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Review

History of Anesthesia in Belgium – VUB

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In 1970 a new Flemish university was established: the "Vrije Universiteit Brussel" or VUB. This institution arose from the split of the bilingual Université Libre de Bruxelles - Vrije Universiteit Brussel, in the aftermath of the student protest of May 1968 in France and the language struggle in Belgium. The ULB itself had been founded in 1835 as a liberal institution to counterbalance the Catholic University of Leuven, and it was initially entirely French-speaking. The first faculty to offer a Dutch-language program at the ULB was the Faculty of Law in 1935, but it took until 1963 for all faculties to offer Dutch-language programs and for the university's name to be completed as Université Libre de Bruxelles - Vrije Universiteit Brussel (ULB-VUB).

After the institutional split, however, the VUB remained faithful to the ideological foundation of the original university (ULB), namely the free inquiry, a principle enshrined in a famous quotation from the French mathematician and philosopher Henri Poincaré: "La pensée ne doit jamais se soumettre, ni à un dogme, ni à un parti, ni à une passion, ni à un intérêt, ni à une idée préconçue, ni à quoi que ce soit, si ce n'est aux faits eux-mêmes, parce que, pour elle, se soumettre, ce serait cesser d'être." (Thought must never submit to dogma, party, passion, interest, preconceived idea, or anything else, except to the facts themselves, because for thought, to submit would be to cease to exist).

When the VUB separated from the ULB-VUB, the creation of its own Dutch-speaking university hospital was also planned. This hospital was officially inaugurated in 1977, under the name Academisch Ziekenhuis Brussel (AZ-Brussel), emphasizing its scientific mission. In 1999, the name was changed to Universitair Ziekenhuis Brussel (UZ-Brussel). The hospital is located in Jette, in the northern part of Brussels.

The establishment and development of the Department of Anesthesiology at the VUB began in 1977 and has continued to the present day. This coincided with an era in which the foundations of modern anesthesia were laid. From the very beginning of AZ-Brussel, enthusiastic and dedicated physicians, already specialized in anesthesiology, were recruited. Many of them were still working in the University Hospitals affiliated with the ULB, such as Hôpital Saint-Pierre and Hôpital Brugman, both in Brussels. These collegues were eager to contribute to the development of safe anesthetic techniques and pharmacological agents.

They not only adhered to the ideological principles of the VUB, expressed in Poincaré's quotation, but they were inspired by the fundamental concept of Claude Bernard which forms the basis for modern experimental biology: scientists must systematically question established ideas and test them through rigorously designed experiments. This fundamental principle was formulated in Bernard's work "Introduction à la médecine experimentale".

However, the anesthetic activity started in 1978 on a small-scale basis as there were only four fully functioning operating rooms at the start of the hospital. These initial four operating rooms were organized, at the same site, where the actual delivery rooms are. Activity was gradually expanding, first to eight and subsequently to fourteen rooms, at the present site, well-known and existing for nearly 50 years. The expansion occurred as a result of new activity needs, compliance to authority regulations and the availability of emerging surgical treatment options.

Staff members at that time practiced anesthesia in the Brugmann Hospital, St Pieters Hospital or Bordet Hospital. They were solicited, principally, because there existed agreements dealing with the formation of VUB medical students and more specifically, in which hospital to deploy them. The agreements were signed between the

VUB and several Hospitals in the Brussels area. Next to the previously mentioned institutions, several other public assistance (OCMW) hospitals (Schaerbeek, Etterbeek, Elsene), were also taking in students from the VUB. This way staff members had teaching experience from the very start of the Academic Hospital.

The first Head of the Anesthesiology Department was Prof. Dr. Fréderic Camu. Prof Camu was trained at the Stanford University, and he was working at the time in Brugmann Hospital. Initial staff consisted of Dr. Andrée Lambin, Dr. Michel Rucquoi and Dr. Elisabeth Gepts, who was recruited from St.Pieter Hospital. Later on they were joined by Dr. Eddy Brillouet, Dr. Lieve Van Den Abeele, Dr. Jan Steppé. Dr. Wouter Govaerts and Dr. George Geldhof joined the staff one year later.

Since subspecialties weren't yet common in anesthesiology, everyone did just about everything, although everyone could still work in their preferred field of interest. For example, anesthesia for cardiac and vascular surgery was handled by Dr. Rucquoi. Dr. Steppé was primarily responsible for anesthesia in abdominal surgery. In addition, interest gradually arose in several areas of research. Dr. Rucquoi focused on the analysis of exhaled gases with mass spectrometry[1]. Dr. Gepts focused more on the pharmacokinetics of intravenous hypnotics and opioids[2]. In abdominal surgery and major vascular surgery, the practice of combining neuraxial anesthesia with general anesthesia emerged, principally to improve perioperative comfort for our patients. Our pediatric anesthesiologist at the time was Dr. Anne Van de Velde, who documented different ways for having children relaxed and cooperative for the upcoming intervention[3].

From the early years onward Prof. Camu focused on expanding patient care, organized by anesthesiologists. Post anesthesia care units at the time were mostly active only during daytime, nursing staff consisted of whoever was available in the operating rooms and extensive surgery patients were mostly referred to Intensive Care, where sometimes non-anesthesiologists were on duty. Thanks to his efforts, the anesthesiologists could rely on a permanently 24-hour available recovery unit, with at least two nursing staff dedicated to all aspects of immediate and mid-term post-surgery care. This resulted in increased and prolonged commitment by the attending anesthesiologist to all events, possibly happening after surgery. More extensive monitoring and hence increased safety were standard and therefore gathering data for study protocols became easier, more accurate and reliable. Untoward side-effects coming from new or experimental pain treatments were readily recognized and treated accordingly without delay. A net improvement as compared to standard care at the ward. Since the space occupied by the recovery ward was nearly half of that of all operating rooms together, specially conceived study hardware could remain in place untouched for prolonged periods, often extending the needed study observation time. For instance, the material used for studying expired volume/etCO2 ramps (2 m^3 space-occupying volume) could remain undisturbed for the whole 20 hour study period[4]. Likewise, laboratory hardware could stay there, to be used day and night, much to the satisfaction of our researchers.

The research efforts of Dr. Gepts, in particular, but also Prof. Camu, focused primarily on creating and applying pharmacokinetic models for alfentanil and sufentanil use. They also proposed models for etomidate and propofol, as well as for the combined administration of these agents[5,6]. From a single-compartment basic model for IV administration, work was done on a three-compartment mammary model for several products, including sufentanil and propofol. The availability of simple neuromonitors then allowed for the design of an effect compartment based on a sigmoid E-model. Because the prediction of a particular model had to be achieved through control analyses of serum concentrations of the product under investigation, intensive collaboration with the Department of Toxicology of the Pharmaceutical Sciences at the VUB was necessary. Several models have been widely accepted in the anesthesiology community and they are still used to control adapted infusion pumps. The GEPTS model for sufentanil is still available as an infusion rate selection for various syringe pumps.

Since this were the early years of propofol, and the product was adopted with great enthusiasm, the availability opened up an opportunity to study the hemodynamic effects during anesthesia, induced and maintained with propofol. Dr. Marianne Claeys, who was primarily involved in the study of postoperative pain relief in orthopedic surgery, published her findings in the British Journal of Anaesthesia in 1988[7].

Another staff member was highly successful in studying malignant hyperthermia and, in particular, in developing the caffeine test for diagnosis. Dr. Luc Heytens was a staff member under Camu when this branch of research inspired him to take various steps to identify at-risk patients. At that time, MH was considered a fatal complication during anesthesia, primarily in young patients with no apparent history[8]. The introduction of the

test became a milestone in guiding these patients safely through the procedure. The embryonic testing hardware was set up in the operating room, where the test could easily be performed in close proximity to the patient, and where it was indeed used for several years, albeit in a more elaborated manner, under the supervision of Dr. Heytens[9,10].

During the early years 90, the Anesthesiology Department started research in laboratory animals, with the help coming from Erasme Hospital. The distribution of liposomes was studied after epidural and intrathecal administration. More specifically a difference was expected between multilamellar and unilamellar liposomes within the first 24 hours after injection. A faster and more extensive systemic spread was observed after unilamellar liposomes. Multilamellar liposomes stayed more local, making them a suitable depot for epidurally administered agents[11,12].

Developing new clinical techniques in other specialties often provides the opportunity to apply and optimize adaptations in anesthesia technique. For example, our colleague Prof. Marc Noppen, while still working as a pulmonologist, made progress in the different fields of interventional pulmonology. To facilitate this, Dr. Jan D'Haese developed a total intravenous technique with high-frequency jet ventilation. This type of ventilation proved to be successful and safe for respiratory support for thoracoscopic sympathectomies[13]. The technique made it possible to use a classical ETT for thoracoscopic intervention in a day-case setting. The technique also created ideal conditions for endotracheal and bronchial interventions, such as laser treatment of tracheal or endobronchial stenoses or tumors, the implantation of tracheal stents or the insertion of bronchial valves as an alternative for lung volume reducing surgery. In this setting the pulmonologist and the anesthesiologist share the same airway.

The postoperative use of NSAIDs for analgesia and the distinction between Cox-1 and Cox-2 and their clinical consequences were the areas of study for Dr. Caroline Vanlersberghe. After a strongly elaborated review of prostaglandin synthetase inhibitors[14], new NSAIDs were thoroughly studied in terms of pharmacodynamics, efficacy, and side effects, particularly in postoperative analgesia. The importance of the Cox-2 inhibitor in pain modulation and the benefits of combining different non-opioid agents in order to minimize side-effects and potentiate pain relief were also reported[15,16].

The combination of general and neuraxial anesthesia for major abdominal procedures was introduced here by Dr. Jan Steppé[17]. Placing an epidural line for continuous perioperative and postoperative use allowed for the study of the effects and pain-free interval of various opioids, administered through the epidural line, with or without local anesthetics[18]. The various options were described by Dr. Christian Verborgh, who further studied various opiates and opioid subtypes in laboratory animals, including after intrathecal and intravenous administration[19,20]. The effects of these opiates and their respective antagonists on respiratory parameters have led to better insights into the antagonization of opioid-induced side effects.

After the retirement of Professor Camu, UZ Brussels appointed Professor Jan Poelaert as Head of Anesthesiology and Perioperative Care. Professor Poelaert had extensive experience in cardiology in intensive care and he was a renowned echocardiographer. His policy, therefore, focused on the extensive use of ultrasound, both in cardiology and for the needle trajectory in locoregional blocks. The use of invasive hemodynamic techniques, such as determining cardiac output using a pulmonary catheter, was therefore diminished in a very short time. The trend toward less invasive hemodynamic techniques had already begun, and Dr. Stefan Beckers extensively studied and refined various devices and methods for non-invasive cardiac output determination.

A fundamental change in the acceptance of propofol administration in heart rhythm surgery, was accomplished by Dr. Panagiotis Flamée. Based on previous publications, administering propofol to patients with Brugada syndrome was considered a near-error. These patients often were scared if they noticed a white substance in the handled syringe, even if told it was etomidate. Dr. Flamée demonstrated with solid studies that propofol could be administered safely to these patients. First by comparing propofol to etomidate[21] and second by evaluating induction and maintenance of propofol in a retrospective cohort analysis[22].

Late in the nineties, our pediatric anesthesia team was reinforced by Dr. Nadia Najafi. Before that time Dr. Najafi worked as a pediatrician specializing in intensive care, which she also practiced in London. Inspired by the care for critically ill children, Dr. Najafi subsequently specialized as an anesthesiologist for children and helped our pediatricians by taking care of the anesthesia for difficult diagnostic or therapeutic procedures ever since. Dr. Najafi has dedicated her life's work to the safety of anesthesia for children in special circumstances. This has enabled her to author several publications that substantially highlighted safety in anesthesia[23-25].

The favorable role of Janssens Pharmaceutica should also be mentioned, on the one hand, because they were the cradle for the development of newer opiates, such as alfentanil, sufentanil, carfentanil, and lofentanil. On the other hand, because they, also through Dr. Theo Meert who was working there at the time, made their facility available to allow a number of fellow anesthesiologists to conduct animal experiments in their area of interest, such as M. Vercauteren, M. De Kock and C. Verborgh.

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