Apoplexy, cerebrovascular disease, and stroke

Historical evolution of terms and definitions

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ABSTRACT. The long-standing concept of “apoplexy” can be followed from Antiquity, passing through the Middle Ages and Renaissance, and reaching the Modern era and the present day, with the new designation of “stroke”. The definition of “apoplexy” can be divided, by the history of autopsy, into a period predating this practice, which spanned from Antiquity until the Renaissance, with a relatively stable clinically-based umbrella concept, and an autopsy period of the Modern era, when the condition was subdivided into several subtypes. Thus, it took about 2,500 years assembling the numerous pieces of information to achieve a fairly well-defined picture. The “stroke” concept inherited the information developed for “apoplexy”, incorporating all historical acquisitions to form the current state of this knowledge.

Key words: “apoplexy”, “stroke”, cerebrovascular disease, history

INTRODUCTION

Cerebrovascular disease refers to a group of disorders of the brain vasculature that may affect the blood supply of the underlying tissues. This condition should be analyzed considering the pathology of the cerebral vessels (extra- and intracranial), as well as the resultant consequences on the brain parenchyma and related structures. The diseases of the vasculature include those of the large arteries (e.g., arteriosclerosis of cerebral arteries), of the small arteries, as well as of the venous vessels, besides cardiovascular conditions (e.g., embolicigenic), and systemic illnesses. The parenchymal lesions are varied, comprising ischemic changes, such as infarcts (large, small, lacunar, microinfarcts, watershed) and white matter ischemia (demyelination and axonal loss [white matter rarefaction], leukoencephalopathy), and hemorrhages (large lobar, basal ganglia, microbleeds, among others).

Cerebrovascular diseases can be asymptomatic or subclinical (silent or covert), or appear as an overtly expressed clinical manifestation in the form of “stroke” (cerebrovascular accident). The term “stroke”, which represents an acute event leading to clinical symptoms of neural dysfunction, is regarded as having evolved from the ancient designations.

This study was conducted at the Cognitive and Behavioral Neurology Unit, INDC – CDA-IPUB – UFRJ, Rio de Janeiro RJ, Brazil.

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tion “apoplexy”, which likewise refers to a clinical concept characterized by rapid loss of consciousness, and various manifestations of brain dysfunction. The “apoplexy” concept used to embrace varied disorders, later identified as acute cerebral events, vascular and non-vascular (e.g., abscess, hydatids, pus, tumors, among others), as well as non-cerebral acute occurrences (e.g., myocardial infarction, pulmonary embolism, intoxications, among others). The term “stroke” was introduced in the course of the historical studies and after a long time came to replace “apoplexy”, a term which has virtually disappeared from the medical literature.7

The historical highlights of the above-mentioned terms and concepts will be outlined, with a focus mainly on Western medicine, from Antiquity to the Modern era.

APOPLEXY: TERM AND CONCEPT

The term ἀποπληξία (apoplexia) (“struck down with violence”, “to strike suddenly”) has been used since Antiquity, identifying, in the ancient and clinical sense of the term, a disorder in which “a person suddenly falls, without consciousness or motion, retaining pulse and respiration”.5,6 This characteristic picture was well known to the ancient Greeks, at least 2,500 years ago, and “in all probability, long before, it was mentioned in writings that have not come down to us, and by authors whose names have been entirely forgotten”9

ANTIQUITY: THE GRECO-ROMAN PERIOD

This period spans about 1,000 years (c. 500 BC-c. 500 AD), when the bases of the concept was established. Many authors contributed with their knowledge, and despite lost documents, a coherent narrative took shape. Some of the many authors will be named.10

Hippocrates (and the Hippocratic Corpus) is responsible for the first recorded appearance of the term “apoplexy”. The concept is mentioned in several parts of his extensive work, describing the clinical picture, with some variations6,11 (Box 1).

The Hippocratic age was followed by numerous personalities, such as Celsus (c. 25 BC-c. 50 AD), Aretaeus (c. I century AD), Archigenes (c. I-II century AD), Galen (129 to c. 210 AD), Caelius Aurelianus (c. IV-V century AD), among many others.10 Galen deserves a special mention. He acknowledged the current notions on the theme, which he developed with ideas somewhat divergent from those of Hippocratic authors, maintaining, however, the original core6,12,13 (Box 1).

It is important to remind that, at the time, the “humoral theory” (humors, spirits), as well as “divine punishment”, was plainly in vogue as a determining factor of the ailment, a notion that would begin to be abandoned only in the 18th century of the Modern era.7,10,13

MIDDLE AGES OR MEDIEVAL ERA

The Medieval history of apoplexy, extending from the 5th to the 14th century, was represented by numerous prominent names. The authors of the early Middle Ages maintained the Hippocratic-Galenic ideas, with minor variations. The high Middle Ages included Byzantine, Persian, and Arabic authors, and in the high and late epoch the authors were from Western Europe, mainly Italy, France, and Germany. The entire period was influenced by ideas from Greco-Roman and Arabic works, but without the introduction of novel concepts.16-18

RENAISSANCE

The Renaissance, between the 14th and 17th century (in Europe), witnessed a renewed rise of interest in the ancient Greco-Roman ideas. At the time, translations of the ancient works were performed. The promotion of human dissection (autopsy) allowed society to use this for forensic, health and scientific purposes, and led to the emergence of new knowledge. The discoveries during the medical Renaissance paved the way for modern medicine.19

During the Greco-Roman, Medieval and Renaissance periods the term “apoplexy” was maintained by all authors, along with its umbrella meaning. Important changes would come with the autopsy findings of the ensuing period.
MODERN ERA

Many changes occurred from the 17th century on with the advent of autopsies, and “apoplexy” began to lose its unitary (umbrella) meaning.20 The non-vascular intracranial and the systemic conditions began to be separated, and only the vascular-related events retained the original designation. A classification started to emerge, based on cadaveric examination, dividing the condition into increasingly numerous subtypes, and laying the foundations of the study of the chapter of “cerebrovascular disease(s)”. Some of the most cited authors of the period,21,22 and their contributions to the theme, will be mentioned, without diminishing the influence of many others (Box 2).

- Wepfer (1658) identified non-traumatic intracranial hemorrhage – “subarachnoid hemorrhage” and “cerebral hemorrhage”, as separate from other “apoplexy” types.23
- Wepfer split, for the first time, the unitary “apoplexy” definition, marking the start of studies on vascular diseases of the brain or “cerebrovascular disease(s)”.24
- Cole (1689) first used the term “stroke” to denote “apoplexy” in English medical writing.24
- The term would be adopted much later.
- Biumi (1765) described a case of a non-ruptured sacular “aneurysm” of the carotid artery.25
- Morgagni (1761) distinguished a “sanguineous” [intracranial hemorrhage], a “serous” [non-hemorrhagic], and a “neither sanguineous nor serous” apoplexy.26
- Blackall (1814) identified a ruptured “aneurysm” of the basilar artery in a case of “subarachnoid hemorrhage”.27

Box 2. “Apoplexy” in the Modern era (from 17th century on); discovery of subtypes timeline – authors and excerpts.

| Author | Year Range | Country | Description |
|--------|------------|---------|-------------|
| Wepfer | 1620-1695 | Swiss | Distinguished for the first time non-traumatic intracranial bleeding - in one case: “…cut the dura mater, much blood discharged from the space between it and the pia-mater [subarachnoid space]…”, in another case: bleeding with ruptured anterior cerebral artery branch; in one more case, with serous liquid (pale-colored serum) accumulation (1658).23 |
| Cole | 1635-1716 | English | The first to use the term “stroke” to denote “apoplexy” in English medical writing (1689).24 |
| Biumi | 1660-1717 | Italian | Described a case of “apoplexy”, without intracranial bleeding, identifying: “…internal carotid aneurysm sack [saccular aneurysm] in the cavernous sinus (Vieussens receptacle)…” [aneurysm - unruptured] (1765).25 |
| Morgagni | 1682-1771 | Italian | Described a “sanguineous” (with bleeding) [hemorrhagic], a “serous” (with intracranial fluid) [non-hemorrhagic], and a “neither sanguineous nor serous” type apoplexy (1761).26 |
| Blackall | 1771-1860 | English | Distinguished: “…haemorrhage in the space between the meninges… [subarachnoid hemorrhage]…traced to the basilar artery…at its bifurcation was dilated into an aneurysmal sac [basilar artery aneurysm]…opened into the cavities” [aneurysm - ruptured] (1814).27 |
| Rochoux | 1787-1852 | French | Defined “hemorrhagic apoplexy” [cerebral hemorrhage], and introduced the term ramollissement du cerveau [softening of the brain] [infarction] (1814).28 |
| Rostan | 1796-1866 | French | Defined “sanguine (hemorrhagic) apoplexy” [cerebral hemorrhage] and extended the notion of (non-inflammatory) “cerebral softening” (ramollissement cérébral) [cerebral infarction] (1819); he considered “apoplexy” only for hemorrhagic events.29 |
| Dechambre | 1812-1886 | French | Introduced the term lacune [lacune] for small rounded cavities probably resulting from the liquefaction after partial resorption within foci of softening (1838).30 |
| Durand-Fardel | 1815-1899 | French | Described “hemorrhage” [meningeal, cerebral] [subarachnoid hemorrhage] [cerebral hemorrhage], “brain softening” [cerebral infarction], “interstitial atrophy of the brain” [white matter rarefaction (demyelination and axonal loss)], “lacune”, and état criblé du cerveau [riddled state of the brain].31 |
| Virchow | 1821-1902 | German | Introduced the terms apoplexia sanguinea (Hämorraghische Apoplexie des Gehirns) [hemorrhagic apoplexy of the brain] [cerebral hemorrhage], and apoplexia ischaemica (ischaemic apoplexy) [Hirnweichung] [cerebral softening] [cerebral infarct], caused by embolism; created the terms “thrombosis” and “embolism”; revived the term “arteriosclerosis” (according to Lobstein, 1829) (1852).32 |
| Laborde | 1830-1903 | French | Described the “pisiform lacunes” (lacunes pisiformes) as “…small cystic cavities…small blood effusions that have suffered a complete resorption…in other cases…their centers…resulting from partial and progressive disorganization…” for “lacunes” [post-hemorrhage and post-softening] (1866).33 |
| Cohnheim | 1839-1884 | German | Introduced the terms Infarct [infarction, infarction], Nekrose [necrosis] and hämorragischer Infarct [hemorrhagic infarct], after embolic obstruction of terminal arteries (1872).34 |
| Wilsanger | 1852-1929 | Swiss | Described marked atrophy of the subcortical white matter he named “Chronic progressive subcortical encephalitis” (1894), later named after him, and subsequently known as “Binswanger disease”.35,36 |
| Alzheimer | 1864-1915 | German | Described diffuse and focal subtypes of vascular injuries of the brain, including focal cortical atrophic changes (senile Sklerose der Hirnrinde and senile Rindenverödung), “cortical microinfarcts” (1899-1902).37,38 |
• Rochoux (1814) defined a “horrhadagog apoplexy” [cerebral hemorrhage] and introduced the term ramollissement du cerveau [softening of the brain] [infarction].

• Rostan (1819) defined “sanguine (hemorrhagic) apoplexy” [cerebral hemorrhage] and extended the notion of non-inflammatory ramollissement cérébral [cerebral softening] [cerebral infarction].

Here, the basic distinction between the two main forms of “apoplexy”, hemorrhagic and ischemic (“cerebral hemorrhage” and “cerebral infarction”) became clearly recognized. This division was set to endure until the present day, maintained also for the “stroke” concept that would follow.

• Dechambre (1838) introduced the term lacune [lacune].

• Durand-Fardel (1843) described “hemorrhage” (meningeal, cerebral) [subarachnoid hemorrhage] [cerebral hemorrhage], “brain softening” [brain infarction, cerebral infarction], “interstitial atrophy of the brain” [white matter rarefaction], “lacune” and état criblé du cerveau [riddled state of the brain].

• Virchow (1852) introduced the terms apoplexia sanguinea [cerebral hemorrhage] and embolic apoplexia ischaemica (ischaemic apoplexy) [cerebral softening, cerebral infarct], created the terms “thrombosis” and “embolism”, and revived the notion of “arteriosclerosis”.

• Laborde (1866) described lacunes pisiformes [lacunes], post-hemorrhagic and post-softening.

• Cohnheim (1872) introduced the terms “infarct”, “necrosis” and “hemorrhagic infarct”, following embolic obstruction of terminal arteries.

•Binswanger (1894) described “Chronic progressive subcortical encephalitis” (later named after him, and subsequently known as “Binswanger disease”).

• Alzheimer (1898) described “cortical microinfarcts”.

At this time, the main subtypes of “apoplexy” due to “cerebrovascular disease(s)” were identified, and would, as a next step, be officially recognized and reunited in a reference report.

STROKE AND ILCD/ICD: PRESENT-DAY TERMS AND DEFINITIONS

The term “apoplexy” was maintained as a medical term in the 4th Revision of the International List of Causes of Death (ILCD-4) (1929). The term was abandoned from the 5th Revision onwards (ILCD-5) (1938).

The term “stroke” (cerebrovascular) appeared first in the ICD-9 (1968). The definition of the concept by the World Health Organization (WHO) appeared soon after (1971 and 1980), and more recently, a new definition was proposed by the American Heart Association-American Stroke Association (AHA-ASA) (2013) (Box 3).

The notion “cerebrovascular disease(s)” was introduced initially as “arteriosclerosis with cerebral vascular lesion” in the ILCD-3 (1920), and replaced by “cerebrovascular disease(s)” from the ICD-8 (1965) onwards.

The current ICD-10 (1990) (version 2016), contains the term “cerebrovascular disease(s)” and “stroke” (cerebrovascular accident), besides “intracerebral hemorrhage”, “subarachnoid hemorrhage”, “cerebral infarction” (thrombosis, embolism), “lacunar” (syndromes), “Binswanger disease”, “cerebral aneurysm”, “subarachnoid hemorrhage”, among others.

Thus, after an extensive period of research, the WHO went on to incorporate progressively, in the official reference report, all subtypes of “cerebrovascular disease(s)” that were so arduously developed. However, the term “apoplexy”, with a more restricted meaning, remains in use in the medical literature to the present day.

Box 3. Definitions of “stroke” in the Modern era (20th–21st century) (excerpts as examples).

| WHO (World Health Organization) |
| --- |
| “Stroke” definition (1971): “A sudden onset of disturbance of focal brain function due to the blockage or rupture of blood vessels.” |
| “Stroke” definition (1980): “Rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin.” |

| AHA-ASA (American Heart Association-American Stroke Association) (2013) |
| --- |
| Ischemic “stroke”: “An episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction.” |
| Intracerebral hemorrhagic “stroke”: “Rapidly developing clinical signs of neurological dysfunction attributable to a focal collection of blood within the brain parenchyma or ventricular system that is not caused by trauma.” |
| Subarachnoid hemorrhagic “stroke”: “Rapidly developing signs of neurological dysfunction and/or headache because of bleeding into the subarachnoid space, which is not caused by trauma.” |
| “Stroke” (not otherwise specified): “An episode of acute neurological dysfunction presumed to be caused by ischemia or hemorrhage, persisting ≥ 24 hours or until death, but without sufficient evidence to be classified as one of the above.” |
CONCLUSION

“Apoplexy” is a long-known condition. Since Hippocrates, or even earlier, numerous authors dedicated their talents to studying this subject. In the days before autopsies were allowed, from Antiquity until the Renaissance, the definition was relatively stable, an all-embracing concept for a broad condition. The advent of autopsies in the Modern era allowed the concept to be further refined and broken down, and several subtypes emerged, furthering understanding on the subject. “Stroke” inherited the information that was developed for “apoplexy”, incorporating all historical acquisitions, to form the current state of this knowledge.

REFERENCES

1. Gorelick PB, Scuteri A, Black SE, DeCarli C, Greenberg SM, Iadecola C, et al. Vascular Contributions to Cognitive Impairment and Dementia. Stroke. 2011;42(9):2672-713.
2. Smith EE, Sapounik G, Biesens GJ, Doubal FN, Fornage M, Gorelick PB, et al. Prevention of Stroke in Patients With Silent Cerebrovascular Disease. Stroke. 2017;48:e44-e71.
3. Grinberg LT. Vascular dementia. Current concepts and nomenclature harmonization. Dement Neuropsychol. 2012;6(3):122-6.
4. Aho-K, Harmesen P, Hatano S, Marquardt J, Smirnov VE, Strasser T. Cerebrovascular disease in the community: results of a WHO collaborative study. Bull World Health Organ. 1980;58:113-30.
5. Clarke E. Apoplexy in the Hippocratic writings. Bull Hist Med 1963;37:301-14.
6. Cooke J. A Treatise on Nervous Diseases, Vol I. On Apoplexy. London: Longman, 1820. [Retrieved from: http://books.google.com].
7. Pound P, Bury M, Ebrahim S. From apoplexy to stroke. Age and Ageing. 1997;26:331-7.
8. Schutta HS, Howe HM. Seventeenth century concepts of “apoplexy” as reflected in Bonet’s “Sepulchretum”: J Hist Neurosci. 2006;15:250-68.
9. Ledel JA. A Treatise on Apoplexy, Cerebral Hemorrhage, Cerebral Embolism, Cerebral Gout, Cerebral Rheumatism, and Epidemic Cerebro-spinal Meningitis. New York: W. Wood & Company, 1873. [Retrieved from: http://books.google.com]
10. Karenberg A, Moog FP. Die Apoplexie im medizinischen Schrifttum der Antike. Fortschr Neurol Psychiatr 1997;65:489-503.
11. Hippocrates. Opera omnia. De morbis liber II. Anca Mos ed. Francfort sur le Main: Wechel héritiers d’André, 1956:534-62. [Retrieved from: http://www.biusante.parisdescartes.fr/histoire/medica/resultats?cote=00002&do=pdf].
12. Galen. Oeuvres anatomiques, physiologiques et médicales de Galien. Vol 2. Darenberg C (trans). Paris: Baléire, 1856. Karenberg A, Blood, Pfiegm and Spirts: Galen on Stroke. Hist Med 2015;20(2):160-8. [Retrieved from: https://archive.org/stream/b28030507_00002&page/n5/mode/2up].
13. Karenberg A, Blood, Pfiegm and Spirts: Galen on Stroke. Hist Med 2015;20(2):160-8.
14. Hippocrates. The Aphorisms of Hippocrates. New York: Collins & Co, 1818. [Retrieved from: https://archive.org/stream/25560688r.nlm.nih.gov/25560688r#page/n5/mode/2up/search/apoplexy].
15. Sacco RL, Kasner SE, Broderick JP, Caplan LR, Connors JJ, Culebras A, et al.; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular Surgery and Anesthesia, Council on Cardiovascular Radiology and Intervention, Council on Cardiovascular and Stroke Nursing, Council on Epidemiology and Prevention, Council on Peripheral Vascular Disease, and Council on Nutrition, Physical Activity and Metabolism. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association Stroke Council, and The Councils on Cardiovascular Disease and Stroke and the Nutrition, Physical Activity, and Metabolism. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association Stroke Council, and The Councils on Cardiovascular Disease and Stroke and the Nutrition, Physical Activity, and Metabolism. Stroke. 2013;44:2064-89.
16. Karenberg A, Hort I. Medieval Descriptions and Doctrines of Stroke: Preliminary Analysis of Select Sources. Part I: The Struggle for Terms and Theories - Late Antiquity and Early Middle Ages (300-800). J Hist Neurosct. 1998;7(3):162-73.
17. Karenberg A, Hort I. Medieval Descriptions and Doctrines of Stroke: Preliminary Analysis of Select Sources. Part II: Between Galenism and Aristotelism - Islamic Theories of Apoplexy (800-1200). J Hist Neurosct. 1998;7(3):174-85.
18. Karenberg A, Hort I. Medieval Descriptions and Doctrines of Stroke: Preliminary Analysis of Select Sources. Part III: Multiplying Speculations - The High and Late Middle Ages (1000-1450). J Hist Neurosct. 1998; 7(3):186-200.
19. Toledo-Pereyra LH. Medical Renaissance. J Invest Surg. 2015;28:127-30.
20. Burton JL. A Bite into the History of the Autopsy. Forensic Sci Med Pathol. 2005;14(4):277-84.
21. Schiller F. Concepts of stroke before and after Virchow. Med Hist. 1970;14(2):115-131.
22. Warlow C, van Gijn J, Dennis M, Wardlaw J, Bamford J, et al. Chapter 2. Development of knowledge about cerebrovascular disease. In: Stroke: practical management. 3rd ed. Massachusetts: Blackwell Publishing, 2008;7-34.
23. Wepfer JJ. Observations anatomicae ex cadaverebus eorum quos sustulit apoplexia. Cum exercitatione de eiusmodi loco afecto. Schaffhausen; O a Waldkirch, 1675:1-19. [Retrieved from: http://books.google.com].
24. Cole W. A physico-medical essay concerning the late frequency of apoplexies together with a general method of their prevention and cure: in a letter to a physician. Oxford: The Theater, 1689;7. [Retrieved from: http://quod.lib.umich.edu/e/ebod/A33733.0001.018?rgn=main;view=fulltext].
25. Bluini F. Observations Anatomicae, Scholis Ilustratae. Observatio V: In Sandfort E (ed): Thesaurus Dissertationum, Vol 3. Leyden: S et J Luchtmans; 1778:373-9. [Retrieved from: http://books.google.com].
26. Morgagni JB. The seats and causes of diseases, investigated by anatomy: containing a great variety of dissections and accompanied with remarks. Cooke, William (translated and abridged). Boston: Wells and Lilly, 1824;1:22-76, 77-87. [Retrieved from: https://archive.org/stream/b21462161#page/710/mode/2up].
27. Blackall J. Observation on the Nature and Cure of Dropoises. 2nd American ed (4th English). Philadelphia: James Webster, 1825:83-5. [Retrieved from: http://books.google.com].
28. Rochoux JA. Recherches sur l’apoplexie. Paris: Mêquignon-Marvis, 1814. [Retrieved from: http://books.google.com].
29. Rostan L. Recherches sur le Ramollissement du Cerveau. 2ème ed. Paris: Béchet, 1823. [Retrieved from: http://gallica.bnf.fr/ark:/12148/bpt6k740989f/image].
30. Dechambre A. Mémoire sur la curabilité du ramollissement cérébral. Gazette Médicale de Paris 1838;6(20):305-14. [Retrieved from: http://194.254.96.52/main.php?key=cGFydGlhbHw5MDE4MnxODM4eDQ1MjAwNzA4Mi].
31. Durand-Fardel M. Traité du ramollissement du cerveau. Paris: Baillière, 1843. [Retrieved from: http://books.google.com].
32. Virchow R. Gesammte Abhandlungen zur Wissenschaftlichen Medicin. Frankurt: Meidinger Sohn & Comp.; 1856. [Retrieved from: https://archive.org/stream/b21462161#page/710/mode/2up].
33. Laborde J-V. Le ramollissement et la congestion du cerveau: principale considérées chez le vieillard: étude clinique et pathogénique. Paris: Adrien Delahaye, 1866. [Retrieved from: http://books.google.com].
34. Binswanger O. Die Abgrenzung der allgemeinen progressiven Paralyse. Berliner Klin Wochenschrift 1894;49:1103-1105, 1137-1139, 1180-6. [Retrieved from: http://www.bium.univ-paris5.fr/histmed/medica/cote?epo1248].
35. Cohnheim J. Untersuchungen über die embolischen Prozesse. Berlin: August Hirschwald, 1872. [Retrieved from: http://books.google.com].
36. Binswanger O. Die Abgrenzung der allgemeinen progressiven Paralyse. Berliner Klin Wochenschrift 1894;49:1103-1105, 1137-1139, 1180-6. [Retrieved from: http://www.bium.univ-paris5.fr/histmed/medica/cote?epo1248].
37. Engelhardt E. Apoplexy, CVD and stroke history. 453

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