The history of parathyroid endocrinology

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ABSTRACT

The parathyroid glands are now recognized as being essential for life. Their structure and function is well delineated, and their disease and dysfunction, well characterized. Diagnosis and management of parathyroid disease has improved in the past few decades. The path of parathyroid science, however, has been far from smooth. This paper describes the early history of parathyroid endocrinology. In doing so, it focuses on major events and discoveries, which improved the understanding and practice of our specialty. Contribution in anatomy, physiology, pathology, medicine, surgery and biochemistry are reviewed.

Key words: Endocrinology, history, parathyroid

INTRODUCTION

The nineteenth century witnessed the boom of endocrinology as a clinical science. Innovations in research, diagnosis and therapeutics stimulated interest in this young branch of medicine.¹

In 1805, Cuvier defined the medulla and cortex of the adrenal gland. A few years later, Alibert described acromegaly (1822), while Rathke described the formation of the pituitary gland (1838). In 1860, Von Luschka was able to describe the pituitary portal circulation.

Maximum attention, however, was focused on reproductive endocrinology. In 1824, Prevost and Dumas described ovulation, and in 1827, von Baer discovered the human ovum. The first suggestion for artificial insemination in man came from John Hunter in 1790. Berthold, in 1849, conducted elegant experiments on testicular transplants in birds, and Brown-Séquard tried organotherapy, using testicular extracts on himself. In such a rapidly evolving, exciting period of scientific discovery, the parathyroids took back seat. The choice of their name itself was unfortunate, as they were considered thyroid appendages, and were not given their due physiological significance too easily.

ANATOMY

In 1852, the parathyroids were described in the rhinoceros by Sir Richard Owen in London. He noted a small compact yellow, glandular body, attached to thyroid, in an Indian rhinoceros cadaver, preserved in London. Virchow described the human parathyroids in 1863, but credit for the first complete description goes to the Swedish doctor Sandstroem, in 1980. He identified two parathyroid bodies in 43 out of 50 autopsies.

In 1890, Anton Woelfler described areas of “young tissue” or “foetal rests” which might have been intrathyroid, as parathyroid glands.² Though the anatomy of the parathyroids had been reasonably well described, their physiology was not understood until much later.

EARLY STUDIES ON PHYSIOLOGY

Eugene Gley studied the parathyroid glands (he thought there were two in each animal) in rabbits, and performed...
Another ten years passed before Talage and Elliott (1903) described Bovine parathyroid tissue epithelium. The anti-calciuric and anti-magnesiuric actions of parathormone were demonstrated a much simpler method of managing tetany by early researchers in the nineteenth century, the first account of parathyroid disease quite early. Tetany in the pediatric age group was described by John Charke in 1815, and carpopedal spasm and glottis spasm by George Kellie in 1816. Steinheim, working in German, described tetany as “acute rheumatism” in 1830. Trousseau’s sign was described in 1862, Erb’s sign in 1873, and Chvostek’s sign in 1876. Though organotherapy had been in vogue as far as testicular and thyroid extracts were concerned, for quite some time, the first account of parathyroid hormone replacement was given in 1898. G. Moussu injected on aqueous extract of 12-20 equine glands and successfully treated post-parathyroidectomy tetany in canine models. In 1909, Berkeley and Beebe described correction of hypocalcemic tetany, with parathyroid extract, in man. In the same year, Mac Callum and Vogelin demonstrated a much simpler method of managing tetany with intravenous calcium chloride.

**Clinical Medicine**

Though the study of anatomy and physiology of the parathyroids proceeded slowly, clinical medicine had recognized the symptoms of parathyroid disease quite early. Tetany in the pediatric age group was described by John Charke in 1815, and carpopedal spasm and glottis spasm by George Kellie in 1816. Steinheim, working in German, described tetany as “acute rheumatism” in 1830. Trousseau’s sign was described in 1862, Erb’s sign in 1873, and Chvostek’s sign in 1876. Though organotherapy had been in vogue as far as testicular and thyroid extracts were concerned, for quite some time, the first account of parathyroid hormone replacement was given in 1898. G. Moussu injected on aqueous extract of 12-20 equine glands and successfully treated post-parathyroidectomy tetany in canine models. In 1909, Berkeley and Beebe described correction of hypocalcemic tetany, with parathyroid extract, in man. In the same year, Mac Callum and Vogelin demonstrated a much simpler method of managing tetany with intravenous calcium chloride.

Parathormone

The first report of isolation of an effective parathyroid extract is by Hanson, who reported his work in cattle in 1923. Yet he is not credited with the discovery of parathormone. This honour goes to the Canadian James Bertram Collip. Parathormone was discovered by Collip in 1925, and used to treat tetany successfully, by Leitch and him, in the same year. It was named as parathyrin. It is surprising that Collip is remembered more for his role in the discovery of insulin (though the Nobel Prize committee did not feel him worthy of the prize), than for his role in the discovery of parathyroid hormone, an equally important feat. The parathyroid hormone was isolated and purified by Ramussen and Craig in 1959, and its polypeptide structure defined by them in 1962. Bovine parathyroid tissue was used by all researchers initially.

In spite of this research, however, scientists such as Noel Paton and Findlay continued to assert that the function of the parathyroid was to detoxify guanidine (1917). The actions of the parathyroid hormone were discovered slowly. Greenwald identified its phosphaturic action in 1911, while Barnicot noted its resorptive effect on bone in 1948. The anti-calciuric and anti-magnesiuric action were described by Jahan and Pitts in the same year. Another ten years passed before Talage and Elliott observed an increase in calcium absorption form the small intestine.

The effectiveness of vitamin D in parathyroidectomized animals was reported by Hanson in 1935. It has taken many years for scientists to understand the actual relationship between vitamin D and parathormone.

In 1962, a new hormone, calcitonin, was discovered, and was initially thought to be secreted from the parathyroid gland. Its thyroid origin and significance was understood later.

**Pathology**

Gerhard Engel described the clinical condition of osteitis fibrosa in 1864. Von Recklinghausen gave a complete description of the disease in 1891. In 1904, Askanasy postulated a connection between parathyroid tumour and osteitis fibrosa cystic. In 1907, Erdheim described osteitis fibrosa in 1864. Von Recklinghausen gave a complete description of the disease in 1891. In 1904, Askanasy postulated a connection between parathyroid tumour and osteitis fibrosa cystic. In 1907, Erdheim described hyperplasia of the parathyroids in osteomalacia in humans, while in 1914; he found the same finding in rachitic rats. This is the first report of secondary hyperparathyroidism.

The most extensive work on hyperparathyroidism was...
done by Fuller Albright in the 1930s. He described parathyroid hyperplasia, and differentiated between primary, secondary and tertiary hyperparathyroidism.[15‑17]

He and his team also described pseudohyperparathyroidism in 1942.[18] The pathophysiology of the parathyroids was put in perspective by Greep RO, in 1963, who studied the comparative endocrinology of the glands. He suggested that as amphibians migrated from calcium- rich marine environment to calcium- poor terrestrial surroundings, and the need for a calcium homeostasis mechanism occurred. This then led to the development, and functioning of the parathyroid glands.[18]

**Conclusion**

The endocrinology of the parathyroids has grown slowly over the nineteenth and early twentieth centuries. Advances in anatomy, physiology, medicine, surgery and biochemistry have contributed to effective modalities of diagnosis and treatment which are in use today. This brief article pays homage to the pioneers of our specialty, while offering tribute to their acumen and perseverance.

**References**

1. Medvei VC. A history of endocrinology. Lancaster: MTP Press Ltd.; 1982.
2. Gley E. Sur Les fonctions du corps thyroide. CR Soc Biol (Paris) 1891;43:841-7.
3. Berkeley YW, Beebe SB. A contribution to the physiology and chemistry of the parathyroid glands. J Med Res 1909;20:149-57.
4. Mac Callum G, Vogelin C. On the relation of tetany to the parathyroid glands and to calcium metabolism. J Exp Med 1909;11:118-51.
5. Halsted WS. Auto- and iso transplantation, in dogs of the parathyroid glandules. J Exp Med 1909;11:175-9.
6. Collip JB. The extraction of a parathyroid hormone which will prevent or control parathyroid tetany and which regulates the level of blood calcium. J Biol Chem 1925;63:395-438.
7. Collip JB, Leitch DB. A case of tetany treated with parathyrin. Can Med Assoc J 1925;15:59-60.
8. Rasmussen H, Craig LC. Purification of parathormone by use of countercurrent distribution. J Am Chem Soc 1959;81:5003.
9. Rasmussen H, Craig LC. The parathyroid polypeptides. Recent Prog Horm Res 1962;18:269-95.
10. Greenwald I. The effect of parathyroidectomy upon metabolism. Am J Physiol 1911;28:103-32.
11. Barnicot NA. The local action of the parathyroid and other tissues on bone in intracerebral grafts. J Anat 1948;82:233-48.
12. Jahan I, Pilts RF: Effect of parathormone on renal tubular re-absorption of phosphate and calcium. Am J Physiol 1948;155:42-9.
13. Tal mage RV, Elliott JR. Removal of calcium from bone as influenced by the parathyroids. Endocrinology 1958;62:217-22.
14. Coop DH, Cameron EC, Cheney BA, Davidson AG, Henze KG. Evidence for calcitonin- A new hormone from the parathyroid that lowers blood calcium. Endocrinology 1962;70:638-49.
15. Albright F, Aub JC, Bauer W. Hyperparathyroidism- A common and polymorphic condition, as illustrated by seventeen proved cases from one clinic. J Am Med Assoc 1934;102:1276-87.
16. Albright F, Bloom berg E, Castlem an B, Churchill E, Churchill ED. Hyperparathyroidism due to diffuse hyperplasia of all parathyroid glands rather than adenoma of one. Arch Intern Med 1934;54:314-29.
17. Albright F, Reifenstein EC. The parathyroid Glands and Metabolic Bone Disease. Baltimore: Williams and Wilkins; 1948.
18. Greep RU. Parathyroid hormone. In: von Euler US, Hel ter H, editors. Comparative Endocrinology. Vol I. New York: Academic Press; 1963. p. 325-70.