Plenary Lecture

Twelve centuries of nephrological writings in the Graeco-Roman world of the Eastern Mediterranean (from Hippocrates to Aetius Amidanus)

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Introduction

The island of Crete is at the centre of the Eastern Mediterranean basin, the birthplace of medical science. The year 450 BC marks the emergence of 'scientific medicine', while 650 AD marks the emergence of 'Islamic medicine', which continued to influence medical practice until modern times. This article reviews 12 centuries of nephrological writings in the Graeco-Roman world of the Eastern Mediterranean, from 450 BC to 650 AD.

Scientific thinking and medicine in ancient Greece

In the Bronze Age, Mesopotamian, Egyptian and Minoan medicine was based on experience, a practice that was fundamentally changed by the Greeks [1]. The Greeks adopted a method used in the Near East—they performed an examination and subsequently made a diagnosis. However, the Greeks also searched for a logical explanation by asking questions and supplying answers. Their fundamental question was: Is Medicine an Art or a Science? [2].

Greek philosophers were divided on this matter. In the 2nd century AD, Galen thought that medicine was mainly an art, the aim of which was to heal and not to theorize. Later, the Arab, Avicenna, was of the same opinion. Aristotle suggested that medicine is a pure science, and in this opinion was followed in the Middle Ages by the Arab, Averroës. Hippocrates forced a compromise between the two ideas on the role of medicine, suggesting that it was pure science, like mathematics and the natural sciences, but that its manifestations differed according to the particular conditions of the patient and the environment. Hence, medicine was more accurately thought of as a Scientific Art [3]. This represented enormous progress from previous Eastern practices. Plato promoted an enduring tradition. For him, medicine was 'one of those arts that lend their aid to nature, ...(in it) judgement and foresight, wisdom, art and law must be prior to hard and soft, heavy and light...For art takes over the primary works from the hands of nature, already formed and then models and fashions the artificial' [4]. Could a more apt description of the idea behind the creation of the artificial kidney ever be made?

Thus, the basic contribution of the Hippocratic era to nephrology was a change in the general way of scientific thinking, which eventually led to the establishment of the precise biomedical model of modern nephrology. However, Greek philosophers had two disadvantages. The first was that the natural theories of Greek Medicine were the cause, among many correct theses, of some naive hypotheses. A well-known example was the theory of the Four Humours [3], which proposed that all diseases resulted from an imbalance of the four humours of the body, i.e. the phlegm, the bile, the blood and the pneumonia. Although this theory was inaccurate in many aspects, it was crucial in establishing the doctrine that metabolic and idiosyncratic abnormalities are the basis of many diseases. Secondly, the lack of established institutions, such as universities, to promote research and to safeguard the rights of scientists later proved to be disadvantageous to Greek medicine, and science as a whole.

Classical writers on renal diseases

Hippocrates (Figure 1) [5] wrote extensively on renal diseases, and hence is justifiably called the 'Father of Clinical Nephrology' [6]. Most of his writings have withstood the passage of time. However, Hippocrates wrote in an era when little was known about the anatomy and physiology of the kidneys, and he therefore did not understand their exact role, believing that urine was formed in the bladder. His main nephrological contributions can be divided into four categories.

(i) Description of four Renal Ailments. Several authors assign to Hippocrates the diatribe About Inner Sufferings, while others consider it to be a work from the neighbouring School of Cnidus. In this work, there are very good descriptions of nephrolithiasis with colic, renal tuberculosis, a syndrome compatible with renal
vein thrombosis or papillary necrosis, and a suppura-
tive chronic renal infection. In the same work, there is
a passage on renal damage due to crush syndrome
[7–9].
(ii) Thirty seven out of 423 of Hippocrates’
Aphorisms (4: 69–72; 5: 74–83; 6: 6, 11, 14, 21, 27,
with renal problems. These included references to gout,
changes in micturition and prognosis in elderly patients
with renal ailments.
(iii) Hippocrates advocated the use of uroscopy in
diagnosis but was not an enthusiastic supporter of the
method. His observation that ‘Bubbles appearing on
the surface of the urine indicate renal disease with a
prolonged course’ [10] is a classic one, and probably
refers to albuminuria due to chronic glomerulo-
nephritis.
(iv) On Lithiasis. Hippocrates wrote about renal
stones, which he linked to the use of drinking
water rich in minerals [11]. He also differentiated
between lithiasis of the kidneys and of the bladder
[12].
A dubious passage in the Oath prohibits medical
doctors from performing lithotomy. Many explana-
tions are given, including the idea that Hippocrates
wanted to protect doctors from being accused of
malpractice (lithotomy was performed mainly by
paramedics at that time). With Hippocrates, as with
many ancient writers, it is sometimes difficult to
understand precisely what is meant by the terms
employed. For example, Hippocrates used the word
‘ureter’ indiscriminately to denote the ureter and the
urethra [13]. Another difficulty is the widespread
plagiarism that occurred during the Middle Ages,
when many copyists were themselves labelled as the
original writers. For example, in the 11th century,
Constantinus Africanus in the Montecassino trans-
lated into Latin Isaac Judeus’ book On Urines, which
was written in the 9th century. The translation subsequently appeared as an original work composed by Africanus himself [14].

Later, Aristotle, in his work *Historia Animalium*, describes his idea about the kidneys [15]. He too failed to realize their purpose, assigning to them a genetic and decorative role. Aristotle also theorized about the diuretic properties of several plants, in a typical archaic way of thinking [16].

**Hellenistic contributions to nephrology (4th–1st century BC)**

In the following discussions about the nephrological writings of the Hellenistic and Roman eras, it should be noted that these two terms are used conventionally to refer to a historical period, and not as an indication of the nationality of the authors. For example, the majority of medical writers from Roman times were of Greek extraction but they are discussed in the section on Roman contributions to nephrology.

Erasistratus, who lived during the 3rd century BC, was the first to declare that urine is formed in the kidneys. However, his idea was challenged by Galen and by later authors, who attributed the discovery to other writers. Ammonius, renowned for his technique for performing a lithotomy, lived during the same period. The Alexandrian doctor Herophilus described the prostate gland, while Lycus was the first to describe the filtration of urine.

Chrysippus, Praxagoras, Euryodes, Kleophantos and Philomelos, all minor medical writers of the Hellenistic period, are referred to by Rufus of Ephesus, the excellent writer of the 2nd century AD [17]. Chrysippus is better remembered for his poultice with soothing and diuretic properties, which he applied over the kidneys. Praxagoras elegantly described a patient with a recto-cystic fissure, who was passing urine from his rectum, and who survived

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Fig. 2. *Asphodelus ramosus*. A wild bulbous plant, recommended by Dioscorides as a diuretic and spasmolytic drug. Codex Vindobonensis Med. Gr. 1, Nationalbibliothek, Wien, fol. 26r. (Reproduced with permission from [23]).
with this condition for at least 12 years. Euryodes reputedly operated on patients with renal problems, following the tradition of Hippocrates. Kleophaunts likened the crust that stands on the surface of thick urine with a medusa, while Philomelos suggested the application of pressure over the lower abdomen in order to facilitate the passage of urine in patients with urine retention.

Roman contributions to nephrology (1st century BC to 4th century AD)

Celsus was a prolific medical writer, although he was not a doctor. The subjects of his many writings included lithotomy, purification from renal diseases, and a bronze urethral catheter, to be used mainly in males but also in females [18]. Pliny the Elder wrote about many subjects of nephrological interest, and insisted on the ritual significance of urine [19].

Aretaeus Cappadoces lived during the same century as Celsus and Dioscorides, and is an excellent link between the better-known Hippocrates and Galen. His works were neglected around the 7th century AD and were rediscovered in the 16th century. He wrote about hydronephrosis from venereal diseases and nephritis, accurately describing the anaemic look of renal patients. His observations were written 18 centuries before the publications of Richard Bright of London, Robert Christison of Edinburgh and Pierre Rayer of Paris, who are conventionally acknowledged as the first to describe the characteristic. Aretaeus also recorded other symptoms of renal patients, such as unhealthy skin and a tendency towards oedema and/or vascular accidents [20]. He also described diabetic nephropathy, and he is popularly believed to have coined the word ‘diabetes’, although it is now known that the term was first proposed by Demetrius of Apameia, three centuries before Aretaeus’s birth [21].

Dioscorides lived during the 1st century AD. He was a Greek doctor from Asia Minor practising later in Rome, who may have been personal doctor to Emperor Nero. His outstanding contribution to medicine in general, and to nephrology in particular, was the extensive Materia Medica. In this publication he described, among other drugs, 300 substances of veget-
able, animal or mineral origin [22] (Figures 2 and 3 [23]) that had a nephrological effect. The work was monumental and, until the last century, served as the basis of all subsequent pharmacopoeias in Europe. Even today, several of the drugs recommended by Dioscorides are still used, or have been reintroduced for the treatment of renal diseases.

Galen was personal doctor to Emperor Marcus Aurelius, and the most prolific medical writer to date. It is said that the surviving volumes of his works alone are more extensive than the whole of Shakespeare’s writings. He successfully showed, by ligating animal ureters, that urine flows from the kidneys to the bladder. He also experimented further on the anatomy and physiology of the urinary tract. Hence, Eknoyan has rightly called him ‘The Father of Experimental Medicine’. Galen also elaborated on several acute and chronic renal ailments. He was a real scientist and was one of the last great medical writers of antiquity.

During the Middle Ages, religious faith favoured a bias towards humanistic values of medicine at the expense, in several cases, of scientific and experimental clarity. Galen, however, survived the change of intellectual climate because he, too, was a deeply religious person. He characterized the human body as ‘a sacred discourse that composed a true hymn to our Creator’ [24], thus later becoming a favourite of the Christian Church.

Cassiodorus, who wrote about renal problems, was favoured mainly in the Latin West. Rufus from Ephesus, according to Wellman, was ‘One of the few independent doctors of the post-classical era’. His treatise On the Diseases of the Kidneys and the Bladder, written around the end of the 1st century, is the only
ancient nephrological treatise that has survived intact. Rufus was not merely a compiler of texts. When he used other writers’ work, he methodically reported his sources. Rufus admired Hippocrates, and several of his passages on renal diseases are quoted verbatim in Rufus’s treatise [25]. In the treatise he correctly describes the signs and symptoms of many renal problems, such as chronic renal failure, abscesses of the kidneys and paresis of the bladder [26]. Rufus studied some specific diseases, such as tuberculosis of the urogenital tract, psoriasis of the bladder and the causes of renal calculi (including diet and quality of drinking water), and recommended flushing the kidneys with huge amounts of water [27, 28]. Among his treatments were many accepted plant and mineral substances but also some strange remedies. For example, a poultice of grilled cicadas as a diuretic, and advising the patient to urinate in a hot bath, measures which both increase the renal blood flow [29]. His description of the role of the healthy kidneys as ‘The filtration of clean urine without blood or thickness’ is a very early and elegant equivalent of the modern definition of a healthy urine sample without haematuria or proteinuria.

**Early Byzantine contributions to nephrology (4th–7th century AD)**

The Byzantine era began when Constantine the Great moved the capital of the Roman Empire from Rome to Constantinople, and ended with the conquest of Alexandria by the Arabs in 642 AD. During this period, the centre of medical knowledge was still Alexandria. For a short time after the Byzantine era,
Arab and Jewish medicine took the lead, but Constantinople was later established as a medical centre par excellence. In the period under discussion, Stephanus of Athens and Theophilus Protospatharius, leaders in the art of uroscopy, were the two most prominent writers who explored scientific diagnosis via a urine sample. Their work, which has been discussed previously [30] (Figure 4) [31], remained basically unchanged until the time of John Actuarius in the 13th–14th centuries. The bulk of their observations passed intact into medical manuscripts both in the East and the West. Oreibasius wrote extensively on renal diseases, and in particular on diabetic nephropathy and gout. Aetius Amidanus compiled a large treatise with many nephrological entries, based mainly on Galen, Hippocrates and Rufus. He was copied extensively by the eminent Arab doctors, Avicenna, Averroës and others. Generally, Byzantine doctors of the period studied acute and chronic renal failure, and in their treatises ‘vulgarized’ traditional Galenism, in order to be functional and homogenous [32].

**Jewish contributions to nephrology (4th–7th century AD)**

Although Jewish physicians contributed extensively to the understanding of renal diseases, their influence was not evident until a later stage. Asaph Judeus is thought to have lived during the 6th century, although this is disputed. He was heavily influenced by Dioscorides and Galen. His main contribution is the differential diagnosis between renal and intestinal diseases. He
also proposed an Oath similar to the Hippocratic Oath [14].

Conclusions

In conclusion, the main contribution of the ancient writers is not so much the many references to nephrology listed here but their philosophical thinking. For example, Plato, in his work Phædrus, cites the following dialogue: ‘If Hippocrates the Asclepiad is to be trusted one cannot know the nature of the body except by such a method.’ To which Socrates, the famous philosopher answered: ‘He is right, my friend; but we must not just rely on the authority of Hippocrates, but must see also if our reason agrees with him on examination...’ [33].

Figures 5 [5] and 6 [23] show ancient Greek medical thinking as being revered and, to some extent, almost static and sanctified. In real life, ancient medical thinking was vivid, challenging and inquiring. Those characteristics are evident in the juxtaposition of two theses by the most eminent ancient Greek writers. Hippocrates, in a famous axiom, rightly condemns the tendency of many doctors to pursue any novelty in order to impress and to commercialize their trade: ‘Not to look after patients with incurable diseases, as it is well known that Medicine isn’t empowered to treat everything’ [34]. His greatest admirer, Galen, did not hesitate to challenge him and to wonder: ‘Would it ever be possible to empty a human body from the corrupted blood and to re-infuse a pure one, hence to treat the most serious diseases?’ [35], a question to which modern haemodialysis gave an affirmative answer. Thus, the idea of blood purification and extra renal clearance was born by the inquiring spirit of our ancestors in the Eastern Mediterranean basin.

References

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