

ONE

THE VENTRICLES

Apoplexy in the Sixteenth Century

SUMMARY

Hippocratic and Galenic texts, fully rediscovered in the first half of the sixteenth century, defined apoplexy as a sudden collapse, with loss of movement and sensation, except for preserved heart action and respiration. Though this definition leaves room for divergent interpretations, early physicians who made the diagnosis rarely specified the symptoms.

Galen explained apoplexy as blockage of the cerebral ventricles by abnormal fluids, most often phlegm; animated spirits, an extremely subtle vapour, could then no longer reach the nerves. Post-mortem examination of human bodies was rare; the first inspections of the brain after apoplexy mentioned extravasated blood at its base or within the ventricles (Fernel, Duret). Varolio developed a method to remove the brain from the body and suggested that it was the substance of the brain, not its ventricles, that transported animated spirits. Two instances of hydrocephalic infants who had nevertheless shown signs of mental activity (Vesalius, Fabricius Hildanus) contributed to establishing the role of brain tissue. Physicians gradually came to use personal observation as a supplement to, or even a replacement of, written sources of knowledge.

The terms ‘apoplexy’ and ‘stroke’ have much in common, since both suggest a sudden collapse from a catastrophic illness. Yet there is a large difference. ‘Apoplexy’ refers to observable phenomena in patients – the manifestations of a brain disease, according to criteria developed in antiquity. By contrast, today the word ‘stroke’ evokes, as dictionaries testify, an anatomically defined cause: a disorder of the brain’s blood vessels. This transition, from a set of clinical features

to a morphological notion, is a metamorphosis many other diseases have gone through in the course of history. The difference between the two points of view, that is, what the doctor observes in the patient versus what the pathologist sees in the brain after death, explains not only why terms have changed, but also what is meant by them. As a consequence, some examples of ‘apoplexy’ would not be called ‘stroke’ today, and vice versa.

This chapter describes the earliest phase in these early developments, in the second half of the sixteenth century. During this period, the heritage of ancient Greek medicine was fully rediscovered, cleansed of Arab interpretations, and disseminated by the growing book culture.¹ Two themes dominate the chapter. The first is the definition of apoplexy as a clinical syndrome or as a set of coherent clinical features. The second theme is the theory of normal brain function and its disturbance in apoplexy. It will be necessary to switch from manifestations to explanations, and back, a few times.

APOPLEXY: AN AFFLICTION DEFINED BY ITS MANIFESTATIONS

Phenomena are recorded through observation – often, if not always, conditioned by interpretation. Readers, please discard all ideas you may have in relation to what is now called ‘stroke’, and open your mind to the observations and interpretations of physicians in a distant past who tried to make sense of an acute disease.

Ancient Descriptions

The cardinal feature of apoplexy, as the original term in ancient Greek implies, is that it strikes suddenly and renders the patient senseless and motionless. It is as if the victim is struck by lightning, hence the Latin synonym *morbus attonitus*, or ‘stunned disease’. The disease is briefly mentioned in Babylonian texts,² and subsequently in Hippocratic writings. Yet the most influential author in antiquity on medical subjects was Galen (129–c.216) (Box 1.1). He was a prolific writer with an adventurous life.³ Galen did not systematically deal with each disease in turn; therefore, the reader has to try and reconstruct Galenic notions from different, and sometimes contradictory, passages. Key features of the disease are found in different sentences, for example:

When all nerves have simultaneously lost sensation and motion, the affection is called apoplexy. But when this happens on one side, the right

¹ Siraisi (1985), *The Canon of Avicenna*, 39–41; French (1985), *Berengario*, 66–71; Maclean (2002), *Medicine in the Renaissance*, 19–20; Wear (1995), *Early modern Europe*, 251–5.

² Reynolds and Kinnier Wilson (2004), *Stroke in Babylonia*.

³ Mattern (2013), *The Prince of Medicine*; Nutton (2020), *Galen*.

Box 1.1 Claudius Galenus (129–c.216).

Galen was the son of an architect and local magistrate in the Greek community of Pergamum (now Bergama, Western coast of Turkey). He studied medicine from the age of 16, first in his home town, then in Smyrna (present-day Izmir) and Alexandria. In 157, he was back in Pergamum, as a physician for the gladiatorial school.

In 162, Galen set out to establish himself in Rome. The professional climate in the capital was highly competitive – apart from educated Greek physicians, also lay citizens or slaves offered their services to the sick. A physician's reputation depended heavily on their ability to predict the outcome of disease and also on anatomical demonstrations in live animals. Galen used pigs, goats, cattle, monkeys, cats, dogs, mice, snakes, fish, and birds. Among the spectators at such sessions was the ex-consul Flavius Boethus; he invoked Galen's help when his wife was ill and became Galen's patron when she recovered. In 166, Galen rather unexpectedly left Rome. Speculations about his motives include an epidemic of infectious disease, rivalry among colleagues, and fear of being conscripted.

He returned two years later to join the medical staff of the joint emperors Marcus Aurelius and Lucius Verus; the latter died soon afterwards. Under subsequent emperors, Galen kept this position, but he did not live in the imperial palace or join military expeditions. This arrangement allowed him to spend much of his time performing private consultations for the Roman elite – and also writing an amazing series of treatises on the structure and function of the body, illustrated with pertinent case histories. Even though, in 192, a fire destroyed his writings on pharmacology, Galen's extant collected works still take up 22 volumes in the nineteenth-century edition by Kühn.

or the left, it is called paralysis, of the part in which the disorder exists – sometimes the right, sometimes the left.⁴

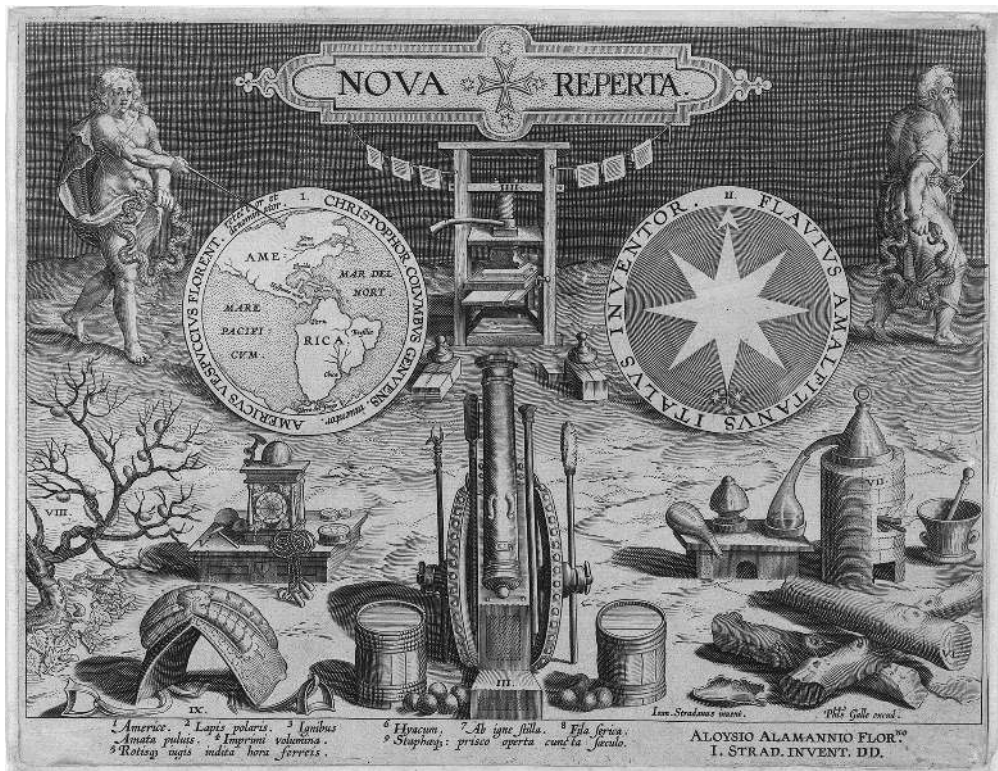
Galen noted elsewhere that respiration was preserved in these patients, though it was laboured. He also found that the pulse of the arteries in the wrist and elsewhere continued to beat in patients with apoplexy:

But when the respiration is affected to such an extent that [the patient] breathes as in deep sleep, then we speak of apoplexy.⁵ [And also:] As long as the disease has not gained the upper hand, you will find [in the pulse] no change at all with regard to magnitude, force, speed, frequency and hardness.⁶

⁴ Galenus (1625b [c.180]), *De Locis affectis* (C4) III, 20H; Kühn, ed. (1821–33), *Galen Opera*, vol. VIII, 208.

⁵ Galenus (1625b [c.180]), *De Locis affectis* (C4) IV, 22H; Kühn, ed. (1821–33), *Galen Opera*, vol. VIII, 231.

⁶ Galenus (1625a [c.180]), *De Causis Pulsuum* (C4) IV, 102G; Kühn, ed. (1821–33), *Galen Opera*, vol. IX, 193.



1.1 New discoveries (*Nova reperta*). A printing press is shown directly under the cartouche. On the left, a young woman with the mythical snake Ouroboros (biting its own tail) indicates the Americas. On the right side is a compass rose, with the name of its supposed inventor; an older man, again with Ouroboros, leaves the scene. In the foreground are inventions symbolizing the sixteenth century: the silkworm, a saddle and spurs, a mechanical clock, a cannon and gunpowder, medicinal bark, and an apparatus for distillation. Engraving attributed to Jan Collaert, after drawing by Jan van der Straet, c.1590. *Source*: Courtesy of Rijksmuseum, Amsterdam.

It is justified to say that, at least with regard to the definition of apoplexy, physicians in the middle of the sixteenth century started where Galen had left off more than 13 centuries ago. The term ‘Renaissance’ may have been coined rather recently, by nineteenth-century historians,⁷ but literary humanists in the fourteenth century, such as Petrarch, already saw themselves as harbingers of a new era, after the ‘dark ages’.⁸ Two hundred years later, many still felt they were living in an age of discoveries (Figure 1.1). In the ‘medical Renaissance’ of the sixteenth century,⁹ recovered and reconstituted Galenic texts came to replace medieval Latino-Arab glossaries on medicine, at a time when prices of

⁷ Burckhardt (1860), *Die Kultur der Renaissance in Italien*.

⁸ Mommsen (1942), Petrarch’s conception of the Dark Ages.

⁹ Wear, et al., eds. (1985), *The Medical Renaissance of the Sixteenth Century*.

printed books allowed doctors to build their own library.¹⁰ The young Jean Fernel (1497–1558), about to become an important physician, used similar terms when young: ‘These disciplines and arts have clearly come to life again, after having been buried, or rather extinct and lifeless, for almost twelve hundred years.’¹¹ It is no surprise, therefore, to find an almost Galenic description of apoplexy in the first known treatise on diseases of the nervous system,¹² published in 1549 by Jason Pratensis (c.1486–1558; Latinized name for ‘van der Velde’); he practised in Zierikzee, in the Southwest of the Low Countries:

Apoplexy is a disease in which an affected person is deprived of motion and sensation; only breathing remains, though not intact, but abnormal in a variety of ways. Most often this illness arrives without fever, and the person suddenly tumbles down on the floor with a great fall. The collapsed person cannot be woken up by any speech, or by any shouting or poking. The numbness keeping the stricken patient down is so severe that no stimulus can overcome it. [. . .] And in the same way, the arteries originating from the heart are less impeded in this disorder, because they retain their pulsations, though these are much more subtle [. . .]¹³

Thus, the standard definition of apoplexy, often repeated and essentially unchanged in the sixteenth and seventeenth centuries, and even later, consists of three main characteristics: (1) a sudden fall; (2) loss of movement and sensation; and (3) preservation of respiration and pulses, at least by and large. Still, there are some loopholes in this definition. A case report can help to clarify this – it is unique for several reasons: it dates from the middle of the sixteenth century and the patient is also the author.

A Self-Reported Case History

Conrad Wolffhart (1518–1561) (Figure 1.2) included an account of his own apoplexy – and his recovery – in a collection he edited of prodigious events spanning from pre-biblical times to the middle of the sixteenth century; his humanist name was Lycosthenes. Born in Rouffach (Alsace), Wolffhart studied philosophy in Heidelberg. In 1542, he moved to Basle where he became Deacon of the Church of St Leonard.¹⁴ This is how he looked back on his disease episode:

On 21 December of the year 1554, on leaving the building where I was already preparing the edition of my collection of ‘Aphorisms’ for the press, a horrible incapacity overwhelmed me. I suddenly collapsed on the floor and in a single moment I lost not only my voice, but also all sensation and movement on the right side, from head to heel (except sight and hearing).

¹⁰ Jones (1995), *Reading medicine*, 155–6; Nutton (2005), *Printing and medicine*, 421–2.

¹¹ Fernelius (1548), *De abditis Rerum Causis*, 2. ¹² Pestronk (1988), *The first neurology book*.

¹³ Pratensis (1549), *De Cerebri Morbis*, 121. ¹⁴ Beyer (2012), *Lycosthenes*.



1.2 Conrad Lycosthenes (1518–1561). Etching by Simon Frisius, c.1610, 150 × 115 millimetres.

Source: Courtesy of Rijksmuseum, Amsterdam.

I could not utter a single word, until 12 days later; I could not stand on my feet or move a finger for three entire months, during which period I was bed-bound. My [right] limbs seemed to be converted not into wood but into the hardest stone; the blood of the affected parts was so much frozen and hardened by the coldness of the humours and the obstruction of my nerves, that rubbing, compresses or any other measures entirely failed to warm them. At that time, owing to the humours that were disappearing from the head and the brain (it is astonishing to say), I lost all memories, to such an extent that the words of my Sunday sermon and all my knowledge of literature had vanished completely. [..]

My excellent friends were witnesses of my disaster. They could not understand me

because I could only communicate by nodding, though I was sound of mind and reason. They held up a slate on which the letters were chalked in alphabetical order, so that I could point out the letters in their proper order with the index finger of my left hand; in this way the letters formed syllables and the syllables sounds, which they, after some mulling on my part, made me utter. But my affliction seemed to be a chronic and irreparable disease. As a result, not only I myself, but all who watched this cruel disease despaired about my life. But God in his mercy, on whose power all infirmity depends, overhearing my persistent prayers and those of his church on my behalf, restored me for the greater part, through the effort of Dr Guglielmo Gratarolo from Bergamo. Therefore, if you have possibly thought that in the part of life left to me some products of my pen have some merit for muses and profession, I would like to thank God Almighty in the first place, and thereafter Dr Gratarolo [..]¹⁵

Ambiguity in the Interpretation of Clinical Symptoms

This unique case history also serves to show that the criteria for the diagnosis of apoplexy are somewhat imprecise, that is, open to different interpretations.

Consciousness. Medical treatises of the sixteenth century often distinguish between external senses (sight, hearing, touch, smell, and taste) and internal senses, viz. intellectual activities such as reasoning, imagination, and memory. So ‘loss of one’s senses’ is practically synonymous with the modern term

¹⁵ Lycosthenes (1557), *Prodigiorum ac Ostentorum Chronicon*, 640–1.

Box 1.2 Pieter van Foreest (1521–1597).

van Foreest was the third child of a wealthy couple in Alkmaar, a city north of Amsterdam. After secondary school, he studied liberal arts and medicine in Louvain (1536–1539), then made a tour of medical faculties in northern Italy. Having graduated in Bologna (1543), he also spent time in Venice, Ferrara, and Padua, made an eventful foot journey to Rome in the company of botanists (1545), and visited Paris and Orléans.



The next year, van Foreest settled in Alkmaar where he married Eva van Teylingen and established a solid reputation. Twelve years later, he accepted the post of city physician in Delft where the plague was raging. He remained in Delft for the next 37 years, a period of political turmoil, religious strife, and revolt of the United Provinces against Spanish rule. In 1574, during the siege of Leiden, he became the personal physician of William the Silent, prince of Orange and leader of the revolt.

In 1595, his wife Eva died, predeceased by their four children; van Foreest, now aged 74, decided to return to Alkmaar as a city physician. Meanwhile he had started to publish a series of books with case histories, followed by comments (*scholia*). These volumes continued to appear after his death, the last with medical subjects (no. 17) in 1606, followed by two more volumes with surgical cases. Reprints of his collected works continued to appear up to 1661.

Source: Portrait courtesy of Rijksmuseum, Amsterdam.

‘unconsciousness’. But either term is based on the absence of reactions from the patient, such as speaking and moving the limbs or eyes. Since Lycosthenes, once recovered, could write about his fall and its circumstances, he must, at the time of the event, have been able to think and remember – or others must have recounted later what had happened. At any rate, the reason why a later medical compiler classified the disease as a case of apoplexy¹⁶ must have been that the patient was unable to speak and could not signify he was sentient. Bystanders – and physicians – depend on verbal communication to find out whether someone can think and feel; at any rate, when a patient had collapsed and was speechless, with their eyes closed, it was assumed that all mental activity had been lost.

Language. If, however, a patient was mute but showed signs of awareness by other means, sixteenth-century physicians tended to diagnose ‘paralysis of the tongue’. An example is found in the *Observationes et Curationes Medicinales* of Pieter van Foreest or Forestus (1521–97) (Box 1.2). This extensive work, often reprinted,¹⁷ contains the following story in the section on apoplexy:

¹⁶ Schenck von Grafenberg (1609), *Paratereseon*, 91.

¹⁷ Breugelmans and Gnirrep (1997), *Bibliografie*.

A high-born and noble young man, Mr van Cruningen, about 29 years old, was melancholical, more than fitting for his age and nature; this melancholy had increased when, long before, he had been kept in custody in Hoorn, together with Mr de Bossu. Early on the night of March 8, 1581, he suddenly sustained a fairly strong apoplexy, which quickly evolved into a paralysis of the entire right side, arm as well as leg, with impairment of the tongue, so that he could hardly speak; also, he could not properly understand.¹⁸

Although the report mentioned difficulty in understanding spoken language, the medical community apparently saw language as a purely motor phenomenon.

Paralysis. Van Foreest's report also shows that he designated right-sided hemiplegia after the patient had come round as 'paralysis', in keeping with the rule that apoplexy was diagnosed only if *all* movement was abolished. Yet it is difficult to be sure that a collapsed patient can move anything at all. Lycosthenes was unable to say this; had he been able to speak, his disease might have been classified as 'paralysis'. Perhaps he made no spontaneous movements with the left limbs because he was lying on this 'good' side, or because he was too frightened to stir at all. Of course, someone might have prodded or pinched him, in order to evoke some sort of response. But if this test was done on the affected side and gave no result, there was no good reason in those times to try the other side. Moreover, if a patient happened to be in deep coma, it would have made no difference. Another source of uncertainty is how violent the stimulus should be. Pratensis recommended the application of white-hot iron,¹⁹ but probably he mentioned it only for the sake of didactic drama and never tried it himself.

Respiration. That breathing was preserved, though with some difficulty, while other movements were suspended, continued to puzzle physicians; a common explanation was that it represented 'a movement of nature, not of the will'. Van Foreest followed Galen in distinguishing four types of respiration in apoplectic patients, with different chances of survival.²⁰ Many authors mentioned frothy sputum around a patient's mouth as an ominous indication of outcome, a sign that goes back to the aphorisms of Hippocrates, though in the context of judicial hanging.²¹ Hercules Saxonia (1551–607), appointed Professor of Practical Medicine in Padua in 1575, thought he could distinguish two kinds of sputum on the lips – if frothy and thick, with bubbles from exhalation, patients might recover; but no hope was left, he wrote, if it consisted of lung tissue liquefied by heat, with bubbles from enclosed spirit.²²

¹⁸ Forestus (1653 [1590]), *Observationes et Curationes*, vol. x, 526.

¹⁹ Pratensis (1549), *De Cerebri Morbis*, 422.

²⁰ Forestus (1653 [1590]), *Observationes et Curationes*, vol. x, 510.

²¹ Hippocrates (1959b [c.400 BCE]), *Aphorisms*, 119 (aphorism 43).

²² Saxonia (1639), *Opera practica*, 39.

Differential Diagnosis. Physicians had to distinguish apoplexy from other conditions with sudden onset in which the senses were affected, for example epilepsy, paralysis, syncope, and ‘suffocation by the uterus’, a kind of swooning attributed to vapours rising up from the womb. Van Foreest stipulated that the distinction was difficult if the patient had already died by the time the doctor arrived. His example was the sudden death of a certain Hugo Grotius (not the famous lawyer of the same name); van Foreest ascertained that eyewitnesses had not observed any signs of breathing or of fluid emerging from the patient’s mouth, so he concluded that the cause of death was not apoplexy, but syncope, a sudden cessation of heart action through loss of ‘innate heat’.²³

Apoplectic or Dead? A related problem was the distinction between severe apoplexy and death. For the detection of barely perceptible respiration, many authors described tests such as applying a piece of cotton wool or a mirror to the mouth and nose, or putting a mug full of water on the patient’s chest.²⁴ Similarly, van Foreest warned that feeling the pulse could be misleading and even treacherous, as illustrated by horror stories of patients deemed dead and about to be buried until their miraculous recovery – hence the statutory delay of three days between apparent death by apoplexy and the burial.²⁵ This precautionary interval is a recurring theme in almost every text on the subject from widely different parts of Europe.

In conclusion, it was up to the physician which observations or tests were necessary in deciding whether the criteria for a diagnosis of apoplexy were met. Such details were almost never recorded, at least not until the middle of the seventeenth century – and even then, by only a minority of physicians. As a rule, the reader was supposed to accept the diagnosis on trust.

BRAIN FUNCTION: SPIRITS PERFECTED IN THE VENTRICLES

Despite the possible differences of interpretation, the written criteria for the diagnosis of apoplexy remained largely unchanged until at least the beginning of the nineteenth century. By contrast, ideas about the location of brain function began to shift at an earlier stage. The most influential ancient medical authority in the sixteenth century was Galen; he is our starting point. However, Galen’s views on brain function are scattered across different texts.²⁶ To obtain a coherent account of how he was understood in the sixteenth century, it is best to consult a distinguished interpreter of that era.

²³ Forestus (1653 [1590]), *Observationes et Curationes*, vol. x, 513–14.

²⁴ Forestus (1653 [1590]), *Observationes et Curationes*, vol. x, 513.

²⁵ Forestus (1653 [1590]), *Observationes et Curationes*, vol. x, 529.

²⁶ Rocca (2003), *Galen on the Brain*.

Box 1.3 Jean Fernel (1497–1558).



Fernel's father was a furrier and innkeeper in Montdidier (Somme); the family moved to Clermont (near Paris) when he was 12 years old. Jean's ambition to continue his education at the university was new in his family, but he got his way and became a Master of Arts at *Collège Ste Barbe* in 1519. At around that time, Fernel discovered that the spirit of the 'new times' had not yet reached the University of Paris and that his teachers had provided only medieval glossaries containing Latino-Arabic interpretations of the ancients. Besides, his Latin was 'barbaric'.

In the next five years, Fernel studied on his own – apart from Plato, Aristotle, and Cicero, he developed a keen interest in mathematics and astronomy. Having finally chosen medicine as his profession, Jean provided for his own upkeep by teaching, since his father had to support the younger children. In 1530, he graduated and obtained a licence to practise; in the meantime, he had published three folio volumes on mathematical and astronomical subjects.

After his marriage to Madeleine Tornebüe in 1531, Fernel had to give precedence to his tasks as a physician, but he continued teaching until 1550 when his medical practice had become too large. His medical lectures were probably private, because he was never officially appointed to the university, while the relations with his colleagues at the medical faculty were strained. In 1542, he was appointed physician to the Dauphin; when the latter became King Henri II in 1547, Fernel excused himself from the function of royal physician but accepted it 10 years later.

Source: Portrait courtesy of Wellcome Foundation.

Spirits and the Brain: Jean Fernel's Interpretation of Galen's Model

A didactic synthesis of Galen's ideas about brain function appeared in 1554, in a seminal book called *Medicina* by Jean Fernel (1497–1558) (Box 1.3). His erudition is the more remarkable since he was largely self-taught after his graduation in Paris;²⁷ unlike young physicians from well-to-do families, he could not finish his education with a tour of foreign universities.²⁸ The first part of Fernel's book is entitled *Physiologia*. This newly coined term means 'Laws of Nature'; the neologism caught on and eventually withstood the test of time, though its meaning evolved. Fernel's book was the first treatise of its kind after Galen's *On the Function of Body Parts (De Usu Partium)*.

Fernel systematically represented the Galenic model of the different spirits, with minor adaptations;²⁹ it is schematically represented in Figure 1.3. The

²⁷ Sherrington (1946), *The Endeavour of Jean Fernel*, 1–17.

²⁸ Frank-van Westrienen (1983), *De groote Tour*; Cunningham (2009), *Peregrinatio medica*; de Ridder-Symoens (2009), The mobility of medical students.

²⁹ Fernelius (1554), *Medicina (Physiologia)*, 120–1.