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Comparative Endocrinology of Serum Calcium Regulation in Lower Vertebrates

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Serum Ca concentration in mammals is precisely controlled by three hormones; parathyroid hormone (PTH), vitamin D derivatives and calcitonin. The former two are hypercalcemic factors and the latter is hypocalcemic. Parathyroid hormone is secreted from the parathyroid gland (PT) which is present in all tetrapods and absent in piscine forms. The removal of this gland causes an acute decrease of serum Ca concentration in the majority of tetrapods. Thus the PT is an essential organ for the maintenance of serum Ca concentration.

In teleosts, serum Ca concentration is maintained by the pituitary gland. Hypophysectomy causes hypocalcemia accompanied by tetanic seizures in some teleosts, which can be corrected by administration of pituitary extracts.

PT emerges from the epithelial remnants of the visceral pouches upon their degeneration during embryonic development. Therefore, the phylogenetically lowest group bearing PT is the urodelan amphibian. However, a question arises as to whether or not the urodelan PT functions as a hypercalcemic organ as in higher tetrapods.

In *Cynops pyrrhogaster* and *Tylotriton andersoni*, which both belong to the Salamandridae, the highest phyletic group among urodelan families, parathyroidectomy (PTX) results in hypocalcemia. In these species the PT plays an important role in serum Ca regulation as a hypercalcemic organ. However, serum Ca concentration shows a recovery from the lowest level to subnormal levels in PTX specimens. Histological examination shows that this recovery is not due to regeneration of the PT, and the pituitary gland seems to be the main organ responsible. No recovery can occur after the removal of the pituitary gland. In this context, the pituitary gland is a potential hypercalcemic

organ, which shows its hypercalcemic effect when the PT is defective. However, hypophysectomy alone exerts only very slight effects on serum Ca concentration if the PT is intact. On the other hand, *Megalobatrachus davidianus* and *Hynobius nigrescens*, which belong to lower families, do not show significant changes in serum Ca concentration after PTX. In these species the PT is not as important as in higher species, and the main organ responsible for maintaining normal serum Ca is the pituitary gland. Thus, control of serum Ca concentration in lower urodeles depends on the pituitary gland as in teleosts even though they have the PT. On the other hand, there is substantial evidence that the PT of these lower urodeles do have a hypercalcemic factor.

In teleosts, the pituitary gland exclusively participates in hypercalcemic regulation. In lower urodeles, the PT appears and secretes PTH, but in fact PTH only plays a minor role in serum Ca control in lower urodeles, perhaps due to the premature state of their target organ system. In these species, the pituitary gland is still responsible for the maintenance of normal serum Ca concentration. In higher urodeles, the PT actually becomes functional and the pituitary gland is no longer required for routine serum Ca regulation, although still bearing potential hypercalcemic function. When the function of the PT is reduced, the pituitary gland resumes its hypercalcemic function.

These steps represent the transition of hypercalcemic organs and their function from piscine forms to amphibian forms during evolution. In anuran amphibians and more higher forms of vertebrates, the PT is exclusively responsible for the maintenance of normal serum Ca levels and its function is never substituted by the pituitary gland.