A Brief Review of the History of Global and Croatian Neurosurgery

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Abstract

Neurosurgery is the oldest, but also the youngest medical discipline. Namely, archaeological findings confirm the existence of cranial bone trepanations in the Late Stone Age, while neurosurgery as a separate discipline was founded only at the beginning of the 20th century. Descriptions of head/spinal injuries, and trepanations, date back to ancient Egypt (Edwin Smith papyrus) and physicians like Hippocrates, the Alexandrian school, and Galen, who described his classification of cranial fractures, perfected trepanation and contributed to neuroanatomy and physiology. Unfortunately, with his disappearance, the study of the central nervous system ceased during the next millennium. Medieval contribution to neurosurgery is due to the work of Arab and Persian physicians (Albucasis, Avicenna), who collected, preserved, and improved the medical knowledge of ancient times, including neuroscience. With the arrival of the Renaissance in the early 16th century, significant advances in anatomy, medicine, surgery, and neuroscience began. Berengario da Carpi, Andreas Vesalius, and Ambroise Paré stood out as progenitors of this era. During the 19th century, at a time of progress in medicine and surgery, preconditions were created for more extensive and long-lasting neurosurgical procedures, while the era of modern neurosurgery began in the early 20th century with the pioneering activities of MacEwan, Horsley, Cushing, Elsberg, Dandy and many others. Further progress in neurosurgery was made through the use of an operating microscope, which from 1965 marked the era of modern microneurosurgery, founded by Yaşargil. The beginnings of neurosurgical activity in Croatia date back to the end of the 19th century when Theodor Wickerhauser published a record of the first craniotomy done in our country in 1886. In conclusion, modern neurosurgery as one of the most advanced medical professions is based on the achievements of its historical leaders, and on the cutting-edge diagnostic and surgical armamentaria, together with the superior neurosurgical service organization.

Keywords: neurosurgery, history, progenitors, world, Croatia

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Introduction

Considering the history of neurosurgery, it is interesting to note that, at the same time, it is the oldest and youngest medical discipline. Archaeological findings confirm the existence of neurosurgical procedures (cranial bone trepanations) already in the Late Stone Age – Neolithic (around 6,400 BC), and the Bronze Age (3,300 BC–1,200 BC)[1], while at the same time, neurosurgery as a separate discipline was founded only at the beginning of the 20th century.

Evidence-based study of Egyptian mummies suggests that more than 6,000 years ago there was a trace of knowledge of certain neurological diseases and permanent spinal deformities including tuberculosis spondylitis[2].

Also, it is evident that since prehistoric times the brain has been considered the organ responsible for human behavior. Therefore, cranial bone trepanation is without a doubt the oldest documented medical procedure[3, 4]. It seems that in prehistory, the habit of opening the skull (trepanation) was widespread, from Europe, North, and South America, all the way to the Middle and Far East[5]. On about 5% of all archaeological findings of skulls from that time, traces of single or multiple trepanations have been discovered[4]. It is assumed that they were made for different, primarily spiritual, religious, and mystical reasons, and ultimately because of changes in human behavior or for possible treatment of craniocerebral injuries. Since traces of bone healing were found around individual samples of trepanned skulls, it can be also assumed that a large number of those undergoing this procedure survived the surgical procedure itself and a certain period after it[4].

In this review article, brief considerations of the global history of neurosurgery were given, ranging from its humble beginnings during prehistoric times up to the modern age. The ever-changing pattern of various neurological diseases urging different neurosurgical procedures was discussed and the most important milestones from medical history were debated being put within the context of time. Lastly, an ephemeral recapitulation of the most notable events in the short history of Croatian neurosurgery was also underlined remembering its founders, as well as its prompt development during the last few decades.

Neurosurgical procedures during Ancient Egypt and the Antiquity

The Edwin Smith Papyrus (c. 1,650–1,550 BC), considered the most important written source of medical knowledge in ancient Egypt, listed cases of craniocerebral and spinal injuries, describing cranial structures, brain coverings, and cerebrospinal fluid. It also contained the first descriptions of some procedures in the treatment of cranial and spinal trauma, as well as a clinically credible assessment of the injury's condition based on which it is possible to predict the need and likelihood of treatment undertaken[6-8]. Based on the same papyrus, it was even possible to identify certain clinical conditions, such as a depressed fracture of the cranial vault with laceration of the dura and/or brain, or infected open head wounds, i.e., penetrating stab brain injuries and spinal cord injuries, which were not treatable at the time[6-8].

Descriptions of head injuries, trepanation, and spinal injuries are also found in the works of ancient physicians from Hippocrates's time, doctors of the Alexandrian school, and Galen of Pergamon[9].

Hippocrates (460–375 BC), generally accepted as the father of medicine, is among others credited with the text *On Head Injuries* (Lat. *De capitis vulneribus*), which describes different types of skull fractures – warns of the possibilities, but also the dangers of trepanation as a method of treatment[10]. There is evidence that in his day trepanation was performed for medical reasons, which represented an epochal advance over the mysticism of his predecessors[11, 12]. He was also the first to notice the clinical features of elevated intracranial pressure[13], as well as the first to describe the possible clinical implications of the vertebral column and spinal cord injury[9].

Physicians of the famed Alexandrian school further contributed to understanding craniocerebral and spinal injuries[9]. Their insights were largely based on the first anatomical dissections of the human body, which became fundamental for the development of medical science. The most prominent representatives of this school Herophilus (335–280 BC) and Erasistratus (304–250 BC) were rightly considered the founders of anatomy and physiology as independent medical disciplines[14]. Finally, the anatomical recess on the inner surface of the occipital bone formed at the junction site of the dural venous sinuses (Lat. *confluence sinuum*) is still called the *torcular of Herophili*, in honor of the founder of anatomy[15].

Galen of Pergamon (129–200 AD) was an ardent supporter of Hippocrates's and Alexandrian medical knowledge, which he upgraded with new ones and further improved[16]. Unlike Hippocrates, who considered the brain a gland, Galen correctly considered it the center of volitional movements and sensory experiences that are transmitted caudally through the spinal cord[17]. His surgical competence, vast medical knowledge, and enviable understanding of neuroanatomy made him the leading physician-surgeon of antiquity, whose scientific observations and expertise, as well as some misconceptions, dominated overall medicine for more than a thousand years[9]. In his time, cranial trepanation was widely accepted and common, and in his teachings, it was emphasized that during the procedure it is important to preserve the integrity of the dura (Lat. *dura mater encephali*), the opening of which inevitably leads to infection and death[18, 19]. He described his own classification system for skull fractures and further refined the surgical technique of trephination and also substantially contributed to the understanding of neuroanatomy and physiology. He was the first to describe the need to remove free bone fragments from the vertebral canal after a spinal fracture with the aim of preventing neurological deficits[9]. Unfortunately, with his disappearance, the study of the central nervous system (CNS) ceased during the next millennium, a need for which it arose again only in the Renaissance period, at the beginning of the 16th century.

Traces of medical knowledge and neurosurgical practice in the Middle Ages

Medieval contributions to medicine and neurosurgery were largely reduced to the work of Arab and Persian physicians, who collected, translated, preserved, and further improved the overall medical knowledge of ancient times, including neuroscience[20-22].

It was an Islamic physician Albucasis (al-Zahrawi, 936–1013) the pioneer of neurosurgery, who in his treatise gave a more precise description of many aspects of neurosurgical pathology, its treatment, instruments, and neurosurgical techniques. He dealt with a multitude of topics concerning neurosurgical pathologies such as head injuries, spinal fractures, tumors, and hydrocephalus, whose surgical treatment he described for the first time[23]. Soon, his encyclopedic book (*Kitab al-Tasrif*), which was published in 1000 AD, was translated from Arabic into Latin, Hebrew, and French, representing the basis for teaching medicine, especially surgery, in many European medical schools of that time[23].

However, the brightest example of this dark period of human history is certainly the Persian physician and scientist Avicenna (Ibn Sina, 980–1037), who in his encyclopedic book Canon of Medicine (Al-Qanun) from 1125 consolidated and published almost all of the previous knowledge of Galenic medicine collected throughout history, and is rightly considered a pioneer of evidence-based medicine[24]. Avicenna also described an instrument, a drill calling it a trepanum or a perforator that did not penetrate the dura[25]. In his Canon of Medicine, Avicenna revised the knowledge of the ancient scholars through critical thinking and relying on observation and testing, systematized the science of medicine, and introduced many ideas and innovations[25-27]. As such, he was regarded the most prominent physician of the Islamic Golden Age.

Progenitors of neuroscience from the Renaissance

Along with the arrival of the Renaissance at the beginning of the 16th century, together with well-known contributions to science and art, significant advances in anatomy, medicine, and surgery began, as well as in neuroscience as the forerunner of neurosurgery. Among the progenitors of this trend, the first to stand out was Jacopo Berengario da Carpi (1460–1530), a professor of medicine from the University of Bologna, who in 1518 published his work *On Skull Fractures* (Lat. *Tractatus de Fractura Calvae gray Cranei*) as the most significant work on craniocerebral injuries of that time in which he described a number of surgical procedures and different surgical instruments used to treat such injuries[28, 29]. He is also among the most deserving scientists responsible for transforming medieval morphological concepts into modern evidence-based science as anatomy will soon become[30].

Rapidly, in the same atmosphere of all scientific progress, the works of the famous Andreas Vesalius (1514–1564), the father of modern anatomy, appeared. They were based on a detailed knowledge of the human body acquired empirically by conducting numerous anatomical dissections[31]. Certainly, the most important of his endeavors was the epochal work from 1543 *On the structure of the human body* (Lat. *De Humanis Corporis Fabrica*), which was particularly distinguished by precise illustrations counted among the most significant pictorial anatomical representations in the overall history of medicine[31]. From a neurosurgical point of view, his works particularly emphasized detailed descriptions of the meninges and cerebral ventricles, as well as

cranial, spinal, and peripheral nerves[32]. After all, it was Vesalius who was the first to challenge Galen's famous pneumatic theory, that is, the ventricular doctrine of cognition, which erroneously claimed that the center of mental functions is located in the brain ventricles[33]. His contribution to the treatment of craniocerebral penetrating injury is also not negligible since Vesalius, in addition to the position of top scientist and professor at the prestigious University of Padua, was also a practicing physician at the court of King Philip II of Habsburg (1527–1598) in Spain[31, 34].

His contemporary and supporter, the French surgeon Ambroise Paré (1510–1590), stood out in this line, and in 1564 he described in detail the comprehensive treatment of wartime craniocerebral injury, which is why he is rightly considered the father of modern surgery[35]. Paré performed various surgeries on skull and brain infections and did not shy away from a craniotomy and the opening of the dura for which he specifically made a kind of craniotome (trepan) similar to the one being used today[34, 36, 37]. He was also the first to spot, clarify and describe the pathophysiology of concussion and contusion of the brain[35].

Significant advances in medicine and neurosurgery during the 19th and early 20th century

The nineteenth century was a time of significant advances in medicine and surgery. The development of anesthesia with ether (Long and Moton, 1842) and chloroform (*trichloromethane*) (Young Simson, 1847) created the preconditions for the development of more extensive and long-lasting surgical and neurosurgical procedures[9].

The next crucial step was the development of antisepsis and asepsis (Lister, 1867), which was based on knowledge from bacteriology about microorganisms as the causative agent of infection (Koch, 1877)[9]. This has enabled the exponential development of surgical professions, but not neurosurgery entirely, which has largely depended, and still depends on today, on technological medical achievements. It was necessary to discover X-rays and make a radiological device (Röntgen, 1895), develop ventriculography and pneumoencephalography (Dandy, 1918 and 1919), and finally, cerebral angiography (Moniz, 1927)[38] to enable approximately accurate topographic diagnosis of various intracranial, and spinal processes. Previously, neurosurgeons depended on the localization diagnosis of neurologists, often done during the operation itself[39].

Since hemostasis in neurosurgery has always been one of the key elements for the outcome of treatment, it was only the development of electrocoagulation (Bovie, 1926) that enabled further progress of the neurosurgical technique as we know it today[40].

Pioneers of modern neurosurgery

William MacEwan (1848–1924) is considered by many to be the father of modern neurosurgery[41]. This Scottish physician founded neurosurgery as a separate medical profession and performed the first successful surgeries on a brain abscess in 1876, and a benign brain tumor in 1879[42].

Victor Horsley (1857–1916), probably the most important neurosurgeon of his time, was the first to use bone wax to stop bleeding after trepanation and craniotomy and created the first assumptions of the future stereotaxic method[43]. He was also the first to successfully surgically remove a spinal extramedullary tumor after a laminectomy in 1887[43]. He was the first surgeon to devote his career entirely to the study and surgical treatment of CNS diseases and the founder of the first independent neurosurgical department in the world founded in London in 1886. (*National Hospital, Queen Square, London*)[39, 43, 44].

Harvey Cushing (1869–1939) was undoubtedly the most significant figure in neurosurgery of the first half of the 20th century[45]. It was he who was responsible for the description of many neurosurgical diseases and conditions (Cushing's disease, Cushing's syndrome), as well as for the development of surgical procedures that are widely used today[45]. Thanks to him, neurosurgery has become a modern science and a kind of paradigm for the use of precise, decisive, and detailed operative techniques[46].

Charles Elsberg (1871–1948), from The New York Neurological Institute, was among the first to successfully remove the intramedullary tumor in 1909, as well as spinal arteriovenous malformation in 1914. Therefore, he is rightly considered the founder of modern spinal surgery[47].

Walter Dandy (1886–1946), performed the first successful operation to exclude the intracranial aneurysm from circulation by placing a metal clip on the neck of the aneurysm in 1937[48], and previously introduced ventriculography and pneumoencephalography into neurosur-

gical diagnostics (in 1918 and 1919), which were then the first successful attempts of indirect imaging of the CNS structures[49]. He was also the first to successfully operate on a hernia of the intervertebral disc of the lumbar spine, in 1929[50]. With his scientific achievements, he contributed to the understanding of the physiology of cerebrospinal fluid and pituitary gland, and advanced surgical approaches to pontocerebellar angle, as well as various pathology of the posterior cranial fossa[51].

The era of contemporary neurosurgery

In 1955, the World Federation of Neurosurgical Societies (WFNS) was founded in Brussels, which was a significant step in the advancement and affirmation of the profession on a global scale, and whose first elected president was the famous British neurosurgeon Sir Geoffrey Jefferson (1886–1961)[52, 53].

Further significant advances in neurosurgery were made possible by the use of an operating microscope (Kurze, 1957), which from 1965 began the era of modern microneurosurgery, founded by Mahmut Gazi Yaşargil (b 1925), one of the most important neurosurgeons of the second half of the 20th century[54-56]. He developed important microsurgical concepts including arachnoid microdissection and segmental exploration of vascular and neoplastic CNS lesions within their predilection sites[57, 58]. Furthermore, he successfully united the microsurgical technique with innovative approaches to the cranial base and vascular tree (pterional craniotomy)[59]. At the same time, he was the first to combine the microsurgical technique with bipolar coagulation, originally invented by Leonard Malis (1919–2005) in 1953[57- 61].

An additional impetus to the development of cranial base surgery was the application of a modern high-speed drill, whose progenitors were Ossama Al-Mefty from the US, Majid Samii from Germany, and Vinko Dolenc from Slovenia.

The subsequent development of neurosurgery was made possible by the introduction and improvement of diagnostic techniques, such as computed tomography of the brain (CT) (Hounsfield, 1971)[62, 63], and magnetic resonance imaging (MRI) (Lauterbur and Mansfield, 1973) which enabled direct and accurate depiction of all neural structures of the CNS for the first time in history.

Hence, contemporary neurosurgery remains one of the most cutting-edge medical professions, which is profoundly based on the accomplishments of its predecessors, as well as on the state-of-the-art armamentarium and instrumentation together with the superb organization of neurosurgical service and healthcare.

A brief history of neurosurgery in Croatia

It can be said that neurosurgery in this region began with the activities of Anton von Eiselsberg (1860–1939) from the University of Vienna[64], who was one of the founders of neurosurgery and spinal surgery in the Austro-Hungarian Monarchy, of which Croatia was then a part. He first described the successful removal of a primary spinal cord tumor in 1907[9].

However, the actual beginnings of neurosurgical activity in Croatia date back to the end of the 19th century, when Theodor Wickerhauser (1858–1946) published his record of the first craniotomy done in our country in 1886, on the pages of the Croatian Medical Herald. On that occasion, he described the surgical management of a complicated temporal bone fracture with bleeding from the middle meningeal artery (Lat. a. meningica media) and the formation of an epidural hematoma. In 1890, he became the primary physician–surgeon of the newly established external ward (composed of surgery, otorhinolaryngology, ophthalmology, and dermatovenerology) of the Public General Hospital of the Sisters of Mercy in Zagreb[65]. At that time, the ward was an innovative one having two rooms for surgery – an aseptic and septic one and patients were assigned to the hospital rooms according to the type of surgery. It is undoubtedly that it was T. Wickerhauser who established the foundations of modern surgical practice in Croatia.

His colleague and later successor, Miroslav Čačković Vrhovski (1865–1930) published in the Croatian Medical Herald in 1886 the first account of the operation of an injured man with a depressed cranial vault fracture accompanied by generalized epileptic seizures, which was performed in morphine and chloroform narcosis. He was soon elected the first dean of the Faculty of Medicine, University of Zagreb, founded in 1917[66].

Aleksandar Blašković (1882–1953) performed the first transnasal pituitary glandectomy in 1922, also at Sisters of Mercy Hospital in Zagreb, while *from the same hospital* in 1927 Ante Šercer (1896–1968) first published his experiences in the surgical treatment of 10 patients with pituitary adenoma[67].

Danko Riessner (1907–1973) founded a separate neurosurgical department in Zagreb in 1946 and thus became the most important person responsible for the further development of the neurosurgical profession in this re-

gion, so he is rightly considered the founder of Croatian neurosurgery[68]. His main scientific contribution was the paper on the shifting of brain masses, which he published in 1939. He also published a paper in the Croatian Medical Herald on the surgical approach in the treatment of late post-traumatic epilepsy, in 1943.

Matija Kožić (1915–1981), the first neurosurgery specialist in Croatia, published in the Croatian Medical Herald the first reports on spinal injury and pathology of the cervical intervertebral disc in Croatia, in 1954. He also published the first papers on the surgical treatment of hydrocephalus and epilepsy and on brain tumors. He was the founder of the Department of Neurosurgery in Zagreb in 1974, one of the first institutions of its kind in this part of Europe.

An important contribution to the further development of Croatian clinical neuroscience in general, and neurosurgery in particular, was the procurement of the first device for computed tomography (CT) imaging of the head (*EMI CT brain scanner*), in 1976 at the hospital in Zagreb's Rebro, just a few years after its first clinical use at Atkinson Morley Hospital in Wimbledon, London, UK, in 1974[62].

Finally, the Croatian Neurosurgical Society has been founded in 1992 with the aim of promoting the neurosurgical profession and science at the national level. The first elected president was Ivan Jeličić (1929–2012), head of the Department of Neurosurgery, Faculty of Medicine, University of Zagreb. At the same time, he was the first neurosurgeon from Croatia to train abroad, with the famous G. M. Yaşargil in Zűrich (Germn. *Neurochirurgische Universitatsklinik Zűrich*)[59], as well as the first one to use the microsurgical technique in this region during operations of intracranial aneurysms, about which he published the first book in Croatian, in 1985. Therefore, he is rightly considered the founder of modern microneurosurgery in Croatia.

Soon after that, there was a general progress of neurosurgical expertise across the country followed by the establishment of a dozen neurosurgical hubs and several centers of excellence in regional capitals in Zagreb, Split, Rijeka, and Osijek, armed with state-of-the-art diagnostic and surgical equipment and teamed with highly educated staff.

Today, we can proudly confirm that the current state of development of the neurosurgical profession in Croatia has reached the standards in providing health care of most developed Western countries and that the profession is successfully progressing further.

Conclusion

The humble beginnings of neurosurgery as a surgical discipline may be traced back to prehistoric times when initial primitive craniotomy procedures (trepanations) were observed according to archaeological findings of skulls from the Neolithic period. However, the progress of neurosurgical practice and knowledge was rather slow due to the intricate pathology of neurological diseases, as well as the lack of adequate knowledge and appropriate diagnostic and surgical equipment needed to perform such complex procedures. Hence, it depended on the reduced number of brave but competent individuals responsible for its development and who, throughout their enormous enthusiasm and endeavors, managed to make and shape modern neurosurgery as we know it today.

Therefore, contemporary neurosurgery is one of the most advanced medical professions, which is heavily grounded on the achievements of its predecessors, as well as on the state-of-the-art armamentaria and instrumentation together with the superb organization of neurosurgical service and healthcare. The same can be said for Croatian neurosurgery as one of the most exclusive medical specializations in the county.

Although one may consider the history of neurosurgery intricate but optimistic, its present existence is even more rewarding. Due to the further development of most modern technologies including robotic neurosurgery, virtual reality, nanotechnology, and artificial intelligence, the bright future of this remarkable discipline is certainly assured.

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Kratak pregled povijesti svjetske i hrvatske neurokirurgije

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Sažetak

Neurokirurgija je istodobno jedna od najstarijih, ali i najmlađih medicinskih disciplina. Naime, arheološki nalazi potvrđuju opstojanje trepanacije lubanjske kosti već u mlađem kamenom dobu, dok je neurokirurgija kao zasebna disciplina utemeljena tek početkom 20. stoljeća. Opisi ozljeda glave i kralježnice, kao i trepanacije potječu već iz doba starog Egipta (papirus Edwina Smitha) te od antičkih liječnika, Hipokrata, aleksandrijske škole i Galena iz Pergama, koji je opisao vlastitu klasifikaciju lubanjskih prijeloma, dodatno usavršio trepanacijsku tehniku i znatno pridonio razumijevanju neuroanatomije i fiziologije. Nažalost, nakon toga prestalo je izučavanje središnjega živčanog sustava tijekom sljedećeg tisućljeća. Srednjovjekovni doprinos medicini i neurokirurgiji svodi se na djelovanje arapskih i perzijskih liječnika (Albukasis, Avicena), koji su prikupili, sačuvali i dodatno unaprijedili medicinsko znanje antičkog vremena, uključujući i neuroznanost. Dolaskom renesanse početkom 16. stoljeća započeo je znatan napredak anatomije, medicine i kirurgije te neuroznanosti kao preteče neurokirurgije. Kao rodonačelnici ovog doba posebice su se istaknuli Berengario da Carpi, Andreas Vesalius i Abroise Paré. Tijekom 19. stoljeća, u vrijeme znatnog napretka medicine i kirurgije, stvoreni su preduvjeti za razvoj opsežnijih i dugotrajnijih neurokirurških zahvata, dok era moderne neurokirurgije započinje početkom 20. stoljeća pionirskim djelovanjem Williama MacEwana, Victora Horsleyja, Harveya Cushinga, Charlesa Elsberga, Waltera Dandyja i mnogih drugih. Daljnji napredak neurokirurgije omogućen je uporabom operacijskog mikroskopa, čime od 1965. počinje era suvremene mikroneurokirurgije, čiji je utemeljitelj M. G. Yaşargil. Počeci neurokirurške djelatnosti u Hrvatskoj datiraju s kraja 19. stoljeća, kada je Theodor Wickerhauser objavio zapis o prvoj kraniotomiji učinjenoj u našoj zemlji 1886. U zaključku, suvremena se neurokirurgija, kao jedna od najnaprednijih medicinskih profesija, temelji na postignućima svojih povijesnih predvodnika te na najmodernijem dijagnostičkom i kirurškom armamentariju, zajedno s vrhunskom organizacijom neurokirurške službe.

Ključne riječi: neurokirurgija, povijest, rodonačelnici, svijet, Hrvatska