
By

MADELINE JOLLEEN HANSEN

A Thesis Submitted to The Honors College

In Partial Fulfillment of the Bachelors degree

With Honors in

Physiology

THE UNIVERSITY OF ARIZONA

MAY 2020

Approved by:

____________________________
Dr. Zoe Cohen
Department of Physiology
# Table of Contents

Abstract ......................................................................................................................... 2

General History of Anesthesia ..................................................................................... 3-14
  Prehistoric-200AD..................................................................................................... 3-5
  200AD- 1846 (historical surgery) .............................................................................. 5-8
  1847-1992 ............................................................................................................... 9-14

Physiology of General Anesthesia ............................................................................. 14-16
  Understanding of anesthesia mechanism .................................................................. 14
  System impacts ......................................................................................................... 15-16
  Description of perioperative assessments and monitoring ...................................... 15-16

Anesthesia and Elderly ............................................................................................. 17-21
  Physiological changes with aging .......................................................................... 17-18
  Pharmacological changes with aging .................................................................... 17-18, 20
  Perioperative differences ......................................................................................... 19-21
  Looking to the future .............................................................................................. 21
  Author recommendations ......................................................................................... 21

References ................................................................................................................ 22
Abstract

Anesthesia today is known as “the controlled state of temporary loss of sensation or awareness that is induced for medical purposes.” Anesthesia has been used in America since 1846, long after surgery, and the associated pain was introduced. This thesis is a literary review of journals, books, and papers. It begins by shedding light on critical historical periods, events, and people that relate to the discovery and development of anesthesiology in order to better understand and appreciate anesthesia. I then discuss how anesthesia impacts an average person and what happens during the perioperative period for a patient. Lastly, the changes that occur during aging and how anesthetics impact the elderly will be analyzed. The main points of the paper are to provide recommendations for the elderly and their family on anesthesia care and to allow the patients to be empowered or more in control of their own care and potentially the outcomes of their surgeries.
General History of Anesthesia

Disease and pain have been around since humans were there to experience it. For much of history, humans needed to "just deal" with the pain. It was not until the 19th century when methods were developed to decrease it.

In prehistoric times (until 3000 BC), the cause of disease, both physical and mental, was believed to be the wrath of a god or gods, magic, or an evil spirit or demon that had entered the body. Therefore, treatment consisted of calming the gods, removing the magic, or removing the demon/spirit by making the ailment so uncomfortable in the host's body, that they leave. Surgery or knowledge of anatomy during this time helped with killing animals for food, first aid for wounds from animals or battle, or ritual operations, which were tests of endurance and evidence of manhood. In the latter case, anesthesia was undesirable.

Figure 1 displays a skull that has undergone trepanation, which is thought to be a prehistoric cure for illnesses such as headaches, a way for demons or spirits to leave the body, or a ritualistic right of passage. No matter the reason for undergoing trepanation, it was always done without any anesthesia or pain reliever.

During the Magico-empiric age (3000-585 BC), the great civilizations were in the Nile Valley (Egypt) and Mesopotamia. Egyptian medicine was made of two parts: magic and rational methods. Diseases were still personified and were treated with rituals, which sometimes were accompanied by drugs or herbs. Surgeries were limited to circumcision and first aid treatment of wounds and fractures. Of the many drugs that the Egyptian's used, only a few can be identified, and there is no evidence that they provided any pain-allaying effects. Depictions of surgeries always show a fully conscious patient, indicating that no anesthetics were used.
Figure 2 depicts what is considered the first brain surgery in ancient Egypt. Notice that the patient is awake and being held down (http://welcome-pharaonic-egypt.blogspot.com/2013/04/the-first-brain-surgery-in-history.html)

Mesopotamian medicine was similar to that of Egypt. Diseases were still caused by demons, and physicians were priests. Surgeries were done by craftsmen, and rewards for successful operations or punishments for unsuccessful surgeries were indicated in the code of Khammurabi. Some of the many drugs that the Mesopotamians used had therapeutic properties. Again, there was no evidence that anesthetics were available or used.

The Hebrews, developing from both previously mentioned cultures, made significant advances in hygiene, but therapeutics remained respectively primitive and magic-based, and anesthetics seem to be unused.

From around 2250-1750 BC in Babylonia, cuneiform tablets were used to treat dental decay by local application of a gum that contained seeds of henbane. It is an extreme stretch to call this the earliest record of local anesthesia. In 1500 BC, Ebers Papyrus recorded opium-like preparations used as anesthetics.

The Scientific age began in 585 BC and ended in 200 AD. This period marks the beginning of Greek science in which the history of diseases was studied, and rational treatments were instituted by physicians. Magical treatments were still practiced by priests in temples worshiping Asklepios, but the procedures here were always moving toward rational therapies. When Greece and later Egypt were conquered by the Romans, the medical center of the time shifted to Rome. The Greeks and Romans seem to have not known about anesthesia, but the soothing and pain-relieving properties of opium were used in the fourth century BC Bloodletting began in 500 BC.
Figure 3 (500 BC) and Figure 4 (Medieval times) are depictions of bloodletting, which was believed to help balance the more important of the four humors: blood. Both are presented here to see better how the practice did not change over time. (https://www.collectmedicalantiques.com/gallery/bloodletting)  
(https://timothyjreveland.com/2019/03/14/medieval-bloodletting-and-the-four-humors/)

In the first- or second-year A.D., Pedacius Dioscorides used the word anaesthesia to describe poppy and mandragora (mandrake). He uses the word in the modern sense rather than the moral sense that was used at that time.

During the age of Superstition (AD 200- 1454), the anarchical state of most of Europe led to a rapid decline in learning, the use of observations was no longer used, and religion, astrology, and alchemy all played a role against science at this time. During this period, reasonable attempts at pain relief occurred very occasionally and had no impact on humankind and played no part in the discovery of anesthesia.

The Renaissance (1454-1754) was the great cultural revival that saw the artistic and scientific advances that overthrew the old Aristotelian and Galenic systems. In 1687, the discovery of the circulatory system was published, which led to the formation of modern physiology and medicine. The most important findings that impacted anesthesia directly were the discovery of di-ethyl ether in 1540, and the experiment of drugs administered intravenously. Other notable moments were the rediscovery of local analgesia by applying cold in 1595 and 1646, but it was soon forgotten again. In 1605, Paracelsus published Paradox in which he described the action of di-ethyl ether on chickens. He states that "it quiets all suffering and relieve[s] all pain."
Figure 5 is a portrait of Paracelsus to give a face to the man that studied the impact of di-ethyl ether on chickens. He also stated that "poison is in everything, and no thing is without poison. The dosage makes it either a poison or a remedy." This idea is prevalent in medicine and especially anesthesia. (https://wellcomecollection.org/works/ugmj98c)

The word anesthesia, more specifically "anaesthesia," was first used in English in 1721, and it is presumed that the meaning then meant to indicate loss of sensation in a part of the body. It was simplified in the early 20th century.

The pre-anesthesia era is considered to be from 1754-1846. In 1800, Humphry Davy published his work that suggested that nitrous oxide could be used to help surgical operations. In 1807, Baron Larrey rediscovered refrigeration anesthesia.

In August 1810, Frances "Fanny" Burney, a well-known author of her time, depicted her firsthand account of pre-anesthesia surgery. She had developed pain in her breast, and through her royal network, she was eventually treated by several leading physicians. A year later, on September 30th, 1811, she underwent a mastectomy performed by "7 men in black". The operation was performed like a battlefield operation, under the command of M. Dubois, a midwife to Empress Marie Louise, Duchess of Parma. Burney would later describe the procedure in detail, since she was conscious through most of it, as it took place before the development of anesthetics.

Part of Fanny's letter to her sister describing her experience went as follows:

"I mounted, therefore, unbidden, the Bedstead – & M. Dubois placed me upon the Mattress, & spread a cambric handkerchief upon my face. It was transparent; however, & I saw, through it, that the Bed stead
was instantly surrounded by the 7 men & my nurse. I refused to be held; but when, Bright through the
cambric, I saw the glitter of polished Steel – I closed my eyes. I would not trust to convulsive fear the
sight of the terrible incision. Yet – when the dreadful steel was plunged into the breast – cutting through
veins – arteries – flesh – nerves – I needed no injunctions not to restrain my cries. I began a scream that
lasted intermittently during the whole time of the incision – & I almost marvel that it rings not in my Ears
still? So excruciating was the agony. When the wound was made, & the instrument was withdrawn, the
pain seemed undiminished, for the air that suddenly rushed into those delicate parts felt like a mass of
minute but sharp & forked poniards, that were tearing the edges of the wound. I concluded the operation
was over – Oh no! presently the terrible cutting was renewed – & worse than ever, to separate the bottom,
the foundation of this dreadful gland from the parts to which it adhered – Again all description would be
baffled – yet again all was not over, – Dr. Larry rested but his own hand, & – Oh heaven! – I then felt the
knife (rack)ling against the breastbone – scraping it!"

(https://www.basicincome.com/bp/surgerywithoutanaesthetic.htm)

Figure 6 portrays an alert woman undergoing a mastectomy in the early 1800s without anesthesia needing
to be held in place and supported by several men. (https://www.moorgatebooks.com/10/fanny-
burney-and-the-seven-men-in-black/)

In 1821, Recamier used hypnotism during a cauterization procedure. During 1829, Cloquet successfully
amputated a breast while his patient was under hypnosis.

Commonly, as mentioned above, surgery and pain have always been linked, but anesthesia set out to
separate the two. Surgery before anesthesia was typically performed at the last possible moment, only
when it was necessary, and executed quickly with little care toward precision due to the pain incurred and
the risk of complications. Later, research found that surgeons perform better knowing that they were not
causing pain during surgery.

Before the 1840s, the mainstream forms of "anesthesia" or helping the patient get through surgery was
with oral opium, laudanum, mandragora, hypnotism, and a generous dose of alcohol.

Although surgeons were aware of some forms of anesthesia, several unknown hurdles had to be overcome
for effective implementation. The ability to inject substances into veins, understanding concepts with
blood transfusion, and inventions for inflating lungs to aid in respiration all became crucial to surgical
success. Suspended animation was first used on animals in the 1820s by Henry Hill Hickman using Sulphuric acid and carbonate of lime, and carbonic acid gas. Henry Hickman is said to have discovered anesthesia's theoretical application, but W. T. G. Morton convinced the medical world of the success of surgical anesthesia. On October 16th, 1846, Morton etherized a patient who then had a tumor removed. The patient Gilbert Abbott said after the surgery that he felt no pain during the operation. In 1844, Horace Wells, W. T. G. Morton's former partner, used nitrous oxide for dentistry, but a tooth extraction demonstration proved unconvincing.

Dr. Morton's sulphuric ether vapor inhalation anesthetic method from the above surgery had been previously applied to his patients during quick dental procedures. At this time, known effects of this vapor included quick coughing, dilated pupils, increased or unchanged pulse, unconsciousness for about two to eight minutes, and euphoric waking sensations. Lassitude, headache, and other symptoms lasted for several hours after the vapor was used. A few months after Morton's debut surgery, he put in for a patent for his anesthetic agent, which led to a large public debate of the practicality and ethicality of patenting anesthetics.

![Figure 7 depicts Morton administering anesthesia before performing a tooth extraction as a live demonstration that anesthesia is safe for use. The demonstration is before doing his famous surgery in 1846.](https://daily.jstor.org/19th-century-anesthesia-and-the-politics-of-pain/)

While A. E. Guedel and John Snow (first physician to only practice anesthesia) are credited with assigning the stages of anesthesia. Francis Plomley published work describing the three stages in 1847 based on his personal experience with ether inhalation. He describes the first stage as a pleasurable feeling of slight intoxication. The second stage is extremely pleasurable, similar to being on nitrous oxide, also known as laughing gas. Francis states that "there exists in this stage a perfect consciousness of everything said or done" and that there is a general inability to move (Cole, 1965). While in this stage, the patient is indifferent to pain, but if the operation began in the second stage, the patient would "recover" from the ether before surgical completion. In the third stage, which is the preferred stage to perform operations in, the patient is extremely intoxicated and numb. In other words, the patient's body cannot feel pain, muscles become limp, circulation decreases, and body temperature falls. The patient is mentally in a dream state.
Figure 8 shows the faces of the three men that helped develop the field of anesthesia by better understanding the stages and effects of anesthesia. (https://www.woodlibrarymuseum.org/ebooks/item/167/the-history-of-anesthesiology-reprint-series:-part-4--signs-and-stages-of-anesthesia.)

It is believed that the first use of ether on an obstetric patient during labor in America occurred at the beginning of 1847. There are contradicting views on whether C.W. Long or James Young Simpson where the first American physician to provide their patients sulphuric ether in between contractions during labor.

During 1847, Nikolai Ivanovich Pirogoff, a well-known Russian surgeon, believed that the rectal route of ether administration would become the most common method of anesthesia administration. Through this method, the ether spread throughout the body within two to four minutes, would be independent of the will of patients, and would replace the pneumatic method which was often inconvenient and painful for patients.

Chloroform had been discovered in 1831 by Soubeiran. In late 1847, James Young Simpson pushed the use of chloroform more common because it was just as fast-acting through pulmonary inhalation as ether. However, chloroform did not have the same potent smell or require as much quantity of the chemical for the same results. Simpson found that chloroform quickly evaporated, had a fruit-like smell, and a sugary, pleasant taste. As an anesthetic, chloroform, compared to ether, requires less quantity, acts faster and more completely, more pleasant experience, more pleasant smell, more portable, and requires no special equipment. John Snow popularized the use of chloroform in obstetric anesthesia and personally administered this anesthesia to Queen Victoria during the births of her last two children.

In January 1848, the first recognized death as a result of anesthesia occurred. It was later determined that the event should have been marked in March of 1847 with the death of Ann Parkinson. While working to remove a tumor on her thigh, medical reports stated she never woke after surgery and died two days later, still in an unconscious state. This report caused a review of whether it was the anesthesia provider's fault or the ether itself to blame for her death. The further debate continued whether a provider of the ether would be answerable for death or if ether was safe enough to use with predictable results.

The first death related to the use of chloroform occurred in 1848. Hannah Greener was a 15-year-old girl who died while undergoing an operation to remove a toenail with chloroform as the anesthetic. During the autopsy, it was discovered that the inferior portions of Hannah's lungs were in a high state of congestion, and there were several emphysematous bubbles on the left lung. The cause of death was attributed to congestion of the lungs due to the inhalation of chloroform.
In 1853, Charles Gabriel Pravaz proposed the protocol of injecting a few drops of concentrated perchloride of iron into arterial vessels to coagulate blood. This process used hypodermic syringes, which were invented by Dr. Pravaz. 1853 also introduced a new method to provide medications to the body by using a hollow needle to enter medicine to or through the skin. The hollow needle was invented by Alexander Wood in 1853, but he did not publish his work until two years later. The hypodermic syringe and hollow needle are instruments that ended up being vital to medicine, surgery, and especially anesthesia.

Before 1879, intubating a patient was done through tracheotomy or laryngotomy. William Macewen changed this then common practice to today's methods of intubation through tracheal tubes by the mouth. He initially practiced on cadavers, slowly perfecting this method, which he used more to treat edema of the glottis or to keep the larynx clear rather than to provide anesthesia to patients. Macewen experimented without a laryngoscope, and tested intubating through the nose but found it to be constricting. He preferred the use of large-caliber instead of smaller sized catheters because the catheter often would get caught on the intricacies of the internal laryngeal surfaces.

In July of 1879, a tube placed in the trachea for breathing during surgery was used. Intubation occurred because the operation involved the removal of epithelioma from the pharynx to the base of the tongue. A sponge at the upper end of the larynx was used to collect the blood that was lost during the surgery so that it would not enter the trachea and cause breathing issues. The tube allowed for continuous administration of chloroform and for the respiration rate to be measured throughout the surgery. The operation had no complications and showed that the tube could be used to administer chloroform in an easy, uniform, and uninterrupted manner. The procedure also demonstrated that chloroform could be delivered and have no impact on the outcome or performance of surgery.

In 1884, the use of topical cocaine as an anesthetic was first studied on the eye by Carl Koller. R.J. Hall and William Stewart Halsted. That same year, they examined how cocaine could be used as an anesthetic on deeper structures in the body, a process that is now referred to as "conduction anesthesia." Four years later, the first spinal-epidural block using cocaine was performed by accident by James Leonard Corning. However, the credit of the first surgery to use spinal anesthesia is often given to August Bier, Theodore Tuffer, Rudolph Matas, Dudley Tait, or Guido Caglieri, whose various operations occurred about fourteen years after Corning's. In these surgeries, the epidural anesthesia were subarachnoid injections. Spinal blocks often come with side effects that include chill, fever, nausea, and occipital headache.

In 1897, George W Crile produced a new surgical anesthetic method of injecting cocaine into the nerve trunk that supplies an injured area. This method was named blocking and evolved into a nerve block. This discovery was significant because general anesthesia did not stop the afferent systems impulses, which often lead to shock in the patient.

In 1900, M.A. Sicard and Fernand Cathelin separately published research on extradural injections of cocaine through the sacrococcygeal route for medicinal purposes. This method was found to have a relatively painless injection, requiring no bed rest after, and none of the side effects that occurred in the subarachnoid method. Its primary purpose was to relieve nerve pain in the lower extremities that occurred with things like surgery, delivery, or chronic pain.
In 1911, Georg Hirschel achieved the first successful brachial plexus block, which is used for operations of the upper extremity. The anesthesia used is a 2% solution of procaine with about two drops of epinephrine. Previous attempts to accomplish this by other surgeons involved exposing the nerve trunk to apply the anesthesia. Hirschel's method interrupts the plexus by blocking it in the axilla. At the same time, D. Kulenkampff had discovered a better approach to the plexus than Hirschel's, and this is the technique that is still used today. His method involves injecting the anesthesia where the plexus emerges, lateral to the subclavian artery and lies on the first rib. Kulenkampff performed the block on himself and believed the procedure to be safe and easy to do after a few trials.

Figure 9 illustrates the Kulenkampff method, and from this, it is easily understood how he could have performed this method on himself. (http://www.noranaes.org/logbook/resources/Ebooks/Miller1/Miller%20-%20Anesthesia%206th%20Ed/das/book/body/0/1255/I10.html)

In 1919, Stanley P. Reimann and Fred L. Hartman were the first scientists to publish about the effects that anesthesia and operations have on specific metabolites. They found that small changes in metabolism occur while under anesthesia. These changes included a decrease in bicarbonate in blood plasma.

In 1923, research on ethylene as a gas anesthetic that started in 1908 was completed and published by Arno B. Luckhardt and J.B. Carter. The gas was invented in 1849 by Thomas Nunneley, who believed that it did not make a decent anesthetic agent. The agent was found to provide a deeper plane of anesthetic but had an unpleasant odor and was flammable. Luckhardt and Carter saw that in proper concentration with oxygen, ethylene had excellent anesthetic properties. Subsequent experiments on humans showed
little to no ill effects. Surgeons felt that the agent was a good or very satisfactory anesthetic that gave better relaxation to the patient's body than nitrous oxide, and this allowed for better manipulation.

After 2.5 years of research and literature review, Ralph M. Waters concluded in 1926 that total rebreathing (filtering carbon dioxide out inhalation anesthesia) of nitrous oxide and other anesthetic drugs could reduce damage to the patient, and significantly decrease the cost of anesthesia. This method also protects the surgical and anesthesia teams and allows for better control of volatile drugs. A rebreathing apparatus ("To and Fro" system) can be used in all closed mouth operations no matter the length of the surgery and is not a difficult technique, the critical points being that the system is air-tight and careful maintenance of the oxygen supply, more economical, smaller size and weight.

Figure 10 shows one of Ralph Water's drawings of his total rebreathing apparatus and the final physical outcome.

(https://www.researchgate.net/publication/323828907_Towards_Quantitative_Totally_Closed-Circuit_Anesthesia_-_Development_over_a_100-year_Period)

About seventy-five years after Morton's demonstration, Howard W. Haggard, a physiologist, published his thorough study of ether in the human body. During his career, he concluded that there were many benefits of using carbon dioxide and is connected to the "HH" inhaler and "carbogen," a mixture of carbon dioxide and oxygen, which is often used to treat asphyxia. In his paper, Haggard discusses the absorption, distribution, and elimination of ethyl ether in the body. He explained the importance of rapid induction of ether anesthesia by increasing respiratory volume, which in turn reduces pulmonary irritation from ether. Prolonged use of ether was also found to be undesirable because of pulmonary irritation due to ether inhalation that increases proportionally with the increase in concentration.

In 1929, G.H.W Lucas and V.E. Henderson published an article about the new anesthetic of the time: cyclopropane. Cyclopropane is a flexible gas, affording rapid induction and emergence, quiet respiration. It also allows little to no blood pressure fall, and little to no nausea; however, it can be toxic to the heart. Cyclopropane at this time was only tested on animals.

A year later, Chauncey D. Leake and Mei-Yü published an article about their research about vinyl ether/oxide, which is often referred to just as "oxide." It was shown to have a similar partition coefficient and anesthetic effects as di-ethyl ether.
Five years after the preliminary studying of cyclopropane on animals, John A. Stiles with W.B. Neff, E.A. Rovenstine, and R.M. Waters introduced cyclopropane into clinical studies. These studies showed no unfavorable complications that were any worse than the current anesthetics that were being used on the general public.

1934 was also the year that two new thiobarbiturates were created to be used as intravenous anesthesia. The leading researcher of this movement was John S. Lundy.

In 1939, William T. Lemmon presented his soon to be published research on a method for continuous spinal anesthesia which uses procaine (Novocain). This method is beneficial in surgeries like gastrectomy, colon resections, and pelvic operations, to name a few.

In 1942, Harold R. Griffith and G. Enid Johnson published their research on curare, which paralyzes muscles. Curare is given intravenously, allowing anesthesiologists to produce muscle relaxation at will, more efficiently, and more safely than ever before.

The next step in anesthesia occurred in 1956 with the introduction of halothane into clinical practice. This development was the first time that drug companies were the originators of advancements in the field of anesthesia drugs. Halothane was first synthesized in 1951 by Imperial Chemical Industries and underwent pharmacology studies by James Raventós over the next four years.

Postwar years lead to many intravenous anesthetic agents such as hydroxydione (1955), propanidid (1966), gamma-hydroxybutyric acid (1960), and Althesin (1971). Most of these drugs did not survive and are not in common use. Time led to the natural evolution of intravenous anesthesia and the development of the agents available at the end of the twentieth century. An example of one of the surviving drugs from this time is thiopentone.

The sixties- introduced methoxyflurane and enflurane into the field of anesthesia drugs. Methoxyflurane had an unpleasant smell but was non-explosive, non-flammable, and was a good analgesic; however, it was metabolized to fluoride, which is toxic to the kidneys. Therefore, this drug could cause high output renal failure. Enflurane leads to the discovery of its isomer, isoflurane. Isoflurane was discovered in 1963 but was not used clinically until 1971. It was accused of causing malignancies or tumors. This accusation was eventually refuted and was subsequently a huge success with minimal vital side-effects.

Etomidate was first synthesized in 1971 and was first used clinically two years later. This agent had the advantage over barbiturates that it did not cause depression of the circulatory system. It was found in 1983 that continuous infusion of etomidate did cause decreased adrenal function.

Propofol was first reported in 1977. This drug has become a famous anesthetic induction agent and led to the development of total intravenous anesthesia in the 1980s. Propofol is relatively safe, has some antiemetic properties, and has a quick offset. Another pro of this agent is it suppresses the laryngeal reflex.

Fentanyl and alfentanil were first used in 1981 and were preferred because their swiftness of onset and duration of use matched a wide range of surgical procedures.
In the 1980s, total intravenous anesthesia gained popularity because propofol and automated infusion programs were written to control their administration.

Desflurane was first used clinically in 1987 and is used for general anesthesia maintenance.

Pregnenolone or eltanolone was synthesized in 1992 and was found to have a high therapeutic ratio and cardiovascular stability. It is still used to this day.

No matter the year, anesthesia and the development of this field has been compared to the most humane discovery the world has ever known.

**Physiology of General Anesthesia**

The general inhaled or volatile anesthetics used today are nitrous oxide, isoflurane, sevoflurane, desflurane, and halothane. The mechanisms of action are not fully understood; however, there are key points that are known. The mechanism is likely at the pre- and/or postsynaptic ligand-gated channels (lipophilic sites) and causes an inhibitory effect of GABA (gamma-aminobutyric acid) at the GABA sub A receptors (Fig below). In mice studies, the alpha1 subunit was deemed responsible for amnesia and sedation, and the alpha 2 subunit was for anxiolysis. Anesthetic agents interrupt or block information processing and memory establishment. Lastly, anesthetics inhibit transmission at excitatory N-methyl-D-Aspartate (NMDA) receptors. Ideal volatile anesthetic agents are agents that are non-toxic, non-allergenic, do not trigger malignant hyperthermia (which is the fast increase in body temperature and severe muscle contractions when given general anesthesia), stable in storage, non-flammable, low blood/gas coefficient, low oil/gas coefficient, CVS stable, does not cause decreased respiration, non-irritant, inexpensive, and no reaction with breathing circuit/ soda lime.

Today's Intravenous anesthetics are thiopental, propofol, etomidate, ketamine, and midazolam. These drugs are used to induce and maintain anesthesia, sedation, and operations with local anesthesia. Intravenous medications are also believed to have a mechanism of action involving either the GABA or NDMA receptors. This technique is technically more challenging to perform but can be an advantage for specific patients like patients with a risk of malignant hyperthermia.
Anesthesia generally affects the central nervous system, respiratory system, the cardiovascular system, skeletal muscle, and basal metabolic rate. Many anesthetic agents reduce myocardial contractility causing myocardial depression, reduce systematic vascular resistance, and change heart rate. All agents produce a net hypotensive effect on the CVS. The respiratory system is affected because the agents reduce the tidal volume and increase respiratory rate causing reduced alveolar minute ventilation. The respiratory system's ability to respond to hypoxia and hypercarbia is diminished. These agents also produce reduced muscle tone and decreased basal metabolic rate. Many anesthetic agents cause a dose-dependent decrease in cerebral activity, which is seen by lower levels of consciousness and EEG activity. Oxygen consumption is also reduced, and cerebral blood flow increases, leading to an increase in intracranial pressure.

The autonomic control of body temperature is also impacted by anesthesia. Meaning that the hypothalamus's control is altered so that heat-conserving measures are implemented at lower temperatures, and processes regulating heat-loss are started at a higher temperature. All of the volatile anesthetics used today can trigger malignant hyperthermia. During anesthesia, there are three phases of heat loss: 1. Redistribution in which heat moves away from the core to periphery with no net body temperature change in the first hour, 2. Linear in which heat loss is greater than heat production, and 3. Plateau in which heat production equals heat loss.

During surgery, anesthesiologists monitor the patient's blood oxygenation, heart's electrical activity, temperature, gas analysis (assessment of the gas that's delivered to and taken from the patient), blood pressure, cardiac output, end-tidal CO2, airway pressure, central venous pressure, and blood volume. Maintenance of fluids and balanced electrolytes are also monitored perioperatively. This monitoring occurs because anesthetics impact these physiological systems.

A risk assessment by an anesthesiologist is usually done by the American Society of Anesthesiologists (ASA) grading system (Table 1). However, other tests include POSSUM (physiology and operative severity score for enumeration of morbidity and mortality), APACHE (acute physiology and chronic health evaluation) and various tests specifically for cardiac risk, since cardiac events during a surgical procedure are not uncommon.
Table 1: ASA Grading, which rates the patient's pre-anesthesia co-morbidities. (Stone)

<table>
<thead>
<tr>
<th>ASA grade</th>
<th>Definition</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>A normal healthy patient</td>
<td>Well-controlled hypertension, asthma</td>
</tr>
<tr>
<td>II</td>
<td>A patient with mild systemic disease</td>
<td>Controlled CHF, stable angina</td>
</tr>
<tr>
<td>III</td>
<td>A patient with severe systemic disease</td>
<td>Unstable angina, symptomatic COPD,</td>
</tr>
<tr>
<td>IV</td>
<td>A patient with severe systemic disease that is a constant threat to life</td>
<td>symptomatic CHF, multifocal failure,</td>
</tr>
<tr>
<td>V</td>
<td>A moribund patient who is not expected to survive without the operation</td>
<td>sepsis syndrome with haemodynamic</td>
</tr>
<tr>
<td>VI</td>
<td>A declared brain-dead patient whose organs are being removed for donor</td>
<td>instability</td>
</tr>
</tbody>
</table>

Emergencies are followed by the letter E.
CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease.

Preoperative assessments include a general medical evaluation for cardiac disease, respiratory disease, GI disease, renal disease, central nervous system disease, musculoskeletal disease, endocrine disease, hepatic disease, medications, non-prescription drugs, herbal remedies, allergies, smoking/vaping, tobacco, alcohol, and recreational drugs usage. Areas specifically important for anesthesia are the airways, past anesthesia history, and family history. Red flags from a patient's history for potentially having problems intubating a patient are as follows: documented difficulties with airway management, cervical spine problems, previous surgery, ankylosis, trauma/infection to the airway, past scarring of the head/neck, and temporomandibular joint dysfunction. For a large number of diseases, the patient's perioperative level of control of the disease must be known. When the patient had their last meal is vital to know because it can impact the induction technique. On visual examination, risks for difficult tracheal intubation are poor mouth opening, missing or loose teeth, cervical range of motion, obesity, inability to protrude the mandible, and receding mandible. It is important to discuss past anesthetic problems and family history of malignant hyperthermia.

Preoperative tests commonly include a full blood count, coagulation screen, electrolytes and urea, urinalysis, ECG, and chest x-ray. More recently, more trials have started to be performed on patients at risk for abnormalities that would change management or act as a baseline for likely changes. At-risk patients and patients undergoing major surgery will also likely receive liver function tests, respiratory function tests, arterial blood gas analysis, and cardiac echocardiography or other imaging to determine heart function.

Perioperatively, all medications are continued except drugs that impact coagulation, hypoglycemics, and some hypotensive medicines such as ACE inhibitors. Drugs that impact coagulation might be stopped, changed for a lower dose, or substituted for heparin, depending on the patient. Generally, diabetic patients will be taken off their long-acting insulin and will be given short-acting IV insulin instead.

Postoperative concerns that are an anesthesiologist's responsibility are nausea/vomiting, pain, and hemodynamic stability. They also are concerned about a patient's airway and level of consciousness.

Overall, the core of anesthesia is the ABCs, as known as airway, breathing, and circulation.
Anesthesia and Elderly

Aging is a gradual, additive process of deteriorations and damage to the body. DNA, proteins, and lipids are always under attack. Functional reserve is how much organ function can increase above the necessary level for essential activity. Functional reserve peaks at about 30 and gradually decreases for several decades, then takes a rapid decline starting at about 80. Interestingly, the older a person gets, the less likely their age reflects their physiological status or functional reserve. Anesthesiologists need to measure the patient's reserve, which is often done with an informal observational assessment of subcutaneous tissue, slowed or an unsteady walk, stooped body habitus, and minimal muscle mass. Diminished mental activity is also a risk for postoperative delirium.

Figure 11 is a graph that represents the age of a patient versus organ function depicting functional reserve with age (https://www.semanticscholar.org/paper/Medical-management-of-hip-fracture.-Aur%C3%B3n-G%C3%B3mez-Michota/8c4cdffdaa22c524b45a2abb2af8198e7a917f74/figure/0).

The physiological changes that occur as we age impacts every bodily system. Basal metabolism decreases with age, which accounted for by a slow decrease in skeletal muscle mass and an increase in body fat. The total water in the body and plasma albumin also decreases. Liver size decreases, which accounts for a reduction of liver blood flow. Renal cortical mass decreases, but more importantly, almost half of glomeruli are lost by the age of 80. Therefore, fluid and electrolyte homeostasis are more vulnerable in elderly patients, especially when eating and drinking often become more difficult.

Concerning the central nervous system and aging, the mass of the brain decreases gradually, starting at about 50 years old. Neurotransmitter functions suffer more significantly, including serotonin, dopamine, acetylcholine system, and GABA. For many intravenous anesthetics, the same brain concentration produces about double the effect in an older person compared to a young adult.

With aging individuals, the cardiovascular system sees a decreased response to receptor stimulation, a stiffening of the myocardium, arteries, and veins, increased sympathetic nervous system activity, conduction system changes, and defective ischemic preconditioning.

Respiratory system changes with aging are stiffening of the chest wall, and the elasticity of the lung parenchyma decreases. Alveolar surface area decreases with age. These changes all contribute to a decline in resting partial pressure of oxygen in arterial blood. The changes in the nervous system with aging also
impacts the respiratory system by causing a decrease in the ventilatory response to hypercapnia and hypoxia. Older people have an increased risk of upper airway obstruction due to loss of muscle tone. Elderly individuals are susceptible to hyperthermia, most likely because aging can impact vasoconstriction and shivering response.

![Visual summary of changes to the body that occur with aging. (Stone)](image)

Some key pharmacological changes with aging are as follows. With aging, there is a decrease in drug metabolism. This is in part because of a reduction in clearance and an increase in body fat.
Table 2: Summarized table of the effects that aging has on drug dosing and other comments about these specific drugs. (Barash)

During the perioperative period, elderly patients are at an increased risk of complications, which is reflected in comorbid diseases and decrease functional reserve with aging. Cardiovascular and pulmonary system complications have the highest perioperative mortality.

Preoperative visits with an anesthesiology team are essential, but in many ways, it is more important for elderly patients. As stated before, this visit will include a detailed review of the patient's medical history, current functional status of organs, and medication list. A mini-mental state examination should be done to compare with after surgery. Important issues that are more prevalent in this age range should be raised with elderly patients. This could include whether the patient's living situation can provide the support the patient needs for a successful recovery. Other areas of concern and conversation should consist of dehydration, malnutrition, and elder abuse. The nutrition status of a patient is an underappreciated risk factor for surgery. It should be mentioned that elderly patients might take a longer time to return to the preoperative level of function.

During operation, a closer level of management is required for elderly patients. The induction of general anesthesia for elderly patients requires a smaller dose than for younger patients. General and neuraxial (not discussed in the paper) anesthesia causes a significant decrease in systemic BP. Currently, there is no

<table>
<thead>
<tr>
<th>Drug</th>
<th>Bollus Administration</th>
<th>Multiple Boluses or Infusion</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propofol</td>
<td>20-60% reduction</td>
<td>50% reduction</td>
<td>Possible increased brain sensitivity</td>
</tr>
<tr>
<td></td>
<td>Dose on lean body mass (1 mg/kg in very old patients)</td>
<td>Infusions beyond 50 min progressively increase the time required to decrease the blood level by 50% (but effect site levels may decrease faster in elderly patients)</td>
<td>Decreased V&lt;sub&gt;ss&lt;/sub&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Slowed redistribution</td>
</tr>
<tr>
<td>Thiopental</td>
<td>20% reduction</td>
<td>20% reduction</td>
<td>Decreased V&lt;sub&gt;ss&lt;/sub&gt;</td>
</tr>
<tr>
<td>Etomidate</td>
<td>23-50% reduction</td>
<td></td>
<td>Slowed redistribution</td>
</tr>
<tr>
<td>Midazolam</td>
<td>Compared to age 20, modest reduction at age 60, 75% reduction at age 90 years</td>
<td>Similar to bolus</td>
<td>Increased brain sensitivity</td>
</tr>
<tr>
<td>Morphine</td>
<td>Probably 50% reduction</td>
<td>Long effect site equilibration time translates into a very slow reduction in the effect on termination of the infusion (4 h for 50% reduction)</td>
<td>Metabolic morphine-6-gluconide buildup requires prolonged morphine use, but its renal excretion makes it very long lasting</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>50% reduction</td>
<td>50% reduction</td>
<td>Increased brain sensitivity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Minimal change in pharmacokinetics Delayed absorption from fentanyl patch</td>
</tr>
<tr>
<td>Alfentanil</td>
<td>50% reduction</td>
<td>50% reduction</td>
<td>Probably increased brain sensitivity</td>
</tr>
<tr>
<td>Sufentanil</td>
<td>50% reduction</td>
<td>50% reduction</td>
<td>Minimal changes in pharmacokinetics Slighter blood-brain equilibration, suggesting slower onset and offset</td>
</tr>
<tr>
<td>Ramifentan</td>
<td>50% reduction</td>
<td>50% reduction</td>
<td>Modest decreased V&lt;sub&gt;ss&lt;/sub&gt;</td>
</tr>
<tr>
<td>Meperidine</td>
<td>Used only for postopera- tine sedation</td>
<td>Do not use</td>
<td>Toxic metabolite normeperidine whose renal excretion decreases with age</td>
</tr>
<tr>
<td>Vecuronium</td>
<td>Slower onset</td>
<td>Slower recovery</td>
<td>Older age severely disables metabolic half-time</td>
</tr>
<tr>
<td>Cisatracurium</td>
<td>Slower onset</td>
<td>No significant changes with age</td>
<td>Liver metabolism slightly greater than renal metabolism</td>
</tr>
<tr>
<td>Rocuronium</td>
<td>Minimally slower onset</td>
<td></td>
<td>Modest increase in metabolic half-time</td>
</tr>
<tr>
<td>Succinylcholine</td>
<td>Slower onset</td>
<td></td>
<td>Modest increase in metabolic half-time</td>
</tr>
<tr>
<td>Ketamine</td>
<td>Similar dosing and onset</td>
<td></td>
<td>Hepatic elimination</td>
</tr>
<tr>
<td>Nesiritidine</td>
<td>Despite pharmacokinetic changes, some studies indicate the need for an increased dose with age</td>
<td></td>
<td>Modest increase in metabolic half-time</td>
</tr>
</tbody>
</table>

V<sub>ss</sub> = central volume of distribution or initial volume of distribution; a smaller V<sub>ss</sub> increases initial plasma levels and enhances transfer of drug to the target organ (brain, muscle).
Evidence that major or minor brief changes in blood pressure can have adverse effects on the patient. Regional anesthesia is sometimes harder to use because hypotension might impact drug treatment, and calcification of ligaments might make positioning difficult.

Immediate postoperative care is no different in younger patients vs. elderly patients. Interestingly, elderly patients seem to under-report their pain level. The adverse outcomes of failure to achieve adequate levels of pain relief are sleep deprivation, impairment of the respiratory system, ileus, suboptimal movement, insulin resistance, tachycardia, and systemic hypertension. Attention should also be paid to fluid management, antibiotics because of decreased immune function, anticoagulation, and oxygen therapy. Postoperative delirium often goes undetected in older patients.

Postoperative delirium is a sudden onset of an acute state of confusion and with varying levels of attention and cognitive skill, which lasts a few hours or days. The risk for elderly patients to have postoperative delirium is about 10%, and the risk level varies with the surgery type. The incident rate of postoperative delirium after hip surgery is the highest at about 35%. The choice of regional anesthesia vs. general anesthesia as a risk factor or if anesthesia is a risk factor still being researched. The highest risk factors in elderly patients for delirium are age, baseline low cognitive function, use of drugs, sleep deprivation, depression, general debility (dehydration, auditory/visual impairment), unfamiliar environment, and postop pain.

Table 3: Summaries table of the above information on the causes of postoperative delirium with specific examples. (Stone)

<table>
<thead>
<tr>
<th>Cause</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections</td>
<td>Urinary tract infection</td>
</tr>
<tr>
<td>Drugs</td>
<td>Opioids, benzodiazepines, anticholinergics</td>
</tr>
<tr>
<td>Drug / substance withdrawal</td>
<td>Alcohol</td>
</tr>
<tr>
<td>Metabolic</td>
<td>Disturbances of sodium, calcium and glucose homeostasis</td>
</tr>
<tr>
<td>Hypoxia</td>
<td>Chest infection</td>
</tr>
<tr>
<td>Sensory withdrawal</td>
<td>Loss of glasses, hearing aide</td>
</tr>
</tbody>
</table>

Table 3: Summaries table of the above information on the causes of postoperative delirium with specific examples. (Stone)

<table>
<thead>
<tr>
<th>Low risk medications</th>
<th>High risk medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticonvulsants</td>
<td>Sedative-hypnotics</td>
</tr>
<tr>
<td>Carbamazepine, phenytoin, valproate</td>
<td>Benzodiazepines: Alprazolam, diazepam, lorazepam, midazolam, others: Zolpidem, zaleplon, alcohol, propofol</td>
</tr>
<tr>
<td>Antiarhythmics</td>
<td>Dopamine agonists</td>
</tr>
<tr>
<td>Beta-blockers, clonidine, digoxin</td>
<td>Amantadine, levodopa, bromocriptine pergolide, ropinirole, pramipexole</td>
</tr>
<tr>
<td>Antiinfectives</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td>Acyclovir, amphotericin B, lioheoloid, aminoglycosides, cephalosporins,</td>
<td>Hydrocortisone, prednisolone, methylprednisolone, dexamethasone</td>
</tr>
<tr>
<td>fluoroquinolocides, macrolides, penicillin, sulfonamides</td>
<td>Antiepileptics</td>
</tr>
<tr>
<td>Gastrointestinal agents</td>
<td>Atropine, benztropine, diphenhydramine, scopolamine</td>
</tr>
<tr>
<td>Histamine-2-receptor antagonists</td>
<td>Analgesics</td>
</tr>
<tr>
<td>Antiemetics-pronethazine</td>
<td>Opioids - meperidine, NSAIDs</td>
</tr>
<tr>
<td>Skeletal muscle relaxants</td>
<td>Antidepressants</td>
</tr>
<tr>
<td>Baclofen, cyclobenzaprine, tizanidine</td>
<td>Mirtazapine, selective serotonin reuptake inhibitors</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Tricyclic antidepressants-amitryptiline, doxepin, imipramine</td>
</tr>
<tr>
<td>First-generation-chlorpromazine, thioridazine</td>
<td>NSAIDs = Nonsteroidal anti-inflammatory drugs</td>
</tr>
<tr>
<td>Second-generation-diazapine</td>
<td></td>
</tr>
<tr>
<td>Other drugs with anticholinergic properties</td>
<td></td>
</tr>
<tr>
<td>Antihistamines: Cyproheptadine, hydroxyzine diphenhydramine</td>
<td></td>
</tr>
<tr>
<td>Antimuscarinics: Oxybutynin, tolterodine</td>
<td></td>
</tr>
<tr>
<td>Poly-pharmacy – using ≥ 5 medications increases risk of delirium</td>
<td></td>
</tr>
</tbody>
</table>

Figure 12: Chart of medications that are prone to increase the risk of postoperative delirium. (Reddy)
Postoperative cognitive dysfunction is a long-term reduction in mental abilities after surgery. It might be caused by cerebral emboli or metabolic disturbances. Research is still being done if anesthesia plays a role. Risk factors include age, history of stroke, lower levels of education, infections, extended operations, and poor pre-existing cognitive function.

After conducting a literary review, it remains unknown whether perioperative stress and medical co-morbidities are related more to postoperative cognitive decline. It is understood that light sedation with regional anesthesia for geriatric patients undergoing hip fracture surgery is better for cognitive outcomes.

Looking to the future of anesthesia and the elderly, improvements in surgical and anesthesia techniques that reduce stress to the patient's body will allow older and sicker patients to get more surgeries. Improved pain management without immediately prescribing opioids would be helpful. The most important issues moving forward are preventing postoperative delirium, cognitive decline, respiratory failure, and pneumonia. As well as long-term studies on the impact of anesthesia on postoperative delirium and postoperative cognitive dysfunction. Overall, identifying the optimal anesthesia care for elderly patients will lead to decreased complications, which will contribute to better outcomes.

It is estimated that by 2050, the elderly will make up 20% of the population. Therefore, we must give them proper care and continue to learn about how anesthesia impacts this population differently. To better care for the elderly, it is recommended that one person is marked as their advocate and is prepared to answer and ask questions to the anesthesia team. In 1983 a list of "Ten Commandments for Effective Consultations" was created, but they can be adapted here to create a good template for both sides of an anesthesia consultation to take part in. These included the following: determine the question asked, gather primary data, establish the urgency of the consultation, communicate as briefly as appropriate, understand one's role in the process, make specific recommendations, provide contingency plans, offer/ask for educational information, communicate recommendations directly, and provide appropriate follow-up. The author recommends that an organized binder or file is made to better track an elderly patient's medical history at home with an emphasis on the areas discussed earlier on average and elderly patient preoperative assessments. A note of cognitive decline after surgery and what anesthetics were used should be told during this assessment to better prepare the anesthesia team.

This author hopes that the information in this paper has shed light on the journey that anesthesia has taken, how anesthetics impacts the average person, and how to better care for elderly patients who are undergoing surgery.
References


Lester, Laeben. "Anesthetic Considerations for Common Procedures in Geriatric Patients."


