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Galenicae Quaestiones Disputatae Duae : rete mirabile and pulmonary circulation

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Summary

The author discusses two points of Galenic medicine that have long interested medical historians: why didGalen describe a non-existent arterial rete mirabile *atthe base ofthe human brain and was Galen the first to discover the pulmonary circulation. After reviewing the evidence, it is concluded that Gglen mistook the venous rete mirabile at the base of the human brain for an arterial one and that he indeed described the passage of blood from the right to the left ventricle although he did not discover the pulmonary circulation.*

Résumé

L'auteur s'interroge sur deux questions de la médecine galénique qui ont longtemps interpelé les historiens de la médecine : pourquoi Galien a-t-il rapporté l'existence d'une rete mirabile *artérielle (qui n'existait pas) à la base du cerveau humain et comment est-il arrivé le premier à reconnaître la circulation pulmonaire ? Après réflexion, l'auteur conclut qu 'en fait Galien a confondu une* rete mirabile *veineuse avec une* rete mirabile *artérielle et a donc décrit le passage du sang du ventricule droit vers le gauche, bien qu'il n'ait pas découvert la circulation pulmonaire.*

The purpose of this paper is to discuss two unsolved long-standing questions of Galenic medicine: one concerns the non-existent arterial *rete mirabilethat* Galen describes at the base of the human brain, the other whether he discovered the pulmonary circulation.

1. Galen's description of an arterial retiform plexus, a rete mirabile (1), at the base of the human brain has puzzled historians for centuries because such a plexus does not exist and it is difficult to understand how Galen, an experimenter of unusual observational skills, could have made such a mistake. Yet, the pertinent passage leaves no doubt:

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"The plexus called retiform (rete mirabile,*) by anatomists, is the most wonderful of the bodies located in this region. It encircles the gland (the hypophysis) itself and extends far to the rear; for nearly the whole base of the encephalon has this plexus lying beneath it. It is not a simple network but (looks) as if you had taken several fisherman's nets and superimposed them... But of course, on account of the delicacy of the members composing it and the closeness of its contexture, you could not compare this network to any man-made nets, nor has it been formed from any chance material. Rather, Nature appropriated as the material for this wonderful network the greatest part* (a.carotid interna*) of the arteries ascending from the heart to the head. Small branches are given off by these arteries to the neck, the face, and the external parts of the head. All the rest of them, as straight as they were formed*

in the beginning, pass up through the thorax and neck to the head and are received there comfortably by a part of the cranium, which is pierced through (by the carotid canal) and admits them with no trouble into the interior of the head. The thick meninx (the dura mater) too was about to receive them and had already been pierced through along the line of their invasion(2) and all these things gave the impression that the arteries were making haste to reach the encephalon. But this was not the case. For when they have passed beyond the cranium, in the space between it and the thick meninx they are first divided into many very small, slender arteries, and then they are interwoven and pass through one another, some toward the front of the head, some toward the back, and others to the left and right, giving the other, opposite impression, namely, that they have forgotten the route to the encephalon. However, this is not true either; for, as roots combine to form a trunk, so from these many arteries there arises another pair of arteries (aa.carotides cerebrales), *equal to the pair that passed upward in the beginning, and so these now enter the encepahlon through the perforations in the thick meninx" (3).*

It is evident that Galen describes here an extradural arterial *rete mirabile.* It must be underlined that this, however, is not a Galenic "discovery", but the confirmation of an alleged observation previously made by Herophilus or his school. As Galen tells us,

"the 'net-like' plexus (rete mirabile), *as it is called by those around Herophilus,...(is formed) when the carotid arteries ascend toward the brain, this is where they are divided in many ways by the dura mater, before they go through it. They twist around in many rows, as they would if you were to conceive of several nets lying on each other, and they occupy a very great area, which they call the 'base' (basis) of the brain" (4).*

One pauses at the thought that the two greatest anatomists of antiquity, both with anatomical knowledge based on dissection, should both have made the same mistake, that is, that they either saw a structure that was not there either in humans or primates or attributed to humans what they had seen only in certain animals (even though Galen frequently dissected primates and Herophilus had experience with the dissection of human bodies) (5).

Although Herophilus was the first to describe it, because of the greater fame of Galen, it is to his *rete mirabile*that reference was made when the topic was discussed throughout the centuries. The question of its presence in human, continued to be debated even after Vesalius, who clearly recognized Galen's error:

"De reticulari vero Galeni plexu...novimus Galenum bourn cerebri dissectione delusum, non hominis cerebrum utineque ipsius vasa, sed bourn recensuisse" (6).

"About Galen's reticular plexus... we know that, misled by dissection of the brain of cattle, he did not describe the human brain, nor its vessels, but that of oxen".

Harvey wrote :

"Bauhinus contra Vesalium esse capitibus hominum; manifestum vero bubus etc. Riolanus amplum dempta dura meninge et aliud rete basi cerebri ex fibris venae ut illud arteriae" (7).

"Bauhin (8), contrary to (the opinion of) Vesalius, (says that) it exists in the human head; it is indeed evident in oxen, etc. Riolanus (9) (says) that, after the dura has been removed, another rete mirabile *(can be seen) at the base of the brain composed of venous strands as the other was of arterial".*

As, subsequently, it has been shown that, without doubt, an arterial rete mirabile does not exist in humans, the most common position, so far, has been that Galen, lacking the possibility of dissecting human bodies, performed his

anatomical studies on animals and described something that, in fact, exists in some of them (e.g., ruminants(IO) and felidae(11)) without realizing that it does not exist in man (12). One attempt has also been made to prove that Galen was right and that such an arterial *rete mirabile* does indeed exist in humans (see below).

The explanation that Galen attributed to men a feature found in some animals appears unsatisfactory, as the following questions present themselves : Why would Galen rely on his dissection of ruminants and felidae and not on his frequent dissection of monkeys ? Why did he fail to note that the plexus did not exist in the monkey, the animal he considered to be most similar to man (13) ? If he found the plexus in other animals, why did he not verify its existence in primates ?

I n view of the fact that at the base of the brain of humans and primates there is a plexus, which had been already been noted by Riolanus (as quoted above), that fits Galen's description although it is venous rather than arterial, a more likely explanation appears to be that he mistook for an arterial plexus this quite large *venous rete mirabile.* This venous network surrounds the sella turcica and the *foramen magnum,* is under the brain, covers a large part of the base of the cranial cavity, and is composed of several intercommunicating sinuses and venous channels : the basilar plexus, the cavernous sinuses, the anterior and posterior intercavernous sinuses, the occipital sinuses, the sigmoid sinuses, the superior and inferior petrosal sinuses and the marginal sinuses. These structures (14) are closely associated with the internal carotid artery (which could explain Galen's belief that they were of arterial origin) and are located between two layers of dura mater, although they appear to be extradural because the parietal layer of the membrane adheres firmly to the bone (15).

The possibility that Galen may have mistaken the *venous* network at the base of the cranial cavity for an *arterial rete mirabile* has been considered "conceivable but unlikely" by Siegel (16), who, on the other hand, tried to prove that Galen was right in that an *arterial rete mirabileat* the base of the human brain does, in fact, exist:

> *"In man, however, the internal carotid artery, after passing through the petrous bone, forms a rete below the dura mater, as Spalteholz showed in his atlas of human anatomy (17), where he wrote that an artery passes through the foramen ovale of the petrous bone to form the rete foraminis ovale* (sic) *below the dura mater. This would be the exact analogy to the* rete mirabile *of Galen" (18).*

The problem with Siegel's position, however, is that it is not clear what he means when he mentions the "foramen ovale of the petrous bone" (the petrous bone is part of the temporal bone and the foramen ovale is in the sphenoid bone); in addition, Spalteholz, in the page indicated by Siegel, does not exactly say what Siegel attributes to him but says instead :

> *"Drilled through the root of the great wings, from above and behind to the front of the fades sphenomaxilaris (is) the* foramen rotundum *(for the nervus maxillaris), from above down to the fades infratemporalis (are)* ffreforamen ovale *(forthe rete foraminis ovalis; nervus mandibularis) and the*\ oramen spinosum *(for the arteria meningea media, venae meningeae mediae, nervus spinosus, plexus meningeus); the latter is located closely in front of the hindmost corner and can be incomplete" (19).*

Morevover, the *rete forminis ovalis,* mentioned by Spalteholz only cursorily, is not to be found in standard anatomy texts, which suggests that, if it exists, it must be small indeed and surely cannot be the rete that, as quoted above, Galen described as large ("It encircles the gland (the hypophysis)... extends far to the rear... nearly the whole base of the encephalon has this plexus lying beneath"). Finally, no rete

is visible in the figure of Spalteholz mentioned by Siegel (20). Harris refers to the possibility advanced and rejected by Siegel that Galen took the venous *rete mirabile* for an arterial one but passes no judgement on the question except to point out that Galen described a conspicuous system whereas the *rete foraminis ovalis* of Spalteholz and the circle of Willis are small structures (21).

In conclusion, considering that, in humans the *venous rete mirabile* appears to be extradu ral, covers a large part of the base of the encephalon and encircles the hypophysis (as Galen described it), considering that such a plexus is easily observed in primates, and considering that the dissection of the base of the skull is difficult (especially with the means available in antiquity), it seems more logical to conclude that Galen mistook the venous *rete mirabile* that he found in the skull of primates for an arterial one, than to think that he attributed to human anatomy observations made in felidae and ruminants and neglected to verify his findings in primates. As the venous *rete mirabile,* because of its close association with intracranial arteries, can be easily mistaken for an arterial *rete mirabile,* it is not surprising that both of antiquity's great anatomists could have taken one for the other, Herophilus in humans, Galen in primates.

2. It is generally assumed that the pulmonary circulation was discovered at least a thousand years after Galen by Ibn an-Nafis, or, even later, by Servetus or Colombo; some, however, have suggested that it was Galen who was the first to describe the passage of blood from the left to the right ventricle through the lungs. The point has been repeatedly debated (22).

Some, including Harvey (23), have held that Galen did, in fact, discover the pulmonary circulation (or at least had an idea of the pulmonary pathway) (24), others that he did not or that somebody else did (25).

Galen's notion of the perfusion of organs by blood was based on the ancient model, which went back to the Egyptian, Hindu and Chinese medical paradigms, of water irrigating fields (that is to say, on the idea that blood was used up at the periphery, like water in the fields) (26). The concept is clearly expressed in *De naturalibus facultatibus*:

"Numerous conduits distributed through the various limbs bring them pure blood, much like the garden water-supply...so that... (all) parts should be plentifully provided..."(27) .

At the time, this model was satisfactory and the circulation of the blood, not being necessary to explain observations, was not even considered. Galen believed that blood, produced by the liver (28), was distributed to the entire body through the veins and that it reached the right heart through the inferior vena cava. Arteries carried from the heart to the periphery not only blood but *pneuma* (29) as well (30). Galen did not recognize the pumping action of the heart; blood was propelled inside the vessels by attraction from the peripheral tissues in need of nutrition (31) or by the squeezing of vessels by thoracic respiratory movements (32).

The picture was complete and everything was reasonably clear except for one problem : how did the blood reach the arterial tree ? That is to say, how did the blood, produced by the liver and carried to the right heart by the vena cava, reach the left heart so that it could be distributed to the arterial tree ? Before Galen the question was not asked because it was generally held that arteries did not contain blood but *pneuma*; however, as Galen had proven that the arteries indeed contain blood, he had to confront the problem.

Galen had a good notion of the aortic, pulmonary and cardiac valves (33) and held that arteries and veins communicate by what we would today call capillaries :

"All over the body the arteries and veins

comunicate with one another by common openings and exchange blood and pneuma through certain invisible and extremely narrow passages" (34).

The quantity of blood that passed through these invisible openings, however, was too small to account for the blood in the arterial tree; most of the blood passed from the right heart to the left through invisible openings in the interventricular septum :

"Similarly, also, in the heart itself, the thinnest portion of the blood is drawn from the right ventricle into the left, owing to there being perforations in the septum between them : these can be seen for a great part (of their length) they are like a kind of fossae (pits) with wide mouths, and they get constantly narrower; it is not possible, however, actually to observe their extreme terminations, owing both to the smallness of these and to the fact that when the animal is dead all the parts are chilled and shrunken" (35).

Again, the model was satisfactory and in reasonable agreement with observation (36). Galen, however, introduced another element as well: a small part of the right-heart blood reached the left heart through what we would call the lesser circulation. Galen's ideas on this point are expressed in the following passage, in which he also explains the function of the pulmonary valve :

"But if the large orifice of the arterial vein (i.e., pulmonary artery) (37) always lay uniformly open and if Nature had not found some device that could close and open it again at the proper times (the pulmonary valve), the blood would never be taken over into the (venous) arteries (i.e., pulmonary veins) through the little, invisible orifices (i.e., pulmonary capillaries) when the thorax contracts... When the thorax contracts, the venous arteries (i.e., pulmonary veins), pushed inward and compressed from all sides, instantly force out the pneuma they contain and receive in exchange a portion of blood through those fine openings, an exchange that would never take place if the blood were able to run back through a very large opening, such as that of the (arterial) vein (i.e., pulmonary artery), into the heart. As it is, however, when the blood is compressed and cut off from returning through the large orifice, some of it trickles through those fine openings into the (venous) arteries (i.e., pulmonary veins)" (38).

The passage is clear: some blood from the pulmonary artery is squeezed by thoracic contraction into the pulmonary veins, where it replaces some of the *pneuma* (39).

Galen's belief that the pulmonary veins contained blood is made clear in two passages:

"I have already shown several times that the smooth arteries (i.e., pulmonary veins) that connect the rough arteries (i.e., bronchi) with the heart contain thin, pure and vaporous (i.e., mixed with pneuma,) *blood and are not organs (i.e., carriers)* o/pneuma *alone"(40).*

"Erasistratus thinks that the other artery, that is the smooth one (i.e., the pulmonary vein), also lacks blood, but he is wrong, as I have often said before; for it does contain a considerable quantity of pure, thin, spirituous blood" (41).

The passing of blood from the pulmonary veins to the left ventricle (the atria were considered mere appendages of the vessels attached to the ventricles) is described as follows (42) :

"And in fact, the heart is able to attract mingled blood and pneuma from the lung too through that opening which I have said is the only one to have placed upon it two tunics growing from the outside inward (i.e., the mitral valve)...I have shown before that in fully formed animals (as opposed to foetuses) this vessel (i.e., pulmonary veins) gets its share of blood... by way of many fine inoculations that escape the sight (i.e., the lungs' capillaries) (43)...

The passage from the *De usu partium* concerning the pulmonary valve quoted above (44) underlines that, as mentioned before, Galen did not recognize the pumping action of the heart and believed that the movement of the blood through the lungs resulted from the compression secondary to thoracic movements (45).

This is the evidence on which the answer to the question "Did Galen discover the pulmonary circulation ? " must be based. As mentioned above, more commonly, the discovery of the lesser circulation is attributed to Ibn an-Nafis (c.1210-1288), or Servetus (1511-1553), or Colombo (c.1515-1599). We quote below the passages of these authors that describe the lesser circulation so that a comparison with Galen's ideas on the subject can be made.

Ibn an-Nafis :

"The blood, after it has been refined in this cavity (i.e., the right ventricle), mustbetransmitted to the left cavity where the (vital) spirit is generated. But there is no passage between these two cavities; for the substance of the heart is solid in this region and has neither a visible passage, as was thought by some persons, nor an invisible one which could have permitted the transmission of blood, as was alleged by Galen. The pores of the heart there are closed and its substance is thick. Therefore, the blood after having been refined, must rise in the arterious vein (i.e.,pulmonary artery) to the lungs in order to expand in its volume and to be mixed with air so that its finest part may be clarified and may reach the venous artery (i.e.,pulmonary vein) in which it is transmitted to the left cavity of the heart. This, after having been mixed with the air and having attained the aptitude to generate the (vital) spirit. That part of the blood which is less refined is used by the lung for its nutrition" (46).

Servetus :

" *The vital spirit has its origin in the left ventricle of the heart, and the lungs assist greatly in its generation... It is generated in the lungs from a mixture of inspired air with elaborated, subtle blood which the right ventricle of the heart communicates to the left. However, the communication is made not through the middle wall of the heart, as is commonly believed, but by a very ingenious arrangement the subtle blood is urged forward by a long course through the lungs; it is elaborated by the lungs, becomes reddish-yellow and is poured from the pulmonary artery into the pulmonary vein. Then in the pulmonary vein it is mixed with inspired air and through expiration it is cleansed of its sooty vapors. Thus finally the whole mixture, suitably prepared for the production of the vital spirit, is drawn onward from the left ventricle of the heart by diastole... (as a consequence), not merely air, but air mixed with blood, is sent from the lungs to the heart through the pulmonary vein; therefore the mixture occurs in the lungs. That reddish-yellow color is given to the spirituous blood by the lungs; it is not from the heart. ...That middle wall (i.e., the interventricular septum), since it is lacking in vessels and mechanisms, is not suitable for that communication and elaboration, although something may possibly sweat through. By the same arrangement by which a transfusion of the blood from the portal vein to the vena cava occurs in the liver, so a transfusion of the spirit from the pulmonary artery to the pulmonary vein occurs in the lung. If anyone compares these things with those which Galen wrote in books Viand VII, De usu partium, he will thoroughly understand a truth which was unknown to Galen" (47).*

Colombo :

"Between these ventricles there is a septum through which almost everyone believes there opens a pa th way for the blood from the

right ventricle to the left, and that the blood is rendered thin so that this may be done more easily for the generation of vital spirits. But they are in great error, for the blood is carried through the pulmonary artery to the lung and is there attenuated; then it is carried, along with air, through the pulmonary vein to the left ventricle of the heart. Hitherto no one has noticed this or left it in writing, and it especially should be observed by all...
But let us return to the aforesaid four vessels (pulmonary artery, vena cava, aorta, pulmonary vein); two of them have been constructed so that they carry inwardly to the heart, that is, when the heart is dilated; but the other two carry outward when the heart is constricted. Therefore when it is dilated, and those membranes are loosened and yield ingress, the heart receives blood from the vena cava into the right ventricle, and also prepared blood from the pulmonary vein, as we said, along with air into the left ventricle. And when the heart is compressed (constricted), these valves are closed lest the vessels receive anything regressing along the same path; and at that same time the valves of both the aorta and the pulmonary artery are opened; they permit the passage of the outgoing spiritous blood which is diffused through the whole body and of the natural blood which is carried to the lungs; and it is always thus when the heart is dilated, as we noted before : (that the) other (valves) open and then shut. And so you will find that the blood which has entered the right ventricle is unable to return to the vena cava" (48).

There is a progression toward the correct picture from Galen to Colombo. Galen thought that most of the blood going through the pulmonary artery was consumed by the lungs for their nutritional needs, that only a trickle would pass from there to the pulmonary veins and into the left ventricle, and that almost all blood going into the left ventricle came directly from the right ventricle through foramina in the interventricular septum. Ibn an-Naf is denies the existence of the foramina in the intrerventricular septum and states that, of the blood coming from the right ventricle through the pulmonary artery, some is used by the lungs for their nutritional needs and some goes into the left ventricle through the pulmonary veins. Servetus also denies the existence of interventricular communication through the septum (although he felt that "something may possibly sweat through") and does not mention the utilization of some of the right ventricle's blood by the lungs for their own nutrition. In other words, he seems to indicate that all the blood received by the right ventricle passes into the left. Finally, Colombo realizes that there is no communication between the ventricles through the septum, clearly understands the function of the heart valves, realizes the function of the heart systole and diastole, and has a clear idea of the function of the aorta in diffusing to the whole body the blood "prepared" by the lungs.

At this point we can try to answer the question : did Galen discover the pulmonary circulation ? The answer can be attempted only after we define what we mean by "pulmonary circulation". The following are four possible definitions:

1) The passage, through the lungs, of *some* (no matter how little) of the blood of the right ventricle into the left ventricle. (Galen)
2) The passage, through the lungs, of a *large part (or* most) of the blood of the right ventricle into the left ventricle. (Ibn an-Nafis)
3) The passage, through the lungs (where it is mixed with air), of a//blood of the right ventricle into the left ventricle. (Servetus)
4) The reception of blood from the vena cava by the right ventricle during diastole, its passage through the lungs where it is "prepared", and its reception by the left ventricle from which, when the heart is constricted, it is distributed to the whole body. (Colombo)

Galen discovered the lesser circulation if we accept our first definition of it, that is to say, if we consider that the most important component in the discovery is the concept that blood goes from the right to the left ventricle through the lungs and we do not concern ourselves with quantitative details. In this case, Galen is the discoverer and Ibnan-Nafis refined the concept; Servetus had an even clearer idea of the smaller circulation, and Colombo further clarified the question.

This conclusion, however, in our opinion, is not justified. It is true that Galen was the first to observe that some blood passes from the right to the left ventricle through the lungs, but in his view this was only a very small amount; in other words, he failed to recognize that the passage through the lungs was not a pleonastic physiological detail (after all, according to him, practically all blood passed through the septum) but that, in reality, all the blood passing from the right to the left ventricle followed that route. In addition, his erroneous notion of interventricular communication through the septum misled the medical community for centuries. The lesser circulation was discovered later.

Notes

1. A *rete mirabile* (remarkable, or wonderful net) is a vascular network that interrupts the continuity of an artery or vein as, for example, in the renal glomeruli (arterial *rete mirabile)* or in the liver (venous *rete mirabile).* It was called *mirabile* because usually a vascular network is interposed between the end of an artery and the beginning of a vein rather than between the end of an artery (or vein) and the beginning of another artery (or vein). In other words, the usual pattern is "artery -> *rete* -> vein" and not "artery -> *rete* -> artery" or "vein -> *rete* -> vein". The imaginary *rete mirabile* of Galen was an arterial one.
2. It is not clear what Galen means by stating that the dura mater "had already been pierced along the line of their invasion". Possibly he refers to the numerous openings through which various structures pierce the *dura mater* in the same area (the internal carotid, the optic, oculomotor, trochlear, trigeminal and abducens nerves).
3. Galen *De usu partium,* IX, iv, K, III, pp 696-698. Translation by Tallmadge May in : *Galen on the Usefulness of the Parts of the Body,* translated by Margaret Tallmadge May, Ithaca, Cornell University Press, 1968.
4. Galen, *De usupulsuum,* ii, K, V, p. 155. Translation by von Staden in: Heinrich von Staden, *Herophilus : the Art of Medicine in Early Alexandria,* Cambridge, Cambridge University Press, 1989, p.223.
5. Herophilus'error is sometimes considered an argument to support the belief that he did not perform human vivisection. See: John Scarborough, "Celsus on Human Vivisection at Ptolemaic Alexandria", *Clio Medica,* XI (1), 25-38,1976; Plinio Prioreschi, *A History of Medicine, Vol. II, Greek Medicine,* 2nd Edition, Omaha, Horatius, 1996, Ch. VII, B.
6. Vesalius, *De humani corporis fabrica libri septem,* Basileae, ex off. Ioannis Oporini, 1543, p. 310. Vesalius repeats the same concept also on pages 524 and 642.
7. *The Anatomical Lectures of William Harvey: Prelectiones Anatomie Universalis, De Musculis,* edited by Gweneth Whitteridge, London, E. & S. Livingstone, 1964, p.336.
8. Caspar Bauhin, *Theatrum Anatomicum,* Basel, 1605,p.609,accordingtoO'Malleyetal. in: William Harvey, *Lectures on the Whole of Anatomy* : An annotated translation of *Prelectiones Anatomiae Universalis by* CD. O'Malley, F.N.L. Poynter, and K.F. Russell, Berkeley, University of California Press, 1961, p.229.
9. Jean Riolan, *Anthropographia,* iv, 2, p. 262, according to *The Anatomical Lectures of William Harvey : Prelectiones Anatomie Universalis, De Musculis,* edited by Gweneth Whitteridge, London, E. & S. Livingstone, 1964, p.336; *Anthropographia, in Anthropographia et Osteologia,* Paris, 1626, p. 389, according to O'Malley et al. in : William Harvey, *Lectures on the Whole of Anatomy* : An annotated translation of *Prelectiones Anatomiae Universalis by CD.* O'Malley, F.N.L. Poynter, and K.F. Russell, Berkeley, University of California Press, 1961, p.229.
10. Robert Getty, *Sisson and Grossman's The Anatomy of the Domestic Animals,* Philadelphia W.B. Saunders, 1975, p. 970; P.M.Daniel et al., "Studies of the Carotid Rete and its Associated Arteries", *Philosophical Transactions of the Royal Society of London, Series Biological Sciences,* CCXXXVII, 173-208,1953; B.A. Baldwin, "The Anatomy of the

Arterial Supply to the Cranial Regions of the Sheep and Ox", *Am. J. Anal* CXV, 101-118, 1964.

11. D. Dwight Davis and H. Elizabeth Story, "The Carotid Circulation of the Domestic Cat", *Zoological Series, Field Museum of Natural History,* XXVIII, 1, 1-47, 1943.
12. See for example, Vivian Nutton, "Roman Medicine, 250 B.C. to A.D. 200" in : Lawrence I Conrad, Michael Neve, Vivian Nutton, Roy Porter, Andrew Wear, *The Western Medical Tradition: 800 B.C. to A.D. 1800,* Cambridge, Cambridge University Press, 1995, p.66. Such a rete is also said to occupy in animals the same place that the circle of Willis occupies in man *(Galen on the Usefulness of the Parts of the Body,* translated by Margaret Tallmadge May, Ithaca, Cornell University Press, 1968, p.430, note 9). This, however, cannot be correct because the circle of Willis is intradural and, in fact, many animals (e.g., cat, sheep, goat, ox, pig) have the extradural rete mirabile and the circle of Willis (intradural) as well (P.M.Daniel et al./'Studies of the Carotid Rete and its Associated Arteries", *Philosophical Transactions of the Royal Society of London, Series Biological Sciences,* CCXXXVII, 173-208,1953 ; B. A. Baldwin, The anatomy of the Arterial Supply to the Cranial Regions of the Sheep and Ox", *Am. J. Anal* CXV, 101-118, 1964.
13. In *De Anatomicis administrationibus* (I, ii, K, II, p.219), Galen says: "Among all animals, the monkey is the most similar to man in viscera, muscles, arteries, nerves and in the form of the bones". See also : Galen, *De usu partium corporis humani,* XI, ii, K, III, p.844.
14. For pictures of these structures see : *Gray's Anatomy,* edited by Peter L. Williams et al., Edinburgh, Churchill Livingstone, Thirty-seventh Edition, 1989, pp. 800,802-805 ; Carmine D. Clemente, *Anatomy : A Regional Atlas of the Human Body,* Baltimore, Urban & Schwarzenberg, Third Edition, 1987, Figs 637, 638, 642.
15. In *Deplacitis Hippocratis etPlatonis*(VII, iii, K, V, p. 607), Galen says that the *rete mirabile* is "surrounded by the dura mater".
16. Rudolf E.Siegel, *Galen's System of Physiology and Medicine,* Basel, S. Karger, 1968, p. 112, footnote 33.
17. Werner Spalteholz, *Handatlas der Anatomie des Menschen,* Leipzig, Verlag von S. Hirzel, 3 Vols, 1913.
18. Rudolf E.Siegel, *Galen's System of Physiology and Medicine,* Basel, S. Karger, 1968, p. 112
19. *Werner* Spalteholz, *Handatlas der Anatomie des Menschen,* Leipzig, Verlag von S. Hirzel, 3 Vols, 1913, Vol. I, p.5. Translations are by the author unless otherwise indicated.
20. Spalteholz, *Handatlas der Anatomie des Menschen,* Leipzig, Verlag von S. Hirzel, 3 Vols, 1913, Vol II, fig. 445, p. 400.
21. C.R.S. Harris, *The Heart and the Vascular System in Ancient Greek Medicine,* Oxford, At the Clarendon Press, 1973, p.358.
22. The notion that the idea of the circulation of the blood was already *in nuce* in the writings of the ancient authors goes back to Littre, who says : "Il n'est pas un developpement, le plus avance de la medecine contemporaine, qui ne se trouve en embryon dans la medecine anterieure... En science, comme en toute autre chose, rien n'est qui n'ait ete en germe". (There is no development of contemporary medicine, including the most advanced, that is not found *in nuce* in the past....In science, as in everything else, there is nothing that did not exist in an embryonic stage before) (E. Littre, *Oeuvres completes d'Hippocrate,* Paris, J.B.Balliere, 10 Vols., 1839-1861, I, p.223).
23. Harvey's Latin reads: "Sed quando aliqui sunt, qui nil nisi adductis autoritatibus admittunt, iidem ex ipsius etiam Galeni verbis hanc veritatem confirmari posse sciant; scilicet non solum posse sanguinem e vena arteriosa in arteriam venosam, et inde in sinistrum ventriculum cordis, et postea in arteria transmitti : sed ex continuo pulsu cordis, et pulmonum notu inter respirandum, hoc fieri". *(Exercitatio anatomica de motu cordis et sanguinis in animalibus Guilielmi Harvei,* Francofurti, Sumptibus Guilielmi Fitzeri, 1628, VII, p. 38). That is : "Those who accept only what is based on authority can find this truth confirmed by Galen himself: not only can blood pass from the pulmonary artery to the pulmonary veins into the left ventricle and then into the arteries, but that this happens because of the pulsation of the heart and the respiratory movements".
24. For example: J. Prendergast, "Galen's View of the Vascular System in Relation to that of Harvey", *Proc. R. Soc. Med.* XXI, 1839-1848, 1928. M. Bahuelos, "Los grandes errores en el estudio de la circulacion" *Gaceta medica espahola,* XX, 360-363,1946 :"DenuevosobreGalenoylacirculacion" Gaceta medica espanola, XXI, 353-355, 1947 ; "Conocio Galeno la circulacion de la sangre ?" Gaceta medical espanola, XXII, 55-57, 1948.; *El problema de la circulacion de la sangre. Nuevos*

hechosynuevas ideas, Editorial Cientifico Medica, Barcelona, 1946. Sigismund Peller, "Harvey's and Cesalpino's role in the History of Medicine", Bull. Hist. Med. XXIII, 213-235, 1949. Leonard G. Wilson, "Erasistratus, Galen and the *Pneuma", Bull. Hist. Med.,* XXXIII, 293-314, 1959. L.G. Wilson, "The Problem of the Discovery of the Pulmonary Circulation", *J. Hist. Med.XVU,* 229-244, 1962. R.E.Siegel, "Galen's expreriments and observations on pulmonary blood-flow and respiration", *Am. J. Cardiol.,* X, 738-745,1962 ; "Why Galen and Harvey did not compare the heart to a pump", *Am. J. Cardiol,* XX, 117,121, 1967 ; "The influence of Galen's doctrine of the pulmonary blood-flow on the development of modern conceptions of the circulation", *SudhoffsArch. Gesch. /*Wecf.XLVl, 311 - 332, 1962 ; *Galen's System of Physiology and Medicine,* Basel, Karger, 1968. Tallmadge May in : Galen, *on the Usefulness of the Parts of the Body,* Ithaca, Cornell University Press, 2 Vols., 1968, p.301, footnote 43.

25. For example : Lain Entralgo, "Conocio Galeno la circulacion de la sangre ?" *Medicina Clfnica,* VII, 464-466, 1946. Antonio De la Granda, "Galeno y Servet", *Gaceta medica espahola* XXII, 124-127, 1948. Donald Fleming, "Galen on the motion of the blood in the heart and the lungs", *Isis,* XLVI, 14-21, 1955. A. Rupert Hall, "Studies in the history of the cardiovascular system", *Bull. Hist. Med.,* XXXIV, 391 -413, 1960. Jerome J. Bylebyl and Walter Pagel, "The Chequered Career of Galen's Doctrine on the Pulmonary Veins", Medical History, XV, 211-219, 1971. C.R.S. Harris, *The Heart and the Vascular System in Ancient Greek Medicine,* Oxford. At the Clarendon Press, 1973, p.322. Alfred P. Fishman, "The Pulmonary Circulation", JAMA, CCXXXIX, 13, 1299-1301, 1978. M.R. Salem, "Discovery of the Pulmonary Circulation by an Arab in the Thirteenth Century", *Anesthesia and Analgesia,* XLVII, 7, 587-588, 1968. Donald Fleming, "Galen on the Motion of the Blood in the Heart and Lungs", *Isis,* XLVI, 14-21,1955. T.V.N. Persaud, "Historical Development of fhe Concept of a Pulmonary Circulation", *Can. J. Cardiol.,* V, i, 12-16,1989. T. Donath, "Who was the first to describe pulmonary circulation ?" *Gegenbaurs Morph. Jahrbuch,* CXXX, 819-826, 1984. G. Whitteridge, "La decouverte de la petite circulation", *Revue Medicate de la Suisse Romande,* CVI,25-33,1986. N. Hamarneh, "On the 700th anniversary of the death of Ibn an-Nafis", *Documenta Ophthalmologica,* LXXI, 143-154,1989. It must be underlined that the bibliography listed in this and in the previous footnote is far from being comprehensive and that the authors listed do not embrace two groups of opposite and incompatible conclusions. In many cases there is overlap in the two ways of thinking : for example, L. Wilson (mentioned in the previous footnote) recognizes that Galen found that a pulmonary pathway for the blood existed although he concludes that he did not discover the lesser circulation.
26. Plinio Pioreschi, *A History of Medicine, Vol. I, Primitive and Ancient Medicine,* Omaha, Horatius Press, 1996, Chs. II, III, IV and General Conclusions.
27. Galen, *De naturalibus facultatibus,* III, xv, K, II, p.211. Translation by Arthur J. Brock, The Loeb Classical Library, London, William Heinemann, 1916.
28. The belief that the liver was the organ that was the center of blood production may have been suggested by its aspect (it looks like a big blood clot) and by the fact that wounds of the liver bleed profusely.
29. A word that can be translated as air, vapor, breath.
30. Galen's distinction between arteries and veins was based on the thickness of their walls and on the fact that arterial blood contained *pneuma.*
31. Galen, *De naturalibus facultatibus,* III, xv, K, II, pp.210-211.
32. Galen, *De usu partium,* VI,x,K,lll, pp.455-457.
33. Galen, *De usu partium,* VI,xiv,K,lll, pp.476-480.
34. Galen, *De usu partium,* VI,x,K,lll, p.455. Translation by Tallmadge May in: *Galen on the Usefulness of the Parts of the Body,* Ithaca, Cornell University Press, 1968.
35. Galen, *De naturalibus factultatibus,* III, xv, K, II. pp.207-208. Translation by Arthur John Brock in : *Galen on the Natural Faculties,* The Loeb Classical Library, London, William Heinemann, 1916.
36. The model was only in *reasonable* agreement with observation because both the communications between arteries and veins and the openings in the interventricular septum were "invisible".
37. Galen called the pulmonary artery "arterial vein" and the pulmonary veins "venous arteries".
38. Galen, *De usu partium,* VI, x, K, III, pp.455-457. Translation by Tallmadge May in : *Galen on the Usefulness of the Parts of the Body,* Ithaca, Cornell University Press, 1968.
39. The pulmonary veins carried not only blood and pneumafrom the lungs to the left ventricle, but also "sooty and fuliginous" residues from the left ventricles to the lungs (whereas the aorta carries the same material at the periphery): "Nature...

opened all the smooth arteries (i.e., pulmonary veins) into one source, the left ventricle of the heart, which is the source of the innate heat... and in the contraction of the heart she pours all that is sooty and fuliginous in it through these same arteries and even more through the great artery (i.e., the aorta) into the others, thus providing safely that the heat in the heart should never be smothered by noxious residues and quenched." (Galen, *De usu partium,* VII, ix, K,lll, p.545. Translation byTallmadge May in : *Galen, on the Usefulness of the Parts of the Body,* Ithaca, Cornell University Press, 1968). This function, of course, presupposes a leaky mitral valve. Although the tricuspid is not supposed to leak, in the Pseudo-Galen we find that blood can reflux through it : "When nutrients have been transformed into blood in the liver, the blood flows from there into the right ventricle of the heart. From the right ventricle it is then distributed to the higher parts through the jugular vein and through the vena cava to the whole body." (Pseudo-Galen, *Introductio sive medicus,* xi, K, XIV, p.718).

40. Galen, *De usu partium,* VII, viii, K, III, p.537. Curiously enough, Harris, after having pointed out that the passage indicated that the pulmonary veins "carry a one-way traffic of light, clean vaporous blood, going in the direction of the heart" (C.R.S. Harris, *The Heart and the Vascular System in Ancient Greek Medicine,* Oxford, At the Clarendon Press, 1973, pp.307-308), two pages later says that "we maintain that Galen thought that only pneuma passes inward through the mitral valve". (C.R.S. Harris, *The Heart and the Vascular System in Ancient Greek Medicine,* Oxford, At the Clarendon Press, 1973, pp.310). In addition, he states that Galen "nowhere says" that some blood enters the left ventricle through the mitral valve (C.R.S. Harris, *The Heart and the Vascular system in Ancient Greek Medicine,* Oxford, At the Clarendon Press, 1973, pp.310). In fact the passage that follows (Galen, *De usu partium,* VII, viii, K, III, p.509-510) states just that.

41. Galen, *De usu partium,* VII, viii, K, III, p.521. Translation by Tallmadge May in : *Galen on the Usefulness of the Parts of the Body,* Ithaca, Cornell University Press, 2 Vols., 1968. Here Galen contradicts himself (a not uncommon occurrence) because, as we have seen, he states also that only "some of it (i.e., blood) trickles through those fine openings into the (venous) arteries (i.e., pulmonary veins'". Elsewhere, Galen seems to indicate that some of the blood contained in the pulmonary veins is used to nourish the lungs (Galen, *De usu partium,* VII, viii, K, III. p.542-544). This would imply a to-and-fro blood movement in the pulmonary veins.

. Bylebyl and Pagel assert that, according to Galen, the blood that passes from the lungs to the pulmonary veins is subsequently reabsorbed by the lungs and does not reach the left ventricle (Jerome J. Bylebyl and Walter Pagel, "The Chequered Career of Galen's Doctrine on the Pulmonary Veins," *Medical History,* XV, 211-219, 1971). This is in contradiction with the Galenic text that follows, in which it is clearly stated that the left ventricle attracts blood through the mitral valve. If the pulmonary veins contain blood, as there are no other vessel ending in the left atrium besides the pulmonary veins, any blood that passes to the ventricle through the mitral valve has to come from the pulmonary veins.

. Galen, *De usu partium,* VI, xxi, K, III, pp.509-510. Translation by Tallmadge May in : *Galen on the Usefulness of the Parts of the Body,* Ithaca, Cornell University Press, 2 Vols., 1968. The fact that, according to Galen, the pulmonary veins carry blood (even if only a trickle) to the left ventricle is evident. Yet, curiously enough, not only Harris but other authors as well disagree on this point. Fleming, for example, says that "whether Galen's venous artery, corresponding to our pulmonary veins, then carried blood to the left ventricle is in question"; yet, in previous pages, he admits that according to Galen, some blood passes into the pulmonary veins and then, discussing the backward passage of the smoky residues from the left ventricle to the lungs (through the pulmonary veins), he states that this flow is "against the natural current of fluids in the heart". (Donald Fleming, "Galen on the Motion of the Blood in the Heart and Lungs", *Isis,* XLVI, 14-21, 1955). Bylebyl and Pagel (Jerome J. Bylebyl and Walter Pagel, "The Chequered Career of Galen's Doctrine on the Pulmonary Veins", *Medical History,* XV, 211 -219,1971) state that there is no evidence that Galen held that there was a transit of blood from the right to the left ventricle through the lungs and that the passage quoted (Galen, *De usu partium,* VI, xxi, K, III, pp. 509-510) refers to the fetal heart (footnote 24). This is evidently not the case as one can see from the complete text of the passage, which reads : "And in fact, the heart is able to attract mingled blood and pneuma from the lung too through that opening which I have said is the only one to have placed upon it two tunics growing from the outside inward (i.e., the mitral

valve). For in animals confined in the uterus this vessel (i.e., the pulmonary vein) receives blood from the vena cava by way of an inosculation of remarkable size (i.e., *foramen ovale).* I have shown before that in fully formed animals this vessel (i.e., the pulmonary vein) gets its share of blood from instruments (i.e., organs) that are sanguineous in fully formed animals and pneumatic in fetuses by way of many fine inosculations that escape the sight (i.e., the lungs' capillaries'". (Translation by Tallmadge May in : *Galen on the Usefulness of the Parts of the Body,* Ithaca, Cornell University Press, 1968, pp. 330-331). The same passage is similarly translated by Daremberg (Ch. Daremberg, *Oeuvres anatomiques, physiologiques et medicates de Galien,* Paris, J.B.Billiere, 2 Vols., 1854,1, pp. 453-454): "Le coeur pouvait meme prendre au poumon du sang et du pneuma melanges au moyen de l'orifice sur lequel seul, disions-nous, s'implantent uniquementdeuxtuniques *(valvule bicuspide)* dirigees de dehors en dedans. En effet, ce vaisseau, chez les animaux enfermes dans l'uterus, regoit le sang de la veine cave par une anastomose d'une grandeur remarquable (i.e., *foramen ovale).* Nous avons demontre precedemment que chez les animaux parfaits, le sang vient d'organes qui sont chez eux des organes sanguins, et chez le foetus des organes pneumatiques, au moyen d'anastomoses nombreuses et d'une finesse qui echappe a l'oeil". It would appear that to interpret the passage as referring only to the fetal heart and not to the heart of the adult as well is unjustified.

44. VI, x, K, III.
45. Galen, however, correctly understood that the movements of the lungs were passive and due to the expansion and contraction of the thoracic walls: "(I have shown) that the lung is moved by the thorax; that when dilated and expanded, it attracts the outer air, and this is inspiration; and when compressed and contracted, it expels its contents into the larynx and mouth and through them into the outer air, and this is expiration...(I also have described) all the muscles, the instruments moved by them, and the nerves conveying the psychic faculty to them from the encephalon." (Galen, *De placitis Hippocratis et Platonis,* II, iv, K, V, p. 236. Translation by Tallmadge May in : *Galen on the Usefulness of the Parts of the Body,* Ithaca, Cornell University Press, 1968, p.279, note 3).
"For when the whole thorax expands in inspiration... (it) causes the entire lung to expand to fill the space left vacant". (Galen, *De usu partium,* VII, iv, K, III, p.523. Translation by Tallmadge May in : *Galen on the Usefulness of the Parts of the Body,* Ithaca, Cornell University Press,1968. Galen applies here the principle of the *horror vacui).*
Another passage in which Galen underlines the relation between the heart, the pulmonary artery and veins, and the lungs is the following : "This organ (i.e., the lung) has no supply of blood to nourish itunless some veins (i.e., pulmonary artery) are attached to it, and... the heart has no way of profiting by respiration unless the lung is connected with it by other arteries (i.e., pulmonary veins)." (Galen, *De usu partium,* VII, viii, K, III, p.536. Translation by Tallmadge May in : *Galen on the Usefulness of the Parts of the Body,* Ithaca, Cornell University Press,1968).
46. Max Meyerhof, "Ibn an-Nafis (XIIIth cent.) and his theory of the lesser circulation", *Isis,* XXIII, 100-120, 1935.
47. C.D.O'Malley, *Michael Servetus. A translation of his geographical, medical and astrological writings with introductions and notes,* Philadelphia, American Philosophical Society, 1953, pp.204-205.
48. Quoted by : Coppola,E.D. "The discovery of the pulmonary circulation : a new approach", The William Osier Prize Essay for 1956, *Bull. Hist. Med.,* 1957, XXXI, 44-47 (pp.62, 65).

Biography

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Dr. Prioreschi is the author of over forty scientific publications in pharmacology and experimental medicine. Trained in internal medicine, he has practiced medicine at university clinics and hospitals; For several years, he has been interested in history of medicine and has published, in this field, papers, books and book reviews; his books on history of medicine are : A Hisotry of Human Responses to Death *(New York, The Edwing Mellen Press, 1990);* A History of Medicine, Vol.I, primitive and Ancient Medicine *(SecondEd., Omaha, HoratiusPress, 1996);* A History of Medicine, Vol.II, Greek Medicine *(Second Ed., Omaha, Horatius Press, 1996). At present, Dr. Prioreschi is working on the third volume of his History of Medicine (Roman Medicine). HisbookMan* and War *(New York, Philosophical Library, 1987) is a historical work not related to medicine.*