SHORT HISTORICAL REVIEW

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Remember the Romanian pioneers: Alexandru Obregia (1860–1937) – first *in vivo* suboccipital puncture

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Abstract

In a time when doctors had limited knowledge about neuroanatomy and were focused primarily on clinical data, paraclinical investigations were overlooked even though they offered much needed information about the patients. Prof. Dr. Alexandru Obregia (1860–1937) is one of the forgotten pioneers of cerebrospinal fluid (CSF) investigation techniques. He envisioned, performed, and wrote about the very first *in vivo* suboccipital puncture, in 1908. The invention of this investigation technique was a considerable step forward in understanding the CSF and was Prof. Alexandru Obregia's most important scientific work. This, in turn, inspired Thoma Ionescu (1860–1926) to create the general rachianesthesia technique, in 1919, which allowed surgeons to perform a new range of procedures safely. The universal medical literature bears witness that this procedure was performed in other countries only after five years by Antonio & Bramman and after 11 years by Wegeforth, Ayer & Errik, thus confirming without a doubt Prof. Alexandru Obregia's priority in this historical finding.

Keywords: Alexandru Obregia, suboccipital puncture, cerebrospinal fluid, history.

Cerebrospinal fluid (CSF) exploration

The investigation and understanding of the nervous system have been historically a tedious endeavor, partly because of its complexity but mostly because of the near impossibility of direct *in vivo* research.

The early steps in the understanding of the cerebrospinal fluid were made in Antiquity by Hippocrates (460–375 BC), who observed "water" surrounding the brain [1]. Later, Galen (130–200) observed an "excremental liquid" in the ventricles of the brain from where he wrongly concluded it is purged into the nose [2].

Although Hippocrates and Galen recognized the presence of CSF, its presence eluded subsequent anatomist for the next 16 centuries – most likely due to their autopsy technique, which involved decapitation of the cadaver prior to the brain's autopsy, thus draining all the liquids from the brain and spine.

The discovery of CSF is historically attributed to Emanuel Swedenborg (1688–1772). He was the first anatomist to understand the nutrition role of the CSF and its location [3].

François Magendie (1783–1855) was the first anatomist to try *in vivo* experiments on animals' central nervous systems, which allowed him to observe that the brain and the spinal cord are submerged and suspended in CSF. With this conclusion, he opened discussions about the roles of CSF in a living being [4].

Four decades after his studies, in 1891, Walter Essex Wynter (1860–1945) treated tuberculous meningitis by tapping CSF from the spinal subarachnoid space, thus relieving fluid pressure [5].

The same year, Heinrich Quincke (1842–1922) formulated the first protocol for lumbar puncture. This technique offered both diagnostic and treatment options.

The next discovery, in chronological order is the invention of the suboccipital puncture of *cisterna magna* by Romanian doctor and scientist, Alexandru Obregia (1860–1937) (Figure 1).

Figure 1 – ***Alexandru Obregia, portrait with autograph (1934).***

He performed it for the first time *in vivo* on human patients with a clear diagnosis and treatment purpose (Figure 2). The technique was perfected, and his experience accumulated after using the procedure on 22 patients. He recorded all his endeavors and published it in 1908 [6].

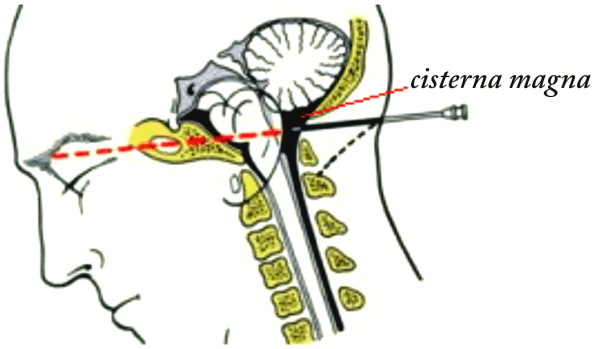

Figure 2 – ***Illustration of suboccipital puncture.***

Alexandru Obregia's work, in turn, inspired the renowned Romanian surgeon Thoma Ionescu (1860–1926) to create the general rachianesthesia procedure, in 1919, which allowed surgeons to operate for longer periods of time until the introduction of ether as general anesthetic in the operating room [7].

The understanding of the CSF is brought into modern era by William Mestrezat (1883–1928), who describes the chemical composition of CSF in detail and by Harvey W. Cushing (1869–1939), who describes the correct flow of the CSF, from its genesis in the choroid plexus to its reabsorption in the dural venous sinuses [8, 9].

Suboccipital puncture of *cisterna magna* – 20th *vs.* 21st century

Literature from the 20th century suggests that the suboccipital puncture was performed daily and was considered a standard tool for the surgeon's arsenal of investigation and treatment procedures.

In a case presented in the "Lancet", in 1924, Dr. Adolf Harwich (Germany) performed suboccipital puncture 13 times in the course of 25 days on a 12 years old girl with cerebrospinal fever. He removed 30 ccm of CSF and injected 20 ccm of anti-meningococcus serum on each occasion. The patient had no major complications (only complained of headache regularly after each injection). In this case, a lumbar puncture could offer only a few ccm of turbid fluid through aspiration, whereas a suboccipital punctured offered 20–30 ccm of fluid. Dr. Adolf Harwich concluded that suboccipital puncture caused less discomfort for the patient and could be more easily carried out than lumbar puncture [10].

Harry C. Saunders and Leo Spiegel (1928) present a comparative study of cisternal and lumbar puncture with a literature review. According to them, up to November 1927, more than 10 000 cases had been reported in literature as having underwent a suboccipital puncture procedure by various surgeons (citing nine doctors) and until September 1928, both authors had performed 620 suboccipital punctures together. Of all 10 620 cases only two (0.01%) deaths were reported. Dr. Harry Saunders presents the Ayer method as being "a great deal of danger". Instead, they followed "the technique used by the German operators", more exactly the Eskuchen method. Upon a closer examination, the Eskuchen method described by the authors is almost the same as the Obregia method from 1908 [11].

This confirms not only that Alexandru Obregia was the first in the world to present this technique in 1908, but quite remarkably would be considered by some as being one of the best.

While the suboccipital puncture was a frequently performed technique in the 20th century and even preferred to the lumbar puncture by some surgeons, today the technique has almost been completely replaced by lumbar puncture. Without a doubt, in the 21st century, the recommended technique for CSF investigation or axial drug administration is the lumbar puncture. In the current practice, performing a suboccipital puncture is considered an exception from the rule.

Literature suggests puncture of *cisterna magna* may still have some use or may even make a return.

Pomerantz *et al.* (2005) presented a rare situation when a suboccipital puncture is performed in the 21st century. In order to circumvent an anomalous course of the posterior inferior cerebellar artery (PICA) they used computed tomography (CT)-guidance with intravenous enhancement. A safe approach was planned specifically for this patient and the procedure was successfully performed without complications. To our knowledge, there has been no other instance of cisternal puncture under CT guidance in literature [12].

Gong *et al.* (2018) performed a retrospective study of 1008 lateral atlanto-occipital space puncture of *cisterna magna* in 667 patients. The results are to say the least promising. Of all 1008 procedures only 17 (1.7%) failed due to technical problems in 15 cases and because of an uncooperating patient in two cases. Although 15 (2.25%) patients reported pain, 32 (4.8%) patients had a transient increase in blood pressure and one patient (0.15%) had intracranial hypotension, all those complications were fully resolved with no sequelae. The procedure was done for both diagnosis (196 patients) and treatment (812 patients) purposes on 10 different kinds of pathologies. Due to its high success rate, no serious adverse effects (all complications completely resolved) and no headache complication (compared to 10–25% in lumbar puncture) this study suggests suboccipital puncture is a viable alternative for the standard lumbar puncture [13].

Alexandru Obregia and his legacy in Romania

Alexandru Obregia was a well-known psychiatrist and university professor at the Faculty of Medicine in Bucharest.

In 1888, when he was only 28 years old, he presented his thesis in medicine, at the Faculty of Medicine in Bucharest. Afterwards, he specialized in psychiatry in Berlin and Paris for three years. Since 1909, he was professor of Psychiatry at the Faculty of Medicine in Bucharest for 25 years and in 1922, he was voted President of the Romanian Society of Psychiatry [14].

His greatest achievement was the inauguration of the Central Hospital for Mental and Nervous Diseases in Bucharest, in 1923 (Figures 3 and 4).

Figure 3 – ***Aerial view of "Prof. Dr. Alexandru Obregia" Clinical Psychiatric Hospital, Bucharest (2012) (Courtesy of Sorin Riga).***

Figure 4 – ***Wagons on Berceni Street, in front of the main building of Central Hospital for Mental and Nervous Diseases in Bucharest ("Ilustraţiunea Română", 16 September 1936).***

It was built in 16 years and represented an important European progress in public health. It was the largest Psychiatry Hospital in Romania and Europe, having 34 buildings and the possibility to hospitalize 2000 patients at a time [14] (Figure 5).

Figure 5 – ***Current Building Plan of "Prof. Dr. Alexandru Obregia" Clinical Psychiatric Hospital, Bucharest; currently can hospitalize 1229 patients at a time. 1: Administrative Building; 2: Psychiatry IV (75 beds); 3: On-call Room & Patient Admission Office (15 beds); 4: Pharmacy; 5: Administrative Building & Kitchen; 6: Administrative Building; 7: Pediatric Neurology I (40 beds); 8: Maintenance Building; 9: Psychiatry X (70 beds); 10: Psychiatry I (75 beds); 11: Psychiatry II (60 beds); 12: Psychiatry VI (75 beds); 13: Psychiatry VII (70 beds); 14: Psychiatry VIII (70 beds); 15: Psychiatry XV (70 beds); 16: Psychiatry XI (80 beds); 17: Infantile Psychiatry Va (35 beds); 18: Psychiatry XIV (65 beds); 19: Psychiatry XII (72 beds); 20: Psychiatry XIII (50 beds); 21: Pediatric Neurology II (40 beds); 22: Infantile Psychiatry Vb (35 beds); 23: Pediatric On-call Building; 24: Paraclinical Investigations Building; 25: Garage; 26: Psychiatry XVI – Toxicomania (25 beds); 27: Psychiatry XVII – Toxicomania (34 beds); 28: Psychiatry IX (90 beds); 28*: Psychiatry III (83 beds); 29, 30, 32, 33: Storage Building; 31: Kinetotherapy; 34: Archives; 35: Autonomous Water Source; 36: Water Tower; 37: "Emil Racoviţă" Gate; 38: Berceni Street Gate – A: National Institute of Neurology and Neurovascular Diseases; B: Vascular Neurology; C: Administration Building; D: Morgue; E: Ambulatory; *"Bagdasar–Arseni" Emergency University Hospital.***

In fact, Prof. Dr. Alexandru Obregia was the one who conceived, founded, localized (outside the City), projected, organized and led the Hospital (between 1923 to 1930). In his honor, since 1935, when Alexandru Obregia celebrated his 75th anniversary, the main entrance of the hospital presents a statue of his bust, which was realized by the Romanian sculptor Frederic Storck (1872–1942) [14] (Figure 6).

Figure 6 – ***Bust of Alexandru Obregia at the front of the Central Building (made by Frederic Storck, in 1935).***

Between 1951 to 1998, the Hospital was named The Unified Hospital No. 9 "Dr. Gheorghe Marinescu", in opposition to historical reality. Over the time, Mrs. Maria Romana Obregia, daughter of Prof. Alexandru Obregia, and the psychiatrist Dr. Paul Cortez (1922–1988) tried to correct the name of the Hospital, without any success. Fortunately, after three years of work to demonstrate the truth, in 1998, Prof. Dr. Dan Riga and Prof. Dr. Sorin Riga managed to change the title of the Hospital in "Prof. Dr. Alexandru Obregia" Clinical Hospital of Psychiatry [15].

It is known that Prof. Dr. Alexandru Obregia had many contributions in psychiatry, introducing new methods of diagnosis and treatment, which gave the possibility of treating mental disorders.

He introduced the anatomo-clinical studies in psychiatry, and the most known are the ones referring to progressive general paralysis, alcoholism and paranoia.

At the Faculty of Medicine in Bucharest, he was for 18 years the head of the Department of Histology and established a new method in the process of making samples for the optic microscope, using celloidin.

Conclusions

The suboccipital puncture of *cisterna magna* is a key historical medical progress, which offered new treatment and diagnosis options for doctors in the 20th century. Even though today its indications are reserved, it still has value in cases when a lumbar puncture is not suitable. Alexandru Obregia is one the first CSF investigation and Psychiatry pioneers in Romania and worldwide. His contributions must not be forgotten, nor replaced from history.

Conflict of interests

The authors declare that they have no conflict of interests.

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