World J Surg (2010) 34:1793–1804
DOI 10.1007/s00268-010-0580-7

World Journal of Surgery

Historical Evolution of Thyroid Surgery: From the Ancient Times to the Dawn of the 21st Century

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Published online: 17 April 2010

Abstract Thyroid diseases (mainly goiter) have been recognized for more than 3500 years. Knowledge of the nature of these diseases was, of course, limited at that time. Thyroid surgery was conceived by the ancients, but it was limited to rare attempts to remove part of an enlarged thyroid gland in cases of impending death by suffocation or, in very rare cases, of a suppurating thyroid. Like other fields of surgery, thyroid surgery was limited by many problems: the lack of anesthesia and antisepsis, the need for appropriate instruments, mainly artery forceps (many deaths after thyroid surgery were due to severe postoperative hemorrhage or infection). Much of the progress in thyroid surgery occurred in Europe during the second half of the 19th century. During the first half of the 20th century, the evolution of thyroid surgery accelerated significantly, based on the contributions of pioneering European and American surgeons. The present status of thyroid surgery was established during the last quarter of the 20th century, when modern imaging methods and technological advances (including progress in applied molecular biology) brought thyroid surgery into the new millennium.

> Only the man who is familiar with the art and science of the past is competent to aid in its progress in the future.
>
> Theodor Billroth

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> The chief legacy which a surgeon can bequeath is a gift of the spirit. To inspire many successors with a firm belief in the high destiny of our calling, and with a confident and unwavering intention both to search out the secrets of medicine in her innermost recesses, and to practice the knowledge so acquired with lofty purpose, high ideals, and generous heart, for the benefit of humanity—that is the best that a man can transmit.
>
> Sir Berkeley Moynihan

Introduction

Surgical management of thyroid diseases evolved slowly throughout the ages. Although thyroidopathies were known from ancient times, thyroid surgery (like all other surgical specialties/subspecialties) was confronted with too many practical problems, limiting its evolution. Much of the progress of thyroid surgery occurred during the second half of the 19th century. During the first half of the 20th century, advances in thyroid surgery were impressive, mainly because of the contribution of pioneer surgeons in Europe and America. The introduction and wide use of modern imaging methods, preoperative fine needle aspiration cytology, the standardization of surgical techniques (including cervical lymph node dissection for thyroid cancer), but also the understanding of the molecular changes in thyroid diseases (including thyroid cancer), characterize the evolution of thyroid surgery during recent decades.

The aim of this review is to present the historical evolution of thyroid surgery up to the dawn of the 21st century. The reader will understand the significant difficulties and limitations with which our ancestors were faced. The important contributions of the great thyroid surgeons of the 19th and early 20th centuries is also emphasized.

From antiquity to the 19th century

Historical writings have described abnormalities of the thyroid gland for more than 3500 years. The Chinese mentioned goiters (the most common type of thyroid disease, appearing as a mass protruding from the neck) as early as 2700 BC. Although some societies considered this neck enlargement to be attractive in women, goiter was usually treated as a curiosity, the subject of ridicule and distain, as shown in the artistic depictions of thyroid disease many centuries ago (Fig. 1) [1]. However, knowledge of thyroid diseases and their causes was very limited. Chinese writings suggest the use of seaweed and sea sponge, significant sources of iodine, in treating "enlargement of the thyroid" [2]. The association of goiter and orbital disease (despite being attributed to Graves and Basedow) was described between AD 1000 and 1110 by two Persian physicians and philosophers, Avicenna and Aj-Jurjani [3]. The Romans also used natural sources of iodine for the treatment of enlargement of the thyroid; they also documented occasional operative treatment for an enlarged thyroid.

Despite the relative frequency of thyroid disease, the gland was not named until the 16th century, when Bartholomeo Eustachius of Rome characterized it as a single "glandulam thyroideam" with two lobes connected via an isthmus [4]. The term "thyroid gland" (*glandular thyroidoeis*, previously "laryngeal gland") is attributed to Thomas Wharton (described in his work *Adenographia*) (1646); he gave this name to the gland because of either its own shield-like shape (*thyreos*: Greek *shield*) or because of the shape of the thyroid cartilage, with which it is closely associated. Accurate anatomical definition of the thyroid (noting both its lobular and bilateral nature) was drawn by Leonardo da Vinci (a visionary of contemporary anatomic sketching) in about 1500 and by Andreas Vesalius in 1543 [5]. However, Leonardo, despite his anatomically correct drawings, incorrectly concluded that the purpose of the thyroid was to "…*fill a void in the neck*…[!]. The Dutch physician-anatomist, Frederik Ruysch, suggested that the gland secreted fluid into the veins. In the late 18th century, Caleb Hillier Parry of Bath, England, who identified exophthalmic goiter in 1786, before Graves' description of 1835, described the thyroid as a vascular reservoir to prevent engorgement of the brain [6].

Interestingly, the idea of surgical treatment of goiter was conceived by the ancients; rare attempts to remove the enlarged thyroid gland were performed for centuries, mainly in cases of impending death from suffocation (due to massive enlargement of the thyroid, causing compressive symptoms, mainly from pressure on the trachea), but also in cases of suppurating glands. Obviously, "thyroid surgery" was undertaken without a clear understanding of thyroid physiology. Accounts of early "operations," performed in Salerno during the 12th and 13th centuries with setons, hot irons, and caustic powders, often with fatal results, were recorded by Roger Frugardi in 1170 [5]. These attempts were horrifying both for the patient and for the surgeon, and they were associated with little success, a prohibitively high mortality, and significant morbidity resulting from massive hemorrhage, asphyxia, infection, hospital gangrene, and air embolism [7]. In these operations, the surgeon's fingers were used for dissection, and finger nails were applied for tissue removal. The appalling procedures led, in 1646, to the imprisonment of a surgeon for his work and to a total ban of the operation by the French Academy of Medicine in 1850 [4]. It is highly probable that the first typical partial thyroidectomy was not successfully performed until the famous French surgeon Pierre-Joseph Desault accomplished it in 1791 [8]. However, as discussed later in this review, technical improvements leading to improvement of the results of surgery did not occur until the middle of the 19th century.

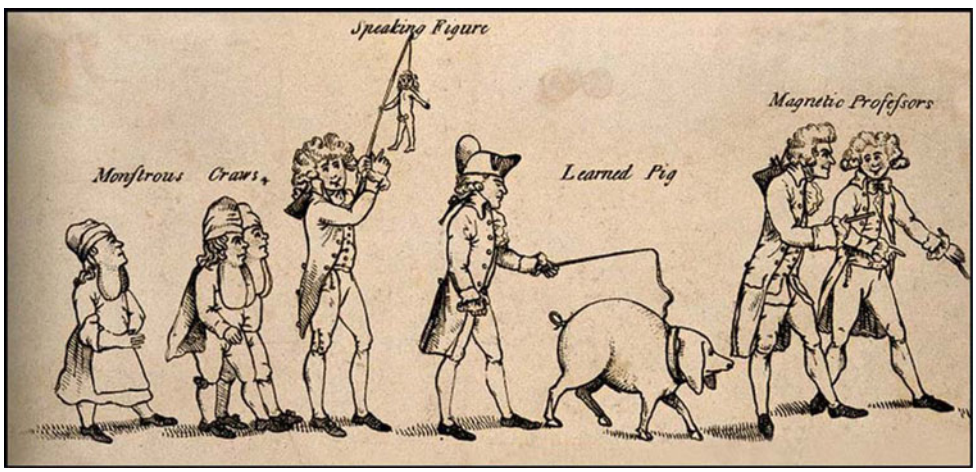

Fig. 1 Etching, 1780s. Note the goiters (from [1])

19th Century

During the first decades of the 19th century, thyroid surgery remained primitive. Mechanical complications of goiter treatment predominated. Debulking or enucleation was initially popular but was then abandoned because it was ineffective and dangerous. Attempts to suppress the gland by superior thyroid artery ligation were first used by William Blizard in 1811. Although relatively easy because it was accomplished via the lateral approach, this operation also fell into disfavor because of minimal long-term benefit.

The development leading to the contemporary era in thyroid surgery began just over a century and a half ago (grossly, from the middle of the 19th century). Since that time, progress in thyroid surgery has been rapid, due to technical advances and to the work and vision of pioneer surgeons (see below). Up until 1849, operation was reserved for the most severe cases of goiter and was associated with a very high (40% or even higher) mortality [9].

Important advances during the 19th century

Beginning in the middle of the 19th century, important steps in the evolution of surgery included the development of anesthesia, the introduction of antisepsis, the development of microscopy and biochemical testing, the use of effective surgical instruments (mainly artery forceps), and the understanding of thyroid physiology.

Antisepsis

Septic complications, often with a fatal outcome, were very common in surgery before the description and the use of the antiseptic technique by Joseph Lister in 1867. Specifically regarding thyroidectomy, many surgeons (including prominent surgeons of that era, such as Theodor Billroth) were unwilling to undertake non-emergent thyroid surgery due to the high incidence of infection that was often fatal.

Anesthesia

In the pre-anesthesia era, surgery was a horrible and terrifying experience. Anesthesia had a particularly significant impact on thyroid surgery. Before general anesthesia was available, there was little to make the patient comfortable during the procedure. Patients were told not to move and were even tied down to the operating table. Chemicals such as ether had been in use for years, but not necessarily in a controlled way. Successful management of the difficult airway was very important, especially for patients with large goiters pressing and causing deviation and stenosis of the trachea. Under these circumstances, it was thought that local anesthesia was the preferred method of anesthesia [1].

Development of microscopy/understanding thyroid physiology

Advancements in microscopes and biochemical testing also evolved during the 19th century. These advances allowed observation of the thyroid tissue (normal and diseased) at the microscopic level. The microarchitecture of the thyroid was recognized, as well as the synthetic activity of the gland. Before the 19th century, most physicians and surgeons believed there was no vital function to the gland. The discovery of iodine in the burned ash of seaweed in 1811 had led to the successful treatment of some goiters by 1820 (the Chinese used seaweed as a source of iodine in treating goiters without knowledge of its mechanism of action, see above). It was observed that if these thyroid masses could be treated with iodine, the gland would shrink, impinge less on the trachea, and subsequently lessen the demand for emergent goiter removal. However, toxicity complicated the picture, and the value of iodine in treating early small goiter, though recognized by Billroth in Vienna in 1877, was frequently disputed [5]. Billroth himself warned of the untoward effects of "iodinism." Iodine therapy was certainly not found to be effective in very large goiters. Gradually, scientists began to realize that the thyroid stored and required iodine to produce "thyroid juice." Classical presentations of hyperthyroidism (exophthalmic goiter) was presented by Parry (1825), Robert Graves (1835), and Karl Adolph von Basedow (1840) [4, 9]. Virulant thyrotoxicosis claimed many young lives and appeared to be best managed by 6 months in bed with a variety of drugs being tried, including: the milk of thyroidectomized goats, serum from various thyroidectomized animals, extracts of all kinds of glands, injection of steam and boiling water, compression (and during the first decade of the 20th century by irradiation and even by insulin therapy). Hypothyroidism (myxedema) was described by Thomas Curling (1850) and William Gull (1875) [6]. Moritz Schiff, in the middle of the 19th century, conducted experiments demonstrating the physiologic importance of the thyroid. Excision in dogs resulted in death, which was found to be preventable by a previous graft of the gland. In 1882, J. L. Reverdin produced experimental myxedema by total or partial thyroidectomy. In 1884 Ludwig Rehn of Germany observed that the effects of thyroid toxicity, for which the thyroid had not yet been credited, abated after thyroid removal for goiter. With this information, Rehn suggested that an overproductive thyroid may be the cause of these symptoms. In 1888 William Grieenfield noted that the symptoms of thyrotoxicity correlated with thyroid gland hyperplasia. Other clinicians began noting similar relationships [1]. In the 1890s, George Murray and Howitz successfully treated patients with sluggish behavior, increased weight, hair loss, and other symptoms of deficient thyroid activity (myxedema) with thyroid extract [6].

Effective surgical instruments

Artery forceps were introduced in clinical practice in 1879 and offered the possibility to perform unhurried and safe thyroid surgery. Although up to the middle of the 19th century infection had been the main cause of death after thyroid surgery, it was the fear of massive hemorrhage (due to the rich vascularity of the gland) that deterred most surgeons from performing thyroid resection. As a consequence, many surgeons (even prominent ones like Theodor Billroth) believed that thyroid surgery was not justified in non-emergent cases [7]. It is extremely interesting to read the notes (dated 1846) of the legendary Robert Liston, who was a gifted, skilled, dexterous, and daring surgeon [10]:

> …It has been proposed again to cut these tumors out, and some surgeons have ventured upon that, but the result has not been at all satisfactory. You could not cut the thyroid gland out of a living body in its sound condition without risking the death of the patient from hemorrhage…It is a proceeding by no means to be thought of….

The famous American surgeon Samuel D. Gross (from Philadelphia) took a similar position. About 20 years later (1886), he noted [11]:

> …Can the thyroid gland when in the state of enlargement be removed with a reasonable hope of saving the patient? Experience emphatically answers, no ! … 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…

It is therefore clear that the introduction and use of hemostatic forceps in the operating theaters, initially in Europe (around 1870) and subsequently in America, represented a significant step in the evolution of thyroid surgery, allowing safe dissection and careful ligation of blood vessels, thereby enhancing the safety and reducing morbidity and mortality of thyroid surgery.

Pioneers in thyroid surgery during the 19th century

Theodor Kocher (1841–1917)

Theodor Kocher is considered the father of thyroid surgery (Figs. 2, 3). He was appointed to the Chair of Surgery in Berne, Switzerland, in 1872 and began his landmark thyroid surgery with the use of antiseptic techniques in the operative environment. His procedure was marked by meticulous care in dissecting and controlling (ligating) blood vessels (thereby avoiding hemorrhage), and precise dissection within the thyroid capsule. His operations were undertaken initially though an oblique incision along the anterior border of the sternocleidomastoid or by a vertical midline approach. Subsequently, he used a transverse incision. Kocher also paid close attention to the anesthesia methods available. One of Kocher's few mortalities was secondary to chloroform anesthesia. From that point onward, he used only local anesthesia with cocaine. During the first

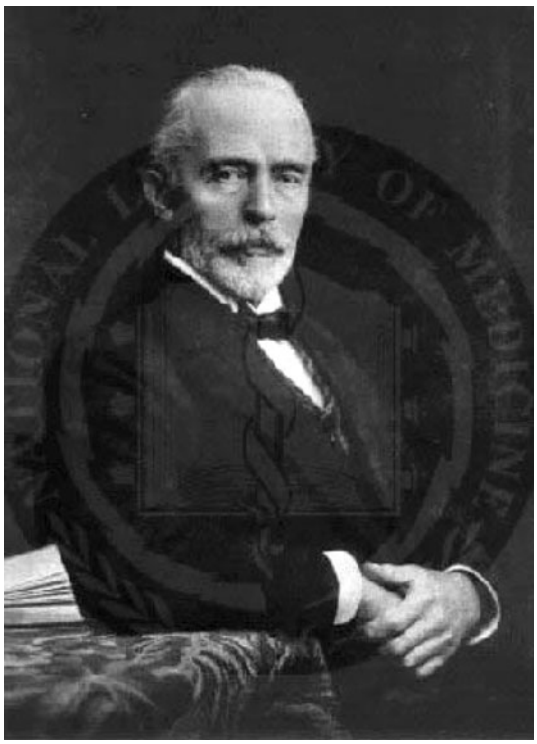

Fig. 2 Emil Theodor Kocher, M.D. (1841–1917)

Fig. 3 A woman from Switzerland operated on by Theodor Kocher [12] (available online at: http://www.thyroidmanager.org/Chapter21/ch01s06.html)

10 years of his tenure at Berne, Kocher excised 101 goiters, with a mortality rate of 12.8%. Another 250 cases were recorded in 1889, with a mortality rate of 2.4%. By 1895, his operative mortality for benign lesions had declined to a little over 1%; and in a new series of 560 nonmalignant cases reported in 1898 the associated mortality was less than 0.2%. In 1917, a few weeks before his death at the age of 76, he made his final appearance before the Swiss Surgical congress, reviewing his entire surgical experience with goiter, reporting on approximately 5,000 operations with a mortality of about 0.5% [7].

It was in 1883 that Kocher published the historic paper [12] in which he considered the ill effects of total thyroidectomy, and he made his greatest contribution to physiology by providing proof that the thyroid gland is an organ essential to health. Speaking before the 12th German Surgical Congress, he presented the now famous case report of Marie Richsel, an 11-year old girl on whom he had done his first total extirpation. He said:

> …Concerning one patient upon whom I had operated on January 8, 1874, the referring physician incidentally reported that the girl had undergone marked change in her personality. Indeed, he finally informed me that she had become quite cretinoid. This seemed to me so important that I made every effort to examine the girl, which was not so easy since this physiciac had died very shortly after making his report. We were all the more intent upon it since our colleague, Reverdin of Geneva, had informed us that he had observed two patients who had suffered diminution of mental capacity following goiter operations. I was highly astonished at the striking appearance of my patient. To crystallize somewhat your impressions, I shall show photographs of the girl and her younger sister, taken before and after the operation. At the time of the operation, according to her mother, both girls looked so much alike that they were frequently mistaken for each other. Whereas in the ensuing 9 years the younger sister blossomed into a very pretty young woman, the one operated upon remained small and has an ugly, almost idiotic appearance. As soon as this was determined I immediately requested all of my goiter patients to return for examination.

Of Kocher's 34 patients with total extirpation, 18 returned for examination. Sixteen of the 18 had the symptoms and signs of what we now know to by hypothyroidism. He described with accuracy the clinical picture, speculated at length the possible causes of the mental and other physical changes characteristic of myxedema, observed the striking resemblance to cretinism, and to the syndrome applied the name *cachexia strumipriva*. This debilitating and potentially fatal complication invariably followed total thyroidectomy, and Kocher was so shocked and saddened that he decided never again to do a total extirpation for benign disease. Thereafter he advocated lobectomy, reserving total excision for malignancy or the unusual instance in which a bilateral procedure was required for adequate tracheal decompression. In his 1909 Nobel Prize acceptance speech for "his work in physiology, pathology, and surgery on the thyroid gland," Kocher discussed the difficulties of recognizing thyroid disease more subtle than goiter, that is hyper- and hypothyroidism. He noted that virtually any organ could be affected by alterations in thyroid function and that the symptoms were often nonspecific. Recognizing the importance of adequate thyroid function and its influence on the "whole" patient was certainly in great contrast to the earlier belief that the thyroid may be functionless.

Kocher also recognized recurrent laryngeal nerve injury and tetany as postoperative complications, implicating the need for a more cautious resection and a more precise technique by extracapsular dissection. It is of interest that only one case of transient tetany was observed in a series of Kocher's patients ($n = 18$) with total thyroidectomy; a striking contrast to the relative frequency of tetany in Billroth's experience (see below). The famed American Surgeon, William Stewart Halsted, proposed the following explanation for this difference regarding the incidence of tetany among the patients of these two great surgeons [7, 9]:

> …I had pondered this 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 his manner—with less regard for tissues and less concern for hemorrhage, might easily have removed the parathyroids or at least have interfered with their blood supply, and have left remnants of the thyroid…

According to Halsted [9], Kocher's most significant contributions in thyroid surgery include:

1. The realization that total thyroidectomy is associated with many consequences from too many organ systems (cachexia thyreopriva or cachexia strumipriva)
2. Study of malignant tumors of the thyroid gland
3. Perfection of the technique of thyroidectomy
4. Consideration about surgical management of Graves' disease and study of the mild forms of hyperthyroidism
5. Use of the ligature of the arteries as a preliminary step in lobectomy, in highly toxic cases

6. Realization of the danger of the indiscriminate administration of iodine to patients with goiter

Theodor Billroth (1829–1894)

Theodor Billroth (Fig. 4) is considered by many medical historians to have been the 19th century's most distinguished surgeon. He graduated in 1852 from the Berlin University and was appointed in 1860 (at the age of 31) chairman of the department of surgery at the University of Zurich. This was an excellent new university hospital located in an area with a very high incidence of goiter. It was in this setting that he started treating surgically patient suffering from large suffocating goiters. During the first six and a half years at Zurich he performed 20 thyroidectomies with a mortality rate of 40%. Seven patients died of sepsis and one of hemorrhage. These tragic results prompted him to abandon thyroid surgery as a treatment for goiter for almost a decade [7]. Billroth noted [13]:

> On carefully reviewing the results of my experience, I have come to the following conclusions…much less favorable in its results is the operation for completely removing deep-seated substernal or unilateral bronchoceles (goiters), accompanied by a high degree of dyspnea; even in cases in which the operation is immediately successful in saving life, the ultimate result is frequently unfavorable….

Fig. 4 Theodor Billroth, M.D. (1829–1894)

We—as surgeons today—should, however, remember among these fatalities only one died from hemorrhage, in an era when artery forceps were not used. At that time, surgeons had to rely on aneurysm needles, sutures, hooks, and the pressure of fingers or sponges for the control of hemorrhage. Later, in Vienna, with increased experience and aftersignificant improvements in surgical technique (antisepsis, artery forceps, etc.) and anesthesia, Billroth ventured again to operate on goiter. Subsequently, he was very successful in treating goiters and he contributed enormously in the advancement of thyroid surgery.

These two phases reflecting his experience in thyroid surgery are clearly seen when analyzing two series of Billroth cases. Over a period of 21 years (1860–1881) he performed 84 thyroidectomies; in the "pre-antiseptic period" (1860–1876), he operated on 36 patients (Zurich 20, Vienna 16), with 16 deaths (mortality, 36%). From 1877 to 1881 ("the antiseptic period") he did 48 thyroidectomies, with four deaths, an operative mortality of 8.3% [7]. By the early 1880s Billroth had become the most experienced thyroid surgeon in the world. He also made important contributions in related fields of surgery (for example, total laryngectomy [1873]). Billroth was also a very good teacher, and his experience was conveyed to his assistants, who later become famous surgeons in their own right (see below).. All these achievements can explain why the Vienna clinic soon became a surgical Mecca, attracting surgeons from all over the world. This time marks the peak of German pre-eminence in surgery. George Crile (see below) visited Billroth's clinic in 1892 and later, in his autobiography, recorded these impressions [14]:

> …Albert Christian Theodor Billroth was the most distinguished surgeon of his day, with von Bergmand of Berlin and Kocher of Berne as close seconds. Billroth was famous for his boldness and initiative in surgery. Through his successful resection of the stomach for cancer about ten years earlier, he had laid the foundation for modern abdominal surgery. He was also famous for his work in cancer of the larynx. In those days a professor of surgery was a personality and Billroth was the most impressive of them all—positively godlike in demeanor. He not only wore a long Prince Albert coat suitable to such a position, but he always performed his work with the utmost formality. Promptly at nine the wide doors of his clinic swung open and Billroth with his staff of 20 assistants made a grand entrance. Everything was organized; each case had been studied. Billroth knew each detail. There was not more chance of an error than there was in the performance of a great play. This was the German system….

Thyroid surgery in America during the 19th century

The important contribution of William Halsted

As already noted, William Stewart Halsted (1852–1922) was one of most prominent American surgeons of the 19th and early 20th century (Fig. 5). Following his graduation from Yale University and the Columbia University College of Physicians & Surgeons, and internships at Bellevue and New York Hospitals, he set off to travel Europe in the fall of 1878. Thus began 2 years of intensive post-graduate study in medicine, surgery, the specialties, and the basic sciences in the most famous clinics in Germany and Austria. His interest in the thyroid can be traced to his time in Vienna in 1879 when, with Anton Wölfler (Billroth's first assistant), he studied the development and structure of the thyroid in fish. Wölfler gave him unrestricted entrée to the surgical wards and Billroth's operating amphitheater.

Between 1880 and 1886, the period of his surgical activities in New York, he neither saw nor heard of an operation for goiter, except that on one occasion he assisted Dr. Henry Sands in the removal of a small tumor of the right lobe of the thyroid. The patient sat erect in a dental chair, with a rubber bag tied around his neck to catch the blood [7]. At that time, no one in the United States did more to stimulate interest in thyroid diseases or to standardize technique and promote advances in thyroid surgery. Halsted was able to find reports of only 45 operations for goiter in America up to 1883. By that time Billroth alone had done 124. Halsted deplored the delayed development of thyroid surgery in the United States and attributed it to the tardy acceptance of antisepsis and to a lack of proper surgical instruments. Whereas most of the better surgeons of Germany, Austria, and Switzerland promptly and eagerly accepted the teachings of Lister, there were few in America who did so until nearly a quarter of a century later. Indeed, the records indicate that of the thyroidectomies done in the United States prior to 1890 not a single one was performed under antiseptic conditions [7]. The Johns Hopkins Hospital opened in 1889, and over the next 10 years only 7 thyroidectomies were done there, 6 by Halsted and one by Harvey Cushing.

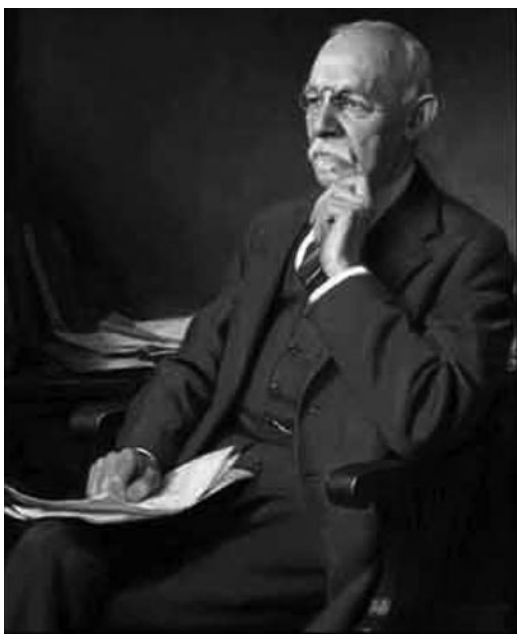

Fig. 5 William Stewart Halsted, M.D. (1852–1922)

The lack of appropriate instruments (mainly artery forceps) was a significant barrier to the development of thyroid surgery in America up to the last decade of the 19th century. The value of these instruments is emphasized by Halsted himself [9]:

> On my return from Germany in 1881, I was impressed with the fact that our surgeons were greatly handicapped in most of their operations for lack of proper instruments, particularly of artery clamps. They were insufficient in number and faulty in design. Rarely had I seen in our country prior to my first visit to Europe (1879), more than one artery clamp at a time left hanging in a wound. Clamps were too few for this—four to three or even two being considered ample for an operation. Few hospitals, in New York at least, possessed as many as six artery clamps in 1880. I recall vividly an operation in Vienna performed by Mikulicz in 1879 in Billroth's clinic. Americans, newly arrived in Austria, we were greatly amused at seeing perhaps a dozen clamps (Schieber) left hanging in a wound of the neck while the operator proceeded with his dissection, and were inclined to ridicule the method as being untidy or uncouth. Slowly it dawned upon us that we in America were novices in the art as well as the science of surgery. The value of artery clamps is not likely to be overestimated. They determine methods and effect results impossible without them. They tranquilize the operator. In a wound that is perfectly dry, and in tissues never permitted to become even stained by blood, the operator, unperturbed, may work for hours without fatigue. The confidence gradually acquired from masterfulness in controlling hemorrhage gives to the surgeon the calm which is so essential for clear thinking and orderly procedure at the operating table….

In the summer of 1899 Halsted first met Theodor Kocher. Thereafter he visited the Berne clinic at every opportunity and was often a guest in the Kocher home. He considered him perhaps the greatest surgeon of his time. Although he patterned his residency system after that of

Langenbeck and Billroth, it was Kocher's technique that evoked his admiration. In 1920 he wrote [9]:

> Many times during the past 20 years I have stood by the side of Professor Kocher at the operating table enjoying the rare privilege of feeling in complete harmony with the method of the operator, and it is a pleasure to give expression to the sense of great obligation which I feel to this gifted master of his art and science….

By 1907, Halsted had performed 90 operations for Graves' disease with a mortality rate of just over 2%. No surgeon had a better record in a sizable series. In 1914, he reported that he had operated on 500 cases of Graves' disease.

The contributions of Halsted in the evolution of thyroid surgery include the following:

1. Development of a standardized technique of thyroidectomy based on precise anatomic and physiologic principles
2. Significant experimental work with thyroid and parathyroid grafts
3. Use and popularization of hemostatic forceps and other surgical instruments (such as retractors, ligature carriers, aneurysm needles, scalpels, dissectors etc.) in the USA
4. Introduction and wide use of local infiltration anesthesia, which greatly reduced morbidity and mortality after thyroid surgery
5. Publication in 1920 of his classic monograph titled *The Operative Story of Goiter* (F-6/8); in the 166 pages of this treatise, which reviewed 375 sources of information, the great experience of Halsted is clearly and precisely presented. In this monograph Halsted noted [9]:

> The art of operating for goiter by Billroth and Kocher and men in their school had been almost perfected, relatively minor problems remaining to be solved. … Greater advance was made in the operative treatment of goiter in the decade from 1873 to 1883 than in all the foregone years, and, I may say, than in all the years that have followed.

Other contributors in the evolution of thyroid surgery during the 19th century

Anton Wölfler served for 10 years as Billroth's first assistant. He was the first to present a detailed description of post-thyroidectomy tetany, and to publish a thorough discussion of the danger of operative injury to the recurrent laryngeal nerve and the anatomical and technical reasons for it. His two classic monographs on the development and structure of the thyroid gland and of goiter were based on his study of Billroth's operative material [15, 16]. These were valuable expositions of the ideas and experiences of what was at that time the world's most active thyroid surgical center [7].

Anton von Eiselsburg's important early experimental work on transplantation of the thyroid and parathyroids was fundamental and attracted wide attention. He continued Wölfler's studies of the tetany material in Billroth's clinic. In 1890, he found that in 30 patients with postoperative tetany the complication was temporary in 7, permanent in 3, and fatal in 13. Even at that late date the etiology of tetany was unclear. In the following year, 1891, *Eugene Gley* reported that post-thyroidectomy tetany was caused either by the removal of the parathyroid glands or interference with their blood supply [7].

Jan Mikulicz in 1886 reported that in his first 3 years as director of the surgical clinic at Krakau (Poland) he had performed 25 thyroidectomies without a fatality. Seven of these were total extirpations, 8 were unilateral lobectomies, and in 2 only the isthmus had been excised and in 8 instances he had done what he termed a "resection" according to a new method of his own, which he described for the first time in this article [17]. He explains how he conceived a new operation, aiming to avoid recurrence of the goiter and injury to the recurrent nerve; he termed this procedure (partial) "resection" to distinguish it from the typical total excision or extirpation of one or both lobes:

> …But it not infrequently happens that having undertaken the operation with the intention of removing only one lobe, the surgeon finds it necessary to remove the other. I have several times found myself in this predicament. After a very large, forwardly displaced lobe had been excised there would appear for the first time the second lobe which had been concealed behind the trachea which is surrounded or had been buried in great part behind the sternum. In such cases one takes a risk if he postpones removing this lobe in the expectation that it may atrophy. It was in a case of this kind that I first practiced the method which I hope may best prevent the evil consequences of total extirpation. I extirpated, namely, the second lobe, only in part, resecting in such a manner that a portion of the lobe remained in the neighborhood of the inferior thyroid artery. The remaining stump of the gland contracted to a nodule the size of a chestnut, resting in the angle between the trachea and the esophagus. Neither the inferior thyroid artery nor the recurrent laryngeal nerve were seen.…

> …I ventured to do this because I had observed that division and ligation of a quite massive isthmus could be accomplished without evil consequence; the parenchyma of the gland must therefore be tolerant of the insult caused by ligature en masse. Hence I need not fear to sever the parenchymal part of the goiter from the remains by means of mass-ligatures passed through the parenchyma….

Thus Mikulicz first demonstrated the feasibility and value of partial thyroid resection; he also showed that thyroid parenchyma can be crushed, divided, and ligated without fear of uncontrollable hemorrhage or impairment of wound healing, thereby forming the basis of modern unilateral and bilateral subtotal lobectomy [7].

It should, however, noted that, despite the important contribution of these great surgeons in the field of thyroid surgery, not all surgeons were aware or practiced these improvements. For example, in 1892, Mathieu Jaboulay of Lyon, France, was still advocating exothyropexy (exteriorization of the gland) and, in 1896, he recommended cervical sympathectomy for toxic patients [5].

20th Century

Pioneers in thyroid surgery during the first part of the 20th century

Thomas Peel Dunhill (1876–1957)

Thomas Peel Dunhill began work on the intractable problems of goiter and thyrotoxicosis in Melbourne, Australia, at the turn of the century, and in 1910 he had done 312 operations, of which 200 were for exophthalmic goiter. This was at a time when treatment of this condition was associated with a formidable mortality (for example, in this era mortality following thyroid surgery at the St. Thomas Hospital in London was 33%) [5]. Dunhill adopted the technique of total lobectomy on one side and subtotal resection on the other for toxic patients. He used cautious, precise technique under local anesthesia at first, and later he put the patients under light general anesthesia. He practiced total lobectomy by a pericapsular dissection technique, which is even now considered by many surgeons to be the optimal method of resection. Despite accepting the most seriously ill patients, many of whom suffered from uncontrolled atrial fibrillation, he achieved a mortality of less than 3%, a standard treated with disbelief and even derision by his hosts at the Royal Society of Medicine [18] when the mortality for the operation in London hospitals was as high as 30%. Later, Dunhill described operation on retrosternal goiter by splitting the sternum. Dunhill served in France during WWI and afterwards was persuaded to take up a post at St. Bartholemew's Hospital, London, where in 1920 he produced his outstanding paper in an early issue of the *British Journal of Surgery* [19]. The illustrations were by A. Kirkpatrick Maxwell who travelled down from Glasgow to draw in the operating theater, elegantly demonstrating the precision of extracapsular dissection to safeguard adjacent structures.

Cecil Joll (1885–1945)

Cecil Joll, also professor of surgery in London, described the treatment of thyrotoxicosis by means of a subtotal thyroidectomy. He published a comprehensive book on thyroid surgery in 1932 (*Diseases of the Thyroid Gland with Special Reference to Thyrotoxicosis*) [20]. He reported on over 2,000 patients with goiter, including only two with abscess [20]. Interestingly, in this book the thyroid remnants after subtotal lobectomy are demonstrated as very large. He used a rather retrograde technique and recorded a relatively high incidence of nerve injury, but a low incidence of tetany. Joll's book also illustrates thyrotoxic crisis, which was not uncommon then.

Charles H. Mayo (1865–1939)

Charles Mayo (Fig. 6) was an extremely popular and highly respected American surgeon and was probably the most experienced thyroid surgeon of his time. He performed his first goiter operation in 1889. Mayo's operative mortality rate for his first 16 cases of exophthalmic goiter was 25%. By 1908 he had operated on 234 patients with thyrotoxicosis with a mortality of 6%. In an effort to improve these results, Mayo in 1908 began to employ in the severe thyrotoxicosis unilateral or bilateral pole ligation as a preliminary to partial thyroidectomy. Although Kocher had for years practiced this staged or graduated operation for exophthalmic goiter, credit is due to Mayo for demonstrating by means of a large group of cases the great value of this principle in reducing mortality in Graves' disease. During the year 1912 he operated on a consecutive series of 278 patients with exophthalmic goiter without a death and with only one case of transient tetany. In 1918 he had completed his large series with 5,000 thyroidectomies. In 1907 Mayo used the term *hyperthyroidism* to describe the cachectic nature of hyperthyroid disease, although it would be some time before the overproduction of thyroid hormone and its effects on cellular and organ function were fully elucidated. Mayo treated hyperthyroidism by thyroidectomy [1]. For these contributions he has been named The Father of American Thyroid Surgery. In collaboration with Henry Plummer, his medical counterpart on the clinic thyroid team, he started using iodine in the preoperative preparation of patients with

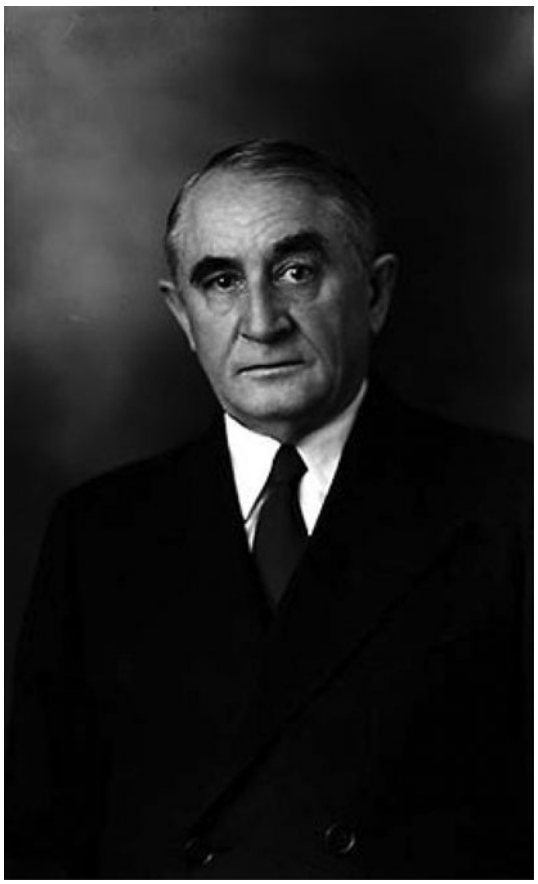

Fig. 6 Charles H. Mayo, M.D. (1865–1939)

hyperthyroidism. This practice resulted in a significant drop in operative mortality from between 3% and 4% to under 1% and a decrease in the incidence of multistage operations from over 50% to 2% [7].

George W. Crile

George W. Crile of Cleveland was a famous and talented thyroid surgeon, very well-known also as a productive research scientist [7]. He was very interested in hyperthyroidism and he observed that the thyrotoxic patient was likely to develop prostration during crisis due to overactivity of the central nervous system. He contended that this condition could be obviated by preventing noxious stimuli from leaving the operative site with local anesthesia, a process to which he applied the term *anoci-association*. The concept of "stealing" the toxic goiter was also a Crile innovation. This concept (the so-called thyroid steal) was based on the fact that there was no way to control thyrotoxicosis; surgeons at that time knew that nervousness would make things much worse. Therefore, they did not tell their patients when they were going to have the operation. Each day, for several days beforehand, the patient was injected with saline into a vein by the anesthesiologist, and, finally, on the day of surgery, without telling the patient, the anesthesiologist injected an anesthetic agent and the patient then underwent the operation. This approach was thought to make surgery much safer for the patient. Crile believed that the surgeon should never expose the recurrent laryngeal nerve during thyroid surgery, as attempts to identify the nerve could lead to recurrent laryngeal nerve paralysis. Unfortunately, this technique led to many recurrent laryngeal nerve injuries by inexperienced surgeons. Crile in 1906 described the procedure of radical neck lymph node dissection for the management of head and neck cancer in 132 patients [21]. He is considered the father of head and neck cancer surgery.

Frank Lahey (1880–1953)

During the second quarter of the 20th century, Frank Lahey did more than any other surgeon to accumulate, impart, and disseminate valuable clinical information about surgical diseases of the thyroid gland; he published more than 150 articles related to thyroid diseases. He proposed the division of the strap muscles, wide exposure of the superior poles, and visualization of the recurrent laryngeal nerve and parathyroids [7]. Thus, it is Lahey who definitely showed that the recurrent laryngeal nerve could be dissected along its course without causing damage, and he showed that this was a safer way of operating on the thyroid. In 1938 he advised lateral ligation of the inferior thyroid artery to avoid nerve injury and recorded a nerve palsy rate of only 0.3% [22]. By the time of his death in 1953 he had personally performed almost 10,000 thyroidectomies.

Harold Foss (1883–1967)

Harold Foss, who worked at the Geisinger Clinic in central Pennsylvania, was known for his balance of careful technique and operative speed. His motto was "speed and accuracy," and he often completed 10 operations in a morning, including 3 or 4 thyroidectomies [23]. He encouraged his colleagues and residents to publish ("obligations of every member of this staff"), and he himself published more than 100 articles and addresses, including 25 related to the thyroid (mainly goiter) [24, 25]. Foss adopted the use of motion pictures to teach surgical techniques (Fig. 7) and was one of the first to show color (Kodachrome) movies—a thyroid operation in 1935—at a national meeting [23].

Advances during the 20th century

The 20th century was marked by significant advances regarding the management of thyroid diseases, including

Fig. 7 Harold Foss was among the first surgeons to use motion pictures to teach surgical techniques (from [23])

thyroid cancer. A detailed discussion of this progress is beyond the scope of this review. Advances include the use of blood transfusions (during the first decade of the 20th century), the introduction of patient follow-up and statistical analysis (a practice that allowed more critical evaluation of the results of treatment), the development of staging systems for all cancers (including thyroid cancer), offering the possibility of selecting the most appropriate method of treatment for each patient depending on the histological type and stage if the thyroid disease, the introduction of frozen section histopathology, which can aid the decision-making process during surgery. The first successful transplantation of a thyroid was reported by *E. Payr* in 1906, who transplanted a portion of the thyroid gland from a woman into the spleen of her myxedematous daughter with "successful" results. Gradually, it was realized that post-total thyroidectomy symptoms could be avoided by supplying patients with transplanted thyroid tissue, which some surgeons took to implant in patients who underwent total thyroidectomy. In time, oral supplements of desiccated animal thyroid extract replaced transplantation of exogenous tissue. Isolation of the hormone thyroxine (T4) was accomplished by Edward C. Kendall in 1914 [26]. Antithyroid drugs and radioiodine therapy were developed in the early 1940s and were used as alternatives to surgery in the treatment of hyperthyroidism. Propranolol was introduced in the perioperative management of patients with thyrotoxicosis in 1965 [27]. Scintigraphy had a significant role in the diagnostic work-up of patients with thyroid diseases during the last quarter of the 20th century, but its role gradually diminished after the introduction and wide use in clinical practice of neck ultrasonography (in the 1980s). Neck ultrasonography can detect very small thyroid nodules ($\sim$3 mm), lesions that are impossible to diagnose based on clinical examination alone. Fine-needle aspiration cytology (FNAC) of the thyroid was described by N. Söderström in 1952 [28] and has been generally available since the 1970s. Nowadays, neck ultrasonography with fine needle aspiration cytology (FNAC—often under ultrasonographic guidance) is considered the gold standard in the diagnostic evaluation of patients with thyroid nodules. By means of FNAC, preoperative diagnosis of a thyroid malignancy can be established, thereby accurately allocating surgical priority. Effective anesthesia and better instrumentation (including modern hemostatic devices, such as LigaSure or Harmonic Scalpel) greatly facilitate operative technique. The use of intraoperative monitoring of the recurrent laryngeal nerve in thyroid surgery was proposed about 40 years ago in an attempt to diminish the risk of injury to the nerve [29]. Its routine use in thyroid surgery remains a highly controversial issue. In selected patients with thyroid diseases (i.e., large retrosternal goiters) the use of modern imaging methods (CT, MRI) allows accurate preoperative evaluation of the disease, useful for the operating surgeon. The last decade of the 20th century and the dawn of the 21st century have been marked by the evolution and clinical use of molecular biology and minimally invasive surgery in thyroid diseases. Specific genetic alterations are now used as criteria to select appropriate management of asymptomatic patients [30]. For example, the children of parents with multiple endocrine neoplasia-2 (MEN-2) syndrome should be tested for *RET* oncogene mutations; in this setting, the detection of specific mutations is considered an indication for total thyroidectomy before the patient reaches the age of five years, at which time the disease is manifest only by C-cell hyperplasia and medullary thyroid cancer has not yet developed. Endoscopic or minimally invasive video-assisted thyroidectomy techniques have recently been used by some groups in selected patients to improve cosmetic results [31].

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