The latest anatomical discovery: the parathyroid glands or *Glandulae parathyreoideae* of Owen-Sandström-Gley

El último descubrimiento anatómico: las glándulas paratiroides o Glandulae parathyreoideae *de Owen-Sandström-Gley*

Carlos Ortiz-Hidalgo
Department of Pathological Anatomy, Hospital and Fundación Médica Sur, Mexico City, Mexico

Abstract

In 1852, Owen, a prominent British anatomist, described the parathyroid glands. While dissecting a rhinoceros, he noted a small compact yellow body, attached to the thyroid. Virchow and later Remak described the human parathyroids around 1960, but credit for the first complete description goes to the Sandström in 1980. More than a decade later Gley, showed that it was the removal of the parathyroids that accounted for the tetany that followed thyroidectomy. The association of parathyroid pathology and skeletal abnormalities was made in 1914 by Erdheim and Schlagenhaufer, and Mandl was the first surgeon to successfully treat a case of osteitis fibrosa by surgical removal of a parathyroid adenoma in 1925. The most extensive work on hyperparathyroidism was done in the 1930s by Albright from Boston, who described parathyroid hyperplasia, and differentiated between primary, secondary and tertiary hyperparathyroidism. Progresses in anatomy, physiology and surgery of the parathyroid glands, have contributed to various effective modalities of diagnosis and treatment.

Keywords: *Parathyroids. History. Richard Owen. Ivar Sandström. Marcel Eugène Émile Gley.*

Resumen

En 1852, Owen, un destacado anatomista británico, describió las glándulas paratiroides. Mientras realizaba la disección de un rinoceronte indio, observó un pequeño cuerpo amarillo compacto, unido a la tiroides. Virchow, y más tarde Remak, describieron las paratiroides humanas alrededor de 1860, pero el crédito por la primera descripción completa es para Sandström en 1880. Más de una década después, Gley demostró que era la eliminación de las paratiroides lo que explicaba la tetania después de la tiroidectomía. La asociación de la patología paratiroidea y las anomalías esqueléticas fue establecida en 1914 por Erdheim y Schlagenhaufer, y Mandl fue el primer cirujano en tratar con éxito un caso de osteítis fibrosa mediante la extirpación quirúrgica de un adenoma paratiroideo en 1925. El trabajo más extenso sobre el hiperparatiroidismo fue realizado en la década de 1930 por Albright, en Boston, quien describió la hiperplasia paratiroidea y la diferenció del hiperparatiroidismo primario, secundario y terciario. Los avances en anatomía, fisiología y cirugía de las glándulas paratiroides han contribuido a diversas modalidades efectivas de diagnóstico y tratamiento.

Palabras clave: *Paratiroides. Historia. Richard Owen. Ivar Sandström. Marcel Eugène Émile Gley.*

Correspondence:
Carlos Ortiz-Hidalgo
E-mail: ortizhidalgocarlos@gmail.com

Date of reception: 26-11-2020
Date of acceptance: 15-01-2021
DOI: 10.24875/CIRUE.M21000306

Cir Cir (Eng). 2022;90(1):136-145
Contents available at PubMed
www.cirugiaycirujanos.com

"Is seems hardly credible that the loss of bodies (parathyroids) so tiny, should be followed by a result so disastrous."

William S. Halsted (1852-1922)

Introduction

Parathyroid glands are essential to life, as they perform a key role in calcium metabolism. Their small size (between 3 and 7 mm) is not in accordance with their important function in homeostasis. It is possible that their small size was the reason for the delay in their discovery and their subsequent physiological understanding[1,2]. The parathyroids are the human glands more recently described. The way in which they were discovered and the events that followed their identification create a chronicle with different protagonists that made significant contributions to the judgment of the development, the histology, the function and the abnormalities of the parathyroid glands[3,4]. Below, there is a summary of the history of these little glands described just over 150 years ago.

Parathyroid glands discovery

Sir Richard Owen

The first description of the parathyroid gland was written on November 19, 1849 by Sir Richard Owen (1804-1892) during the autopsy he performed on a rhinoceros who had died in the London zoo[5] (Fig. 1A). Owen was born in Lancaster, England, on July 20, 1804, and started to study medicine in Edinburgh in 1820. It was in that University where he learnt to dissect cadavers, which later had a crucial role in his academic career. Apparently, the poor and boring anatomy classes of Alexander Monro III (tertius) (1773-1859) lead him to leave Edinburgh and move to London, to be admitted at St. Bartholomew's Hospital, where he graduated as surgeon *Fellow of the Royal College of Surgeons*, at age 23[5,6]. In 1834, he held the position of professor of compared anatomy in St. Bartholomew's Hospital, and was in charge of organizing the whole collection that John Hunter (1728-1793) had left, reason why he was appointed Hunterian Professor[5,6]. After the death of Charles Bell (1774-1842), who was known for the description of facial paralysis, he was chosen as professor of anatomy and physiology. Owen developed a great interest in the study of paleontology, and it was him who gave the name "dinosaurs" to that group of sauropsids that appeared during the Triassic (from the Greek δεινός*[deinos],* dreadful, and σαύρος*[sauros],* lizards; that is, dreadful lizards!)[5]. This name is not absolutely precise, as dinosaurs are not lizards. However, Owen pretended to evoke their majesty and terrific size[7].

Owen was a prolific writer and his literary production adds up to more than 600 articles and various books. His most prominent titles are: *Lectures on Comparative Anatomy and Physiology of the Vertebrate Animals* (1846), *A History of British Fossil Mammals and Birds* (1846), *A History of British Fossil Reptiles* (1849-84), and *On the Anatomy of Vertebrates* (1866-68)[8]. In the book *Odontography* (1840-45) he meticulously studies the structure of teeth and describes the dentine irregular lines, today called "contour lines of Owen"[6,8].

Owen knew how to become established at the peak of the scientific community. Nevertheless, as he was one of the strictest critics of Charles Darwin (1809-1882) because of his outspoken opposition to the theory of evolution, Owen not only lost his good name, but also earned the designation of "the great villain of science"[9]. Darwin, who had been his friend for more than 20 years, felt betrayed; and it is said that Owen was the only scientist the naturalist ever hated[8].

On September 20, 1834, the Zoological Society of London bought an Indian rhinoceros *(Rhinoceros unicornis)* for 1000 guineas (the guinea was the currency then used in England, and 1000 guineas were approximately $25,249.60 Mexican pesos or $1422.85 US dollars at present exchange rate) and it quickly became the main attraction at the London zoo[5,6,8]. This animal was placed together with the elephants, but it was not well received, as one of them attacked it. Not long after the incident, and probably due to the harm caused by the elephant, the rhinoceros died, on November 19, 1849. Perhaps nobody imagined that the death of this animal would contribute some really important knowledge about human anatomy. Owen dissected the 2-ton animal during the winter months from 1849 to 1850, and by the time the work was over, he mentioned that the cadaver "was already in an advanced state of decomposition"[6].

Owen's report included the last days of the rhinoceros, according to the registers in the minutes book of the Chief Zookeeper, as well as the whole dissection process[9]. Because of this, we can read that the animal lost its appetite as of July 1849 and had vomited viscous mucus and blood for a week before its demise. Owen discovered a rib was fractured and that it had injured the left lung, so he concluded this had

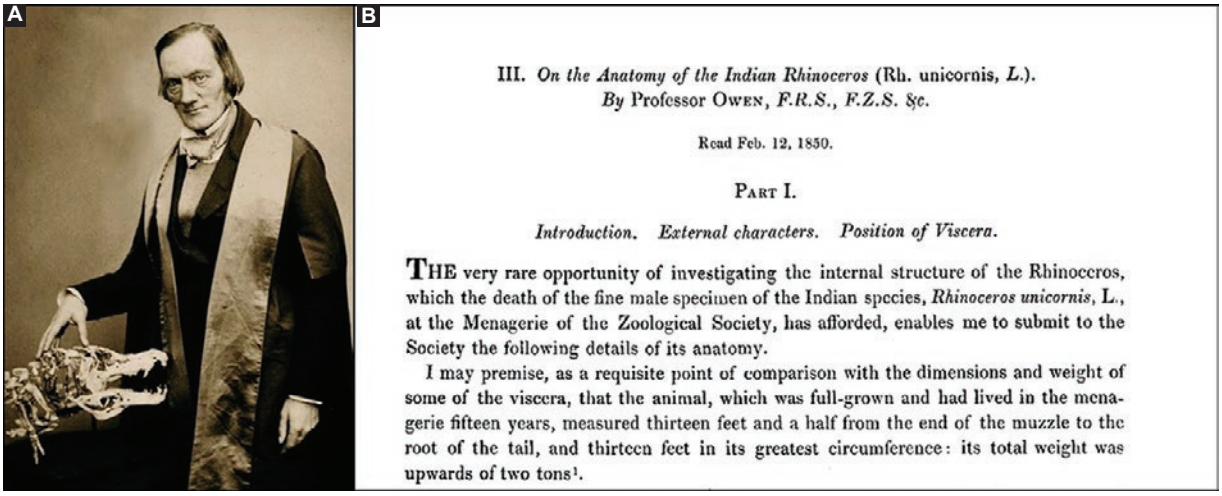

Figure 1. A: *Sir Richard Owen (1804-1892). Photograph, Maull & Polybank. Source: https://wellcomeimages.org/indexplus/obf_images/1e/cc/fb3a20c6b142ff5619e472cbc930.jpg.* **B:** *cover of the paper in which Owen describes the parathyroid glands in a rhinoceros. Source: Owen R. On the Anatomy of the Indian Rhinoceros (Rh. unicornis, L.). Zool Soc. 1852;IV:31-58.*

been the cause of death, probably a side effect of the harm produced by the elephant[8].

In a letter Owen wrote to his sister, he said:

"Amongst other matters time-devouring, and putting out of memory mundane relatives, sisters included, has been the decease of my ponderous and respectable old friend and client the rhinoceros. I call him 'client' because fifteen years ago I patronised him, and took it upon my skill, in discerning through a pretty thick hide the internal constitution, to aver that the beast would live to be a credit to the Zoological Gardens, and that he was worth the 1000 guineas demanded for him. The Council had faith, and bought him, and he has eaten their hay, oats, rice, carrots and bread in Brobdignagian quantities daily ever since, and might have gone on digesting, had he not, by some clumsy fall or otherwise inexplicable process, cracked a rib; said fracture injuring the adjacent lung and causing his demise. His anatomy will furnish forth an immortal 'Monograph', and so comfort comes to me in a shape in which it cannot he had by any of my brother Fellows"[8].

With the title *On the anatomy of the Indian Rhinoceros (Rh. unicorni L),* on February 12, 1850, Owen presented the results in a monograph to the Zoological Society (Fig. 1B)[10]. This manuscript appeared in the fourth volume of the journal *Society's Transactions,* which covers the period from January 1851 to September 1862. In those first publications of the Zoological Society, documents were informed as a group and included various years, so Owen's work was published in the volume dated in 1862, even though he had made his discovery 10 years before, which is an important piece of information in relation to the priority in the discovery of the parathyroid glands[5,8].

In section III of the report named *Thoracic viscera,* Owen described: *"a small compact yellow glandular body, attached to the thyroid at the point where the veins emerge".* This description corresponds to the parathyroid glands, but he did not perform a histological study nor did he ponder over the possible function of such structures[10]. The specimen that shows the rhinoceros parathyroid gland is classified under RCS-HM/L333.1 and is displayed at the Hunterian Museum, in The Royal College of Surgeons of England, in London. This specimen consists of part of the rhinoceros' larynx and trachea, and shows the lateral lobe of the thyroid: the "small compact yellow glandular body, attached to the thyroid at the point where the veins emerge", connected to its upper part and partially embedded in the tissue (Fig. 2). Due to all the information mentioned, the parathyroids had been named "the glands of Owen".

Owen died at 88 years old and is known as one of the most brilliant minds of Victorian England. He surely did not imagine that his description of the parathyroid glands of his "ponderous and respectable old friend and client the rhinoceros" would turn into one of the most memorable moments of his long and profitable life[5].

Figure 2. A: *indian rhinoceros (Rhinoceros unicornis), similar to the one Owen dissected. Source: https://www.freepik.es/vector-gratis/rinoceronte-indio-rhinoceros-unicornis_3098888.htm.* **B:** *larynx of the rhinoceros where the parathyroid gland is located (arrow) (Royal College of Surgeons of England, Mus., Physiol. Series, L 331.1).*

Ivar Viktor Sandström

Three years after Owen's publication, the Polish histologist Robert Remark (1815-1865), and subsequently in 1863 the German pathologist Rudolf Ludwig Karl Virchow (1821-1902), both working in Berlin, described some similar glands in cats and in humans, but did not assign them names nor did they ponder over their function[3,4]. It was not until 1880 that Viktor Sandström (1852-1889) described their exact localization and precise histological structure, and proposed the name (Fig. 3A)[11].

Sandström was born on March 22, 1852, in Stockholm and studied medicine in Uppsala University. By 1877, when he had just turned 25 years old and was still a medicine student, Sandström made the first anatomical and histological description of the parathyroid glands during the dissection of a dog's neck in the Department of Anatomy of the Uppsala University[3,11]. The work in which he described his findings was written in German and sent to the journal edited by Virchow for its publication. However, it was rejected because, as he was informed, it had an excessive length! There is a belief that, as Virchow had already seen some structures similar to those described by Sandström, he was not willing to give priority to the young Swede for the discovery, and that was the reason why he rejected the article[11]. Finally, the manuscript was published in Swedish in 1880 in the journal *Upsala Läkareförenings Förhandlingar,* with the title *Om en ny körtel hos menniskan och åtskilliga däggdjur* (About a new gland in humans and some mammals)[3,12,13]. In this 30-page article, Sandström said:

"About three years ago, I found in the thyroid gland of a dog a small organ, barely the size of a hemp seed, which was inside the thyroid connective tissue, but could be distinguished by its lighter color. The microscopic examination revealed a glandular tissue completely different from the thyroid's and with rich vascularization". (Figs. 3 B-C)[12].

Sandström named these structures *glandulae parathyroidea*, and assumed they were non-developed embryo parts of the thyroid gland. Afterwards, he dissected cats, rabbits and humans, and found some similar glands. He carefully dissected 50 autopsies, and in 43 of them he found four glands, two at each side of the thyroid. He then described in detail the position, size, color and various forms of the glands, and showed that they were always in close proximity to the thyroid and were between 3 and 15 mm in diameter. He pointed out that:

"The existence of a gland that, until today, was unknown in animals and that so often has been a matter of anatomic examination, required an exhaustive focus in the region around the thyroid gland, even in humans. Although the probability of finding something unrecognized seemed so low, I began a careful examination of this region not with the hope of finding something new, but solely with the purpose of completing the investigation. I was astonished when, in the first examined individual, I found at both sides to the lower edge of the thyroid gland an organ of the size of a small pea that, judging by its exterior, did not seem to be a lymph gland, nor an accessory thyroid gland, and that showed a peculiar structure in the histological examination."[12]

Sandström was awarded two Swedish medical medals and was invited to present his discovery before the Society for Natural Sciences, in Stockholm[11]. Nevertheless, his finding did not have much impact at that moment. His promising researcher career was cut short by a tragedy, as some chronic depression problems led him to commit suicide at the young age of 37[14]. Nevertheless, the originality and precision of his discovery had secured him a place in the history of medicine for ever. In R. L. Thomson's words: "This article Sandström wrote is so thorough that so little has been added to our knowledge since his discovery, and it is so complete that there is no doubt he well deserves the whole credit for the description of these organs"[15]. For this reason, the parathyroid glands have also been called "glands of Sandström".

Contributions to the study of parathyroids after Owen and Sandström

Almost a decade after Sandström's publication, the French physiologist and endocrinologist from Hôtel-Dieu,

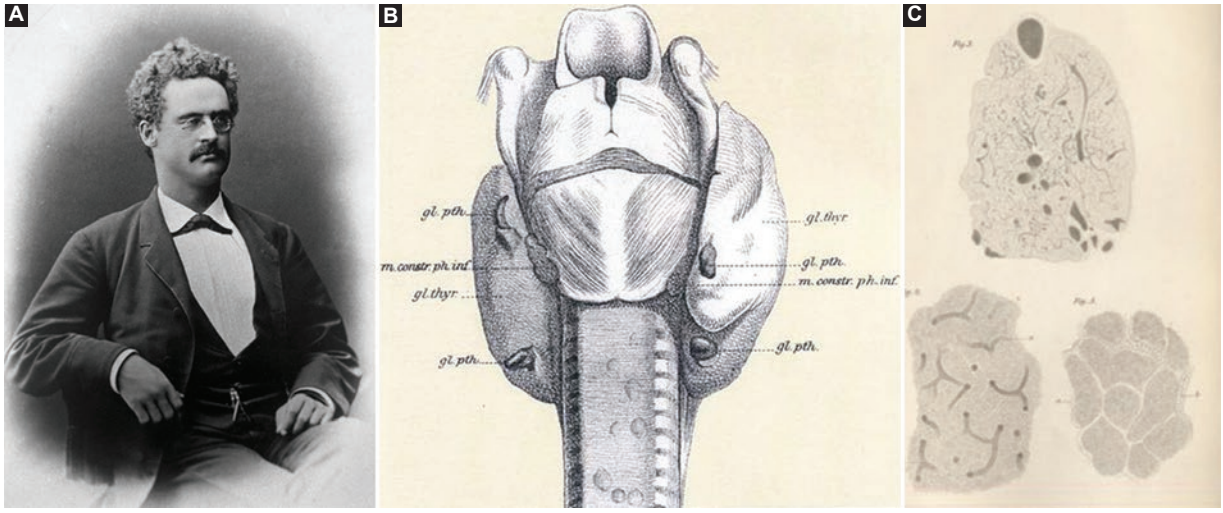

Figure 3. A: *Ivar Viktor Sandström.* **B:** *drawing that shows the anatomic localization of the parathyroids.* **C:** *first drawings of the histology of the parathyroid glands. Source: Sandström IV. On a new gland in man and several mammals – glandulae parathyroideae. Upsala Läk Förenings Förh. 1879-80;15:441-71. Source: https://wellcomeimages.org/indexplus/obf_images/c9/d5/ace8e8ed53e91666002e726e2c00.jpg.*

Marcel Eugène Émile Gley (1857-1930), who was the successor of Charles-Édouard Brown-Séquard (1817-1894) in the Collège de France, discovered the importance of these glands and published the first report about the relationship between the parathyroid glands and tetany (Fig. 4)[3,4,11].

Gley was born in the city of Épinal, located 400 km east of Paris, and studied physiology in Nancy. He later moved to Paris, where he received the title of *Professeur agrégé,* and in 1908, he was designated professor at the Collège de France. Gley noted during some experiments performed on dogs that these presented tetany after the unnoticed destruction of the parathyroids during the removal of the thyroid gland. He proved that when the parathyroid glands were removed from laboratory animals, these died of tetany, and mistakenly thought that the *glandules thyroidiennes,* as he called them, completed in some way the function of the thyroids[3,4]. He was not able to realize that these glands had a completely different role. In spite of this misinterpretation, Gley had found an essential function of these glands and, as a consequence, sometimes they have also been called "glands of Gley"[3,4].

Based on the studies by Gley, William George MacCallum (1874-1944), back then Chief of the Department of Pathology at Johns Hopkins Hospital, described that tetany was the direct result of calcium deficiency. During the same period, it was proved that tetany due to hypocalcemia could be treated with parathyroid extract injections[16].

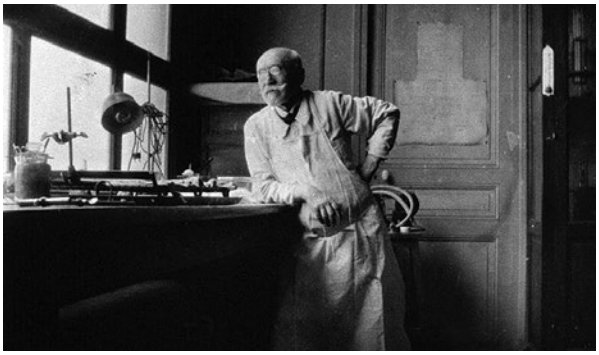

Figure 4. *Marcel Eugène Émile Gley (1857-1930) in his laboratory at Hôtel-Dieu, Paris. Source: https://wellcomeimages.org/indexplus/image/V0026444.html.*

The relation that exists between the parathyroids and bone disease was initially described by the pathologist from the Institute of Pathology in Strasbourg, Friedrich Daniel von Recklinghausen (1833-1910). In 1891, in order to celebrate Virchow's 71th birthday, 13 of his students, among them Edwin Klebs (1834-1913), Paul Grawitz (1850-1932) and Von Recklinghausen, published a commemorative book*(Festschrift Rudolf Virchow zu seinem 71. Geburtstage)* (Fig. 5A)[17]. One of the chapters was written by Von Recklinghausen under the title *Die fibröse oder deformirende Ostitis, die Osteomalacie und die osteoplastische Carcinose in ihren gegenseitigen Beziehungen* (Osteitis fibrosa or deforming, osteomalacia and osteoplastic calcinosis) (Fig. 5B)[17]. In it, Recklinghausen reported the autopsy study of 16 patients whose bones had been replaced

by fibrosis and cysts, and he called this osteitis fibrosa cystica (today known as Von Recklinghausen's bone disease; not to be confused with the other Von Recklinghausen's disease, which is the neurofibromatosis type I). Actually, Recklinghausen was very fortunate to be part of history because of this description, as 50 years later, Fuller Albright (1900-1969), who will be mentioned below, while revising the manuscript, came to the conclusion that only one of his 16 patients had the clinical and pathological characteristics typical of the hyperparathyroidism[18,19]. Albright concluded that four patients had had Paget's disease, three polyostotic fibrous dysplasia, and the rest, other conditions, including a metastasic carcinoma in the bone[18,19]. The only case that had what we now know as osteitis fibrosa was a 40-year-old patient, called S. Bleich, who in April 1888 had fallen from a staircase over his left side and was admitted to the hospital for pain in the hip joint[19]. It was not clear if it was a femoral neck fracture or a coxitis, and he was treated with general measures and discharged. In October of that same year, the patient slipped and fractured his clavicle, was readmitted to the hospital, where he fractured the right femur diaphysis, as he slipped with the bedpan! His pain continued and he also had an excessive deformity in various bones, and even though the fractures seemed to be healing, the patient was not able to lift his leg. His overall poor condition deteriorated and he died on October 4, 1889. Recklinghausen practiced patient Bleich autopsy and put emphasis on three of the principal pathological characteristics of the bone disease that is so often present with hyperparathyroidism: generalized fibrosis, cysts, and brown tumors (or giant cell tumors) (Fig. 5C). This case was diagnosed as *Ostitis de Fibröse Osteosarkome* multiple and was classified as “metaplastic malacia”, which refers to the replacement of the compact bone by recently formed fibrous osteoid. He used the word *Osteosarkome* to refer to the brown tumors called *Myeloidtumoren* or *Riesenzellensarkomen,* that possibly correspond to those we now know as “brown tumor of hyperparathyroidism”. He also described that Mr. Bleich had “a small reddish-coffee color gland in the left part of the thyroid”, which seems to be the description of an abnormal parathyroid gland[19].

Later, the relationship between bone disorders and the parathyroid disease was confirmed, when in 1904 the German pathologist Max Askanazy (1865-1940), born in Stallupönen, East Prussia (today Nesterov, Russia), described a 51-year-old woman with bone changes due to osteitis fibrosa and a soft, red-white parathyroid tumor of 4.5 x 2 x 2 cm attached to the left lobe of her thyroid[20]. Afterwards, the relationship between the glands and bone alterations was confirmed by a pathologist from the University of Vienna, Jakob Erdheim (1874-1937), also known for the description of the Erdheim-Chester disease and the craniopharyngioma (Fig. 6A)[21]. Erdheim proved, in experiments with rats, that the presence of the parathyroid glands was necessary for a good bone and dental development, and reported that the four parathyroid glands were bigger in patients with osteomalacia and rickets, so he assumed this was a compensatory hyperplasia[13]. There were two crucial observations: 1) the parathyroidectomy produced decalcification of the dentine in the rats' teeth, similar to what was observed in rickets, and 2) all parathyroids were bigger in rats with spontaneous rickets. Erdheim also proposed that the growth of parathyroids that appears along bone changes was a compensatory phenomenon and that the bone disease should be treated with parathyroid extract[11,13]. However, the Austrian pathologist Friedrich Schlagenhaufer (1866-1930) questioned the validity of this interpretation, as he had observed in two patients with osteomalacia that only one of the four glands was bigger, and proposed that the changes in the parathyroid glands were the main reason for the bone problem. According to this reasoning, it was logical for him to treat these patients through the removal of the sick gland[11,22].

The first parathyroidectomy in a patient with Von Recklinghausen's bone disease was performed by Félix Mandl (1892-1957) (Fig. 6B), professor of surgery at the University of Vienna[13,19]. The 38-year-old patient Albert Jahne, who was a streetcar driver, suffered from serious osteitis fibrosa cystica with femoral fracture and elevated serum calcium. In 1924, he was admitted to the Department of Surgery II, at the General Hospital of Vienna, and Mandl thought that the problem was a deficiency in the parathyroids, so he was treated with parathyroid extract pills (pills of *parathyreodin* or Collip extract), cod liver oil and mud baths, thinking in the possibility that his suffering was a secondary effect of rheumatism or arthritis[19]. In 1925, Albert was readmitted to the hospital and Mandl transplanted him four parathyroid glands from a man that had died in an accident. However, there was no improvement, so out of desperation he decided to perform a parathyroidectomy, a surgery he had never performed before. On July 30, 1925, under local anesthesia, the patient had his left inferior parathyroid gland removed, which was described as yellow-coffee in color, of 25 x 15 x 12 mm

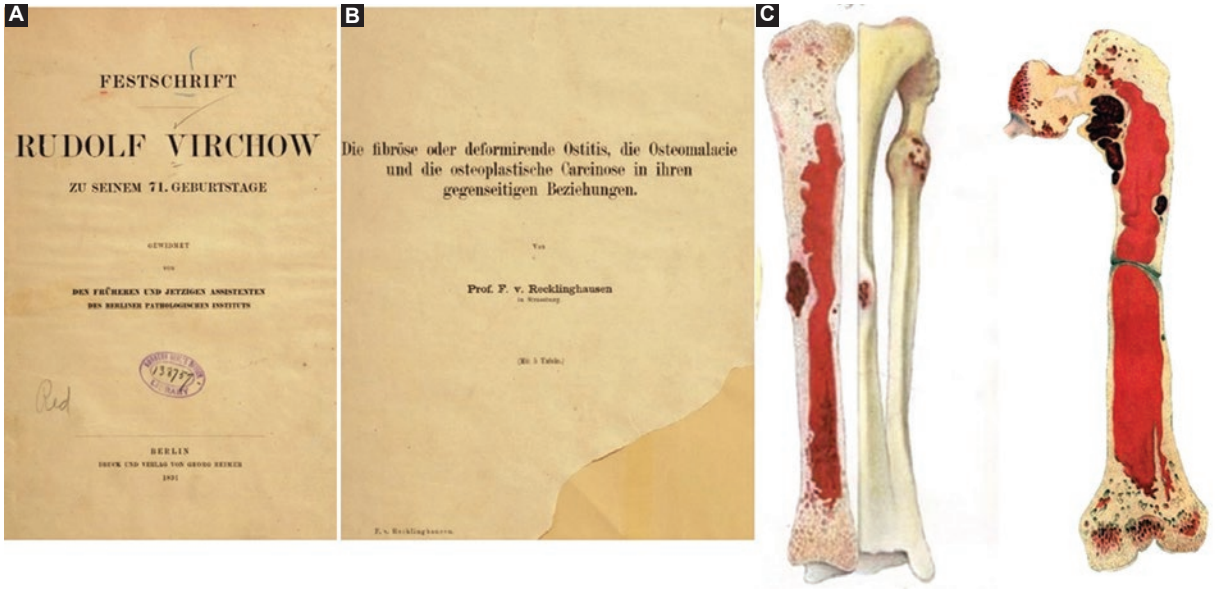

Figure 5. A: *publication of the commemorative book Festschrift Rudolf Virchow zu seinem 71. Geburtstage. Source: The Virchow "Festschrift". Lancet. 1891;138:1187.* **B:** *Die fibröse oder deformirende Ostitis, die Osteomalacie und die osteoplastische Carcinose in ihren gegenseitigen Beziehungen, of Von Recklinghausen, where he describes the osteitis fibrosa cystica.* **C:** *drawings of patient Bleich that show the main pathological characteristics of the bone disease that is so often present with hyperparathyroidism: generalized fibrosis, cysts and brown tumors. Source: https://collections.nlm.nih.gov/catalog/nlm:nlmuid-62130340R-bk.*

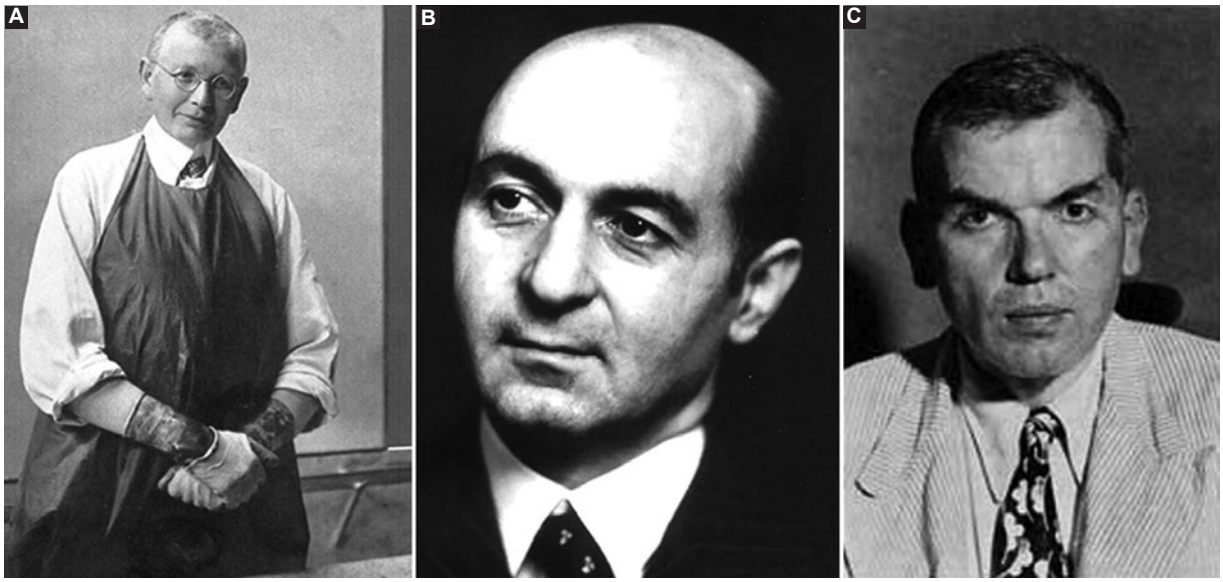

Figure 6. A: *Jakob Erdheim (1874-1937). Source: https://kehilalinks.jewishgen.org/Drohobycz/families/erdheim.html.* **B:** *Félix Mandl (1892-1957). Source: https://www.trendsmap.com/twitter/tweet/1235716632376377344.* **C:** *Fuller Albright (1900-1969). Source: http://collections.countway.harvard.edu/onview/items/show/5897.*

(the normal dimensions are 5 x 3 x 1 mm) and as being adhered to the recurrent laryngeal nerve. The other three parathyroid glands were normal. The patient improved spectacularly, his bones did not hurt anymore and the concentrations of serum calcium also improved. Mandl had demonstrated for the first time that Schlagenhaufer's hypothesis was correct, that is, that the bone disease was a consequence of a lesion in the parathyroid gland. “It was an experiment with fortunate results”, said Mandl, and he made history as

the first surgeon to resect a parathyroid tumor, and Albert as the first patient to be cured from a parathyroid tumor[23].

The removed gland was studied by Erdheim, who described it was made up of:

"... alveolar or plexiform and cohesive strains that were separated from each other by narrow strains of connective tissue with low cell count. The epithelial cells that form the alveolus lied side by side as a mosaic, separated by thin and red lines, and had a protoplasm that was sometimes clear and with a nucleus apparently free, sometimes it seemed to be full of thin particles and eosinophilic granules. The nucleus was generally round, vesicular, bright and of variable size. A nucleus can be five times bigger than another one, but it is rare to find one of excessive size. Where the epithelium was directly above the stroma, it sometimes showed a disposition in stockade... Normal parathyroid tissue cannot be found in the cut, in any place... One can assume it is a malignant tumor due to the inconstant size of the cellular nucleus and the mitotic figures and the cell polymorphism..."

Years later, Mandl considered this tumor to be an "adenoma"[3].

The patient Albert was able to walk with the help of a cane, and both the pelvic and extremity pain disappeared. However, 6 years later, he had a recurrence, and in September 1932 he presented a kidney stone, hypercalcemia again, decrease in the blood phosphatase, his bones were decalcified and he was once again incapacitated. Mandl operated again on Albert on October 18, 1933, but he did not find any tumor in the whole neck region nor in the mediastinum, and he removed two normal parathyroid glands. The patient died in February 1936 and the autopsy did not reveal any parathyroid tumor. Various bones showed changes as consequence of the serious hyperparathyroidism, and both kidneys had nephrocalcinosis[3]. It is assumed that Albert died from metastatic parathyroid carcinoma, but that is something that will never be resolved[24]. Two years after the surgery, Mandl received the *Venia Legendi,* that is the highest academic qualification to be professor of surgery at the University of Vienna, which was also revoked by the nazi regime because he was Jewish. He had to leave Vienna and continued his surgical practice at the Haddassah Hospital, in Jerusalem. He returned to Vienna when the Second World War was over, in 1947, and was appointed chief of surgery at Kaiser Franz Josef Spital. He died at age 65 due to an influenza complication[13,24].

As we have seen, patient Albert received the parathyroid extract that Collip and Hanson had isolated years before. The first report of the isolation of an effective parathyroid extract is that of Adolph Melanchthon Hanson (1880-1959), in 1923, when he was still a medicine student at the University of Minnesota. Hanson, who had been a student of Harvey W. Cushing (1869-1939), developed a method to extract the parathyroid hormone from the bovine parathyroid glands for the treatment of tetany, in a laboratory prepared in his house[25]. By the same period, the Canadian biochemist James B. Collip (1892-1965) isolated from the parathyroid glands a substance he called *parathyrin,* and was convinced that the parathyroid glands had a regulating calcium hormone[26]. The method used by both of them to extract the hormone was similar. They grinded the parathyroids of an ox and treated them with diluted hydrochloric acid. A concentrate was then prepared by evaporation, which was then titrated to neutral pH, and with that they isolated the paratohormone[25,26]. Collip is better known for having participated in the insulin isolation (although the Nobel Prize committee did not consider him worthy of it) than for his role in the discovery of the parathyroid hormone, an achievement of the same importance. The parathyroid hormone was purified in 1959 by Howard Rasmussen (1925-1999) and Lyman C. Craig (1906-1974) of the Rockefeller Institute, in New York. Its peptide structure was also defined by them in 1962[27]. Craig received the Albert Lasker price in 1963 and was nominated in 29 occasions for the Nobel Prize in chemistry.

Finally, an immunoassay to measure the different hormones, the parathyroid hormone among them, was developed in collaboration by Solomon A. Berson (1919-1972) and Rosalyn S. Yalow (1921-2011) in 1963. This made Yalow worthy of the Nobel Prize in medicine or physiology in 1977 (Berson did not received the prize as he had died from a heart attack at the early age of 53 years old in 1972, and Nobel Prizes are not awarded posthumously)[28,29].

In the advancement of current concepts in the physiology of the parathyroid glands, Fuller Albright cannot be omitted, as he devoted almost his entire academic life to the study of the parathyroids (Fig. 6C)[30]. Albright was born in Buffalo, New York, on January 12, 1900, and studied medicine at Harvard University. When he finished the internship, he firstly dedicated a year to the research of calcium metabolism with professor Joseph C. Aub (1890-1973), then one rotation at Johns Hopkins University

under the tutelage of professor Warfield T. Langcope (1877-1953), and then one year together with Erdheim in Vienna. These three public figures were of great inspiration for his later interest in the study of parathyroids[30,31].

When he returned from Vienna, Albright settled in the Massachusetts General Hospital and organized the endocrinology area. His work was really productive and he described various diseases, such as the polyostotic fibrous dysplasia associated with milky coffee skin spots and precocious puberty (McCune-Albright syndrome), the nephrocalcinosis with hyperchloremic acidosis (Lightwood-Albright syndrome), the amenorrhea-galactorrhea syndrome for pituitary prolactinoma (Forbes-Albright syndrome), the importance of menopause in osteoporosis, the different forms of congenital adrenal hyperplasia and the various types of hyperparathyroidism, among many other original contributions[30]. His prediction, around 1945, about the eventual birth control as a secondary effect of the hormone therapy is known as "Albright's prophecy"[30,31].

While Albright was still a medicine student, he discovered his passion for the study of the parathyroid glands. Since the year he presented the work entitled *The Physiology and Physiological Pathology of Calcium,* until his death in 1969 due to a pallidotomy complication because of Parkinson's disease, Albright dedicated almost his entire career to the study of these glands. At the age of 36, he was diagnosed with Parkinson's disease, and in 1956, against the opinion of many doctors, he decided to undergo a pallidotomy. Unfortunately, the surgical procedure had complications because of a hemorrhage, which left him aphasic and comatose for the remaining 13 years of his life, a period during which he was attended at the General Hospital of Massachusetts[31].

Conclusions

Just over 150 years have passed since Owen, Sandström and Gley's descriptions lead to an endless number of studies about the ultrastructure, the biochemistry, the function, and the pathology of the parathyroid glands. The names of the discoverers have been forgotten little by little, but without a doubt, they deserve to be remembered. The term "parathyroids" may be a bit imprecise, as they are not always *para-,* they can also equally be *intra-, epi-* or *extra-* in relation to the thyroids. Besides, they only have an anatomical relation with it, but no physiological connection. These glands have historically received names such as *glandules thyréoïdennes, glandules thymiques, glandules branchiales* or *parathymus III, IV*. Unfortunately, many eponymous have disappeared, as they do not contribute anything to the meaning or the function of the referenced organ. However, to those who still use eponyms, the parathyroid glands have the best name: "glands of Owen-Sandström-Gley".

Funding

This paper did not receive funding.

Conflicts of interest

The author declares not to have any conflicts of interest.

Ethical disclosures

Protection of people and animals. The authors declare that no experiments have been made on human beings or animals for this research.

Data confidentiality. The authors declare that they have followed the protocols of their work center regarding the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appears in this article.

References

1. Erraez-Jaramillo PJ, Ortiz-Hidalgo C. Anatomía microscópica de las glándulas paratiroides normal. Principios generales para residentes de endocrinología y patología, con una breve nota histórica. Rev Mex Endocrinol Metab Nutr. 2020;7:43-53.
2. van der Walt J. Pathology of the parathyroid glands. Diag Histopathol. 2012;18:221-33.
3. Carney JA. The glandulae parathyroideae of Ivar Sandström. Contributions from two continents. Am J Surg Pathol. 1996;20:1123-44.
4. Eknoyan G. A history of the parathyroid glands. Am J Kidney Dis. 1995;26:801-7.
5. McAneny D, Beazley RM. The glands of Owen. Who was Owen? Surgery. 2016;159:7-10.
6. Modarai B, Sawyer A, Ellis H. The glands of Owen. J R Soc Med. 2004;97:494-5.
7. Torrens H. When did the dinosaur get its name? New Sci. 1992;134:40-4.
8. Wessels Q, Taylor AM. Anecdotes to the life and times of Sir Richard Owen (1804-1892) in Lancaster. J Med Biogr. 2017;25:226-33.
9. García Bartual M. ¿Fue Richard Owen un villano de la ciencia? Available at: https://www.lavanguardia.com/historiayvida/historia-contemporanea/20170620/47313745809/fue-richard-owen-un-villano-de-la-ciencia.html
10. Owen R. On the Anatomy of the Indian Rhinoceros (Rh. unicornis, L.). Zool Soc. 1852;IV:31-58.
11. Johansson H. The Uppsala anatomist Ivar Sandström and the parathyroid gland. Upsala J Med Sci. 2015;120:72-7.
12. Sandström IV. On a new gland in man and several mammals – glandulae parathyroideae. Upsala Läk Förenings Förh. 1879-80;15:441-71.
13. Vermeulen AHM. The birth of endocrine pathology. How Erdheim misunderstood parathyroids. Virchows Arch. 2010;457:283-90.
14. Breimer L, Sourander P. The discovery of the parathyroid glands in 1877: triumph and tragedy of Ivar Sandström. Bull Hist Med. 1981;55:558-63.

15. Thomson RL. A study of parathyroid glands in paralysis agitans. J Med Res. 1906;15:399-424-5.
16. Mac Callum G, Vogetlin C. On the relation of tetany to the parathyroid glands and to calcium metabolism. J Exp Med. 1909;11:118-51.
17. Editorial. The Virchow "Festschrift". Lancet. 1891;138:1187.
18. Cherian ET, Guttenberg KB. Osteitis fibrosa cystica. QJM. 2018;111:487.
19. Albright F. A page out of the history of hyperparathyroidism. J Clin Endocrinol. 1948;8:637-57.
20. Askanasy M. Uber Ostitis deformans ohne ostoides gewebe. Arb Geb Path Anat Inst Tubingen. 1903;4:398-422.
21. Pascual JM, Rosdolsky M, Prieto R, Strauβ S, Winter E, Ulrich W. Jakob Erdheim (1874-1937): father of hypophyseal-duct tumors (craniopharyngiomas). Virchows Arch. 2015;467:459-69.
22. Schlagenhaufer F. Über diffuse ossifizierende Periostitis. Ztsch f Heilk. Abt pathol Anat. 1904;25:364-80.
23. Nordenström J, Marcus R. History of the parathyroid gland and their secretory product. Parathyroid hormone. In: Biliezikian J, editor. The parathyroid gland. Basic and clinical concepts. 3rd ed. Amsterdam: Elsevier; 2015. p. 1-17.
24. Niederle BE, Schmidt G, Organ CH, Niederle B. Albert J and his surgeon: a historical reevaluation of the first parathyroidectomy. J Am Coll Surg. 2006;202:181-90.
25. Hanson AM. An elementary chemical study of the parathyroid glands of cattle. Mil Surg. 1923;53:280-4.
26. Collip JB. The extraction of parathyroid hormone which will prevent or control parathyroid tetany and which regulates the level of blood calcium. J Biol Chem. 1925;63:395-438.
27. Rasmussen H, Craig LC. Purification of parathormone by use of countercurrent distribution. J Am Chem Soc. 1959;81:5003.
28. Friedman A. Remembrance: the Berson and Yalow saga. J Clin Endocrinol Metab. 2002;87:1925-8.
29. The Endocrine Society Staff. In Memoriam: Dr. Rosalyn Yalow, PhD., 1921-2011. Mol Endocrinol. 2012;26:713-4.
30. Kleeman CR, Levine BS, Felsenfeld AF. Fuller Albright: the consummate clinical investigator. Clin J Am Soc Nephrol. 2009;4:1541-1546.
31. River V. Dr. Fuller Albright. Biografías Médicas Ilustradas. Available at: https://biografiasmedicasilustradas.blogspot.com/2015/06/dr-fuller-albright.html