

The history of cerebrospinal fluid analysis in Brazil

História do estudo do líquido cefalorraquidiano no Brasil

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ABSTRACT

Analysis on cerebrospinal fluid (CSF) in neurological diagnosis has always been considered to be a strong point among the main complementary examinations in Brazil. The present paper reviews the main events in the history of CSF in the neurological sciences, with emphasis on the founders of several CSF schools in our country from the beginning of the 20th century to the present time.

Keywords: cerebrospinal fluid, history, CSF laboratories in Brazil.

RESUMO

No Brasil o estudo do líquido cefalorraquidiano (LCR) como arsenal diagnóstico para a neurologia sempre foi considerado um ponto forte entre os principais exames complementares. Neste artigo são revisados os fatos principais da história do LCR dentro das ciências neurológicas, com ênfase aos fundadores das diversas escolas de LCR do nosso país desde as primeiras décadas do século XX até o momento atual.

Palavras-Chave: líquido cefalorraquidiano, história, laboratórios de LCR no Brasil.

The first evidence of fluid inside the brain cavities is found in Edwin Smith's surgical papyrus, probably written in the 17th century BC. In the 6th century BC, Hippocrates carried out the first postmortem ventricle access by needle in a case of hydrocephalus. In the second century AD, Galenus reported that the ventricle cavities were filled with a "vital gaseous spirit".

It was only in 1543 that Vesalius published the first information that the brain ventricles are filled with an aqueous fluid. In 1764, Cotugno presented the first description of brain ventricles and the subarachnoid space, after studying them in 20 cadavers subjected to lumbar puncture and anatomical dissections.

In 1825, after the initial studies on access to the cisterna magna in animals, Magendie gave the name cerebrospinal fluid (CSF) to the liquid found in the ventricle cavities and subarachnoid space.

In 1891, in Germany, Quincke started a new era in studies on CSF, carrying out the first *in vivo* lumbar puncture with measurements of intracranial pressure. He used a needle and a scalpel, which were similar to the needles currently used for puncture. This was the time when CSF puncture turned daily practice for diagnostic purposes. Quincke's studies on

CSF included cytomorphological analysis, protein assay, spinal glucose levels and bacteriological examination. Within a short period of time, CSF examinations became common in other European countries.

At the beginning of the 20th century, several studies were published regarding CSF. In 1912, Mestrezat published the first book about the CSF examination for many neurological diseases, and this became an essential reference point worldwide.

Suboccipital puncture was carried out *in vivo* for the first time by Obregia in 1908, but its use in neurological practice following precise recommendations only began after Ayer's studies in 1920¹⁻⁴.

The beginning of CSF studies in Brazil

Miguel Couto, in Rio de Janeiro in 1897, carried out the first lumbar puncture in a patient at Hospital de Misericórdia, in that city. Correa, in the same year, defended his thesis on "The diagnostic and therapeutic value of lumbar puncture" also in Rio de Janeiro.

In 1923, in Bahia, Pondé presented his thesis on "Semiological value of cerebrospinal fluid" based on data from over 100 examinations collected and analyzed in his service⁵.

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In 1926, suboccipital puncture was carried out for the first time in São Paulo, by Vamprè and Camargo, and in Rio de Janeiro by Esposel. In the same year, Waldomiro Pires, also in Rio de Janeiro, became the greatest exponent of cisternal puncture in our country, together with Cerqueira da Luz. In 1928, they reported that they had performed more than 5000 punctures using the cisternal approach. Waldomiro Pires was probably the person who contributed the most in the whole world towards definitive inclusion of cisternal puncture in daily practice. At that time, three large CSF study centers were established in Brazil, supervised by Cerqueira da Luz and Waldomiro Pires in Rio de Janeiro, by Alcides Benício in Recife and by Oswaldo Lange in São Paulo^{4,5}.

CSF in Brazil: Oswaldo Lange

Oswaldo Lange graduated in medicine in 1927 at the Medical and Surgical School of São Paulo, later renamed the Medical School of the University of São Paulo (FMUSP). From that time onwards, he joined the group of Enjolras Vamprè's direct collaborators, together with Adherbal Tolosa and Paulino Watt Longo. Oswaldo Lange dedicated himself to studies and clinical research on CSF.

He learned the technique for cisternal puncture in Rio de Janeiro in 1928, with Cerqueira da Luz. In October 1929, he started working in his own CSF specialized laboratory.

Together with Vamprè, he published results from his initial work on CSF.

In 1936, Oswaldo Lange published his first paper on CSF and neurocysticercosis in the *Revista de Neurologia e Psiquiatria de São Paulo*. In 1940, in the same journal, he published his most important work "*Cerebrospinal fluid syndrome in encephalomeningeal cysticercosis*", a paper that is still cited in the worldwide literature⁶⁻⁸.

In 1938, Lange was confirmed as the greatest specialist in CSF in our country when he published the first Brazilian book on the subject: "*Cerebrospinal fluid in clinics*" (São Paulo, Melhoramentos, 1938). In the same year in the United States, Merrit and Fremont-Smith published the book "*The cerebrospinal fluid*", which was similar to what was published by Lange and had great international acclaim.

Lange founded *Arquivos de Neuro-Psiquiatria* in 1943, and was its Editor for 44 years. He passed away after completing issue 4 of volume 44, in 1986. *Arquivos de Neuro-Psiquiatria* was the climax of his work and remained his greatest passion.

In the 1940s, Lange continued to work with CSF in his laboratory, and he was also PhD, and Head of the Clinic at the Department of Neurology in FMUSP, where he taught about CSF and infectious diseases of the nervous system. He was responsible for the creation of a subspecialty on CSF in that medical school.

In 1960, Oswaldo Lange finished his professional activities and handed the supervision of the CSF laboratory to Antonio Spina-França Netto⁶⁻⁸.

CSF in Brazil: Spina-França

Antonio Spina França Netto graduated in medicine from FMUSP in 1951. He was the first resident in neurology at that medical school. Already during his residence, he attended Oswaldo Lange's CSF laboratory and learned the techniques and details of the examination.

There, he met Marília, Lange's daughter, who was then working as the laboratory technician. Within two years, they were married and remained together till the end of their lives. Together with great charisma, they attended all CSF meetings in Brazil and abroad.

From 1960 onwards, Spina-França took over the coordination of the laboratory and made it his favorite working place, where he worked until the end of his life. Spina-França was responsible for the systematization and modernization of CSF in Brazil.

Still in the 1960s, Spina França brought to Brazil the accelerated gravitational sedimentation chamber for cytomorphological examinations (Suta's chamber) and CSF protein electrophoresis, after working for a period with Prof. Armand Löwenthal in Antwerp, Belgium. From that time onwards, they became very good friends.

Spina França's two theses, for his doctorate in 1963 and full professorship in 1968, were about CSF in neurocysticercosis. This subject became his main line of research.

In the neurological clinic of FMUSP, he was named Head of the Clinic in 1968 and Head of the Postgraduate Program in 1970. In 1982 he became Full Professor of Neurology and in 1991, Emeritus Professor.

In 1973, he founded the Center for Neurological Investigations in FMUSP, with a research laboratory mainly concentrating on CSF studies.

From 1980 onwards, this Center became part of the Medical Investigations Laboratories (LIMs) of FMUSP, known as LIM-15.

With the establishment of the Brazilian Academy of Neurology (ABN), he was accepted as a titular member in 1963 and was elected President for the period 1970-1972. As President, he organized the 1st Brazilian Congress of the ABN in São Paulo and the 1st Pan-American Congress in Brazil.

He was the founder of the Working Group on CSF at ABN in 1976, and he was also its first president. This group is now named the Scientific Department of CSF at ABN and remains active throughout Brazil.

He was the ABN Delegate to the World Federation of Neurology for eight years (1978-1986), and participated in all its congresses and meetings.

In 1998 he received the highest homage from ABN, the Golden Owl prize.

Spina-França was a great enthusiast for creation and reinforcement of several CSF units in Brazil and in other South American countries. He received many doctors to learn in his laboratory and created a large number of disciples who spread their knowledge on this field in their original localities in the country.

He worked every day of his life in the laboratory that carries his name until the May 17, 2010, when he passed away.

José Antonio Livramento joined the laboratory in 1970 and Luís dos Ramos Machado in 1976. They were direct and beloved collaborators of Spina França, and they are responsible for the laboratory at present.

In 1988, Lílíana Scaff Vianna joined the Spina França laboratory team and is now a full member of its core group of activity and competence.

The Spina-França CSF laboratory continues to provide CSF analysis services for the whole of Brazil, as it has done throughout its 84 years of existence.

CSF in Brazil: other prominent schools

The largest centers of CSF studies in Brazil, since the beginning, were in the states of São Paulo, Rio de Janeiro and Pernambuco.

In São Paulo, from the start of the 1940s, other centers became created based on Oswaldo Lange's CSF laboratory of 1929.

In 1940, João Batista dos Reis founded the Reis laboratory, which was responsible for CSF in Hospital Juquery, São Paulo, and Escola Paulista de Medicina, now known as the Medical School of the Federal University of São Paulo. From 1950 onwards, Antonio Bei joined that unit and, in 1968, João Batista dos Reis Filho also joined the team. The latter continues to be active as the present supervisor of that laboratory.

Also in the 1940s, José Mario Taques Bittencourt, who had studied with Lange, started to work in Fleury Laboratory as the doctor responsible for CSF. Gilberto Bassi and Marcelo Fortuna Santiago were his disciples. The latter continues to work with CSF, coordinating his own CSF unit up to the present time. The CSF unit in Fleury laboratory is still active, under the supervision of Aurélio Pimenta Dutra.

In 1972, Carlos Augusto Senne Soares, who had graduated from the Medical School of Santa Casa de Misericórdia de São Paulo in 1968, created his own CSF laboratory, known as Senne Liqueur, which is now one of the largest laboratories in Brazil.

In 1981, Sergio Rivas Cunha also founded his own service, which is still active and is one of the highly qualified services for CSF in São Paulo.

Hélio Rodrigues Gomes started to work with CSF in 1988 at Spina França Laboratory, where he stayed for 15 years. He

then transferred to the CSF unit in Fleury Laboratory where he worked for another 10 years. He is now responsible for the Central CSF Laboratory of Hospital das Clínicas at FMUSP.

In Ribeirão Preto, in the 70s, Oswaldo Massaiti Takayanagui started to work with CSF and still remains as the head of the Medical School Laboratory at the Ribeirão Preto campus of the University of São Paulo.

From the late 1980s in São José do Rio Preto, Elisabete Liso, one of Spina França's disciples, became responsible for the CSF laboratory of the Medical School of São José do Rio Preto. She presented her doctor degree thesis on neurocryptococcosis. She still remains as the head of that laboratory.

In Rio de Janeiro, following the work of Waldomiro Pires and Cerqueira da Luz, there are now two large CSF units. One is Neurolife, under the supervision of Carlos Otávio Brandão, who holds a doctorate from the State University of Campinas (UNICAMP); and the CSF laboratory of the Federal University of Rio de Janeiro (UFRJ), under the supervision of Marzia Puccioni-Sohler, who specialized in CSF at Göttingen University, Germany.

In Recife, Antonio Alcides Benício, who was an assistant to Ulisses Pernambucano, founded his own CSF unit at the same time that Lange created his laboratory in São Paulo. Benício remained in activity up to the 1970s. After his passing away, the laboratory was supervised by Taciana Antunes, who later associated with Solange Dorneles Mesquita. They both still work in that unit.

Also in Recife, Fernando Mauricio de Mello Travassos created a CSF unit in 1970, now supervised by Patricia Tereza de Melo Travassos.

In Curitiba, from the early 1990s and after completing two theses about CSF in UNIFESP and a postdoctoral thesis at the Neurological Investigation Center in FMUSP, Sérgio Monteiro de Almeida started his activities in a specialized CSF unit in the Hospital de Clínicas at the Federal University of Paraná.

In 1988, Otávio Moreno de Carvalho, after two years of residence in Infectious and Parasitic Diseases at Hospital das Clínicas of FMUSP, one year of practice in the Neurological Clinic of the same hospital and five years of activities at Spina França Laboratory, moved to Salvador, Bahia. He widened his activities and revitalized the CSF laboratory of the José Silveira Foundation in that city. He is now the greatest specialist on neuroschistosomiasis in Brazil and coordinates his own CSF laboratory in Salvador.

Other Brazilian states have also been able to count on collaboration from medical doctors responsible for CSF units for many decades. These services are integrated with general clinical analysis laboratories, and therefore, their participation has not been specified in the present paper.

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