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Medicine in the Hippocratic and post-Hippocratic age

Medicina u doba Hipokrata i posle Hipokrata

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Introduction

From a historical aspect, medicine is divided into pre-Hippocratic, Hippocratic, and post-Hippocratic medicine. Hippocratic medicine represents a period in which medicine developed under the influence of Hippocrates. The Hippocratic period includes the time when he lived, but also several centuries later. People who studied and practiced medicine according to his doctrine formed a kind of direction in medicine called Hippocratic medicine. It is not possible to precisely define the date range of the actuality of Hippocratic medicine, but its influence on medicine today is realistically immeasurable ¹.

Hippocrates was a Greek physician who lived from 460 to 377 BC and who belonged to the period of the highest scope of the classical Hellenic science of medicine. His father was Heraclides. He worked within the Medical School in Kos. He traveled extensively and died in Thessaly 1 . Hippocrates's portrait is shown in Figure 1 2 .

Hippocrates was the first to separate medicine from superstition, which was a kind of turning point in medicine. Because of that, he became a legend of medicine. The title "father of medicine" rightly belongs to him since it represents the prototype and ethical ideal of the doctor, who spoke about human life and the doctor's attitude towards the patient. He influenced medical practice centuries in advance. He put the patient at the center of the treatment process and the patient's well-being, that is, the welfare of the patient, as a priority in treatment. He believed that people were a part of nature and diseases were a natural phenomenon. According

to that belief, people were treated with natural methods. He believed that a man was treated, not a disease. He was the first doctor to ask a person how they felt. There are a lot of

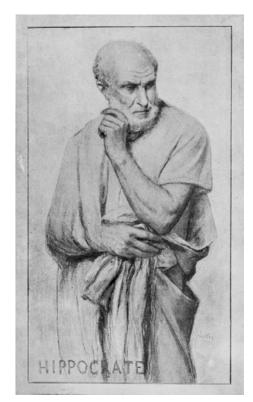


Fig. 1 – Hippocrates: portrait. Available from: https://schoolhistory.co.uk/early-modern/hippocrates/2.

valid terms and methods of treatment that he left us. He was the originator of the concept of humoral medicine, which marked the diagnosis and understanding of pathology until the end of the New Century. He individualized medical therapy and pioneered medical propaedeutic. Medical ethics, as we call it, began with him. He practiced surgery, orthopedics, pharmacology, diet therapy, and philosophy. A well known Hippocrates's aphorism is: "Human life is short, medical skill is enormous; a favorable moment passes quickly; experience is deceptive, making a decision is difficult" ¹.

After Hippocrates, medicine was marked by the Dogmatic and Alexandrian schools. The most valuable representatives of the Dogmatic school were Diocletian and Praxagoras. The Alexandrian school was marked by Herophilus and Erasistratus. Aristotle made a great contribution to medicine in this period. Another physician who marked the Hippocratic period was Galen. Galen was a Roman physician who was claimed to have lived between 125 and 215 AD. His life expectancy was almost three times longer than expected in the Old Century, which raises doubts about the reliability of this information. Like Hippocrates, Galen developed the idea of humoral medicine, which practically meant that human health was defined by body fluids. Galen influenced medicine so much that his name bears not only the vein but also the methods of preparing medicines in the pharmacy, and the prepared medicines are called Galena preparations. His teaching was considered dogmatic for 15 centuries. Roman medicine did not leave anything original on its own, except for a few personal discoveries. It mainly elaborated on the ideas and methods of Greek medicine. Notable Roman physicians in this period were Themison, Soranus, and Celsus 1,3.

It is important that the doctors of that time had open access to museums and other selections of archeological discoveries. The concept of pathogenic factors varied depending on the cultural context and historical period. In this sense, subdisciplines developed, such as paleopathology. Old methods and treatments that we neglected and overlooked may prove useful. Modern medicine should take into account past experiences in treatment, at least as a basis for research ⁴.

Ancient Greek medicine of the Hippocratic period

Greek medicine was a turning point in human treatment. The ancient Greeks separated medicine from superstition and divine manipulations and turned it towards a naturalistic concept. That paved the way for the development of scientific medicine, and in the 5th century BC, Greek doctors already had their own association. There were permanent doctors (demiurges) and traveling doctors (periodeutes). Demiurges performed interventions in surgeries, where patients sometimes stayed in recovery without charge. The concept of hospitals did not exist at the time, but it can be said that this was its beginning. Periodeutes went to places where there were no doctors, and they charged according to the agreement. In treatment, they

used herbs, examination, observation, and surgery, not prayers and spells. Nevertheless, Hippocrates made medicine a science ^{1,3,4}. The most famous schools of medicine were in Kos, Kroton, Cnidus, and Alexandria ^{1,5}.

Nemesius was the first to theorize about the division of the brain in the 4th century BC. He believed that feelings and imagination were located in two lateral chambers in the frontal lobe of the brain, and he called it the first cell. The mind was the function of the second cell, and in the posterior part of the brain was the third cell, which was in charge of remembering ⁶.

Chrysippus of Soli, who lived between 279 and 206 BC, was the first to mention cataract surgery ⁷.

Theophrastus is considered the father of botany. He wrote *De Causis Plantarum* and *De Historia Plantarum*, important collections of herbal medicines ⁸.

Hippocratic teaching

Hippocrates claimed that people were a part of nature. Hence, the disease had natural causes. He believed that climate, atmosphere, pollution, miasmatic fumes, food, colds, and other external influences significantly affected human health. He assessed the signs and symptoms by following human feelings as well as objective factors. He adjusted the therapy to the patient. A significant part of his treatment was diet therapy. Many aspects of which medicine is proud today, we really owe to him. The saying "Let food be your medicine" is attributed to him. He viewed people as beings who functioned in harmony with their environment. A person was treated as a complete being, and everything related to his external and internal interactions was seen as a factor of illness. Therefore, Hippocrates is considered the originator of the concept of holistic medicine. Today, holistic medicine is seen as the ideological forerunner of complementary medicine. He laid important foundations of medical ethics. Hippocrates did not distinguish veins from arteries. All blood vessels were called phlebes, hollow tubes. He understood the brain in the same way as Alcmaeon: its function was to analyze information from the outside world, which created our thoughts and feelings 1,8.

By the term 'neura', he meant fibers such as veins, nerves, tendons, and ligaments, and he believed there were also hollow neurons such as pores, which could be opened to enter fluid if necessary. He claimed that the compression of the leg caused pallor or blue discoloration of the extremities. He described how a carotid artery injury caused contralateral hemiplegia. He introduced inspection, palpation, and the primitive variant of auscultation ^{5–8}.

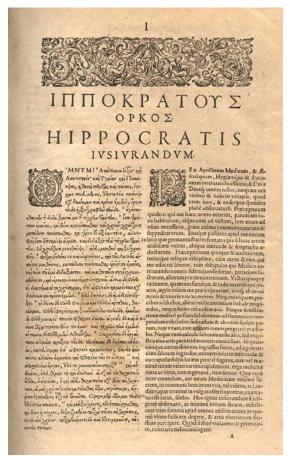
Hippocratic humoral medicine

Hippocrates based his teaching on Empedocles's idea of four elements: water, fire, air, and earth. Thus, humans were a phenomenon, a consequence of the activity of four fluids: blood, phlegm, and yellow and black bile. These liquids had four properties: hot, cold, dry, and wet. He believed that these aspects were governed by the force of physics. All

harmful liquids tended to be expelled from the body after cooking (pepsis), which gave a fever. All these aspects formed the disease, as well as the symptoms. He observed the appearance and behavior of the person and considered the examination to be the main moment in the treatment.

The famous *facies hippocratica*, *digiti hippocratica*, and much more were a consequence of his observation of patients. Practically, he laid the foundations of propaedeutics as the point of humoral medicine. Humoral means wet. In his treatment, he relied heavily on herbal medicines as essential elements of his work. Not only did he base his entire doctrine on that, but he also significantly influenced his students, particularly Galen, and Galen was practically the basis of Avicenna's work. Avicenna (Ibn Sina) gave his concept of four types of persons (choleric, phlegmatic, sanguine, and melancholic) based precisely on humoral medicine. The repercussions of this physical classification have not subsided to date, especially in psychiatry and psychology, even though they are no longer part of standardized diagnostics ⁸.

We learn about Hippocratic teaching from a work called the "Hippocratic Corpus" (*Corpus Hippocraticus*) ⁸ (Figure 2).



 $\label{eq:Fig.2-Corpus} Fig.\ 2-Corpus\ Hippocraticus.\ Available\ from: \\ https://schoolhistory.co.uk/early-modern/hippocrates/\ ^2.$

The "Hippocratic Corpus" is believed to have been compiled in the Library of Alexandria in 250 BC. It is a collection of 70 works in the ancient Greek language, which

mostly deal with medical issues. In addition to medicine, there are also philosophical texts. Authorship was not identified in the Old Century as it is today. Authorship had nothing to do with the creator but authority, which gave the concepts within which the work was created. If you established yourself as an authority, the work would be attributed to you.

Therefore, when we come across something that Hippocrates said, the chances that these were really his words are not that big. Entire texts were attributed to him. However, everything that was attributed to him was completely within the framework of his doctrine ⁸.

The works that are known to be his are: "Of the Epidemics", "The Book of Prognostics", "On Airs, Waters, and Places", "On the Sacred Disease (Epilepsy)", "On Ancient Medicine", "Aphorisms", and "The Hippocratic Oath" ^{1, 3, 8}.

Hippocrates's contribution to the understanding of specific diseases

The Hippocratic method for manual repositioning in glenohumeral dislocation and shoulder fractures is known and described in the section "On fractures": The upper arm is fixed in extension and under load while the patient is sitting. After returning the humerus, unless the head is broken, the bandages are dipped in oil, and the fracture is bandaged. The arm remains fixed for 40 days with diet therapy. The problem of poor healing was also pointed out. That clearly indicates that the students of the Hippocratic school understood the dynamics of articulation ^{3,8}.

The Hippocratic School saw diseases of the urinary tract as a problem in the swelling of the semen. It was thought that both men and women could suffer from it and that sometimes sex could be the cause. However, they had trouble distinguishing sexually transmitted diseases from other urinary tract diseases. Interestingly, they linked urinary tract disease to decay or spinal cord phthisis. The connection between seminal diseases and the condition of the spinal cord has survived to this day, even in popular culture and jargon. Here is an extract from the "Hippocratic Corpus", which illustrates how much Hippocratic doctors actually relied on inspection: "Most often it attacks the youth and those who like intercourse. They do not have a fever but still excrete something. If you ask the patient, he will say that he feels something coming from his head, down his spine, like ants. When he urinates or has a bowel movement, watery liquid comes out. He will not make children, and at night he urinates whether he has intercourse with a woman or not. When he walks or runs, especially uphill, he is out of breath, feels weak and dizzy, and it rings in his ears. When he finally gets a fever, he dies of it" 9.

In the section "On joints", from the book "Mohlikon", nasal injuries and the procedure of repositioning the nose were described ¹⁰. Traction therapy of scoliosis is still used today in the form it was proposed by the Hippocratic school ¹¹. The treatment of lower jaw dislocation was taken over from the Hippocratic school ¹². The term and description of clubbed fingers came from Hippocrates ¹³. Hippocrates considered urine a blood filtrate that had passed through the kidneys. In

the "Aphorisms", he stated that bubbles in fresh urine were a sign of long-term kidney disease, and urine sediment was a sign of fever ¹⁴.

Hippocrates coined the term *chylos*, and in the book "Peri Adenoma", he tried to explain lymphatics, calling them a branched and complex network ¹⁵. He associated sciatica with claudication and thought it was more common during summer, and prescribed rest and diet to the patient ¹⁶. He is thought to have performed abortions with a special instrument for that ¹⁷.

Ancient Greek medicine after Hippocrates

Hippocrates practically defined Greek medicine after the period of his work. His work was continued by his sons and a son-in-law. After him, two important schools of medicine stood out: Dogmatic and Alexandrian ¹⁸.

Dogmatic School

The Dogmatic School of Medicine considered the Hippocratic teachings a dogma, which was, ironically, diametrically opposed to the Hippocratic principle. The main teachers of the dogmatic school were Diocles, Praxagoras, and Crisipus. The Dogmatic School was the ideological and personnel predecessor of the Alexandrian school. Diocles wrote his first work on anatomy, the book "Anatomy". He practiced embryology and believed that both mother and father participated in the creation of embryos. They called him another Hippocrates. Praxagoras was Diocles's successor. He was the first Greek physician to deal with the pulse and the first to distinguish between arteries and veins. As Herophilus, who was his student, Praxagoras thought there was air in the arteries ^{1, 18}.

Aristotle was the son of the philosopher and mathematician Nicomachus. He was not a doctor but he knew about medicine and wrote about it. He claimed that the basis for a human being was determined by the father and the mother only gave what was needed for growth. In addition to the known four elements, he added the fifth – "the principle of life" ^{1, 18}. Aristotle thought that the heart was the center of emotions and intelligence. He thought that we learned from memory and with the help of feelings. In his book *Historia Animalium*, he gave the first description of the lymphatic system. He believed that some of the fibers between nerves and veins contained *sanies*, a colorless fluid ^{1, 15, 18}.

Alexandrian school

The Alexandrian School of Medicine was under the patronage of a pharaoh from the Ptolemaic dynasty. That means they were allowed vivisections and, in a short period of time, even dissecting people.

That influenced the accelerated development of clinical knowledge, primarily in the field of anatomy. The two most famous students were Herophilus and Erasistratus. The Alexandrian School also left vague anatomical descriptions concerning the lymphatic system ^{15, 18}.

Herophilus of Chalcedon is considered the father of anatomy as we know it today. He was born in 325 and died in 255

BC. He was a big name of the Alexandrian School of Medicine. He dissected human corpses, which led to comprehensive anatomical knowledge at the time. However, this practice was not allowed for a long time. He described the brain and spinal cord, as well as the seven nerves that came out of the brain. He explained the structure of the eye, described the intestines and gave the name to the duodenum. He distinguished between porous sensory fibers and hard fibers that moved muscles ^{15, 18}. Herophilus wrote the work "On the Eyes". He is thought to have discovered the optic nerve. He also practiced obstetrics and performed abortions with an instrument called 'fetal destroyer'. Demosthenes Philalethes, who wrote the work *Ophthalmicus* in the first century, was a student of Herophilus ^{7, 18}.

Crisipus was at the head of the Cnidian School. He worked between 320 and 280 BC. He wrote about the importance of vegetables in medicine, and he especially appreciated the cabbage compresses. He wrote the work "The Treatment of Vision". Unfortunately, that work has been lost. His grandfather and son bore the same name and were famous physicians ^{7, 18}.

Erasistratus of Chios was born in 304 and died in 250 BC. Erasistratus relied on Herophilus's anatomy, but his personal work was more based on physiology. He described 4 chambers of the brain. He claimed that the fourth ventricle was below the third and that it was used for communication. That was the first mention of a cerebral aqueduct in the literature. He compared the cerebral convolutions with the convolutions on the intestines, which indicated that he had seen them. He described the heart valves and thought they moved the blood in one direction. He claimed that the heart worked on the principle of a pump. He considered the ends of the arteries to be the beginnings of the veins. He thought there was only blood in the veins and that the arteries contained breath ^{5, 18}. Erasistratus rejected the humoral theory ^{1, 18}.

Roman medicine

Roman medicine was practically a continuation of Greek medicine. The Romans were often treated by Greek doctors. Ancient Rome relied on hygiene. The brothels were outside the towns, and the prostitutes were strictly controlled. Cemeteries and cremation sites were also outside the cities. They introduced sewerage and public baths. Spa healing literally originated from the Romans. In ancient Rome, being a doctor was a shameful occupation. They had the status of slaves. The only hospitals were *valetudinaria*, and these were places for the recovery of slaves so that their value would not fall. The first significant physician, who received civil rights, was Archagathus ^{1,18}.

Asclepiades of Bithynia was a famous Roman physician of Greek origin. He rejected the humoral theory and believed that solid parts of the body were more important than fluids in the human body ¹⁸. He believed that the human body was composed of pores and channels. He understood disease as the stagnation of atoms. That was called solidarity medicine ¹. Asclepiades was among the first to advocate a naturalistic approach to healing. He strongly opposed superstition in treatment and believed that the main medicines were heat, cold,

sun, and plants. He made balsams, medicines for the eyes and ears, vaginal suppositories, etc. ^{8, 18}.

Themison of Laodicea worked in the second half of the first century. His teacher was Asclepiades. He also adhered to solidarity medicine. As with Asclepiades, solidarity medicine meant that health was determined by solid parts of the body. It was important to strengthen the tone of the organism in order not to burden the sick person. For this purpose, baths, astringents, carrying in a stretcher, and massage were given. Themison relied on the systematic determination of the causes and consequences of the disease. For this reason, he founded the Methodic School. The Methodic School respected the solidarity medical principle ^{1, 18}.

Aulus Cornelius Celsus was a Roman physician who lived between 25 BC and 50 AD. He wrote a collection of eight books, *De Medicina* (Figure 3) ¹⁹.



Fig. 3 – De medicina, Celsus. Available from: https://www.historyofinformation.com/detail.php?id=1765 19.

It was the first saved manuscript in Latin, printed in 1478. He significantly influenced the spread of ancient medical thought in Renaissance Europe. He based his work on Hippocratic medicine ³. He was the first to identify four signs of inflammation: tumor, rubor, dolor, and calor ¹⁷.

His record of genital infections was interesting, and in the thirties of the new era, he described *profusio seminis*. He claimed that he based his medical information on Greek sources. Here is an extract for which he attributed the data to an anonymous Greek source: "In those who suffer from gonorrhea, we notice reluctant, constant swelling (*rhein*) of the semen (*gonos*), without pleasure. They decay, lose color and strength, get a fever with the loss of appetite, and their pulse weakens." As a remedy, he cited cold compresses with vinegar, rest, and not to lie on the back. He also left records about

cataracts and other eye diseases. He described the decapitation of the fetus with a metal hook during abortion ^{7, 9, 18}.

Soranus of Ephesus was the author of the first gynecology. He is considered to have been the greatest obstetrician of the Old Age. He wrote "The Biography of Hippocrates" ^{9, 18}.

Aretaeus of Cappadocia wrote the work "On Acute and Chronic Diseases" in the second century. Aretaeus claimed that apoplexy was the cause of paralysis. Furthermore, if the left side of the head was injured, the right side would be paralyzed and vice versa ^{9, 18}.

Rufus of Ephesus, who lived in the first and the second century of the new era, described the mesenteric, inguinal, and axillary lymph nodes and the thymus ^{9, 15, 18}.

Dioscorides was a Greek pharmacologist of the first century. He wrote the book *Materia medica*, which is considered to be the most important pharmacological book of the Old Century. It consists of five parts. It describes the procurement, preparation, and application of medicines from parts of plants, seeds, oils, metals, aromas, fruits, animals, waxes, milk, cereals, and minerals. He ground the ingredients in a special oven ^{8, 9, 15, 18}.

In the first and second century, unsigned Egyptian papyri of medical content were created based on the teachings of Hippocrates ^{7-9, 18}.

Galen

Galen was born in Pergamon, today's Bergama in Turkey. The exact year of birth and death are unknown but it is believed that he was born in 129 and died around 215 AD ¹⁸ (Figure 4).



Fig. 4 – Galen of Pergamum: an eighteenth-century portrait by George Paul Bush (The history of medicine, public domain image files).

He worked as a famous doctor for 50 years and as a surgeon of the gladiator Marcus Aurelius. He studied medicine in Alexandria and Smyrna 18. He considered the brain to be the center of emotions and intelligence. Since it was forbidden to dissect people in Rome, the fact that he was watching the dissection of corpses in Alexandria for four years was of undeniable importance for his knowledge 3, 18. Galen was a medical authority for almost 15 centuries, until the 17th century. Of the 600 texts that he wrote on over 1,300 pages, only a third survived. He introduced the experimental method into medicine, as well as research. He was known for his medical ethics. He contributed a lot to pharmacology and philosophy. He was notable as a good diagnostician. He relied heavily on the pulse in his diagnosis. He began to systematize the organs. He realized that blood was carried by the body through the vessels. He was the first to mention anastomoses between arteries and veins, but he thought it was a way of communication between arteries and veins globally, but he could not know where they were. He was called the "divine Galen" 19. He believed that three pneumas went through the liver, heart, and brain, which were separated from the blood vessels: natural, vital, and animal spirit. Natural went through the heart, animal through the liver, and vital through the brain ^{6, 9, 20}. He significantly influenced the development of Persian medicine. He later advocated Islamic medicine as well. In Avicenna's "Canon of Medicine", Galen was cited over 300 times 21. He believed that vital pneuma was created in the heart and carried by arteries to the brain, and then transformed into the animal one in the retiform plexus (a formation he claimed to have been localized near the pineal gland) ^{20, 21}.

Pneuma is actually what we would now call a ghost. Animal pneumas were stored in the ventricles of the brain. If necessary, it was the drive for the transmission of motor and sensory information to the periphery 18, 21. Galen believed that we received external information from the five senses - sight, hearing, touch, smell, and taste, which processed common sense and formed perception and thought. That process, according to him, took place in the brain chambers. By "internal processing", the thought would further have gone into the processes of memory, evaluation, cognition, and imagination. Practically, he laid the foundations of neuropsychiatry. That was one of the first descriptions of what we now call the perceptual process ²². Galen was a proponent of humoral medicine. Here is how he described the stroke: "The phlegm is cold and moist. When the blood vessels attract the phlegm into themselves, the body must calm down. If the phlegm prevails, the blood cools and gelatinizes. Then the person dies. The accumulation of phlegm blocks the animal pneuma. This causes dizziness, loss of consciousness, and possibly death. That is why, as we get older, there is more and more phlegm." That is why he considered cleansing from mucus or phlegm a priority, so hygiene and proper nutrition were a priority ²². He associated everything with stroke because stroke mainly occurred in old age, even today. What he considered old was not the same as what we consider today because life expectancy is getting longer ²².

Galen made a huge contribution to pharmacology. He acquired part of his knowledge from Dioscurides's book De Materia Medica. He wrote "On the Mixtures and Powers of Simple Drugs", "On the Composition of Drugs According to Kind", and "On the Composition of Drugs According to Places" 8, 23. He considered that breast cancer was a consequence of the accumulation of black bile and treated it with opium. He took it from Hippocrates 23. In the books De usu partium and De Anatomicis administrationibus, Galen described mesenteric lymph nodes, thymus, and pancreas. He distinguished between the milky and clear contents of the lymph nodes. He thought that Hippocrates's chyle was transmitted from the intestine to the liver through small branches of the portal vein in order to turn it into blood, which went to all tissues. He called this process anadosis. He thought, relying on Herophilus, that the pancreas and mesenteric lymph nodes fed the intestines 15, 23. He discovered that there was blood in the veins 15. He was the first to notice a double pulsus bisferiens and used it to diagnose 24. Interestingly, he called polyuria urine diarrhea¹⁴. Galen considered inflammation to be a struggle with the disease, and as a fifth sign, he added reduced function (functio laesa) 17,24. He put a lot of effort into experimental work in medicine. He tied nervus (n.) laryngeus recurrens to prove the assumption that it had a role in a pig's squealing. Due to such research in the creation of the voice, in his honor, the nerve loop between the posterior branch of n. laryngeus recurrens and the internal branch of n. laryngeus superior was called the Ansa Galeni. In fact, the scale of his work on dissecting animals instead of humans throughout his career led him to warn students of the potential differences in anatomy ²⁴. That also led to his errors in anatomical descriptions, unprovoked until the New Century 5. There was also a medical scholar named Pseudo-Galen. He lived around the time when he did, too, and got his name in that way. He wrote "Introduction Sive Medicus" 7, 22.

Medicine today, after Hippocrates, is becoming a complex science and the "art of healing" (ars medicina), based on scientific principles, biomedical research, contemporary medical technologies for modern diagnostics, and actual treatment ^{23, 24}.

Conclusion

The history of medicine is a science that deals with the traces of the past, which exist in the present. The history of Hippocratic medicine is not exact. A lot of works have been lost; we learn about many authors from the mentions of other authors, so we have to take their word for it. Doctors of that time, for the most part, were not allowed to dissect corpses. That is why there are a lot of anatomical errors. Even Galen's mistakes were widely discussed in world literature. However, due to the lack of imaging methods and limitations in dissection, the doctors of Hippocratic medicine left us extraordinary anatomical records. If it had not been for Hippocrates, for example, we would not have propaedeutic today because he was the one who laid the foundations of what is the essence of medical science today: rationalism, nature,

ethics, patient care, observation skills, and clinical experience. For centuries, Hippocrates and Galen's knowledge was considered the absolute truth. We learned a lot that allowed us to refute them. Precisely, constant suspicion and constant improvement of knowledge are the key elements to the progress of medicine. That is why it is important to know the history of medicine, especially the entire Hippocratic and post-Hippocratic period. The skill of observing the physicians of the Hippocratic period points us to things that today, perhaps due to reliance on image and laboratory methods, we professionally miss. Furthermore, there are forgotten pieces of information, which we can use again, or at least research further. It is enough to understand even

why mistakes were made sometimes. Today, malicious people are abusing the concept of holistic medicine and healthy eating to disavow the achievements of evidence-based medicine and promote pseudoscience and financial gain. In that way, people are deterred from visiting doctors, and trust in the medical profession and science is being actively destroyed. The duty of medicine as a science in the coming period dictates that we protect Hippocrates's legacy. We must not allow Hippocrates's teaching to be tarnished by someone's lucrative motives, even to the detriment of the patient's existence. The oath is the least that Hippocrates left us and intended in post-Hippocratic medicine.

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