

Hippocrates and cardiology

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Background Although Hippocrates has been traditionally recognized worldwide as the father of medicine, the fact that he was seminal in the development of cardiology is much less well appreciated. Therefore his role in forming the foundation of scientific practice of cardiology needs to be defined.

Methods This article was based on a personal 3-day visit in 1999 to the island of Kos, the birthplace of Hippocrates, and further research on the subject on return to the United States.

Results Considering the fact that all the references to the heart and diseases of the heart were recorded almost 2500 years ago at a time when knowledge of anatomy was fragmentary and pathophysiology practically nonexistent, Hippocrates had truly accomplished a remarkable task in describing the various disorders of the heart and blood vessels, defining the methods of diagnosis and treatment, and outlining the prognostic factors and preventive measures.

Conclusions Hippocrates was the pioneer in carefully documenting and thoughtfully interpreting case studies, an essential prerequisite to the coupling of clinical, physiologic, and pathologic features of diseases in the practice of cardiology that characterized the beginning of modern scientific medicine in the Renaissance. (*Am Heart J* 2001;141:173-83.)

Although Hippocrates has been traditionally recognized worldwide as the father of medicine, the fact that he was seminal in the development of cardiology is much less well appreciated. Recently I had an opportunity to visit the island of Kos, the birthplace of Hippocrates. I spent 3 days there and gathered much relevant information. On my return to the United States, I did further research on the subject. Following is my assessment of Hippocrates and his role in forming the foundations of the scientific practice of cardiology.

Pre-Hippocratic medicine

Medicine has existed on earth—either in the form of primitive medicine or magico-religious medicine—from the first days that humans appeared on the planet.¹ Religion and medicine, priest and physician, worked toward the same end: the defense of the individual against evil forces.² Ancient Greece during the pre-Hippocratic period was the time of the priestly Asclepian medicine. Asclepios is the Greek God of the healing art, who is also known by his more familiar Roman name Aesculapius, although Asklepios or Asclepius is the preferred spelling because it more closely transliterates the original Greek spelling of Ασκληπιος.³

According to earliest known writings, dated around 1500 BC, Aesculapius was the son of Apollo and his mortal mistress Coronis. Apollo killed Coronis in a fit of jealous rage after she was unfaithful to him. As her body was placed on the funeral pyre, he discovered that she was pregnant. He was stricken with remorse. He delivered their unborn child, Aesculapius, from her womb and gave him to Chiron, the centaur, to raise and to train in the art of healing.⁴ Aesculapius became the symbol of the healer in ancient Greek society and, later, throughout the Roman Empire. For centuries physicians were referred to as followers of Aesculapius.⁴ Hippocrates referred to himself as such and appealed to Aesculapius in the first line of the Hippocratic Oath (Figure 1).

To Asclepios were dedicated many therapeutic centers, temples around the Mediterranean Sea, the so-called Asclepieia.^{1,6} One such sanctuary of Asclepios existed on the island of Kos (Figure 2). Pre-Hippocratic medicine was based on religious belief, on surgery, and on regimen. The physician was closely connected with religion and was, predominantly, an herb gatherer.

Hippocratic medicine

Hippocrates (460 to c 375 BC) (Figure 3) was born on the island of Kos (Cos). This Greek island in the Aegean Sea, which is geographically much closer to Turkey across from Halicarnassus (now Bodrum) than Greece, is dedicated to its native son, although there is little evidence of his existence at the present time except for the plane tree under which Hippocrates is said to have instructed his students in the arts of empirical medicine

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Figure 1



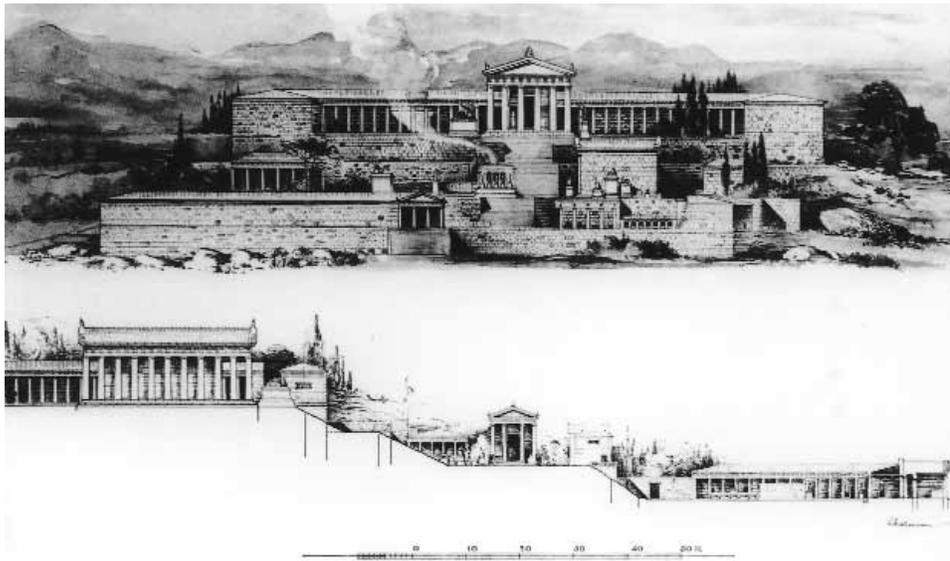
The Oath of Hippocrates in which Hippocrates referred to himself as a follower of Aesculapius and appealed to Aesculapius in the first line. The leaf on the bottom came from the Hippocratic tree on the island of Kos. This is, of course, not the original Oath of Hippocrates but a translated version I purchased at a shop near the Hippocratic tree. Of note is the absence of the quote "first do no harm" in this or other versions of the Hippocratic Oath. I was somewhat surprised when I could not find the quote in the Oath, because I have seen the quote cited frequently as such in reputable books and medical journals. The closest Hippocrates (or any of the unknown authors of the Hippocratic Corpus) came to expressing it is in the work *Epidemics* book I, where it is stated, "As to diseases, make a habit of two things—to help, or least to do no harm."⁵

and the attending moral responsibilities (Figure 4, A). The Hippocratic tree may well be one of Europe's oldest, if not the oldest, but certainly not old enough to have been there since the time of Hippocrates (probably a descendent of the original). The main trunk of the tree is almost 10 feet thick⁷; the tree is so old that it must be extensively supported by beams and marble pillars and protected by rails and fences. Its academic name is *Platanus orientalis*. I picked up several leaves that had landed outside the protective iron rail that circled the tree (Figure 4, B); to me, these leaves bridged

the gap between antiquity and the current era. Regardless of whether this was indeed the tree under which Hippocrates taught, the tradition is surely worth maintaining, and the tree should remain a living memorial to the greatest of the Greek physicians.⁷

Hippocrates is stated by Plato to have learned medicine from his father and grandfather; his father was supposedly a direct descendent of Asclepius, the god of healing, his mother of Herakles. Hippocrates was the first to distinguish between philosophy and medicine and to separate religion from scientific medicine. He

Figure 2



The Asclepieion on Kos, built after the 4th century BC, is laid out on three terraces. It is impressive as well as beautiful. (Reproduced with permission from Roy Porter's *The Cambridge Illustrated History of Medicine*, 1996.)

created the art and science of medicine and removed it from the realm of superstition and magic. Our medical terminology really begins with Hippocrates (his own name means “horse driver” from ἵππος, horse, plus κρατέέ, I govern) because he was the first to record terms in writing.⁸

Hippocratic medicine was based on a right way of thinking (rationalism) and on a whole, humane approach to the patient.⁹ The Hippocratic physician treated the whole patient, not only the organs of the body. It is obvious that when a sick patient was not cured by the rational medicine then an attempt was made to find healing in religious and/or alternative types of medicine, as occurs even today.

Hippocrates' writings on the heart

Hippocrates' writings on the heart contain some of the best clinical descriptions recorded in history. Descriptions of the heart and blood vessels, the method of their examination, coronary artery disease, cardiac risk factors, valvular heart disease, congestive heart failure, pulse, arrhythmias, sudden death and circadian rhythm, and the various therapeutic modalities including techniques of abdominal and thoracic paracentesis and acupuncture indicate that Hippocrates and other Greek physicians of the fifth century BC had experiences with many disorders of the heart.¹⁰

There are 70-odd books attributed to Hippocrates.^{10,11} But questions arose as to how many of them were actu-

ally written by Hippocrates. According to Katz and Katz,¹⁰

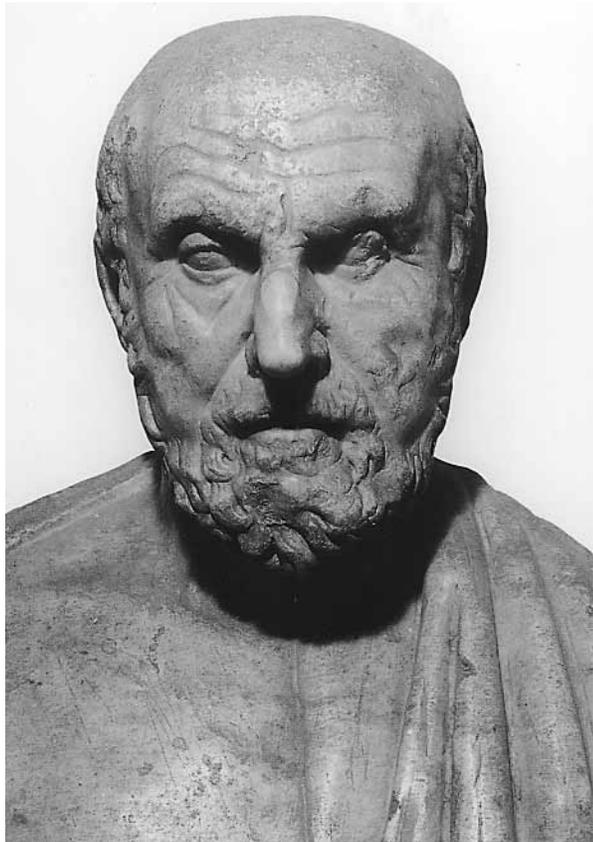
[i]t has been suggested that the Hippocratic collection might be the library of Hippocrates' school of medicine on the island of Cos (Jones, 1923-31).^[12] Several of the books are distinguished for their carefully recorded histories and detailed observations of the diseases then prevalent. These clinical books have been ascribed by some modern commentators to Hippocrates and the present paper follows the classification of Jones (1923-31) who regarded the books *Prognostic*, *Regimen in Acute Diseases*, and *Epidemics I and III* as likely to be genuine works of Hippocrates while *Aphorisms*, *Airs, Waters, Places*, *Fractures*, and *Wounds in the Head* are closely related to Hippocratic thoughts, if not genuine. Another aphoristic book that will be referred to is *Coan Prognostics*; this was probably written at the medical school of Cos during the early part of Hippocrates' lifetime and may represent the work of his teachers. The books *Diseases II* and *Internal Affections* were probably written at the medical school of Cnidus, on the mainland of Asia Minor, less than fifty miles from Cos, possibly during the lifetime of Hippocrates (Littré, 1839-1861; Jones, 1923-1931).

Heart or head

According to Katz and Katz,¹⁰ the location of the intellect was an important question being debated at the time of Hippocrates. They wrote:

Some writers placed consciousness in the heart while others said it rested in the brain. The author of a book that was closely related to Hippocratic thought supported the latter hypothesis: “the parts by the heart called ears [ὄτια, ie, the auricles] contribute nothing towards hearing. Some people

Figure 3



Bust of Hippocrates. (Courtesy of Professor S. G. Marketos, president of the International Hippocrates Foundation of Kos.)

say that it is the heart that is the organ with which we think and that it feels pain and anxiety. But it is not so . . . it is the brain which is the [interpreter of consciousness]" *The Sacred Disease* XX (Jones, 1923-1931).

On the other hand, a reference to pyogenic pericarditis complicating pneumonia appears to support the view that the heart is the seat of awareness by attributing unconsciousness to cardiac involvement: "In cases where the whole lung is inflamed, together with the heart . . . the patient is wholly paralyzed and lies cold and insensible. He dies on the second or third day." *Coan Prognostics* 395 (Littré 1839-1861; Chadwick and Mann, 1950^[13]).

The surgical book, *Wounds in the Head*, deals extensively with the effects of trauma and the contralateral paralysis resulting from head injury was clearly described: "if the patient has the lesion on the left side of the head, spasm seizes the right side of the body, if he has the lesion on the right side of the head, spasm seizes the left side of the body. Some also become apoplectic and die. . . ." *Wounds in the Head* XIX (Withington, 1927).^[14] From this, and similar references in *The Sacred Disease*, it is unlikely that Hippocrates considered consciousness to have resided in the heart.

But, in the treatise "*The Heart*" (vide infra), it was said "for man's intelligence, the principle which rules over the rest of the soul, is situated in the left ventricle."¹⁵

The heart and blood vessels

"*The Heart*"¹⁵ is an outstanding work in the Hippocratic Collection dealing with an anatomic subject; it is the first extant treatise to mention the pericardium, the four chambers and four valves of the heart, and the great vessels. According to "*The Heart*,"¹⁵

[i]n shape the heart is like a pyramid, in colour a deep crimson. It is enveloped in a smooth membrane. In this membrane there is a small quantity of fluid, rather like urine, giving one the impression that the heart moves in a kind of bladder. The purpose of the fluid is to protect the pulsation of the heart, but there is just about sufficient of it to alleviate the heat of the heart as well. The heart filters out this fluid after it has received it and made use of it, drinking it up from the lung. [What a succinct description of the pericardium except perhaps for the last sentence].

. . . The heart is an exceedingly strong muscle—"muscle" in the sense not of "tendon" but of a compressed mass of flesh. It contains in one circumference two separate cavities, one here, the other there. These cavities are quite dissimilar: the one on the right side lies face downwards, fitting closely against the other. By "right" I mean of course the right of the left side, since it is on the left side that the whole heart has its seat. Furthermore this chamber is very spacious, and much more hollow than the other. It does not extend to the extremity of the heart, but leaves the apex solid, being as it were stitched on outside.

The other cavity lies somewhat lower, and extends towards the line of the left nipple, which in fact is where its pulsation is observed. It has a thick surrounding wall, and is hollowed out inside to a cavity like that of a mortar. It is enwrapped and cushioned in the lung, and being surrounded by it, it controls and tempers its own heat. For the lung is both cold in itself and is also cooled by respiration.

The inside surface of both chambers is rough, as though slightly corroded; the left more so than the right, for the innate heat is not situated in the right. It is therefore quite to be expected that the left chamber should be rougher than the right, being filled as it is with untempered heat. Hence it is of such massive construction—to protect it against the strength of the heat.

The orifices of the cavities are not exposed until one cuts off the tops of the ears [By "ears" Hippocrates evidently means the auricles along with the atria because he does not otherwise refer to the atria] and removes the heads [ie, the base] from the heart. Once they are cut off, a pair of orifices for the two chambers is revealed. For the thick vein, running up from one, escapes our eye unless we dissect. [Dissection reveals four orifices, which are the sites of the four valves of the heart. The "thick vein" is the superior and inferior venae cavae.]

The independent contraction of the atria was described as follows: "Here is the evidence for my statement: you

Figure 4



A, The plane tree of Hippocrates in the shade of which Hippocrates taught in the 4th century BC and present-day merchants sit to make souvenirs for tourists. **B**, Several leaves from the tree that had landed outside the rails surrounding the tree.

can see the heart pulsating in its entirety, while the ears have a separate movement of their own as they inflate and collapse.”¹⁴

The following is the description of the heart valves from “*The Heart*”¹⁵:

The rest of my account will be concerned with the hidden membranes of the heart—a piece of craftsmanship deserving description above all others. There are membranes in the cavities, and fibres as well, spread out like cobwebs through the chambers of the heart and surrounding the orifices on all sides and emplanting filaments into the solid wall of the heart. [Hippocrates apparently recognized the chordae tendineae, the papillary muscles, and the trabeculae carneae.] In my opinion these serve as the guy-ropes and stays of the heart and its vessels, and as foundation to the arteries. Now there is a pair of these arteries, and on the entrance of each three membranes have been contrived, with their edges rounded to the approximate extent of a semicircle. When they come together it is wonderful so see how precisely they close off the entrance to the arteries. And if someone who fully understands their original arrangement removes the heart from a cadaver and while propping up one membrane he leans the other against it he will find that neither water nor air can be forced into the heart. This is especially true in the case of the membranes in the left chamber, which are engineered more precisely.

Hippocrates did not clearly distinguish the arteries from the veins and used the same term for both. As Katz and Katz¹⁰ described,

[f]or example, the temporal artery was described as a “large and thick vein (φλέψ) that extends through the temporal region,” *Wounds in the Head II* (Withington, 1927). The same root word described the vein in the antecubital fossa: “the bend of the elbow, about the bifurcation of the vein [φλεβος] which passes upwards along the [biceps] muscle.” *Fractures XLIV* (Withington, 1927). Necrosis following tight bandaging was discussed in relation to splinting of fractures, and a symptom of arterial occlusion was described: “Should minor veins be so compressed that the breath cannot pass through the vein, a numbness immediately seizes [that part of the body],” *The Sacred Disease VII* (Jones, 1923-1931). [It might be amusing to note such ancient terms as Galen’s “artery-like vein” which is the pulmonary artery and the “vein-like arteries” which are the pulmonary veins (Katz AM, personal communication).] One additional statement may be quoted from a book added to the Hippocratic collection by a later Greek writer. This indicates some understanding of vasomotor tone: “The changing colours [of the skin] are produced by the heart by constricting or relaxing the veins; when it relaxes them, the complexion becomes animated, of good colour and translucent; when it constricts them, pale and livid.” *The Nature of Bones XIX* (Littre, 1839-1861).

Although motion of blood in a circle had to wait for William Harvey for its full elucidation, the first suggestion that blood does circulate in this manner can be found in the Hippocratic Corpus.¹⁶ The following paragraph from this work¹⁷ appears to substantiate this premise:

The vessels communicate with one another and the blood

flows from one to another. I do not know where the commencement is to be found, for in a circle you can find neither commencement nor end, but from the heart the arteries take their origin and through the vessel, the blood is distributed to all the body, to which it gives warmth and life; they are the sources of human nature and are like rivers that purl through the body and supply the human body with life; the heart and the vessels are perpetually moving, and we may compare the movement of the blood with courses of rivers returning to their sources after a passage through numerous channels.

This paragraph not only demonstrates a loop concept but, in the analogy of “courses of rivers returning to their sources after a passage through numerous channels,” it also provides a concept of the microscopic anatomy of the capillaries.¹⁶

Another Hippocratic document, *On the Heart*, also describes several physiologic notions pertaining to the cardiovascular system: “The auricles regulate respiration . . . the vessels originating from the right ventricle supplies the lung with blood which serves as its nourishment . . . the blood leaks back through a weak pulmonary valve allowing some air to pass through in small quantity.”¹⁸ These statements are remarkable in that they antedate Galen’s conceptions by five centuries.¹⁶

Physical examination

As Katz and Katz¹⁰ told us,

Hippocrates’ clinical observations were unsurpassed in antiquity and his moderation in reaching conclusions remains an example even today. . . . Hippocrates was a strong advocate of the importance of physical contact between the physician and his patients. . . . Various parts of the body palpated, and sputum, urine, feces and other bodily secretions examined in detail.

The Hippocratic collection mentioned physical examination of the chest and auscultation. According to Katz and Katz,¹⁰

[t]he succussion splash was noted in empyema: “Those who, when shaken by the shoulder make a lot of noise. . . .” *Coan Prognostics 424* (Littre, 1839-1861; Chadwick and Mann, 1950) and this sign was utilized to locate the side of pleural effusions. Succussion was carried out as follows: “One seats [the patient] on an immobile stool; an assistant holds his arms, and you, shaking him by the shoulders, listen to which side the noise is heard.” *Diseases II XLVII* (Littre, 1839-1861). There are also references to the pleural friction rub: “a noise like two leather straps being rubbed together”; and to râles: “when the ear is held to the chest, and one listens for some time, it may be heard to seethe inside like the boiling of vinegar” (*Diseases II LIX and LXI* (Littre, 1839-1861).

The latter passage was also cited by Laennec in his “*A Treatise on the Diseases of the Chest*.”¹⁹ Therefore it is reasonable to suppose that Hippocrates indirectly inspired Laennec to invent the stethoscope.²⁰

Clubbing of the fingers (digitus hippocraticus or Hippocratic digits) was described by Hippocrates in cases of empyema, although not in cases of cyanotic congenital heart disease: "All sufferers from empyema may be distinguished by the following symptoms . . . the fingernails are bent and the fingers grow hot, especially at the tips." (*Prognostics XVII*).^{10,12}

Although Hippocrates did not actually feel the pulse at the wrist, vascular pulsation was mentioned by him.²¹ For example: pulsation of the temporal artery was noted: "in fevers, when the veins of the forehead are throbbing . . ." (*Coan Prognostics 125*).^{10,11,13} Ozanam cited several references to the pulse from the Hippocratic works.²¹

Hippocrates also described Cheyne-Stokes respiration when he said: "Respiration rare and large with long intervals, becoming afterwards short" (*Epidemics III*, case 5).¹⁰ "The breathing throughout, as though he were recollecting to do it, was rare and large" (*Epidemics I*, case 1).^{10,12} "The patient seemed to forget the necessity of breathing and then to remember it and breathe consciously."^{10,12}

Hippocrates was the originator of the eponym Hippocratic facies or "facies hippocratica" when he described the appearance of approaching death: "a sharp nose, hollow eyes, collapsed temples; the ears cold, contracted, and their lobes turned out; the skin about the forehead being rough, distended, and parched; the colour of the whole face being green, black, livid, or lead-coloured."⁸

Coronary artery disease

The Greek word for angina is κύνναγγη, which derives from κύων (dog) and ἄγγω (angina, literally "squeeze"). Galen considered this word to mean an inflammation of the throat, but it is clearly used to describe the choking symptom of tetanus and possibly of cardiac pain as well.¹⁰ The description of angina pectoris is often presented in very brief terms. For example, "Sharp pains, irradiating soon towards the clavicle and towards the back are fatal" (*Coan Prognostics*).^{10,11} "Frequent recurrence of cardialgia, in an elderly person announces sudden death" (*Coan Prognostics*).^{10,11} "Should, however, the pain show signs of extending to the collar bone or should there be a weight in the forearm, or in the region of the breast . . ." (*Regimen in Acute Disease XXII*).^{10,12} "In every movement of the body to rest at once when pain begins relieves the suffering" (*Aphorisms II*, 48).¹⁰⁻¹³

Although many kinds of pain react favorably to rest, this is certainly most characteristic of angina. The aggravation of angina by cold winds may be the subject of the following aphorism. According to Leibowitz,²²

[t]he aphorism denotes its Mediterranean origin and praises the salutary influence of a bracing northerly wind, so welcome in a hot country. However, in pointing to the less

agreeable consequences of this cold spell the author [Hippocrates] stresses its provocative and noxious influence on preexisting pain localized in the chest. This is a rather common clinical observation and fits again into the frame of precordial pain which is often provoked by walking against a cold wind.

This description by Hippocrates is certainly consistent with the characteristic features of angina pectoris as we understand them in modern times. It was unfortunate that those writers who have tried to trace the evolution of the medical knowledge of coronary artery disease have not for some reason used the information found in the Hippocratic writings. Perhaps it was Hippocrates' lack of mentioning the heart as the seat of the disease that was responsible for this neglect.²²

It is significant that Hippocrates also stressed the conjunction of chest pain with dyspnea.²² Patients with angina may have dyspnea without pain, known as blockpnea, which is an angina equivalent.²³ The word "blockpnea," coined by Gallavardin²⁴ in 1933, is a very descriptive term, although a somewhat awkward combination of Latin and Greek. This variety of angina is not rare, and, when identified, will lead straight to the correct diagnosis and appropriate treatment.²⁵

In a discussion of the causes of angina, Hippocrates may have been describing myocardial infarction when he wrote: "Angina is serious and rapidly fatal when no lesion is to be seen in either throat or neck, and moreover, it causes very great pain and orthopnea; it may suffocate the patient even on the first day, or on the second, third or fourth" (*Prognostics XXIII*).^{10,12}

Of course, Hippocrates' view on the myocardium that "the heart is an exceedingly strong muscle"¹⁵ (vide supra) had an important bearing in the history of myocardial infarction.

The most provocative statement made by the followers of Asclepiades is that "cardiac disease is an inflammation in the region of the heart due to a heaping-up or stoppage of the corpuscles."²² This inflammatory theory of atherosclerosis antedated the current debate on the role of inflammation in coronary atherosclerosis²⁶ by 2500 years!

Obesity as a cardiac risk factor

That obesity is a risk factor in coronary artery disease was recognized by Hippocrates. In *Aphorism 44* he pointed out the shortened life expectancy of the obese compared with those who were slender.^{10,12} To think that he came to this conclusion without benefit of the computerized actuarial statistics so beloved by the life insurance companies of today!¹⁶ Hippocrates condemned overeating: "Repletion, carried to extremes, is perilous" (*Aphorisms I*),^{10,12} and warned against exercise after eating: "Fat people who want to reduce should take their exercise on an empty stomach."²⁷

According to Katz and Katz,¹⁰

the correlation between overweight and atherosclerosis may have been responsible for the following statements, made in a catalogue of the infections and constitutional diseases that occur in temperate and tropical climates: "A city that lies exposed to the hot winds. . . . Most of [the inhabitants] have a rather flabby physique. . . . When they are more than fifty years old they are paralyzed by catarrhs supervening from the brain. . . ." "But the following is the condition of cities with the opposite situation, facing cold winds. . . . The natives must be sinewy and spare. . . . These men were more likely to be long-lived than are others." *Airs, Waters, Places* III, IV (Jones, 1923-1931). The conclusion in this work was that climate influenced both body habitus and longevity. A modern interpretation of the same observations would probably be that obesity predisposed to cerebrovascular disease and the slender person is likely to outlive his heavier neighbour.

Valvular heart disease

Rheumatic fever existed in Hippocrates' time. According to Katz and Katz,¹⁰

[i]n the paragraph following a discussion of the diseases of the throat, Hippocrates wrote: "If a fever be protracted, although the patient is in a state indicating recovery, and pain does not persist through inflammation or any other obvious cause, you may expect an abscession, with swelling and pain, to one of the joints, especially to the lower ones . . . other descriptions indicate the appearance of rheumatic nodules as well as arthritis: "in protracted fevers, tumours and pains at the joints come on" *Aphorisms VII*, 64 (Jones, 1923-1931). The author of another work in the Hippocratic collection, referred to previously, provides the most convincing description of acute rheumatic fever: "In arthritis, fever sets in, sharp pains seize the joints of the body; and these pains, often sharper, often milder, attack one joint, then another [a typical description of migratory polyarthritis. Hippocrates' succinct description of two major (subcutaneous nodules and migratory polyarthritis) or one major (subcutaneous nodules or migratory polyarthritis) and two minor Jones criteria (fever, arthralgia, or previous rheumatic fever) certainly met the current criteria for the diagnosis of rheumatic fever.²⁸]. . . . If rheumatic fever was prevalent in Greece at this time, one might expect to recognize rheumatic heart disease as it appears in young adults. Such a case is that of heart failure occurring in pregnancy: "Harpalida's sister, in the fourth or fifth month of her pregnancy, had watery swellings in her legs, swellings in the hollows of her eyes, and her whole body puffed up. . . . Besides these she had a dry cough, sometimes orthopnoea, dyspnoea and suffocation. Sometimes she was so near to suffocation that she was obliged to sit up in her bed without being able to lie down; and if she tried to sleep it was in a sitting position. Yet there was not much fever. For a long time the foetus did not move, as if it were dead. . . ." *Epidemics VII VI* (Littre, 1839-1861; Clifton, 1734^[29]). . . . dyspnoea lasted for two months, resolving at the same time she was delivered of a child. [The description would be typical for a patient with rheumatic mitral stenosis developing symptoms as a consequence of expanded blood volume typically seen during the second trimester of pregnancy and recovering spontaneously post partum.]

Mitral valve prolapse is the most common valve disorder in the United States.³⁰ It occurs in 50% of patients with Behçet's disease.³¹ Although the triad of iritis and mucocutaneous and genital ulcers, known as the Behçet's disease, was named after the Turkish dermatologist from Istanbul, Hulusi Behçet, who first encountered such a patient in 1924,³² the symptoms of this disease was actually reported by Hippocrates in his third book of epidemiology: "There were other forms of fever. . . . Many developed aphthae, ulcerations. Many ulcerations about the genital parts. . . . Watery ophthalmies of a chronic character, with pains; fungus excretions of the eyelids externally, internally, which destroyed the sight of many persons. . . . There were fungous growths on ulcers, and on those localized on the genital organs. Many anthraxes through the summer . . . other great affections; many large herpes."³³

Although Hippocrates did not mention the association of mitral valve prolapse, it is well known that there is a high prevalence of mitral valve prolapse in patients with Behçet's disease, first reported from China in 1985.³⁴ Behçet's disease occurs most frequently in Japan and the Mediterranean countries but also in the population linking these two areas to each other. It occurs most frequently between latitudes 30 degrees and 45 degrees north, in Asian and Eurasian populations.³⁴ This area coincides with the old Silk Route. Thus Behçet's disease is often called the "Silk Route disease."³⁴

Heart failure

The writings attributed to Hippocrates include dozens of clinical case histories, some of which probably represent descriptions of heart failure.¹⁰ These books contain examples of dyspnea that could represent left heart failure and of dropsy that could represent right heart failure. Hippocrates viewed dyspnea as the result of "phlegm" (the cold humor) passing from the brain to the heart. As Katz and Katz¹⁰ mentioned,

for when the phlegm descends cold to the lungs and heart, the blood is chilled; and the veins, being forcibly chilled, beat against the lungs and heart, and the heart palpitates, so that under this compulsion difficulty of breathing and orthopnoea result. *The Sacred Disease IX* (Jones, 1923-1931).

An excellent description of what may be congestive heart failure with cardiac cirrhosis is found in one of the *Cnidan* books: "[the patient] appears yellow; the whole body is edematous; the face is red; the mouth dry; he is thirsty; and when he eats, respiration quickens. In the same day at some times he may appear better while at others he is suffering acutely and seems on the verge of dying" (*Internal Affections XXI*).^{10,11}

Hippocrates distinguished between the soft pitting edema of the legs seen in chronic heart failure and the indurated edema in acute cellulitis: "Swellings that are painful, big and hard indicate a danger of death in the near future; such as are soft and painless, yielding to

the pressure of the finger, are of a more chronic character" (*Prognostics VII*).^{10,12}

Hippocrates also provided an important description of the wasting of the body ("cardiac cachexia") in patients with heart failure. As mentioned by Katz and Katz,¹⁰

[d]ropsy is usually produced when the patient remains for a long time with impurities of the body following a long illness. The flesh is consumed and becomes water . . . the abdomen fills with water; the feet and legs swell, the shoulders, clavicles, chest and thighs melt away. If you begin treatment at the beginning, before the accumulation of water becomes excessive, you must administer purgatives which evacuate water or phlegm . . . the regimen of food, drink, exercise and walking will be until the patient becomes thin and dry, but only until the flesh becomes as strong as possible . . .

Hippocrates used paracentesis, thoracocentesis, and acupuncture in the management of advanced heart failure. As mentioned by Katz and Katz,¹⁰

[i]f the patient is relieved by the medication, and the rest of this regimen, the abdomen may be emptied as well; if not, one drains off the water by means of an incision; the incision used is either beside the umbilicus or behind at the flank." *Affections XXII (Littre, 1839-1861)*. Further comment about paracentesis is found in a sophisticated essay of the Hippocratic collection probably written during Hippocrates' lifetime: "Patients [suffering from dropsy] already at death's door are pumped dry of the water. Now the water appears to come copiously from the cavity at first, becoming less plentiful after a time. . . . When the cavity has been completely emptied, not even three days elapse before [it is] full again." *Breatbs XII (Jones, 1923-1931)*. . . . Directions for . . . thoracocentesis are found in one of the Cnidan works: "Incise over the third rib, down to the bone; then drill through the rib with a trephine. The perforation completed, remove a little water, and after the evacuation, put in a plug of raw flax, and over this, a soft sponge; you must then apply a bandage so that the plug does not fall out. You must take off the water over a period of twelve days, once daily; after the twelve days, on the thirteenth, evaluate all of the water. For the remaining time, if more water forms, you must remove it . . ." *Internal Affections XXIII (Littre, 1839-1861)*. Hippocrates warned of the danger of too rapid drainage by thoracocentesis or paracentesis: "Those cases of empyema or dropsy which are treated by incision or cautery, if the water or pus flow rapidly, all at once, prove fatal." *Aphorisms VI 27 (Littre, 1839-1861; Jones, 1923-1931; Adams, 1849^[35])*. At the conclusion of the passage describing thoracocentesis, acupuncture was advised in cases where edema arose as a complication: "If the genitals and thighs become edematous, one must, without fear, scarify them." *Internal Affections XXIII (Littre, 1839-1861)*.

Hippocrates also recommended venesection and dietary therapy in the treatment of heart failure. One example of the latter was written as an aphorism: "Starving should be recommended for persons with moist flesh, for starving dries bodies. (*Aphorisms VII, 60*)^[12]."¹⁰ Although Hippocrates was aware of the

diuretic effect of strong wine, which "passes readily into the bladder,"¹² he did not mention its use in heart failure.¹⁰

Pulse, arrhythmias, syncope, and sudden death

It has been recorded by Galen that Hippocrates was the first to use the word "pulse."³⁶ In the *Corpus Hippocraticum* one can find references such as "In the most acute fevers the veins around the umbilicus pulsate with greater strength and frequency."³⁷ A reference to arrhythmias was present in the comment that "there was violent palpitations of the heart" (*Epidemics III, case 16*).¹²

Cardiogenic syncopal attacks were described in one of Hippocrates' aphorisms: "Those who suffer from frequent and strong faints without any manifest cause, die suddenly" (*Aphorisms II, 41*).^{10,12,13,22} "This appears to be Adams-Stokes syndrome, although Hippocrates would not have noted the slow pulse if, indeed, he was referring to cases with complete heart block."¹⁰

Hippocrates also made other references to sudden deaths resulting from cardiovascular causes: "Heart pain which occurs frequently in an elderly man indicates sudden death" (*Coan Prognosis*)³⁸; "Pain at the mouth of a ventricle, accompanied by a swollen precordium and headache is sometimes malignant and causes some shortness of breath. For they suddenly die, as in the case of Dysodes"³⁸; "Those who have lost blood and who have subsequently suffered rigors and malignant sores die unexpectedly even when in conversation" (*Coan Prognoses*)³⁸; "Those who by nature are somewhat stout die sooner than those who are lean."³⁸

Circadian rhythm and seasonal variation

That circadian rhythm (from the Latin *circa diem*, meaning "about a day"³⁹) and seasonal variation affect many physiologic and biochemical parameters of the body has been in recent years well documented in cardiology—in acute myocardial infarction, acute coronary syndromes, sudden cardiac death, and thrombotic stroke.⁴⁰ Hippocrates theorized nearly 2500 years ago that the seasons affected the human constitution and various physiologic functions: "Every disease occurs at all seasons of the year but some of them occur more frequently and are of greater severity at certain times" (*Aphorism*).²⁷ This theory of Hippocrates is clearly an early precursor of the modern idea of circadian rhythm and seasonal variation of diseases.

Although romanticists may argue that the heart influences the head, Hippocrates long ago postulated that the reverse might also be true. Modulation by the autonomic nervous system, hormone release, and a variety of other possible pathways offers a potential mechanism by which the chronobiologic rhythms controlled by the suprachiasmatic nucleus could affect cardiovascular events, including sudden cardiac death.⁴¹

Conclusion

It has been said that Hippocrates did for medicine what Socrates and Plato did for philosophy.⁴² From the writings of Plato we may gather many details about the status of physicians in his time. It is evident that the medical profession had been progressively developing for a long time before Hippocrates. But it was Hippocrates who developed medicine as a science. The critical sense and skeptical attitude of the Hippocratic school laid the foundation of modern medicine on broad lines, and we owe it for this.

Hippocrates left his mark on the course of history and a great deal can be learned by studying his works and following his example. Many of the teachings attributed to him may have been written by his disciples, but they are nonetheless significant because they are based on his method and describe the different procedures used for treating diseases. Perhaps most important, he was the first known practitioner to adopt a rational method in diagnosis and therapy, which subsequently developed into the scientific method of today.

In Hippocrates' time medicine was also practiced by priests and was seen more or less as a magical art.²⁷ Hippocrates, however, said that "the gods rule in heaven and earth, but their fateful influence is remote. In medicine, natural causes immediately prevail. Diseases are natural events. They must be observed, followed, and treated by natural means. The place of the physician is not in the temple but at the bedside."⁴³

Hippocrates knew that as long as the art of medicine was kept secret it could make no real progress or offer any real benefit for humanity. He was the first to make the precious gift of medicine available to all by publicizing all the aspects that were at that time kept secret and establishing clinical practice based on human values. Consequently physicians in subsequent centuries were able to follow his examples and developed his methods and theories.²⁷ Hippocrates is the visual personification of the oft-quoted Chinese proverb "To plan for a year, plant rice; to plan for a decade, plant acorns; to plan for a century, teach men." Thus it was no exaggeration that in the first century AD Galen in Greece and Celsus in Rome were popularly known as "the second Hippocrates" and the "Roman Hippocrates," respectively. In the 10th century Avicenna was called the "Persian Hippocrates," in the 17th century Sydenham was called the "English Hippocrates," in the 19th century Lannec was called the "French Hippocrates," and in the 20th century Osler was known as the "Canadian Hippocrates."²⁷

Considering the fact that all the references to the heart and diseases of the heart were recorded almost 2500 years ago at a time when knowledge of anatomy was fragmentary and of pathophysiology practically nonexistent, Hippocrates had truly accomplished a remarkable

task in describing the various disorders of the heart and blood vessels, defining the methods of diagnosis and treatment, and outlining the prognostic factors and preventive measures. He was the pioneer in carefully documenting and thoughtfully interpreting case studies, an essential prerequisite to the coupling of clinical, physiologic, and pathologic features of diseases in the practice of cardiology that characterized the beginning of modern scientific medicine in the Renaissance.

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