Thyroid surgery before the technological revolution: from Samuel Gross' "torrents of blood" to Paolo Miccoli's video-assisted thyroidectomy

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Abstract. "Can the thyroid gland...be removed with a reasonable hope of saving the patient?...If a surgeon should be so foolhardy as to undertake it...every step he takes will be followed by a torrent of blood, and lucky will it be for him if his victim live long enough to enable him to finish his horrid butchery...no honest and sensible surgeon would ever engage in it". With this renowned posthumous declaration, in 1886, Samuel D. Gross proposed that thyroid surgery should have been abandoned by surgeons. Despite this, subsequent improvements in anesthesiology, antisepsis strategies and better surgical instruments allowed to significantly decrease the mortality rates of this surgery to nearly zero percent, as is the case now. This paper aims at highlighting the most important steps and Mentors that led thyroid surgery to become one of the safest and most widespread surgical procedures.

Key words: thyroid surgery, Samuel D. Gross, Paolo Miccoli, Theodor Kocher, Theodor Billroth, minimally-invasive veideo-assisted thyroidectomy, MIVAT

Can you imagine how a person living before the first half of the nineteenth century could survive a giant-size thyroid goiter, or how he/she might be treated to avoid suffocation or strangling? The existence of goiter has been described since very early in recorded history. An enlargement of the neck was already reported in Chinese populations as far back as 2700 BC (1). Due to the widespread incidence of this disease, which is related to the low iodine content in the environment, goitrous people have long been depicted in drawings all over the world. Since goiter is an active and progressive disease, it is reasonable to assume that people with goiter reaching a certain age would likely display serious and life-threatening compressive complications from the significantly bulky disease.

So, back to our initial questions. How could doctors in the early ages deal with this sort of life-threatening problem? At a time when anesthesia did not exist, how could the primitive surgeon deal with a

giant-sized, highly vascularized thyroid gland, a fully awake patient, and no electrocautery or proper surgical instruments designed to control bleeding?

The answer to these questions can now be found by looking back at centuries of surgical history.

Despite the well-known incidence of thyroid diseases, and the description of clearly-defined physiopathologic effects of the gland, the thyroid was not described in great detail until the XVI century, in the works of Andreas Vesalius (1514-1564) and Bartolomeus Eustachius (1520-1547). The latter was the first to use the term "isthmus" for the bridge that connects the two lobes of the gland. The gland itself was described by its Latin name ("glandulam thyroideam") only after the works of Thomas Warton (1614-1673), although he misinterpreted its role, and in his work "Adenographia", he was unable to distinguish the gland from the maxillary glands (1). Iconographically, the first anatomical representation of the thyroid was

the one drawn by Leonardo da Vinci (1452-1519), that was depicted in a sketch currently hosted in the Royal Library, which was drawn around the year 1500 (https://www.rct.uk/collection/themes/publications/leonardo-da-vinci-the-mechanics-of-man): the Italian genius was nevertheless far from reality in his interpretation of its correct role in the human body (2).

Thyroidectomy before the nineteenth century

From a surgical point of view, some treatments to remove life-threatening bulky thyroid glands in cases of impending death due to compressive symptoms were carried out, most of which ended with distressing results in terms of intraoperative mortality. Among the primitive descriptions of thyroidectomies, we must cite the work of the Arabic surgeon Albucasis (936-1013) who performed surgery on opium-sedated patients with the help of a bag tied around their neck to collect the blood flowing from the incision. We must also mention the "noncutting operation" performed by Ruggero Frugardo (1140-1195) of the Salernitan Medical School, that included the use of setons, hot irons and caustic powders (all of which were used on the neck of an awake patient!). These techniques, together with others that were attempted in patients who were suffocating from large thyroid masses, were burdened by a degree of mortality that was not tolerable by the medical and surgical arts (2, 3). Operations on the thyroid were therefore long banned in several countries, and a report exists of a French surgeon who was imprisoned in 1646 (evidently after an "ante-litteram" litigation) for having performed a thyroidectomy in a patient who died immediately afterwards (3, 4).

The first description of a successful partial thyroidectomy dates back to 1791, and is attributed to Pierre-Joseph Desault (1738-1795) (5). Nevertheless, until 1850, the vast majority of surgical procedures performed on the thyroid proved to be either ineffective in managing the disease (e.g. ligature of the vessels of the superior pole, enucleations of the nodules, debulking of any sort) or burdened with a mortality rate as high as 50% (when more extensive procedures were attempted). The thyroid patient undergoing unfortunate surgery usually died of massive and uncontrollable

bleeding or of acute asphyxia, while the luckier ones who survived the procedure usually died of other late complications such as infections or embolism (3,6).

These appalling results contributed to the idea, which was shared by many famous and skilled surgeons, that surgery of the thyroid was "not to be ventured upon" (7). In 1886, after his death, a statement by the American surgeon Samuel D. Gross (1805-1884) was reported: "Can the thyroid gland...be removed with a reasonable hope of saving the patient?...If a surgeon should be so foolhardy as to undertake it...every step he takes will be followed by a torrent of blood, and lucky will it be for him if his victim live long enough to enable him to finish his horrid butchery", concluding that "...no honest and sensible surgeon would ever engage in it" (3). This publication appeared, at that point, very late, since thyroid surgery in Europe was quickly changing...

"Modern" thyroid surgery: the impact of the German-speaking European school

The most important steps that led to the incredibly fast progression of thyroid surgery started in the 19th century, immediately after the posthumous statements from otherwise memorable surgeons: the introduction of anesthesia, the description and introduction of an antiseptic technique (Joseph Lister, 1867), and the introduction of surgical instruments designed to control bleeding (introduced in 1879 in Europe, much later in the US) (3,6,8-10).

Europe, and, more precisely, German-speaking countries such as Germany and Switzerland, were the core of the revolutionary development of thyroid surgery, mainly thanks to Theodor Billroth (1829- 1894) (Fig. 1) and Emil Theodor Kocher (1841-1917) (Fig. 2), two surgeons who hugely contributed to the improvements of modern surgery.

Emil Theodor Kocher and his impressive impact on mortality

Kocher held the chair of surgery in Bern, Switzerland from 1872 to 1917 (the year he died) and con-

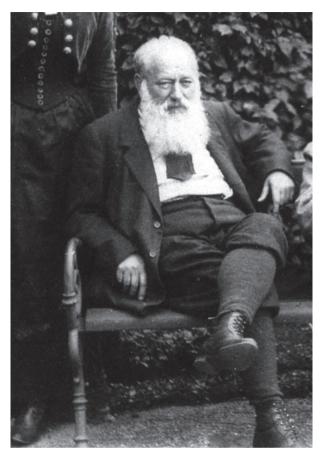


Figure 1. Theodor Billroth (1829-1894).

tributed significantly to both the technique of thyroid surgery itself and the understanding of the physiology of the gland. He was awarded the Nobel Prize in 1909 for his "work on the physiology, pathology and surgery of the thyroid gland".

He was extremely curious and scientifically ready to accept new medical and surgical solutions, thus once he arrived in Bern in 1872, he introduced both antisepsis (which had only been described a few years earlier) in his operating theaters, and a surgical technique that was meticulous and respectful of the anatomical structures surrounding the thyroid. He also introduced chloroform anesthesia for his patients undergoing thyroid surgery, though with often unexpected results, since among the few mortalities in his initial experience there were some caused by the uncontrolled use of chloroform itself. He then decided to switch to a "safer" (at the time) type of local anesthesia, i.e., cocaine. Curiously, the incision that is currently used for

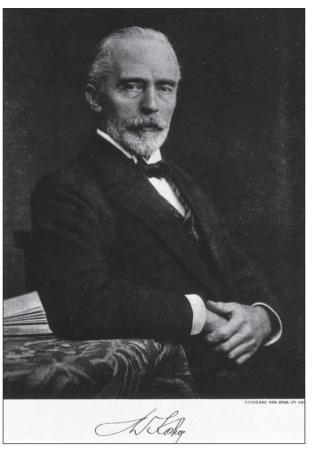


Figure 2. Emil Theodor Kocher (1841-1917).

thyroid surgery throughout the world, named after him, was adopted by Kocher only at the very end of his career, since he initially started performing surgery through an oblique incision in the neck, then through a vertical incision and only afterwards by the transverse incision that is still currently used.

In his hands, thyroid surgery mortality decreased from 13% at the beginning of his experience in Bern, to 0.5% at the end of his career, when he died in 1917. This astonishing result was not obtained easily, and presented several critical phases that required eventual improvements and relative technical adjustments (3).

Total thyroidectomy and the onset of cachexia strumipriva

After his first case series, Kocher was appalled when he met one of his patients and noticed how she

had changed in what he called a "cretinoid way". The patient displayed a marked modification of her personality and had become psychically and physically slow, and she had also completely changed physical shape. Despite various attempts to cure her, she would never regain a normal quality of life. Based on this experience, he decided to review all his cases of thyroidectomy and concluded that "cachexia strumipriva" was present in all subjects who underwent total thyroidectomy: his conclusion was that total thyroidectomy should not have been indicated except in carefully selected cases (e.g. in the presence of malignancy). This unfortunate and sad evidence was extremely useful in understanding the many roles of thyroid hormones, and of hypothyroidism. All Kocher's reports perfectly exemplify how the effects and actions of several, if not all, endocrine glands could have been described in patients who underwent removal of the glands themselves (3, 4, 10).

Theodor Billroth and an inexplicable postoperative tetany

Unlike Kocher, Billroth, a German surgeon "positively godlike in demeanor" as described by the American, George Crile (1864-1943) (9), was an extremely daring surgeon who contributed to several innovations in abdominal and thyroid surgery. In his first six years as chairman of the Department of Surgery at the University of Zurich (1860-1866) he performed 20 thyroidectomies and reported a 40% mortality rate. Billroth then decided to abandon thyroid surgery, only to begin again some years later, after the benefits of anesthesia, antisepsis and the improvement in surgical instruments had been well established. After he moved to the University of Vienna, mortality rates in Billroth's hands decreased to 8% between 1877 and 1881. What was later found to be interesting with regard to Billroth's experience are the observations made by Anton Wolfler (1850-1917) and later by Anton von Eiselburg (1860-1939) and Eugène Gley (1857-1930) that patients operated on by the great mentor developed postoperative tetany which was likely caused by the removal of the parathyroid glands during surgery (10-12). The differences between Kocher and Billroth's

surgical techniques, as well as an interpretation of their postoperative complications, are best described by another famous American surgeon, William Halsted (1852-1922), who wrote: «I have pondered the question for many years and conclude that the explanation probably lies in the operative methods of the two illustrious surgeons. Kocher, neat and precise, operating in a relatively bloodless manner, scrupulously removed the entire thyroid gland doing little damage outside its capsule. Billroth, operating more rapidly and, as I recall, with less regard for the tissues and less concern for hemorrhage, might easily have removed the parathyroids or at least have interfered with their blood supply, and have left fragments of the thyroid» (13). Halsted was among the first surgeons to publish a technique for parathyroid preservation (14). Billroth's postoperative tetany had been therefore solved after a few years...

"...Do you fancy a fried thyroid?" Or "how to cure postoperative hypothyroidism".

The problem Kocher had encountered was at least partially solved when, in 1891, George R Murray (1865-1939) injected an extract of the thyroid gland and later showed how it benefited patients who had undergone total thyroidectomy (15, 16). Immediately afterwards (1892), Frederick Y Fox (1856-1938) demonstrated that the same benefits were present when half a lightly fried sheep's thyroid obtained the same excellent results (17). These studies are now considered the cornerstones of modern replacement therapy with levothyroxine.

Thyroid surgery in the XX century: the "New wave" of surgeons from the New Continent

In the 20th century, thyroid surgery spread from Europe all around the world thanks to the many surgeons who had visited the two most famous European surgical schools and had been mentored by Kocher and Billroth. In this century, attention was focused more on the various diagnoses of thyroid disease requiring different preoperative and operative treatments than on the technique itself, which was at that time already fairly well standardized.

William Halsted's epiphany following his encounter with both Kocher and Billroth, helped him understand how one of the possible reasons American surgery was so underdeveloped as compared to the European schools, was the use of vascular clamps. In his observations, he concluded that "the value of artery clamps is not likely to be underestimated, since they determine methods and results impossible without them. They tranquilize the operator. In a wound that is perfectly dry...the operator, unperturbed, may work for hours without fatigue" (13). He therefore decided that a number of these clamps should have been present in every operating theater around his country, where they had previously been limited to very small numbers in very selected centers.

Thomas Dunhill (1876-1957) was an Australian surgeon who started working on patients with "exophthalmic goiter", a condition that was considered extremely severe and was burdened by high rates of mortality in surgical case series, mainly due to the onset of uncontrollable atrial fibrillation. By 1910, Dunhill had reached an astonishing 3% mortality rate in his series of patients affected with this disease, while in London the standard mortality rate exceeded 30%. He was among the first surgeons to use and describe a thorough extracapsular dissection of the gland, although he performed a total lobectomy on one side and a subtotal lobectomy on the other, in patients undergoing surgery for toxic thyroid disease (18).

Charles Mayo (1865-1939), an American surgeon, is considered the father of American thyroid surgery: working with the famous endocrinologist, Henry Plummer (1874-1936), he was probably the surgeon with the largest case series. Their studies on hyperthyroidism are very well known, also because they were likely the first to use this definition for patients displaying "cachectic thyroid disease". Mayo and Plummer further decreased the mortality of thyroidectomy in patients with hyperthyroidism (from 4% to 1%) thanks to the preoperative use of iodine compounds given to patients undergoing surgery (12).

Other pioneers contributed to the dissemination of the principles emerging in thyroid surgery, and among them, the most important surgical improvement was described by Frank Lahey (1880-1953), who advocated the full dissection of the inferior laryngeal nerve during every thyroidectomy, thus limiting its injuries to only 3% of his cases. Lahey's technique for

nerve dissection is still valid in modern thyroid surgery and is carried out to limit the incidence of postoperative vocal cord palsy (19).

The great mentors of thyroid surgery in the last decades of the XXth century

A relatively long time passed without any significant jolts in the field of thyroid surgery, but another "New wave" was brewing in Europe. Starting in 1971, a new current was taking shape in London, and more precisely at the Hammersmith hospital, where some prestigious British surgeons and endocrinologists met to organize what was the first Course on Endocrine Surgery dedicated to a European audience. This course, which was organized by Selwyn Taylor and Richard Welbourn, brought together a group of young endocrine surgeons from around the continent, all of whom would eventually become great mentors of the discipline in later years. This group was made up of the immense (in all senses) Charles Proye from Lille, Antonio Sitges-Serra from Barcelona, Sten Tibblin from Malmo, Hans-Dietrich Roher from Dusseldorf, and Matthias Rothmund from Mainz. In these courses (a regular appointment for anyone interested in the field of thyroid and endocrine surgery coming from all over the world in the '70s) the most recent knowledge the endocrinologists had merged with the technical notes provided by the most experienced and renowned British surgeons. In those years, London was attracting more and more experts in the field and creating further followers. The faculty included two other then-young American surgeons, Norman Thompson and Orlo Clark, who would later have spread their technical skills all over the new continent, becoming icons of the discipline, and founders of the American and International Societies that were to appear shortly afterwards (20).

In the 80's and '90s, France became a fervent territory for endocrine surgery in general and thyroid surgery in particular, with the previously cited Charles Proye (1938-2007), Jean-Francois Henry from Marseille, Jacques Marescaux from Strasbourg, and Jean-Louis Kraimps from Poitiers.

Charles Proye was, as already stated, a huge figure in thyroid surgery. Trained by his mentor, Georges La-

gache, he became a great mentor himself for hundreds of disciples all around the world. He always worked in Lille, where he would host surgeons coming from all around the globe. In his preoperative morning meetings you could hear several different languages (he could handle many of them, including his native Flemish), with people from nearby England, but also from the US, Mexico, Uzbekistan, Australia, New Zealand, Belarus, Switzerland, Germany and Italy, among others. He was a workaholic, working till all hours, 6 if not 7 days a week with the only exception of the Five Nations' match days, when his beloved French rugby team played (the signpost affixed on his office in the hospital claiming: "Closed for Five Nations match" was famous in those days). Charles Proye generously dispensed his unlimited knowledge and talent for research, and taught his skills about thyroid and parathyroid surgery every single day to whomever was willing to follow him into the operative room. Having the honor of assisting him on a surgery was always a gratifying moment. He was a fascinating man, a mentor for a lot of present-day thyroid surgeons, a friend to most of them, a scuba diver, a shark chaser, and, basically, one of those few who "invented" endocrine surgery as a discipline itself.

Proye contributed to the development of endocrine surgery in his country by being one of the founders of the extremely active French Association of Endocrine Surgery (AFCE) in 1989, as well as its first President (20), and became a founding member of the International Association of Endocrine Surgeons (IAES), and its President between 1997 and 1999. In his last years, still working hard despite an aggressive disease that was consuming him but not his untamed spirit, he became President of the French Academy of Surgeons (an honor he was very proud of) and was awarded the "Legion d'honneur". Despite the loss of the man, legends about him are still firmly rooted and widespread in operating theaters all around the world by his beloved disciples and friends (21).

France had indeed been the hub of endocrine surgery as a discipline, but in the last decade of the 20th century technology overtook science: laparoscopy impacted the surgical world...and the surgical world itself fell into turmoil.

The Italian revolution: the impact of an endoscope on thyroid surgery

At a time (late '80s to early '90s) when the biggest goal was to laparoscopically remove organs before other surgeons did, the thyroid was approached relatively late due to its limited anatomical region and the bulky instruments that could not be considered appropriate for such surgery. Despite these difficulties, two surgeons, both from Italy, reported their endoscopic approach to the neck: Cristiano Huscher, a pioneer of laparoscopic surgery (22), and Francesco Paolo Mattioli from Genoa, a true gentleman who, despite his advanced age, decided to dedicate himself to laparoscopic surgery and achieved excellent results (23). Nevertheless, these new techniques were clearly unsuccessful for the previously cited reasons: there was too little room in the neck for such instruments.

Many other surgeons also more or less successfully tried to perform endoscopic thyroidectomy via the neck, but always encountered major problems due to the fact that they wanted to adapt the neck region to the laparoscopic technique, and not the other way around. The main clinical problems, some of which were life-threatening, included: the CO2 pressure that was initially used was too high for a region (the neck) that is not confined, but that is in direct communication with the chest. This led to severe and long-lasting hypercapnia during operations which lasted more than 3 hours, often requiring postoperative recovery in the ICU. Another significant problem was the length of the surgical instruments: those dedicated to laparoscopic surgery were too long to be used in the neck region. Therefore, the main issue related to this was that the surgeon was performing a long operation in an anti-ergonomic position that could not be effective in terms of the fine movements required for this kind of surgery.

Then, in 1997, an Italian surgeon started to think that the thyroid was not the best choice organ of the neck on which to start developing a minimally invasive technique, when his surgical center was performing hundreds of...parathyroidectomies every year. Paolo Miccoli (born in Leghorn in 1947, but who always worked in Pisa, together with the immense endocrinologist Aldo Pinchera) (Fig. 3) then envisioned

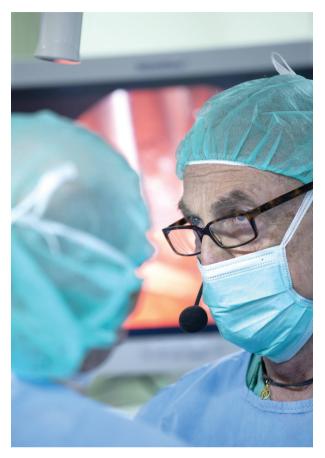


Figure 3. Paolo Miccoli. Photo by: Philippe Eranian. With permission from Paolo Miccoli.

a technique that was not adapted to, but specifically created for the neck region. It involved dedicated instruments (that he designed together with his collaborators) and an endoscope smaller than the one commonly used for laparoscopy, i.e., a 30° 7mm caliber endoscope usually used by urologists for cystoscopy. The idea behind the technique was to take advantage of the endoscopic magnification (as high as 20x) during an operation in which the aim of the surgeon was to identify small lesions. In an effort to carry out a thorough exploration of the neck, he decided to make the 2cm incision on the midline, thus allowing him to work on both sides of the neck. To avoid the problem of hypercapnia, in a country where operating rooms used to be full of young surgeons wishing to observe, he decided that the best way to create the operative field was to rely on external retraction maintained by an assistant surgeon, and not on CO2 insufflation. The technique was therefore named "Minimally-Invasive Video-Assisted Parathyroidectomy", better known by the acronym MIVAP (24).

The die was cast and after a few months the technique was used for small-sized thyroid nodules, when a lobectomy was indicated mainly to perform diagnostic surgery, in the presence of a thyroid that was otherwise normal. The first series of MIVAT operations was published in 1999 (25), and the Pisa technique immediately spread throughout the world, with great help from the Roman School of Rocco Bellantone, who, together with his collaborators, published the description of their first case that same year (26), and several other studies in the years to follow. MIVAT was initially recommended for "diagnostic" surgery, thus only lobectomies were indicated, but within a few years it proved its value for total thyroidectomies (27, 28), for the treatment of thyroid cancer (29, 30), and for lymphadenectomy of the central neck (31). In just a few years this Italian technique spread throughout the world, and its effectiveness and reproducibility was shown in multicentric studies (32, 33).

Will other Mentors be able to override technological successes or will we be tied to 2.0 versions?

From that point on, the new millennium witnessed a major development of technology over the gigantic figures of Men, and, indeed, thyroid surgery advanced further and further, but new surgical techniques became more and more dependent on technical support (e.g. Leonardo da Vinci robotic system) or on derivatives of new surgical philosophies (e.g. the all-new transoral approach deriving from the Natural Orifice Transluminal Endoscopic Surgery). These new techniques are still under development and are far from being globally accepted, due also to the ethical issues they inevitably carry with them.

This is why we should never forget our origins or our Fathers since great Mentors and huge personalities will always override mere technology in a discipline that requires human contact between surgeons and their patients (34, 35).

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