Da descoberta da circulação sanguínea aos primeiros factos hemorreológicos (1.ª Parte) § [99]

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RESUMO

Neste artigo, o primeiro de duas partes sobre o mesmo tema, procede-se a uma breve revisão histórica sobre os conceitos que prevaleceram, relativamente à natureza do sangue e circulação sanguínea, desde a Antiguidade e até à resolução do problema por William Harvey, no século XVI. Pela vivissecção de diversos tipos de animais, pôde Harvey definir um modelo geral e lógico para toda a circulação sistémica que contradizia conceptualizações anteriores, designadamente as que haviam sido definidas por Galeno, cerca de catorze séculos antes. A influência que Galeno ainda exercia sobre, virtualmente, todos os assuntos médicos terá justificado as hesitações e escrúpulos de Harvey, que publicou somente as suas conclusões treze anos depois de as ter obtido. Também explica a polémica estabelecida com colegas sobre o assunto, que se manteve até ao seu falecimento. Todavia, através de cuidadosa observação e investigação perseverante, Harvey demonstrou claramente que o coração era o órgão central do sistema, de que dependia a propulsão do sangue para as artérias e, depois o seu retorno por vasos diferentes, as veias, até ao ponto de partida. O sangue proveniente do coração seria diferente do que regressasse aquele órgão, atribuindo essa diferença (em cor e fluidez) à presença de conteúdos próprios, nutritivos para o organismo por ele

ABSTRACT

From the discovery of the circulation of the blood to the first steps in hemorheology: Part 1

In this article (the first of two on the subject) a brief historical review is presented of the prevailing ideas on the nature of the blood and its circulation from antiquity to the 16th century, when the problem was solved by William Harvey. On the basis of vivisection of various types of animals, Harvey constructed a general and logical model for the whole systemic circulation, which contradicted previous concepts, mainly those that had been put forward by Galen fourteen centuries before. The influence that Galen still exercised on virtually all areas of medicine justified Harvey's hesitations and scruples, forcing him to delay publishing his conclusions for thirteen years. It also explains the controversy with fellow physicians on the subject, which continued until his death. However, through careful observation and painstaking investigation, Harvey demonstrated clearly that the heart was the central organ of the circulatory system, on which depended the propulsion of the blood to the arteries and its subsequent return by different vessels, the veins, to its starting point. The blood coming from the heart was different from that which returned

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irrigado. Caracterizou a pulsação sanguínea como resultante do enchimento das artérias pelo sangue arterial veiculado a cada contracção cardíaca. Revelou que o sangue arterial saía do coração pela contracção do ventrículo esquerdo, a qual ocorria em simultâneo com a do ventrículo direito e, em ambos, depois da contracção das aurículas. Confirmou que o sangue passava do ventrículo direito para a aurícula esquerda e, desta, para o ventrículo esquerdo, através da circulação pulmonar. Pelo cálculo do volume de sangue debitado diariamente pelo coração, considerou que o sangue não poderia ser consumido pelo corpo e teria de circular continuamente pelo coração e rede vascular. Ainda que não tenha confirmado completamente a continuidade da rede circulatória, não deixou de considerar a existência de passagens minúsculas ou imperceptíveis entre as artérias e veias, que seriam posteriormente confirmadas, por Marcello Malpighi, sob a forma de redes capilares. O sentido unidireccional do fluxo sanguíneo era assegurado também por válvulas presentes no coração e nas veias. O modelo estabelecido por Harvey para a circulação sanguínea foi extrapolado para o Homem sendo corroborado nos séculos seguintes. Malpighi e, depois, Van Leeuwenhoek contribuíram, em especial, para um melhor esclarecimento da composição e características do sangue e a importância exercida sobre a respectiva perfusão através dos diferentes vasos da rede circulatória.

to the organ, the difference (in color and fluidity) being attributed to the presence of constituents which nourished the organism it irrigated. Harvey characterized blood pulsation as the result of the arteries filling with arterial blood during each heart contraction. He demonstrated that the arterial blood left the heart by contraction of the left ventricle, which happened simultaneously with contraction of the right ventricle and, in both, after the contraction of the atria. He confirmed that blood passed through the lung circulation from the right ventricle to the left atrium and from there to the left ventricle. By calculating the volume of blood pumped daily by the heart, Harvey reasoned that the blood could not be consumed by the body and would have to circulate continually through the heart and vascular network. Although Harvey did not confirm the continuity of the circulatory network, he went so far as to hypothesize the existence of minuscule imperceptible passages between arteries and veins, which was later confirmed by Marcello Malpighi, in the form of networks of capillaries. The one-way direction of blood flow was ensured by valves in the heart and veins. The model established by Harvey for blood circulation in animals and extrapolated to humans was confirmed in the following centuries. Malpighi and van Leeuwenhoek, in particular, helped clarify the composition and characteristics of blood and their importance for its perfusion of the different vessels of the circulatory network.

INTRODUÇÃO

A constituição e funções genéricas da circulação sanguínea são do conhecimento comum desde o século XVII. Para esse conhecimento foi decisiva a contribuição de William Harvey, culminando um conjunto de hipóteses e modelos elaborados a partir da Antiguidade.

Cerca de dezasseis séculos antes da descoberta de Harvey já se afirmava no

INTRODUCTION

The general constitution and functions of the blood circulation have been common knowledge since the 17th century. The contribution of William Harvey was fundamental to this understanding, which was the culmination of a series of hypotheses and models that go back to ancient times.

Sixteen centuries before Harvey, the *Huangdi Neijing*, the Inner Canon of Huangdi,

"*Huangdi Neijing*" (*Canon da Medicina de Huangdi*)[i] que "*todo o (movimento do) sangue é controlado pelo coração; o sangue flui continuamente em círculos sem nunca parar… alguns vasos sanguíneos transportam o ar necessário à vida*" [(1)].

A etapa seguinte ocorreu na Grécia Antiga, ao ser comprovado, pela dissecção de cadáveres humanos, que o sangue circulava em canais próprios de dois tipos; um dos tipos, que transportaria ar, foi denominado *arteria*[ii] (significava tubo de ar, sendo este gás designado também por pneuma ou "espírito vital"), enquanto os do outro tipo, que continham sangue[iii], recebiam a designação de veias (*phleps ou phebos*, tubo transportador de sangue).

Segundo Aristóteles, e depois com os seus discípulos da escola de Alexandria, Erasistratus e Herofilus (séc. IV-III aC), admitia-se que o sangue era formado no fígado a partir dos alimentos, donde seria transportado para o coração, que o distribuiria para todo o corpo, para consumo. As artérias e veias emanariam do coração. Pelo contrário, para Hipócrates (séc. V-IV aC) o sangue circularia num só vaso (em circuito fechado) que se ramificava por todo corpo. [(1, 2)]

Claudius Galenus, conhecido simplesmente por Galeno (131-201? A.C.), adoptou os conceitos originais da escola de Alexandria, alterando-os de acordo com as suas próprias observações anatómicas. Desde modo, as artérias não transportariam somente ar mas também sangue (como Herofilus propusera) de composição e cor distintas das

stated that "all the [movement of the] blood is controlled by the heart; the blood flows in never-ending circles... some blood vessels transport the air that is necessary to life" [(1)].

The next step was taken in ancient Greece, when dissection of human cadavers showed that the blood circulated in special vessels of two types; one, which was thought to transport air, was called "artery" (meaning tube for air; this gas was also known as *pneuma*, or vital spirit), while the other type, which contained blood, was termed "vein" (from the Greek *phleps*, *phlebos*, tube carrying blood).

According to Aristotle and his disciples at the school of Alexandria, Erasistratus and Herophilus (4th-3rd century BC), the blood was formed in the liver from food, and was thence transported to the heart, which distributed it throughout the body, where it was consumed. Arteries and veins emanated from the heart. By contrast, according to Hippocrates (5th-4th century BC), the blood circulated in a single vessel that branched throughout the body, in a closed circuit [(1, 2)].

Claudius Galenus, known as Galen (131-201?AD), adopted the concepts of the Alexandria school and altered them in accordance with his own anatomical observations. According to him, as well as air, the arteries carried blood (as also proposed by Herophilus) of a different composition and color from venous blood. The two types of blood were distributed throughout the body and consumed as and when required, but their origin and transport system were different. The darker

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NB- As transcrições de parte de textos originais citados foram adaptados à grafia actual.

[i] Compêndio médico chinês atribuído ao Imperador Amarelo (Huang di), cerca de 2400 aC, foi transmitido oralmente durante muitos séculos. Parece ter sido compilado em forma escrita somente no 3º século aC.
[ii] Deu origem à designação actual dos vasos que transportam sangue arterial
[iii] Pensava-se na época que as veias continham sangue e as artérias ar porque, post-mortem, o sangue era evidente somente no sector venoso.

Spelling in the quotations has been modernized.

[1] A Chinese medical compendium from around 2400 BC, attributed to the reign of the Yellow Emperor (Huang Ti); it was transmitted orally for centuries and was only written down in the 3rd century BC.
[2] Hence the modern term for the vessels that transport arterial blood.
[3] At the time it was believed that the veins contained blood and the arteries contained air because after death blood was only found in the veins.

do sangue venoso. Os dois tipos de sangue seriam distribuídos por todo o corpo e aí consumidos quando e enquanto necessário; porém, as suas origens e vias de transporte eram diferentes: o sangue mais escuro, formado no fígado a partir do quilo, seria veiculado para o coração direito, onde daria origem a duas partes, uma distribuída por todo o organismo, teria funções de nutrição e crescimento, enquanto a outra atravessaria directamente o septo interventricular (portanto, sem passar pelos pulmões) para o ventrículo esquerdo, onde se misturaria com o *pneuma* (transportado pelas veias pulmonares), originando o sangue arterial (de cor vermelho clara, mais fino e cheio de vitalidade), por sua vez também veiculado para todo o organismo por uma rede vascular própria, e aí também consumido. Por conseguinte, Galeno também admitia que ambos os tipos de sangue seriam consumidos pelo organismo, à semelhança de qualquer outro alimento. Por sua vez, o ventrículo esquerdo seria o local onde o *pneuma* se misturava com o sangue. O sangue movimentar-se-ia pela pulsação das artérias e pela sucção do coração durante a diástole. Estas ideias, que definiam o essencial da circulação sanguínea, foram preservadas e transmitidas a sucessivas gerações de médicos, quase sem alterações, até ao século XVI [1-3].

Em meados do século XIII, Ibn al-Nafis, de Damasco, apresentou as primeiras discordâncias aquele sistema ao afirmar, no seu mais famoso tratado médico "*Sharh Tashrih al-Qanun Ibn Sina*" (*Comentários ao Canon de Anatomia de Avicena*)[iv], que o sangue circulava através dos pulmões e não através do septo interventricular; admitiu a existência de pequenas passagens (ou poros) entre as veias e as artérias pulmonares (o que tem sido interpretado como uma referência a capilares, cerca de 400 anos antes da sua visualização); adicionalmente apresentou, também pela primeira vez, o conceito da circulação coronária, pela qual o sangue proveniente do ventrículo esquerdo e transportado através de pequenos vasos, nutria o coração [4]. Não há a certeza de que forma Ibn al-Nafis chegou

blood, formed in the liver from chyle, was carried to the right heart, where it divided into two parts: one was distributed throughout the organism for the purposes of nutrition and growth, while the other crossed the interventricular septum (and thus did not go through the lungs) and passed directly into the left ventricle, where it mixed with *pneuma* from the pulmonary veins, giving rise to arterial blood, lighter in color, thinner and full of vitality, which was in turn carried to the rest of the organism via its own system of vessels, there to be consumed. Galen thus believed that both types of blood were consumed by the organism, like other types of food. The left ventricle was where the *pneuma* combined with the blood, which was then transported by the pulsation of the arteries and the suction of the heart during diastole. These ideas, Galen's explanation of the circulation of the blood, were transmitted, virtually unchanged, to successive generations of physicians up to the 16th century [1-3].

In the mid-13th century, Ibn al-Nafis of Damascus put forward the first alternative to this system in his best-known medical treatise, *Sharh Tashrih al-Qanun Ibn Sina* ("Commentary on Anatomy in Avicenna's Canon"), in which he stated that the blood circulated via the lungs and not through the interventricular septum and proposed the existence of small passages or pores between the pulmonary veins and arteries (which has been interpreted as a reference to capillaries 400 years before they were first observed). He presented, also for the first time, the concept of the coronary circulation, in which blood from the left ventricle nourishes the heart through small vessels [4]. It is not known how Ibn al-Nafis arrived at these conclusions, whether by conjecture, observation of animals such as monkeys, or by autopsy studies of humans [5, 6].

The subject of the pulmonary circulation was taken up again in Europe three centuries later by Miguel de Servetus and Matteo Realdo Colombo. The fact that both published their works within a few years of the appearance of a translation of a work by Ibn al-Nafis[4], and the similarities between some of

aquelas conclusões: por conjectura, observação em animais (p.ex., macacos) ou pela autópsia[v] sistemática de humanos [5,6].

O tema da circulação pulmonar seria retomado na Europa, três séculos depois, por Miguel de Servetus[vi] e Matteo Realdo Colombo[vii]. O facto de os trabalhos de ambos terem sido divulgados poucos anos depois da divulgação de uma obra traduzida de Ibn al-Nafis[viii] [4], e a semelhança de redacção entre algumas das descrições, têm suscitado posições contraditórias quando à primazia da descoberta.[7-10]

Nos primórdios do Renascimento, os magníficos desenhos e descrições do coração e aparelho circulatório que Leonardo da

the descriptions, have aroused disagreement as to who first made the discovery [7-10].

In the Renaissance, the magnificent drawings and descriptions of the heart and circulatory apparatus that Leonardo da Vinci and Andreas Vesalius produced on the basis of autopsy studies of human cadavers, together with the contributions of Servetus, Colombo and other anatomists, rendered untenable the model of the circulation that had prevailed since Galen. Among the most important of the new concepts were the following: (a) the interventricular septum was not permeable to blood, which therefore could not pass directly from the right to the left ventricle; (b) the vena

[iv] Ibn al-Nafis (1210-1285) publicou o volume referido aos 29 anos de idade, enquanto médico do Hospital Al-Mansouri, no Cairo. A sua obra terá sido conhecida na Europa somente em 1924, por via de uma tese de doutoramento em Medicina submetida por um bolseiro médico egípcio na Universidade de Freiburg im Breisgau, Alemanha. A tese nunca foi publicada e, só por um acaso, veio a ser conhecida por Max Meyerhof (4), da qual divulgou partes relevantes.

[v] O que se afigura pouco provável devido às restrições estabelecidas pela religião muçulmana, mas não impossível, atendendo às descrições incluídas no texto, que contrariam postulados de Galeno.

[vi] Miguel de Servetus (1511-1553), natural de Navarra Espanha), foi teólogo, geógrafo e anatomista, foi autor de diversos livros relevantes na sua época. Foi condenado à morte pela justiça religiosa (de católicos e protestantes), com base no que publicara no livro "Christianismi Restitutio" . Esta obra, em grande parte devotada à interpretação e discordância de alguns dogmas e comportamentos religiosos, também incluía, em alguns parágrafos, somente, a descrição de observações anatómicas realizadas por Servetus. Nessas observações era rejeitada a existência de qualquer comunicação entre a s câmaras direita e esquerda do coração; como alternativa, indicava que o sangue passava pelos pulmões, onde se misturaria com o ar, mudando de cor vermelha escura para mais clara, após o que reentrava no coração pela aurícula esquerda, donde passava, através de uma válvula, para o ventrículo do mesmo lado. Seguidamente, indicava que o coração impulsionava o sangue para as artérias. Porém, mais do que uma exposição anatómica, Servetus pretendia definir a alma (como sinónimo de "espírito vital" ou pneuma, que seria a expressão do poder divino eterno) como o resultado de uma mistura do ar inspirado com o sangue nos pulmões. A vida continuaria enquanto houvesse aquela mistura e, portanto, a circulação intrapulmonar do sangue.

[vii] Realdo Colombo (1516-1559), anatomista italiano, baseou os seus estudos anatómicos, que publicou em "De Re Anatomica" (1559), na dissecção de criminosos, religiosos e portadores de defeitos morfológicos congénitos, e na vivissecção animal. A parte referente à circulação pulmonar terá sido redigida após 1553, ou seja, bastante depois da divulgação dos resultados de Servetus. As suas conclusões eram substancialmente idênticas às de Servetus, com a diferença de ter enfatizado o grande volume de sangue transportado pela veia pulmonar, depois de se ter misturado com o ar nos pequenos vasos intrapulmonares (esclarecendo assim que o "espírito vital" do sangue arterial era gerado nos pulmões e não no coração). Adicionalmente, resolveu as fases (de contracção e relaxamento) do ciclo cardíaco, além de associar a presença de válvulas nos vasos que entram e saem do coração ao sentido do fluxo sanguíneo (do ventrículo direito para os pulmões, destes para o coração esquerdo e, por fim, do ventrículo esquerdo para a aorta). O facto de ter sido médico da corte papal e as relações desta com a Inquisição, ter-lhe-ão dado acesso a cópias do volume proscrito "Christianismi Restitutio" e de outros textos de Servetus.

[4] Ibn al-Nafis (1210-1285) published this treatise at the age of 29 while working as a doctor at the Al-Mansouri Hospital in Cairo. It only became known in Europe in 1924 through the PhD thesis of an Egyptian medical student at the University of Freiburg im Breisgau in Germany. The thesis, which was never published, happened to be discovered by Max Meyerhof [4], who published relevant extracts.

[5] Given the restrictions on dissection in Islam, this is unlikely but not impossible, since the descriptions in the text contradict those of Galen.

[6] Michael Servetus (Miguel Servet) (1511-1553), of Navarre in Spain, theologian, geographer and anatomist, was the author of a number of important works. He was condemned by the religious authorities (both Catholic and Protestant) and burned at the stake for his book *Christianismi Restitutio*, most of which deals with the interpretation of and disagreements between various religious dogmas and practices. It also contains a few paragraphs on Servetus' own anatomical observations, on the basis of which he rejects the possibility of any communication between the right and left chambers of the heart and proposes instead that the blood passes through the lungs, where it mixes with air, changing from dark to lighter red, after which it re-enters the heart via the left atrium, whence it passes through a valve to the left ventricle. The heart then pumps the blood to the arteries. However, this was not merely an anatomical explanation; Servetus also set out to define the soul (which was synonymous with the *pneuma* or "vital spirit", the expression of the eternal divine power) as resulting from the air breathed in mixing with the blood in the lungs. Life continued so long as this mixture was available, in other words so long as intrapulmonary blood circulation continued.

[7] Realdo Colombo (1516-1559) was an Italian anatomist who based his studies (published in 1559 as *De Re Anatomica*) on his dissection of criminals, members of religious orders and those with congenital morphological defects, as well as vivisection of animals. The section on the pulmonary circulation was written after 1553, and thus well after the publication of Servetus' work, and his conclusions are broadly similar. However, Colombo highlighted the large volume of blood transported by the pulmonary vein after being mixed with air in the small intrapulmonary vessels, thus showing that the "vital spirit" of arterial blood was generated in the lungs rather than in the heart. He also described the phases of contraction and relaxation in the cardiac cycle, as well as linking the presence of valves in the vessels entering and leaving the heart with the direction of blood flow (from the right ventricle to the lungs, from the lungs to the left heart and finally from the left ventricle to the aorta). His position as physician at the papal court, and the relationship between the papacy and the Inquisition, meant he would have had access to the proscribed *Christianismi Restitutio* and other works by Servetus.

Vinci[ix] e Andreas Vesalius[x] obtiveram a partir de cadáveres humanos autopsiados, e os contributos de Servetus, Colombo e de outros anatomistas, puseram definitivamente em causa o modelo de circulação que vigorava desde Galeno. Entre as reformulações conceptuais então apresentadas merecem referência as seguintes:

(a) o septo interventricular não era permeável ao sangue, donde este não poderia passar directamente do ventrículo direito para o esquerdo;

(b) a veia cava não provinha do fígado;

(c) foi demonstrada a existência de um percurso intrapulmonar entre o coração direito e o esquerdo;

(d) em lugar da diástole (que aspiraria os sangue para o coração), seria a sístole cardíaca a determinar a função contráctil do coração e subsequente descarga do sangue para as artérias, que assim se encheriam com o volume debitado; a pulsação resultaria do enchimento das artérias com sangue, debitado

cava did not originate in the liver; (c) an intrapulmonary route was demonstrated between the right and the left heart; (d) it was not diastole, sucking the blood into the heart, but rather systole that determined the heart's contractile function and the expulsion of the blood into the arteries, pulsation resulting from the arteries filling regularly with blood during each systole, and not as a result of the expansion caused by mixing the blood with *pneuma*; and (e) the direction of blood flow was determined by valves in the heart and in the veins.

However, none of these works showed that, *in vivo*, the blood circulated constantly and regularly in a closed circuit and that the heart was the dynamo of this movement. Although the term *circulatio* had been proposed by Andrea Cesalpino, he meant no more than a slow and irregular movement, like air moving around a dwelling, caused by evaporation and condensation, as warm blood continually rose in the arteries and cool blood descended in

[viii] Na origem desta hipótese estaria a tradução para Latim (por Andrea Alpago de Belluno, em 1547) de outras obras de Ibn Nafis(designadamente, o texto "Comentários sobre Drogas Compostas"), que incluíram críticas aos conceitos de Galeno sobre o coração e os vasos sanguíneos, contrapondo as suas próprias descobertas; acresce o facto de Servetus ter estudado anatomia, em Paris, com Guenther von Andernach (ou Johannes Guinter) e, por essa via, lhe ter sido possível aceder às muitas obras dos clássicos Gregos e de outros médicos da Antiquidade, que Guenther traduzira para Latim.

[ix] Leonardo di ser Piero da Vinci (1452-1519), polímata italiano e um dos maiores génios da Humanidade. Entre os seus múltiplos interesses incluía-se o estudo da anatomia humana, realizada em cadáveres e ilustrada em magníficos desenhos de grande precisão e sob diferentes perspectivas. As observações morfológicas do coração e dos grandes vasos foram completadas por hipóteses fisiológicas baseadas na hidrodinâmica. Quer os desenhos quer as observações e conjecturas ficaram dispersos em múltiplas folhas e cadernos de anotações, de que foi recuperada apenas uma parte.

[x] Andries van Wesel (1514-1564), conhecido pelo nome latinizado de Andreas Vesalius, nasceu em Bruxelas (então Habsburg, Holanda). Foi autor do primeiro e mais influente tratado de anatomia dos tempos modernos (" HYPERLINK "http://en.wikipedia.org/wiki/De_humani_corporis_fabrica" \o "De humani corporis fabrica" De humani corporis fabrica", 1ª edição em 1543, ilustrado com muitos desenhos minuciosos do corpo humano em diversas posições comuns), no qual demonstrou diversos erros que vinham sendo ensinados desde Galeno (alegadamente por este se ter baseado mais na anatomia de gorilas e cães do que em humanos) e de outros seus antecessores. Designadamente, esclareceu que o coração era constituído por quatro câmaras e que era o órgão donde emanavam os grandes vasos, corrigindo o que Aristóteles, Galeno e Mondino de Liuzzi haviam descrito. Vesalius tem sido considerado o fundador da Anatomia Humana.

[8] The work in question was a translation into Latin by Andrea Alpago of Belluno, in 1547, of other works by Ibn al-Nafis, particularly his "Commentary on Compound Drugs", which included criticisms of Galen's ideas on the heart and blood vessels and put forward his own. There is the added factor that Servetus studied anatomy in Paris with Guenther von Andernach (Johannes Guinter) and would thus have had access to many works on medicine by the Greeks and other ancient authors that Guenther had translated into Latin.

[9] Leonardo di ser Piero da Vinci (1452-1519) was an Italian polymath and one of the greatest geniuses in history. Among his many interests was human anatomy, which he studied by dissecting corpses and illustrating them with superb drawings of great accuracy and from different perspectives. On the basis of his observations of the structure of the heart and great vessels, he went on to develop conjectures on physiology based on hydrodynamics. His drawings and observations and conjectures were scattered among numerous notebooks and loose pages, only some of which have survived.

[10] Andries van Wesel (1514-1564), known by the Latinized name of Andreas Vesalius, was born in Brussels (then in the Habsburg-ruled Low Countries). He was the author of the first and most influential treatise on anatomy in modern times, *De humani corporis fabrica*, first published in 1543, which was copiously illustrated with detailed drawings of the human body in various common positions. In it he pointed out a number of errors that had been perpetuated since the time of Galen (supposedly because the latter's teaching had been based on the anatomy of gorillas and dogs rather than humans) and by other anatomists. In particular, he demonstrated that the heart consisted of four chambers and that it was the origin of the great vessels, contradicting the teachings of Aristotle, Galen and Mondino de Liuzzi. Vesalius is considered the father of human anatomy.

regularmente a cada sístole (e não, como resultado da expansão da mistura do sangue com o *pneuma*);

(e) o sentido da deslocação do sangue seria determinado por válvulas existentes no coração e nas veias.

Porém, nenhum daqueles estudos evidenciou que, *in vivo*, o sangue circulava constante e regularmente em circuito fechado, e que seria o coração o dínamo desse movimento. Ainda que o termo *circulatio* tivesse sido proposto na época por Andrea Cesalpino[xi], não significava mais do que um movimento lento e irregular (à semelhança das deslocações de ar num aposento) induzido por evaporações e condensações, durante o qual o sangue quente subia nas artérias e o sangue frio descia nas veias continuamente, portanto nada condizente ao que veio a ser demonstrado[1,11].

O esclarecimento do modelo de circulação sanguínea

Coube a William Harvey (*Fig1*), médico e anatomista inglês do século XVII, a descoberta do modelo da circulação sanguínea sistémica. Após uma primeira fase educacional, graduou-se em Artes no Gonville e Caius College de Cambridge (1597), onde permaneceu até finais de 1599 para completar os estudos de medicina. No ano seguinte Harvey foi para Pádua, para aprender anatomia e medicina na que, na época, era considerada a melhor escola médica europeia. Durante dois anos, Harvey foi discípulo de Hieronymus Fabricius (também conhecido por Girolano Fabrizi d'Aquapendente)[xii], após o que regressou a Inglaterra, sendo investido como Doutor em Medicina pela Universidade de Cambridge e iniciando o exercício da profissão prática, em 1602 [11].

Nos anos seguintes, Harvey praticou e ensinou medicina em Londres[xiii], mantendo-se interessado numa questão então por esclarecer, que era a do fluxo sanguíneo no organismo humano [12]. As investigações de Fabricius sobre as válvulas venosas e a sólida formação anatómica cultivada em Pisa, desde

the veins, which bore no resemblance to what came to be demonstrated [1, 11].

The circulation of the blood elucidated

It fell to William Harvey (*Figure 1*), a 17th-century English physician and anatomist, to discover the true nature of the systemic blood circulation. In 1597 he was awarded the degree of Bachelor of Arts from Gonville and Caius College, Cambridge. After graduating, Harvey remained in Cambridge until the end of 1599, to complete his studies

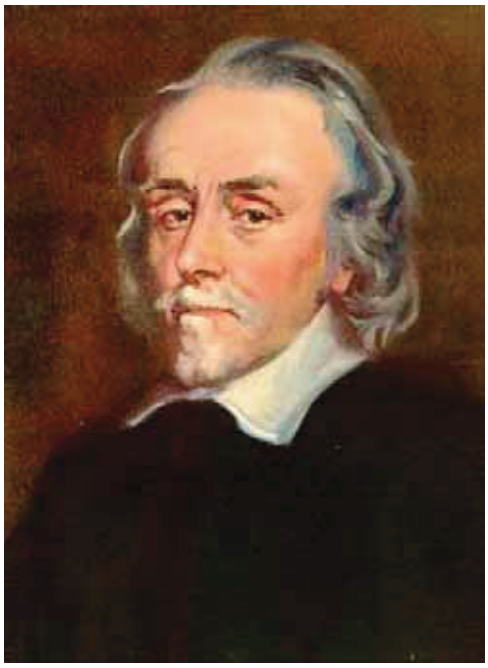

Figura 1- William Harvey (1578-1657), natural de Folkstone in Kent, Inglaterra, foi o primeiro a identificar o movimento do sangue na circulação sistémica com a exactidão ainda hoje reconhecida. Na época, representou uma total ruptura conceitos anatómicos e funcionais de Galeno. Harvey descreveu em pormenor a sua descoberta em "Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus" (Exercício Anatómico sobre o Movimentos do Coração e do Sangue nos Seres Vivos), com 1ª edição publicada em 1628.O volume contém duas partes: na primeira anota as falhas de Galeno, enquanto a segunda evidencia os factos verificados nas suas experiências que conduziram à descoberta do modelo circulatório do sangue.
Cortesia/ Courtesy: "Wikimedia Commons".

Figure 1. William Harvey (1578-1657), born in Folkstone, Kent, England, was the first to describe the movement of blood in the systemic circulation, with an accuracy still acknowledged today. At the time, this represented a complete break with the anatomical and functional teachings of Galen. Harvey described his discovery in detail in Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus *("An Anatomical Exercise Concerning the Motion of the Heart and Blood in Animals"), first published in 1628. The volume consists of two parts: the first details Galen's errors, while the second sets forth the results of Harvey's experiments that led him to develop his model of the circulatory system.*
Image courtesy of Wikimedia Commons.

Vesalius, foram determinantes para as pesquisas que Harvey projectava realizar. Por duvidar das teorias então vigentes no ensino médico tradicional, decidiu basear o seu trabalho em observações e não em conjecturas. Para o efeito realizou numerosas dissecções e investigações experimentais em diferentes espécies animais, de sangue frio e quente, entre os quais veados das coutadas reais, decerto beneficiando do apoio e interesse de dois soberanos (James I e, depois, de Charles I) e do estatuto de médico da corte [12-15].

Além de descobrir que o sangue circulava nos animais, inclusive em humanos, foi o primeiro apresentar um modelo lógico para a

in medicine. A year later he went to study anatomy and medicine in Padua, then considered the finest medical school in Europe. For two years he studied under Hieronymus Fabricius, after which he returned to England to be incorporated as Doctor of Medicine at Cambridge and to begin professional practice in London, later in 1602 [11].

In the following years, Harvey practiced and taught medicine in London, and kept up his interest in the still unresolved question of the flow of blood in humans [12]. Fabricius' investigations of the venous valves and the meticulous study of anatomy that had been a tradition in Pisa since Vesalius were essential

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[xi] Andrea Cesalpino (latinizado para Andreas Caesalpinus;1519-1603), médico, filósofo e botânico italiano, foi discípulo de Realdo Colombo em Pisa. Na continuidade das investigações deste, apresentou uma boa descrição das válvulas cardíacas, desenvolveu o conceito da pequena circulação e previu a existência de vasos muito finos a conectarem as artérias às veias. Também observou que, ao comprimir uma veia superficial, provocava a sua distensão abaixo e o seu esvaziamento acima do ponto de interrupção (precedendo observações semelhantes que Harvey viria a utilizar para o seu raciocínio sobre o circuito da circulação sistémica). Porém, não se demonstrou que as investigações de Cesalpino sobre a circulação sanguínea tivessem fundamento anatómico adequado. Por exemplo, ao verificar que a veia cava tinha um diâmetro maior junto à aurícula direita do que perto do fígado, concluiu que seria uma prova de que aquela veia transportava o sangue do coração. Entre outras ideias rudimentares, admitia que o sangue tinha origem no coração, do qual saía por 4 veias para irrigar todo o corpo, "à semelhança dos 4 rios que saem do Paraíso".

[xii] Fabricius (1537-1619), anatomista Italiano e um dos expoentes médicos da época, fora discípulo de Gabriello Fallopio (1523-1562), que por sua vez fora aluno de Vesalius na escola médica de Pisa. Fabricius redescobriu as válvulas venosas em 1574, porém nunca entendeu a respectiva função, pois continuou a admitir que o sangue fluía nas veias do coração para a periferia do corpo e que as válvulas serviam para obstruir parcialmente o lúmen. Não tem sido fácil identificar quem primeiro demonstrou a existência daquelas válvulas, cerca de 30 anos antes de Fabricius. Entre os que reuniam maiores possibilidades têm sido citados o professor de Anatomia de Ferrara, Giambattista Canano (1515-1579), também médico do Papa Julius II, e o anatomista e médico português João Rodrigues Castelo Branco (1511- 1568), mais conhecido por Amato (us) Lusitano (us). Canano terá anunciado a Vesálio, num encontro havido em 1545, que descobrira válvulas nos orifícios de entrada de diversas veias (designadamente na ázigos e veias renais) embora nunca a publicasse os seus resultados. Por seu lado, Amatus , em 1547, no período em que viveu em Ferrara (Itália), demonstrou numa aula de Anatomia (em cuja assistência estaria Canano) , em diversos cadáveres de homens e animais , a presença de uma válvula na intercomunicação da veia ázigos com a veia cava que impedia que o ar soprado na ázigos não passasse para a veia cava. Estas observações, mencionadas em 1551 num dos seus tratados (Curationum Medicinalium Centuria Prima) levaram – no a concluiu (erradamente) que o mesmo sucederia com o sangue.

[xiii] Após o seu regresso, Harvey começou a exercer clínica; em 1607 foi eleito "Fellow" do Royal College of Physicians ; em 1609 assumiu um cargo médico no St. Bartholomew's Hospital; em 1615 foi nomeado docente "Lumleian"de Anatomia e Cirurgia, em Londres (em cujas atribuições se incluía a efectivação de dissecções públicas); três anos depois foi designado médico extraordinário do rei James (I de Inglaterra e VI da Escócia), sendo, após a morte deste, nomeado médico ordinário de Charles I.

[11] Andrea Cesalpino (Latinized as Andreas Caesalpinus;1519-1603), an Italian physician, philosopher and botanist, was a disciple of Realdo Colombo in Pisa. Continuing the latter's research, he accurately described the valves of the heart, developed the concept of the lesser circulation and predicted the existence of very small vessels connecting arteries and veins. He also observed that compression of a superficial vein caused distension below and emptying above the point of pressure, anticipating similar observations by Harvey, who used them as a basis for his reasoning regarding the systemic circulation. However, Cesalpino's theories on the circulation of the blood do not appear to have had a real basis in anatomy. For example, on discovering that the vena cava was wider at the right atrium than at the liver, he concluded that this was evidence that it transported blood from the heart. Among other erroneous ideas, he thought that blood originated in the heart, whence it emerged through four veins to irrigate the rest of the body, "like the four rivers flowing out of Paradise".

[12] Fabricius (1537-1619) (also known as Girolano Fabrizi d'Aquapendente), Italian anatomist and one of the outstanding physicians of his day, was a disciple of Gabriello Fallopio (1523-1562), who in turn had studied under Vesalius at the medical school in Pisa. Fabricius rediscovered the venous valves in 1574, although he never understood their function and continued to believe that the blood left the heart through the veins to the rest of the body and that the valves served to partially obstruct the lumen. It is not known with any certainty who first discovered the existence of the venous valves, some 30 years before Fabricius. Among the most likely candidates are the professor of anatomy at Ferrara, Italy, Giambattista Canano (1515-1579), who was also physician to Pope Julius II, and the Portuguese anatomist and physician João Rodrigues Castelo Branco (1511-1568), better known as Amatus Lusitanus or Amato Lusitano. Canano informed Vesalius, during a meeting in 1545, that he had discovered valves in the ostia of various veins, particularly the azygos and renal veins, although he never published his findings. Amatus, while living in Ferrara in 1547, in an anatomy class at which Canano was present, demonstrated in human and animal cadavers the presence of a valve at the junction of the azygos vein with the vena cava, which prevented air blown into the azygos from entering the vena cava. This observation, mentioned in his 1551 tract Curationum Medicinalium Centuria Prima, led him to conclude (erroneously) that the same was true for blood.

[13] After his return, Harvey began to practice and in 1607 was elected a Fellow of the Royal College of Physicians in London. In 1609 he took up a post at St. Bartholomew's Hospital; in 1615 he was appointed Lumleian Lecturer in Anatomy and Surgery at the Royal College (among the duties of which was to perform public dissections); and three years later he was appointed physician extraordinary to James I, after whose death he became Charles I's personal physician.

circulação sanguínea, baseado na observação e experimentação, e que continua a ter aceitação genérica. Porém, aqueles resultados e conceitos, alguns dos quais divulgados Harvey vinha divulgando desde 1615 aos seus alunos viriam a ser publicados somente treze anos mais tarde, no famoso livro "*Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus*" (que ficou conhecido por "*De Motu Cordis*) (*Fig 2*). Nesse pequeno volume de 72 páginas (da edição original em latim), Harvey apresentou com elegância o que observara nas dissecções realizadas e as conclusões a que havia chegado [16]. Entre outras, merecem particular destaque as seguintes [17]:

(a) A disposição das válvulas cardíacas permitia que o sangue fluísse somente num sentido[xiv]:

"*If the three tricuspid valves placed at the entrance into the right ventricle prove obstacles to the reflux of the blood into the vena cava, and if the three semilunar valves which are situated at the commencement of the pulmonary artery be there, that they may prevent the return of the blood into the ventricle; why, when we find similar structures in connexion with the left ventricle, should we deny that they are there for the same end, of preventing here the egress, there the regurgitation, of the blood?*"

(b) Os ventrículos contraíam-se simultaneamente, depois das aurículas, passando o sangue do ventrículo direito para a aurícula esquerda e, daqui, para o ventrículo esquerdo através dos pulmões (refutando assim o disposto por Galeno, em que o sangue seria directamente encaminhado de um ventrículo para o outro através de perfurações invisíveis do septo interventricular) [18]:

"*…we find …the pulmonary vein and left ventricle so full of blood, of the same black colour and clotted character as that with which the right ventricle and pulmonary artery are filled, is because the blood is incessantly*

to the research that Harvey was about to embark upon. Since he questioned the contemporary theories that dominated traditional medical teachings, he decided to base his work on observation rather than conjecture. To this end, he performed numerous dissections and experiments on various animal species, both cold- and warm-blooded, including deer from the royal parks, made possible no doubt by the support and interest of two sovereigns, James I and Charles I, and his status as court physician [12-15].

Besides discovering that the blood circulated in animals, including humans, he was the first to present a logical model for this circulation, based on observation and experimentation, which in general terms is still accepted today. Although some of his findings and theories were introduced into his lectures from 1615 onwards, they were only published thirteen years later in his famous book *Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus* (which became known as *De Motu Cordis*) (*Figure 2*). In this slender volume of 72 pages, originally published in Latin, Harvey elegantly presented the results of his dissections and the conclusions he had reached [16]. Among these conclusions, the following are of particular importance [17]:

Figura 2-Capa da 1ª edição do tratado Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus
Imagem: Cortesia/ Courtesy: "College Librarian, The Royal College of Surgeons of Edinburgh".

Figure 2. Cover of the first edition of Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus.
Image courtesy of the College Librarian, The Royal College of Surgeons of Edinburgh.

passing from one side of the heart to the other through the lungs."

(c) Os movimentos do sangue eram determinados pelo coração e não pelo fígado; também rejeitou a ideia de que o sangue seria movimentado por sucção cardíaca, pois que ao removê-lo do animal, o coração continuava a contrair-se, à semelhança de um saco muscular[xv]; nessa base propôs que aquela função se assemelhava à de espremer o sangue para a aorta e artéria pulmonar [19]:

"*From these particulars it appears evident to me that the motion of the heart consists in a certain universal tension-both contraction in the line of its fibres, and constriction in every sense…. We are therefore authorized to conclude that the heart, at the moment of its action, is at once constricted on all sides, rendered thicker in its parietes and smaller in its ventricles, and so made apt to project or*

(a) The arrangement of the cardiac valves means that the blood can flow in only one direction:

"*If the three tricuspid valves placed at the entrance into the right ventricle prove obstacles to the reflux of the blood into the vena cava, and if the three semilunar valves which are situated at the commencement of the pulmonary artery be there, that they may prevent the return of the blood into the ventricle; why, when we find similar structures in connexion with the left ventricle, should we deny that they are there for the same end, of preventing here the egress, there the regurgitation, of the blood?*"

(b) The ventricles contract simultaneously, after the atria, the blood passing from the right ventricle to the left atrium and thence to the left ventricle via the lungs. This contradicts Galen's theory that the blood goes directly from one ventricle to the other through invisible perforations in the interventricular septum [18]:

[xiv] Esta conclusão é original somente por sido observada *in vivo*. Já no século IV aC, o grego Erasistratus havia afirmado que as válvulas do coração asseguravam a corrente unidireccional do sangue; interpretava a hemorragia subsequente ao corte de uma artéria como o resultado do "horror ao vazio": primeiro sairia o ar das artérias, imediatamente substituído pelo sangue proveniente de pequenos vasos situados entre as veias e as artérias; desde modo parece que Erasistratus admitia a existência de vasos equivalentes aos capilares, embora a circulação seguisse sentido inverso ao que sucede na realidade. No início do Renascimento, o estudo das válvulas do coração humano, quer no seu aspecto anatómico quer na interpretação das respectivas finalidades hemodinâmicas, foi uma das geniais e inéditas descobertas que Leonardo da Vinci realizou em cadáveres autopsiados, nos seus últimos anos de vida, na sequência de observações prévias em animais viviseccionados. (15,16) A teorização sobre a repleção de sangue durante a diástole e a sequência da respectiva ejecção para a aorta (extrapoladas da observação minuciosa dos fluxos de água corrente e dos redemoinhos originados por obstáculos) levou a que Leonardo concluísse que o encerramento da válvula aórtica seria induzida pelos vórtices gerados na aorta e pelo subsequente refluxo pós-sistólico do sangue. Concebeu ainda a existência de diversos tipos de fluxo e a interacção parietal do sangue ejectado ao longo da crossa da aorta (aparentemente com o auxílio de modelos de cera e de um modelo mecânico que construiu). No conjunto, aqueles estudos representam uma fase pioneira da Hemodinâmica e também da Hemorreologia. Harvey não terá tido conhecimento da obra anatómica e das teorias que Leonardo elaborara sobre as válvulas cardíacas, a sua contribuição para o fluxo sanguíneo e, ainda, o ter admitido a hipótese de um circuito sanguíneo. De facto, não só Leonardo morreu quase 60 anos antes de Harvey nascer como não deixou nenhum livro sobre os seus estudos, somente folhas soltas com apontamentos e desenhos de assuntos misturados, redigidos em código e com imagem revertida. A compreensão do legado científico de Leonardo foi conseguida séculos mais tarde, pelo que será muito improvável que Harvey o tivesse conhecido.

[xv] A natureza muscular do coração fora já admitida por Aulus Cornelius Celsus (25 aC - 50 dC) e, depois também, por Claudius Galeno dC). Leonardo da Vinci descreveu e desenhou com grande exactidão a conformação muscular do órgão e a respectiva função contráctil, bem como a distribuição dos feixes musculares que accionavam o movimento das válvulas cardíacas.

[14] This conclusion is only original in that it was observed *in vivo*. As early as the 4th century BC, the Greek physician Erasistratus had stated that the valves of the heart made the blood flow in one direction. He interpreted the bleeding that resulted from cutting an artery as the result of "Nature abhorring a vacuum": firstly air left the artery, to be replaced immediately by blood from the small vessels between the veins and the arteries. It thus appears that Erasistratus believed in the existence of vessels equivalent to the capillaries, although with flow in the wrong direction. In the Renaissance, study of the valves of the human heart from dissections of cadavers, following on from his earlier observations from the vivisection of animals, led to some of Leonardo da Vinci's most brilliant and original discoveries in terms of their anatomy and hemodynamic function (15, 16). His theorizing about the refilling of blood during diastole and the sequence of its ejection into the aorta (extrapolated from his meticulous observation of currents of flowing water and eddies caused by obstacles) led him to conclude that closure of the aortic valve was induced by vortices generated in the aorta and by subsequent post-systolic blood reflow. He also hypothesized the existence of different types of flow and that the ejected blood interacted with the walls of the aortic arch (apparently with the aid of wax casts and a mechanical model that he constructed). Taken together, these discoveries represent a pioneering stage in hemodynamics and, indeed, hemorheology. Harvey would not have known Leonardo's anatomical studies and theories concerning the valves of the heart and their role in blood flow, or the fact that he postulated the circulation of the blood. Not only did Leonardo die nearly 60 years before Harvey was born, but he left no published record of his studies, merely loose pages of notes and drawings on miscellaneous subjects, in code and in mirror writing. Leonardo's scientific legacy was only recognized centuries later and it is therefore extremely unlikely that Harvey would have known of him.

[15] The fact that the heart is composed of muscle was already known to Aulus Cornelius Celsus (25 BC-50 AD) and later to Galen. Leonardo da Vinci described, and drew in great detail, the configuration of the heart's muscles and its contractile function, as well as the distribution of the bands of muscle that activated the cardiac valves.

expel its charge of blood… Neither is it true, as vulgarly believed, that the heart by any dilatation or motion of its own, has the power of drawing the blood into the ventricles; for when it acts and becomes tense, the blood is expelled; when it relaxes and sinks together it receives the blood in the manner and wise which will by-and-by be explained … Finally, it is not without good grounds that Hippocrates in his book, "De Corde," entitles it a muscle; its action is the same; so is its functions, viz., to contract and move something else - in this case the charge of the blood."

(d) No seguimento desta conclusão estabeleceu que o sangue proveniente do coração circulava num sistema de vasos diferentes daquele que o transportava em sentido inverso da periferia [20]:

"*…that the arteries are the vessels carrying the blood from the heart, and the veins the returning channels of the blood to the heart…*"

(e) O sangue que circulava nas artérias e nas veias era o mesmo, assim como as artérias e as veias faziam parte do mesmo sistema transportador de sangue [21]:

"*…we may fairly conclude that the arteries contain the same blood as the veins, and nothing but the same blood.*"

(f) A pulsação resultava do enchimento das artérias com sangue; por esse mecanismo as artérias dilatavam e não o contrário, como se julgava (ou seja, primeiro alargariam e só depois ficariam cheias de sangue) [18]:

"*From these facts it is manifest, in opposition to commonly received opinions, that the diastole of the arteries corresponds with the time of the heart's systole; and that the arteries are filled and distended by the blood forced into them by the contraction of the ventricles; the arteries, therefore, are distended, because they are filled like sacs or bladders, and are not filled because they expand like bellows. It is in virtue of one and the same cause, therefore,*

"*...why... we find... the pulmonary vein and left ventricle so full of blood, of the same black colour and clotted character as that with which the right ventricle and pulmonary artery are filled, is because the blood is incessantly passing from one side of the heart to the other through the lungs.*"

(c) The movement of the blood is determined by the heart and not by the liver. He also rejects the idea that the blood was moved by cardiac suction, since when removed from an animal, the heart continues to beat, like a muscular bag. On the basis of these observations, he proposes that its function was to squeeze the blood into the aorta and the pulmonary artery [19]:

"*From these particulars it appears evident to me that the motion of the heart consists in a certain universal tension - both contraction in the line of its fibres, and constriction in every sense.... We are therefore authorized to conclude that the heart, at the moment of its action, is at once constricted on all sides, rendered thicker in its parietes and smaller in its ventricles, and so made apt to project or expel its charge of blood... Neither is it true, as vulgarly believed, that the heart by any dilatation or motion of its own, has the power of drawing the blood into the ventricles; for when it acts and becomes tense, the blood is expelled; when it relaxes and sinks together it receives the blood in the manner and wise which will by-and-by be explained... Finally, it is not without good grounds that Hippocrates in his book,* "De Corde" *entitles it a muscle; its action is the same; so is its functions, viz., to contract and move something else - in this case the charge of the blood.*"

(d) Based on this conclusion, he establishes that blood from the heart circulates in a different system of vessels from that which carries it in the opposite direction from the periphery [20]:

"*...that the arteries are the vessels carrying the blood from the heart, and the veins the returning channels of the blood to the heart...*"

that all the arteries of the body pulsate, viz., the contraction of the left ventricle; in the same way as the pulmonary artery pulsates by the contraction of the right ventricle...it clearly appears that the artery is dilated with the impulse of the blood…. and lead us to conclude that the pulsative property proceeds along them from the heart….;Why does an artery differ so much from a vein in the thickness and strength of its coats? Because it sustains the shock of the impelling heart and streaming blood."

(g) Ao multiplicar o número de batimentos cardíacos por dia pelo volume residual de sangue colhido no coração de um cadáver humano, demonstrou ser impossível que o sangue fosse consumido quando chegava aos tecidos e constantemente substituído por novas quantidades formadas pelo fígado a partir do quilo alimentar, conforme fora admitido por Aristóteles e depois incorporado no ensino médico desde Galeno; por conseguinte, a quantidade de sangue bombeado diariamente pelo coração seria muito superior à quantidade de líquidos e alimentos ingeridos por dia e à capacidade da hipotética regeneração do sangue pelo fígado; em alternativa, Harvey considerou que o sangue existente teria de circular continuamente na rede vascular, sempre no mesmo sentido, passando das artérias para as veias, destas para o coração, e depois de novo para as artérias, em circuito fechado constante [26]:

"… I conceive it will be manifest that the blood circulates, revolves, propelled and then returning, from the heart to the extremities, from the extremities to the heart, and thus that it performs a kind of circular motion…Let us assume, either arbitrarily or from experiment, the quantity of blood which the left ventricle of the heart will contain when distended, to be, say, two ounces, three ounces, or one ounce and a half - in the dead body I have found it to hold upwards of two ounces…. and let us suppose as approaching the truth that the fourth, or fifth, or sixth, or even but the eighth part of its charge is thrown into the artery at each

(e) The blood circulating in the arteries is the same as that in the veins, and they are both part of the same system for transporting blood [21]:

"*...we may fairly conclude that the arteries contain the same blood as the veins, and nothing but the same blood.*"

(f) Pulsation results from the arteries filling with blood; this is what causes them to dilate, and not the reverse, as had been thought (i.e. first dilating and then filling with blood [18]:

"*From these facts it is manifest, in opposition to commonly received opinions, that the diastole of the arteries corresponds with the time of the heart's systole; and that the arteries are filled and distended by the blood forced into them by the contraction of the ventricles; the arteries, therefore, are distended, because they are filled like sacs or bladders, and are not filled because they expand like bellows. It is in virtue of one and the same cause, therefore, that all the arteries of the body pulsate, viz., the contraction of the left ventricle; in the same way as the pulmonary artery pulsates by the contraction of the right ventricle. .... it clearly appears that the artery is dilated with the impulse of the blood.... and lead us to conclude that the pulsative property proceeds along them from the heart....) Why does an artery differ so much from a vein in the thickness and strength of its coats? Because it sustains the shock of the impelling heart and streaming blood.*"

(g) By multiplying the number of heartbeats per day by the residual volume of blood that gathers in the heart of a human cadaver, Harvey proved that the blood could not possibly be consumed when it arrived in the tissues and be constantly replaced by new blood formed in the liver from alimentary chyle, as claimed by Aristotle and a tenet of medical teaching since Galen. He reasoned that the volume of blood pumped every day by the heart must be much greater than the quantity of liquid and food ingested daily and far more than the liver could possibly regenerate.

contraction; this would give either half an ounce, or three drachms, or one drachm of blood as propelled by the heart at each pulse into the aorta; which quantity, by reason of the valves at the root of the vessel, can by no means return into the ventricle. Now, in the course of half an hour, the heart will have made more than one thousand beats, in some as many as two, three, and even four thousand. Multiplying the number of drachms propelled by the number of pulses, we shall have either one thousand half ounces, or one thousand times three drachms, or a like proportional quantity of blood, according to the amount which we assume as propelled with each stroke of the heart, sent from this organ into the artery - a larger quantity in every case than is contained in the whole body! … But, supposing even the smallest quantity of blood to be passed through the heart and the lungs with each pulsation, a vastly greater amount would still be thrown into the arteries and whole body than could by any possibility be supplied by the food consumed. It could be furnished in no other way than by making a circuit and returning."

(h) À semelhança das válvulas cardíacas, a existência e funcionamento de válvulas no sistema venoso (*Fig 3*) asseguravam a unidireccionalidade do fluxo sanguíneo [22]:

"…the veins, in fact, collapsing, and being without any propelling power, and further, because of the impediment of the valves, as I shall show immediately, pour out but very little blood; whilst the arteries spout it forth with force abundantly, impetuously, and as if it were propelled by a syringe."

Robert Boyle[xvi], no único encontro em que conheceu Harvey, pouco antes de este falecer, Harvey proposed that the blood must circulate continually in the vascular network, always in the same direction, from the arteries to the veins, from the veins to the heart and back to the arteries, in a constant closed circuit [26]:

"... I conceive it will be manifest that the blood circulates, revolves, propelled and then returning, from the heart to the extremities, from the extremities to the heart, and thus that it performs a kind of circular motion.... Let us assume, either arbitrarily or from experiment, the quantity of blood which the left ventricle of the heart will contain when distended, to be, say, two ounces, three ounces, or one ounce and a half – in the dead body I have found it to hold upwards of two ounces.... and let us suppose as approaching the truth that the fourth, or fifth, or sixth, or even but the eighth part of its charge is thrown into the artery at each contraction; this would give either half an ounce, or three drachms, or one drachm of blood as propelled by the heart at each pulse into the aorta; which quantity, by reason of the valves at the root of the vessel, can by no means return into the ventricle. Now, in the course of half an hour, the heart will have made more than one thousand beats, in some as many as two, three, and even four thousand. Multiplying the number of drachms propelled by the number of pulses, we shall have either one thousand half ounces, or one thousand times three drachms, or a like proportional quantity of blood, according to the amount which we assume as propelled with each stroke of the heart, sent from this organ into the artery – a larger quantity in every case than is contained in the whole body! ... But, supposing even the smallest quantity of blood to be

[xvi] Boyle(1627-91),físico, químico, fisiologista e filósofo inglês, foi um dos grandes cientistas do século XVII. Em 1684 publicou, em "Memoirs for the Natural History of Human Blood", o seu primeiro e mais importante estudo sobre o sangue, recebido na época com opiniões contraditórias. O seu principal mérito terá sido o de demonstrar que o sangue podia ser submetido a diversos tipos de reagentes químicos, sendo por isso um precursor da Química Fisiológica.

[16] Robert Boyle (1627-91), the English physicist, chemist, physiologist and philosopher, was one of the great scientists of the 17th century. In 1684 he published "Memoirs for the Natural History of Human Blood", his first and most important study of the subject, which was given a mixed reception. Its main merit was to demonstrate that blood could be subjected to various types of chemical reagents, and it was thus a precursor of physiological chemistry.

perguntou-lhe como lhe ocorrera a possibilidade da circulação do sangue. Harvey respondeu que fora no momento em que soubera que as válvulas venosas estavam localizadas no corpo de modo a darem passagem ao sangue no sentido do coração e impedirem o seu fluxo em sentido contrário[14].

(i) Harvey admitiu a variabilidade da fluidez do sangue, ao observar que o sangue (venoso) se tornava mais fluido quando, de volta ao coração, recebia os "espíritos" (presumivelmente, depois ser arterializado)[23]:

"*And similarly does it come to pass in the body, through the motion of the blood, that the various parts are nourished, cherished, quickened by the warmer, more perfect, vaporous, spirituous, and, as I may say, alimentive blood; which, on the other hand, owing to its contact with these parts, becomes cooled, coagulated, and so to speak effete. It then returns to its sovereign, the heart, as if to its source, or to the inmost home of the body, there to recover its state of excellence or perfection. Here it renews its fluidity, natural heat, and becomes powerful, fervid, a kind of treasury of life, and impregnated with spirits, it might be said with balsam. Thence it is again dispersed. All this depends on the motion and action of the heart.*"

(j) Tendo por base as considerações anteriores, o coração passou a ocupar, primordialmente para Harvey, a posição de órgão que impulsiona o sangue e não o local onde este se misturaria com o ar; esta função passou a ser identificada com os pulmões (ainda que permanecesse o conceito de que ambos os órgãos seriam a origem e o reservatório de sangue, assim como o local onde o sangue se misturaria e era aquecido, antes de ser transportado para resto do organismo com o pneuma, quer o vital quer também o alimentício[24]:

"*…and since all living things are warm, all dying things cold, there must be a particular seat and fountain, a kind of home and hearth, passed through the heart and the lungs with each pulsation, a vastly greater amount would still be thrown into the arteries and whole body than could by any possibility be supplied by the food consumed. It could be furnished in no other way than by making a circuit and returning.*"

(h) As with the cardiac valves, the position and function of the valves in the venous system (*Figure 3*) ensure that the blood flows in only one direction[22]:

"*...the veins, in fact, collapsing, and being without any propelling power, and further, because of the impediment of the valves, as I shall show immediately, pour out but very little blood; whilst the arteries spout it forth with force abundantly, impetuously, and as if it were propelled by a syringe.*"

Robert Boyle, at his only meeting with Harvey shortly before the latter's death, asked him how the idea of the circulation of the blood had occurred to him. Harvey replied that it was the moment when he realized that the venous valves were positioned so as to allow the blood to travel to the heart and to prevent it flowing in the opposite direction[14].

(i) Harvey pointed out that the fluidity of blood varied; he observed that venous blood became more fluid when it returned to the heart and received "spirits" (presumably after being arterialized)[23]:

"*And similarly does it come to pass in the body, through the motion of the blood, that the various parts are nourished, cherished, quickened by the warmer, more perfect, vaporous, spirituous, and, as I may say, alimentive blood; which, on the other hand, owing to its contact with these parts, becomes cooled, coagulated, and so to speak effete. It then returns to its sovereign, the heart, as if to its source, or to the inmost home of the body, there to recover its state of excellence or perfection. Here it renews ts fluidity, natural heat, and becomes powerful, fervid, a kind of treasury of life, and impregnat-*

where the cherisher of nature, the original of the native fire, is stored and preserved; from which heat and life are dispensed to all parts as from a fountain head; from which sustenance may be derived; and upon which concoction and nutrition, and all vegetative energy may depend. Now, that the heart is this place, that the heart is the principle of life, and that all passes in the manner just mentioned, I trust no one will deny…(14, pag 37)…because the blood has its fountain, and storehouse, and the workshop of its last perfection, in the heart and lungs."

(k) Embora tivesse esclarecido o processo não deixou de manifestar perplexidade quanto à origem do sangue e a "finalidade última", teleológica, da circulação. Na tentativa de a explicar, Harvey não hesitou em recorrer aos argumentos de Aristóteles para justificar o ciclo da água na biosfera[24]:

"*And so also of the blood, wherefore does it precede all the rest? And in what way does it possess the vital and animal principle, and show a tendency to motion, and to be impelled hither and thither, the end for which the heart appears to be made?*"…*Which motion we may be allowed to call circular, in the same way as Aristotle says that the air and the rain emulate the circular motion of the superior bodies; for the moist earth, warmed by the sun, evaporates; the vapours drawn upwards are condensed, and descending in the form of rain, moisten the earth again; and by arrangement are generations of living things produced; and in like manner too are tempests and meteors engendered by the circular motion, and by the approach and recession of the sun.*"

Um pouco mais adiante, baseando-se novamente nos conceitos Aristotélicos e talvez influenciado pela interpretação mágica dos fenómenos, vivida durante o Renascimento, Harvey estabeleceu que a posição do coração como órgão central do corpo humano (equiparado a um microcosmo) se assemelhava à posição heliocêntrica do Sol no macrocosmo[25]:

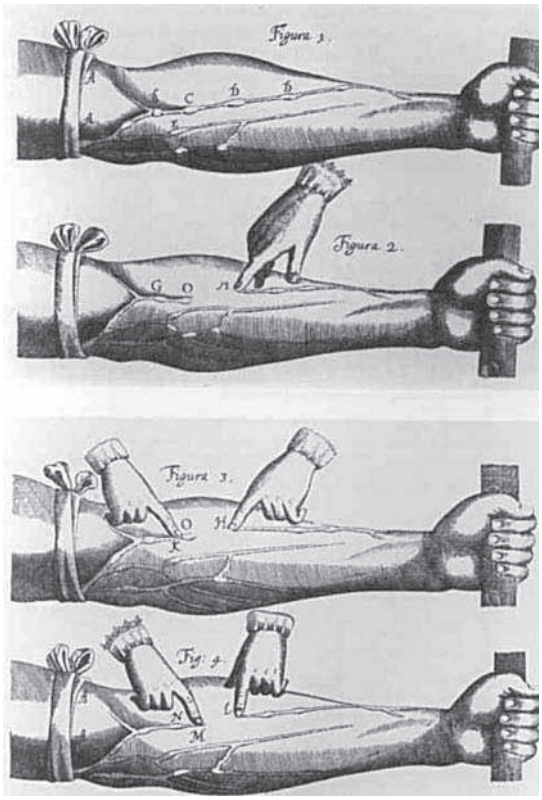

Figura 3- Para explicar que o sangue nas veias seguia para o coração e não retornava em sentido oposto, Harvey realizou uma experiência simples. Garrotando o braço de um voluntário de modo a interromper a circulação venosa e arterial., ao fim de pouco tempo o segmento distal do membro estava mais frio e pálido, enquanto acima da compressão estava mais quente e inchado. Ao aliviar a compressão pelo garrote de modo a possibilitar a circulação arterial no sector, o segmento distal recuperava a cor e a temperatura, ainda que continuasse inchado e as veias estivessem mais salientes e evidenciassem pequenas saliências no seu trajecto. Para Harvey a explicação era simples: quando a circulação era interrompida o sangue não fluía nas artérias e por isso não chegava às veias, acumulando-se a montante, o que explicava que este inchasse e ficasse mais quente, enquanto a jusante, sem sangue, perdia a cor e arrefecia. Ao aliviar a compressão, o sangue passava pelas artérias (localizadas mais profundamente que as veias) para todo o membro, pelo que este recuperava a cor, aquecia e inchava.
Porém. como o garrote ainda impedia o sangue circular pelas veias, estas ficavam visíveis e túrgidas; os pequenos nódulos ao longo do trajecto das veias foram interpretados como válvulas venosas. Numa experiência complementar, Harvey demonstrou que o sangue venoso seguia no sentido proximal, da extremidade do membro para o coração; quando tentava empurrar (com um dedo na sobre uma veia) o sangue no sentido oposto não conseguia, ao contrário do que sucedia quando o empurrava do antebraço para o braço (H). Com base nestas observações, extensíveis a outras partes exteriores do corpo, Harvey concluiu que o sangue era impulsionado pelo coração para as artérias para a pequena circulação e para a circulação sistémica, retornando depois pelas veias para o coração; este órgão actuava como uma bomba propulsora e não, como até então e desde Galeno era aceite, em que sangue seria movimentado por sucção, pelo coração e pelo fígado ,ou que o trabalho cardíaco resultaria dos movimentos do sangue (como fazem os rios com a s azenhas). Por sua vez, a continuidade da circulação do sangue arterial para as veias fê-lo pressupor a existência de uma conexão vascular, que viria a ser demonstrada por Malpighi, quase 40 depois.
Cortesia / Courtesy: "Public Services Group, Rare Books and Special Collections, Princeton University Library".

"*The heart, consequently, is the beginning of life; the Sun of the microcosm, even as the Sun in His turn might well be designated the heart of the world; for it is the heart by whose virtue and pulse the blood is moved, perfected, made apt to nourish, and is preserved from corruption and coagulation; it is the household divinity which, discharging its function, nourishes, cherishes, quickens the whole body, and is indeed the foundation of life, the source of all action.*"

Apoios e rejeições do novo paradigma

A impossibilidade de encontrar uma explicação para a circulação contínua do sangue terá sido uma das razões para Harvey ter demorado treze anos a publicar o seu livro, depois de esclarecer o processo. O outro motivo apontado seria a sua própria hesitação em divulgar factos que contradiziam toda a doutrina conhecida, ensinada e praticada sobre a circulação do sangue, em parte também do conhecimento popular [26]:

"*Thus far I have spoken of the passage of the blood from the veins into the arteries, and of the manner in which it is transmitted and distributed by the action of the heart; points to which some, moved either by the authority of Galen or Columbus, or the reasonings of others, will give in their adhesion. But what remains to be said upon the quantity and source of the blood which thus passes is of a character so novel and unheard-of that I not only fear injury to myself from the envy of a few, but I tremble lest I have mankind at large for my enemies, so much doth wont and custom become a second nature.*"

Esta prudência tinha plena justificação, já que as suas observações e conceito foram recebidos com cepticismo ou, mesmo, rejeitadas entre os contemporâneos, não só colegas de profissão como também clientes que abandonaram a sua clínica. Nessas críticas destacaram-se o seu compatriota médico James Primerose (em livro publicado em 1630, Exercitationes, et Animadversiones in Librum, De Motu Cordis, et Circulatione

Figure 3. To demonstrate how blood in the veins traveled to the heart and not in the opposite direction, Harvey performed a simple experiment. After a ligature was placed around the arm of a volunteer in order to cut off both the arterial and venous circulation, the distal part of the limb soon became cold and pale, while above the compression it became swollen and warmer. When the ligature was loosened sufficiently to enable arterial circulation to return to the sector, the distal part recovered its color and temperature, although it remained swollen, and the veins were prominent, with small bulges along their course. To Harvey, the explanation was simple: when the circulation was interrupted, the blood could not flow in the arteries and thus did not arrive in the veins but accumulated upstream, which caused the upper part to swell and become warmer, while the tissue downstream, deprived of blood, lost color and cooled. When the constriction was removed, the blood began to flow once more in the arteries (which are deeper than the veins) throughout the limb, which accordingly regained its color, warmed and swelled. However, since the ligature still prevented blood from flowing in the veins, they became swollen and more visible; the small nodules along their course were interpreted as venous valves.
In a related experiment, Harvey demonstrated that venous blood flowed in a proximal direction, from the extremity of the limb to the heart. When he tried to force the blood in the opposite direction, with his finger against a vein, he was unable to do so, unlike when he pushed blood up a vein from the lower to the upper arm (H).
On the basis of these observations, which held for other peripheral parts of the body, Harvey concluded that the blood was impelled from the heart into the arteries to the lesser circulation and the systemic circulation, returning via the veins to the heart. The latter acted as a pump, unlike in the model that had been accepted since the time of Galen, in which the blood was moved by suction through the heart and liver, the work of the heart resulting from the movement of the blood, like a water-wheel in a river. The continuity of the blood circulation between the arteries and the veins led him to assume the existence of a connection between the vessels, which was only demonstrated by Malpighi almost forty years later. Image courtesy of Public Services Group, Rare Books and Special Collections, Princeton University Library.

ed with spirits, it might be said with balsam. Thence it is again dispersed. All this depends on the motion and action of the heart."

(j) On the basis of this reasoning, Harvey came to the fundamental conclusion that the heart is the organ that impels the blood and not the place where it mixed with air, which he identified as the lungs, although he did not abandon the notion that both organs were the source and reservoir of the blood as well as the site where blood was mixed with air and the mixture heated before being transported to the rest of the organism together with the *pneuma*, both the vital spirit and the animal spirit [24]:

"*...and since all living things are warm, all dying things cold, there must be a particular seat and fountain, a kind of home and hearth, where the cherisher of nature, the original of the native fire, is stored and preserved; from which heat and life are dispensed to all parts as from a fountain head; from which sustenance*

Sanguine.Adversus Guilielmum Harverum Medical Regium,& Anatomes in Collegio Londinensi Professorem), e o influente anatomista e professor da Faculdade de Medicina de Paris Jean Riolan, o Novo (em Opuscula anatomica, 1649), ambos acérrimos defensores dos ensinamentos de Galeno e, portanto, oponentes das concepções e do modelo circulação propostos por Harvey para a circulação do sangue[27]. Em resposta a Riolan, Harvey publica, também em 1649, um segundo livro (De Circulatione Sanguinis), basicamente constituído por duas cartas, em que suplementa o "De Motu Cordis" nas partes criticadas por aquele seu opositor.

Numa outra carta que endereçou, em 1651, a Paul Marquard Schlegel (seu colega e amigo de Hamburgo), Harvey comentou algumas das críticas de Riolan, em particular quando este punha em causa a evidência da circulação pulmonar e permanecia convicto de que o sangue passava directamente do ventrículo direito para o esquerdo por "porosidade" do septo interventricular. Nessa carta, Harvey refutava aquelas críticas, ao mesmo tempo que divulgava, utilizando uma preparação de coração-pulmão, os resultados experimentais que obtivera posteriormente na presença de várias testemunhas credíveis. Deste modo, quase trinta anos depois da publicação das suas primeiras observações directas in vivo, e já septuagenário, Harvey confirmava inquestionavelmente ("*… there is no means of escape for…*") o que antes observara, isto é, a inexistência de qualquer comunicação interventricular para o circuito sanguíneo e, por consequência, a sua passagem natural através dos pulmões[28]:

"*…it may be well here to relate an experiment which I lately tried in the presence of several of my colleagues, and from the cogency of which there is no means of escape for him. Having tied the pulmonary artery, the pulmonary veins, and the aorta, in the body of a man who had been hanged, and then opened the left ventricle of the heart, we passed a tube through the vena cava into the right ventricle of the heart, and having, at the same time, may be derived; and upon which concoction and nutrition, and all vegetative energy may depend. Now, that the heart is this place, that the heart is the principle of life, and that all passes in the manner just mentioned, I trust no one will deny) … because the blood has its fountain, and storehouse, and the workshop of its last perfection, in the heart and lungs.*"

(k) Although he had clarified the process of blood circulation, he remained perplexed concerning the origin of blood and the final purpose of the circulation. In his attempts to find an explanation, Harvey went back to Aristotle's theories on the cycle of water in the biosphere[24]:

And so also of the blood, wherefore does it precede all the rest? And in what way does it possess the vital and animal principle, and show a tendency to motion, and to be impelled hither and thither, the end for which the heart appears to be made? … Which motion we may be allowed to call circular, in the same way as Aristotle says that the air and the rain emulate the circular motion of the superior bodies; for the moist earth, warmed by the sun, evaporates; the vapours drawn upwards are condensed, and descending in the form of rain, moisten the earth again; and by arrangement are generations of living things produced; and in like manner too are tempests and meteors engendered by the circular motion, and by the approach and recession of the sun."

Later, again drawing on Aristotle and perhaps influenced by the belief in a magical interpretation of phenomena that was widespread during the Renaissance, Harvey put forward a view of the heart as the central organ of the human body, which was seen as a microcosm, in a similar way to the central position of the sun in the heliocentric macrocosm[25]:

"*The heart, consequently, is the beginning of life; the Sun of the microcosm, even as the Sun in His turn might well be designated the heart of the world; for it is the heart by whose virtue and pulse the blood is moved, perfected,*

attached an ox's bladder to the tube, in the same way as a clyster-bag is usually made, we filled it nearly full of warm water, and forcibly injected the fluid into the heart, so that the greater part of a pound of water was thrown into the right auricle and ventricle. The result was that the right ventricle and auricle were enormously distended, but not a drop of water or of blood made its escape through the orifice in the left ventricle. The ligatures having been undone, the same tube was passed into the pulmonary artery, and a tight ligature having been put round it to prevent any reflux into the right ventricle, the water in the bladder was now pushed towards the lungs, upon which a torrent of the fluid, mixed with a quantity of blood, immediately gushed forth from the perforation in the left ventricle ; so that a quantity of water, equal to that which was pressed from the bladder into the lungs at each effort, instantly escaped by the perforation mentioned. You may try this experiment as often as you please; the result you will still find to be as I have stated it."

Questões que ficaram por esclarecer

Harvey não poderia entender a fisiologia da circulação pulmonar sem a contribuição dos resultados que Lavoisier apresentaria somente dois séculos mais tarde[xvii]. Embora não tivesse também conseguido esclarecer a intercomunicação entre os sistemas arterial e o venoso - o que constituiu uma lacuna importante do modelo proposto - Harvey admitiu ser inevitável a respectiva conexão, propondo para tal as seguintes três hipóteses: anastomoses arterio-venosas, porosidades dos tecidos (que ficariam embebidos em sangue proveniente das artérias, como se fossem esponjas, de onde seria recolhido por outros canais) ou ambas as possibilidades [29]:

made apt to nourish, and is preserved from corruption and coagulation; it is the household divinity which, discharging its function, nourishes, cherishes, quickens the whole body, and is indeed the foundation of life, the source of all action."

Support and criticism for the new paradigm

Harvey's inability to find an explanation for the continuous circulation of the blood was one of the reasons that, having clarified the process, he waited thirteen years before publishing his book. Another reason was his reluctance to publish facts that contradicted all known doctrine and practice concerning the movement of the blood, part of which was also popular knowledge [26]:

"Thus far I have spoken of the passage of the blood from the veins into the arteries, and of the manner in which it is transmitted and distributed by the action of the heart; points to which some, moved either by the authority of Galen or Columbus, or the reasonings of others, will give in their adhesion. But what remains to be said upon the quantity and source of the blood which thus passes is of a character so novel and unheard-of that I not only fear injury to myself from the envy of a few, but I tremble lest I have mankind at large for my enemies, so much doth wont and custom become a second nature."

This caution was fully justified, for his observations and theories were received with skepticism or rejected outright by his contemporaries, not only his fellow physicians but patients who left his practice. Among his most prominent critics were the English physician James Primrose or Primerose, in his book

[xvii] Antoine Lavoisier (1743-1794), químico Francês, considerado o fundador da química moderna. Verificou que o ar se compunha de duas partes, uma responsável pelas combustões e que conferia também acidez, que designou por "oxigénio", sendo a outra o "azoto". A combinação de oxigénio com hidrogénio originava água. Demonstrou, por experimentação animal, que a respiração era uma espécie de combustão, concluindo que as trocas gasosas pulmonares eram uma combustão semelhante "à de uma vela a arder".

[17] Antoine Lavoisier (1743-1794), the French scientist who is considered the founder of modern chemistry. He showed that air is composed of two parts, one, responsible for combustion and also involved in the production of acids, he called *oxygène*, the other being *azote* (nitrogen). The combination of oxygen and hydrogen produced water. He demonstrated by experiments on animals that respiration was a type of combustion, and concluded that gas exchange in the lungs was a combustion "like that of a candle burning".

"*Finally, we are now in a condition to suspect wherefore it is that no one has yet said anything to the purpose upon the anastomoses of the veins and arteries, either as to where or how it is effected, or for what purpose…. it seems obvious that the blood enters a limb by the arteries, and returns from it by the veins; that the arteries are the vessels carrying the blood from the heart, and the veins the returning channels of the blood to the heart; that in the limbs and extreme parts of the body the blood passes either immediately by anastomoses from the arteries into the veins, or mediated by the porosities of the flesh, or in both ways,*"

Mais adiante, procurou esclarecer um pouco melhor essa comunicação [30]:

"*Farther, when we see the veins below the ligature instantly swell up and become gorged, when from extreme tightness it is somewhat relaxed, the arteries meantime continuing unaffected, this is an obvious indication that the blood passes from the arteries into the veins, and not from the veins into the arteries, and that there is either an anastomosis of the two orders of vessels, or porosities in the flesh and solid parts generally that are permeable to the blood.*"

A polémica manteve-se em aberto enquanto Harvey foi vivo. As dúvidas e rejeição que o "*De Motu Cordis*" suscitou na época justificaram que Harvey, através de correspondência que manteve com individualidades médicas de diversos países, entre apoiantes e antagonistas, tentasse esclarecer alguns dos pontos mais controversos ou, inclusivamente, acrescentando outros pontos de vista. Entre as questões por esclarecer e para as quais Harvey também não tinha resposta, encontrava-se a de passagem do sangue das artérias para as veias. Embora por diversas vezes tivesse excluído a existência de anastomoses, por nunca as ter observado senão em três locais, e por considerar a inevitabilidade de um processo próprio, muito elaborado (e portanto distinto das anastomoses) que completaria o circuito da circula-

Exercitationes, et Animadversiones in Librum, De Motu Cordis, et Circulatione Sanguine. Adversus Guilielmum Harverum Medicum Regium, & Anatomes in Collegio Londinensi Professorem, published in 1630, and Jean Riolan the Younger, the influential anatomist and professor at the Faculty of Medicine in Paris, in his *Opuscula anatomica* (1649). Both were fervent supporters of Galen's teachings and accordingly opposed the model of the blood circulation put forward by Harvey [27]. Harvey published *De Circulatione Sanguinis*, his response to Riolan's criticisms, in 1649; it took the form of two letters, in which he expanded upon the parts of *De Motu Cordis* that his opponent had criticized.

In another letter, to his friend and colleague from Hamburg, Paul Marquard Schlegel, in 1651, Harvey refutes some of Riolan's criticisms, particularly the latter's questioning of the evidence for the pulmonary circulation and his insistence that blood passed directly from the right to the left ventricle through the "porous" interventricular septum. Harvey also announces the results of an experiment he had subsequently performed using a heart-lung preparation in the presence of several credible witnesses. Thus, nearly thirty years after the publication of his first discoveries *in vivo* and now in his seventies, Harvey confirmed unequivocally ("there is no means of escape") his previous observation, that there is no interventricular communication in the circulation of the blood, which must therefore pass through the lungs [28]:

"*...it may be well here to relate an experiment which I lately tried in the presence of several of my colleagues, and from the cogency of which there is no means of escape for him. Having tied the pulmonary artery, the pulmonary veins, and the aorta, in the body of a man who had been hanged, and then opened the left ventricle of the heart, we passed a tube through the vena cava into the right ventricle of the heart, and having, at the same time, attached an ox's bladder to the tube, in the same way as a clyster-bag is usually made, we filled it nearly full of warm water, and forcibly*

ção sistémica, também admitia, em meados de 1651, a teoria da porosidade [28]:

"*I confess, I say, nay, I even pointedly assert, that I have never found any visible anastomoses… — anastomoses in the way the word is commonly understood, and as the meaning has come down to us from Galen, viz, a direct conjunction between the orifices of the arteries and veins — I still admit…that I have found what is equivalent …in three places, namely, in the plexus of the brain, in the spermatic or preparing arteries and veins, and in the umbilical arteries and veins. I shall now, therefore, for your sake, my learned friend, enter somewhat more at large into my reasons for rejecting the vulgar notion of the anastomoses, and explain my own conjectures concerning the mode of transition of the blood from the minute arteries into the finest veins.… I imagined that the transference from the extremities of the arteries into those of the veins could not be effected without some other admirable artifice, at least wherever there was no transudation through the pores of the flesh. I therefore held the anastomoses of the ancients are fairly open to suspicion, both as they nowhere presented themselves to our eyes, and as no sufficient reason was alleged for anything of the kind. But you will ask, what is this artifice? What these ducts? viz. the small arteries, which are always much smaller — twice, even three times smaller — than the veins which they accompany, which they approach continually more and more, and within the tunics of which they are finally lost. I have been therefore led to conceive that the blood brought thus between the coats of the veins advanced for a certain way along them, and that the same thing took place here.*"

O novo modelo da circulação colocava igualmente em causa a tradição e a racionalidade das flebotomias[xviii] (local do corpo onde era feita, em que quantidade, com que frequência, perto ou afastada da lesão, do mesmo lado ou do oposto à lesão), então um dos principais recursos terapêuticas disponíveis na prática médica, como eram[16].

injected the fluid into the heart, so that the greater part of a pound of water was thrown into the right auricle and ventricle. The result was that the right ventricle and auricle were enormously distended, but not a drop of water or of blood made its escape through the orifice in the left ventricle. The ligatures having been undone, the same tube was passed into the pulmonary artery, and a tight ligature having been put round it to prevent any reflux into the right ventricle, the water in the bladder was now pushed towards the lungs, upon which a torrent of the fluid, mixed with a quantity of blood, immediately gushed forth from the perforation in the left ventricle; so that a quantity of water, equal to that which was pressed from the bladder into the lungs at each effort, instantly escaped by the perforation mentioned. You may try this experiment as often as you please; the result you will still find to be as I have stated it."

Questions that remained unanswered

Without the discoveries of Lavoisier nearly two centuries later, Harvey was unable to understand the physiology of the pulmonary circulation. Although he was also unable to explain the communication between the arterial and venous systems, which was a significant weakness of his proposed model, Harvey believed that they must be connected, and suggested three possible mechanisms: arteriovenous anastomoses, porous tissues (which would be soaked like sponges in blood from the arteries, which would then be drawn off through other channels), or both [29]:

"*Finally, we are now in a condition to suspect wherefore it is that no one has yet said anything to the purpose upon the anastomoses of the veins and arteries, either as to where or how it is effected, or for what purpose ... it seems obvious that the blood enters a limb by the arteries, and returns from it by the veins; that the arteries are the vessels carrying the blood from the heart, and the veins the returning channels of the blood to the heart; that in the limbs and extreme parts of the body the blood passes either immediately by anasto-*

Por outro lado, atendendo às circunstâncias sociais e ao estado do conhecimento da época, o esclarecimento da circulação sanguínea dificilmente originaria consequências clínicas imediatas, apesar dos esforços envidados por Harvey nesse sentido. Dando mostras de notável perspicácia, explicou como o modelo da circulação que defendia alterava os conceitos de doença, exemplificando as possíveis repercussões de uma infecção ou envenenamento em todo o organismo, em antecipação ao que, séculos mais tarde, constituíram quadros nosológicos bem definidos[31]:

"*There are still certain problems, which, taken as consequences of this truth assumed as proven, are not without their use in exciting belief, as it were, a posteriori; and which, although they may seem to be involved in much doubt and obscurity, nevertheless readily admit of having reasons and causes assigned for them. Of such a nature are those that present themselves in connexion with contagions, poisoned wounds, the bites of serpents and rabid animals, lues venerea and the like. We sometimes see the whole system contaminated, though the part first infected remains sound; the lues venerea has occasionally made its attack with pains in the shoulders and head, and other symptoms, the genital organs being all the while unaffected; and then we know that the wound made by a rabid dog having healed, fever and a train of disastrous symptoms may nevertheless supervene. Whence it appears that the contagion impressed upon or deposited in a particular part, is by-and-by carried by the returning current of blood to the heart, and by that organ is sent to contaminate the whole body.*"

Apesar de ter dado sobejas provas de espírito inovador e capaz de enfrentar os seus oponentes tradicionalistas, Harvey não rejeitara completamente os ditames clássicos. Ainda admitia, à semelhança da medicina tradicional, que o coração forneceria o "espírito vital" ao *moses from the arteries into the veins, or mediated by the porosities of the flesh, or in both ways.*"

Further on, he sought to clarify this communication[30]:

"*Farther, when we see the veins below the ligature instantly swell up and become gorged, when from extreme tightness it is somewhat relaxed, the arteries meantime continuing unaffected, this is an obvious indication that the blood passes from the arteries into the veins, and not from the veins into the arteries, and that there is either an anastomosis of the two orders of vessels, or porosities in the flesh and solid parts generally that are permeable to the blood.*"

The controversy continued during Harvey's lifetime. The questions and criticisms that *De Motu Cordis* aroused at the time prompted Harvey to attempt to clarify some of the more controversial points and to put forward further ideas, through his correspondence with physicians in various countries, both supporters and critics. Among the issues still to be clarified, and for which Harvey had no answer, was how the blood passed from the arteries to the veins. On various occasions he excluded the possibility of anastomoses since he had only observed them in three sites, and considered that a special system must be involved to complete the circuit of blood circulation that would be far more elaborate than simple anastomoses. However, in 1651 he did admit of the possibility of porosity as the mechanism[28]:

"*I confess, I say, nay, I even pointedly assert, that I have never found any visible anastomoses... – anastomoses in the way the word is commonly understood, and as the meaning has come down to us from Galen, viz., a direct conjunction between the orifices of the arteries and veins – I still admit...that I have found what is equivalent ...in three places,*

[xviii] Entretanto, alguns anos mais tarde já se registavam algumas modificações práticas, p.ex., as sangrias deixaram de ser praticadas em situações de síncope cardíaca.

[18] Within a few years, the practice of blood-letting underwent certain modifications; for example, it was no longer performed in cases of cardiac syncope.s

sangue a ser distribuído por todo o corpo e, tal como Servetus um século antes, embora não o citando, afirmaria em 1651 (invocando a autoridade dos antigos filósofos mas sem implicações religiosas aparentes) que "*o sangue era a sede primordial da alma*" [32]:

"*From this it clearly appears that the blood is the generative part, the fountain of life, the first to live, the last to die, and the primary seat of the soul… how much it concerns our welfare that by a wholesome and regulated diet we keep our blood pure and sweet. When I have accomplished this it will no longer, I trust, seem so improbable and absurd to any one as it did to Aristotle 1 in former times, that the blood should be viewed as the familiar divinity, as the soul itself of the body, which was the opinion of Critias and others, who maintained that the prime faculty of the living principle (anima) was to feel, and that this faculty inhered in the body in virtue of the nature of the blood. Thales, Diogenes, Heraclitus, Alcmeon, and others, held the blood to be the soul, because, by its nature, it had a faculty of motion.* "

O cepticismo e a controvérsia gerados pelo modelo de circulação sanguínea proposto por Harvey arrastaram-se por mais uns vinte anos, sendo praticamente encerrados, somente depois da sua morte, por Marcello Malpighi. Para a História, Harvey será sempre um precursor da ciência moderna em geral, e da fisiologia em particular, em que a observação atenta e a evidência pela experimentação constituíram-se em metodologias precedentes ao desenvolvimento natural das conclusões e dos conceitos. Por seu lado, "*De Motu Cordis*" foi o instrumento que marcou a separação entre passado e futuro, entre um novo modo de pensar e de resolver problemas do conhecimento, e o outro, o das tradições antigas, do conservadorismo e da ignorância, propalados desde a Antiguidade.

namely, in the plexus of the brain, in the spermatic or preparing arteries and veins, and in the umbilical arteries and veins. I shall now, therefore, for your sake, my learned friend, enter somewhat more at large into my reasons for rejecting the vulgar notion of the anastomoses, and explain my own conjectures concerning the mode of transition of the blood from the minute arteries into the finest veins.... I imagined that the transference from the extremities of the arteries into those of the veins could not be effected without some other admirable artifice, at least wherever there was no transudation through the pores of the flesh. I therefore held the anastomoses of the ancients as fairly open to suspicion, both as they nowhere presented themselves to our eyes, and as no sufficient reason was alleged for anything of the kind. But you will ask, what is this artifice? What these ducts? viz. the small arteries, which are always much smaller – twice, even three times smaller – than the veins which they accompany, which they approach continually more and more, and within the tunics of which they are finally lost. I have been therefore led to conceive that the blood brought thus between the coats of the veins advanced for a certain way along them, and that the same thing took place here."

The new model of blood circulation also cast doubt on the traditional practice of blood-letting[18], at that time one of the main treatments available to physicians, questioning the reasoning behind the part of the body where blood was taken, in what quantity, how often, and whether it should be near or distant from the lesion and on the same side of the body or not [16].

At the same time, bearing in mind the social conditions and the state of medical knowledge of the time, an explanation of the circulation of the blood would be unlikely to lead to immediate clinical improvements, despite Harvey's best efforts in this regard. Demonstrating remarkable insight, he explained how his model of the circulation changed the concept of disease, such as the possible implications of infection or poisoning for the whole organism, anticipating what cen-

turies later became well-defined nosological settings [31]:

"*There are still certain problems, which, taken as consequences of this truth assumed as proven, are not without their use in exciting belief, as it were,* a posteriori; *and which, although they may seem to be involved in much doubt and obscurity, nevertheless readily admit of having reasons and causes assigned for them. Of such a nature are those that present themselves in connexion with contagions, poisoned wounds, the bites of serpents and rabid animals, lues venerea and the like. We sometimes see the whole system contaminated, though the part first infected remains sound; the lues venerea has occasionally made its attack with pains in the shoulders and head, and other symptoms, the genital organs being all the while unaffected; and then we know that the wound made by a rabid dog having healed, fever and a train of disastrous symptoms may nevertheless supervene. Whence it appears that the contagion impressed upon or deposited in a particular part, is by-and-by carried by the returning current of blood to the heart, and by that organ is sent to contaminate the whole body.*"

Although he had provided ample evidence of his innovative spirit and his willingness to confront his traditionalist opponents, Harvey did not completely reject classical teachings. He still believed that, as in traditional medicine, the heart supplied the blood with "vital spirit", to be distributed throughout the body, and like Servetus a century before (although without quoting him), in 1651 he stated (invoking the authority of the ancient philosophers, but with no apparent religious implications), that the blood was the primary seat of the soul [32]:

"*From this it clearly appears that the blood is the generative part, the fountain of life, the first to live, the last to die, and the primary seat of the soul... how much it concerns our welfare that by a wholesome and regulated diet we keep our blood pure and sweet. When I have accomplished this it will no longer, I trust, seem so improbable and absurd to any one as it did to Aristotle in former times, that the blood should be viewed as the familiar divinity, as the soul itself of the body, which was the opinion of Critias and others, who maintained that the prime faculty of the living principle (*anima*) was to feel, and that this faculty inhered in the body in virtue of the nature of the blood. Thales, Diogenes, Heraclitus, Alcmeon, and others, held the blood to be the soul, because, by its nature, it had a faculty of motion.*"

The skepticism and controversy surrounding Harvey's model for the circulation of the blood continued for another twenty years, and was only effectively ended after his death by Marcello Malpighi. Historically, Harvey will always be considered a pioneer of modern science in general and physiology in particular, his careful observation and experimental methods leading naturally to the development of his theories and conclusions. The publication of *De Motu Cordis* marked a dividing line between past and future, between ancient traditions mired in conservatism and ignorance that had come down from antiquity and a new way of thinking, of solving problems and of gaining new knowledge.

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