

**Dementia &
Neuropsychologia**

Dementia & Neuropsychologia

ISSN: 1980-5764

demneuropsych@uol.com.br

Associação Neurologia Cognitiva e do
Comportamento
Brasil

Engelhardt, Elias

Apoplexy, cerebrovascular disease, and stroke. Historical evolution of terms and
definitions

Dementia & Neuropsychologia, vol. 11, núm. 4, octubre-diciembre, 2017, pp. 449-453

Associação Neurologia Cognitiva e do Comportamento
São Paulo, Brasil

Available in: <http://www.redalyc.org/articulo.oa?id=339554592016>

- How to cite
- Complete issue
- More information about this article
- Journal's homepage in redalyc.org

redalyc.org

Scientific Information System

Network of Scientific Journals from Latin America, the Caribbean, Spain and Portugal

Non-profit academic project, developed under the open access initiative

Apoplexy, cerebrovascular disease, and stroke

Historical evolution of terms and definitions

Elias Engelhardt¹

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

APOPLEXIA, DOENÇA CEREbroVASCULAR E ACIDENTE VASCULAR CEREBRAL: EVOLUÇÃO HISTÓRICA DOS TERMOS E DEFINIÇÕES

RESUMO. O conceito de “apoplexia”, conhecido há muito tempo, pode ser seguida desde a Antiguidade, passando pela Idade Média e a Renascença e alcançando a era Moderna e os dias presentes, com uma nova designação, “acidente vascular cerebral”. A definição de “apoplexia” pode ser dividida, pela história da autópsia, em um período precedendo essa prática, que durou da Antiguidade até a Renascença, com um conceito guarda-chuva relativamente estável baseado na clínica, e em um período de autópsia da era Moderna, quando foi alcançada a separação dessa condição em diversos subtipos. Assim, levou cerca de 2.500 anos reunindo os numerosos fragmentos de informação para chegar a um quadro satisfatoriamente bem definido. O conceito de “acidente vascular cerebral” herdou tal informação desenvolvida para a “apoplexia”, incorporando todas as aquisições históricas, para formar o presente estado de conhecimento.

Palavras-chave: “apoplexia”, “acidente vascular cerebral”, doença cerebrovascular, história.

INTRODUCTION

Cerebrovascular disease refers to a group of disorders of the brain vasculature that may affect the blood supply of the underlying tissues.^{1,2} 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., emboligenic), and systemic illnesses.³ The parenchymal lesions are var-

ied, 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).³

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).^{1,2} The term “stroke”, which represents an acute event leading to clinical symptoms of neural dysfunction,⁴ is regarded as having evolved from the ancient designa-

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

¹Cognitive and Behavioral Neurology Unit, INDC – CDA-IPUB – UFRJ, Rio de Janeiro RJ – Brazil.

Elias Engelhardt. Av. N.S. de Copacabana, 749/708 – 22050-002 Rio de Janeiro RJ – Brazil. E-mail: eliasz@centroin.net.br

Disclosure: The authors report no conflicts of interest.

Received September 13, 2017. Accepted in final form October 16, 2017.

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).^{5,6} 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”.^{5,6,8} 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 variations^{5,11} (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 core^{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 fac-

Box 1. Definition of “apoplexy” in the Greco-Roman era.

Hippocrates. “Apoplexy” definition (not explicit) (De Morbis II): “Suddenly a healthy person is seized with head pain, immediately the voice fails, he snores, and the mouth is open (gapes), and if someone calls or moves, he only groans, nothing with meaning, gives (releases) copious urine, and does not perceive. If the fever does not seize (appears), he dies in seven days. Because it seizes (comes), the health is generally spared”.⁵ And: “Suddenly seized with pain to the head, immediately the voice fails, and he becomes incapacitated (powerless). Here, within seven days, unless the fever seizes, he dies. If the attack is strong”.¹¹

“Apoplexy” definition (explicit) (Aphorisms II-42): “It is impossible to remove a strong attack of apoplexy, and not easy to remove a weak attack”.¹⁴

Galen. Definition (De loci affectis, Commentary on Hippocratic Aphorisms): “Apoplexy is an unconsciousness of the mind, with a privation of the senses and a palsy of the body.” Also: “Apoplexy is a privation of sense and motion in all the nerves”. And: “In apoplexy the whole body suddenly is deprived of sensation and motion, with only respiration remaining, and if it is prevented, the apoplexy is maximum and very severe”.^{12,13}

tor 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 “cere-

bral 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)”.

- 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.

Johann Jakob 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

The (non-traumatic, spontaneous) “hemorrhagic apoplexy” [intracranial hemorrhage], [subarachnoid hemorrhage], and [cerebral hemorrhage] due to vascular cause, and a non-hemorrhagic variety, emerged.

William Cole (1635-1716) (English). The first to use the term “stroke” to denote “apoplexy” in English medical writing (1689).²⁴

Franciscus (Francesco) Biumi (xxxx-xxxx) (Italian). Described a case of “apoplexy”, without intracranial bleeding, identifying: “...internal carotid aneurysmal sack [saccular aneurysm] in the cavernous sinus (Vieussens receptacle)...” [aneurysm - unruptured] (1765).²⁵

Giovanni Battista Morgagni (1682-1771) (Italian). Distinguished a “sanguineous” (with bleeding) [hemorrhagic], a “serous” (with intracranial fluid) [non-hemorrhagic], and a “neither sanguineous nor serous” type apoplexy (1761).²⁶

John Blackall (1771-1860) (English). Described: “...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

Jean André Rochoux (1787-1852) (French). Defined “hemorrhagic apoplexy” [cerebral hemorrhage], and introduced the term *ramollissement du cerveau* [softening of the brain] [infarction] (1814).²⁸

Léon Louis 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

Amédée 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

Charles Louis Maxime 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

Rudolf Ludwig Karl Virchow (1821-1902) (German). Introduced the terms *apoplexia sanguinea* (*Hämorrhagische Apoplexie des Gehirns*) (hemorrhagic apoplexy of the brain) [cerebral hemorrhage], and *apoplexia ischaemica* (ischaemic apoplexy) (*Hirnerweichung*) [cerebral softening] [cerebral infarct], caused by embolism; created the terms “thrombosis” and “embolism”; revived the term “arteriosclerosis” (according to Lobstein, 1829) (1852).³²

Jean-Baptiste Vincent 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

Julius Friedrich Cohnheim (1839-1884) (German). Introduced the terms *Infarct* [infarct, infarction], *Nekrose* [necrosis] and *hämorrhagischer Infarct* [hemorrhagic infarct], after embolic obstruction of terminal arteries (1872).³⁴

Otto Ludwig Binswanger (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}

Alois (Aloysius) 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 “hemorrhagic apoplexy” [cerebral hemorrhage] and introduced the term *ramollissement du cerveau* [softening of the brain] [infarction].²⁸
- Rostan (1819) defined “sanguine (hemorrhagic) apoplexy” [cerebral hemorrhage] and extended the notion of non-inflammatory *ramollissement cérébral* [cerebral softening] [cerebral infarction].²⁹

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].³⁰
- 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].³¹
- 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”.³²
- Laborde (1866) described *lacunes pisiformes* [“lacunes”], post-hemorrhagic and post-softening.³³
- Cohnheim (1872) introduced the terms “infarct”, “necrosis” and “hemorrhagic infarct”, following embolic obstruction of terminal arteries.³⁴
- Binswanger (1894) described “Chronic progressive subcortical encephalitis” (later named after him, and subsequently known as “Binswanger disease”).³⁵

- Alzheimer (1898) described “cortical microinfarcts”.³⁷

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).³⁹

The term “stroke” (cerebrovascular) appeared first in the ICD-9 (1968).³⁹ The definition of the concept by the World Health Organization (WHO) appeared soon after (1971 and 1980),^{4,39} and more recently, a new definition was proposed by the American Heart Association-American Stroke Association (AHA-ASA) (2013)¹⁵ (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.³⁹

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.³⁹

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.”⁴⁰
- “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.”⁴

AHA-ASA (American Heart Association-American Stroke Association) (2013)¹⁵

- 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

- 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.
- Smith EE, Saposnik G, Biessels GJ, Doubal FN, Fornage M, Gorelick PB, et al. Prevention of Stroke in Patients With Silent Cerebrovascular Disease. *Stroke*. 2017;48:e44-e71.
- Grinberg LT. Vascular dementia. Current concepts and nomenclature harmonization. *Dement Neuropsychol*. 2012;6(3):122-6.
- Aho K, Harmsen P, Hatano S, Marquardsen J, Smirnov VE, Strasser T. Cerebrovascular disease in the community: results of a WHO collaborative study. *Bull World Health Organ*. 1980;58:113-30.
- Clarke E. Apoplexy in the Hippocratic writings. *Bull Hist Med* 1963;37:301-14.
- Cooke J. A Treatise on Nervous Diseases. Vol I. On Apoplexy. London: Longman, 1820. [Retrieved from: <http://books.google.com>].
- Pound P, Bury M, Ebrahim S. From apoplexy to stroke. Age and Ageing. 1997;26:331-7.
- Schutta HS, Howe HM. Seventeenth century concepts of “apoplexy” as reflected in Bonet’s “Sepulchretum”. *J Hist Neurosci*. 2006;15:250-68.
- Lidell 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>]
- Karenberg A, Moog FP. Die Apoplexie im medizinischen Schrifttum der Antike. *Fortschr Neurol Psychiat* 1997;65:489-503.
- Hippocrates. Opera omnia. De morbis liber II. Anuce Foes ed. Francfort sur le Main: Wechel héritiers d’André, 1595:534-62. [Retrieved from: <http://www.biusante.parisdescartes.fr/histoire/medica/resultats/?cote=00002&do=pdf>]
- Galen. Oeuvres anatomiques, physiologiques et médicales de Galien. Vol 2. Darenberg C (trans). Paris: Ballière, 1856. Karenberg A. Blood, Phlegm and Spirits: Galen on Stroke. *Hist Med* 2015;2(2):160-8. [Retrieved from: https://archive.org/stream/b28035070_0002#page/n5/mode/2up]
- Karenberg A. Blood, Phlegm and Spirits: Galen on Stroke. *Hist Med* 2015;2(2):160-8.
- Hippocrates. The Aphorisms of Hippocrates. New York: Collins & Co, 1818. [Retrieved from: <https://archive.org/stream/2556068R.nlm.nih.gov/2556068R#page/n57/mode/2up/search/apoplexy>]
- 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/American Stroke Association. *Stroke* 2013;44:2064-89.
- 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 Neurosci*. 1998;7(3):162-73.
- 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 Neurosci*. 1998;7(3):174-85.
- 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 Neurosci*. 1998;7(3):186-200.
- Toledo-Pereyra LH. Medical Renaissance. *J Invest Surg*. 2015;28:127-30.
- Burton JL. A Bite into the History of the Autopsy. *Forensic Sci Med Pathol*. 2005;1(4):277-84.
- Schiller F. Concepts of stroke before and after Virchow. *Med Hist*. 1970;14(2):115-131.
- 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.
- Wepfer JJ. Observationes anatomicae ex cadaveribus eorum quos sustulit apoplexia. Cum exercitatione de eius loco affecto. Schaffhausen: O a Waldkirch, 1675:1-19. [Retrieved from: <http://books.google.com>]
- 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/eebo/A33733.0001.001?rgn=main;view=fulltext>]
- Blackall J. Observations Anatomicae, Scholiis illustratae. Observatio V. In: Sandifort E (ed): *Thesaurus Dissertationum*, Vol 3. Leyden: S et J Luchtmans; 1778:373-9. [Retrieved from: <http://books.google.com>]
- 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://ia600704.us.archive.org/3/items/seatscausesofdis01morg/seatscausesofdis01morg.pdf>]
- Blackall J. Observation on the Nature and Cure of Dropsies. 2nd American ed (4th English). Philadelphia: James Webster, 1825:83-5. [Retrieved from: <http://books.google.com>]
- Rochoux JA. Recherches sur l’apoplexie. Paris: Méquignow-Marvis, 1814. [Retrieved from: <http://books.google.com>]
- Rostan L. Recherches sur le Ramollissement du Cerveau. 2ème ed. Paris: Béchét, 1823. [Retrieved from: <http://gallica.bnf.fr/ark:/12148/bpt6k774099/f9.image>]
- 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=cGFyZGhHw5MDE4MngxODM4eDA2fDMwNnwzMTc>]
- Durand-Fardel M. Traité du ramollissement du cerveau. Paris: Baillière, 1843. [Retrieved from: <http://books.google.com>]
- Virchow R. Gesammelte Abhandlungen zur Wissenschaftlichen Medicin. Frankfurt: Meidinger Sohn & Comp.; 1856. [Retrieved from: <https://archive.org/stream/b21462161#page/710/mode/2up>]
- Laborde J-V. Le ramollissement et la congestion du cerveau: principalement considérés chez le vieillard: étude clinique et pathogénique. Paris: Adrien Delahaye, 1866. [Retrieved from: <http://books.google.com>]
- Cohnheim J. Untersuchungen über die embolischen Prozesse. Berlin: August Hirschwald, 1872. [Retrieved from: <http://books.google.com>]
- 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>]
- Engelhardt E. Binswanger: mais que um epônimo [Binswanger: more than an eponym]. *Rev Bras Neurol*. 2015;51(1):24-27.
- Alzheimer A. Beitrag zur pathologischen Anatomie der Seelenstörungen des Greisenalters. *Neurologisches Centralblatt*. 1899;18:95-96.
- Engelhardt E, Grinberg LT. Alzheimer and vascular brain disease: Focal and diffuse subforms. *Dement Neuropsychol*. 2015;9(3):306-10.
- ICD. 2007 [Retrieved from: <http://www.wolfebane.com/icd/index.html>].
- WHO Technical Report Series, No. 469, 1971 (Cerebrovascular diseases: prevention, treatment, and rehabilitation. Report of a WHO Meeting).