Review

Hippocrates of Kos, the Father of Clinical Medicine, and Asclepiades of Bithynia, the Father of Molecular Medicine*

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Abstract. Hippocrates of Kos (460-377 Before Common Era, BCE) is universally recognized as the father of modern medicine, which is based on observation of clinical signs and rational conclusions, and does not rely on religious or magical beliefs. Hippocratic medicine was influenced by the Pythagorean theory that Nature was made of four elements (water, earth, wind and fire), and therefore, in an analogous way, the body consisted of four fluids or 'humors' (black bile, vellow bile, phlegm and blood). The physician had to reinstate the healthy balance of these humors by facilitating the healing work of 'benevolent Nature'. The Hippocratic Oath contains the Pythagorean duties of justice, secrecy, respect for teachers and solidarity with peers. The clinical and ethical basics of medical practice as well as most clinical terms used even today have their origins in Hippocrates. His contribution in clinical medicine is immense. Asclepiades of Bithynia (124-40 BCE) was the first physician who established Greek medicine in Rome. Influenced by the Epicurean philosophy, he adhered to atomic theory, chance and evolution, and did not accept the theory of a 'benevolent Nature'. He suggested that the human body is composed of molecules and void spaces, and that diseases are caused by alteration of form or position of a patient's molecules. Asclepiades favored naturalistic

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therapeutic methods such as a healthy diet, massage and physical exercise. Above all, he introduced the friendly, sympathetic, pleasing and painless treatment of patients into medical practice, influenced by the teachings of Epicurus on pleasure and friendship. He was the first who made the highly important division of diseases into acute and chronic ones and to perform an elective non-emergency tracheotomy. As the founder of the Methodic School, Asclepiades was the first known physician who spoke about what is known today as molecular medicine.

It is widely accepted that medicine, like many other scientific endeavors, has its origin in Hellenic civilization (1-3). Religious and/or magical beliefs dominated the minds of humans for millennia, until, in the 6th century. Before Common Era (BCE), philosophy started to flourish in Greek cities of the Aegean islands and the nearby Ionian coast of Asia Minor (1). In a long tradition started by Thales of Miletus, philosophers ('wisdom lovers' in Greek) attempted to explain nature using their experience based on senses, as well as their imagination based on empirical analogies and rational assumptions (1).

It was precisely this environment of intellectual freedom that enabled scientific medicine to be born. Empirical knowledge from cooking and gymnastic accidents as well as philosophical ideas had all been suggested in antiquity as the grounds on which Greek medicine first stood (1, 2). This paper is dedicated to the pioneers who, more than two thousand years ago, introduced the basics of medical theory, practice and ethics that are still with us today: the legendary Hippocrates of Kos and the mysterious Asclepiades of Bithynia. Their life, medical philosophy, legacy and relevance to clinical and molecular aspects of modern medicine are discussed. The relatively unknown Asclepiades is presented in greater detail, since his pioneering contributions were understood only in recent decades with the advent of the molecular era of medicine (2-4).

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Hippocrates of Kos (460-377 BCE)

The Life and Medical Philosophy of Hippocrates

Hippocrates of Kos is universally recognized as the father of modern medicine, which is based on observation of clinical signs and rational conclusions (1, 2, 5, 6). Before him, therapeutic attempts were based on religious or magical beliefs and were commonly practiced by priests, spiritual healers and witch-doctors (1, 2).

Hippocrates was born in Kos, a Greek island of the southeastern Aegean (7, 8). He was the son of Heraklides and belonged to a family of physicians who claimed their ancestry from Asclepius, the god of medicine (7, 8). Hippocrates worked mainly in Kos and the nearby coast of Asia Minor (corresponding to present-day Turkey), but he also traveled extensively visiting other Greek regions including Athens, Thessaly and Thrace (5-8). His contribution to medical practice is characterized by ethical rules of conduct, close observation of clinical symptoms, an open mind for any ideas, and willingness to explain the cause of diseases.

Hippocrates based medicine on the philosophical idea that Nature was made of four elements, namely water, earth, wind and fire, according to the Pythagorean philosopher Empedocles (493-433 BCE) (1, 9-11). The Pythagoreans were an elite philosophical group who believed that benevolent Nature was divinely created by musically harmonious and numerically defined laws (1, 9, 10). They believed that through a series of reincarnations human souls were destined to be immortal ethereal stars (9, 10). The founder of this philosophical sect, the legendary Pythagoras, had claimed that he was able to remember his past lives (9, 10). Pythagoreans respected hierarchy and observed an oath of secrecy, since they believed that sacred knowledge was meant to be shared by the select few (9, 10). They believed that justice should be involved in all human relations, just like divine law governs all natural phenomena (9, 10).

In a way analogous to the concept of the four elements, Hippocrates believed that the body consisted of four fluids or 'humors' (black bile, yellow bile, phlegm and blood) and four elemental conditions (cold, hot, dry and moist) (1, 2, 5, 6, 11, 12). Therefore, the state of health existed when these humors and qualities were in balance (1, 2, 5, 6, 11, 12). In a case of disease, the physician had to disclose the imbalance of humors and facilitate the healing work of benevolent Nature by use of bleeding, emetics, purgatives, or even surgery (1, 2, 5, 6, 12).

According to Hippocrates, the physician had to examine a patient, observe symptoms carefully, make a diagnosis and then treat the patient (1, 2, 5, 6, 12). Therefore, Hippocrates established the basics of clinical medicine as it is practiced even today (1, 2, 5). He introduced numerous medical terms universally used by physicians, including *symptoma*,

diagnosis, therapy, trauma and sepsis (12). In addition, he described the presentation of a great number of diseases without superstition. Their names are still used in modern medicine including diabetes, gastritis, enteritis, arthritis, cancer, eclampsia, coma, paralysis, mania, panic, hysteria, epilepsia and many others (12). The latter disease was called 'divine' before Hippocrates, and a passage attributed to him underlines his rational way of thinking: "Epilepsy is not more divine a disease than any other disease. People call it divine because they do not understand it. But if we call divine all things we do not understand, then divine things will be endless" (1, 12).

Hippocrates lived in an era of great epidemics. There are several reports that he was invited by Persians and Illyrians to visit their countries and treat people with plague, but he declined the offers preferring to fight the epidemic in Thessaly (7, 8, 12). This was the same plague of 429-426 BCE that decimated about one fourth of the population of classical Athens, including its charismatic leader Pericles, and precipitated the decline of the Athenian empire, as the historian Thucydides vividly described (13). The epidemic was probably typhoid fever, as recent molecular evidence has indicated (14). Genomic sequences of the agent of typhoid fever Salmonella enterica Typhi were identified in skeletal remains of a mass burial pit found in the Kerameikos ancient cemetery of Athens and dated to the era of the plague (14). It has been proposed that the severity of the epidemic was possibly due to an ancient strain of high virulence based both on Thucydides' narration and on detected DNA variations of the ancient versus modern sequences of S. enterica Typhi (13-15). Interestingly, typhoid fever was well known to Hippocrates because he described the symptoms of that disease in great detail and named it 'typhos', possibly because of its typhoon-like impetuous character (12). There are even ancient reports that place Hippocrates in Athens during the period of the plague, allegedly trying to confine the epidemic by purification of the air with fires (2, 6, 12). Nevertheless, most modern scholars have dismissed this information as fictitious because the physician was rather young and unknown at that time, while the eyewitness Thucydides did not mention Hippocrates and reported that all attempts of physicians to cure the epidemic had failed (12, 13).

Hippocrates and his followers wrote many works, which are now included in the *Hippocratic Corpus*, a collection of texts regarding medical theory and practice (12). Some of them contain anachronistic language styles and dissident philosophical views, indicating that they were clearly composed several centuries after the father of clinical medicine (1, 12). The famous *Hippocratic Oath* was probably written down at least two centuries after Hippocrates, although he most certainly had established orally a sacred vow of similar ethical rules regarding proper

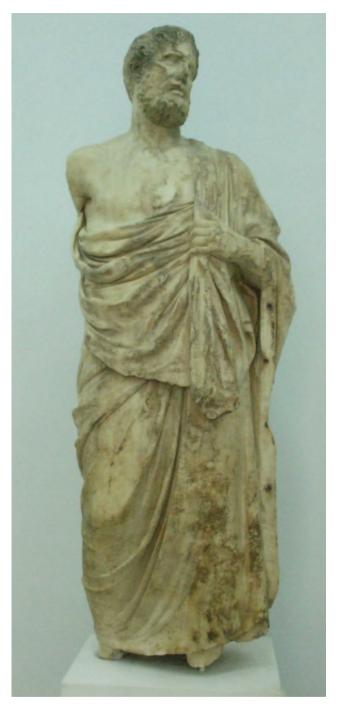


Figure 1. Hippocrates of Kos: It has been suggested that this statue represents the famous physician at a young age. It is housed at the Archeological Museum of Kos, Greece.

medical conduct (2, 12). This notion is supported by the fact that the Oath has clearly a Pythagorean influence (2, 12). The pledging physician promises wherever he goes to assist the sick, refrain from injustice and sexual mischief, and keep secrets. The Pythagorean duties of justice, respect for



Figure 2. Asclepiades of Bithynia: This is the only known bust of Asclepiades. It is located among other Epicureans in the Room of Philosophers at the Capitoline Museum in Rome, Italy.

teachers, solidarity with peers and secrecy are the most important requirements (2, 12). That the exclusive purpose of the physician should be to provide help to his patient is a command that seems obvious.

The Legacy of Hippocrates

Hippocrates died in old age and was buried by his physician sons near Larissa, Thessaly, according to Soranus of Ephesus (7, 8). His legacy remained for about two and a half millennia as the mainstream medical tradition (2, 3, 5, 6). The Hippocratic beliefs of a benevolent Nature formed by four elements were revived by the Neoplatonic physician Galen of Pergamon in the 2nd century of the Common Era (CE), and later were endorsed by the Neoplatonicallyinfluenced Christian and Muslim physicians of the Middle Ages (2, 3, 5, 6, 16). Some manuscripts of the Eastern Roman Empire illustrate this trend of endorsement. A 14thcentury manuscript portrays Hippocrates as a Christian saint, while in another one of the 12th century the Oath is inscribed in the sign of a cross substituting the gods Apollo, Asclepius and goddesses Hygeia and Panacea with the unique Judeo-Christian God (3).

Several sayings from Hippocratic works became for millennia the emblems of medical profession. For example, the famous mottos "Life is short but the art is long" (O $\mu \acute{e}\nu$ $\beta \acute{l}o \varsigma$ $\beta \varrho \alpha \chi \acute{v} \varsigma$ $\dot{\eta}$ $\delta \acute{e}$ $\tau \acute{e} \chi \nu \eta$ $\mu \alpha \varkappa \varrho \acute{a}$) and "Do good or at least do not harm" ($\Omega \varphi \epsilon \lambda \acute{e} \epsilon \iota \nu \eta$ $\beta \lambda \acute{a} \pi \tau \epsilon \iota \nu$) (12). The latter saying in De morbis popularibus 1.2 is followed by the text: "The art consists of three things: the disease, the patient, and the physician. The physician is the servant of the art, and the patient must combat the disease along with the physician". In his Commentary, Galen remarks that in some of the manuscripts instead of "art" he found "nature" in the last sentence. He states that either of the readings will agree very well with the meaning of the passage. Therefore, according to Galen "the physician is the servant of (benevolent) Nature" (12).

The Hippocratic Oath and mottos still inspire contemporary doctors of medicine, although no physician with scientific knowledge and self-respect believes in a benevolent Nature any more (3, 4, 16, 17). Despite some wrong assumptions, the contribution of Hippocrates to clinical medicine is nevertheless immense. The clinical and ethical basics of medical practice as well as most clinical terms used even today have their origins in the legendary physician from the island of Kos.

Asclepiades of Bithynia (124-40 BCE)

The Life and Medical Philosophy of Asclepiades

Asclepiades of Bithynia is recognized as the first physician who established Hellenic Medicine in Rome (2, 3). Nevertheless, he is surprisingly unknown given the important fact that he was the first physician who created a health and disease theory with apparent similarities to what is known today as molecular medicine.

Asclepiades was born in Prousias (also called Cius), a Greek seaside port in Bithynia, the northwest region of Asia Minor (18). His father Andreas was also a physician. There are reports that as a young practitioner Asclepiades visited Pergamon and Parium in Asia Minor (18). He was further educated in medicine at the famous Medical School of the Museum in Alexandria and in philosophy at the Epicurean School in Athens, called 'Keepos' ($K\hat{\eta}\pi o\zeta$ meaning garden). Asclepiades refused the enticing offer to serve as official physician of Mithridates Eupator, the king of Pontus who was interested in medicine and natural science in general (18). Instead, he moved to Rome at the age of around 30 years, where he first taught philosophy and later on practiced medicine (18). Asclepiades must have been proficient both in philosophy and in medicine as his contemporaries Antiochus of Ascalon and Cicero, a Greek Platonic philosopher and a Roman Stoic philosopher respectively, attest admirably (18).

The dual competence of Asclepiades has puzzled many modern scholars, but it is easily explained by the fact that he was influenced by the teachings of the Epicurean philosopher Zeno of Sidon (in present-day Lebanon), who was then the leader of the Athenian Keepos (19, 20). We know from surviving works of the Epicurean philosopher Philodemus of Gadara (in present-day Jordan or Syria), another disciple of Zeno's, that the Sidonian was teaching philosophy as medicine for the soul (20). In his lectures, he emphasized recognition of behavior signs and use of empirical records for the treatment of vices and passions of the Epicurean community members (20, 21). Zeno used a combination of friendly approach and frank criticism in a practical way, much like modern day behavior analysis and group psychology (20). Philodemus used the same approach in philosophical lessons he gave to outstanding Romans such as Lucretius, Horace and Virgil in Herculaneum, a town near Naples (20-22). Like Asclepiades, Philodemus was another Greek of the eastern Mediterranean who was educated both in Alexandria and Athens and then moved west to Italy to teach Epicurean philosophy (20, 22).

The founder of this philosophy was the Athenian Epicurus (341-270 BCE) who combined the atomic physics of Democritus and the naturalistic ethics of Aristotle in order to form a humanistic philosophy that spread in the Hellenistic and Roman worlds influencing many people (19, 22). Epicurus thought that eternal Nature consisted of atoms and void space, as well as that the sum of all matter was conserved, but atoms were perpetually used by necessity and chance in an endless process of construction and decay of material objects (22, 23). He considered the sun and stars as spheres of fire, the earth as a spherical planet, and suggested the existence of an infinite number of other planets like or unlike earth, with some of them supporting life (22, 23). As Lucretius attests, Epicurus spoke about evolution of living organisms based on survival of the fittest in a Darwinian manner (22-24). He maintained that the best way to understand nature was through our senses, since we developed them during evolution and we are adapted to live in this world (22,23). His contemporary Strato of Lampsacus, the third leader of Lyceum after Aristotle and Theophrastus, was the first man who conducted actual experiments in order to test Epicurus' ideas about atoms and void (1). As a result, Strato agreed with Epicurus renouncing Aristotle's teleological theories (1).

Epicurus observed that we are naturally inclined towards pleasure, which is measured by the absence of pain (22, 23). He defined happiness as a condition in which the body does not feel pain and the soul is not anxious (22, 23). Epicurus taught that the right philosophy, which is based on scientific knowledge, cures the anxieties of the soul in a similar manner that the right medicine cures the pains of the body (20, 22-24). He tried to free people from superstition and unsubstantiated fears of the unknown (20, 22-24). Death destroys our soul and senses; therefore we will never

experience it (23). There is no destiny, thus the existence of chance atomic movements permits free will in people (23). Gods do exist but they are not concerned with people or the celestial bodies, which is why the world is so imperfect (23). We should not be afraid of gods but rather use them as examples of perfect happiness (23). The message of Epicurus was that all people (including poor men, women, even slaves) may achieve happiness if their way of living is based on prudence, virtue, justice, friendship and objective knowledge (22, 23).

Influenced by the Epicurean philosophy, Asclepiades rejected the Hippocratic doctrines of four elements and humors as well as the benevolent Nature axiom (2, 18). He adhered to atomic theory, chance and evolution, insisting that "Nature does not look after living organisms" (18, 19). He warned that in most cases if proper care is not provided by a physician the condition of a patient will deteriorate (18). He suggested that the human body is composed of a) molecules $(\mu \epsilon \rho \eta$, 'meree' or 'corpuscula') that are made of atoms (ἄναρμοι ὄγκοι, 'anarmoi ongoi'), and b) void spaces $(\pi \acute{o} \rho o \iota, 'poroi')$ (18). According to Asclepiades, diseases are caused by alteration of form, position or free flow of a patient's molecules; thus, he introduced molecular stereopathology (18). In order to restore health status, he favored mild therapeutic methods such as a healthy diet, exposure to light, hydrotherapy, massage, physical exercise, although he also employed herbal remedies and surgery if judged appropriate (18). He was named Philosophicus because of his knowledge of philosophy and Pharmacion because of his knowledge of medicinal herbs, such as his favorite chamomile (18).

Another characteristic of Asclepiades was the friendly support of patients (18). His sympathetic consideration for the feelings and comfort of his patients was in great contrast with the infamous callousness of physicians of his era. His motto was "treat the patient swiftly, harmlessly and pleasantly" (18). In order to offer treatment as painless and pleasing as possible to his patients he even recommended the use of wine in some cases (18). He maintained that "a physician who respects his profession has a few patients because he attends them very closely" (1, 18). He advocated the equal treatment of women because most diseases are common to both genders (7, 8, 18). Asclepiades was a pioneer in the humane treatment of patients with mental disorders (2, 18). He freed insane persons from confinement in the dark and treated them using labor and music therapy, in addition to healthy diet and massages (2, 18).

He was the first physician who introduced the highly important division of diseases in acute and chronic ones (2, 18). Freed by the misconception of a benevolent Nature and influenced by one of the principal sayings of Epicurus regarding pains ("those that are acute are more intense, while those that are lasting are milder"), Asclepiades recognized

that some diseases have a short duration, while others are incurable (23). He realized that the physician has to act swiftly in order to have an opportunity to cure the acute diseases, while the best thing to do in incurable chronic diseases is to comfort the patients. Asclepiades, who charged Hippocratic physicians preceding him with having being "concerned with death instead of life", was the first to study chronic diseases systematically (18). It was only after him that the cure of chronic diseases rather than the cure of acute ones became the outstanding accomplishment of doctors (2).

The humane and naturalistic approach of the Bithynian physician, as well as his medical skills gave him a great reputation in Rome (2, 3, 18). He wrote many medical works but none remains and his views are known by other writers. Interestingly, the book 'Precepts' ($\Pi \alpha \rho \alpha \gamma \gamma \epsilon \lambda i \alpha \iota$), which is oddly included in the *Hippocratic Corpus*, contains so many of Asclepiades' ideas that either he or one of his early students is probably the author (12). It contains references to acute and chronic diseases, proper medical practice with sympathy, caring and friendliness toward patients (12). The book begins with the dictum that "healing is a matter of time, but sometimes also is a matter of opportunity" (12). It bases medical practice "not on theories but on experience combined with reason" underlining Zeno the Sidonian's pragmatic approach based on observation and inference by means of signs (12, 20). It includes several Epicurean terms and views, including the concept of senseperception, the consideration of patients' pleasure, and the avoidance of physicians' flamboyant pretense (12, 18, 23). Most importantly, it contains the Epicurean motive of 'philia' (φιλία, friendship or friendly love) for compassion to patients: "For where there is love of human, there is also love of the art" ("Ην γάρ παρή φιλανθρωπίη πάρεστι καί φιλοτεχνίη). Last but not least, the Greek text contains latinisms, indicating that the author spoke Latin and lived in Roman era (12).

Scattered information, recorded by various writers, reveals that Asclepiades was an extraordinary man. He was the first physician who performed an elective non-emergency tracheotomy, according to Galen and Aretaeus (18). Once, according to Pliny the Elder, in a passing funeral procession Asclepiades noticed that the presumed dead person was not really deceased and he 'revived' him (saved him) to the amazement of everybody around (18). Probably his is the impressive theory that in stagnant waters there are "invisible tiny animals" (microbes!), which if inhaled may cause disease, recorded by his contemporary Roman Marcus Terentius Varro (11). Asclepiades might have conceived this hypothesis using the Epicurean inference of invisible things by analogy to evident ones, in order to explain the observation that people who drank stagnant water, even diluted in fresh water, usually became sick. Varro had ideas with many Epicurean influences, ranging from the nature of gods to the perception of language (25). Another contemporary Roman, the Epicurean poet Lucretius, evidently shared Asclepiades' way of thinking by referring to molecules ('corpora') as clusters of atoms attached to each other ('primordia'), as well as the void that facilitates their movement in material bodies (24). Lucretius incorporated much of the language and imagery of medical practice and epicurean psychotherapy throughout his poem *De Rerum Natura* ('On the Nature of Things') and the climax is the final episode regarding the Plague of Athens (24, 26).

The Legacy of Asclepiades

Asclepiades died in Rome at an advanced age according to Pliny the Elder (18). His influence lasted for about half a millennium through the Methodic School of Medicine, which was established by his students (2). The name of the School is derived from Greek 'methodos' ($\mu\epsilon\theta\sigma\delta\sigma\varsigma$), which implies a systematic line of scientific investigation (2, 3). Accordingly, Methodic Medicine was based on atomic theory and was free of metaphysical ideas.

Among many famous Methodic physicians are Asclepiades' Greek students Themison (c.100-20 BCE) and Titus Aufidius of Sicily (c.90-10 BCE) (1, 2). The latter wrote a book, which was later translated into Latin by the Roman Cornelius Celsus under the title 'De Re Medica' and became one of the most popular medical texts until the 19th century (1, 2, 16). The Greek physician Antonius Musa notably cured the emperor Augustus of typhoid fever with cold baths (2). A probable explanation of the successful treatment is that by decelerating the reproduction of the microbial agent in a cold environment, the Methodic physician gave the opportunity to his patient's immune system to combat the disease. Other famous followers of Asclepiadian medicine include Thessalus of Tralles, the official physician of emperor Nero (1st century CE), Soranus of Ephesus, who is considered the father of Gynecology, Obstetrics and Neonatology (early 2nd century CE) and Caelius Aurelianus of Numedia (early 5th century CE) (2, 7, 8, 16, 27-29). It is worth mentioning that in his surviving Greek texts, Soranus refers several times to Asclepiades and other Methodic physicians (7, 8). Most importantly, he also once mentions Zeno the Epicurean together with the philosopher Aristotle and once, elsewhere, Phaedrus together with the philosopher Empedocles (7, 8). Phaedrus, probably a close friend of his contemporary Asclepiades, was another famous Epicurean who taught philosophy in Rome for many years according to Cicero and returned to Athens after 86 BCE (22). It is tempting to assume that Soranus knew the views of Epicureans Zeno of Sidon and Phaedrus from references in the works of Asclepiades. After all, the Bithynian physician was greatly influenced by his teacher Zeno in treating his patients with sympathy and kindness.

Asclepiades' ideas of molecules and void were heavily attacked by Neoplatonic physicians such as Galen and philosophers such as Apuleius in the 2nd century CE and

subsequently by Christians and Muslims who favored Hippocratic medicine (1-3, 6, 16). Most of the contributions of the Bithynian physician were forgotten for about 15 centuries, except very few such as the division of diseases into acute and chronic ones.

Then, some of the basic ideas of Asclepiades were rediscovered by modern Science. In the 19th century, Dalton proved that the atomic theory was indeed true and Pasteur showed that microbes may cause disease. In the 20th century, it became apparent that all diseases have a molecular basis (3, 4). The structure of DNA provided a biochemical model of life at its first level of organization initiating the era of molecular biology (4). Medicine entered its molecular phase, too, in the past decades (3, 4, 17). No self-respecting physician or life scientist believes in the incorporeal healing powers of a benevolent Nature any-more. Psychological support of patients is currently considered a necessary component of medical conduct (3, 17). Patients with mental disorders are now respected and treated with music and labor therapy, in addition to appropriate drugs (3, 30). There are even recent reports that massage may have a beneficial effect in reducing physical symptoms of pain and anxiety in patients of cancer (31). And yet, Asclepiades of Bithynia still remains widely unknown.

Recent Debate about Asclepiades

It is worth mentioning that in the last three decades some scholars advanced certain curious assumptions regarding Asclepiades, possibly in an attempt to obscure either his direct contribution to Methodic medicine or the Epicurean origin of his corpuscular theory. Rawson postulated that Asclepiades died before 91 BCE, taking literally a past tense meaning "he was a physician and a friend of ours" in a text Cicero wrote at that time (32). But Cicero does not actually mention that Asclepiades was dead at the time in this or any other text, while several other reliable authors such as Pliny, Cornelius Celsus (Titus Aufidius), Galen and Sextus place the Bithynian physician well in the 1st century BCE (18). Nevertheless, Polito considered Rawson's hypothesis as proven and he went further to suggest that Asclepiades was born in the late 3nd century BCE and his physician father Andreas had been the student and successor of Herophilus in Alexandria, therefore Asclepiades must have been a Herophilean (33). To agree with Polito one has not only to disregard all reliable ancient authors but also one has to believe that Asclepiades lived about 100 years or more (!) and that he spent his childhood (or even he was born) in Alexandria and not in Bithynia (33). Obviously, it is rather difficult to accept the hypotheses of either Rawson or Polito.

Furthermore, Vallance wrote a book aiming to support his opinion that Asclepiades' corpuscular theory was not influenced by Epicurus but rather by the platonic philosopher Heraclides of Pontus (34). The arguments of Vallance are

purely philological: for example he stresses the fact that Galen never calls atoms the 'anarmoi ongoi' of Asclepiades (34). At the same time, he easily dismisses as a misunderstanding the compelling testimony of Galen that Asclepiades was a follower of Epicurus (18, 34). Furthermore, Vallance chooses to disregard the testimony of two other Methodic physicians: Soranus who writes in Greek and uses the term 'ongoi' and Caelius Aurelianus who translates Soranus' texts in Latin using the term 'atomi' (7, 8, 29, 34). As Vallance himself acknowledges on page 25 of his book, there are "no cases of atomi being applied specifically to non-Abderite (i.e. Democritean) or Epicurean particles" (34). Apparently, most other historians and philologists disagree with his interpretation of texts (2, 18, 35, 36). The exception was once again Polito, who recently attempted to sustain Vallance's obscure position stating that Caelius Aurelianus "appears to identify these fragments with atomi, but the question is controversial" (37).

A number of reasons support beyond any reasonable doubt the thesis that Asclepiades was influenced by Epicurean philosophy and not by the Platonic philosopher Heraclides of Pontus:

- 1. Asclepiades accepted the notion that the soul was made of atoms like any other part of the body and therefore dissolved after death. This was an Epicurean and not a Platonic doctrine (10, 18, 23). If belief in afterlife is denied, it follows that life and health of body and soul becomes the most precious possessions of mortal man. Describing the practice of previous physicians as a 'preparation for death', Asclepiades thought that the Methodic physician had to assist people to achieve physical and mental health as well as to subsequently let them hope that they would keep this pleasant state of life for long.
- 2. The consideration of patient's pleasure is an integral component in Asclepiades' medical practice (18). Pleasure was for Epicurus the primary good and the most familiar to human nature, while for Plato it was the last of the minor goods (10, 23). Both philosophers and physicians were divided two ways according to their attitudes toward pleasure and pain. The Cynic philosopher Antisthenes, who like Plato had also been a student of Socrates, said that he lashed out his pupils savagely because physicians of his time did the same with their patients. The same Antisthenes maintained that pain was a good thing and that he would rather go mad than feel pleasure (10).
- 3. The vast majority of Greek physicians admitted that divine dream-healings and mantic dreams were real and effective (2). Hippocratic physicians including Galen, as well as Herophilus and the Empiricists all believed in them (2). The Methodic physicians were the only ones that apparently did not believe in divine dreams and they never mention them (2). This exception parallels the fact that almost all Greek philosophers believed in mantic dreams except

Epicurus (10, 23). He alone objects to such a theory and it must be on account of Epicurean influence that Asclepiades and his followers are the only physicians to disapprove of the value of dream-healings.

- 4. Heraclides of Pontus indeed proposed a corpuscular theory using the term 'ongoi', but his works were also loaded with supernatural narrations and imaginary miracles (10, 36). He was famous for his egocentric attitude, vain personality, extravagant appearance and flamboyant pretense. He even bribed the envoys of his city to the Oracle of Delphi in order to falsely proclaim him a divine hero. Heraclides does not fit at all the personality model for a science-oriented, decent and compassionate physician like Asclepiades. On the contrary, the Bithynian shares many qualities of Epicurus, who was famous for his naturalistic thinking, modesty, kindness and friendliness.
- 5. On page 41 of his book Vallance claims that "there is no evidence for an 'Epicurean' school of medicine" (34). On the contrary, there is mounting evidence for the existence of Epicurean physicians. In Rhodiapolis, a city of Asia Minor, there is a 2nd century CE inscription honoring the physician and philosopher Heraclitus, who was affiliated with the Epicureans of Athens (22). In the Italian city of Rimini, a 2nd century CE house was recently unearthed that belonged to a Greek surgeon named Eytyches, who was apparently an Epicurean, as archeological findings attest (38). As mentioned before, 'Precepts' is an astonishing text that combines ideas of Epicurus and Asclepiades (12). Its existence suggests that this early Methodic text survived only because it was incorporated in the Hippocratic Corpus.

Conclusion

The great Hippocrates of Kos laid the basic foundations of medical practice and ethics. The brilliant Asclepiades of Bithynia offered a more realistic and humane refinement of the medical art in ways that only recently have been appreciated. It is time that Asclepiades be recognized for his contributions as the father of molecular medicine and take his rightful place as a pioneer physician next to Hippocrates, the justly recognized father of clinical medicine.

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References

- Farrington B: Greek Science: Its Meaning for Us. Spokesman Publications, Nottingham, UK, 2000.
- 2 Edelstein L: Ancient Medicine. Johns Hopkins University Press, Baltimore, USA, 1967.
- 3 Porter R (ed.): The Cambridge Illustrated History of Medicine. Cambridge University Press, Cambridge, UK, 1996.
- 4 Runge MS, Patterson C and McKusick VA: Principles of Molecular Medicine, 2nd ed. Humana Press, New York, USA, 2006
- 5 Kiapokas MS: Hippocrates of Kos. Heptalophos, Athens, Greece, 2003
- 6 Temkin O: Hippocrates in a World of Pagans and Christians. Johns Hopkins University Press, Baltimore, USA, 1991.
- 7 Ilberg J: Sorani Gynaeciorum libri IV, De signis fracturarum, De fasciis, Vita Hippocratis secundum Soranum, Corpus medicorum Graecorum 4 (With Latin translation). Berlin, Germany 1927.
- 8 Cactus Philological Group: Soranus Collected Works (With modern Greek translation). Cactus, Athens, Greece, 1996.
- 9 Kingsley P: Ancient Philosophy, Mystery, and Magic: Empedocles and Pythagorean Tradition. Oxford University Press, Oxford, UK, 1995.
- 10 Bakalis N: Handbook of Greek Philosophy from Thales to the Stoics: Analysis and Fragments. Trafford Publishing, Victoria, Canada, 2005.
- 11 Hart GD: Descriptions of blood and blood disorders before the advent of laboratory studies. Br J Haematol 115: 719-728, 2001.
- 12 Jones, WHS: Hippocrates Collected Works I. Harvard University Press, Cambridge, USA, 1868. View in http://daedalus.umkc.edu/hippocrates/HippocratesLoeb1/page.ix.php>.
- 13 Thucydides: History of the Peloponnesian War. Books I & II, 2.47-2.55. Harvard University Press, London, UK, 1919.
- 14 Papagrigorakis MJ, Yapijakis C, Synodinos PN and Baziotopoulou-Valavani E: DNA examination of ancient dental pulp incriminates typhoid fever as a probable cause of the Plague of Athens. Int J Infect Dis 10: 206-214, 2006.
- 15 Papagrigorakis MJ, Synodinos PN and Yapijakis C: Ancient typhoid epidemic reveals possible ancestral strain of Salmonella enterica serovar Typhi. Infect Genet Evol 7: 126-127, 2007.
- 16 Sullivan R: Thales to Galen: A brief journey through rational medical philosophy in ancient Greece. Proc R Coll Physicians Edinb 26: 487-499, 1996.

- 17 Harper PS: A Short History of Medical Genetics. Oxford University Press Inc., New York, USA, 2008.
- 18 Gumpert CG: *Asclepiadis Bithyniae Fragmenta*, Weimar, 1794. (View in http://books.google.com).
- 19 DeWitt NW: Notes on the History of Epicureanism. Transact Proc Am Philol Assoc *63*: 166-176, 1932.
- 20 Tsouna V: The Ethics of Philodemus. Oxford University Press Inc., New York, USA, 2007.
- 21 Konstan D, Clay D and Glad CE: Philodemus: On frank criticism. Society of Biblical Literature, Atlanta, USA, 2007.
- 22 Clay D: Paradosis and Survival: Three Chapters in the History of Epicurean Philosophy. University of Michigan Press, USA, 1998
- 23 Inwood B, Gerson LP and Hutchinson DS: The Epicurus Reader: Selected Writings and Testimonia. Hackett Publishing Company, Indianapolis, USA, 1994.
- 24 Smith MF: On the Nature of Things by Lucretius: Translation and notes. Hackett Publishing Company, Indianapolis, USA, 2001
- 25 Joseph JE: Natural grammar, Arbitrary lexikon: An enduring parallel in the history of Linguistic thought. Language & Communication 15: 213-225, 1995.
- 26 Kilpatrick RS: 'Amicus Medicus': Medicine and Epicurean Therapy in 'De Rerum Natura'. Memoirs Am Acad Rome 41: 69-100, 1996.
- 27 Todman D: Soranus of Ephesus (AD 98-138) and the Methodist sect. J Med Biography *16*: 51-53, 2008.
- 28 Gerdtz J: Mental illness and the Roman physician: the legacy of Soranus of Ephesus. Hosp Commun Psychiat 45: 485-487, 1994.
- 29 Drabkin IE: On Acute Diseases and On Chronic Diseases by Caelius Aurelianus, Chicago, USA, 1950.
- 30 Silverman MJ: The influence of music on the symptoms of psychosis: a meta-analysis. J Music Ther 40: 27-40, 2003.
- 31 Wilkinson S, Barnes K and Storey L: Massage for symptom relief in patients with cancer: systematic review. J Adv Nurs *63*: 430-439, 2008.
- 32 Rawson E: The Life and Death of Asclepiades of Bithynia. Class Quart 32: 358-370, 1982.
- 33 Polito R: On the Life of Asclepiades of Bithynia. J Hellen Stud 119: 48-66, 1999.
- 34 Vallance JT: The lost theory of Asclepiades of Bithynia. Oxford University Press Inc., New York, USA, 1996.
- 35 Pigeaud J: La physiologie de Lucrèce. Revue des Etudes Latines 58: 176-200, 1981.
- 36 Gottschalk HB: Heraclides of Pontus. Oxford University Press, Oxford, UK, 1980.
- 37 Polito R: Frail or monolithic? A note on Asclepiades' corpuscles. Class Quart *57*: 314-317, 2007.
- 38 Jackson R: A Roman Doctor's House in Rimini. British Museum Magazine 44: 20-23, 2002.

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