www.surgicalneurologyint.com

ScientificScholar® Knowledge is power
Publisher of Scientific Journals

Surgical Neurology International

Editor-in-Chief: Nancy E. Epstein, MD, Clinical Professor of Neurological Surgery, School of Medicine, State U. of NY at Stony Brook.

SNI: History of Medicine

Editor
Miguel Faria
Clinical Professor of Surgery (Neurosurgery, ret.), Mercer University School of Medicine, US.

SNI® Open Access

Review Article

The historic evolution of intracranial pressure and cerebrospinal fluid pulse pressure concepts: Two centuries of challenges

Nicollas Nunes Rabelo[1], Josué da Silva Brito[2], Jassiara Soares da Silva[2], Nicolli Bellotti de Souza[2], Giselle Coelho[3], Sérgio Brasil[1], Gustavo Frigeri[4]

[1]Department of Neurology, University of São Paulo, São Paulo-SP, [2]Department of Neurology and Neurosurgery, University Center Atenas, Paracatu-MG, [3]Department of Neurosurgery, Santa Marcelina Hospital, São Paulo-SP, [4]Department of Phisycs, Braincare Technological Development and Innovation, São Carlos-SP, Brazil.

E-mail: *Nicollas Nunes Rabelo - nicollas@gmail.com; Josué da Silva Brito - josuedasilvabrito1998@gmail.com; Jassiara Soares da Silva - soaresjassiara@gmail.com; Nicolli Bellotti de Souza - nicolli.atenas@hotmail.com; Giselle Coelho - gigicoelho7@hotmail.com; Sérgio Brasil - sergiobrasil@usp.edu; Gustavo Frigeri - gustavo.frigieri@brain4.care

***Corresponding author:**
Nícollas Nunes Rabelo,
Department of Neurology,
Scholl of Medicine, Passos-MG,
Brazil.

nicollasrabelo@hotmail.com

Received : 20 January 2021
Accepted : 13 May 2021
Published : 14 June 2021

DOI
10.25259/SNI_53_2021

Quick Response Code:

ABSTRACT

Background: There is a consensus on the importance of monitoring intracranial pressure (ICP) during neurosurgery, and this monitoring reduces mortality during procedures. Current knowledge of ICP and cerebrospinal fluid pulse pressure has been built thanks to more than two centuries of research on brain dynamics.

Methods: Articles and books were selected using the descriptors "ICP," "cerebrospinal fluid pulse," "monitoring," "Monro-Kellie doctrine," and "ICP waveform" in electronic databases PubMed, Lilacs, Science Direct, and EMBASE.

Results: Several anatomists and physiologists have helped clarify the patterns of intracranial volumes under normal and pathological conditions. Monro-Kellie doctrine was an important step in a story that is reconstructed in this article. Through documentary research, we report the contribution of important medical figures, such as Monro, Kellie, Abercrombie, Burrows, Cushing, Langfitt, Marmarou, and other physiologists and anatomists who left their marks on the history of Medicine.

Conclusion: Understanding intracranial dynamics is an unfinished historical construction. Current knowledge is the result of two centuries of research that began with the investigations of Alexander Monro *secundus*.

Keywords: Cerebrospinal fluid pulse pressure, History of medicine, Intracranial pressure

INTRODUCTION

In neurosurgery, there is a consensus on the importance of monitoring intracranial pressure (ICP), which reduces mortality.[28,31] Both invasive and non-invasive monitoring techniques depended on the evolution of anatomical and physiological concepts.[32]

For more than 200 years, anatomists and physiologists have investigated brain dynamics in an attempt to understand how intracranial volumes affect ICP and also the different behavior of the cerebrospinal fluid (CSF) pulse at different pressure stages.[20,25,28]

The present paper reports several findings that contributed to the current knowledge of intracranial dynamics and to the use of CSF pulse pressure (CSFPP) in the interpretation of intracranial dynamics.

MONRO-KELLIE DOCTRINE

The Monro-Kellie doctrine was built on different researchers [Figure 1] and results from investigations of human and animal brain circulation carried out in different centuries. Doctrine is a fundamental starting point for understanding ICP, its regulation, and the influence of disease states.[20,25]

Alexander Monro *secundus* (1733–1817) is responsible for the first great contribution for the doctrine. Monro was born in Edinburgh and obtained his medical degree at the University of Edinburgh, where his father, Alexander Monro *primus*, was a professor of Anatomy and Surgery. At the same university, he became an adjunct professor even before finishing the course, and, from 1758 on, a full professor in his father's place.[36] He investigated the structure of the nervous system and carried out studies on comparative anatomy, thus publishing books and articles on various topics, including the famous *Observations on the Structure and Functions of the Nervous System: with Illustrated Tables*. In his book, published in 1783, the author defined fundamental aspects on intracranial dynamics of volumes inside the skull. According to his observations, the brain tissue volume was static, the blood volume inside the skull hardly varied, regardless of the individual health conditions or even whether alive or dead. Furthermore, in the book, he set the need to expel blood in an amount equal to any foreign liquid inserted in the skull.[26]

The physiologist and anatomist George Kellie (1770–1829), a former student of Monro *secundus* in the University of Edinburg, deepened investigations on brain circulation.[21] In 1824, he launched a study based on the dissection of two individuals found dead after a storm in the city of Leith.

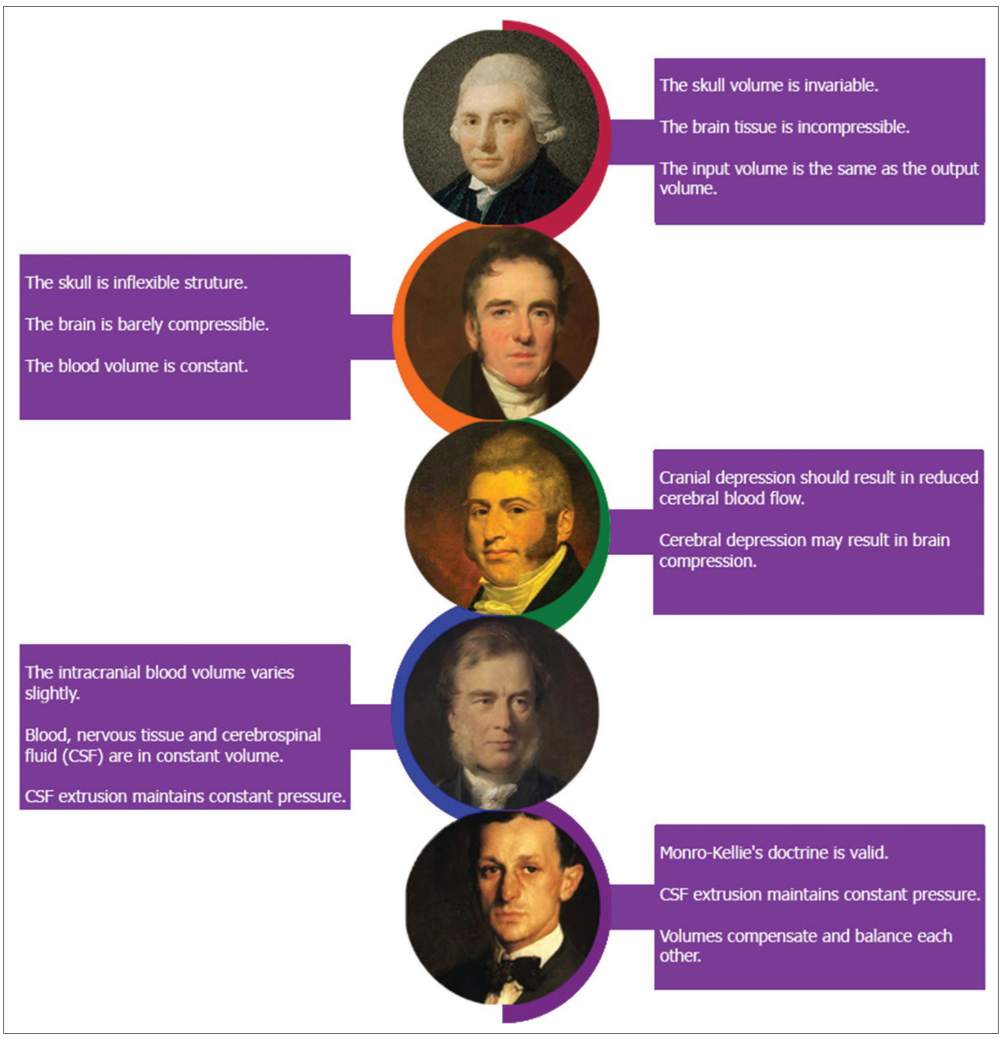

Figure 1: Evolution of Monro-Kellie doctrine. At the top of the figure Monro *secundus*, followed by, respectively, Kellie, Abercrombie, Burrows and Cushing. The authors' contribution to the Monro-Kellie doctrine is highlighted.

Based on this study, he stated that the skull was a firm and inflexible structure in adults, capable of isolating its interior from external mechanical pressures, with the brain occupying almost its interior totality, whereas the integrity of this system was in strict relation with intracranial volume, that is, the addition of any kind of volume would lead to the reduction of another equivalent.[16] He also stated that intracranial dynamics occurred independently of atmospheric pressure. In his various studies with animals and humans who died under different circumstances, he observed that the blood volume was almost always the same, reaffirming the concept on total volume of blood circulating inside the skull is constant.[20,25]

John Abercrombie (1780–1844), a pathologist also graduated at the University of Edinburgh, an eminent surgeon and physician of the King of Scotland, was actually responsible for spreading the doctrine among the medical community. Although his first publication occurred in 1811 — prior to Kellie's —, his most famous manuscript[21] was only published in 1828, therefore after Kellie's contributions. The book *Pathological and Practical Researches on Disease of the Brain and Spinal Cord* attributed the doctrine to Monro and Kellie. The Edinburgh's pathologist reinforced, like Kellie, that cranial depression should result in reduced cerebral blood flow,[1] adding that compression of intracranial nervous tissue could also occur.[21]

However, Monro, Kellie, and Abercrombie were unable to complete the theory due to limitations of knowledge on the anatomy and physiology of the nervous system in that time. They ignored the role and even the presence of the CSF in the regulation of ICP.

Although most of what has been described about CSF and ICP is owed to Western researchers, the first reference to the CSF is found in an Egyptian manuscript dated from 1500 BC, which probably dates back to another document from 3000 to 2500 BC of uncertain authorship, perhaps from Imhotep.[4,5,14] It reports a case of traumatic brain injury, describing the meninges and the fluid around the brain.[5]

In the Western world, both Hippocrates (460–375 BC) and Galen (AD 130–200) recognized the presence of some liquid around the brain.[11,13,15] Galen, the author of the pneuma theory, postulated on the *Rete mirabile* that the *Pneuma zooticon* (vital spirit) became the *Pneuma psychicon* (animal spirit) and filled the cerebral ventricles. The author already believed the choroid plexuses as producers of the CSF and that it circulated from the lateral ventricles to the third and IV ventricles.[11]

The ancient anatomists either ignored the existence of any liquid filling the cerebral ventricles or admitted that it only existed after death, resulting from the condensation of vapor after death. This erroneous idea was conceived from autopsies in which incisions in the cervical region resulted in fluid drainage. As it was not found, its existence was denied.[19]

The absence of dissections during the Middle Age restricted anatomical studies as a whole, with no major advances in the field. CSF and brain structures were again investigated only during Renaissance, after reintroduction of dissections.[2,9,14]

During the Renaissance, different authors reinforced the existence of the CSF, such as Leonardo da Vinci (1452–1519), Andreas Vesalius (1514–1564), and Constantius Varolius (1543–1575), and started the basis for understanding the CSF circulation. Gerard Blasius (1627–1682), in 1666, named the arachnoid membrane and several authors expanded their knowledge about it well as subarachnoid space, such as Raymond Vieussens (1635–1715), Frederik Ruysch (1638–1731), and Antonio Pacchioni (1665–1726), who described the arachnoid granulations.[10] Furthermore, Emanuel Swedenborg (1688–1772), a mining engineer almost unknown in his days, described the presence of CSF around the spinal cord and brain stem.[33]

The understanding of the liquid and its flow has advanced with the discovery of CSF in different spaces and with greater understanding on the anatomy of the nervous system. Domenico Cotugno (1736–1822), in 1764, described CSF around the spinal cord, in the ventricular spaces, below the spinal cord, and also in the labyrinth of fishes and turtles. Alexander Monro *secundus* described the intraventricular foramen and François Magendie (1783–1855) discovered the communication between the lateral ventricles and the third ventricle. It also led to the idea that the medulla and the brain were suspended in the liquid, along with the erroneous conclusion that it was produced by the pia mater. Hubert von Luschka consolidated the idea that the choroid plexus was in fact responsible for the production of CSF, defended by Willis.[9,33]

In 1842, Magendie's publication defined CSF as a physiological fluid inside the skull. Despite creating the notion of a third volume, it did not lead immediately to the reformulation Monro-Kellie doctrine. Only in 1846, the English physician George Burrows clarified some mistakes made in the initial formulations.[20] Burrows contested several points listed by his predecessors such as the view of the skull as a perfect sphere and the notion of the invariability of blood volume, since he found a difference in several positions when trying to reproduce part of the studies carried out by Kellie and Abercrombie. He also attributed to the CSF a prominent role in the regulation of ICP. The physiologist admitted that inside the skull there were three volumes: brain, blood, and CSF in harmonic volumes, whereas the increase in intracranial volume over the ability to expel some amount of its components would result in pathological states. He pointed to the importance of the CSF in ensuring equivalent pressure distribution, and was the first to consider pressure when analyzing skull interior.[6] The author was not able to define well, however, what happens in the face of the volume withdrawal: if the CSF would be responsible for filling the space or if the cerebral content would adapt.[34]

Many other researchers after Burrows helped clarify the missing points. Henry Duret (1849–1921) showed that increased pressure could cause blood vessel compression, reducing cerebral blood flow, and also demonstrated that CSF absorption, vertebral ligament extensibility and venous sinus collapse would alleviate the increase in pressure in the early stages of intracranial hypertension. Ernst von Bergmann (1836–1907) demonstrated CSF drainage into the elastic spinal canal as a mean of controlling this pressure. Theodor Kocher (1841–1917), in turn, established that in ICP first stage of the elevation there would be compensation through drainage of the CSF, compression of veins and capillaries and displacement of brain tissue through the foramen magnum, adding to Bergmann and Duret contributions.[20]

In the 20th century, it was Harvey Cushing (1869–1939), the father of modern neurosurgery, who demonstrated the clinical and physiological importance of the doctrine. Indeed, he consolidates Burrows' discoveries regarding CSF importance in intracranial dynamics and the presence of three volumes that act compensating the depletion or insertion of volume inside the skull.[8]

Neurosurgeon Lewis H. Weed (1886–1952)[34] also wrote an important chapter in this doctrine, in his article *Some Limitations of the Monro-Kellie Hypothesis*, published in 1929. He postulated the possibility of brain volume variation during life, the need for a cranial vault aiding the maintenance of intracranial dynamics, and that the theory should not be employed in the case of children with open fontanelles since the skull is not yet rigid.

Since Cushing, little progress in the theory was made. Therefore, the assumptions of constant intracranial volume and inelastic skull are accepted worldwide.[35] Nevertheless, Mascarenhas *et al*. threatened the theory in the study *The New ICP Minimally Invasive Method Shows That the Monro – Kellie Doctrine Is Not Valid* published in 2012.[24] This work challenged a fundamental aspect of the theory: it questioned the inextensibility of the skull and created a method capable of measuring PCI from cranial extensibility. These authors demonstrated that even after closure of fontanelles there are small volumetric changes in the skull due to volume changes, in linear relation with ICP increase, the wave form analysis and P2/P1 ratio. However, they did not consider that such fact may suggest that the millimeter expansion of the skull is also a compensatory element of the pressure rise.

CSF PULSE PRESSURE OR ICP WAVEFORM

Monro-Kellie's theory was a starting point for understanding pathological phenomena and possible variations on ICP. One of the elements investigated, even during the consolidation of the theory, was the intracranial pulse. Furthermore, Burrows,[6] in his 1846 book, pointed to pulsations in the meninges following arterial systole and respiratory movements. However, the author did not give any clinical interpretation to this phenomenon.

Angelo Mosso (1846–1910), an Italian physiologist born in Chieri, Piemonte, was a prominent researcher on brain activity, having laid the foundation for the current understanding of functional neuroimaging.[27] In his book *Sulla Circolazione del Sangue nel Cervello Del'Uomo: Ricerche Sfigmografiche*, published in 1880, he described the variability of cerebral blood pulse, in a way that produced waves with a variable shape. However, according to the author, the normal shape would probably be tricuspid, that is, three peaks of ICP during a normal blood flow cycle. He also observed changes in blood flow during breathing, walking, and cognitive processes.[27]

In 1955, Edgar Bering Jr. (1917–1994)[3] recorded the CSFPP in cisterna magna, cerebral ventricle and in the lumbar subarachnoid space during an electrocardiogram, demonstrating a relationship between the wave generated in the CSF space and the cardiac cycle, with the choroid plexus responsible for the transmission of the arterial pulse for CSF.

Furthermore, obstinately studying cerebral blood flow, Thomas Langfitt (1927–2005) and collaborators carried out different investigations in monkeys during the 1960s, in which they gradually increased intracranial volume by means of an extradural supratentorial balloon. The authors found that the pressure did not increase linearly. At first, the CSF was drained, preventing significant pressure variation, however, after overcoming the compensation mechanisms, the increase would occur exponentially. Therefore, even small volume variations would produce a large increase in volume. In the experiments, 1 mL, at the end of the curve, was able to raise the ICP by 70 mmHg, although at the beginning of the curve there was almost no pressure change.[17,18]

For some years, the pressure x volume curve and the understanding of the intracranial pulse seemed disconnected. Marmarou's investigations contributed to a better understanding of the relationship between these two phenomena. In his study on intracranial compliance, he demonstrated changes in the amplitude of this pulse at different points on the volume and pressure curve.[22,23]

Portnoy and Chopp,[30] after more than half a century from Mosso's observations, gave an interpretation to the wave. According to the authors, it would have a shape similar to an arterial pulse wave, with an abrupt rise followed by an equally rapid decrease. In conditions of pressure deregulation, the wave would exhibit a more rounded shape.

Gega *et al*.[12] and Cardoso *et al*.,[7] both in the 1980s, were responsible for bringing back the three-phase wave. Gega *et al*. observed that the existence of three components of the CFSPP wave was common, although he did not make any clinical interpretation about the findings: P1 (percussion wave), a wave with a sharp peak and relatively constant amplitude, P2 (tidal wave), a wave of variable shape and amplitude, and P3 (dicrotic wave), a wave after the dicrotic notch that marks the end of P3.[12] Cardoso *et al.*[7] further investigated the wave shape and established the pattern of variation in relation to the increase in ICP. These authors observed a progressive increase in P2 and a slighter increase in P3 in relation to the pressure increase so that, as Portnoy and Chopp had already observed,[30] the wave would exhibit a rounded shape.

In 2016, Nucci *et al.*[29] were responsible for another leap in understanding the behavior of the CSF pulse wave after classifying four types of wave. In the Class I wave, P1 is superior to the other two peaks. In the Class II wave, also said to be potentially pathological, P2 rises slightly, becoming equal or slightly higher than P1 or P3 equal or slightly lower than P1. In Class III, the wave is probably already pathological, and P2 and P3 exceed P1. In the pathological or Class IV wave, the peaks are no longer identifiable, or P2 and P3 become markedly higher than P1. In this study, the possibility of recognizing pathological conditions was identified by an artificial neural network.

CONCLUSION

Understanding intracranial dynamics is an unfinished historical construction. Current knowledge is the result of two centuries of research that began with the investigations of Alexander Monro *secundus*. From the Monro-Kellie doctrine, it was possible to understand the behavior of intracranial volumes and to investigate new pressure parameters such as CSFPP.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

Financial support and sponsorship

Publication of this article was made possible by the James I. and Carolyn R. Ausman Educational Foundation.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Abercrombie J. Pathological and Practical Researches on Disease of the Brain and Spinal Cord. Edinburgh: Waugh and Innes; 1828.
2. Arribas MA. The history of cerebrospinal fluid: From classical antiquity to the late modern period. Neurosci Hist 2017;5:105-13.
3. Bering EA Jr. Choroid plexus and arterial pulsation of cerebrospinal fluid; demonstration of the choroid plexuses as a cerebrospinal fluid pump. AMA Arch Neurol Psychiatry 1955;73:165-72.
4. Blomstedt P. Imhotep and the discovery of cerebrospinal fluid. Anat Res Int 2014;2014:256105.
5. Breasted JH. The Edwin Smith Surgical Papyrus: Published in Facsimile and Hieroglyphic Transliteration with Translation and Commentary in Two Volumes. Vol. 3. Chicago: University of Chicago; 1930.
6. Burrows G. On Disorders of the Cerebral Circulation and on the Connection between Affections of the Brain and Diseases of the Heart. Philadelphia, PA: Lea and Blanchard; 1848.
7. Cardoso ER, Rowan JO, Galbraith S. Analysis of cerebrospinal fluid pulse wave in intracranial pressure. J Neurosurg 1983;59:817-21.
8. Cushing H. The Third Circulation in Studies in Intracranial Physiology and Surgery. London: Oxford University Press; 1926. p. 1-51.
9. Deisenhammer F. The history of cerebrospinal fluid. In: Deisenhammer F, Sellebjerg F, Teunissen C, Tumani H, editors. Cerebrospinal Fluid in Clinical Neurology. Cham: Springer; 2015.
10. di Ieva A, Yaşargil MG. Liquor cotunnii: The history of cerebrospinal fluid in Domenico Cotugno's work. Neurosurgery 2008;63:352-8.
11. Galen. In: CG Kühn, editor. Opera Omnia. Lipsiae: C. Cnoblock; 1821-1833.
12. Gega A, Utsumi S, Iida Y, Tsuncda S. Analysis of the wave pattern of CSF pulse wave. In: Shulman K, Marmarou A, Miller JD, Becker DP, Hochwald GM, Brock M, editors. Intracranial Pressure IV. Berlin, Heidelberg, New York: Springer-Verlag; 1980. p. 188-90.
13. Hajdu SI. A note from history: Discovery of the cerebrospinal fluid. Ann Clin Lab Sci 2003;33:334-6.
14. Herbowski L. The maze of the cerebrospinal fluid discovery. Anat Res Int 2013;2013:596027.
15. Hippocrates. In: Jones WH, editor. Collected Works. London: W. Heinemann; 1923.
16. Kellie G. An account of the appearances observed in the dissection of two of three individuals presumed to have perished in the storm of the 3D, and whose bodies were discovered in the vicinity of Leith on the morning of the 4th, November 1821 with some reflections on the pathology of the brain. Trans Med Chir Soc Edinb 1824;1:84-169.
17. Langfitt TW, Kassell NF, Weinstein JD. Cerebral blood flow with intracranial hypertension. Neurology 1965;15:761-73.
18. Langfitt TW. Increased intracranial pressure. Neurosurgery 1969;16 Suppl 1:436-71.
19. Longatti P. Domenico Felice Cotugno and the rationale of his discovery of CSF. Childs Nerv Syst 2008;24:161-2.
20. Lundberg N. The saga of the Monro-Kellie doctrine in intracranial pressure V. In: Ishii S, Nagai H, Brock M, editors. Proceedings of the Fifth International Symposium on Intracranial Pressure, Tokyo, Japan, May 30-June 3, 1982. Berlin: Springer-Verlag; 1983. p. 68-76.
21. Macintyre I. A hotbed of medical innovation: George Kellie (1770-1829), his colleagues at Leith and the Monro-Kellie doctrine. J Med Biogr 2014;22:93-100.

22. Marmarou A, Shulman K, LaMorgese J. Compartmental analysis of compliance and outflow resistance of the cerebrospinal fluid system. J Nenrosurg 1975;43:523-34.
23. Marmarou A. A Theoretical and Experimental Evaluation of the Cerebrospinal Fluid System, PhD Thesis. Pennsylvania: Drexel University; 1973.
24. Mascarenhas S, Vilela GH, Carlotti C, Damiano LE, Seluque W, Colli B, *et al*. The new ICP minimally invasive method shows that the Monro-Kellie doctrine is not valid. Acta Neurochir Suppl 2012;114:117-20.
25. Mokri B. The Monro-Kellie hypothesis: Applications in CSF volume depletion. Neurology 2001;56:1746-8.
26. Monro A. Observations on the Structure and Function of the Nervous System. Ediburgh: Creech and Johnson; 1783.
27. Mosso A. Sulla Circolazione del Sangue nel Cervello Deel'Uomo: Ricerche Sfigmografiche. Roma: Coi Tipi del Salviucci; 1880.
28. Nag DS, Sahu S, Swain A, Kant S. Intracranial pressure monitoring: Gold standard and recent innovations. World J Clin Cases 2019;7:1535-53.
29. Nucci CG, de Bonis P, Mangiola A, Santini P, Sciandrone M, Risi A, *et al*. Intracranial pressure wave morphological classification: Automated analysis and clinical validation. Acta Neurochir (Wien) 2016;158:581-8.
30. Portnoy HD, Chopp M. Spectral analysis of intracranial pressure. In: Shulman K, Marmarou A, Miller JD, Becker DP, Hochwald GM, Kasner M, editors. Intracranial Pressure IV. New York: Springer-Verlag; 1980. p. 167-72.
31. Shen L, Wang Z, Su Z, Qiu S, Xu J, Zhou Y, *et al*. Effects of intracranial pressure monitoring on mortality in patients with severe traumatic brain injury: A meta-analysis. PLoS One 2016;11:e0168901.
32. Sonig A, Jumah F, Raju B, Patel NV, Gupta G, Nanda A. The historical evolution of intracranial pressure monitoring. World Neurosurg 2020;138:491-7.
33. Swedenborg E. The Brain, Considered Anatomically, Physiologically and Philosophically. London: Andesite Press; 1887.
34. Weed LH. Some limitations of the Monro-Kellie hypothesis. Arch Surg 1929;18:1049-68.
35. Wilson MH. Monro-Kellie 2.0: The dynamic vascular and venous pathophysiological components of intracranial pressure. J Cereb Blood Flow Metab 2016;36:1338-50.
36. Wu OC, Manjila S, Malakooti N, Cohen AR. The remarkable medical lineage of the Monro family: Contributions of Alexander primus, secundus, and tertius. J Neurosurg 2012;116:1337-46.
37. Zago S, Ferrucci R, Marceglia S, Priori A. The Mosso method for recording brain pulsation: The forerunner of functional neuroimaging. Neuroimage 2009;48:652-6.

How to cite this article: Rabelo NN, da Silva Brito J, da Silva JS, de Souza NB, Coelho G, Brasil S, *et al*. The historic evolution of intracranial pressure and cerebrospinal fluid pulse pressure concepts: Two centuries of challenges. Surg Neurol Int 2021;12:274.