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LABORATORY PROCEDURE
ΕΡΓΑΣΤΗΡΙΑΚΗ ΜΕΘΟΔΟΣ

Urine specific gravity according to ancient and medieval Greek sources

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ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2020, 37(Συμπλ 2):97–103

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Το ειδικό βάρος των ούρων σύμφωνα με αρχαίες και μεσαιωνικές ελληνικές πηγές

Περίληψη στο τέλος του άρθρου

The original relevant works by Hippocrates, Galen, Anonymi Medici Minores, Stephanus, Theophilus, Aetius, Joannes Zacharias Actuarius and Avicenna's Canon were read in order to find out if they contained any reference to urine specific gravity (s.g.) and its correlation with the natural history of renal diseases. The term "specific gravity" was of course never mentioned by ancient and medieval writers. Indirectly, they referred to it by discussing the different location of a semisolid formation in the matula (urine examination vial). If it lay on the bottom, it was cold "hypostasis" (sediment), if suspended in the middle "enaeorema" (suspension) and if floating on the top "nephelion" (nebulum). All above medical authors agreed that sediment usually testifies a healthy condition and a floating formation a very severe disease. The suspension could either be a sign of recovery if it followed a nebulum and was thus descending or of deterioration if it followed a sediment and was thus assenting. As its location depended on the difference in weight between the semisolid formation and the liquid part of the urine, in a sense, it measured its specific gravity. Very recently, urine specific gravity gained ground as an accurate renal function marker, equal to creatinine clearance.

Key words

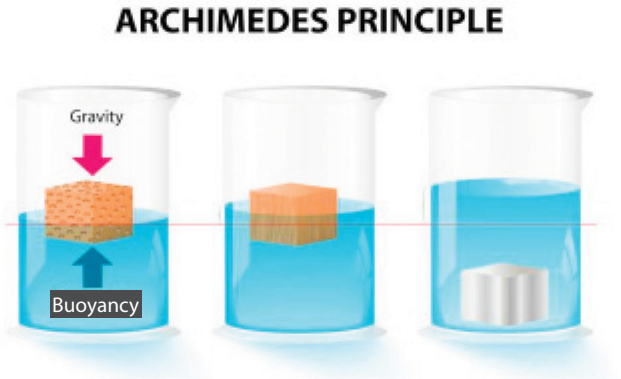
Byzantine medical authors
Classical medical authors
Proteinouria
Specific gravity
Urinometer

1. AIM

The aim of this paper was to try to find out if there was any reference to urine specific gravity in Ancient and Medieval Greek literature and its correlation with the natural history of renal diseases.

2. INTRODUCTION

Any discussion on specific gravity should start with Archimedes' fundamental principle, as presented in his treatise on Floating Bodies: *Any object, totally or partially immersed in a fluid or liquid, is buoyed up by a force equal to the weight of the fluid displaced by the object*[1] (fig. 1). The principle found a practical application as early as in Pliny's times. It was subsequently used for verifying the purity of precious stones and metals as described in the *Carmen de ponderibus et mensuris*, an anonymous Latin poem, dated between the late 4th and the early 6th cent. AD, and dedicated to a Symmachus, perhaps the father-in-law of Boethius; it is a skilfully formed and clearly structured didactic poem in 208 hexameters, concerning weights and measures.[2] It describes the function of a hydrometer in an embryonic form. An early description of this instrument appears in the 5th century AD fifteenth letter from Synesius of Cyrene to the Greek scholar Hypatia of Alexandria.[3] It has a glass shaft with numerical markings and a bulb ending, filled with ball bearings. When immersed in a fluid, it measures its specific gravity. The lower the density of the fluid, the deeper a hydrometer of a given weight sinks; and



The physical law of buoyancy stating that any body completely or partially submerged in a fluid (gas or liquid) at rest is acted upon by an upward, or buoyant, force the magnitude of which is equal to the weight of the fluid displaced by the body. **In an embryonic form it describes the use of a hydrometer and a urinometer.**

Figure 1.

conversely, the higher the density of the fluid, the higher the hydrometer floats. A urinometer is a medical hydrometer designed for urinalysis. As urine specific gravity is dictated by its ratio of solutes (wastes) to the loose portion of the urines, a urinometer allows a quick assessment of a patient's overall hydration level and or the amount of the solutes excreted in the urine and the kidneys' ability to respond appropriately, in order to dilute or concentrate urine over that of plasma. This instrument, in the simple form of a thermometer-shaped mercury-based floating urinometer, was introduced in 1849 by the Viennese scientist Johann Florian Heller (1813–1871).[4] As Ancient and Medieval medical writers lacked the knowledge of the urinometer or of the practical application of the specific gravity principle to body fluids, they never mentioned it in connection to urine examinations.

3. MATERIALS

We read the original relevant works by Hippocrates, Galen, Anonymi Medici Minores, and Stephanus, Theophilus, Aetius, Joannes Zacharias Actuarius and correlated them with Avicenna's Canon. Before proceeding to the presentation of particular authors' writings on the subject, it would be useful to define some of the terms they used (a) and their proposed equivalent in current medical knowledge (b).

3.1. Glossary

3.1.1. Digestion. In a broad sense, it denotes the metabolism. It was based on the theory of the Four Humors and was generally subdivided into three stages. (a) *The First Digestion happens in the gastrointestinal tract (GI) where food is bound with the pneuma and produces chyle; its waste product is the faeces.* (b) Digestion in the intestine requires oxygen. If the blood flow is compromised, the intestine opens more capillaries.[5] *The Second Digestion takes part in the liver where the chyle, or digested food, is brought from the GI and is worked up into an impure blood, imbued with the first form of pneuma innate to all things, the natural spirits. There, the Innate Heat is converted into the Metabolic Heat, or Ignis* (whence etymologically the word ignition as e.g. in cars). *Together with the Natural Force, the Metabolic Heat generates the Four Humors and cooks or concocts the humors in a process of pepsis* (whence etymologically the word Pepsi cola). (b) The hepatic circulation perfuses one of the largest organs and maintains the organic composition of the blood [...] It consists by 80% of venous blood from the GI and the rest from the hepatic artery. For this double perfusion, the liver requires the largest oxygen consumption.[6] (a) *The concocted humors enter the veins where the Third Digestion takes place. The waste products are eliminated via the bile, the urine and sweat. Any imperfect digestion there causes abnormal urine. From the veins, the blood returns to the heart whence it captures peuma from the lungs and little by little reaches all tissues where the Fourth Digestion occurs.* (b) The blood from the liver, full of processed nutrients, enters the heart via the hepatic vein where it is reoxygenated and returns to the general circulation.[7]

3.1.2. Pneuma. We propose that this corresponds to oxygen. This is backed by the fact that the ancients described as pneuma the content of the arteries, not meaning air but aerated blood; hence the arteries were naturally, but in fact wrongly, described by later commentators as empty.

3.1.3. Concoction. (a) Breaking down via metabolism the various nutrients and /or renal handling of the useless residue resulting in transparent urine. This idea was proposed in a rudimentary form by Aristotle.[8] (b) The kidneys are essential for homeostasis (maintaining a constant internal environment) of the body's extracellular fluids. Their basic functions include, between others, the filtration of a variety of water-soluble waste products and environmental toxins into the urine for excretion.

3.1.4. Hypostasis (sediment). This is the matter containing the insoluble components of urine, separated or aggregated with protein or mucus, and laying at the bottom of the uroscopy vial (matula/amis in Greek).

3.1.5. Enaeorema (suspension). This is the same matter, suspended somewhere in the middle of the matula.

3.1.6. Nepheloma (cloud). The same matter floating on the urine surface.

Although the presented comparison between the ancient and modern ideas of the body functions is exciting if just only based on extrapolation, the use of current medical knowledge, as well as logic and philosophy, to interpret ancient bio-medical texts makes them relevant to modern readers.[9]

4. METHOD

We put forward the hypothesis that the location of insoluble urine components depends on the weight difference between these components and the loose part of urine. As the urine examination is "the window to the kidney" any correlation between their location and the underlying renal pathology depends on the "eye of the beholder". Hence, we present some ancient Greek and Byzantine statements on the issue.

5. RESULTS

Hippocrates was the earlier writer correlating the location of the non-soluble particles of the urine with the course of a disease: *"The sediment or cloud is more favourable when it occupies the bottom, than when it floats towards the surface of the fluid".*[10]

"The bowels, in all diseases, were disordered, and in a bad state, but worst of all in these. The urine, in most of them, was either thin and crude, yellow, and after a time with slight symptoms of concoction in a critical form, or having the proper thickness, but muddy, and neither settling nor subsiding; or having small and bad, and crude sediments; these being the worst of all".[11] *"And one should consider respecting the kinds of urine, which have clouds, whether they tend upwards or downwards, and the colours which they have and such as fall downwards, with the colours as described, are to be reckoned good and commended; but such as are carried upwards, with the colours as described, are to be held as bad, and are to be distrusted".*[12] The 10th aphorism reports that when the ripeness is complete, sediments settle at the bottom of vessel, and when it is intermediate, these [the sediments] are suspended, and when it is at the beginning, these float. The 11th aphorism clarifies that bright white sediments are the best indicators of complete cooking: The bright white sediment is praiseworthy and indicative of complete ripeness because cooking power is complete.[13,14]

Because as the urine is coming from the blood and filtered through the kidneys and ends at the bladder, anything abnormal appearing in it originates from the circulation or from these two organs, […] thus the thin ones indicate a disease of the veins; While the no thin (thick) the bladder,[15] referred by Deros.[16]

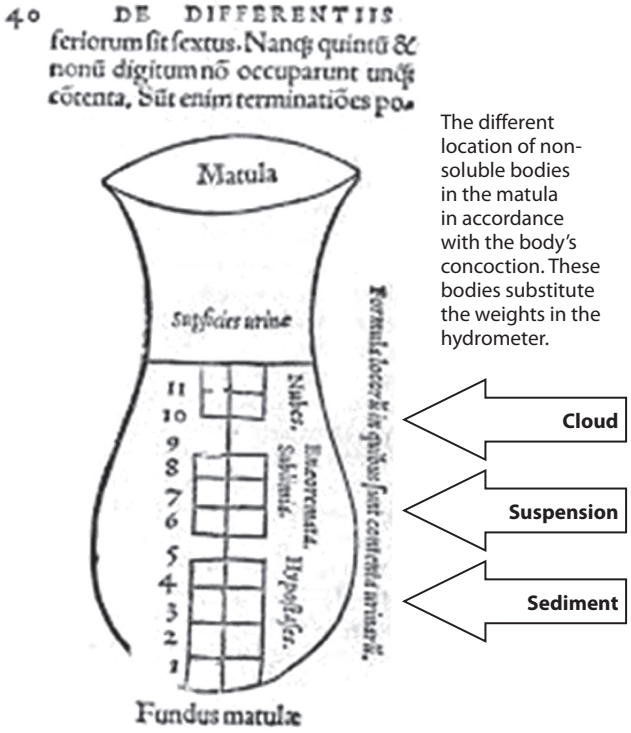
Another interesting reference is that of Stephanus of Athens (7th cent A.D.) in "De urinis". He wrote about bubbles in urine during the course of fever: *"...if bubbles show on the upper surface of urine, just like when a crystal is in fire, this means that urine consist of thick substance; if thick urine are observed during fever and after this they become thin and excess in volume, this means that the fever will subside...".*[17] Here, he probably talks about albuminous urine, as it is known today that during fever there is excess excretion of albumin in urine. *"Again, there is another complexity, having the sediment white colour but its location is in the middle and it is then called suspension […] because … the excess of a spread out wind made it lighter has lifted it in the middle. In addition, if in many cases the spread out wind is in abundance and pushes the sediment it lifts it from the middle in the surface and then it is called cloud.*[18]

The idea of this spread out wind, *pneuma* in the original language, requires a more detailed discussion. According to Ancient Greek writers, there are two kinds of pneuma; respiratory and digestive.[19] The second promotes digestion. Later, a third one was added, the *psychic*, involved in all neurological functions.[20]

When concoction is completed the pneuma is consumed; hence, no wind is left in the urines to push the sediment, which then floats to the bottom. The less the digestion is completed, the more pneuma is left and the higher the location of the particles in urine. Other medical writers of the era followed the same model of thought. Aetius Amidenus (6th cent) detailed the underlying cause of the upwards movement of urine sediment to enaeorema and then nepheloma, calling the "spread out wind" an "invisible force" pushing the formed particles from the bottom upwards.[22] Theophilus Protospatharious (7th cent?) explained the location of the nepheloma and enaeorema in a similar manner.[23] The close similarity between Aetius', Stephanus', Theophilus' Magnus Emesius' (an obscure author of contested date who is believed to be the proposer of the tripartite location of urine cellular components) treatises on uroscopy and their hypothesised connection with Pseudo-Galen's *De urinis Compendium* make it very difficult to be certain about the authentic authorship of any such document. The matter is complicated by the existence of manuscripts haphazardly put together. But generally, they all adhere to the described model.[24] Before proceeding to a medical writer of Late Byzantium, an overview is necessary for comparison of the Islamic views on the subject, mainly of its more prominent author, Avicenna (10th/11th cent). He defined "sediment" with foresight as regards its relation to specific gravity. "In the first place one must specify the meaning of the term "sediment". It is not "that which sinks to the bottom of the vessel". It is "that whole substance is denser in essence than wateriness, which separates out from the wateriness - regardless of whether it settles down. or not, floats or not".[25] Ten verses later, he continues in line with Greek writers: *"If a cloud appears floating in the upper portion of the vial, it indicates crudeness of the illness. If a certain maturity exists in the urine, wind is causing the sediment to renascent to the surface. If the sediment is half way up, be aware that the wind is in a small quantity […] The sediment remains suspended when air is captured in the organic matter, which nature doesn't ripen and digest".*[25]

Joannes Zacharias Actuarius (13th/14th cent) adhered to the tripartite location of urine cellular components. He correctly noted that the more severe the disease or the fever (causing presumably heavier proteinuria and a higher specific gravity), the higher these formed elements stand

in the amis (the examining bottle, which he was the first to insist that it should be made from an excellent quality of glass). When the disease subsides (and hence, proteinuria decreases) the sediment precipitates. However, Joannes goes a step further. He introduced a uroscopy vial with eleven horizontal lines numbered from the bottom upwards. When the cellular components occupy the second to fourth line, they are called Hypostasis, when the sixth to the eighth enaeorema, while the nepheloma lays in the 10th to 11th line. Using this vial, a more accurate description of the cells' location was possible. There are also intermittent zones (figures 2, 3). In his treatise on urines, he also expressed the overall parallelism in Byzantine thinking between the microcosm and macrocosm. Acturius e.g. writes: *"Because it has also been said that during obstructions the excreted urines may appear to be thin, it is worth mentioning the presumed causes. [...] Because whenever some people had a muddy and thick wine, they had passed it repeatedly through a straining cloth, and satisfactorily thinned it, having taken away the thickness through the passage, [...] similarly, it must be considered that the same may happen if during obstructions in any quarter the urine is seen thin, [hence] someone would rather blame the material obstructing the passages than a metabolic disorder".*[26] The notion that a renal obstruction may cause thinner urine has been recently verified when it was stated that the most sensitive test that obstruction and renal limitation is occurring is the urine's concentrated specific gravity.[27,28]



The different location of non-soluble bodies in the matula in accordance with the body's concoction. These bodies substitute the weights in the hydrometer.

Figure 2. Woodcut De Urinis by Joannes Actuarius, translated by Leo of Nola, published: 1529. Wellcome L0012935.

Figure 3. MS copy of Ioannes Actuarius' De Urinis. On the right hand margin a drawing of his vial with the various zones of the non-soluble mater (scribal addition?) MS.MSL.52 (f. 54r). Welcome Library), London.

6. DISCUSSION

With Zacharias, Byzantine uroscopy came to an end and about a century later so did the Byzantine Empire itself. Nevertheless, in its last days, a didactic poem, *"On urines",* was written by Nicephorus Vlemmydes (13th cent) about the same time with Zacharias' works. Both were cultural products of the Imperial Court in Nicea and later in Constantinople. The manuscript has been edited and revived in music by the author of this article in a small volume also containing a similar medical poem by Michael Psellus (11th cent).[29] In the same volume, the author discussed the importance of medical didactic poems in Antiquity and

the Middle Ages and beyond. There follow only few lines implying urine specific gravity.

Psellus verses 510–525:

"[the sediment's] is again triple and depends on its location and site.
[…] Well, since the urines' nature is three fold
All elements cannot be mixed at random.
Because the thin, white and undigested urine
Obviously cannot be mixed with the cloudy material body.
Because how could ever be possible to fuse digestion with indigestion"

Vlemymydes' Ode I:

"The milky urine when it is completely coagulated
Be aware that in all cases this implies imminent death for the patient"

With the presented extracts from Ancient and Byzantine medical texts, we reached the twilight of indirect references to urine specific gravity. A new dawn started in the West with a trend for a more scientific approach. Its prophet can be considered the renowned 15th century theologian and scientist Nicholas of Cusa who in *The Layman: Experiments with Weights* writes that, in creation, God ordered "all things in measure, number and weight."

In the background stands the saying from the *Book of Wisdom:* 11.21. This way number and mathematical ideas take on more than their usual employment for human ends and become a way to the Creator always present in human thought.[29] *"Orator: Do you think that in all cases the situation is as you indicated it to be in the case of water? Layman: Yes, I do. For identical sizes, of whatsoever different things, are not at all of the same weight. Accordingly, since the weight of blood or the weight of urine is different for a healthy man and for a sick man or for a youthful man and an elderly man or for a German and an African, wouldn't it be especially useful to a physician to have all these differences recorded? Orator: Most certainly. Indeed, through the recorded weights, the physician could render himself admirable. Layman: I think that a physician can make a truer judgment from the weight of urine together with its colour than from just its colour, which is misleading.*[30] Two centuries later this became a dictum: *"Neither the naked hand nor the understanding left to itself can effect much. It is by instruments and helps that the work is done"* – Francis Bacon, Novurn Organum (1620).[31] The path to a more scientific evaluation of specific gravity was thus opened.

7. CONCLUSIONS

7.1. General

Several ancient and medieval medical writers had suspected that the floating of the urine's non-soluble materials correlates with the course of a renal disease. As the positioning of these materials depends on the difference between their weight and that of the soluble material, we propose that, in essence, these writers measured urine specific gravity (although they ignored the term) and hence disease severity. They hypothesised that an invisible force was responsible for the upwards movement of non-soluble materials. We now know that such an invisible force exists; it is called buoyancy and its strength depends on the difference of the liquid and solid parts of urine, which in turns depends on proper kidney function and the kind of circulating blood in them. We could not trace any similar hypothesis in the current literature. This was our final remark when presenting this paper at the Larissa XIth IAHN Congress on 13 September 2019 and this was also published as the colophon of the corresponding abstract.[32]

7.2. A belated moral lesson

Surprisingly, while searching the literature for writing the full paper, a 200-year-old book was found, stating the same similarity! *"When a mucous cloud is present [in the urine] it ascends and descends in the fluid according to specific gravity, thus serving the purpose of a hydrometer".*[33] However, as a consolation, Osborne concludes the preface of his book by declaring "*Thus the following treatise may be regarded as an index of what has been hitherto discovered concerning the urinary secretion, and is an attempt to frame for any person interested in the subject, such a sketch as I should have been desirous to possess, when I commenced my inquiries".*[34]

Poetry may better, although crudely, highlight the different changes that the description of urine specific gravity underwent through the centuries:

[…] Later will our enemies the new sophists come
When we in our old age will lie wretchedly.
And some of us will have gone to Hades.
Our present words and works will appear strange
(and ridiculous perhaps) since the enemies will change sophistics' style and tendencies. Like me and them who some much transformed the past things.
What we portrayed as beautiful and proper The enemies will reveal to be foolish and useless, repeating the same things differently (without much effort).
Just as we spoke the old words in another manner.[35]

ΠΕΡΙΛΗΨΗ

Το ειδικό βάρος των ούρων σύμφωνα με αρχαίες και μεσαιωνικές ελληνικές πηγές

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Τα σχετικά πρωτότυπα κείμενα του Ιπποκράτους, Γαληνού, Ανωνύμων Ελασσόνων Ιατρών, του Στέφανου, Θεόφιλου, Αέτιου, Ιωάννη Ακτουάριου και Αβικένα μελετήθηκαν με σκοπό να εντοπισθούν αναφορές τους στο ειδικό βάρος των ούρων. Αν και ο όρος δεν χρησιμοποιήθηκε ποτέ, εν τούτοις ο σχολιασμός τους για τη θέση των αδιάλυτων συστατικών των ούρων μέσα στην ουροσκοπική φιάλη είναι απόλυτα ενδεικτικός της υποψίας που είχαν για το θέμα. Η χαμηλή θέση τους (υπόσταση), η μεσαία (εναιώρημα) και η ανωτέρα (νεφέλη) συσχετίζονταν με την ποιότητα του προσαγομένου στους νεφρούς αίματος και με τη λειτουργία των ιδίων των νεφρών. Επειδή η θέση τους εξηρτάτο από τη διαφορά βάρους του υδαρούς και του εμμόρφου στοιχείου των ούρων, έμμεσα δήλωνε το ειδικό βάρος τους.

Λέξεις ευρετηρίου: Βυζαντινοί ιατρικοί συγγραφείς, Ειδική βαρύτητα, Κλασικοί ιατρικοί συγγραφείς, Ουρινόμετρο, Πρωτεϊνουρία

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