

HISTORY OF MEDICINE / ИСТОРИЈА МЕДИЦИНА

The history of pediatric anesthesia

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The beginnings of pediatric anesthesiology go back to the middle of the 19th century and it is associated with a rural physician Crawford W. Long, MD, who in the 1842 recorded the first case of giving diethyl ether anesthesia to an eight-year-old boy.

The start of development of contemporary pediatric anesthesia is considered to be in 1930, which marked two periods of progress. In the first period, anesthesia techniques and accessories adjusted to different children's ages were developed. In the second period, modern anesthetic medications and supervision were introduced into everyday clinical practice in order to better protect vital organs and their functions in the child's body. The first multidisciplinary pediatric intensive care unit at the Children's Hospital of Gothenburg in Sweden was established in 1955. Dr. Branka Mitrović is considered to be the founder of pediatric anesthesiology in Serbia, as she founded the Department of Anesthesiology and Reanimation at the University Children's hospital in 1955. The history of pediatric regional anesthesia began after its introduction in adults, which occurred after the invention of cocaine in 1884. The Ministry of Health of the Republic of Serbia approved a specialization in pediatric anesthesiology in 2018.

The development of pediatric anesthesia is fascinating because it completely followed the development of pediatric surgery. Modern pediatric anesthesiology is entirely prepared to meet the needs of the most complex surgical interventions, as well as the treatment of critically ill children, and significantly contributes to better treatment outcomes of pediatric surgical patients.

Keywords: children; pediatric anesthesia; history; development

INTRODUCTION

Today it is impossible to understand how even the simplest surgical procedures could be performed without all the benefits provided by anesthesia. The beginnings of anesthesia go back to the 19th century, which enabled many of the advances that occurred in the 20th century that compose everything what we currently take for granted.

Children received anesthesia from the start of the earliest clinical applications [1]. During the first decades of the 20th century, most doctors treated children as "little adults," which we all know today is an incorrect view. At the onset of developing pediatric anesthesia, all equipment, techniques, and medications were founded in the literature concerning adults. Most medications utilized in children were not tested or researched, or recommended to be used in children, so their use was based on adult studies and expert consensus. Morbidity and mortality were high [2].

During the history of the development of pediatric anesthesiology in our country, many pediatric anesthesiologists have contributed to the fact that we follow world trends in the development of pediatric anesthesiology. We hope we have not omitted any of the early contributors to the development of our specialty.

FROM THE BEGINNING OF THE 19TH CENTURY

On March 30, 1842, Crawford W. Long, MD provided diethyl ether to a patient named James Venable to incise a cyst on the patient's neck [3]. His third patient was an eight-year-old boy, about whom he said the following: "My third experiment in etherization was made on the 3rd July 1842, and was on a Negro boy, the property of Mrs. S. Hemphill, who resides nine miles from Jefferson. The boy had a disease of the toe, which rendered its amputation necessary, and the operation was performed without the boy evincing the least sign of pain" [3, 4]. He did not publish his experiments until 1849. It is obvious that anesthesia care of children had primacy from the start, within the surgical records of the Massachusetts General Hospital from 1846 to 1947, when 80% of all pediatric patients received anesthesia [1]. It absolutely was noticed, from the earliest beginning, that children were at higher risk than adults for complications associated with anesthesia [1]. In 1846, Bigelow published a paper about the use of ether in the Boston Society for Medical Achievements, when he warned of the use of ether in young children [5].

The first anesthetic death (1846) comes from the report in an issue of the London Gazette about the use of ether in an 11-year-old boy, in which it was reported that the anesthesia "was not totally effective and, in addition, death

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occurred shortly following the surgery” [1]. The cause of death was considered to be associated to the injuries the boy had. Two years later (1848), the Edinburgh Medical and Surgical Journal published a case report of a 15-year-old girl, named Hannah Greener, who had a heart attack after chloroform anesthesia was applied [6]. The autopsy of the girl was negative except for pulmonary edema and the stomach full of food [7]. The conclusion of this case report was that the death was secondary to the anesthetic.

John Snow, from London, was the first physician who specialized in anesthesia and who is considered the father of anesthesia practice [8]. He began providing anesthesia with diethyl ether for adults and children in 1847 [9]. Soon he switched to chloroform, more potent and rapidly acting halogenated ether, but dangerously toxic [9]. After one decade into practice, Snow reported his experience with chloroform anesthesia on several hundred children, including 186 under the age of one year [8]. His observation was that in children “the effects of chloroform are more quickly produced and also subside more quickly than in adults, owing no doubt to quicker breathing and circulation” [8]. Throughout the time of John Snow, thousands of newborns, infants, and children survived surgery and anesthesia in North America and Europe. However, in the hands of those less experienced, the use of chloroform brought on an unacceptably high incidence of complications. However, though widespread application diethyl ether showed to be the most effective, even anesthesia with diethyl ether posed significant hazards and side effect – but there was no better alternative [1].

A few decades later (1897), due to great concern over deaths associated with the use of chloroform, the Boston Society for Medical Achievement Committee made a decision that the use of ether was safe, while the use of chloroform was not [10]. At that time, chloroform made up 50% of all anesthetics in the USA. In 1888, Buxton described the use of a mixture of N₂O and ether [11]. However, Buxton is also remembered for making a misconception that lasted for the next 50 years and served as an excuse for anesthesiologists whose pediatric patients died under anesthesia, and the claim was that the condition of the thymus lymph tissue changed during anesthesia [11]. Despite the fact that chloroform was declared unsuitable for use in the human population, its use was continued until incidental cardiac arrest and fatal hepatotoxicity occurred in children, first described in 1894 [8].

THE FIRST HALF OF THE 20TH CENTURY

The greatest advance of anesthesia in the early 20th century was primarily due to progress of surgery in treating congenital and acquired diseases and the need for anesthesia to follow it. Any development before the 1940s was exclusively the result of individual efforts. Between 1846 and the 1940s, anesthesia was a dangerous procedure for children due to poor anesthesia equipment not adapted to children, insufficient training in the placement of vascular lines, poor understanding of resuscitation, surgical techniques

were primitive and antibiotics did not exist [12]. William Ladd as one of the pioneers of modern pediatric surgery, initiated the inevitable evolution of pediatric anesthesia [1]. From 1917 to 1945, he introduced surgical procedures for many congenital anomalies and a number of diseases primarily related to young children, thus imposing the need to develop clinical and academic specialties in pediatric anesthesia [1]. For this work he is considered the father of pediatric surgery. Another anesthesiologist, Dr. Charles Robson, is one of the pioneers of this early period who deserves to be mentioned, and he is the first person who could be marked as a pediatric anesthesiologist [13].

In those years, ether and ethyl chloride became the main anesthetics in pediatric anesthesia and were applied by “dropwise” until the 1920s, when reliable evaporators and precise gas flow meters for the simultaneous use of N₂O and oxygen were invented and produced [14, 15]. James Gwathmey in his book “Anesthesia” (1914) describes the techniques of pediatric anesthesia, emphasizing the importance and tenderness of gentle treatment of children during the introduction of anesthesia, all in order to keep the course of anesthesia calm [16]. Arthur Guedel recommends holding the mask a few inches from the face of a small child, and sticking to the face only when the child falls asleep. This method of induction, better known as “stolen induction,” is used today, primarily because it allows a peaceful anesthesia induction [16]. Charles Robson in 1920 and Langton Hewer three years later advocated mandatory intubation of children during all surgical procedures. However, in that period, there was no adequate equipment for the pediatric population, so intubation with the help of a laryngoscope was performed very rarely [14]. The beginning of the development of modern pediatric anesthesia is considered to be in 1930. For the next two decades, anesthesia techniques and equipment adapted to children were developed, and then new and safer intravenous and inhalation anesthetics were introduced [11]. The first tubes for children, made of red rubber, were constructed by Ivan Magill in 1930. Soon after, Philip Woodbridge developed the idea of latex tubes with a metal spiral that could not be bend (reinforced tubes) [11].

Dr. Philip Ayre is one of the prominent figures in the history of pediatric anesthesia. In 1938 he was a visiting anesthetist at the Babies’ Hospital, Newcastle-Upon-Tyne, England, when he developed an especially suitable pediatric anesthesia breathing system in the shape of the letter T, which is called “T system without back breathing” [17]. It was used with tracheal intubation during the operation of cleft lip and palate malformations in infants. This year is also significant because the American Board of Anesthesiology was formed, giving anesthesiology a professional status. In 1941, Robert Miller described his own modification of a flat spatula, which was slightly longer and narrower than the others, it had a thinned and gently rounded tip [18]. Slightly later, in 1943, Robert Macintosh constructed the first laryngoscope spatula, which was curved along its entire length [18]. Due to its anatomical characteristics, Miller’s spatula is used in infants, while Macintosh’s spatula is used for older children.

AFTER WORLD WAR II

The first book “Pediatric Anesthesia” was published in 1948 by Digby M. Leigh and Kettlin M. Belston [19, 20]. The use of halothane began in 1956, and soon became the most popular anesthetic in pediatric anesthesia [21]. Three years later, the era of neuroleptic anesthesia begins, first in the adult population, and then in children. In the same year (1956), ketamine was introduced into clinical practice, and still is most commonly used in children. After World War II and into the 1960s, a group of dedicated anesthesiologists made efforts in developing pediatric anesthesia into a subspecialty. Members of this group were the following: Dr. Leigh, Dr. Jackson-Rees, Dr. Smith, Dr. C. Ronald Stephen, Dr. Digby Leigh’s successor in Montreal; Dr. Margot van Deming, the first director of anesthesia at the Children’s Hospital of Philadelphia, who worked with the pediatric surgeon C. Everett Koop, who demonstrated the relationship between anesthetic blood levels and the anesthetic state in infants [22]; and Dr. Robert Cope, who set new standards for British pediatric anesthesia practice during his long residence at London’s Great Ormond Street Hospital for Sick Children. In 1989, Federation of Associations of Pediatrics Anesthesia (FEAPA) was founded, and Dr. Ljubinko Tonić, who worked at the University Children’s Hospital, participated in the founding assembly. From the first day of its establishment, our country is a member of FEAPA. Ten years after the founding of FEAPA, it changed its name to European Society of Pediatric Anesthesia (ESPA).

Robert M. Smith, MD, a Harvard Medical School graduate, significantly contributed to the understanding of how important it is to know the unique anatomy and physiology of the newborn and young infant as they apply to anesthetic care, researched the safety and efficacy of tracheal intubation and muscle relaxants in children [22]. He also trained future specialists, and he wrote the first extensive book of pediatric anesthesia, still current (the newest one is the 10th edition, released in 2021) [23]. Dr. Virginia Apgar merits special attention as a figure from this period: her one- and five-minute Apgar physical assessment scores for the newborn are the standard of care in hospitals throughout the world [24, 25]. The score was designed to define which babies required reanimation.

Some great individuals of the period between 1960s and 1970s investigated and defined many important processes – fetal transitional circulation and metabolism, birth asphyxia, neonatal metabolism, respiratory control, thermoregulation, body fluid volumes, pulmonary surfactant and its absence in the premature infant – thus establishing the scientific impulse for modern anesthesiology and neonatal intensive care [26]. Monitoring vital parameters such as measurement of arterial pH level and blood gas tensions and interventions like mechanical ventilation, the administration of buffers, and infusion of vasoactive drugs became standards of care [24]. Anesthesiologists who worked with pediatricians, surgeons, and researchers who made these discoveries played the central role by implementing these treatments and interventions [24]. The neonatal care was not restricted to nutrition and

support with minimal intervention any more. In 1955, Dr. Goran Haglund, a pediatric anesthesiologist, established the first multidisciplinary pediatric intensive care unit at the Children’s Hospital of Gothenburg in Sweden [27]. In 1965, a group of anesthesiologists who specialized in the care of children created a committee within the American Academy of Pediatrics (AAP) dedicated to pediatric anesthesia; later, the Committee officially became the AAP Section on Anesthesiology (AAP SOA) [2].

During the period between 1980s and 1990s, pediatric anesthesiology departments or services, training programs and researches in many of the major children’s hospitals and university medical centers were founded. It has become expected that the perioperative survival rate is higher in all but the most moribund infants and children, including preterm infants weighing under 1000 g and those with complex structural heart disease. Enflurane and isoflurane were developed in 1970s and 1980s, and had a better safety profile than halothane. However, these agents did not completely replace halothane because of its benefit during inhalation induction of infants and young children. Recently, sevoflurane has replaced halothane [21]. During this period, pulse oximetry, capnometry, oscillometric monitoring of systemic arterial pressure, and intraoperative neurologic monitoring were introduced to clinical practice.

REGIONAL ANESTHESIA

The history of pediatric regional anesthesia began after its introduction in adults, which occurred after the discovery of cocaine in 1884 [28]. In 1898, August Bier tried to induce spinal anesthesia with cocaine: all of his six patients (two children) had postoperative vomiting and headache [28]. Epidurals came into use in children much later. In this period surgeons dominated the scene, as they performed these blocks. Gaston Labat, a French surgeon, wrote a widely referred book titled “Regional Anaesthesia: Its Techniques and Clinical Applications” [29]. The surgical contribution continued for many years, until anesthesia became an established specialty. Caudal blocks were first reported for cystoscopies in children by Meredith Campbell – this work was presented in the paper to the American Society of Regional Anesthesia in 1933 [30]. The discovery of lidocaine (1943) and bupivacaine (1963) and the increasing concern about postoperative analgesia in the 1970–1980s led to the increased use of blocks [28]. After 1980, the interest in regional anesthesia in children increased, but it is still insufficiently used in clinical practice, probably due to the improvement of standards of general anesthesia, as well as insufficiently trained staff.

DEVELOPMENT OF PEDIATRIC ANESTHESIOLOGY IN SERBIA

The development of pediatric anesthesiology as a distinct specialty in Serbia was, as in the rest of the world, associated with the development of pediatric surgery. In the beginning,

the surgical problems of pediatric patients were solved by general surgeons, and the anesthesia of children was performed by the same people who performed anesthesia in adults. Dr. Dimitrije Jovčić was the first teacher of pediatric surgery at the Faculty of Medicine in Belgrade and a member of the Serbian Academy of Sciences and Arts [11]. The development of pediatric anesthesiology and intensive care was longer and more laborious because it was very difficult to find the right understanding in the medical circles, as well as due to the slow development of technology and the pharmaceutical industry. The introduction of modern methods of anesthesia and intensive care required a specialist of anesthesia. For that purpose, at the Department of Pediatric Surgery, the first specialist of anesthesiology in our country, who worked at a military hospital, Dr. Sever Kovačev, remembered as one of the doyens of our anesthesiology, was occasionally hired. He was probably the first to introduce endotracheal anesthesia in children in our country.

The following years proved crucial for the further development of pediatric anesthesia. Dr. Branka Mitrović (the first educated anesthesiologist next to prof. Predrag Lalević) is considered to be the originator of pediatric anesthesiology in our country. Firstly, she founded the Department of Anesthesiology, Reanimation and Intensive Care at the University Children's Hospital (1955), and a few years later (1965), she established the same department in the newly founded the Institute for Health Protection of Mother and Child. Several decades (1994) after the establishment of the Department at the University Children's Hospital, for the first time the Intensive Care Unit was separated as a new department.

In 1985, the first association of pediatric anesthesiologists was formed at the Section for Anesthesia and Reanimation of the Serbian Medical Society, called Pediatric Anesthesiologists Work Group (*Aktiv pedijatrijskih anesteziologa*), which for decades has regularly organized professional meetings dedicated to pediatric anesthesiology, reanimation, and intensive care [31]. Previous presidents of the Section were Prim. Dr. Aleksandar Milenković (wrote the first study guide on pediatric anesthesiology from which the residents learned), Dr. Branka Mitrović, and Prim. Dr. Božidar Mijomanović (one of the founders of the European Association of Pediatric Anesthesiologists). Today the president is Prof. Dr. Dušica Simić.

The Section of Anesthesiology with Reanimation was established for the first time at the Faculty of Medicine of the University of Belgrade (MFUB), founded by Prof. Predrag Lalević, who also designed the first specialist internship curriculum. At that time, the specialization lasted three years, and within that, two months of education for pediatric anesthesiology. The establishment of the Section at the University of Belgrade was followed by the establishment of specialist sections in Novi Sad, Niš, Kragujevac, and Priština, which had the same curriculum. Since 1990, the specialization in Anesthesiology with Reanimation lasts four years, within which four months are provided for pediatric anesthesiology.

The first professor of pediatric anesthesiology, Dr. Zvonimir Budić, from the Faculty of Medicine in Niš, was

promoted in 1997. The first professor from the University of Belgrade is Dr. Dušica Simić (since 2003). She is the author of the textbook titled "Fundamentals of Pediatric Anesthesiology," the first one approved by the Faculty of Medicine in Belgrade [14]. At the University of Novi Sad, the first professor is Biljana Drašković, who was elected in 2012. Today, at MFUB, there is (only) one full professor from the ranks of pediatric anesthesiologists and four assistant professors. At the Faculty of Medicine in Novi Sad, there is one full professor, two associate professors, and two assistant professors, while in Niš, there are two associate professors. There are no pediatric anesthesiologists at the faculties of medicine of the universities of Kragujevac and Kosovska Mitrovica. The Ministry of Health of the Republic of Serbia approved a specialization in pediatric anesthesiology in 2018 [32]. In four years since the establishment of the specialization in pediatric anesthesiology, four anesthesiologists have already been promoted to specialists, and 15 candidates enrolled for specialization.

In Serbia today, there are four specialized clinics for children's surgery and anesthesia – two in Belgrade and one each in Niš and Novi Sad, which is perhaps enough for our small country, but there are child surgical patients in other cities and smaller places as well, and specialists of pediatric anesthesia will play a crucial role in improving the outcome of surgical treatment of pediatric patients.

In the 2012–2016 period, Prof. Dr. Dušica Simić was the President of the Committee for Pediatric Anesthesia in the World Federation of Anesthesia Associations. In 2013 and 2015, pediatric anesthesiologists from Serbia participated in the two largest pediatric studies – APRICOT and NECTARINE. The first ESPA congress in Belgrade was held in 2016. In 2017, the Association of Pediatric Anesthesiologists and Intensivists of Serbia was founded by Prof. Dr. Dušica Simić.

Despite humble beginnings, with an insufficient number of pediatric anesthesiologists, today this is changing and pediatric anesthesiology is experiencing a bloom.

CONCLUSION

Today, even the smallest operation in pediatric population without anesthesia is unimaginable, primary thanks to many pioneers in this field, as well as their students who continued the further development of pediatric anesthesia. Unfortunately, it is impossible to provide a complete history of pediatric anesthesia because so many names and institutions have made us grow as a distinct specialty.

It seems that the defining issue of pediatric anesthesia in the 21st century will be how to respond to the worldwide workforce deficit in the face of the increasing demand for skilled pediatric anesthesiologists, and how to correct it.

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Историја дејче анестезије

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САЖЕТАК

Почеци педијатријске анестезијологије датирају из средине деветнаестог века, а везани су за сеоског лекара Крофорд-а Лонга (*Crawford W. Long*), који је 1842. године први пут забележио како је применио диетил-етарску анестезију на осмогодишњем дечаку. Почетком развоја савремене педијатријске анестезије сматра се 1930. година. Од тада се бележе два периода развоја. У првом периоду развијене су технике анестезије и прибор прилагођен различитим узрастима деце. У другом периоду се у свакодневну клиничку праксу уводе савремени анестетички медикаменти и мониторинг како би се што боље заштитили витални органи и њихове функције. Године 1955. основана је прва мултидисциплинарна педијатријска јединица интензивне неге у Дејчој болници у Гетеборгу у Шведској. Др Бранка Митровић се сматра

зачетником педијатријске анестезијологије у нашој земљи, јер је 1955. године основала Одељење за анестезијологију и реанимацију Универзитетске дејче болнице. Историја педијатријске регионалне анестезије почела је након њеног увођења код одраслих, што се догодило после открића кокаина, 1884. године. Министарство здравља Републике Србије је 2018. године одобрило ужу специјализацију из педијатријске анестезијологије.

Развој педијатријске анестезије је фасцинантан, јер је потпуно пратио развој дејче хирургије. Савремена педијатријска анестезијологија је потпуно спремна за задовољи потребе најсложенијих хируршких интервенција, као и лечење критично оболеле деце и тиме значајно допринесе бољим исходима лечења педијатријских хируршких пацијената.

Кључне речи: деца; дејча анестезија; историја; развој