

# Science in Greece: from the age of Hippocrates to the age of the genome

Matthew E. Falagas,<sup>\*,†,1</sup> Efstathia A. Zarkadoulia,<sup>\*</sup> Ioannis A. Bliziotis,<sup>\*</sup> and George Samonis<sup>‡</sup>

<sup>\*</sup>Alfa Institute of Biomedical Sciences (AIBS), Athens, Greece; <sup>†</sup>Department of Medicine, Tufts University School of Medicine, Boston, Massachusetts, USA; and <sup>‡</sup>Department of Medicine, University of Crete School of Medicine, Heraklion, Crete, Greece

## INTRODUCTION

THE CONTRIBUTIONS OF CLASSICAL GREEK CULTURE to science, including medicine, were considerable. Happily, Greece is again becoming a force in modern biomedicine. Bibliometric analysis shows that, compared to the rest of the world, Greece has achieved a steady, gradual increase in research productivity during the last 10 years both in absolute and relative terms. However, that increase has come in selected fields and despite the fact that the proportion of the gross domestic product (GDP) devoted to research and development has been stable at around 0.6% (i.e., 3–5 times lower than that of the European Community, the United States of America, and Japan, where the relevant values are 1.9%, 2.7%, and 2.9%). In addition, there are serious problems related to the adequacy of the infrastructure that supports research in Greece. This article outlines the classical contributions to biomedical science in the cradle of Western civilization and the state of science in Greece today.

## MEDICINE IN ANCIENT GREECE (1100–323 BCE)

### Preclassical era

Greek ancient history is divided into the Homeric (1100–750 BCE), the Archaic (750–480 BCE), and the Classical (480–323 BCE) periods. During these periods, medicine underwent considerable transformation and evolution. Earlier, during the Minoan (3500–1700 BCE) and Mycenaean (1600–1100 BCE) periods medicine was closely connected to religion and magic, since disease was solely attributed to gods who had the power to provide and destroy a human health (1).

Ancient Greek medicine was influenced by other civilizations, such as the Egyptian, Babylonian, and Indian. During the Homeric period (1100–750 BCE), various aspects of medicine were described (2, 3). In Homer's *Iliad* and *Odyssey*, there are descriptions of wounds and lesions and information about trauma management (2). The most developed sections of Homeric medicine were anatomy and traumatology.

Therapists of the time not only resorted to magic and exorcisms, but also used healing herbs and bandages for fractures, and performed surgical procedures.

Asclepius is considered the founder of ancient Greek medicine and he is depicted holding a rod with a snake coiled around it (4). He was sanctified during the 6th–5th centuries BCE (3, 5) and gave his name to the “Asclepiads” who were priests-healers serving in the “Asclepieia” (4, 5). Asclepiads exerted beneficial influence on patients suffering mainly from psychosomatic diseases. Asclepieia were both temples dedicated to Asclepius and healing centers (3–5). Asclepieia were located in scenic and rather isolated regions, near mountains or natural springs and can be imagined as modern spas (4, 5). They were well organized and many of them included a library, a stadium, and a theater (5). Moreover, medical schools existed within these temples (4, 5). Proper diet, baths, and exercise played key therapeutic roles (5). Asclepieia were still active even when medicine based on more scientific grounds took over in the 5th century BCE. Today there are remains of Asclepieia in Cos, Pergamos, Epidaurus, Cnidus, Corinth, Delphi, Aegina, and other locations.

### Naturalistic philosophy and the establishment of philosophical and medical schools

In the course of time, Greeks gradually became skeptical of the supernatural influence upon their well-being and became more interested in explaining natural phenomena and understanding human nature, life, and disease on grounds of rational thought. This innovative approach began in the 6th century BCE due to the development of naturalistic philosophy (1, 3). The Greek pre-Socratic philosophers tried to discover the true substance of life and the world (3). Notable representatives of naturalistic philosophy were Thales of Miletus, Anaximenes, Anaximander, Heraclitus, Empedocles, Pythagoras, Democritus, and others. Thales,

<sup>1</sup> Correspondence: Alfa Institute of Biomedical Sciences (AIBS), 9 Neapoleos St., Marousi 151 23, Greece. E-mail: m.falagas@aibs.gr  
doi: 10.1096/fj.06-1002ufm



Relief depicting Asclepius providing treatment to a recumbent patient (circa 400 BCE). From the archeological museum of Pireus (printed with permission).

Anaximander, and Heraclitus founded the Ionian School around the 7th century BCE, which influenced the evolution of sciences including medicine (1, 6). Pythagoras (580–489 BCE), who believed that the brain is the center of higher activities and introduced the importance of numbers, founded a school of philosophy in Croton in southern Italy (530 BCE) (1). Other significant schools of that time were the medical school of Cnidus in Asia Minor and the Coan School on the island of Cos. These two schools developed during the 5th century BCE (the school of Cnidus predates the one of Cos) and their leaders were Euryphon and Hippocrates, respectively (1, 6). There were differences between these schools, as the Coans focused more on the patient than the disease, insisted more on the prognosis than the diagnosis, and had a holistic-psychosomatic approach towards patients. On the other hand, the Cnidians focused more on the suffering organs and mainly observed the physical symptoms and signs of the diseases. Among the prominent physicians preceding Hippocrates were Alcmaeon of Croton, Empedocles, Demokedes, and Democretus (1, 3).

### The era of Hippocrates

Hippocrates (460–377 BCE) is the predominant physician of the classical period of Greek history (480–323 BCE). Part of this period is the “golden era” of the 5th century BCE during which significant progress was made in all fields of science and arts, such as the establishment of democracy (Pericles; 490–429 BCE), impartial recording of history (Thucydides, 460–400 BCE), creation of tragedies (Aeschylus, 526–456 BCE; Sophocles, 496–406 BCE; and Euripides, 480–406 BCE) and comedies (Aristophanes, 460–380 BCE), and progress in medicine. Hippocrates was born on the island of Cos and died at an old age in Larissa. He studied medicine under his father Heraclides who was a physician in the Asclepieion of Cos and Democretus. He traveled to many neighboring countries and created a famous medical school on Cos around 430 BCE (6, 7).

### Characteristics of Hippocratic medicine and contributions to medical science

Hippocrates took into consideration the existing knowledge of medicine and, incited by the movement of naturalistic philosophy, ultimately changed the course of medical study by becoming the leader of scientific medicine. He distinguished medicine from philosophy, setting medicine free from philosophical speculation, superstitions, magic, and religion. He supported the idea that medical treatment must depend on clinical observation and experimentation (1, 4–7). By searching for the natural causes of diseases and by recording the existing knowledge, he set the grounds for medicine to develop as a systematic science. The three fundamental principles of Hippocratic medicine were observation, experience, and rationale (1).

Hippocrates conceived the theory of the four bodily humours (i.e., blood, phlegm, yellow, and black bile) (2, 5). These humours correspond to four qualities, which are warmth, cold, dryness, and moisture. He also believed in the theory of the four elements (fire, air, water, earth). According to Hippocrates, health is the outcome of harmony among the four humours. This normal state is called *eukrasia*. Whenever this natural balance is disturbed, disease appears and the state of disharmony is called *dyskrasia*. Hippocrates saw the patient as an entity and examined the human as a whole, promoting the holistic approach in medical science (4). He proposed a detailed history taking from the patient and his environment, evaluation of the symptoms, the living conditions including age, sex, and behavioral features, and the outcomes of a meticulous clinical examination. Hippocrates’ methods of clinical



Temple-like relief depicting Asclepius treating the shoulder of a young man. The patient is also shown in the background asleep, while the holy snake tends to the wounded shoulder (first half of the 4th century BCE). From the archeological museum of Athens (printed with permission).

examination were inspection, direct auscultation, and palpation. Declaring that diseases are caused and influenced by natural laws, he believed the physician's role lies in helping the therapeutic power of nature, which gradually leads to restoration of a patient's health. The three famous clinical signs described by Hippocrates are the "Hippocratic face" of a patient approaching death, the "Hippocratic fingers" of patients suffering from cardiorespiratory syndromes, and the "Hippocratic *sisis*" (shake) in the case of thoracic suppuration.

He discussed epilepsy and in his treatise "On the Sacred Disease," he supported the idea that, like all other diseases, epilepsy had a natural cause and that its supposed divine origin stems from human inexperience (5). Hippocrates is also considered the father of environmental medicine because he pointed out that air and water may cause epidemics, and that food habits, climate, and occupation are connected with several diseases (5). He stressed the importance of proper diet and preferred to use drugs in moderation. Hippocrates's works are gathered in a collection named *Corpus Hippocraticum* which includes treatises written by him as well as his students (5). *Corpus Hippocraticum* discusses mental illness (1) and various medical specialties, such as anatomy (1), general pathology (1), gynecology and obstetrics (1), surgery (1, 2, 8), otorhinolaryngology (1), ophthalmology (9), and cardiology (4, 7).

In regard to cardiology, Hippocrates suggested that blood flows in a circle, described the manifestations of rheumatic fever, made clinical descriptions and expressed biological ideas pertaining to coronary thrombosis and stroke, and introduced the use of aspirin by recommending chewing willow tree leaves for analgesia (4, 7). He also described the anatomy of the heart, circadian rhythm, some cardiac risk factors (e.g., obesity), congestive heart failure, and sudden death. His works contain references to abdominal and thoracic paracentesis and acupuncture (4, 7).

As for the discipline of ophthalmology, several eye diseases and symptoms, such as pterygium, cellulites, ectropion, diseases of the cilia, prolapse of the iris, amaurosis, amblyopia, photopsia, and nystagmus, can be found in the *Corpus Hippocraticum* (9). Hippocrates contributed to the management of facial injuries—his treatise "Joints" contains information about diseases of the oral cavity, mandibular dislocation and fractures, depressed and deviated nasal fractures, and ear injuries (6).

Hippocrates is also considered the father of spinal surgery—he described the segments and the normal curves of the spine, the structure of vertebrae, the

tendons attached to them, and the blood supply to the spine (8). Kyphosis, scoliosis, concussion, dislocations of the vertebrae, and fractures of the spinous processes, are diseases of the spine that are described in the treatise "Joints." Because he made important diagnostic and clinical observations regarding the macroscopic examination of patients' urine (Hippocratic uroscopy) and differentiated upper from lower urinary tract infections, Hippocrates is considered the father of clinical nephrology (10). In the specialty of gynecology and obstetrics, he introduced the removal of protruding uterine fibroma via the vaginal route, the diastole of the cervical cavity with the use of metallic instruments and the abrasion of the uterus with pessaries.

Hippocrates believed that drugs should benefit or at least not harm the patient, that surgical approach is necessary whenever drugs prove to be ineffective, that in order to cure a patient the doctor should know him well, and that wherever there is love for the human being there is love for medicine as well. He was deeply concerned about medical ethics and although the Hippocratic Oath is wrongly attributed to him, it is certainly influenced by his teaching—the codes of medical conduct and attitude contained in the oath represent a priceless heritage. Along with issues, it refers to the ever-crucial matters of abortion, euthanasia, and medical confidentiality; and the universal declarations regarding peoples' (Genoa 1948) and patients' rights (Lisbon 1981) depend on the Hippocratic Oath.

## BIOMEDICAL RESEARCH IN MODERN GREECE

We performed a bibliometric analysis in order to estimate the biomedical research productivity in modern Greece. By making use of the PubMed search engine we identified the number of biomedical articles for the years 1995–2005 in which the first author's address was in Greece. The total number of articles originating in Greece was also calculated and compared with worldwide productivity. We used a methodology similar to other bibliometric studies performed by our group (11, 12). Search terms included in the address fields were Greece and major Greek cities. We also examined the percentage of publications originating from Greece that were categorized by PubMed as "journal articles," and excluded publication types, such as letters, editorials, and news reports.

In addition, we used the Essential Science Indicators (ESI) database of the Institute for Scientific Informa-

TABLE 1. Number and proportion of articles originating from Greece in PubMed database during the time period 1995–2005

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	TOTAL
Greek papers	1,026	1,149	1,286	1,441	1,452	1,853	2,201	2,372	2,689	3,209	3,844	22,522
World papers	433,323	443,627	441,900	460,375	479,150	520,513	532,280	551,809	582,607	622,096	672,996	5,740,676
% of total	0.24%	0.26%	0.29%	0.31%	0.30%	0.36%	0.41%	0.43%	0.46%	0.52%	0.57%	0.39%

TABLE 2. Absolute and relative research productivity of Greece in the 8 biomedical fields of the Essential Science Indicators (ESI) database, during the time periods 1995–1999 and 2000–2004

	Clinical medicine		Biology and biochemistry		Molecular biology and genetics	
	1995–1999	2000–2004	1995–1999	2000–2004	1995–1999	2000–2004
Greek papers	4,777	7,521	833	1,204	303	474
World papers	800,192	859,835	247,473	255,233	109,505	118,092
% of total	0.60%	0.87%	0.34%	0.47%	0.28%	0.40%
Greek citations	12,823	25,663	2529	4910	2,071	6,286
World citations	3,316,995	4,322,602	1,649,164	1,869,310	1,250,411	1,429,745
% of total	0.39%	0.59%	0.15%	0.26%	0.17%	0.44%
Greek citations/paper	2.68	3.41	3.03	4.07	6.83	13.26
World citations/paper	4.14	5.02	6.66	7.32	11.41	12.1
% of world average	64.73%	67.93%	45.50%	55.60%	59.86%	109.59%

tion (ISI). The ESI provides data from other ISI databases. Approximately 5000 journals were included in the ESI database for the 11-year period examined (January 1, 1995–December 31, 2005), categorized into 22 broad scientific categories. We focused our search on 9 biomedical categories: biology and biochemistry, clinical medicine, immunology, microbiology, molecular biology and genetics, multidisciplinary, neuroscience and behavior, psychiatry/psychology, and pharmacology and toxicology. ESI provides rankings of each country in each category based on scientific output indices. A cumulative citation count threshold is set by ESI in order to allow for a country to be included in the rankings of a scientific category.

Data pertaining to the total number of publications, total number of citations, as well as to the number of citations per paper was collected for Greece and compared with the relevant figures of the rest of the world. ESI provides some of the aforementioned data organized into 5-year periods. Thus, we evaluated the periods 1995–1999 and 2000–2004. It should be noted that articles attributed to a country are those in which at least one author's address is located in the country examined. Hence, publications that result from multinational cooperation are accredited to more than one country in the ESI database. Nevertheless, the absolute total number of articles of each scientific category, regardless of the country of origin, is also provided by the database.

**Table 1** presents the number of articles originating from Greece, as well as from the whole world for the years 1995–2005 and is based on data retrieved from PubMed (April 18, 2006). As shown, the proportion of biomedical articles of Greek origin gradually increased during the examined years. Overall 0.39% of all reviewed articles originated in Greece during the studied 11-year period. In all years from 2001–2005, the scientific output of Greece was higher than the average output for the study period. The relevant proportions and trends were similar when only the category of “journal articles” was evaluated, since in this subset analysis the first author was based in Greece in 0.43% of all 5,232,611 publications (full data not shown).

The analysis of biomedical research productivity of Greece adjusted for demographic and economic indices, namely total population and gross domestic product (GDP, in constant US 1995 dollars) suggests two facts. First, the proportions of articles and global GDP originating in Greece are almost identical (0.43% for research productivity during 1995–2005 and 0.41% for the GDP for the years 1995–2002 for which relevant data were available). Second, the proportion of articles originating in Greece (0.43%) is considerably higher than the proportion of the global population living in this country (0.18%, data from the World Bank). This is not surprising since not only its total population but also the welfare and the infrastructures of a country are important for research production. In addition, a great proportion of the global population lives in poverty, a situation that inhibits scientific activities and progress.

The research productivity of Greece and of the world during the periods 1995–1999 and 2000–2004 in 8 biomedical categories is presented in **Table 2**. Greece did not surpass the cumulative citation count threshold set by ESI for the 9th scientific category of interest, which includes articles published in multidisciplinary journals. As shown in Table 2, the proportion of articles in which authors from Greece participated during the 2nd period (2000–2004) was higher than that of the 1st period (1995–1999) in all categories evaluated. One may also note that the proportion of citations per paper for Greece is lower than the respective value for indexed articles from all areas of the world as a total (in 15 out of 16 comparisons). We found that the proportion of articles in which authors from Greece participated (as well as the relevant citations) was higher in the category of clinical medicine, compared to all other biomedical categories ( $P < 0.001$  by chi-square test).

## CONCLUSION

Despite the recent increase in research productivity, Greece has a long way to go to close the gap with countries such as the United States, Canada, the Scandinavian countries, and the Netherlands, in terms of

TABLE 2. (continued)

Neuroscience and behavior		Immunology		Microbiology		Psychiatry/psychology		Pharmacology and toxicology	
1995–1999	2000–2004	1995–1999	2000–2004	1995–1999	2000–2004	1995–1999	2000–2004	1995–1999	2000–2004
276	455	180	284	168	325	190	343	232	407
122,626	131,265	55,199	55,593	64,783	68,357	94,820	98,757	68,537	73,543
0.23%	0.35%	0.33%	0.51%	0.26%	0.48%	0.20%	0.35%	0.34%	0.55%
1,070	1,898	781	1,849	451	1,301	245	532	432	1,053
809,203	1,006,037	479,614	534,177	392,200	450,849	260,936	338,535	256,791	344,585
0.13%	0.19%	0.16%	0.35%	0.11%	0.29%	0.09%	0.16%	0.17%	0.31%
3.87	4.17	4.33	6.51	2.68	4	1.28	1.55	1.86	2.58
6.59	7.66	8.68	9.6	6.05	6.59	2.75	3.42	3.74	4.68
58.73%	54.44%	49.88%	67.81%	44.30%	60.70%	46.55%	45.32%	49.73%	55.13%

both quantity and quality of research productivity per capita. An increase in GDP would certainly help: a rising tide would lift all boats, including the ship of science. But a change in the cultural climate is also needed—an atmosphere of scholarship as in classical times that would encourage the scientists of the future to devote their lives to learning, science, and wisdom. The accomplishments of a handful of excellent scientific institutes and research groups in Greece already demonstrate that science can flourish and develop in modern Greece. Finally, scientists of Greek origin who live and work abroad are significant sources of inspiration and of training for domestic Greek scientists—an intranational exchange without borders.

## REFERENCES

1. Manolidis, L.S. (2002) Otorhinolaryngology through the works of Hippocrates. *ORL J. Otorhinolaryngol. Relat. Spec.* **64**, 152–156
2. Pikoulis, E. A., Petropoulos, J. C., and Tsigris, C. (2004) Trauma management in ancient Greece: value of surgical principles through the years. *World J. Surg.* **28**, 425–30. Epub.
3. Angeletti, L. R. (1991) Views of classical medicine. Theurgical and secular rational medicine in the healing-temples of ancient Greece. *Forum* (Genova). **1**, 1–11
4. Cheng, T. O. (2001) Hippocrates, cardiology, Confucius and the Yellow Emperor. *Int. J. Cardiol.* **81**, 219–233
5. Luce, J. V. (2001) Greek medicine from Asclepius to Hippocrates. *Ir. J. Med. Sci.* **170**, 200–202
6. Gahhaos F, Ariyan S. Facial fractures: Hippocratic management. *Head Neck Surg.* 1984 Jul-Aug;6(6):1007-13.
7. Cheng, T. O. (2001) Hippocrates and cardiology. *Am. Heart J.* **141**, 73–83
8. Marketos, S. G. Hippocrates. The father of spine surgery. *Spine* **24**, 1381–1387
9. Lascaratos J., and Marketos, S. (1988) Ophthalmological lore in the Corpus Hippocraticum. *Doc. Ophthalmol.* **68**, 35–45
10. Eknoyan, G. (1988) Origins of nephrology: Hippocrates, the father of clinical nephrology. *Am. J. Nephrol.* **8**, 498–507
11. Soteriades, E. S., Rosmarakis, E. S., Paraschakis, K., and Falagas, M. E. (2006) Research contribution of different world regions in the top 50 biomedical journals (1995–2002). *FASEB J.* **20**, 29–34
12. Bliziotis, I. A., Paraschakis, K., Vergidis, P. I., Karvasiou, A. I., and Falagas, M. E. (2005) Worldwide trends in quantity and quality of published articles in the field of infectious diseases. *BMC Infect Dis.* **5**, 16

The opinions expressed in editorials, essays, letters to the editor, and other articles comprising the Up Front section are those of the authors and do not necessarily reflect the opinions of FASEB or its constituent societies. The FASEB Journal welcomes all points of view and many voices. We look forward to hearing these in the form of op-ed pieces and/or letters from its readers addressed to journals@faseb.org.