

Chapter 2

The Cardiovascular System and Its Modes of Operation

ὁμοιον γάρ τό τ' ἐν τῇ δεξιᾷ κοιλίᾳ τῆς
χαρδίας αἷμα καί τὸ κατὰ πάσας τὰς
φλέβας ὅλῳ τῷ ξώῳ. καθάπερ γε καί τὸ
κατὰ τὰς ἀρτηρίας ἀπάσας ὁμοιόν ἐστι
τῷ κατὰ τὴν ἀριστερὰν κοιλίαν.

— Galenus (ca. 131–ca. 201, first name unclear).
From Kühn, vol. v, p. 537, 1823.

Digest: The oldest known symbols for the heart are reproduced. King Hammurabi's code introduces legal liability, which makes Mesopotamian medicine literally superficial and stimulates development of mathematical and astronomical studies instead, unlike concurrent Egyptian developments in medicine. After a long interlude, Greek civilization takes over and Hippocrates assembles his *Corpus*, which assimilates old Egyptian knowledge, but does not offer a comprehensive concept for the operation of the cardiovascular system. Erasistratos subsequently develops such a concept, which is only known through Galenós after the modifications he introduces in it. The Galenic concept survives until Caesalpinus and Harvey replace it by proposing that the same blood circulates in a closed loop. The heart becomes the central and only pump to sustain this circulation, though a number of researchers become convinced that it is too weak to assume this responsibility alone and suggest that other mechanisms must be existent to provide support. Liebau shows empirically that steady flow can be induced in a closed circuit free of valves and ventures to suggest that cardiac valves may be superfluous. This eventually leads to the concept of impedance-defined flow and offers a quantitative mathematics based interpretation of flow phenomena not considered possible at the time.

The cardiovascular system continues to reveal additional flexibility.

2.1 Antiquity

2.1.1 Introduction

In the civilizations that developed in major river valleys such as the fertile Euphrates-Tigris and Nile regions, curiosity and training of the human mind led to the formation of cultures. The dawn of Western science and thinking may be traced to these valleys. Some of what these people knew and thought may have roots in even older centers of civilization (Table 1.1).

In the centers of cultural activity in Mesopotamia and Egypt, awareness of the beating heart may well have preceded the development of script, because pictograms of the heart appear in the oldest known forms of writing. Figure 2.1 shows the development of the Sumerian pictogram (about 2500 BCE) to late Assyrian and Babylonian (around 500 BCE) cuneiform. Likewise, during the earliest Egyptian dynasties (2900–2700 BCE) hieroglyphs for the heart were employed; they display their own development. In both river valleys, the peripheral arterial pulse was palpated, indicating factual knowledge of at least a few of the locations where the pulse can be felt.

2.2 Mesopotamia

No evidence has been found of any Mesopotamian concept of the circulation: the heart beat and the appearance of the peripheral arterial pulse were not perceived in a cause and effect relation. Instead, the peripheral pulse was used to help identify the nature of the sickness and the likelihood of the patient's recovery. Information from the venous system was also utilized since the color, degree of filling, and the distribution of superficial veins were noted in pregnant women as well as on

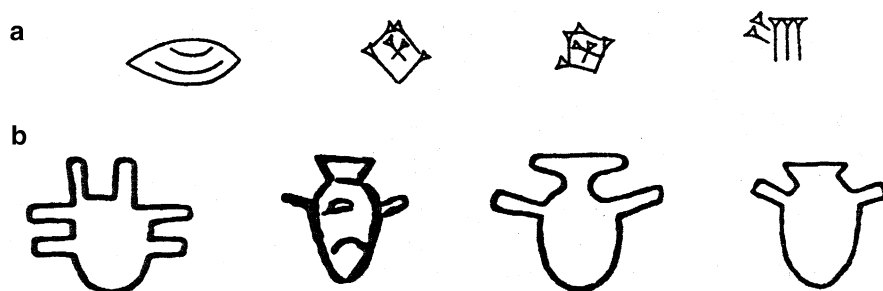


Fig. 2.1 (a) The heart from Sumerian pictogram (at left) to late Assyrian and Babylonian cuneiform. (b) Hieroglyphs for the heart during the first two Egyptian dynasties (2900–2700 BCE) (Reprinted by permission of the publisher from Majno. Copyright @ 1975 by the President and Fellows of Harvard College)

swollen feet. Instead of considering the heart as a pump, it was viewed as the seat of intelligence (Majno 1975).

In Nineveh, tablets have been found which claim that King Assurbanipal registered the three ways available to people who fall sick: healing with drugs, surgery with a brass knife, and prescriptions by sorcerers (Majno 1975). If treatments were recorded, virtually all were anonymous (Leichty 1988). Much of this dealt with superficial wounds, nothing with major surgery. As a consequence, it is not surprising that insight in the anatomy and operation of the cardiovascular system hardly evolved.

The reason for being circumspect about surgical intervention is found in the code assembled by the Babylonian King Hammurabi. This code contains 282 laws, chiseled in a large black stone of diorite around 1700 BCE. The separate laws are traditionally referred to as paragraphs.

Figure 2.2a shows a reproduction of a small part of the original text (Harper 1904), while Fig. 2.2b reproduces Harper's transliteration and translation of paragraph 215. This paragraph is just one example of where the law sets the physician's fee for performing a specific, successful, operation. Ten shekels have been estimated as covering the labor cost of building a substantial house (Majno 1975). The risk of performing surgery is defined in paragraph 218 (Fig. 2.2c). Hammurabi's code tends to mete out severe penalties for failure. There was no liability involved in the administration of drugs or with prescriptions ordered by a physician or a sorcerer. Taking no action at all was not considered malpractice. This may represent the first instance of an effort to distinguish between invasive and noninvasive treatment (Noordergraaf A 1998).

Mesopotamian medicine comes across as restrictive. Little progress appears to have been made over a period of many centuries after their civilization peaked during the period of around 1800–1600 BCE.

The same period of peak activity witnessed rapid progress in mathematics and activity in astronomy. In mathematics, a simple number theory, based on the sexagesimal system (base 60) was developed. The Pythagorean theorem became known. Squares and cubes could be calculated as well as the corresponding roots. The precursor of the logarithm became available. Consequently, the areas and volumes of simple shapes could be calculated. This facility was used to solve irrigation problems, subdivide land, figure the number of bricks required for a given construction project, etc. Under restricted conditions, linear and quadratic equations could be solved, e.g., the relative growth predicted for two flocks of sheep comprising different numbers, and having different birthrates (Neugebauer and Sachs 1945).

Hence, mathematical considerations entered the life sciences very early. Such was not the case with astronomy. Dating of tablets, much extended and refined over the last century, indicates that early Babylonian astronomy was restricted to crude observations of the stars, the planets, and the moon; this information was applied to calculate time (e.g., of the seasons) and in astrology. Although a few tablets appear to suggest a concept of a universe of eight spheres, one of the moon, it took about ten centuries before astronomy acquired a consistent mathematical theory (Neugebauer 1957).

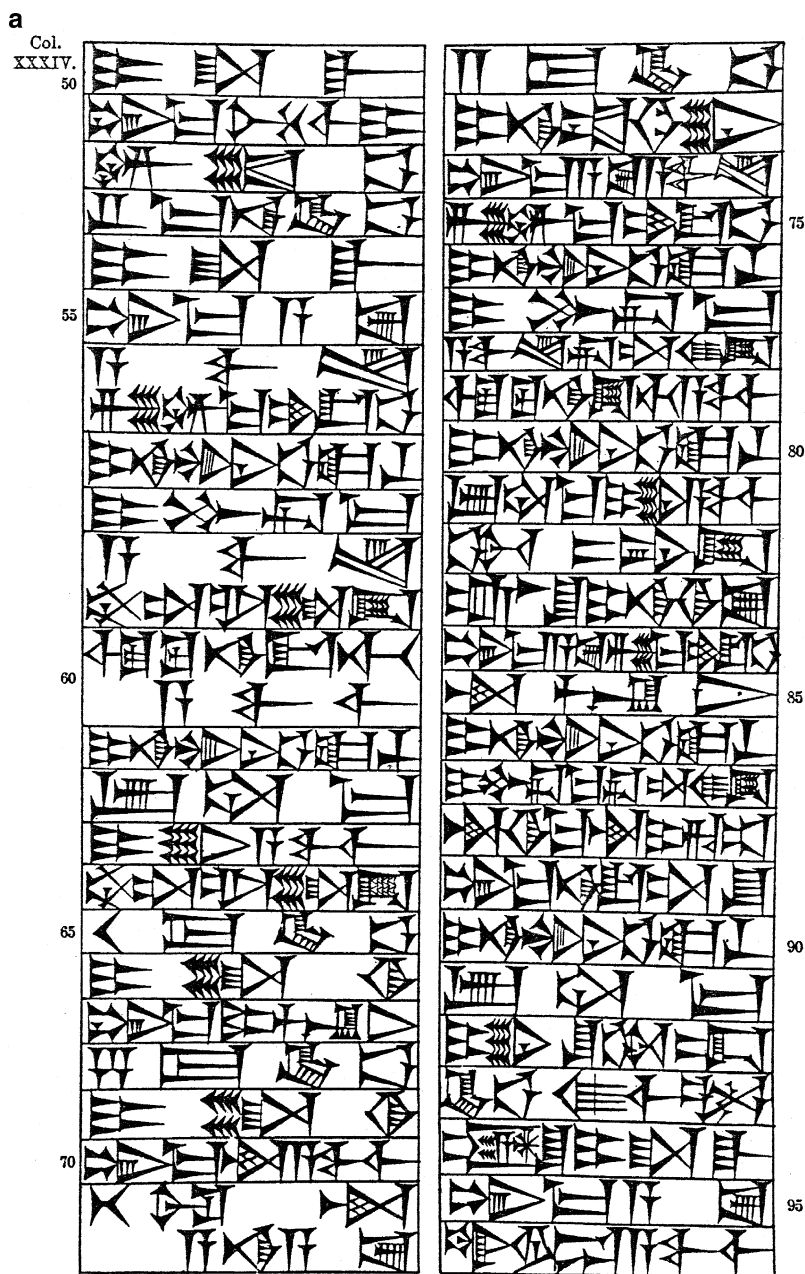


Fig. 2.2 (a) Lines 50–96 of column 34 of Hammurabi's Code in the original cuneiform script. This text reads from *left to right* and from *top to bottom*. (Reproduced by permission from Harper (1904).) (b) Harper's transliteration and translation of paragraph 215 (lines 55–66 in the *left hand column* of Fig. 2.2a). In the transliteration, *lower case* letters indicate Akkadian words, *upper case* Sumerian words. (Reproduced by permission from Harper (1904).) (c) Transliteration and translation of paragraph 218 (lines 74–83 in the *right hand column* of Fig. 2.2a) (Reproduced by permission from Harper (1904))

b § 215—XXXIV, 54-65.

55 šum-ma A.ZU 56 a-wi-lam ^bzi-im-ma-am kab-
 tam 57 i-na GIR.NI siparrim 58 i-bu-uš-ma 59
 a-wi-lam ^bub-ta-al-li-iṭ 60 u lu na-gab-ti ^ba-wi-lim
 61 i-na GIR.NI siparrim 62 ip-te-ma 63 i-in a-wi-
 lim 64 ub-ta-al-li-iṭ 65 X šikil kaspim 66 i-li-ḫi

§ 215.

¶ If a physician operate on a man for a severe wound (or make a severe wound upon a man) with a bronze lancet and save the man's life; or if he open an abscess (in the eye) of a man with a bronze lancet and save that man's eye, he shall receive ten shekels of silver (as his fee).

c § 218.—XXXIV, 73-82.

74 šum-ma A.ZU a-wi-lam 75 zi-im-ma-am kab-
 tam 76 i-na GIR.NI siparrim 77 i-bu-uš-ma 78
 a-wi-lam uš-ta-mi-it 79 u lu na-gab-ti a-wi-lim 80
 i-na GIR.NI siparrim 81 ip-te-ma i-in a-wi-lim 82
 uḫ-tab-bi-it 83 rittē-šu i-na-ki-su

§ 218.

¶ If a physician operate on a man for a severe wound with a bronze lancet and cause the man's death; or open an abscess (in the eye) of a man with a bronze lancet and destroy the man's eye, they shall cut off his fingers.

Fig. 2.2 (continued)

2.3 Egypt

Unencumbered by a bureaucracy surrounding their legal system, and active in embalming and mummification, the Egyptians of the Old Kingdom had ample opportunity to observe the body's internal anatomy. In addition, treatment of battle victims and victims suffering from accidents occurring during the construction of the pyramids provided frequent opportunities for observation of the living. The combination, as became clear from the study of Egyptian papyri (Breasted 1930; Bardinet 1995), generated insights superior to that of their Babylonian counterparts during roughly the same era.

The brain as an organ appeared for the first time. Neural control of movement was assigned to the brain and the spinal cord, though their connection was not appreciated. The heart was recognized as the center of distributed vessels (cf. Fig. 2.1). To evaluate

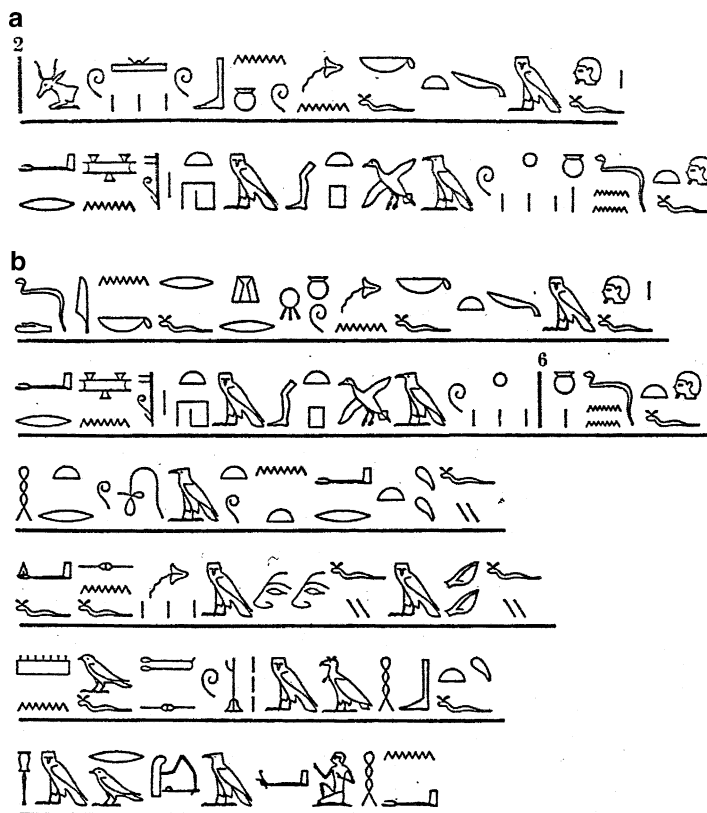


Fig. 2.3 (a) Part of case 7 as recorded in the Edwin Smith surgical papyrus: The title, and an announcement of the instructions. The translation reads: Instructions concerning a gaping wound in his head, penetrating to the bone, (and) perforating the sutures of his skull. (Adapted from Breasted (1930)). (b) The patient's examination, and the first diagnosis. The original text is written in hieratic, a cursive, much more difficult to read form of hieroglyphic writing. The figure displays the conversion into hieroglyphics. (By permission from Breasted (1930)). (c) Examination after the first treatment. Conclusion: treatment is not to be continued (Adapted from Breasted (1930))

a patient's condition, the action of the heart beat was observed peripherally including on the surface of the brain, expressed as “the heart speaks in all the limbs of the body” (Oppenheim 1962; Bardinet 1995), but blood vessels and nerves were not distinguished. Two main vessels were known in the thorax, one to the lungs and one to the heart. Blood was conceived to play an active role. Blood in the lobes of the lungs was thought to receive life spirit (i.e., air). The distinction between “vessels” filled with blood or with air remained vague.

Figure 2.3a–c reproduces part of Case 7 (of 48) as described in the Edwin Smith Surgical Papyrus and addresses evaluation, diagnosis, and treatment of a gaping head wound. In this particular example, the heart's activity enters into the physician's examination.

The Smith papyrus is dated to the seventeenth century BCE. It is written in the form of a document for instruction. This papyrus is considered to be a (an edited)

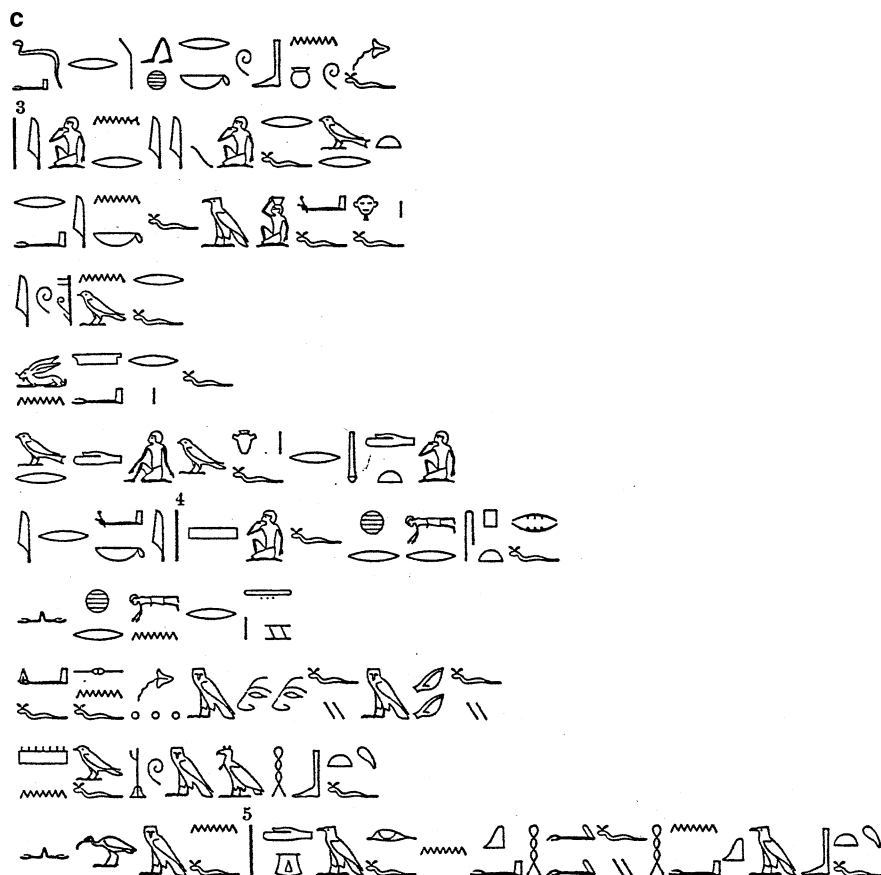


Fig. 2.3 (continued)

copy of a much older document, perhaps going back to Imhotep (thirtieth century BCE) the deified Egyptian physician. The Greek and Roman gods of medicine Asklepios and Aesculapius possibly identify with him.

No evidence has been found in support of Old Kingdom contributions to the development of mathematics. Its computational system remained a primitive additive procedure. In astronomy, the most significant contributions were the introduction of the “Egyptian year,” consisting of 365 days (Neugebauer 1975) and the division of the day and the night in 12 h each (Wells 1996).

2.4 Mesopotamia and Egypt After 1600 BCE

After the cultures passed their respective zeniths in the development of mathematics and in biomedicine, in both areas around the same time (circa 1600 BCE), a long period prevailed of editing and copying tablets and papyri for linguistic adaptation

and preservation of traditional knowledge and wisdom (Oppenheim 1962). It appears that the decline in conceiving new material was more pronounced in Mesopotamia than in Egypt. In Egypt, this activity was primarily in the hands of physician-priests (Breasted 1930).

2.4.1 *Classic*

The early stirrings of the Greek Empire may be placed around 600 BCE when Egypt lived under its 26th dynasty with Sais in the Nile delta as its capital. A new era of growth in medical science, in mathematics and in astronomy was about to manifest itself.

Hippocrates of Cos (460 – ca. 370 BCE) assembled his famous Corpus, a collection of works by a range of authors, which in Littré's Greek/French edition comprises nine volumes (Littré 1839–1861). This work has been hailed as a work of Greek genius, based on the assumption that it resulted from spontaneous generation. The assumption is likely based on the fact that the key to reading hieroglyphics had been lost. Akerblad (1802), Young (1818), and especially Champollion (1822) contributed to its decipherment by analyzing the Rosetta stone (Budge 1976). It has since become evident that Hippocrates as well as other Greek intellectuals lived and studied in Egypt (Breasted 1930). The resulting close contacts facilitated the transition from Egyptian to Greek medicine: Hippocrates' practice of treating a dislocated mandible is identical to the one described in the Edwin Smith papyrus of some 20 centuries earlier (Breasted 1930). Iversen (1939) found that the Hippocrates treatise on gynecology follows its Egyptian precursor dating back at least 10 centuries. There is a broad array of additional examples in medicine available, as well as in a variety of other fields, including mathematics and astronomy, of straightforward transfer of knowledge and ideas from Egypt and Mesopotamia to Greek culture (Pirenne 1963; Steuer and de Saunders 1959). Supporting evidence is furnished by Plato, a younger contemporary of Hippocrates, in the *Timaeus* dialogue (Hamilton and Cairns 1987).

Ptolemy (ca. 130 BCE) devised his geocentric system for the movement of the planets, though the heliocentric system had been formulated earlier. Recent analysis of Ptolemy's work has cast a shadow on his scientific integrity (Newton 1977). Astrology became deemphasized.

It should not come as a surprise that the Hippocratic Corpus contains a diversity of opinions. This diversity is so wide that the debate on what really belongs to it and what is of later vintage has not been closed.

A number of common views in the Corpus may nevertheless be recognized. These views are that the body is totally irrigated by vessels. There are two major vessels in the thorax, one of which provides mechanical suspension for the heart. Arteries furnish suspension for the lungs and this term is sometimes used for vessels that carry blood through the legs. There is a generic term (phlebs) for all sorts of conduits, some of which are fluid filled and provide cooling. Blood nourishes the

whole body. The source of nourishment is in the abdomen. Air is supplied to the entire body via breathing and transportation through vessels (Oppenheim 1962).

The teaching, in the Corpus as well as in general practice, on the heart varies enormously. Some authors view it as a respiratory organ with the lungs containing a reservoir of blood. Others allow that all blood carrying vessels may ultimately be connected to the heart, a view reflected by Plato: “the fountain of the blood which races through all the limbs.” Arteries and veins by the modern definition were not distinguished (Hamilton and Cairns 1987). The Hippocratic Corpus does not recognize a circulatory system (Duminil 1983).

Alexander the Great made both Mesopotamia and Egypt part of the Greek empire which must have intensified intellectual contact between Mesopotamia and Egypt on the one hand and Greece on the other. After his death in 323 BCE, one of his generals proclaimed himself King of Egypt, as Ptolemy I, Soter. Ptolemy I founded the Museum in Alexandria to which he and his son, Ptolemy II attracted a number of the prominent scientists of their time. Here, Greek intellectuals could draw on the ancient wells of knowledge. Alexandria, founded by Alexander, as a Greek city located in Egypt was ideally located for that function.

In the Museum, anatomical investigations were pursued in a consistent fashion under patronage of the rulers, uninhibited by religious prejudice. Two of the physicians who benefitted from this opportunity by settling in Alexandria in the third century BCE were Herophylos of Chalcedon and Erasistratos of Chios.

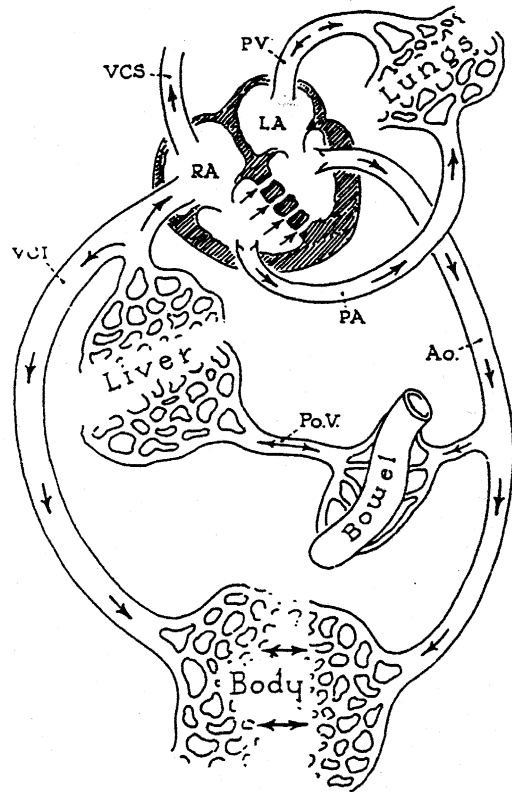
Herophylos is credited with the introduction of the distinction between arteries and veins, primarily by observing that the wall of arteries is at least six times as thick as that of veins. He taught that the heart pumps blood into the arteries and measured the heart’s rhythm from the arterial pulse, probably using the Egyptian waterclock (*klepsydra*) as his time base (Duminil 1983). He also found the connection between the brain and the spinal cord.

Erasistratos, who studied in Athens before settling in Alexandria, is viewed as having contributed the distinction between nerves and vessels (Breasted 1930). He is the first known scientist who made an ambitious effort to synthesize several thousand years of observation into a comprehensive system that included transport through arteries, veins, and nerves. This work became known to, and strongly influenced the thinking of, Galenós of Pergamon (131–ca. 200 CE) about four centuries later.

Galenós became physician to the gladiators in Pergamos, then moved to Rome where he was appointed physician to the Roman Emperor Marcus Aurelius. After Latinizing his name, Galenus, a prolific writer, left a multitude of inconsistent statements, as had his predecessors. Being familiar with the heart valves, he modified the synthesis, written by Erasistratos at a few significant points.

The essence of the Galenic system, as distilled by Siegel (1968, Fig. 2.4), but not necessarily fully subscribed to by others (e.g., Harris 1973), may be summarized as follows. Blood is formed in the liver where it assimilates natural, i.e., nutritive spirit. This blood is distributed by the veins to nourish all parts of the body. The heart, which he distinguished from voluntary muscle, draws a fraction of this venous blood into the right ventricle through its active dilation. Some of this

Fig. 2.4 Diagram of Galenus' description of the operation of the cardiovascular system in the adult. Vena cava superior (VCS), vena cava inferior (VCI), right atrium (RA), left atrium (LA), pulmonary vein (PV), pulmonary artery (PA), aorta (Ao.), portal vein (Po. V.) (By permission from Siegel (1968))



blood is forced into the pulmonary artery toward the lungs through contraction of the thorax, and some penetrates into the left ventricle via pores in the interventricular septum.

The blood in the left ventricle acquires vital spirit with air from the lungs transported via the pulmonary vein. Sooty residues (waste products) move through the same vessel in the opposite direction, i.e., from the left chamber to the lung (two arrows in the pulmonary vein in Fig. 2.4). Blood endowed with vital spirit is distributed throughout the body by the arteries, it being drawn from the left ventricle by the pulsatile properties of the arteries.

The brain, one recipient of vital spirit, transforms part of it into the third kind of spirit, animal spirit. Animal spirit is distributed over the body through the hollow nerves, thereby enabling the body's locomotion (Siegel 1968).

Although Galenus' exposition was found lucid, convincing, and flexible, it became the subject of criticism during its long lifetime. The criticism tended to focus on two aspects: two-way transport through the pulmonary vein, and the pores in the interventricular septum.

Ibn an-Nafis (1210–1288), an Arab physician and autodidactic commentator on the Koran (Qur'an in modern transliteration, Abdel Haleem 2004), criticized

Avicenna, Galenus' translator into Arabic, by rejecting the presence of septal pores and by arguing that blood moves from the right ventricle via the pulmonary artery to the lungs, then via the pulmonary veins to the left ventricle (i.e., unidirectional transport). In the lungs the blood mixes with air and is purified (Meyerhof 1931). Ibn an-Nafis' writing on the circulation remained unknown to the Western world until 1922.

In 1553, Michael Servetus, a physician and scholar with a broad interest who taught mathematics at the University of Paris, anonymously published a book that critically addressed two topics. In Chapter V he criticized the same two items in the teaching of Galenus as had, unbeknownst to him, Ibn an-Nafis', while reaching similar conclusions. No one seems to have paid attention to this chapter for more than a century. In the other chapters, Servetus criticized the doctrine of the Holy Trinity, the first explicit formulation of which is attributed to Tertullianus, a contemporary of Galenus, though its root may lie in the monotheism of Egyptian origin (Kirsch 2004). These chapters received prompt attention. Servetus was accused and convicted of heresy and burned at the stake outside Geneva in the same year that his book appeared (Cournand 1964).

With the European Renaissance in full development, and the rise of interest in experimentally oriented investigations, e.g., how the mammalian body operates, more critical commentaries appeared in rapid succession. Vesalius, reportedly a fellow student of Servetus in a dissection course, expressed his doubts about the existence of the septal pores in 1543. Columbus described the pulmonary circulation once more in 1559. Canano as well as Vesalius announced their discovery of valves in certain veins in or around 1537, which Fabricius definitely established in his book published in 1603. Vesalius' book, published in 1543, is claimed to deviate from Galenus' teaching in more than 200 instances. Peripatetically, i.e., on theoretical grounds, Caesalpinus offered his view of the circulation as a closed circuit in 1593. These developments culminated in William Harvey's work which appeared in book form in 1628, well before Newton's *Principia Mathematica* (1687). All of this caused deep chagrin to Galenus' devotees.

In addition to the criticism on Galenus' teaching, there was also inspiration to modify and update his theory. Friedrich Hoffmann proposed a hydrodynamic machine: Three fluids circulate in the body, blood, lymph, and nerve spirit. They have to flow with appropriate relative magnitudes to prevent diseased states. Hoffmann's book appeared in 1695, i.e., more than 60 years after Harvey's.

2.4.2 *Renaissance/Contemporary*

Harvey's central consideration was that his experimental observations in conjunction with his calculations revealed that the heart ejects more blood in half an hour than the body contains. Hence, his conclusion that the same blood must continuously perform a circular motion. Since this contradicted basic tenets of the Galenic model, Harvey rejected formation of blood in the liver, cardiac suction of blood, the

presence of septal pores and two-way transport through vessels. Instead, he made the heart the central blood moving organ, a consequence of the alternate contraction and relaxation of its muscular walls and the presence of valves.

Acknowledging the contributions made by Columbus and by a number of other predecessors, including his teacher Fabricius, but not by Caesalpinus, Harvey argued that blood moves through a wide open channel from the right ventricle through the pulmonary artery to the lungs, through pores in the lungs to the pulmonary veins on its way to the left auricle. Therefore, there was no need to assume invisible pores in the often thick septal wall. Then it moves from the left auricle to the left ventricle which forces blood into the aorta. Branches of the aorta provide channels to the peripheral organs, from where the blood reaches the veins through pores in the tissue. The veins return the blood to the right auricle, from where it moves to the right ventricle, thus completing a circular pathway. Harvey pointed out that the direction of opening of the valves in the heart fits this picture perfectly. This primarily descriptive interpretation will acquire causal features in Chap. 10.

The only part missing from the circular pathway was the connection between arteries and veins, the pores. He postulated their existence, thereby furnishing a heavy weapon to his many opponents, until Malpighi, born in the year Harvey's book was published, discovered the capillaries in 1661 by applying an improved version of the recently invented microscope. Together, Harvey and Malpighi established the paradigm closely resembling the currently accepted closed system (Fig. 2.5), the gross anatomy for the major vessels being essentially the same as that proposed by Galenus (Fig. 2.4).

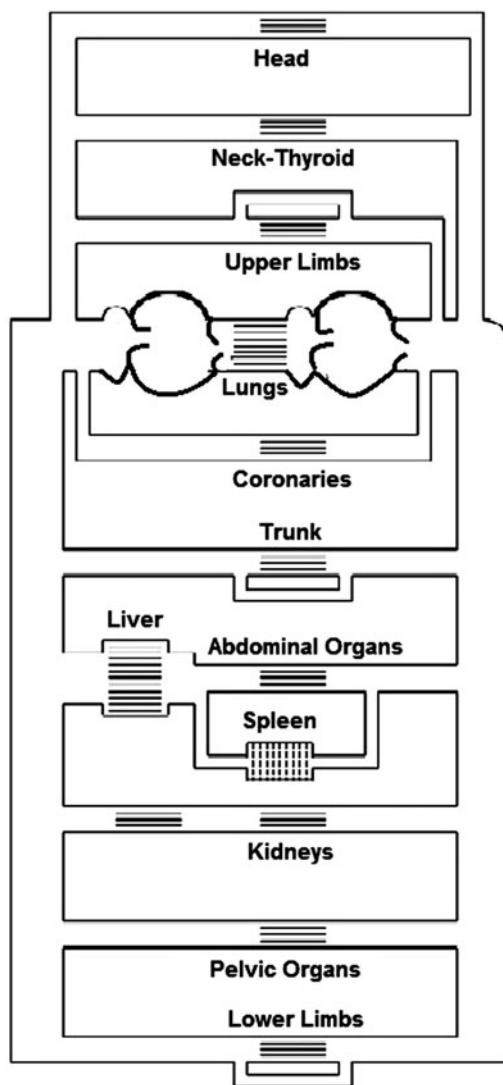
Since normally there is fluid-mechanical separation, though incomplete functional separation, between the two sides, it is appropriate and has proven useful to regard the heart as two pumps, i.e., the left heart and the right heart, each consisting of two contractile chambers.

Considering the manner in which the vascular beds connect the pumps, the closed loop may be schematized as in Fig. 2.6. This diagram illustrates what Harvey had conceived when he spoke of the "circular" motion of blood (clockwise in Fig. 2.6). In Fig. 2.7, the heart itself and major circulatory structures are shown schematically in somewhat greater detail. The four cardiac chambers are indicated, as well as the four sets of leaflets that impose unidirectional flow. This gives rise to a condition of profound significance: average flow through the two pumps and the two vascular beds must be equal. It should be noted that the coronary circulation, i.e., the vascular bed of the heart itself, is a component of the systemic circulation.

The four valves lie in the plane which separates atria and ventricles (Fig. 2.8). Their names are, in the direction of flow, tricuspid (a) and pulmonary valve (b) (in the right heart), and mitral (c) (or bicuspid) and aortic valve (d) (in the left). The leaflets of the atrioventricular valves are supported by chordae tendineae and papillary muscle (Fig. 2.9).

The two vascular beds, designated "systemic" and "pulmonary" (Fig. 2.7), exhibit similarities in architectural pattern. In the direction of blood flow, the vessels first exhibit prolific branching such that the total cross-sectional area increases despite the fact that daughter vessels are narrower than mother vessels.

Fig. 2.5 Contemporary view of the cardiovascular system as diagrammed by Wiggers in 1954



The number of capillaries, the smallest blood vessels, is estimated to exceed 10^9 in the human. Subsequently, beyond the capillary beds, the inverse occurs: small vessels combine to form larger vessels.

Galileo Galilei taught the heliocentric system of planetary motion, proposed (again) by Copernicus, at the University of Padua, Italy, at about the time that Harvey pursued his medical studies there. It has been suggested that Galilei's teaching of the circular movement of the planets around the sun, inspired Harvey to conceive his circular movement of blood.

Harvey reported that he had to overcome "evil criticism of his discovery of the circulation of the blood, such as a feeble infant as yet unworthy to have seen the

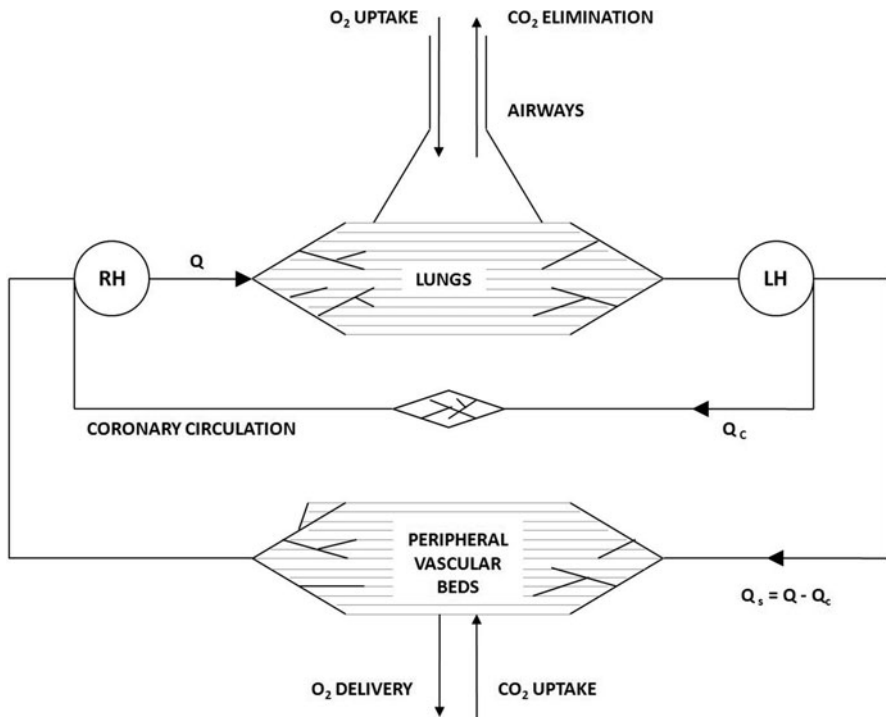


Fig. 2.6 The mammalian circulatory system forms a closed loop containing two sizable fluid pumps in series: the right heart (*RH*) and the left heart (*LH*). Q denotes total blood flow in the closed loop, Q_c flow through the coronary circulation, Q_s through the systemic peripheral beds

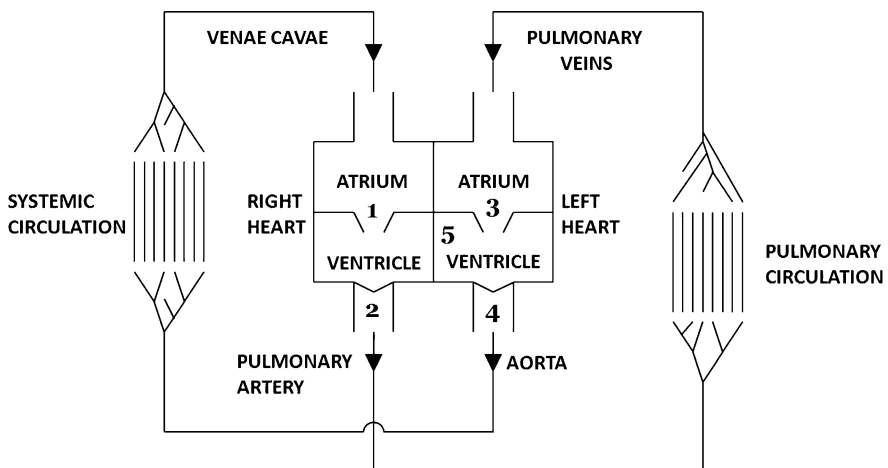


Fig. 2.7 Sketch of the circulatory system indicating the four chambers of the heart and its system of valves. In the normal case, complete fluid separation between the left and right sides of the heart is provided by the septum. Arrows indicate direction of positive flow, Q_s flow through the systemic vascular beds. (1) the tricuspid valve; (2) the pulmonary valve; (3) the mitral valve; (4) the aortic valve; (5) the septum separating the right and left heart

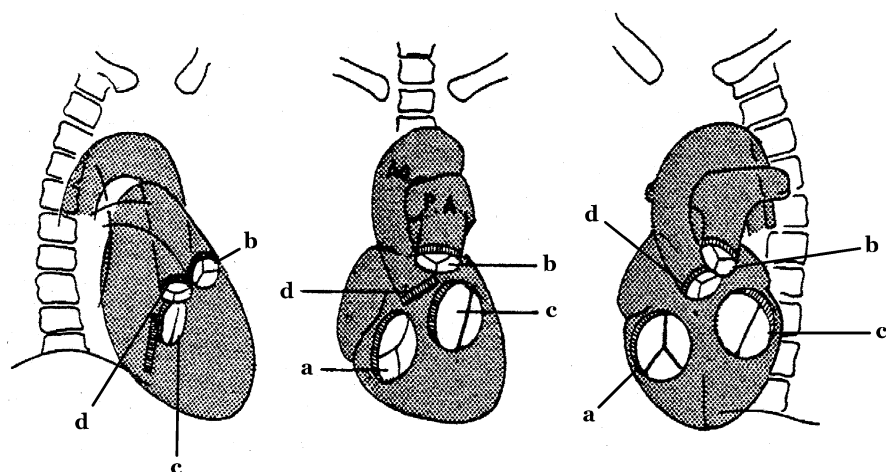


Fig. 2.8 Three views of the human heart with the valves drawn in. *Ao* denotes the aorta, *PA* the pulmonary artery, *a* the tricuspid valve, *b* the pulmonary valve, *c* the mitral valve, and *d* the aortic valve. The first heart sound coincides with the closure of the atrioventricular valves (*a* and *c*), the second with the closure of the pulmonary and aortic valves (*b* and *d*)

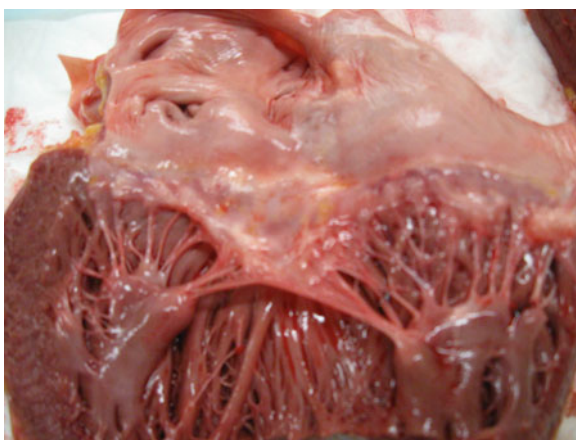


Fig. 2.9 Mitral valve apparatus of a human in the open position. The chordae run from the heads of the papillary muscle to the border as well as to other locations of the leaflets. The papillary muscles themselves are anchored in the ventricular wall

light” (Harvey 1952), but gradually, his concept of the circulation gained acceptance. His monumental work retained a number of features embodied in Galenus’ theory such as the abdominal source of nutrition and gas exchange occurring in the lungs, while introducing new interpretations, such as one way transport of the same blood, abolition of the spirits, and rejection of suction. It opened the way for his followers to study the function of the respiratory system, the digestive system, etc. and the concurrent roles of the blood transport system in these and many other aspects of life-sustaining functions.

In his book, Harvey made the heart the exclusive pump that propels blood around the circle. Eventually, this idea was criticized, notably by Weber in 1834, who claimed that other (unspecified) forces help support the circulation; by Jones in 1852 who felt that “the supplementary force of rhythmical contraction of the veins [...] is called forth to promote the flow in the [bat’s] wings, which [...] are, in a considerable degree, though not entirely, beyond the sphere of the heart’s influence”; by Donders, who proposed in 1856 that the respiratory system assists the heart in its pumping effort by periodically increasing and decreasing the pressure around the thoracic vena cava; and by Ozanam in 1881 and 1886, who concluded from his experiments that pulsation of arteries modify flow to the heart in some of their companion veins.

Before the issue passed out of style temporarily, the proposal by Donders resulted in a vigorous debate between opponents and proponents flaring up intermittently for more than a century without achieving a satisfactory solution. The basic question remained why when blood, displaced by vessel compression and escaping in two directions, should not just return from those two directions in the exactly the same proportion, yielding no net forward flow (Chap. 8).

2.4.3 *Contemporary/Future*

The conversion of fluid flow, or electrical current, from unsteady to steady, or vice versa, has intrigued artists, physicians, physicists, and engineers of various specialties over time. A number of solutions have been found, of which placement of one or more valves, such as in the heart, is a relevant example for the generation of steady flow by a pulsatile source, as argued effectively by Harvey.

Commencing in 1954, and perpetuating his work for decades, the physician Liebau constructed hydraulic models, free of valves, to demonstrate the occurrence of steady flow in response to periodic compression at a particular site. Reconstruction of one of his models confirmed Liebau’s observations (Moser et al. 1998). His motivation was to show that similar compression of veins, free of valves, can aid blood flow around the cardiovascular circuit, even in the absence of cardiac valves (Liebau 1956). Despite support by contemporary fluid-dynamicists, he was unable to offer an interpretation why, and under what conditions, steady flow could be generated in such fluid-dynamic models. The issue continues to fascinate fluid-dynamicists, e.g., Manopoulos et al. (2006).

Taking a different approach, Moser et al. (1998) identified the mechanism as well as a set of conditions that must be satisfied for steady flow to occur. They also found that periodic compression is not the sole way to generate steady flow: periodic linear or rotational acceleration and deceleration of blood containing vessels may achieve the same purpose. Since one of the conditions is the presence of different impedances, steady flow so generated was called impedance-defined flow. Inasmuch as impedances are often frequency dependent, the magnitude of the steady flow achieved may depend on the frequency with which compression, or

acceleration, is applied. As a further consequence, the direction of the steady flow may be in opposite directions for different frequencies.

The presence of a valve, if properly located, may increase the magnitude of the steady flow or it may facilitate the provision of special features, such as the creation of a high pressure reservoir as in the aorta and the pulmonary artery. Valves that open and close periodically may make an impedance of time-varying interest, thereby possibly introducing strong nonlinearities. As the mechanism behind impedance-defined flow allows for the presence of valves, the heart's pumping, as advocated by Harvey, is a special case of impedance-defined flow.

Figure 2.10 shows a closed loop in fluid-mechanical symbols as well as its electrical equivalent utilizing electrical symbols to illustrate some of the key features of impedance-defined flow. The circuits are reduced to their bare bones to prevent distraction from the essential properties. Focusing on Fig. 2.10a, the circuit consists of two elastic reservoirs, marked C_0 and C_1 , connected by two rigid tubes, one of which is narrow, the other wide. The system is fluid filled. Reservoir C_0 is compressed by an external force, then allowed to relax, in a periodic fashion. The narrow tube is assumed to have a sufficiently small radius for the viscous effects to dominate inertial effects of the fluid. In the wide tube, the conditions are assumed to be reversed. These conditions appear more clearly in Fig. 2.10b. The cycle of events may be separated into two parts: (a) the compression phase displaces fluid from C_0 to C_1 via the narrow channel, or the wide channel, or both, and (b) during the relaxation phase, a fraction of the fluid stored in C_1 will return to C_0 , the fraction depending on the duration of the time interval to the next compression.

Pressures $p_0(t)$, $p_1(t)$, flows $Q_0(t)$, $Q_1(t)$, $Q_2(t)$ and volumes $V_0(t)$, $V_1(t)$ prevailing in the circuit may be computed from two sets of four simultaneous equations, one set for phase (a), another for phase (b). They read:

Phase a

$$Q_0(t) = Q_1(t) + Q_2(t) \quad (2.1)$$

$$p_0(t) - p_1(t) = R_1 Q_1(t) \quad (2.2)$$

$$p_0(t) - p_1(t) = L_2 dQ_2/dt \quad (2.3)$$

$$Q_1(t) + Q_2(t) = C_1 dp_1/dt \quad (2.4)$$

Phase b

$$Q_1(t) + Q_2(t) = -C_0 dp_0/dt \quad (2.5)$$

$$p_0(t) - p_1(t) = R_1 Q_1(t) \quad (2.6)$$

$$p_0(t) - p_1(t) = L_2 dQ_2/dt \quad (2.7)$$

$$Q_1(t) + Q_2(t) = C_1 dp_1/dt \quad (2.8)$$

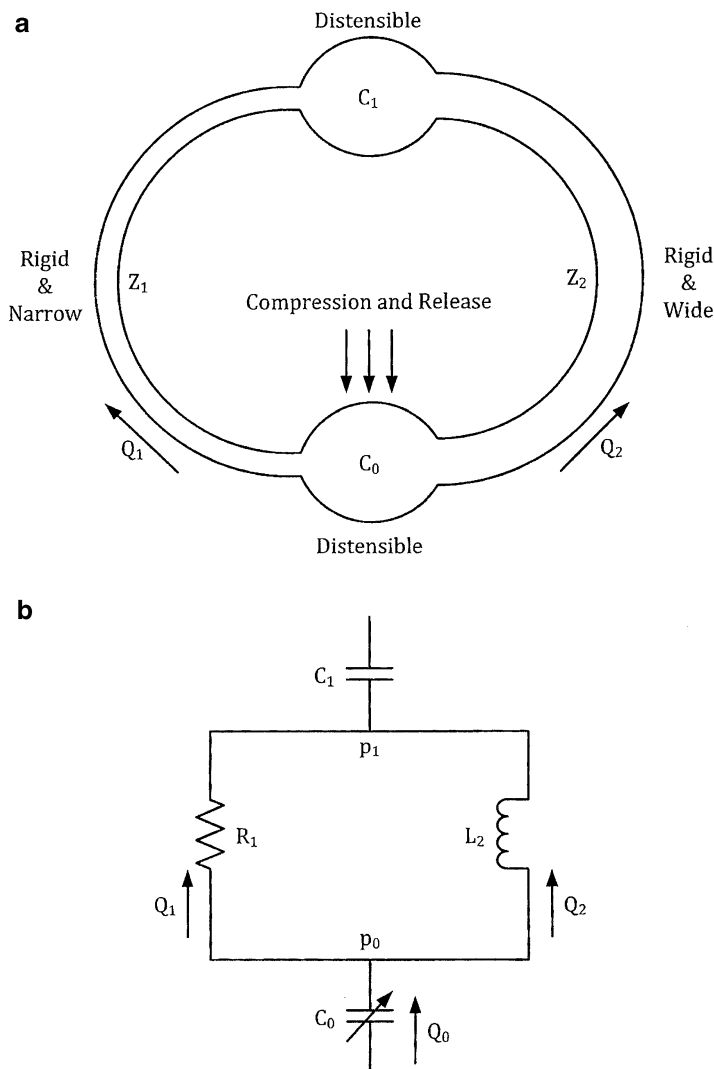


Fig. 2.10 This instructional model, drawn in fluid mechanical (a) and in electrical (b) symbols, consists of two compliant reservoirs C_0 and C_1 , connected by two rigid pathways, one narrow and one wide. The flow impedance Z_1 of the *narrow* channel is R_1 (frequency independent), of the *wide* channel $j\omega L_2$ (frequency dependent) $j = \sqrt{-1}$. In (a) the single arrows mark Q_1 and Q_2 and define the positive direction of the flows Q_1 and Q_2 ; in (b) the vertical arrows define the positive direction of Q_0 , Q_1 , and Q_2

In these equations, R_1 denotes the viscous effect in the narrow channel, L_2 the inertial effect in the wide one. To keep the equations transparent, nonlinear elastic phenomena in reservoir C_0 were bypassed by setting $p_0 = 0$ at the onset of the relaxation phase, thereby introducing a simple discontinuity instead.

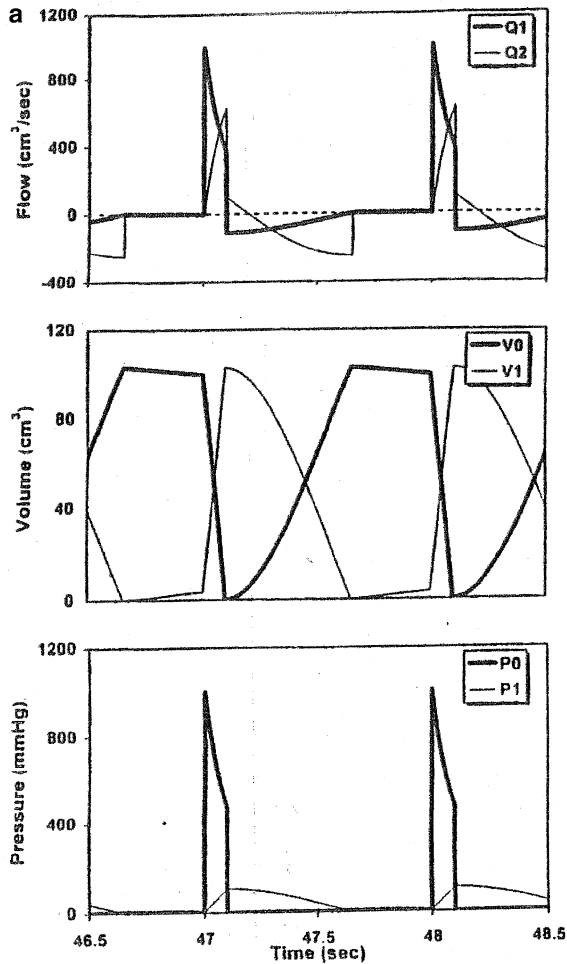


Fig. 2.11 (a) Pressures, flows, and reservoir volumes, V , as functions of time, calculated with the aid of Eqs. 2.1–2.8 for the valveless closed loop depicted in Fig. 2.10. (b) Same after placement of a valve that restricts flow Q_1 to nonnegative values. (c) Computed values of steady flow around the closed circuit of Fig. 2.10 for three cases: valveless (dots), with a valve that prevents Q_1 from going negative (squares), with a valve that keeps Q_2 from going negative (triangles). Positive values signify clockwise, negative values counterclockwise steady flow. Efficiency is defined as percentage of maximum possible flow. All graphs are displayed as a function of compression frequency (Adapted from Moser et al. (1998))

Figure 2.11a–c display results selected from the solution of Eqs. 2.1–2.8. In Fig. 2.11a the circuit is free of valves. During the compression phase, flow is seen to prefer the narrow channel, during the relaxation phase the wide channel. In Fig. 2.11b the solution is shown when a valve restricts Q_1 from going negative. Steady flow around the circuit,

$$\bar{Q}_1 = \bar{Q}_2 = \frac{1}{T} \int_0^T Q_1(t) dt \quad (2.9)$$

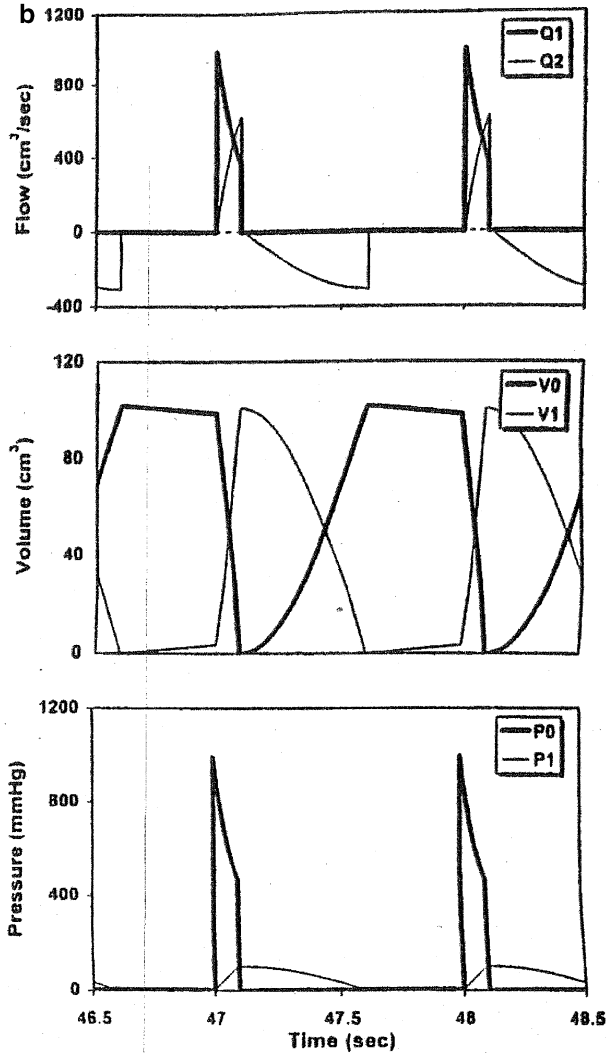


Fig. 2.11 (continued)

(T denotes the duration of one cycle) is reproduced in Fig. 2.11c for three conditions.

Figure 2.12 shows similar results for a more complex analysis of the same valveless condition as above in which introduction of the discontinuity was avoided by taking into account the compliant properties of the collapsed segment, using material presented in Chap. 3, Fig. 3.3, which impacts on Eqs. 2.5–2.8. Inspection disclosed that the magnitude of steady flow around the circuit is sensitive to the speed with which release is effected (Question 2.5; Patel 2004).

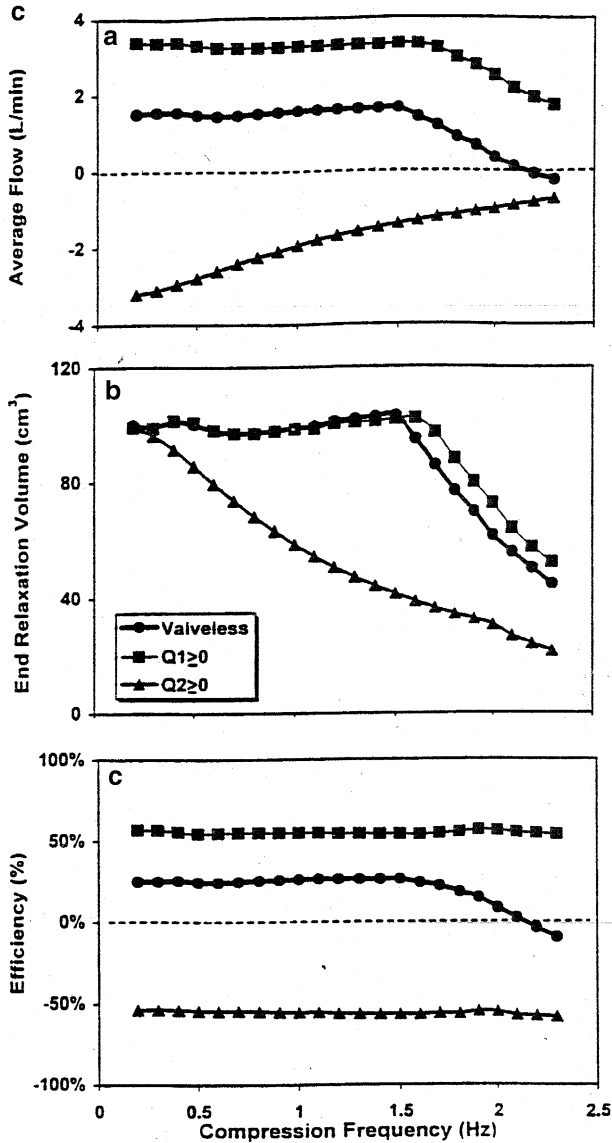


Fig. 2.11 (continued)

The key to understanding the origin of steady flow around the circuit is the presence of different impedances. When C_0 is compressed, outflow will be larger along the path with the smaller impedance, in casu the resistive pathway, which is frequency independent. During the relaxed phase the inductive path offers the smaller impedance, since its expression, $j\omega L_2$, contains $\omega = 2\pi f$, with f = frequency

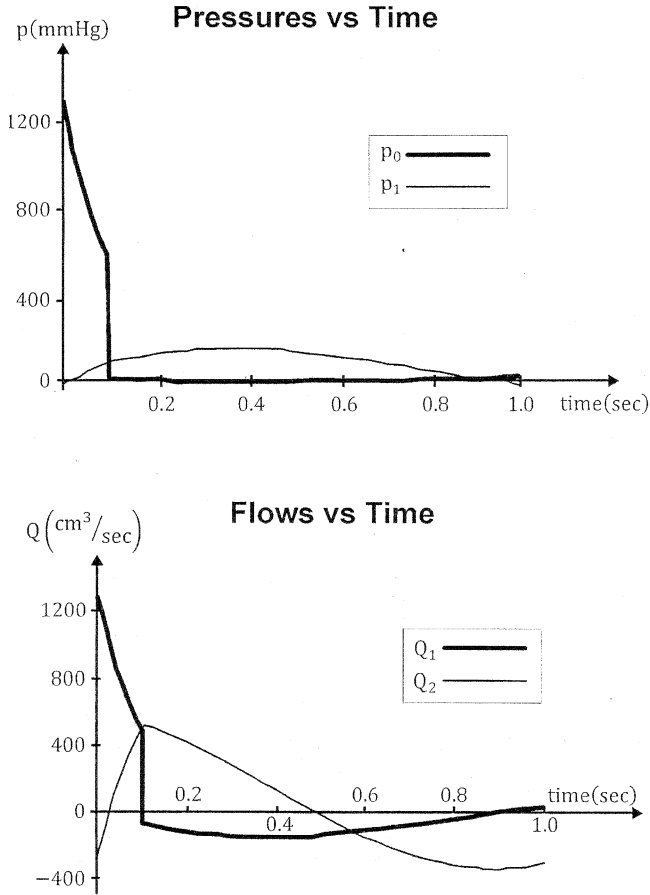


Fig. 2.12 Steady state results for pressures and flows during compression and release after elimination of the discontinuity in Fig. 2.10. Graphs computed by Patel (2004). See text for explanations for p_0 , p_1 , Q_1 and Q_2

of the components of the signal. As a consequence, rapid compression tends to generate more steady flow around the circuit than slow compression.

It is now possible to formulate general conditions that allow the generation of steady flow. These are: (1) Energy must be furnished to the system to move the fluid. $Q_1 = 0$ without compression of the passive vessel; (2) the circuit must contain a compliant reservoir to allow for storage of the displaced fluid; (3) The impedance of the two pathways must be different and at least one must be a complex number. If both are complex numbers, their phases must be different (Moser et al. 1998). Bovard et al. (2004) carried out flow measurements as a function of compression site in a fluid filled two tube model similar to one of Liebau's originals.

Chapter 8 addresses severe limits of applicability of this valveless closed loop to the mammalian cardiovascular system, such as its inability to generate or sustain high pressure arterial reservoirs (Sect. 5.1).

Harvey, in his book, advances three prime considerations in support of his view that the same blood performs a circular movement. The third of these deals with return, to the heart, of blood in the veins. In his argument, Harvey relies heavily on the abundance of valves in superficial arm veins. He apparently failed to observe that skeletal muscle contraction and relaxation promotes blood flow in the direction of the heart. Had he made this observation, he might have felt compelled to modify his statement that the heart alone is responsible for the circulation of blood; in everyday life, it clearly is not.

One is then forced to think in more general terms about what makes blood move. Blood can move in response to any one, or a combination of the following causes:

- A pressure gradient is created along a vessel, or along the vasculature, e.g., by the heart.
- Contraction and relaxation of a blood vessel, or a cardiac chamber, in response to pressure augmentation, or neural or metabolic stimuli.
- Compression, or expansion, and release of a blood vessel, or vessels, e.g., by the respiration, or by skeletal muscle contraction and relaxation.
- Acceleration and deceleration of part, or the whole, of the cardiovascular system, e.g., during walking (active) or shaking (passive).
- Alteration of the gravitational field with respect to the body, e.g., by changing body orientation (change in vector direction), or in space (change in vector magnitude).
- Conversion of steady flow to pulsatile flow, which affects load impedance.
- Compression, or expansion, and release by artificial means, e.g., by an intra-aortic balloon pump, or a foot pump.

In addition, for distribution purposes, the resistive and inertial effects of blood itself can be manipulated by control mechanisms. The applicability and utilization of these causes will form one of the major foci of this book, operating in the interest of many functions, including

- Transporting oxygen from the environment and delivering it to the body tissues
- Collecting carbon dioxide from the tissues and eliminating it from the body
- Performing many other transport functions, such as of metabolites, hormones, etc.
- Allowing for the control of many of these features

2.5 Conclusions

Despite ancient Mesopotamian and Egyptian scientific, factual, knowledge, even as late as Hippocrates' Corpus, the need to see the circulation as a system as opposed to loosely connected pieces, did not reach cognition. This contrasts with the

development of a system for the protection of patients from inappropriate invasive care and the collection of factual anatomical information.

Retrospectively, one recognizes the pervasive tendency to collect and connect facts, adding convenient truths such as the “intraventricular pores” and “two way motion in vessels” to facilitate the chosen explanation. Further discussion then no longer focused on the base idea, but gravitated toward discussions of the distracting factors.

2.6 Summary

Covering history from antiquity, this chapter characterizes the major difference between Mesopotamian and Egyptian interest and activity, and identifies the birth of the concept that mammals possess a cardiovascular system, endowed with three spirits, during the classic Greek period. Since Egyptian documents were anonymous, with rare exceptions and their early translations into Greek were signed, the Western world interpreted them as Greek originals. It took a long time for this to be corrected, in particular, as Egyptian (hieroglyphic) script could not be read any longer until the Rosetta stone had become available (1799). Mesopotamian law introduced medical liability. Andreas Caesalpinus and William Harvey upgraded the classic ideas to the Renaissance level.

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Appendix

Questions

- 2.1 Compare Galenic to Harveyan concepts of the circulation. (List at least five concepts on which their theories differ.)
- 2.2 Which of Harvey's criticisms of Galenus' theory must be deemed to be incorrect?
- 2.3 Since Harvey rejected the existence of pores between the ventricles, could he sensibly be criticized for peripheral pores in his own theory?
- 2.4 Integration of Eq. 2.2

$$\int_0^T p_0 dt - \int_0^T p_1 dt = R_1 \int_0^T Q_1 dt = R_1 T \left[\frac{1}{T} \int_0^T Q_1 dt \right] = R_1 T \bar{Q}_1 = 0,$$

because the two integrals on the far left are each over one period and therefore vanish. With Eq. 2.9, $Q_2 = 0$, hence there is no steady flow around the circuit. This result does not square with the direct solution of Eqs. 2.1–2.8 and the resulting curve marked with dots in the top panel of Fig. 1.11c. Identify the cause of the contradiction.

- 2.5 Average flow in a closed loop, free of valves as in Fig. 2.10b, depends on the speed of release at the end of the compression phase. The faster the release, the smaller the steady flow around the loop. Explain this result.
- 2.6 Can shaking the two elastic tube model in its own plane along a straight line generate flow around the loop, if (a) the line is parallel to the line through the points where the elastic tubes connect, (b) if the line is perpendicular to the line under (a)?
- 2.7 In a normal cardiovascular loop with a beating heart, are all four cardiac valves ever open at the same instant of time?

Answers

- 2.1 Galenus: New blood is manufactured continuously in the liver; Harvey: The same blood flows around the closed system continuously.
 Galenus: Blood contains spirits; Harvey: It does not.
 Galenus: Blood flows from the liver to the organs through the veins; Harvey: Blood flows from the organs to the heart through the veins.
 Galenus: Blood flows from the right ventricle to the left ventricle through the interventricular pores; Harvey: Those pores do not exist.
 Galenus: The pulmonary vein carries two-way flow; Harvey: One-way, toward the left atrium.
 Galenus: There is blood flow through the hollow nerves carrying animal spirit; Harvey: There is no such flow.
 Galenus: The heart sucks in blood; Harvey: The heart does not exert suction.
 Galenus: Contraction of the thorax forces blood into the pulmonary artery; Harvey: Right ventricular contraction is responsible for this.
 Galenus: Blood is drawn from the left ventricle by the pulsatile properties of the arteries; Harvey: The other way around. The contractile properties of the heart make the arteries pulsate.
- 2.2 Actually, the heart does exert suction (Sect. 4.3; Chap. 8).
- 2.3 Pores provided the continuous pathway between the smallest arteries to the smallest veins in Harvey's thinking. The capillaries had not been seen yet (Sect. 5.1).
- 2.4 The function $p_0(t)$ contains a discontinuity that disallows integration.
- 2.5 Faster release, like faster compression promotes flow preference for the resistive channel, but in opposite directions.
- 2.6 (a) yes; (b) no.
- 2.7 No, not in the normal system.



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