

A Brief Historical Survey of Nephrology

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Introduction

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 papyri, 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 2,000 years B.C.), as well as in the Indian medical treatises preserved with the names of Suçruta and Caraka (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.

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 at all about it.

However they surely knew that urine reached the kidney together with blood, was somehow 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 bladder and the urethra. This opinion lasted at least until the 16th 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 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 through the ureters.

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

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 16th century.

That the human kidney is multilobate, most probably because he observed either foetal or bovine kidneys and referred their external shape 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.

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 18th 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.). He deals with the kidneys in chapter 1, 5-10 of the 4th book of his De medicina. The brief chapter reads as follows: “The kidneys are opposed to each other, adhere to the loins above the hips; their side facing the backbone is concave whilst their opposite side is convex; branches of veins run through their substance; in their internal cavity there are ventricles and their external surface is covered with a tunic...a whitish duct start from each kidney and reaches the urinary bladder. The Greeks call them “ureters” because they maintain that urine flows down from these ducts to the urinary bladder”.

However 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 that they didn't study and describe also the anatomical structure of the kidneys; second: as they gave a “mechanical” interpretation of uropoiesis, their opinion could surely be only founded on as careful as skilful autopsies. Although unfortunately none of their works was 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) in the natural faculties (I, 15, K., II, 57 ff.).

Celsus did surely derive 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 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 authors the kidneys were an absolutely useless part because urine transuded directly from the intestines and gathered into the bladder to be discharged through the urethra. As Celsus says "the Greeks believe", the legitimate suspicion arises that he is arguing just with both Asclepiades, who was not a Greek, but was born in Bithynia, on the southern coast of the Black Sea, and Themison, who was born in Laodicea, in the Middle East.

Galen engaged in controversy not only against Asclepiades and Themison (whom he literally ridiculed as absolutely ignorant both of anatomy and physiology of the kidneys) 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 (i.e., 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 the 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. The fact being so, the kidneys were not at all simple "filtering" and passive organs to him and uropoiesis wasn't at all a mechanical operation: it was the final result of the cooperation of the "attractive virtue" (the kidneys attracted blood mixed with "superfluities"), the "retentive virtue" (the kidneys restrained the "watery humour"), the "transforming virtue" (the kidneys transformed the mass of "superfluities" into urine) and the "expelling virtue" (the kidneys expelled urine with the aid of the "attractive virtue" of the ureters). Galen's theory triumphed, together with "Galenism" in general, till the 17th century, that's to say till the "Galilean scientific revolution". Notwithstanding 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 figures and the pertinent captions (Figure 1).

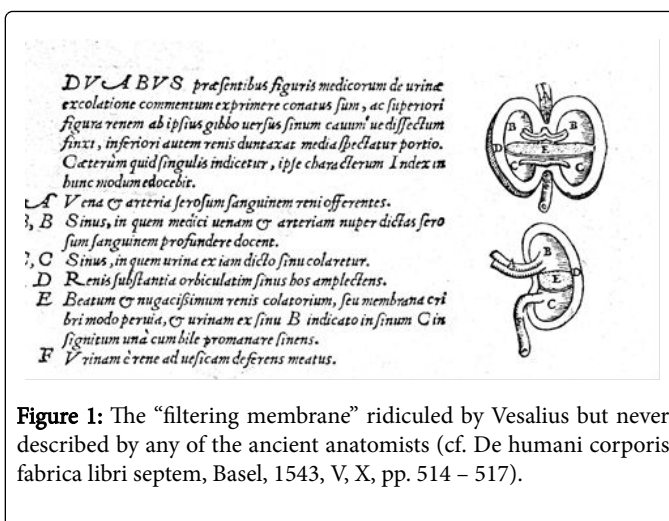


Figure 1: The "filtering membrane" ridiculed by Vesalius but never described by any of the ancient anatomists (cf. *De humani corporis fabrica libri septem*, Basel, 1543, V, X, pp. 514 – 517).

And this may easily be confirmed first of all by Galen himself, who maintained that a network of subtlest venous and arterial capillaries "perialéphetai" (= spreads) on the walls of the internal cavity of the kidney; then 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 and later misinterpreted and ridiculed by Vesalius "panniculus" just – and erroneously – 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. Nonetheless he confined himself to summarise what he found in Galen's great treatises, most probably only for practical use.

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 Coppho the Younger's (†1110) *Anatomia porci* and the anonymous *Demonstratio anatomica* (preserved in the code Q2 of the Maria Maddalena Library of Breslaw), whose author was surely a contemporary with Coppho, because he argues with him. Although both the works are based on autopsy of the kidneys of a pig (as usually was done during the middle ages), nonetheless nothing new can be found about the anatomo-physiology of the kidney, and only one particular is worth mentioning: the two authors describe correctly the pelvis, the calyces and the ureters; both the authors maintain that stones form into the calyces, but we must emphasize an exceptional particular: neither Coppho, nor his opponent allude to any "filtering membrane" dividing the pelvis into an upper and a lower cavity! Suffice it to read two brief passages, one from Coppho's *Anatomia porci*, the second from the anonymous *Demonstratio anatomica*. The first reads as follows: "At this point (i.e., after having observed the abdominal viscera) you must eliminate the whole mass of the bowels. This done, you will see a big artery (the aorta), which descends along the backbone and under which there is also a big vein (the vena cava). The big artery consists of the joining of all the arteries of the head, which form a unique big artery, which descends downward and branches at both the right and the left side. As for the big vein, it too consists of the series of veins starting from the head and reaches the kidneys. At this point it branches off and forms the so-called "vena chili" (the inferior vena cava), into which as subtle as hairs veins (venous capillaries) – which cannot be seen because of their exceptional thinness – insert. Urine mixed with the four humours

is brought to the kidneys just through them. Going on, you will find two vessels called “ureters”, through which urine flows into the urinary bladder”. As one can clearly realize Copho does not describe any “filtering membrane” dividing the pelvis into an upper and a lower cavity!

The passage from the anonymous *Demonstratio anatomica* reads as follows: “After having observed all the above mentioned parts (i.e., the bowels, the liver and all the adjacent viscera), you must extract all of them from the pig in order to observe better the other parts. This done, you will see the kidneys, which lay at the right and the left side of the backbone. They are fleshy and rounded; veins run through their substance and form heir-like corpuscles and their inner part is full of cavities (the calices), into which stones form. Two thin ducts start from them and run downward: the physicians call them “emunctories” (obviously the ureters), one of which inserts into one side, the other into the other side of the urinary bladder...The big artery that starts from the heart....proceeds close to the backbone; then it branches off into two ducts that reach the right and the left side of the urinary bladder”.

Neither in this passage of the anonymous author one can find even the faintest description of any “filtering membrane”, which divides the pelvis into a higher and a lower cavity!

The same description and the same statements may be found in the chapter entitled On the anatomy of the vena cava and the emulgent veins of the kidneys of Mondino de' Liuzzi's (1270 c. – 1326) famous *Anothomia* (sic!) (first edition printed in Padua in 1475) where the author does nothing else than repeat the “galenic” anatomo-physiology on the basis of very few autopsies of human corpses (perhaps only two female corpses in 1315). As regards the kidneys, he too doesn't mention any “filtering membrane”, but confines himself to describe erroneously the galenic “panniculus” as a closest network of arterial and venous capillaries that covers the internal cavity of the kidney and through which the urine drops “downwards” – as he writes – into the pelvis, i.e., from upward to downward, to reach the bladder through the ureters and be discharged through the urethra. His passage reads as follows: “After having cut the kidney from the convex part with a longitudinal incision reaching the cavity, you will observe immediately a “panniculus”, i.e., a thin cloth that consists of the emulgent vein rarefied to form a sort of filter, through whose pores urine but not blood may flow. This is why the urine drops downwards into the kidney towards the orifice of the so-called ureter, which descends into the urinary bladder”.

Although one could mistake the adverb “downwards” for an allusion to the lower cavity separated from the higher one by the “filtering membrane”, this would be a really anti-historical mistake. Indeed the “lowest” point with respect to all the points a circle, a sphere or any other circular or even oblong body, is its centre to all the ancient mathematicians, astronomers and anatomists!

Suffice it to remember that not only according to Ptolemy (2nd century A.D.) and all the subsequent astronomers till Copernicus (1473-1543) the Earth was lying in the lowest point of the spheres of the Universe, i.e., just in their centre, but – according to Holy Scriptures, the Fathers of the Church and even Dante Alighieri (1265-1321) – also the Devil, the most horrendous enemy of God, was thrown “downwards” from the Sky and is driven in the lowest point of the spherical Earth, i.e., just in centre of the centre of the Universe, that is to say in the farthest point from Him! This being the fact, when Mondino writes that urine flows “downwards”, he doesn't mean at all

that it drops from an upper to a lower cavity of the kidney, but just from its internal wall towards its centre, that is to say towards the unique cavity of the kidney!

But the clearest proof that no medieval author thought of a “filtering membrane” dividing the pelvis into two cavities can be found in Henri de Mondeville's (1260-1320) *Surgery* (cfr. 1st 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 difficulty 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.

Although Henri is partly deriving from Aristotle and partly from Celsus, nonetheless his description of the renal pelvis is, generally speaking, sufficiently correct and, most of all, there is no mention of any “filtering membrane”. By contrast, 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 anathomie corporis humani et singulorum membrorum illius* (Book on the anatomy of the human body and each part of it) (Venice, 1502) (cfr. p. 34rb ff.).

The first author who misunderstood both Galen and the following authors and supposed they were speaking about a “filtering 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) he clearly maintains that “as it 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 subsequent authors, Zerbi included, and supposed they were describing just the “transverse filtering membrane”, which he could not find in the pelvis and which none of the previous anatomists had ever found and described!

And this misunderstanding was inherited – as pointed out above – 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 referring erroneously its structure to the human kidney, moreover understanding nothing at all even of what he was observing!

Indeed in his relentless debate with Gabriele Falloppio (or Falloppia) (1523-1562) he clearly mistook the arcuate vessels he had observed in the monopapillary kidney of a dog for the calices renales described by Falloppio [2].

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 hot 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 hot 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 female nipples (Figure 2).



Figure 2: The dissected kidney of a pig illustrates Berengarius’ description of the “papillae”.

Moreover he correctly realized that the internal wall of the kidney is not at all a network of arteriovenous capillaries (as maintained by Galen and all the subsequent anatomists), but an enlargement of the ureter.

But it is worth reading the most important passage of his treatise (pages CLXXViv-CLXXXr). It reads as follows: “Then 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 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 of 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 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 and description – which were confirmed by Niccolò Massa (1499 – 1559) in his *Anatomiae liber introductorius* (Introductory book of anatomy) (Venice, 1536) – are really astonishing, most of all if one considers that he had not and could not have recourse to any magnifying instrument and made his observations with the naked eye! Suffice it to observe that he had already discovered and described what Lorenzo Bellini (1643-1703) will re-discover and re-describe more than two centuries later.

However both Berengarius and Massa and their fundamental discoveries and descriptions were strangely ignored not only by Andreas Vesalius, who ridiculed – as said above – in the text, in the figure and in their captions the idea of a “panniculus” spreading out at the middle of the pelvis like a filter, without taking pains to ascertain whether Ferrari’s statement about the former anatomists was correct, but also by Lorenzo Bellini.

Moreover Vesalius made Three Great Mistakes

He still maintained (like Aristotle and Galen and all the subsequent authors) that the right kidney was higher than the left (Figure 3).



Figure 3: The 22th figure of the 5th book of Vesalius’ *De humani corporis fabrica*: the right kidney is clearly and erroneously 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.

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 the unique "papilla"!

Moreover he conferred the resulting structure to the human kidney, although Berengarius had already described it as "pluripapillary".

He carried on a controversy against Gabriele Falloppio (1523 – 1562) that was absolutely groundless owing to his misunderstanding of Fallopio's description of the calyces. Indeed he made the great mistake of taking the arcuate vessels he had observed in the unipapillary kidney of a dog (Figures 4 and 5) for the calyces perfectly observed and described by Falloppio in the human kidney.

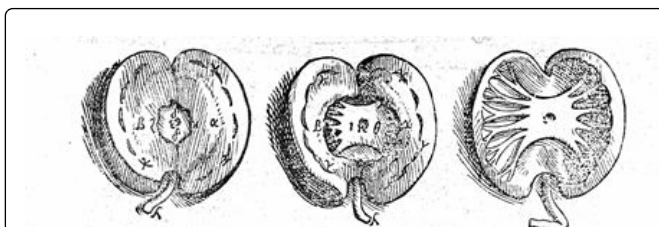


Figure 4: Vesalius' illustration of the dissected monopapillary kidney of a dog. The 3rd figure proves Vesalius' mistake.



Figure 5: The monopapillary kidney of a kid we have dissected and abraded as Vesalius did of the monopapillary kidney of a dog. His great mistake is clear mainly in the 3rd particular.

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 and absolutely more correct than Vesalius' ones.

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