

## Blood, Phlegm and Spirits: Galen on Stroke

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**Abstract.** This paper will use original sources to examine Galen's contributions to the doctrine of stroke, or, in ancient terminology, "apoplexy". Following a rough outline of some methodological issues and pre-Galenic concepts of the disease, Galen's definition and construction of the clinical symptoms will be presented in detail. These include sudden onset, comatose state, serious impairment of movement, lack of sensation, shallow respiration, low pulse, damage of voice and usually fatal outcome. Galen distinguished "apoplexy" from other diseases such as "karos", "lethargy" and "paralysis". In retrospect, his definition includes a number of modern disease categories, such as myocardial infarction and fatal pulmonary embolism. As for the origin of the attack, Galen's fundamental explanation centered on the Hippocratic concept of humoral imbalance, and he distinctly rejected Aristotle's teaching of the involvement of the heart. According to Galen's teaching, stroke resulted either from an influx of blood into the brain or from the accumulation of phlegm and black bile in the cerebral ventricles blocking the transmission of the animal spirit. Prophylaxis and treatment included dietetic, pharmacological, and surgical measures and corresponded to the supposed "hidden cause" as well as observable factors. Galen's Greek texts on stroke remained an authoritative source until the early 19th century.

**Keywords:** Galen, history of cerebrovascular disorders, nervous system diseases, history of Ancient medicine, ancient brain research

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### Introduction<sup>1</sup>

More than 150 years ago, the famous French medical historian Charles Daremberg declared: "The true protagonists on the stage of medical history are the diseases". Unfortunately, historical research has not always conformed to this aphorism. Much is known about famous physicians and the social framing of medicine in the past, but comparatively little is known about the story of diseases themselves. When diseases are studied by historians, the focus is usually placed on epidemics and infectious diseases, and 95 out of 100 publications deal with the history of plague, tuberculosis, syphilis, and AIDS. In contrast, this paper will argue that one can learn much more about the medical past from non-epidemic illnesses, and an excellent example of this approach can be given by studying the history of stroke.

Stroke is today the second most common cause of death worldwide, second only to heart disease, but before cancer. In 2010, approximately

17 million people suffered a stroke and there are 33 million living survivors of a previous stroke [1]. Of course there are no exact epidemiological data available from the more distant past. Yet Celsus, the Roman encyclopedist of the 1st century AD, described stroke and paralysis as "frequent medical conditions" [2]. Obviously stroke is a brilliant "model" to exemplify the statement by Daremberg, and Galenic medicine is an excellent starting point, because it integrated various ancient doctrines and influenced medical practice for more than one and a half millennia [3-5]. However, the emergence of Galen's discussions cannot be understood without a preliminary assessment of earlier ancient teachings related to this disease. Thus a short summary of pre-Galenic doctrines of stroke seem to be a suitable starting point for this paper.

### Pre-Galenic concepts of stroke

During the early history of stroke, a constant terminological struggle between physicians and natural philosophers can be observed [6]. In the Hippocratic writings, the term "stroke", or "apoplexy", had two different meanings. It usually referred to a sudden loss of consciousness including a paralysis of all muscles. Sometimes, however, the term could also signify a paralysis of

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only a certain part of the body. Paradoxically, this condition of partial paralysis was sometimes called “paraplexy”, “paraplegia”, and “paralysis” [7-8]. Between the 4th century BC and the 2nd century AD, some medical authors identified apoplexy with paralysis, while others distinguished them as two separate conditions. The problems with nomenclature continued when Celsus declared that both illnesses were designated by the term paralysis by his contemporaries [2].

Another important issue was related to the supposed pathogenesis of the symptoms. For most of the Hippocratic authors, diseases characterized by an impairment of motion, sensation and mental functions were somehow linked to the brain, thus echoing the “encephalocentric” view propagated by Alcmaeon, Plato, and later the Alexandrians Herophilus and Erasistratus [9]. But the earliest pioneers of brain research in the West were split on this issue. Following Empedocles and Aristotle, the physician Diocles subscribed to the “cardiocentric” theory and pointed out that apoplexy was generated in the heart and the blood vessels [6, 10-11]. These discussions about the origin, naming and clinical features of apoplectic attacks continued well into Roman times. Soranus of Ephesus, one of the foremost exponents of the so-called Methodical School, regarded a state of stricture and a narrowing of all pores that were supposed to exist between the particles of the patient’s body as the ultimate cause of the attack [6]. Thus many conflicting theories about the delineation and origin of stroke existed when Galen entered the field in the second half of the second century AD.

### Methodological considerations

Before starting with an in-depth analysis of Galen’s ideas about stroke, it is important to avoid a multitude of methodological pitfalls in pursuing this research avenue. First, there is no text, full or partial, in the Galenic corpus dealing exclusively with the subject of stroke. Therefore, a number of fragments from more than fifteen works must be located, identified and linked together. About a third of these statements can be found in *De locis affectis* and Galen’s commentaries on the Hippocratic writings; further relevant passages are included in the works on bloodletting, on pulse, healing, hygiene, and in various other writings (Table). Second, on several occasions Galen’s statements are discordant or even outright

**Table 1.** Galen’s writings related to stroke

1.	De locis affectis
2.	In Hippocratis aphorismos commentarii
3.	De venae sectione adversus Erasistratum
4.	De curandi ratione per venae sectionem
5.	De pulsibus ad tyrones
6.	De causis pulsuum
7.	De Methodi medendi
8.	Ad Glauconem de medendi methodo
9.	Quos, quibus catharticiis medicamentis et quando purgare oporteat
10.	De sanitate tuenda
11.	De morborum causis
12.	De symptomatum causis
13.	De placitis Hippocratis et Platonis
14.	In Hippocratis librum de acutorum victu commentarii
15.	In Hippocratis praedictionum librum primum commentarii
16.	De symptomatum differentiis
17.	De temperamentis

contradictory, and thus far there is no reliable chronology of the Galenic corpus that may help to solve this problem. Third, and most important: one has to make painstaking efforts to avoid the pitfall of presentism. Although it is impossible to analyse Galen’s thoughts without being influenced by the contemporary view of disease, one always has to emphasize one fact: Galen’s brain is not our brain, Galen’s arteries, veins and nerves are not our arteries, veins and nerves, and therefore Galen’s concept of stroke is not even close to the present-day conception of the disease [12-18]. This surprising interrelation will be analysed in detail in the following paragraphs.

### Galen’s definitions of the disease

For which medical condition did Galen use the Greek term apoplexy? In one of his definitions in *De locis affectis III, 14* he asserts: “When all nerves have simultaneously lost sensation and motion, the affection is called apoplexy [19, vol. 8, p. 208; 20, p. 100]”.<sup>2</sup> In another passage which, found in *De symptomatum differentiis 3*, he states: “Apoplexy is a palsy of the whole body, accompanied by impairment of its main functions [19, vol. 7, p. 59]”.<sup>3</sup> Al-

<sup>2</sup> πάντων μὲν οὖν ἅμα τῶν νεύρων ἀπολεσάντων αἰσθησίν τε καὶ κίνησιν, ἀποπλεξία τὸ πάθος ὀνομάζεται [19].

<sup>3</sup> ...ἀποπλεξία ἢ παντὸς τοῦ σώματος παράλυσις ἅμα ταῖς ἡγεμονικαῖς ἐνεργεσίαις [19].

though the various definitions and descriptions he gives of the attack differ slightly, they can be summarized with a basic set of signs and symptoms:

(1) sudden onset [19, vol. 8, p. 200; 20, p. 97], with no or few antecedent indications such as acute headache, dizziness, swelling of the jugular veins, or fainting following digestive trouble [19, vol. 11, p. 48];

(2) falling into a comatose state [19, vol. 10, p. 931];

(3) serious impairment of movement, especially of voluntary actions [19, vol. 18A, p. 87; vol. 7, p. 59 and p. 144];

(4) lack of sensation during the attack [19, vol. 8, p. 208; 20, p. 100];

(5) shallow respiration or respiration with great effort [19, vol. 8, p. 231; 20, p. 110];

(6) low, weak and slow pulse [19, vol. 9, p. 193];

(7) damage to the voice [19, vol. 8, p. 270; 20, p. 125];

(8) absence of fever [19, vol. 16, p. 673];

(9) chronic progression with usually fatal outcome or debilitating sequelae [19, vol. 8, p. 230].

The Spanish medical historian Lain-Entralgo and many others have emphasized that the Greek word *diagnostikein* and the modern practice of diagnostics have very little in common [21]. In this context, it is important to note that Galen's delineation of apoplexy is not static but dynamic. If the same combination of symptoms occurred

but respiration remained undisturbed, then Galen called it "karos" [19, vol. 8, p. 231]. Moreover, karos was not followed by an impairment of motor functioning. If fever occurred, then "lethargos" was given as the appropriate name for the condition [19, vol. 11, p. 931]. If the loss of motion and sensation was restricted to a certain part of the patient's body, the affliction was simply called paralysis [19, vol. 8, p. 208]. It is therefore quite certain that some cases, today recognized as cerebro-vascular disorders were not identified by Galen as apoplexy (Figure 1).

On the other hand, Galen's understanding of "apoplexia" was much broader and more comprehensive than our modern one. A case of more or less sudden, simultaneous, complete and non-febrile loss of motion and sensation, including loss of consciousness and respiratory failure, easily falls within a number of modern disease categories ranging from brain trauma, myocardial infarction or pulmonary embolism with loss of consciousness to acute endocrine and toxic comate (Figure 1). It is essential to realize that the relation of symptom and disease and the distinction between symptom and disease remained problematic at a time when the classification and naming of diseases were not supported by anatomical and etiological research. Thus, an uncritical and simplistic identification of Galen's apoplexy with modern concepts of stroke is misleading.

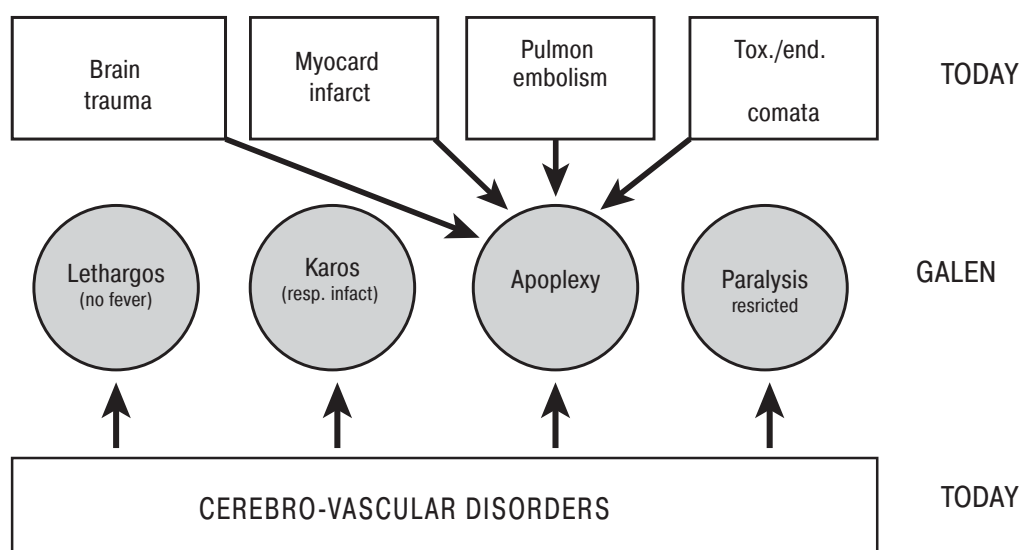


Fig. 1. Galen's definition of apoplexy/stroke in relation to modern nosology.

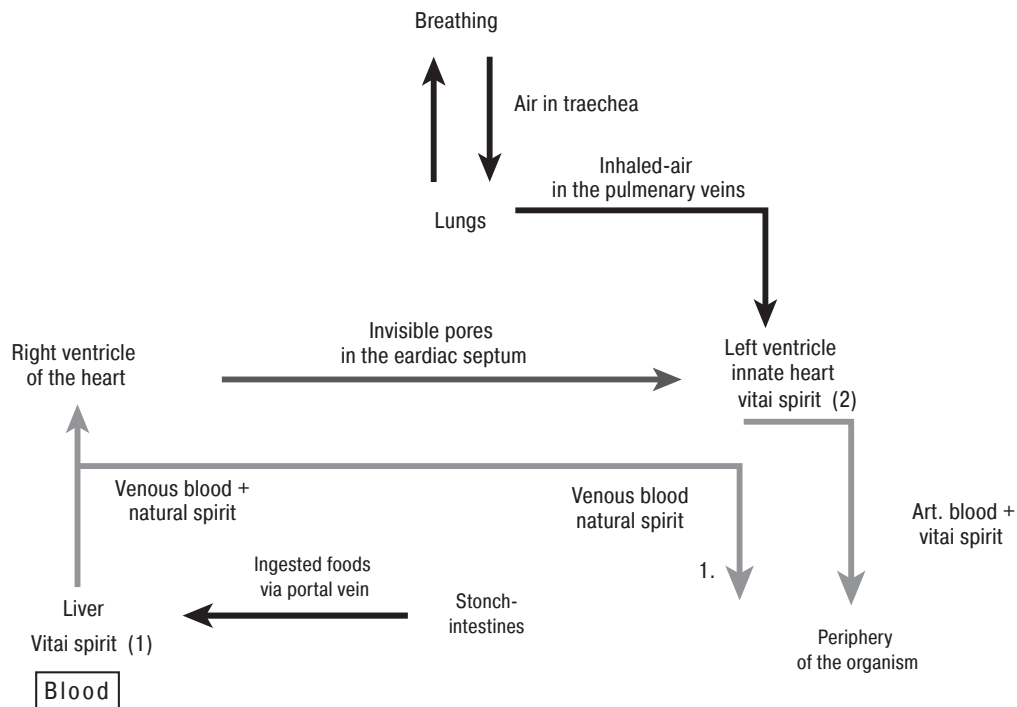


Fig. 2. Galen's doctrine of blood motion.

### The issue of prognosis

To ancient physicians formulating a correct prediction of the course and outcome of a disease was more important than finding the right name for a medical condition. A severe apoplectic attack was, according to Galen, always fatal. Often, however, the disease could take a chronic form: an acute attack was followed by a so-called "paraplegia", consisting of a permanent impairment of movement [19, vol. 8, p. 230; 20, p. 109]. Paraplegia would usually involve the muscles of one side of the body from the head to the tip of the feet. It could also be rather limited, affecting only one half of the tongue.

Following the Hippocratics, Galen distinguished two types of apoplexy according to severity, although he also introduced new criteria. A maximal deviation from the natural rhythm of breathing and the occurrence of a small, weak, narrow and slow pulse indicated a fatal type of apoplexy. Minor disturbances of respiration and pulse were associated with a better prognosis [19, vol. 9, p. 193 and vol. 17B, p. 542]. These observations would be striking to anyone working on a modern stroke unit. However, Galen did not

explicitly characterize respiration and heart-beat as "vital functions". Rather, he viewed respiratory failure exclusively as the result of the patient's inability to move the thoracic muscles necessary for respiration.

### Theoretical background

The most important issue, however, is the way in which Galen explained the origin of an apoplectic attack, an area which goes to the core of his medical thinking. To understand his theoretical background, we must briefly review two of the cornerstones of his medical teaching: first, his own theory of the motion of blood, and second, the centuries-old doctrine of the four humors.

In Galen's doctrine of bodily functions, blood was continuously synthesized from ingested food. The useful part of the food was transported from the intestines via the portal vein to the liver, where, by an innate faculty of the liver, it was transformed into venous blood and a mysterious second product, the "natural spirit". This natural spirit supported the functions of growth and nutrition and was distributed to all parts of the body by the veins (see Figure 2).

Galen further assumed that a certain quantity of venous blood could pass from the right side to the left side of the heart by means of invisible pores in the cardiac septum. Inhaled air was also brought to the left side of the heart, where it was transformed into “vital spirit”. The heart and the arteries were responsible for the maintenance and distribution of the “innate heat” or “indwelling warmth”, a key principle of Aristotelian and also Galenic biology, which explained the body’s functioning. Both arterial blood and the vital spirit, by ebbing and flowing back and forth in the vessels, were thought to be necessary to warm and vivify the peripheral organs. Like the venous blood and the natural spirit, arterial blood and the vital spirit were used up after their distribution to the periphery [13].

According to Galen, further refinement of the vital spirit was accomplished in the arteries that formed the *rete mirabile* or *retiform plexus* – a network of vessels located at the base of the brain – that Galen had seen when dissecting animals, but which does not exist in humans (Figure 3). During its passage through this network, the vital spirit was transformed into the “animal spirit”. Galen considered this spirit,

stored in the cerebral ventricles, to be essential for the transmission of movement and sensation to all parts of the body by the hollow nerves [12]. It is essential to recognize that Galen had no notion of general or cerebral circulation. Nevertheless he established a complex scheme of interplay between blood motion and nervous function – a concept of cerebral function that was based on the Platonic idea of a threefold division of the soul, the tenet of the three spirits, and the idea of the brain as the governing center. Galen even tried to prove his theory using a simple experiment: if the ventricles of an animal were opened by a surgical incision, its body would be deprived of motion and sensation, and the animal would die. This occurred, Galen concluded, because the animal spirit had escaped [12].

The second cornerstone of Galen’s doctrine was the Hippocratic concept of the four humors: blood, phlegm, black bile and yellow bile, and their associated qualities: warm, cold, moist, and dry (Figure 4). According to ancient philosophy and medicine, health was the harmonious balance and blending of these four humors, or “eukrasia”. An excess of one of the humors resulted in an abnormal mixture. “Dyscrasia”

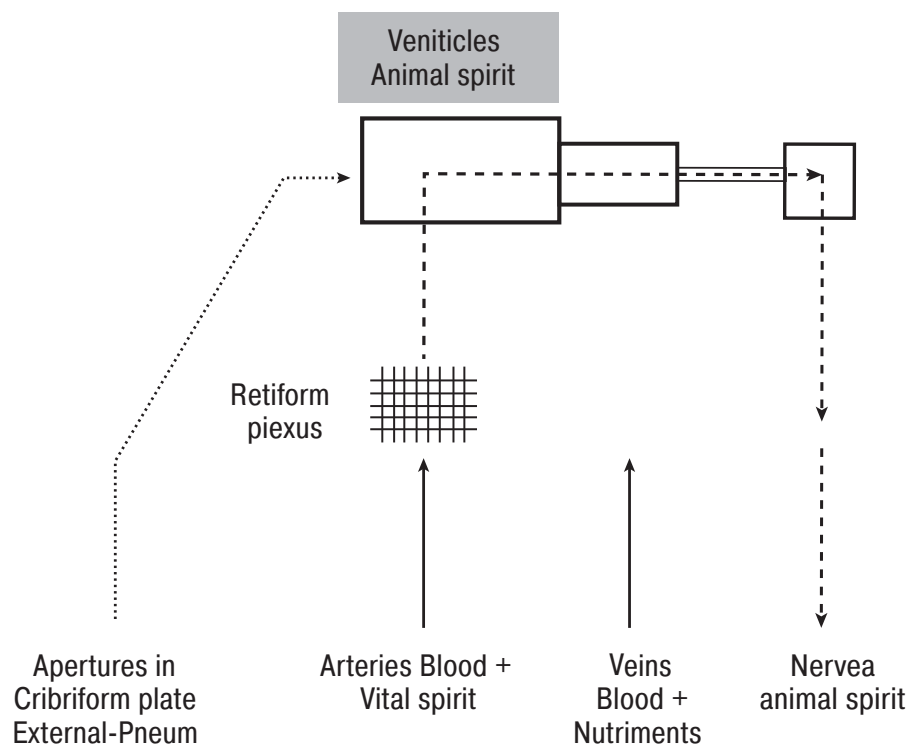


Fig. 3. Galen’s theory of brain function.

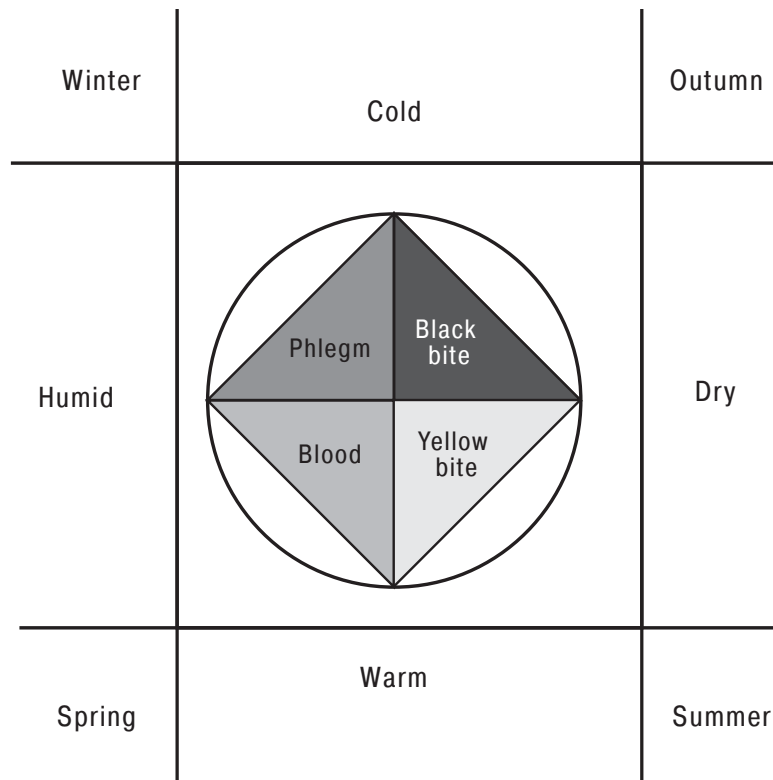


Fig. 4. Ancient doctrine of the four humors.

or “cacochymia”, as this abnormal blending was referred to in ancient terminology, was thought to be the basic disruption of bodily functioning that underlay every internal disease.

How did Galen use these principles to explain the origin of an apoplectic attack? The brain, he argued, can be affected in two different ways. In “apoplexy by local dyscrasia” he viewed the disease as the result of the accumulation of a thick, viscous and sticky humor in the cerebral ventricles which obstructed the flow of the animal spirit [19, vol. 7, p. 201, vol. 8, p. 200 and 232; 20, p. 97 and 110]. Because of the blocked passage, neither motion nor sensation could be transmitted via the animal spirit to and from the periphery [19, vol. 17B, pp. 541-542]. In general, phlegm and black bile took much of the blame for causing the attack. Phlegm was characterized by the qualities “cold” and “moist”, black bile by the qualities “cold” and “dry”. Both these humors shared the quality “cold”, and therefore apoplexy was in both instances a “cold” disease.

More appealing to modern physicians is the second pathway discussed by Galen, “apoplexy by local plethora”. “Sometimes the plethora of

blood...” – he wrote in *De curandi ratione per venae sectionem* 5 – “arrives in force at some part, so as to destroy its function, or inflict notable damage. The apoplexies originate in this way, by a concerted rush of a quantity of blood to the governing center of the animal” [19, vol. 11, p. 265; 22, p. 73]<sup>4</sup>. However, Galen did not elaborate on the issue of whether the superfluous blood in the brain resulted in a hemorrhage or in some alteration of the cerebral ventricles. He simply stated that the abnormal filling of the cerebral veins, by attracting phlegm, caused a diminution of natural heat leading to an abnormal cooling of the brain. Thus both origins of the disease discussed by Galen led, at the final stage of the pathway, to a change of the cerebral warmth and to a consecutive stoppage of the flow of the animal spirit [19, vol. 17B, p. 541-542]. In short, Galenic brain pathology was the pathology of the animal spirit.

<sup>4</sup> ἐνίοτε δὲ πρὶν ἄρχεσθαι σήπεσθαι τὸ πλῆθος τοῦ αἵματος, ἐπὶ τι μῶριον ἀθρώως ἀφικόμενον ἥτοι τελέως ἐνέκρωσεν, ὥστε διαφτεῖραι τὴν ἐνέργειαν, ἢ βλάβην ἀξιολόγον ἐνεγκεῖν. αἱ γοῦν ἀποπληξίαι κατὰ τοῦτον γίνονται τὸν τρόπον, ἐπὶ τὴν ἀρχὴν τοῦ ζώου ῥυέντος ἀθρώως αἵματος πολλοῦ [19].

### Observable factors

For a modern scientist all this theorizing about the so-called “hidden causes” of the illness seems to be quite logical and rational, despite being very speculative. However, many ancient physicians, including Galen, linked their etiological hypotheses to a variety of external factors open to observation.

One of these observable phenomena was the fact that most victims were in the later stages of life, as most apoplectics would succumb to the disease between the ages of 40 and 60 [19, vol. 17B, p. 649-651; vol. 5, p. 694; vol. 7, p. 13-14; 23, vol 2, p. 519]. Galen, like many of his predecessors, explained this fact by a constitutional difference between ages: older people were generally thought to be colder than younger people and thus more susceptible to a cold disease produced by phlegm or black bile. Of similar importance was the climatic factor, namely the influence of the seasons. Winter, the cold and moist season in the Mediterranean, and autumn, the cold and dry period, could provoke a prevalence of phlegm and black bile in the body [19, vol. 5, p. 694 and vol. 18A, p. 95]. Therefore, it was not surprising that phlegmatic or melancholic apoplexies occurred at this time of the year, especially in patients with an inclination to a phlegmatic or atrabilious temperament. Finally, an abnormal cooling of the brain with subsequent attacks could also be provoked by faulty customs in food and drink [19, vol. 7, p. 13]. Any immoderate consumption of nourishment was regarded as harmful. Particularly, excessive ingestion of wine reduced natural warmth and was to be avoided. This is a perfect example how the interaction of external or macrocosmic factors, such as climate and season, and internal or microcosmic elements, such as age and disposition, led to a general cooling of the body resulting in a “cold” disease.

### Prophylaxis and treatment

Therapeutic and prophylactic strategies both included dietetic, pharmacological, and surgical measures and followed the two main principles of ancient therapy: the “rule of contraries”, i.e. the attempt to correct a complexional imbalance by application of its opposite, and “somatocatharsis”, i.e. cleansing the patient’s body by removal of superfluous and noxious humors. In cases of

imminent or manifest apoplexy, the physician’s actions were primarily directed at fighting the underlying cause of the disease. Thus different procedures were recommended for different etiologies.

Prophylactic measures were simple to prescribe. A phlegmatic individual had to avoid all nourishment and beverage that could provoke a further diminution of the “natural warmth”, and moderate exercise was thought to preserve this “natural warmth”. Therefore walking and sports were especially recommended for these patients. Individuals with a high risk for an attack caused by “the plethos of blood” could be identified by an abnormal filling of their veins. For these high-risk patients, blood-letting was preferred [19, vol. 11, p. 344]. The proper time for prophylactic venesection was spring, because this was the season in which the blood humor predominated [19, vol. 18A, p. 78-80; see Figure 4]. As always, Galen felt very confident about the effectiveness of his regime, maintaining that by these strategies he had prevented the disease in many patients.

Immediate evacuation of blood by means of phlebotomy was also the preferred treatment for manifest cases of this type [19, vol. 11, p. 226]. In cases of acute apoplexy by local dyscrasia in the brain, Galen detailed in *Methodi medendi XIII, 21* three principle therapeutic actions, which became axiomatic for later centuries: (1) local evacuation, (2) indirect dilution, and (3) focal heating. First, the physician should use sternutatories to promote sneezing and place anti-phlegm remedies on the palate of the patient. These applications were thought to “cut” the semi-fluid material and to evacuate superfluous mucus via the nose. In chronic cases, warming substances like strong mustard plasters were added on the forehead. A particular therapeutic strategy made use of the hypothetical connection between the cerebral ventricles and the nasal cavities (see Figure 3). Thyme, flea-bane and oregano, all regarded as “heating” substances, were boiled in vinegar and applied under the patient’s nose. The ascending vapor was supposed to generate a dilution and heating of the cold and viscous fluids in the brain [19, vol. 10, p. 931]. On the whole, however, Galen viewed the apoplectic’s chance of recovery with pessimism, quoting the Hippocratic aphorism that it is impossible to cure a severe at-

tack and difficult to cure a mild one [19, vol. 18A, pp. 87–88]. Therefore it is understandable that he stressed the necessity and usefulness of prevention in his writings more than once.

### The aftermath

Galen's doctrine of apoplexy remained an authoritative source until the beginning of the 19<sup>th</sup> century. The leading Byzantine encyclopedist-physicians of the sixth and seventh century, Aetius of Amida, Alexander of Tralles and Paulus of Aegina, simply compiled Galen's teachings, sometimes copying almost verbatim from their sources. Islamic physician-philosophers, particularly Avicenna (10<sup>th</sup>/11<sup>th</sup> century), tried to reconcile Galenic encephalocentrism with Aristotelian cardiocentrism – a wonderful topic for verbose Scholastic writers such as Pietro d'Abano (around 1300) and Jacobo da Forlì (circa 1400) [24]. The rise of dissections and the multitude of case histories compiled in early modern times generally confirmed Galen's observations. The Swiss physician Felix Platter, for example, found around 1600 “a phlegmatic humor obstructing the passages of the brain” when performing a brain dissection of a woman who had died from apoplexy. Even the famous 1658 monograph by his fellow countryman Johann Jakob Wepfer,

sometimes hailed as a “milestone” in the history of stroke, was not at all the end of the ancient doctrine. Although he was the first to rely on Harvey's discovery of the circulation, Wepfer characterized the thrombi he found in the carotid artery as “corpora pituitosa” – phlegm clots – which were obstructing the route of the vital spirits towards the brain. Herman Boerhaave, the 18<sup>th</sup> century star of the Leyden faculty, still used the names “cacochymia leukophlegmatica” and “interception of spirits” to delineate the origins of stroke. It was only when Parisian doctors, guided by the new conception of the disease as a “lesion” and the power of statistics, systematically autopsied hundreds of brains in the 1810s and 1820s, that new morphological and etiological findings, such as cerebral hemorrhage and softening of the brain, spread to the medical community. Almost 100 years after Rudolf Virchow's experiments on thrombosis, embolism and vascular occlusion, the US National Library of Medicine replaced in 1936 the old term “apoplexy” by “brain, hemorrhage”, which was again substituted by “cerebrovascular disorders”, and recently by “stroke”. Thus the disappearance of the term apoplexy marked the very last chapter in the centuries-long history of Galen's doctrine of stroke.

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