MEDICAL VS. SURGICAL TREATMENT FOR PRIMARY HYPERPARATHYROIDISM

ESSAY

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BY

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Historical Review

The History of the Parathyroids

The parathyroids are the last mammalian organ to be discovered. **(Claude H Organ Jr 2000)** They are formed of four small glands lying next to the thyroid in the neck. Sir Richard Owen [Fig. 1], the curator of the Natural History Museum, discovered them in 1852 when he was dissecting a great Indian rhinoceros that had died in the London Zoo. **(Owen R 1862)** It is no wonder that some writing describe the parathyroid glands "the glands of Owen". **(B Modarai 2004)**

Figure 1 : **Sir Richard Owen, KCB, FRS (1804–1892)** (Courtesy of Royal College of Surgeons of England, London)

In his detailed description of the anatomy, Owen refers to 'a small compact yellow glandular body attached to the thyroid at the point where the vein emerged'—a structure we now know as the parathyroid gland. The original preparation in which Owen made the observation is still to be seen in the

Hunterian Museum of the royal College of surgeons in London. It measures 30×14×8 cm and consists of part of the larynx and trachea of the rhinoceros, showing the lateral lobe of the thyroid with a parathyroid attached to its upper extremity and partly embedded in its substance [Fig. 2].

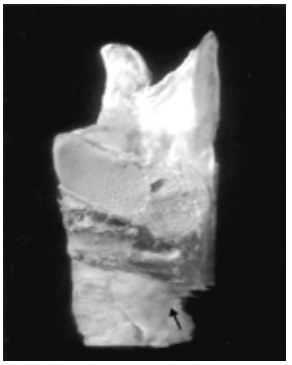

Figure 2: Specimen L333.1, Hunterian Museum, Royal College of Surgeons, London**.** The specimen, showing 'parts of the larynx and trachea of a rhinoceros (*R. indicus*), was added to the museum before 1858.' Courtesy of Royal College of Surgeons of England, London

Discovery of Tetany: In 1879, Anton Wölfer an assistant to C.A. Theodor Billroth was the first to describe postoperative tetany in a patient whom Theodor Billroth had performed his first total thyroidectomy. This patient recovered after 3 weeks of extremity convulsions. Tetany was attributed to hyperemia of the brain from the total thyroidectomy. This was the beginning of the detoxification theory for tetany. Nathan Weiss, another Billroth student,

collected 13 cases of tetany, 8 of which followed total thyroidectomy performed by Billroth. **(N. Weiss 1881)**

Discovery of the new gland: In 1880 Sandström (1852–1889) [Fig.3] a medical student, while working as a summer research assistant in department of anatomy at the University of Uppsala Sweden, observed a new small gland hardly the size of a hemp-seed, while dissecting the neck of a dog. This led to his classic monograph entitled "*On a New Gland in Man and Several Animals*." He had found also this gland on the thyroid of cat, rabbit, ox, and horse and noted "the existence of a hitherto unknown gland in animals that has so often been a subject of anatomical examination and called for a thorough approach to the region around the thyroid gland in man." Sandström's dissection of 50 human bodies confirmed his findings in animals.

Figure 3: **Ivar Sandström**, Uppsala, Sweden, 1877

Sandström suggested the name “glandulae parathyroidae”.**(Sandström IV 1880, Seipel CM 1938)** The function of these structures was unknown at that time. Sandström was not aware of Owen’s description, being published in a journal with a limited circulation at the time. His report was not well received, German editors rejected it being lengthy although carefully detailed both in gross and microscopic drawings and the work remained barely noticed for several years. Later his manuscript was published in Swedish in Uppsala medical journal. Indeed, Sandström did not receive the acclaim he deserved during his short lifetime. He suffered later from a hereditary mental disorder and later he committed suicide at age 37 years. **(Breimer L, Sourander P 1981)**

Discovering the relation between Tetany and the new gland: The significance of Sandström’s discovery was not appreciated until Eugene Gley (1857–1930), a French physiologist successor to Brown-Séquard at the Collége de France, observed that the tetany and death caused by experimental thyroidectomy in dogs, rabbits and rats occurred only

if the excised material included the glands described by Sandström. A selective parathyroid injury model alone also caused tetany. His report (1891) was immediately appreciated by European thyroid surgeons. **(Gley, M. E 1891)**

Discovery of Osteitis Fibrosa Cyctica: In 1891, Friedrich Daniel von Recklinghausen [Fig.4] (1833–1910) professor of pathology at Strasbourg, reported a patient who had experienced recurrent fractures of several bones with negligible trauma and had subsequently shown 'bending' of the long bones

Fig. 4 Friedrich Daniel von Recklinghausen

with extensive fibrosis, cysts and brown tumours. This group of findings was subsequently termed '**osteitis fibrosa cystica of von Recklinghausen**' **(Von Recklinghausen, F. D 1891, Ellis H. Bailey and Bishop's 1983)** now recognized as one of the most severe findings in advanced parathyroid disease. Although this important clinical observation had been

made, von Recklinghausen did not link the described bone disease with any parathyroid abnormality.

The first association of hyperparathyroidism with osteitis fibrosa cystica (von Recklinghausen's disease) was made by Askanazy in 1903. He reported a patient with bone disease associated with a large parathyroid tumor, and speculated, “This might be the cause”. **(Askanazy, M 1904)**

In the same year, Jacob Erdheim from the University of Vienna recorded the coexistence of a parathyroid tumor and a pituitary tumor, foreshadowing the description of multiple endocrine neoplasia almost 50 years later.

At the Johns Hopkins Hospital, William J MacCallum a pathologist in 1903 described the relief of tetany in experimental animals with parathyroid extract. He considered those glands function as neutralizers of a circulating toxin. Soon after in 1909 McCallum and Carl Voegtlin demonstrated that, the low blood calcium (hypocalcaemia) and tetany that followed removal of the parathyroids could be

controlled by parathyroid extract or by calcium administration but not potassium or sodium. They further demonstrated a decrease in tissue calcium in tetany. MacCallum and Voegtlin identified the cause of tetany as hypocalcemia resulting from insufficient parathyroid secretion, not the detoxification theory. **(MacCallum W.J., and Voegtlin C 1909)**

Determination of serum calcium level: In the same year that is 1909 serum calcium level determination became possible, and the association between serum calcium level and the parathyroid glands was established.

Parathyroid Transplantation: The first attempted of experimental parathyroid transplantation was in 1892. It was performed by Anton von Eiselsberg, a pupil of Theodor Billroth, approximately 1 year after Gley's report on post-thyroidectomy tetany. He transplanted it deep in the rectus sheath of a cat. **(A. von Eiselsberg 1892)**

Debate on parathyroid function and its relation to bone diseases continues until 1915 when Friedrich

Schlagenhaufer (1866–1930), professor of pathology in Vienna, suggested that an enlarged parathyroid might be the cause of bone disease and not the result of it. He presented two patients with osteomalacia each of whom was found to have a single parathyroid tumour at necropsy. **(Schlagenhaufer F 1915)**

Despite this finding, it took 10 years before the first attempt at removal of a parathyroid tumour. This happened in Vienna on 30 July 1925, a 38 years old Herr Albert Gahne, had been discharged from the Austrian army with tuberculosis. He then became a tramcar conductor then developed later “osteitis fibrosa cystica”. The Symptoms of this disease dated back to 1921. Bone x-rays in 1923 showed numerous cysts. In 1924, Mr. Albert Gahne sustained a fracture of the femur for which he was admitted to the Hochenegg Clinic under the care of Felix Mandl (1892–1957) [fig. 5].

Fig. 5 Felix Mandl

His blood and urinary calcium

levels were found to be elevated, with an observed white urinary precipitate.

Mr Gahne was unsuccessfully treated with parathyroid extract. Mandl then grafted fresh parathyroid tissue from an accident victim into Mr Gahne. In presenting this to the Vienna Surgical Society, he was caustically criticized by his colleagues because the graft(s) had not been microscopically confirmed as parathyroid tissue. In July 1925 at the University Surgical Clinic, and under local anaesthesia Felix Mandl explored Gahne's neck and removed a 'yellowish-brown almond shaped parathyroid tumour' measuring 25×15×12 mm from the left inferior area behind the thyroid gland. Felix Mandl was then widely credited with performing the first parathyroidectomy. Postoperatively his condition dramatically improved after the operation. Within a few days the blood and urine calcium content was considerably lower and the patient was soon able to walk. He was well for the next six years before developing recurrent hypercalcaemia and a renal calculus. Mandl operated once again but this time could not find any abnormal parathyroid tissue. There

was no postoperative improvement and the patient died in February 1936. The recurrence was probably due to aberrant parathyroid tissue, but none was found at necropsy. **(Mandl F. 1947)**

Although Felix Mandl has long been acclaimed as having carried out the first parathyroidectomy for primary hyperparathyroidism in 1925, yet there is some evidence that Sir Bland Sutton [fig.6] at London's Middlesex Hospital UK (1855–1936) in fact performed the first intentional removal of a parathyroid tumour at least a decade earlier. **(Welbourne RB 1990)**

Fig. 6 Sir Bland Sutton

Indeed, Sir John Bland-Sutton appeared to have been very much aware of the parathyroid gland and the pathology associated with it for many years, even before this first parathyroid operation. He described a post-mortem specimen of a parathyroid tumour in 1886; he surgically removed a parathyroid cyst in 1909; and then carried out

parathyroidectomy for a parathyroid tumour some time before 1917.

The diagnosis of hyperparathyroidism in the United States was initially made in January 1926 by Eugene F Dubois at the Bellevue Hospital in New York City. The patient was the famous 30-year-old Captain Charles Martell of New York City [fig.7]. (**Schwartz Principals of Surgery 1999**) Seven parathyroid exploration was performed on him between 1926 and 1932. The patient was a vigorous marine sea captain until 3 years before admission, when generalized skeletal decalcification set in. Extensive calcium metabolism studies were performed on Captain Martell until April 1927, when he was transferred to Dr Aub, at the Massachusetts General Hospital (MGH), with calcium and phosphorus levels of 14.8 and 3.3 mg/dL, respectively.

Fig.7: Captain Charles Martell, before and after the onset of hyperparathyroidism