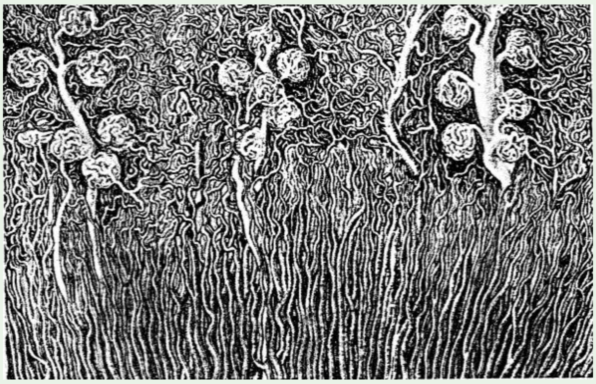

Figure 22: A medium network joins the efferent tubules according to Berres.

Schumlansky's studies and exposed the results of his researches in the treatise De Structura Renum Observationes Microscopicae (Microscopical observations on the structure of the kidneys) published in Berlin in 1818. In this work he maintained that the thinnest tubules radiated from each glomerulus and joined together in a network, the meshes of which contained the "Malpighian corpuscles" The vessels of the medullar substance originated just from this network, changing their shape to become straight and gathering together to reach the renal papilla (Figure 21).

This description seems to correspond to the vascular network observed and described by both Joseph. Berres (1796 - 1844) (cfr. Anatomie der mikroskopischen Gebilte des menschlichen Körpers (Anatomy of the microscopical structure of the human body), Wien, 1836) and his disciple Joseph Hyrtl (1811 - 1894) in a saw kidney. According to them the capillary peritubular networks they thought they had discovered derived from the loops of the glomerules and changed into tubules (Figures 22 and 23).

Is The Kidney A Gland?

Bertin's and Ferrein's theory of tubular secretion in the kidney was resumed by Emil Huschke in his famous essay Ueber die Textur der Nieren (On the structure of the kidney), published in Isis, 21:1828 (cfr. pp. 560 -569). On the sound basis of several experiments he criticised Schumalnsky's theories because they seemed to him to have been founded upon too scanty and inadequate experiments. From his numerous and careful ones, Huschke drew the conclusion that the

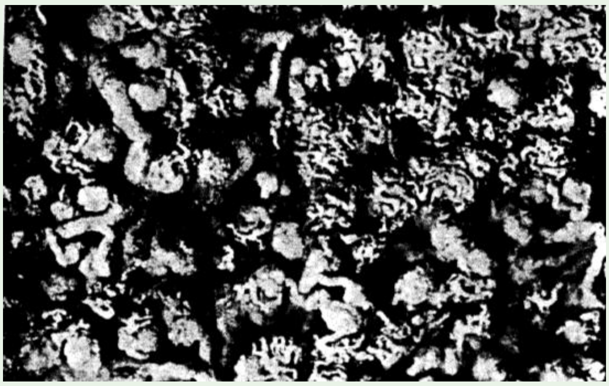

Figure 23: Hyrtl emphasized the same network by injecting a frustum of the kidney of a saw.

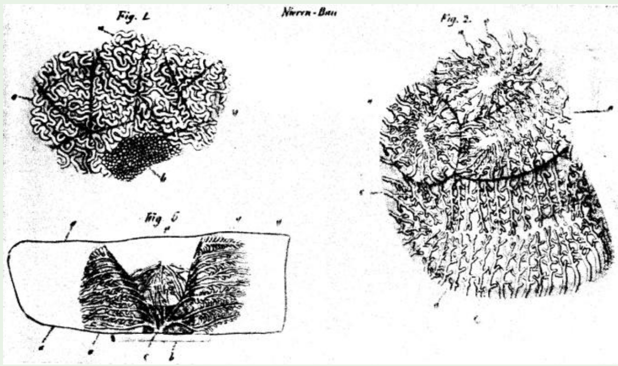

Figure 24: plate VIII illustrating of Huschke' article: (left, above): the outer surface of the kidney of a three years old baby; (left, below): the uriniferous tubules of the kidney of a snake: (right): the outer surface of four lobules of the kidney of a duck.

kidney was a gland like the testicle, because it too was composed of tubules, though the tubules of the kidney were infinitely thinner and softer than those of the testicle. These tubules were embraced by a network of very thin blood capillaries and ended with a blind pouch ampulla (Figure 24).

The only function of the tubules was to secrete urine. Thanks to his exceptional studies and observations Huschke started the final resolution of the problem of uropoiesis, a new and fundamental contribution to which was given by Johannes Müller. He presented the results of his observations in the essay De glandularum secernentium structura penitiori earumque prima formatione in homine atque animalibus (On the internal and deeper structure of the secretory glands and their first formation in man and animals) published in Leipzig in 1830. His conclusions about the structure of the kidney (cfr. book X, De penitiori structura renum, On the deeper structure of the kidneys, p. 84 ff.) were very similar to those of Emil Huschke. Müller agreed with Ruysch that the "Malpighian corpuscles" were balls of vessels, but made the mistake of maintaining that they had no connection with the uriniferous tubules (Figure 25).

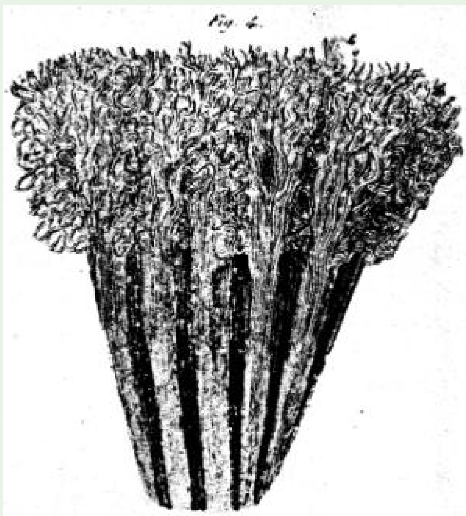

Figure 25: Figure 4 of the Plate XIV of Müller's treatise: it represents the kidney of a squirrel.

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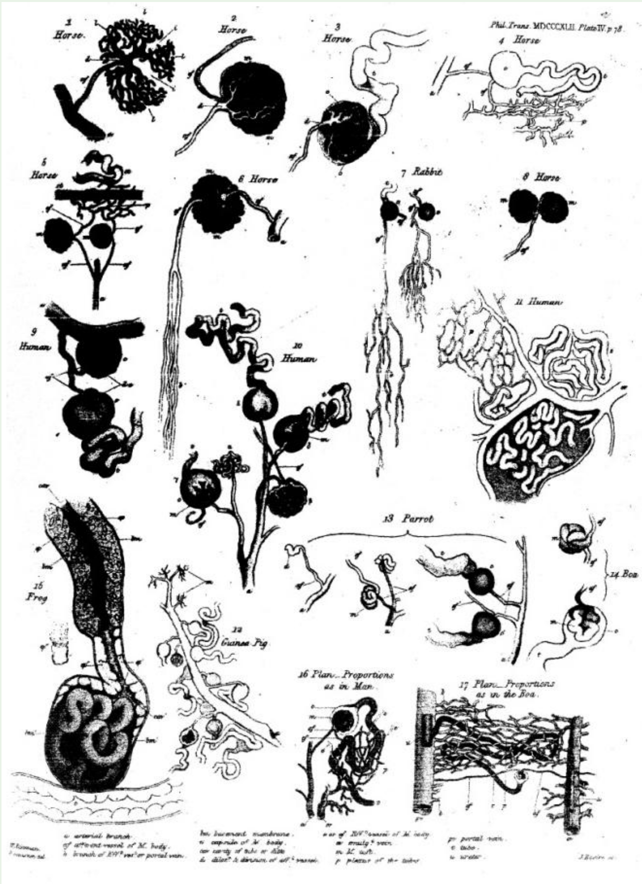

Figure 26: Plate IV of Bowman's work: (left) the pertinent captions; (right) the plate.

This mistake was later corrected by William Bowman (1816-1892) [9-11].

The Final Discovery: "Bowman's Capsule"

Sir William Bowman owes his right glory to his most famous work: On the structure and the use of the Malpighian bodies of the kidney, with observations on the circulation through that gland, published in the Philosophical Transactions of the Royal Society (1842/1, pp. 57 - 80). In this exceptional work he described and proved the connection between the vascular glomerulus and the uriniferous tubule thanks to the capsule that was called after him. He could make this fundamental discovery thanks to a double endovascular injection of two saturated solutions, one of lead acetate and the other of potassium dichromate. In doing so, he put an end to the centuries-old research on the structure of the nephron (Figure 26), although his theory of ultrafiltration of blood plasma through the membranes of the vascular glomerulus in the cortical substance was still imperfect. This was because it assigned to the kidney only the simple and passive function of delivering blood from the waste substances, someway inheriting - although unawares - Erasistratus' theory, so relentlessly opposed by Galen!

However one can well understand and justify such a mistake if only considers the perspective of the Positivism that was dominating in that time.

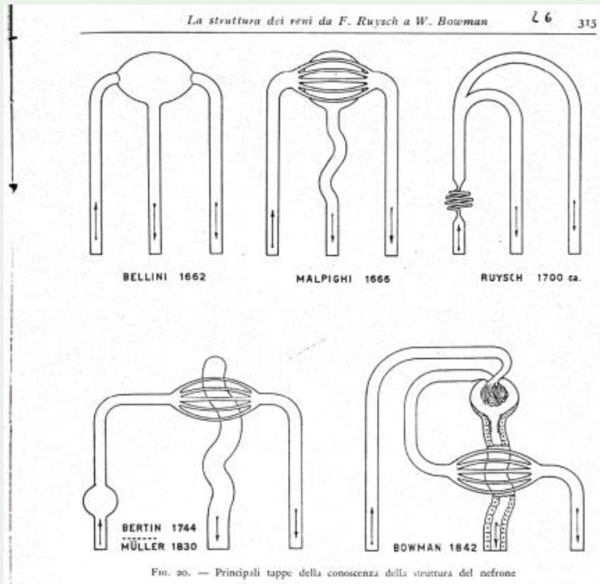

Figure 27: The stages of the conquest - so to say - of the nephron were perfectly summarized.

Conclusion

The stages of the conquest - so to say - of the nephron were perfectly summarized by F Grondona in the following figure 27.

A briefer and different version of this article (only From the origins to Berengarius of Carpi (1470-1530) and Vesalius (1514-1564) was published in Jacobs Journal of Nephrology and Urology, 01-20-2016, p. 1 ff.

Footnotes

1. Expert of the History Office of the EAU (European Association of Urology).
2. Dedicate also this article to the memory of my adored son Giulio, who was killed on 14/05/2012 by a criminal driver, who did not observe a STOP sign.
3. Head of the Complex Operative Department of Andrology at the Azienda Ospedaliera Universitaria Pisana.
4. Read "ç" like "-sh-" of "shameful".
5. Read "C"- like "chi-"of child.
6. K. means "Claudii Galeni Opera Omnia, edited by Carl Gottlob Kühn, Lipsiae, 1921 ff. The Roman numbers correspond to the volume; the Arab ones to the chapter or the page.
7. He succeeded in proving that urine gathered into the renal pelvis and reached the urinary bladder through the ureters by tying up one of the two ureters "in vivo" and emphasizing that the corresponding kidney swelled owing to the accumulated urine!
8. Cf. S. De Renzi, Collectio Salernitana, Filiatre Sabezio Publisher, Naples, 1852-1859, II, p. 388 ff.
9. It is the 9th book of the most famous treatise Kitāb aṭ-Ṭibb al-Manṣuri (Medical treatise dedicated to the King Almansur) in

10 books, written by Abū Bakr Muhammad ibn Zakariyā ar-Rāzī (abbreviated into Rhazi/Rhazes/Rases/Rasis, etc.) (865-c.925). The 9th book deals with pathology from the head to the feet.

10. In the original plate the three figures are put vertically.

11. Galen had already correctly likened the shape of the kidney to the ancient Greek letter "sigma" (= C) and the male urethra to the Latin letter "S".

12. Cf. S. Musitelli, The Galilean revolution, in Europe-The cradle of Urology, edited by Johan J. Mattelaer and Dirk Schultheiss, History Office of the European Association of Urology, Arnhem, 2010, p. 40 ff.

References

1. Hall M. Vesals Darstellung des Baues der Niere in Archiv für Geschichte der Medizin added to Sudhoffs Archiv für Geschichte der Medizin und Naturwissenschaften. 1934.

2. Benjamin J A. A discussion of the twenty-first illustration of the fifth book of De humani corporis fabrica in Bulletin of the History of Medicine. 1943.

3. Klemperer P, Federn W. The dilemma of Johann Jacob Wepfer. The history of the contracted kidney in Bulletin of the History of Medicine. 1959.

4. Belloni L. La conquista del nefrone in Atti della Accademia Medica Lombarda. 1963.

5. Grondona F. Strutturistica renale da Galeno al Highmore. in Physis. 1963.

6. Grondona F. L'esercitazione anatomica di Lorenzo Bellini sulla struttura e funzione dei reni. in Physis. 1963.

7. Belloni L. Dall' "occhiale" di Galileo all'anatomia microscopica di M. Malpighi: il "Testis examinatus" (Firenze 1658) di Claudius Auberius, in Rendiconti dell'Istituto Lombardo di Scienze e Lettere, Classe di Scienze. 1964.

8. Grondona F. Il trattato di Luigi Galvani sui reni e gli ureteri degli uccelli, in Bollettino dell'Istituto Medico Chirurgico Giuseppe Ronzoni. 1964.

9. Grondona F. "De renibus" di Marcello Malpighi. in Physis. 1964.

10. Grondona F. La struttura dei reni da F Ruysch a W Bowmann. in Physis. 1965.

11. Grondona F. Trattato di William Bowman sulla struttura e funzione del rene in Bollettino dell'Istituto Medico Chirurgico Giuseppe Ronzoni. 1965.