

## Ancient medicine after Herophilus. Part 1

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**Abstract.** The article continues a series of publications on research results of a reconstruction of the history of ancient medicine as a protoscience phenomenon. Special aspects of ancient Greek rational medicine (from its inception to the work of Herophilus) were earlier identified. Herophilus' work was experimental in its research methodology and fundamental in its influence on the constitution of a rational view of anatomy and physiology. It has been assessed in the light of the continuity of the natural-philosophical ideas of Hippocrates, Plato, Aristotle.

This article outlines an approach to studying the development of ancient medicine from Herophilus to Galen. The fact that the history of ancient medicine from the 3rd century BC to the 1st century AD is virtually unexplored by Russian experts is recognized, while this period has been sufficiently studied in Western historiography. According to the author, Herophilus' priority was the understanding of medicine as a theoretical and rational knowledge, based on the results of systematic anatomical studies and the use of experimental methods. However, as noted in this article, the explanatory potential of the natural-philosophical systems of the 3rd century BC was not sufficient, and attempts to create a universal medical theory led to certain errors. Apparently, this was one of the reasons why the empiricists' medical school not only appeared, but soon became dominant in the post-Herophilus era. It was characterized by a negative attitude to the development of medical theory, to the extent of completely rejecting the need to study human anatomy.

The author of the article attempts to analyze particular concepts of medical theory and practice of some of the most well-known post-Herophilus doctors. It is concluded that the most famous doctors prior to the 1st century BC belonged to two medical schools – empiricists and rationalist-Hippocratists.

**Keywords:** history of medicine, ancient medicine, Herophilus, empiricist physicians, rationalist physicians, natural philosophy

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### Introduction

This article continues a series of publications on the results of research works that aim to reconstruct the history of ancient medicine as a protoscience phenomenon. Earlier, we established the necessity of analyzing the works of ancient Greek physicians in the light of the dominant views found in various natural-philosophical schools, taking into account the aggregate of phenomena, referred to in the philosophy of science as the “scientific picture of the world”, and factors that we refer to as “religious-philosophical systems” [1].

Previously, we gave an overall assessment of Galen's legacy as the first dominant theoretical and practical system to emerge in the history of medicine [2, 3]. We have traced the emergence of ancient Greek rational medicine from its beginnings up to the work of Herophilus [4]. This was based on an assessment of the natural-philosophical ideas of Plato and Aristotle as having decisive importance for the further development of the ideas of Hippocrates (c. 460–370 BC). The works of Herophilus have been assessed by us in light of the continuity of these ideas as an experimental research methodology and fundamental in their influence on the institutionalization of a rational view of anatomy and physiology [5–7]. However, at the same

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time, the circumstances ancient medicine's development "from Galen to Herophilus" still remain to be clarified.

The history of ancient medicine from the 3rd century BC to the 1st century has been virtually unexplored by Russian experts. Russian language readers have at their disposal a small source base – a number of texts were published in the 1950s and 1960s (for example, the works of Aulus Cornelius Celsus [8]), which offer an impression of that time. However, they are not enough to provide a holistic understanding of events to the medical historian. In Western historiography, this period in the history of ancient medicine has been studied well enough – it is enough to mention the works of V. Nutton and J. Longrigg [9, 10]. A significant amount of information about this period in the development of medicine is contained in the texts of Galen: in his criticism or, on the contrary, appreciation of earlier colleagues, the great Roman physician, as a rule, tried to convey to the reader the essence of the views of his predecessor. In addition, the writings of Pliny the Elder, Celia Aurelian, Erotian and others serve as well-known sources of evidence about doctors and medicine of the Hellenistic period and the early Roman Empire [11, 12].

Of particular importance for the understanding of the history of ancient medicine is the seminal monograph by H. von Staden – Herophilus [13]. The author of this article heard from foreign colleagues that von Staden's research is exhaustive, and further works on the subject are unnecessary. This monograph is definitely a brilliant example of conscientious and professional source-based research. It's hard to add anything to the information on Herophilus' works, meticulously collected by the author. Von Staden's book is made up of small chapters that provide a brief assessment of the activities of doctors, who lived at the end of the 3rd century BC to the 1st century. This small story about the most famous figures of medicine "post Herophilus" confronts historians of medicine with an important question: have they been correctly associated with one or another medical school? An answer to this would clarify the importance of this or that direction in medical thought at a particular historical juncture.

### **The origin of the empiricists' school and questions on the interpretation of Herophilus' body of work**

Of the doctors who worked in the post-Herophilus era, we, in the first place, are most interested in the well-known figures – Bacchius, Andreas of Alexandria, Callimachus, Zeno, Gegetor, Mantias and Demetrius of Apamea. Von Staden calls all of them "Herophileans", considering them followers of Herophilus. From our point of view, this presents certain difficulties in interpreting specific physicians' views and associating them with a particular medical school. Herophilus, in our opinion, was a supporter of the Hippocratic rationalist trend in medicine. It is natural to assume that his followers were like-minded and sympathetic to his way of thinking, which is characterized as "theoretical medicine" (the term is sometimes used in historiography to describe the doctrine of rationalist physicians). However, it is namely post-Herophilus that the medical school of empiricists appears and soon begins to dominate. It is characterized by a negative attitude towards theoretical medicine, to the extent of a complete rejection of the use of the study of human anatomy. Furthermore, attention is drawn to the fact that the doctors considered the founders of the school of empiricists – Philinus of Cos and Serapion – lived in Alexandria during the second half of the 3rd century BC and, no doubt, were well acquainted with the work of Herophilus. Nutton, for example, even uses term "a dissident disciple of Herophilus" in relation to Philinus [9, p. 149].

Von Staden considers certain doctors to be Herophileans, seeing a "clear thread of continuity from the founding teacher to his successors". As an example of such a thread, he attributes the continued interest of several generations of physicians to the pulse theory: from Bacchius (3rd century BC) to Demosthenes Philaethes (1st century). "Herophilus' followers" maintained a tradition of sphygmology, established by their school's founder teachers. However, can we consider all these doctors Herophileans on the grounds that they were interested in sphygmology? This is an extremely unreliable criterion, in our opinion. In fact, the value of studying the pulse for clinical diagnosis was recognized by doctors in all fields – Hippocratic-rationalists, methodists

and empiricists. Naturally, within each school of teachings, there were well-known interpretational variants. It could not have been any other way because we are talking about a period of more than 400 years.

What is most important with Herophilus is not the theory of the pulse, but the understanding of medicine as a theoretical-practical specialization, which is based on anatomical research and experimental method. Can we consider doctors, who in principle rejected the value of anatomical dissections and medical theory, to be Herophilus' followers? Of course, not. Sphygmology in Herophilus' legacy is just one of medical practice's applied aspects. For example, we know that Andreas of Alexandria was interested in the problems of physiology, in particular, the nature and location of the control center for arbitrary functions. According to him, there existed a higher power, possessing the ability to guide human life and the mind, which was equated with the "soul". He equated the concepts of "soul", "mind" and controlling abilities (i.e. the concept of "feelings"). In our opinion, the elements of materialism discernible in this interpretation are not important: the works of Andreas of Alexandria have not survived, and his ideas about this issue cannot be reliably reconstructed. However, it is clear that his professional views fit into the concept of theoretical medicine. In our view, categorizing a doctor as a Herophilean on the basis of only one of the traits inherent in Herophilus' legacy (in this case an interest in sphygmology) is not correct. In fact, we need a comprehensive analysis of the views of doctors, including their approaches to general pathology, clinical practice and natural philosophy. Only in this way will we be able to reconstruct the history of ancient medicine in a historically accurate way.

Obviously, the explanatory potential of natural-philosophical systems of the 3rd century BC was not been sufficient in relation to such a complex subject as medicine. Any attempts to construct a universal medical theory will, no doubt, lead to certain errors. Doctors, having extensive practical experience, could come to the unpleasant conclusion that a large part of their teacher Herophilus' discoveries were virtually useless in daily life due to a limited therapeutic arsenal. Conclusions about the fallibility of all (or almost all) theories followed

as a result. We are talking about a very delicate moment, when the prominent founders of the school of empiricists were convinced of the limited potential of theory and called for more attention to be paid to the systematization of practical experience, and their less talented pupils even completely abandoned the use of anatomical and physiological data. It should always be remembered that a medical school's image on the scale of the whole Mediterranean was defined by the level of knowledge and skills of its practitioners.

Development of ancient Greek medicine in the 6th to 4th centuries BC can be described as the emergence of rational methods of knowledge and, in fact, the appearance of the medical profession in the modern sense of the word. Even in the text of the Hippocratic Corpus (for example, "On ancient medicine") we find echoes of the debate on the art of healing: is medicine an independent profession or some specialized skill? Accordingly, can a person who possesses such a skill (i.e., a physician), achieve greater success in the treatment of diseases than the priest-exorcist, calling on the help of spirits and numerous gods, or simple city-state citizens, relying on common sense in caring for their own health? We have already touched on this topic in the context of describing the conflict between the emerging social class of rationalist doctors and representatives of the pagan clergy, as well as all kinds of itinerant quacks [14, p. 514–543]. Doctors fighting for the prestige of their profession came to the conclusion that in the acquisition of additional theoretical knowledge about the structure and functioning of the human body, they could expand their therapeutic arsenal (discovering new pharmacotherapy methods, inventing new tools, etc.). In other words, the development of a new theory can expand practical possibilities. Education at that time was primarily associated with the study of philosophy. A variety of schools offered various views of the world, which ideally could help to explain physical phenomena – including health and disease. The natural-philosophical ideas of Plato, and following on from them the brilliant practical results achieved in the natural science of Aristotle and his followers, inspired considerable hope. However, in the 3rd century BC, after the work of Herophilus, doctors could already come to the conclusion that the accumulation of

additional theoretical knowledge had not led to the expansion of practical possibilities.

M. Frede characterizes the appearance of the empiricists' school as follows: "Empiricists were doctors who believed that all medical theories have something in common – they were based on questionable assumptions, the truth of which could not be definitively established... From this, in their view, it followed that the validity of such assumptions could not be established and that, even with the help of the mind, such issues could not be resolved" [15, p. 82–83].

This position holds rather scant internal logic: if all existing theories either are somehow incorrect or do not fully clarify the issues faced by researchers, it can be assumed that no theory will reveal the full truth in the future. Moreover, if such sustained efforts, sanctified by the authority of Hippocrates, Aristotle, etc., had not led to a significant expansion of medicine's practical possibilities, it is possible that these efforts are pointless and should not be undertaken. It seemed more reliable and safe for empiricists to rely on a specific set of well-proven concepts and approaches. The empiricists pointed to the dubious endless discussions on general pathology and their ultimate uselessness in practice. At the level of common sense, the mind can offer different plausible arguments in favor of one or another point of view, however, the credibility of these arguments does not testify to their truthfulness. Of course, the doctor who feels responsibility to the patient will never rely on assumptions, the accuracy of which is uncertain. We once again emphasize that the rejection by empiricist doctors of everything that seems to us today an integral part of medical science (anatomy, physiology, principles of pathogenesis), should not lead us to see them as uneducated people. Their methods can be regarded as the result of the caution of medical practitioners who chose a conservative approach towards their patients. In fact, what they expected from the science of their time was well-founded evidence of the truth of a theoretical belief. Galen repeatedly criticized empiricists for excessive distrust of theory, including the fact that even those pharmaceutical substances that empiricists actively used were available due to serious theoretical work on understanding the principles their components' actions. As

evidence of empiricists' professional inability, Galen gives examples of case histories in which he first describes how prescribed treatment helped a patient, and then describes how understanding of similar cases provides practical experience that can be used in new clinical cases [14].

Empiricists often refer to the senses and memory as two "abilities" which should be relied upon. Their practice is based on the assertion that a doctor can see a disease's main symptoms immediately, after a cursory examination of the patient. Nowadays, there is a concept in the doctor's vocabulary of "a symptom's manifestation". This refers to the main characteristic of a disease, which attracts the attention of the doctor most of all. For example, with the vast majority of infectious diseases, these are pyrexia and chills, and surgical disorders of the abdominal cavity are manifested by severe pain in the abdomen (known as the acute abdomen). Any doctor knows that the clinical treatment for different surgical disorders of the "acute abdomen" proceeds differently. These nuances are important these days, when the doctor is in possession of a wide variety of pharmacological agents and surgical options with which the patient can be treated. Let us not forget that such opportunities did not exist for doctors in the 3rd century BC. Furthermore, we understand that for a number of diseases (such as ARVI), symptomatic treatment can be effective and sometimes is the only possible treatment. Empiricist doctors not only criticized their colleagues for, in their opinion, overly enthusiastic theoretical constructions but often successfully treated their patients. After all, they used the same arsenal of therapeutic agents as their opponents. Based on this, empiricist doctors thought that it was their task to quickly make a diagnosis based on the idea of identifying the manifest symptoms of the disease itself, and based on their own experience or that of their mentor, offer the most appropriate therapeutic agent for the case given. Furthermore, they did not reject the need for reflection and practiced it to the level of common sense. Firstly, this reflection helped detect phenomena that could be observed but were not immediately clear. Secondly, they contributed to refuting the arguments of those doctors who objected to the obvious. By following common sense, in an effort

to theorize something clear and understandable, discussions with opponents were made easier, and they were able to resist their opponents' erroneous arguments.

The nihilism of empiricists in relation to theoretical medicine not only meant the rejection of experience derived from anatomical dissections but also extended to the denial of the fundamental necessity of studying the etiology of diseases. Researching the causes of diseases seemed unnecessary precisely because of empiricists' extremely practical view of medicine, relegating the doctor's art to the level of a craft. Even recognizing that diseases may have had some physical cause, representatives of the empiricists' school considered that it was useless to establish the mechanism of influence of the etiological factor and the pathogenesis of diseases. Most important for them was an effective treatment aimed at combating the symptoms of the disease. We have already noted that in the empiricists' world view, diseases' symptoms were, in fact, equivalent to the disease itself.

Many empiricists, who knew Herophilus' work perfectly well, did not deny the results of anatomical studies, but considered them unnecessary and of little use due to one very important argument: these studies were carried out on corpses and a living body differs significantly from the non-living. To the modern reader, this argument may seem somewhat sophisticated, but we should not forget the significant influence of skepticism in the philosophical gamut of the time. It seemed logical to assume that the anatomical and physiological patterns established in experiments on the dead did not necessarily provide adequate information on the body's functions in living people. Empiricists' clinical practice was based on three factors – a thorough examination of the patient, analysis of prior experience (their own or colleagues'), as well as an analysis of the results of measures previously taken by the physician in similar cases.

#### **On the most well-known Hellenistic-period doctors' association with different medical schools**

All of the aforementioned does not by any means indicate that fundamental theoretical reasoning was ignored – for example, the surviving evidence of the life and practice of Heraclides

of Tarentum, who worked in the beginning 1st century BC, testifies to this. For example, it is known that Heraclides believed lethargy was the result of the accumulation of a large amount of undigested substances and a thickening of fluid in the human body (it is a rational theoretical explanation!). Galen testifies to an interesting discussion between Heraclides and the physician Hegetor, a follower of Herophilus, who lived at the end of the 2nd century BC [16, 17]. The discussion dealt with important practical issues – the possibility of repositioning a dislocated hip bone. Hegetor believed that there was a strong short tendon restraining the hip bone in its normal position. From this position, he drew the quite rational conclusion that the pelvic bone could be displaced only in the case of rupture of the tendon holding it in place. Accordingly, Hegetor did not recommend resetting a pelvic bone, since the ruptured tendon, which held it in place, would cause it to move again, and the patient will experience double the suffering from the ineffective medical manipulation and the failure to eliminate the ailment. Empiricist doctors essentially ignored the results from Herophilus' anatomical studies and did not pay attention to rational logic – on the contrary, they tried to reset the pelvic bone in the case of its displacement. In some cases, they succeeded. Accordingly, Heraclides, summarizing practical experience, including his own, pointed to the obvious fact that the rationalist physicians, with their attention to anatomy, were not right, as evidenced by well-known cases of patients being cured. Interestingly, Heraclides did not deny the existence of such a tendon. He just suggested that it might not be completely torn, but only weakened, and in this case the resetting of the pelvic bone was possible. Heraclides was criticized by his colleague Caelius Aurelianus. The subject of his criticism was Heraclides' choice of treatment for phrenitis out of several possible methods, based on the theoretical understanding of the causes of the disease. Caelius Aurelianus believed, that in doing so, Heraclides deviated from the main empiricist school of thought, which was based solely on experience [13, p. 555–559]. An example of such doctrinal inflexibility was Serapion, one of the founders of empiricism, who believed that a specific doctor's medical knowledge was based

only on his own experience and knowledge of the experience of others.

However, studying the few extant sources of evidence about the early empiricists, who existed before Heraclides, we find no clear indication of explicit rejection of the use of reason and theory, which is, first of all, demonstrated by the fact that a voluminous treatise was created on the art of medicine. Thus, Apollonius of Kition, a well-known empiricist physician – a younger contemporary of Heraclides – was the author of essays that refuted critical work of Heraclides dedicated to Hippocrates. Apollonius of Kition's work consisted of 18 books [18]. There is no doubt that only an educated person possessing logic and dialectics, i.e., capable of leading scientific debate according to the rules of the time, could write such a vast polemical treatise. It can be assumed that Heraclides' text refuting Apollonios was no less voluminous.

Apollonius' position on the resetting of the pelvic bone is quite revealing. He does not speak of his own successful experiences and does not essentially argue with Hegetor, but simply draws attention to Hegetor's erroneous conclusions that did not match observed results: a pelvic bone can sometimes be successfully reset. Moreover, he points out that this issue was discussed by Hippocrates, and that such a discussion would be absurd if Hippocrates did not know from personal experience that the pelvic bone could be successfully reset. This is a prime example of empirical logic, paying attention to the experience of colleagues, which could be used to confirm the truth while being sufficiently flexible in understanding the methodology of one's opponents. Apparently, the intellectual image of representatives from the empiricist school has changed over time. M. Frede believes that "even in Soranus' times empiricists tended to deny the positive role played by reason or theory. But when we turn to Menodotus and Theodosius, we see that in the middle of the 2nd century the situation changes considerably. For example, Galen said that Menodotus, like Heraclides, did not deny the importance of the mind" [15, p. 94–95]. This supports our hypothesis that there were considerable differences of opinion on specific issues among empiricist doctors – their doctrine was as flexible as doctor's hands-on experience was varied. However, the most important issue,

which is almost unexplored in the historiography of the subject, is the natural-philosophical basis of their views. We repeat: they were educated people of their time, and we should not suspect them of ignorant stubbornness.

In the text below, we, for the first time in Russian historiography, try to analyze the particular conceptual features of medical theory and practice inherent in the most famous doctors of the post-Herophilus era.

A prominent figure in the post-Herophilus history of medicine is Bacchius, a native of the Boeotian town of Tanagra, who studied and made a career in Alexandria. It is believed that he lived in 275–200 BC, and the heyday of his work took place during the reign of Ptolemy III Euergetes (246–221 BC) and Ptolemy IV Philopator (221–205 BC). Bacchius' most important work consisted of three "Lexicon" books, which were a commentary on Hippocrates, compiled taking into account his own clinical experience. Von Staden points to the mention of Bacchius' name in more than 60 texts of antiquity [13, p. 486]. Bacchius' medical interests included pulse theory, general pathology and pharmacology. His doxographical work "Recollections of Herophilus and members of his household" is considered an important historical record. Bacchius sequentially (as they appear in the text) examined key concepts in the Hippocratic Corpus, unlike later works of Epicles of Crete, whose Lexicon listed terms used by Hippocrates in alphabetical order. In the first book, there is an explanation of concepts from the works of Hippocrates on "Prognostics", "On the sacred disease", "On the joints", "On the lever or reposition joints" and "Epidemics I and VI". The second explains the words used by Hippocrates in the treatise on "Prognostics", "On the joints", "On the lever or repositioning of joints", "On diet in acute diseases" and "Epidemics II". The third book is a glossary to the texts "On the nature of bones", "Fractures", "On the joints", "On the doctor's office", "On the places in man" and "Epidemics V" [13, p. 486–488].

As Bacchius' written legacy is well-studied, we will not dwell on it in detail, but refer only to the relevant part of von Staden's book *Herophilus* [13, p. 484–495]. Actually, most of these studies are not of significant importance for this article, as the focus of their research is concentrated on Bacchius' works from philological and

philosophical points of view. Analysis of lexicographical works dedicated to Hippocrates by physicians of antiquity is essentially a continuation of research into the Hippocratic Corpus that was carried out earlier [19–23]. Unfortunately, glossaries, epos, dialectics, and an understanding of the morphological or semantic richness of certain texts will not help us to solve the main task of the research – dealing with the epistemological essence of the views of various schools of medicine in diagnosing and treating diseases.

The most important (as per the importance of his own works) is considered to be the previously mentioned follower of Herophilus, Andreas of Alexandria.<sup>1</sup> Prominent writer Eratosthenes (275–194 BC) wrote of Andreas as his contemporary and called him a “literary Aegisthus”. There is also the testimony of the doctor Serapion, historiographically recognized as one of the founders of the school of empiricists, who wrote of Andreas as his older contemporary. This allowed von Staden to set the date Andreas of Alexandria’s birth as being in the 370s BC. It is believed that Andreas of Alexandria’s father’s name was Chrysaor and he came from the town Carystus located on the island of Euboea. Von Staden’s reconstruction seems quite important, as it allows us to connect the nickname mentioned in the sources – “Andreas from Carystus”, “Andreas – son of Chrysaor” and “Andreas – follower of Herophilus” (there are about 50 such mentions) – with Andreas of Alexandria, court physician of Ptolemy IV. Thus, based on the frequency of references in the sources, Andreas’ historical significance becomes clearer. It is believed that Andreas of Alexandria wrote the considerably large essay on medicines and cosmetics titled “Casket”, the historical and medical work “On the genealogy of doctors” and “On false beliefs”, the treatise “On poisonous animals”, dedicated

to the problem of poisons and antidotes as well as essays concerning almost all obstetrics issues. Heraclides of Taranto mentions the trustworthy, in his opinion, comments of Andreas on the works of Hippocrates (we can assume that they were part of the treatise “On the genealogy of doctors”.) Approval of Andreas’ works by the well-known empiricist school representatives Heraclides and Serapion is, in our opinion, important for the historical reconstruction of medicine in the Hellenistic period. Apparently, the writings of Andreas of Alexandria held much significance in the tradition of ancient medicine: Celsus spoke positively about them, Pliny the Elder repeatedly refers to them in his “Natural history”, Soranus and Athenaeus mentioned them. Moreover, Galen spoke quite kindly of them, as did even the well-known Christian apologist Tertullian. The writings of Oribasius (4th century) contain a description of the technical devices proposed by Andreas for the resetting of dislocated limbs [24–27].

Another interesting figure in the history of Alexandrian medicine is Callimachus. Von Staden called him an example of a perpetuator of the fundamental ideas of Herophilus’ school [13, p. 481]. Callimachus devoted considerable attention to the study of symptoms (or signs) of diseases, which indicates his commitment to the ideas of Herophilus. He was known for his studies into individual medical preparations and wrote about the toxic properties of wreaths, which was very characteristic of the Hellenic tradition. Renowned historian Polybius, speaking of the “theoretical” school of medicine in Alexandria, mentioned Callimachus immediately after Herophilus. Callimachus’ work is commented upon by later authors much less frequently than Andreas’: Celsus, Soranus and Caelius Aurelianus do not mention Callimachus; Galen quotes him in passing. [28] However, Callimachus was praised by Rufus of Ephesus. [29] Interestingly, Polybius pointed to the independence of Callimachus in his views on medicine and his critical attitude to Herophilus’ legacy [30]. It is practically impossible to clarify the essence of this criticism due to the lack of sufficient sources.

Following in chronological order, an important doctor of the post-Herophilus era is Zeno, who worked in Alexandria in the 2nd century BC. Historiographically, Zeno is customarily classified as a staunch empiricist

<sup>1</sup> Andreas of Alexandria, personal physician of Ptolemy IV. His exact birth date is not known; his death was in 217 BC. He died on the eve of the battle of Raphia, accompanying his highest patron and patient Ptolemy IV Philopator. As the personal physician of the king, he spent the night in his tent, while Ptolemy himself spent the night elsewhere. The king’s inner circle plotted to assassinate him on the eve of battle. The traitor Theodotus, a native of Aetolia, broke into the royal tent at dawn, and probably in error, killed the doctor and not Ptolemy.

[13, p. 501–506]. Zeno, as did his colleagues, commented on Hippocrates: obviously, lexicographical analysis of the works of the great native of Cos was important for apologetics of the empirical approach. The fact that almost all known doctors of the post-Herophilus era saw fit to express their views on this issue is noteworthy. This may explain Galen's careful attention to terminology issues.<sup>2</sup> Empiricist doctors believed that symbols and terms were of paramount importance in the formation of their systems. Note the similarity of their reasoning with the logic of the Stoics, who believed the correct explanation was one of the criteria for demonstrating the truth. However, the clarity of the definitions by which medicine should regard specific general pathology phenomena has always been an integral part of the adequate medical theory. The blurring of these definitions, or the possibility of their different interpretations, is always a great danger. This was significant to the ancient doctor's practice, as well as for the modern historian of medicine, risking a mistake when one and the same term represents completely different meaning for different schools. Von Staden called Zeno a "relatively orthodox Herophilean" referring to his sphygmology. According to Zeno, the pulse is a mixture of contraction and distention, having the same sequence in all its parts, regardless of whether it occurs in equal or unequal time units. Furthermore, Zeno did not mention the significance of cardiac function in the generation of a pulse, and accepts Bacchius' term "arterial parts", in such a way linking the generation of the pulse with the artery function.

Demetrius of Apamea is considered a prominent figure in 2nd century BC medicine. Demetrius is definitely accepted as among the rationalist physician followers of Herophilus because of his interest in general pathology. It is known that he was the author of the treatises "On diseases", "Symptoms" and "Semiotics" [12]. Demetrius of Apamea was interested in the nature of mental disorders, priapism, satyriasis, hydrophobia, drowsiness, and bleeding. He tried to understand the causes of edema, disturbances of the heart, the development of diabetes,

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<sup>2</sup> We pay attention to it in their commentaries on the treatises, which came in the second volume of collected works of Galen.

pneumonia, and pleurisy. Von Staden doubts that Demetrius can be considered a member of the rationalist doctors due to the fact that there is a lack of sources clearly pointing to this. In our opinion, given that there is good evidence that Demetrius proceeded from general principles on the course of pathological processes and attempted to understand the etiology of specific diseases, he can be considered an apologist for "theoretical medicine". Demetrius was a well-known and successful practitioner. He was interested in the causes of pregnancy complications. He divided the causes of labor complications into three groups – those related to the health of the mother, those due to an ill fetus, and those related to problems with "the passage, through which the birth takes place" [31]. He was interested in the causes of endometriosis and described six types of abnormal vaginal discharge caused by this disease. Obviously, Demetrius, following on from Herophilus, paid special attention to the pathophysiology of the reproductive system. Demetrius' work was valued highly by Soranus of Ephesus, whose works on obstetrics and gynecology are considered classics [31].

The doctor Hegetor, who we mentioned earlier, was a prominent representative of Alexandrian medicine in the 2nd century BC. He is considered a rationalist and a follower of Herophilus. Hegetor wrote the treatise "On causes", fragments of which are known to us by the essays of the well-known Alexandrian empiricist doctor Apollonius Cittensis [18]. Apollonius sharply criticizes Hegetor, but his criticism helps clarify the renowned Herophilean's own views. It is evident that Hegetor developed the doctrine of disease etiology, seeing medical practice through the prism of scientific methodology, and he believed that the results of surgical treatment could be significantly improved thanks to the knowledge of anatomy. According to the empiricist Apollonius, a doctor only needs to know what kind of treatment is effective in a given situation, and what is not. The question of why a treatment is effective it is not important, and attempts to discover a disease's cause are futile, according to Apollonius. J. Kollesch believes Hegetor followed the classical teachings of Herophilus on the pulse and believed that an understanding

of the causes of a disease contributed to success in its treatment [17].

Galen names the doctor Mantias, who lived at the end of the 2nd to the beginning 1st century BC, as the first person to record the composition of many medicines deserving of attention [32]. He considered Mantias to be a follower and supporter of Herophilus, unlike Heraclides of Tarentum, who studied with Mantias, but later became an empiricist. Mantias wrote a fundamental description of laxatives, “carminatives”, enemas and locally applied therapeutic preparations. Apparently, Mantias’ pharmacological works not only contained a description of certain drugs, but were clinical in nature, recommending when, how and, most importantly, why a particular formulation should be used. So, Galen refers to Mantias’ explanation of the nature of the staphyline inflammatory disease. Mantias’ works in the field of gynecology are also known. For example, he described “hysterical asphyxiation” syndrome – shortness of breath, loss of speech, fainting, convulsive clenching of teeth and limb contraction, connected with an abnormal state of the cervix (hystera), coming as a result of premature childbirth, prolonged sexual abstinence, etc. The next point is of particular interest – Mantias advised treating hysterical asphyxiation syndrome by playing a flute and beating a drum in the presence of the patient. In our opinion, this testifies to Mantias’ understanding of the disease as a psychosomatic condition and allows us to speak of him as a Platonist-rationalist follower.

The life and work of another prominent follower of Herophilus – Alexandrian physician Dioscorides Phacas – can be quite accurately dated. Dioscorides was a court physician for Ptolemy at the time of King Auletes and his famous children – Ptolemy XIII and Cleopatra (in the middle of the 1st century BC). Dioscorides mentions Gaius Julius Caesar in his diaries and is complimentary in his assessment of Galen. Later sources speak of Dioscorides – works by Paul of Aegina, and the Suda.<sup>3</sup> The Suda mentions 24 books on medicine by Dioscorides. Erotian, the renowned composer of the Hippocratic glossary, who lived during the time of Nero,

parses the polemical work of Dioscorides on Hippocratic lexicography in seven books. Dioscorides Phacas’ association with any of the schools of philosophy is difficult to determine due to insufficient sources. Our only guideline is his positive assessment of Galen’s work. On this basis, with a certain degree of doubt, we can consider Dioscorides as a follower of Herophilus.

Chrysermus, the renowned Alexandrian doctor of the 1st century BC, with whom Heraclides of Erythrae and Apollonius Mus studied, is usually referred to as a rationalist doctor and Herophilus follower. He devoted much attention to the theory of the pulse and the practical issues of pharmacology. He is known for his work dedicated to the treatment of suppuration of the parotid and salivary glands, as well as the creation of medical preparations in tablet form [28].

Sources often refer to the physician Apollonius Mus – Strabo wrote about him, he is quoted by Soranus, Athenaeus, Celsus, Plutarch, Pliny the Elder, he is mentioned by Hippocrates commentators John of Alexandria and Palladius. A contemporary of Strabo, Apollonius lived in Alexandria in the second half of the 1st century BC to the beginning of the 1st century AD. Three significant works of his are known – the doxographical treatise “On the school of Herophilus” in 29 books, the essay “On incense and ointments” and the pharmaceutical and clinical work “On conventional medicines” [33, 34]. Apollonius can be considered a supporter of “theoretical medicine”. His essay “On the school of Herophilus” is of particular interest, as it is apologetic of Herophilus’ approach to medicine. We draw attention to the fact that in the 1st century BC, similar doxographical works were written by a number of authors. Von Staden believes that the need for these works, which set out to defend the views of their authors via an appeal to ancient and respected tradition, arose due to the appearance on the historic proscenium of the Pneumatics’ and Methodists’ medical schools, which quickly gained popularity. Narrating on the work of Herophilus and his numerous followers, these doctors simultaneously presented their own views on the treatment of diseases, based on personal experience.

The essay “On incense and ointments” may be considered to only partially deal with issues of cosmetology: at that time the preparation of

<sup>3</sup> The renowned Byzantine encyclopedic dictionary, dating from about 1000.

pharmacological and cosmetic products was technically no different. In both cases, it was necessary to know the properties and effects of saffron, incense, rose oil, vinegar, nardus, olive oil, bitter almond oil, etc. Of course, the obvious commercial appeal of the production and sale of cosmetic products was important. Furthermore, as is the case now, topical therapeutic agents were used in cosmetics. A logical extension of this treatise is found in the essay “On conventional medicines”<sup>4</sup> [33, 34]. It can, with certain reservations, be called the Alexandrian practitioners’ directory of the 1st century BC. Apollonius introduced a set of detailed recommendations about treatment methods for common ailments – headache, toothache, dandruff, skin irritation, ear pain, infections of the oral cavity and more. The text of this book is a true guide to the world of Mediterranean medical botany. Galen, who was on the whole sympathetic to the works of Apollonius, focused on some of its recommendations that were exotic and demanding in nature [33, 34]. For example, to get rid of dandruff, Apollonius recommended wiping the head with bull or camel urine for a few days, and for a sore throat, he advised drinking hot urine of a donkey. Sneering at those recommendations, Galen rightly points out that patients are of sound mind and have an idea of hygiene, and cannot carry out such medical advice. Galen had grounds for more serious criticism of Apollonius Mus – the great Roman physician considered it necessary to have a clear indication for the use of every drug. Speaking of headache treatments, Apollonius adequately distinguished between different forms of headache, those caused by heat stroke, cold, intoxication, hangover, trauma (a fall or blow), etc. Actually, this was the essence of Galen’s polemic with empiricists: in his opinion, every disease had a cause, and the appropriate remedy was to act on this cause. A symptomatic approach, typical of empiricist doctors, ruled out a pathogenetic view of disease that was inherent in Galen. According to the great Roman physician, Apollonius Mus did not always provide details for his approach, as was the case with a headache. M. Wellmann found significant similarities between the work of Dioscorides “On simple

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<sup>4</sup> Sometimes its name is translated as “On readily available medicines”.

medicines” and more than 30 fragments from the works of Apollonius [22]. In our opinion, this fact is not critical, given the commonality of sources on which the majority of the ancient authors’ works were based.

Another famous student of Chrysermus – Heraclides of Erythrae – seems to have been a consistent supporter of the Hippocratic tradition and continued Herophilus’ work. We know that he wrote comments to the second, third and fourth books of Hippocrates’ “Epidemic” [35]. Apparently, it was not a glossary, but an actual commentary, refracting his own clinical experience through the prism of Hippocratic tradition. Galen argues that Heraclides was one of the first to properly interpret the sixth book of “Epidemic”, stating that it was uncharacteristic for Heraclides to talk nonsense [35]. However, Galen would not be Galen if he did not accuse Heraclides of “verbosity” and of occasional errors. Heraclides wrote the doxographical treatise “On the school of Herophilus” which consisted of seven books. Heraclides is known for his original interpretation of pulse theory: he returned to the concept of “diastole”, abandoning his teacher Chrysermus’ use of the term “diastasis”. For Chrysermus, the pulse only represented the stretching and contraction of the arteries, while Heraclides recognized the importance of cardiac activity in the formation of the pulse. Chrysermus believed that the pulse occurs “by virtue of spiritual and physical abilities”, Heraclides also added to this remark the dominant role of these abilities. Furthermore, he excluded from the definition of the pulse something that was an important characteristic for Chrysermus – the raising and lowering of the arterial wall, which generally indicates Heraclides’ more thorough understanding of the physiological nature of artery pulsation and allows us to consider him a staunch Hippocratic rationalist.

We have repeatedly pointed to the limited arsenal of therapies available to the ancient physician. However, this does not mean that for centuries this arsenal remained unchanged from the moment when the hands-on experience was recorded in the Hippocratic Corpus. This period described by us (the 3rd to 1st centuries BC is sometimes referred to in historiography as “medicine of the Hellenistic period”) saw significant advances in pharmacology.

Knowledge of medicines became a separate important branch of medicine, like dietology – historians are unanimous that dietology took on significance in the 4th century BC. Theophrastus, a pupil and successor of Aristotle (c. 371–287 BC), had already compiled a list of medicinal plants, significantly exceeding those that we see in the Hippocratic Corpus texts. In the 3rd to 2nd centuries BC, considerable attention was paid to the study of poisons, which is associated with the peculiarities of the political and military intrigues of the time. Diocles of Carystus suggested that poison, even when used in small quantities, could cause significant changes in the human body. Later, these ideas were developed by Erasistratus and Andreas of Alexandria. Doctor Mantias goes further and shows great skill in the preparation of complex multicomponent medications. We know of the pharmacist and the physician Apollodorus (c. 280 BC), who Nutton believes was the author of the first specialized study of poisons [9]. The well-known poet of antiquities Nicander (c. 180 BC), wrote two poems based on the research of Apollodorus – *Theriaca* and *Alexipharmaca*, which can also be regarded as important sources of information about the plant and animal poisons known at the time. The social context of this research helps to understand the surviving information about rulers' experience in this field. Attalus III Philometor Euergetes (who ruled from 138 to 133 BC) conducted pharmacological experiments with poisons on his slaves, and Mithridates VI of Pontus (132–63 BC) tried to protect himself from poisoning by regularly taking poison in small doses. The last example is well known to historians of antiquity, and demonstrates that by the middle of the 2nd century BC, Diocles' ideas had taken on the character of clinical-based recommendations – so firmly founded that the private physician could afford to offer them to influential patients. Moreover,

Mithridates VI's experiments can be considered quite successful: the creation of a multi-purpose antidote was established, named after the king – *mithridatium*. It is believed that while working on them, Mithridates' doctors followed the advice of the famous physician and botanist Crateus (c. 90 BC) – author of one of the first illustrated atlases of medicinal plants in the history of medicine.

Heraclides of Tarentum wrote a special treatise on preparation and quality control rules for drugs, and also compiled a practical collection of recipes related to military medicine. It is interesting that the first work was dedicated to a certain Antiochis. Nutton suggested that it was a female doctor, well known in her time.

It is concluded that the most famous doctors prior to the 1st century BC belonged to two medical schools – empiricists and rationalist-Hippocratists. Historiography accounts have repeatedly pointed out that regular anatomical dissection, characteristic for doctors' work in 3rd century BC Alexandria, disappeared from medical practice over the following centuries [36–38]. However, the reasons for this phenomenon cannot be considered fully clarified. We proceed from the possibility of empiricist doctors' conscientious objection to anatomical studies and lack of demand for Herophilus' legacy. The significant influence of the empiricists' school in the 3rd to 1st century BC, as we have shown above, supports this hypothesis. The impression that there was a certain predominance of the supporters of empirical medicine, from our point of view, requires an explanation.

In our earlier papers, we paid great attention to natural philosophy based on the teachings of the rationalists' medical school – the ideas of Plato and Aristotle. The next part of this article will be devoted to the views of empiricist doctors on principles of cognition.

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