The discovery by Gudernatsch (53) of the role of the thyroid in the control of metamorphosis in amphibia quickened interest in this field, with the result that an overwhelming number of papers has appeared since 1912 on the thyroid gland and its functions in amphibia and other cold-blooded vertebrates. Much of the literature has been reviewed elsewhere (75), and a complete analysis of all the publications will not be attempted here. The present review concerns, primarily, those papers dealing with the thyroid gland of Necturus; as also, secondarily, some papers treating of other animals, which were important in the development of our present understanding of thyroid function in Urodela.

The Thyroid Gland in Necturus, and Comparisons with other Urodela

The thyroid gland of the adult Necturus was first recognized by Swingle (106, 107, 108) and by Adams (7) as a pair of small but perfectly formed glands. The presence of a median portion of the thyroid in Urodela was first recognized by Uhlenhuth (121), who described the median thyroid in Ambystoma as the “main portion of the left gland.” Shumway & Sanders (101) identified the follicles constituting the median thyroid in Necturus, and noted their positional relations in the early embryology of the gland. Charipper (30) considered the median thyroid of Necturus comparable to the isthmus of the thyroid in higher forms, and the lateral masses to right and left lobes. Webster (134) confirmed the presence of a median thyroid in Necturus. Sanders (94) found that the thyroid may occasionally be Y-shaped (due to incomplete separation of the lobes) or that there may be only lateral lobes, or lateral lobes plus a median or accessory lobe.

The thyroid gland in the adult Necturus is essentially bilateral, its stroma containing a number of colloid vesicles... each main lateral mass of which is attached closely to the medio-caudal surface of the first ceratobranchial cartilage, usually also covers the entire ventral surface of the second ceratobranchial, and may spread partly over the ventral surface of the proximal end of the first epibranchial cartilage. Often a more or less complete line of colloid vesicles can be found along the medio-ventral border of the first ceratobranchial cartilage, extending forward to the ventral surface of the first basibranchial element. On the first basibranchial element there is a group of vesicles, never fewer than three nor more than seven (30), that constitute the median thyroid; or the median thyroid on occasion may be absent (94). When present, the median vesicles occur on the posterior two-thirds of the first basibranchial; their arrangement in quite varied. The median portion of the gland is covered ventrally by the elongate geniohyoid muscle, and its lateral masses by the sternohyoid muscle.

The general shape and configuration of the thyroid is fairly constant, but there are many individual variations. In animals 29-30 cm. long the main lateral masses average 2 mm. diameter, while the train of follicles leading to the median group of follicles averages in length 45 cm. (30). In some Necturus, there may be chains or clusters of follicles along the first ceratobranchial, or there may be isolated fol-
licles. Some of my specimens seem to be without follicles along the first ceratobranchial; though Charipper (30) says that in most cases there is a compact linear mass of follicles connecting median and lateral masses. The number of follicles appears to increase with increasing age of *Necturus* (30).

In *Necturus* the blood supply to the thyroid is primarily arterial (29,30). Each external carotid artery sends a branch out from under the external ceratohyoid muscle to the region of the median thyroid. The internal carotid (arising from the first afferent branchial artery) sends on each side a large branch to the main lateral masses of the gland. Both arterial sources supply a complex and superficial capillary network which appears to be better developed about the more caudal follicles. The capillary network communicates with the jugular venous sinuses, but no large vein drains the gland. The blood supply to the thyroid gland in several species of Urodela (*Ambystoma opacum*, *A. jeffersonianum*, *Notophthalmus torosus*, *Eurycea rubra*) has been described as primarily venous (18,120,121). Charipper (30) found that the “vascular relationships of the thyroid gland in *Necturus* are like those found in completely metamorphosed Amphibia, and not at all similar to the condition reported for other urodèles.”

The morphology of the thyroid gland has been described in several species of Urodela (See, esp., numbers 4,25,30,72,77,78,80,95,107,117, 124,132,136 in the “Literature Cited.”). In all of them, the thyroids are similar in form, and occupy comparable positions. The thyroid of *Necturus* can be thought of as an “average” urodele thyroid, though Versluys (132) considered it “reduced.” *Siren lacertina* has the largest urodele thyroid; five lobes are present, including a median lobe, two long lateral lobes, and a pair of small accessory lobes (136). *Typhlomolge rathbuni* sometimes lack a thyroid gland (108,115,117); when present, the gland is at best rudimentary, and consists of a few epithelial masses scattered along the path of migration of the thyroid primordium. The epithelial cell masses may contain a lumen, but never colloid (117). The thyroid of *Proteus* is intermediate between that of *Necturus* and *Typhlomolge* (132).

There is considerable variation in the number of follicles in urodele thyroids though there is only one report that gives actual numbers. The average number of follicles in *Ambystoma maculatum* is 39.7; Uhlenhuth & Schwartzbach say that the number of follicles in each thyroid remains constant through the life of the individual, with growth occurring entirely through increase in the size of individual follicles (128). On the other hand, increase in the number of follicles has been reported in one series of young *Triturus* which had been subjected to stimulation by light (104).

The thyroid glands of all vertebrates from lamprey to man afford strong evidence of phylogenetic relationships; this is supported by commonality of function among the vertebrate animals (46).

Seasonal variation in the form and function of the thyroid of all Amphibia probably should be expected. External effects, especially extremes of temperature, influence specific morphological differentiation of the thyroid in frogs (8); these changes undoubtedly affect endocrine functions, and may give a clue to neoteny. Cyclic activity of the thyroid of adult *Triturus viridescens* involves moderate activity in winter, increasing activity in spring, and peak activity at the breeding season; after which the activity abruptly declines, with a summer phase varying from moderate activity to marked inactivity.
Light stimulates the thyroid of *Triturus viridescens* to increased activity; increased temperatures also cause an increase in activity which may be as great as, or greater than, the increase caused by light (104). In *Triturus torosus* there is a definite seasonal cycle, with thyroid activity lowest during the spring mating season and highest during the summer months when spermatogenesis and oogenesis are in progress. Thyroids of female *T. torosus* are said to be more active than those of males (125). To date, cyclic activity of the thyroid of *Necturus* has not been investigated.

The thyroid gland in *Necturus* arises as a median diverticulum from the floor of the pharynx between, or opposite to, the first visceral pouches (38,87,94,101,134). Platt (87) found the thyroid diverticulum to be hollow; in this she was supported by Webster (134), and in part by Baldwin (18) who said the thyroid anlage in *Ambystoma* is a hollow cup-like depression in the floor of the pharynx. A slightly different description of the early origin of the thyroid in *Necturus* was given by Shumway & Sanders (94,101); they found that the thyroid arises, as in most other urodeles, as a solid epithelial bud at the base of a transverse groove in the pharyngeal floor. The thyroid anlage is recognizable even in 5-mm. *Ambystoma* larvae (18).

The thyroid diverticulum of *Necturus* grows caudad until it reaches the pericardium (18,38,89,94,134). Its posterior end grows wider in contact with the pericardium, then splits; this splitting begins at the posterior end of the primordium, and then proceeds forward. [The second basibranchial cartilage of *Hyla regilla* is apparently the cause of division of the thyroid in that animal, for when the second basibranchial is absent, the thyroid does not divide (67).] Division into right and left lobes is completed in 10-mm. larvae of *Ambystoma* (18), and probably also in *Necturus*. As the thyroid divides, the general pharyngeal region elongates, with the result that the thyroid loses its contact with the floor of the pharynx and with the pericardium. The anterior portion is not entirely split; this becomes the median thyroid (94). The whole gland may be Y-shaped (94), or ‘usually is’ Y-shaped (30); or there may be only lateral thyroid glands, or lateral thyroid glands plus a median lobe (94).

After the gland splits, there is differentiation of the follicles. Follicles are present in 15-mm. *Ambystoma* (18). Small follicles are first formed; these fuse to form larger ones. The process of follicular fusion in *Necturus* is said to be suddenly stopped by an outflowing of colloid from them. Follicle-formation is rapid; each small half of the thyroid of a 39-mm. *Necturus* larva already contained 20-30 follicles (38).

There are great differences in the size and shape of individual follicles, even in a single gland, as well as marked variations in the size and shape of the cells in a single follicle. Individual follicles may be in outline irregular, rounded, oval, elongated, or collapsed into a star-shaped mass — all of varying dimensions. Each follicle is lined by a single layer of epithelial cells varying in shape from low cuboidal to high columnar, with its lumen filled with a homogeneous acidophilic colloid substance, containing, regularly, a number of characteristic vacuoles. The number and size of these vacuoles vary from follicle to follicle.

The histology of the thyroid gland of *Necturus* has been described by Charipper (29,30). Much on histology is included in papers by Adams, Algire, Allen, Hoskins, Uhlenhuth and their associates. Though
there are differences in details of structure, the follicles of the thyroids of all vertebrates fit the same general description.

An early indication of colloid formation has been seen in 26-mm. *Necturus* (101); colloid is definitely present in 33-mm. larvae (30), and in 39-mm. *Necturus* (38). Colloid has been reported in 30-mm. *Ambystoma*; its time of earliest appearance is probably close to that of *Necturus* (120). *Necturus* and *Cryptobranchus* of the same lengths have similar conditions of the thyroid; this is also true of the earlier stages of *Ambystoma* and *Eurycea* (94).

Several urodele species have been used in studies designed to discover the method of discharge of the colloid from the follicles. It was apparently never doubted that the colloid is the "active" secretion of the urodele thyroid, which, on being released, produces the effects attributed to thyroxin. This may be due to the fact that Bensley (20) demonstrated that follicular colloid is definitely produced by the follicular cells of the opossum thyroid. Bensley suggested that the colloid is stored as an excess secretion and that it is so stored only when the thyroid is producing more than is needed for ordinary maintenance.

The possibility that the discharge of the colloid might be under the control of the autonomic system was investigated by Uhlenhuth & Schwartzbach (118,128). It was their idea that pilocarpine increases glandular secretion through vagus nerve stimulation, and should induce metamorphosis; while atropine, which inhibits glandular secretion, should thereby inhibit metamorphosis. Larvae of *Ambystoma maculatum* and *A. tigrinum* reacted to the pilocarpine by vomiting, defecation and slime-secretion, but metamorphosis was neither accelerated nor enforced. Conversely, atropine (as well as adrenaline and ergotamine) did not inhibit metamorphosis. It was concluded that the vagus nerve and nervous system are not primarily involved in the releasing mechanism of the thyroid gland in Urodela; or, that the nervous system does not respond to these drugs in the same way as it does in warm-blooded animals.

Many investigators have contributed data indicating that the pituitary, especially the anterior lobe, exercises a controlling influence over the urodele thyroid gland, and helps to regulate the release of the colloid. (See esp. the papers by Uhlenhuth, Allen, Adams, Grant, and their associates.)

The path the colloid follows in its release from the follicles has been described as intercellular in several urodele species (120). Conversely, the path of release has been described as intracellular in *Necturus, Ambystoma jeffersonianum, A. opacum*, and *Triturus torosus* (47,48, 49,126); it has also been so described in a variety of other animals including (among others) the duck, monkey and sheep (100), and mammals in general (15). The preponderance of data seems to favor the intracellular route for release of the colloid. Absorption of the intrafollicular colloid, and secretion of it into circulation, causes the cells of the follicular epithelium to increase in height. Large cells are a prerequisite for colloid release; but both high and low cells of the thyroid follicular epithelium can elaborate colloid for follicular storage (126).

Near Function of the Thyroid Glands

Demonstration of the role of thyroid-feeding in accelerating metamorphosis led inevitably to further investigation of the relationship of thyroids and metamorphosis. The positive hastening of metamorphosis through thyroid treatment of many species of salamanders (including
several neotenous ones) was soon tested and proved. Thyroid tissue, thyroid extracts, iodine and several iodine-containing compounds were tried experimentally (21, 54, 57, 62, 63, 65, 108, 116, 138, and others). In 1929, Allen concluded that iodine is the effective agent in inducing metamorphosis, though its effectiveness varies with the chemical combination in which it occurs.

The effects of thyroxin in producing metamorphosis in many amphibia are so dramatic that for a time other effects were somewhat obscured. It is evident now that induction of metamorphosis is only one effect of thyroid feeding, and that it is not consistent among Urodela, for many respond to thyroid treatment by limited metamorphosis, or none at all.

The perennibranchiate amphibia, and a few caducibranchiate ones, have stubbornly resisted all experimental efforts to induce metamorphosis. All attempts to metamorphose *Necturus*, *Proteus*, young or old *Siren*, *Amphiuma means*, adult *Cryptobranchus*, recently hatched or adult *Pseudobranchus*, have ended in failure (13, 14, 17, 55, 62, 63, 68, 69, 80, 93, 96, 97, 108). While little experimental work has been done on *Typhlomolge rathbuni*, it should be included in the perennibranchiate list (93, 115, 117).

"Partial" metamorphosis characterizes some forms. *Cryptobranchus* larvae reared in solutions of dessicated thyroid undergo metamorphosis of the skin, but no other metamorphosis-changes (83). It should be kept in mind that adult *Cryptobranchus* have a completely metamorphosed skin, though the hellbender is considered incompletely metamorphosed (86). Thyroid injection reduces the gills of *Siren* (34, 80); the skin also completes its metamorphosis, though *Siren* is essentially larval in its other characteristics (26, 85). Neotenic *Triturus viridescens* forced to live in a dry environment, when given homoplastic transplants of pituitary and thyroid grafts, yet retain their gills; many of the experimental animals molted, and several became sexually mature (79). The retention of the gills was "attributed to a genetic cause more deep-seated than mere failure to complete the full genetic expression" (79). In an experiment in which a metamorphosed male *Triturus taeniatus* was bred with a neotenous female, thirty young were produced, half of them neotenous (130); so neoteny is, at least in part, genetic.

"Complete" metamorphosis follows thyroid treatment of many Urodela. Normal metamorphosis of many Urodela seems to be associated with altered activity of the thyroid, as shown by many investigators. A striking example is afforded in the life-cycle of *Plethodon cinereus* (36). This species lays terrestrial eggs from which hatch young salamanders that quickly assume adult form. During the development within the egg, certain urodele characters (such as external gills) appear, which seem to correspond to metamorphic changes of other urodèles. At this stage the thyroid gland first shows marked signs of secretory activity (36); the activity of the thyroid gland initiates the metamorphic change. The idea that thyroid activity is essential to metamorphosis is strengthened by the results of some experiments in which *Plethodon* eggs were kept in thiourea and phenylthiourea. Larvae hatched from the eggs failed to shed their larval skins, and showed no differentiation of eyelids as long as the treatment continued. Thyroid-inhibiting drugs thus produced an "aquatic"-type larva in this normally "terrestrial" species (74).

It is well known that metamorphosis in anurans and urodèles is
associated with increased metabolism (56,62,99). Thyroid activity increases during metamorphosis of Urodela just as it does in Anura. A much more marked release of colloid takes place in urodeles (75). Structures of the skin seem especially sensitive to thyroid and pituitary products, as is shown by the beginning of molting and differentiation of the integument at metamorphosis in anurans and many urodeles. Changes in skin pigmentation at metamorphosis depend upon the thyroid (113,125). The skin changes appear in natural metamorphosis and also in induced metamorphosis whether produced by iodine treatment, thyroxin injection, thyroid feeding or injection, pituitary hormones or pituitary transplants (13,32,48,49,65,66,85,128). Skin changes have therefore been extensively used as criteria for judging metamorphosis. However, as indicated above, many species of urodeles never metamorphose and others have an incomplete metamorphosis, due to the fact that certain tissues are no longer sensitive to the thyroid hormone (80). Even when the tissues fail to react by metamorphosis, there is response to the thyroid injection, demonstrated in a variety of ways.

A few reports have indicated that thyroid treatment of cold-blooded animals is ineffective. *Necturus* seems insensitive to enormous dosages of thyroid (106,108). It has been reported that the metabolism of the frog, turtle, small poeciliid fishes (*Lebistes reticulatus*) and *Triton cristatus* is not increased by injection of thyroxin or thyrotropic hormone (37).

The normal polynuclear blood-count in *Necturus* is similar to that of man and rabbit. Thyroid injection produces an increase in the percentage of Class I polynuclear neutrophil leukocytes, reaching a maximum within 12 hours; there is, of course, a proportional decrease in the percentage of other classes. After about 9 days, the count returns to normal. The extent to which the blood count is altered is directly proportional to the dosage of thyroid administered (27,28). The injection of thyroid produces similar effects in man and rabbit (88). In spite of differences in the principal hemopoietic centers in mammals and amphibians, the effects of thyroid injection on the white-cell count correspond closely. In rabbits, thyroidectomy does not alter the normal polynuclear count (89); it is probable the urodele count also is not altered. Thyroid treatment may initiate a shift in the hemopoietic center; thyroid-treated *Rana catesbiana* tadpoles shift their hemopoiesis from kidney to spleen, and the shift to bone-marrow hemopoiesis at metamorphosis may be correlated with a still higher metabolic requirement (70).

An antagonistic effect between thyroxin and vitamin-A in producing metamorphosis of *Ambystoma* has been reported (44), although it is denied there is any such antagonism in the metamorphosis of *Rana clamitans* (71).

In metamorphosed urodeles, molting is inhibited by hyperthyroid as well as hypothyroid conditions (111). Hyperthyroid *Triturus torosus* have much higher metabolic rates, as shown by their increased use of oxygen (111).

More has been discovered about the effects of the thyroid glands in Urodela and Amphibia generally by thyroidectomy than has been discovered by injection of thyroid materials. Hoskins & Morris (58,59) developed a method of thyroidectomizing Amphibia that has proven extremely valuable. They removed the thyroids from *Ambystoma* larvae in which circulation of the blood had not begun. The larvae
grew large, but did not show any metamorphic changes. There was no regeneration of the thyroids.

Generally, thyroidectomy seems to stop somatic differentiation of tissues, but apparently does not affect the gonads. Thyroid-less frog tadpoles grow larger in size by proportional increase in size of all the organs; there is little ossification. Thyroid-, as well as pituitary removal, stops metamorphosis in larvae of the Urodela (81). Germ cells seem to be unaffected by the thyroid, and may mature in thyroid-less tadpoles; conversely, frog tadpoles metamorphosed by thyroid feeding do not show any change in the gonads (10,11,60,92,105,112).

Possibly the most noticeable effect produced by thyroidectomy of urodeles is that of stopping the molt. Thyroid implantation or injection restores the molt very quickly (1,2,4,5,86,110,111). Interestingly, molting of adult urodeles is stopped by hyperthyroid conditions as readily as by hypothyroid (111). Hypophysectomy also inhibits molting in a number of Urodela (86). The integument of thyroidless *Triturus* becomes thick and leathery (but more permeable to water!), the glands are disturbed, and the cells of the skin appear to age faster (5,110); similar changes have been observed in several other urodeles (86). Less oxygen is used by the thyroidless *Triturus torosus* (111). The animal is more edematous, has a lower erythrocyte- and a higher leukocyte count. The spleen tends to necrosis, liver sinusoids enlarge, and the cells of the epithelium and intestine are greatly modified. Gonadal tissue becomes disorganized. These facts indicate that the lowered metabolic rate in thyroid-less *Triturus* may be due to lowered sensitivity of the tissues and to disturbances in the exocrine glands which are associated with digestion and assimilation of food (111).

**Metamorphosis and Neoteny**

Many explanations have been advanced to account for the failure of several neotenous and perennibranchiate salamanders to metamorphose, either normally or as a result of thyroid treatment.

Failure of metamorphosis in *Typhlomolge* has been attributed to the absence of the thyroid (115). Even when the thyroid is present in *Typhlomolge* there is no colloid present in the lumen of the follicles (117); in this respect the follicles of *Typhlomolge* resemble those of *Necturus* in which the thyroids have been made hyperactive by experimental treatment (51). It seems remotely possible that the cave-waters in which *Typhlomolge* lives may contain enough iodine to satisfy its needs.

The permanent neoteny of *Necturus*, *Proteus*, and *Typhlomolge* has been attributed to the thyroid gland, which Versluys (131) said is “reduced to rudimentary, with hypofunction.” The assumption may be correct so far as *Typhlomolge* is concerned, but is not correct for *Necturus*, *Proteus*, and several other neotenous urodeles. Thyroids of *Necturus* injected into immature *Rana clamata* produced signs of marked hyperthyroidism (108). The thyroids of *Proteus* and *Triton alpestris* also produce metamorphosis when injected into other amphibia (133). Neotenous thyroids may contain enough colloid to produce metamorphosis of several other individual amphibia. For example, the thyroid of an axolotl known to be at least four years old was cut into six parts and grafted into *Rana clamata* tadpoles (108); one tadpole died, but the other five developed fore- and hind-limbs, and showed resorption of the tail.

To test the hypothesis that failure to metamorphose might be due to failure of a releasing mechanism that would allow the thyroid to
put its secretion into circulation, Swingle (109) thyroidectomized eleven Colorado axolotls and then put the thyroid into the coelom of the animal from which it was removed. There was no subsequent metamorphosis. Two thyroid glands in the coelom of each of ten thyroidectomized axolotls also were ineffective in inducing metamorphosis. Five hypophysectomized axolotls also failed to metamorphose, so Swingle concluded that the hypophysis did not block the release of the thyroid secretion. It is of interest that three of twelve control animals completed metamorphosis while the experiments were in progress!

It has been amply demonstrated that a thyrotropic hormone produced in the anterior lobe of the pituitary exercises a distinct control of thyroid function. Both thyroid and anterior lobe of the pituitary are needed to produce metamorphosis (12, 13). The thyrotropic hormone may not be released during larval life, as has been claimed for Ambystoma maculatum and A. tigrinum (98, 99, 127, 128). There may be an unknown inhibitor of the pituitary, or a retarded formation of a releasing mechanism for the anterior lobe, or a delayed development of the anterior lobe with consequent failure to elaborate enough of the metamorphosis-inducing hormone as suggested for certain Anura (1928, 1929). Some species may fail to release enough thyrotropic hormone to produce metamorphosis; for example, reciprocal transplants of the pituitary between easily-metamorphosed Ambystoma tigrinum and the less-readily metamorphosed A. mexicanum induced metamorphosis in A. mexicanum but not in A. tigrinum (23). The anterior pituitary of Necturus releases a thyrotropic substance, as shown by the induction of metamorphosis in Rana clamitans that had been implanted with Necturus anterior-pituitary; metamorphosis is speeded up in proportion to the size of the implant (32).

Frog anterior-pituitaries implanted into the body cavity of Necturus cause colloid release from the thyroid follicles (47). Implants of anterior-pituitary from large (300-cm.) into small (47-mm.) Necturus uniformly produced hyperactive thyroids, with a marked reduction in the amount of stored colloid (51). The process of refilling the thyroid follicles with colloid may also be initiated by the anterior pituitary (50).

Schreiber (95, 96) considered the endocrine system of Proteus and found no evidence to show that it lacked function. Proteus has no endochondral ossification — all its ossification being perichondral; this pattern of bone formation was interpreted by Schreiber as being principally under the control of the anterior hypophysis. Necturus also has perichondral ossification. The failure of Necturus and Proteus to produce bone by endochondral ossification may be due to an altered thyroid function; for in the frog tadpole, where endochondral ossification is normal, there is nearly complete absence of ossification after thyroidectomy (112).

Hypophysectomized newts do not molt (3). Grafts of anterior pituitary activate the thyroid and produce molting; but in the absence of the pituitary, neither thyroid grafts, thyroxin nor iodine will cause molting. The thyroid is inactivated by hypophysectomy; also, thyroid injection inactivated the thyroid gland (3). Ambystoma larvae with triple pituitaries show an increase in stored colloid, while hypophysectomized donors show a decrease (22).

Basophil cells of the anterior pituitary of metamorphosing Rana sylvatica, R. pipiens, and R. palustris are involved in the elaboration of the thyrotropic factor (33). There is evidence that there are two
types of thyrotropic hormones, one controlling the storage of the colloid, the other is discharge; it has been suggested that the pituitaries of neotenic Amphibia produce the storage factor but lack the releasing factor (24).

Some of the data published on the pituitary-thyroid relationship have been contradictory. As early as 1920, Hoskins & Hoskins reported that beef-hypophysis containing iodine (1/200,000) when fed to thyroidless larvae brings about metamorphosis in 24 hours. They found that other tissues with equal iodine content would not produce metamorphosis, and suggested that the initial stimulation in hypophysis feeding is exerted on the calcium and phosphorus metabolism, as indicated by skeletal changes. Swingle (108) also induced molting in hypophysectomized Colorado axolotls by injection of iodine. Spaul (102) claimed that injections of anterior hypophysis induced metamorphosis in the Mexican axolotl, even when the thyroid had been removed. On the other hand, Figge & Uhlenhuth (43) could not induce metamorphosis in thyroid-less Colorado axolotls (A. tigrinum) by transplants of anterior lobe of the pituitary. It is reported (102, 103, 128) that the injection of extracts of the posterior lobe of the pituitary retarded the development of axolotls and tadpoles, and also counteracted the influence of injected iodine and of injected pars anterior of pituitary as well; more informations is needed to verify this function of the posterior pituitary (13).

The presence of thyroxin in circulation does not guarantee its delivery to the specific end-organs that would undergo metamorphosis, for the thyroxin in some instances might not transfuse the tissues. Several papers have included data which directly or indirectly argue against this probability. Axolotl-skin transplants may molt with the host or before the host-skin molts (135). Transplants of the skin of Ambystoma become pigmented and molt in the same time-sequence as the host, no matter if host-skin and graft-skin are of different ages (113). Ambystoma punctatum skin grafted upon A. tigrinum metamorphoses on this host species, but only when the host molts (113). The skin of larval Gyrinophilus porphyriticus, Pseudotriton ruber, and Eurycea bislineata transplanted to Necturus maculosus of the same body-length completes metamorphosis when the host is reared in 1/20,000 solution of thyroxin; the Necturus skin shows no change. Conversely, Necturus skin grafted on metamorphosing plethodontid salamanders is absorbed without metamorphosis (85). Grafts of axolotl skin on adult salamanders change to skin of adult type and pigmentation. It is reported that Proteus skin transplanted to Triton, Salamandra, or Ambystoma also undergoes typical metamorphosis, though skin of Proteus never changes in nature, and cannot be induced to change when Proteus is treated with thyroid (90, 91). Axolotl skin grafted on Proteus shows effects of hypothyroid conditions; but when Proteus is injected with thyroid, the axolotl skin undergoes metamorphosis-changes, indicating that thyroid hormone can circulate in the body of Proteus (97). Proteus skin on axolotl shows no metamorphic changes even when the host is undergoing metamorphosis due to thyroid injections (97).

The failure of Necturus to metamorphose has been attributed to factors other than endocrine (47). Necturus lacks the 6th (pulmonary) arch, as well as a spiral valve and septum in the truncus arteriosus. Without these structures, Figge (39, 40, 41) said Necturus is unable to separate systemic and pulmonary circulation, and so can-
not establish efficient pulmonary circulation to meet the heavy metabolic demands of metamorphosis. To test this hypothesis, Figge ligated the ventral ends of the sixth aortic arches in some larval *Ambystoma*, thus (in part) duplicating conditions in *Necturus*. Ligated *Ambystoma* in his first experiments (39,40,41) did not respond to metamorphosis-inducing substances, while controls kept in the same tank successfully completed metamorphosis. Later, Figge (42) discovered that metamorphosis may be produced in ligated *Ambystoma* if they are kept in an atmosphere of relatively high oxygen-tension.

Efficient pulmonary circulation is not an absolute prerequisite for metamorphosis. Removal of the lungs from axolotls (45) and *Rana pipiens* tadpoles (56), and removal of the fourth and sixth aortic arches of *Hynobius* larvae (64) does not prevent metamorphosis induced by thyroid feeding. For that matter, it has been known for a long while (77) that there is a relatively large by-pass between the branchial and pulmonary arteries in many Urodela (16,34), so that an ample supply of pulmonary blood is available if needed. However, it is probable that under ordinary circumstances *Proteus* (95,96) and *Necturus* do not use their pulmonary systems in respiration.

Undoubtedly most of the preceding data were sifted by Noble (82). He recognized that some urodeles metamorphose completely; that others begin the process and do not complete it; and that others do not metamorphose at all. It is evident that failure to metamorphose is not due to the absence of the thyroid hormone, but to the fact that certain tissues have lost the capacity to respond to the hormone by metamorphosis. It is not known what specific differentiation the tissues of non-metamorphic urodeles have undergone to block their metamorphosis but yet permit them to react to thyroid treatment in various ways. Possibly the physiological changes produced by thyroid in non-metamorphosing Urodela are as extensive as those produced in metamorphosing forms; but are of such nature that they are not considered metamorphosis. Metamorphosis is complex, involving much more than changes in Leydig cells, loss of gills, etc. (49,137). As a result, the criteria of metamorphosis are variable, and cannot be applied in the same manner to all urodeles (85). Thus, shedding of the skin in large patches is a criterion of metamorphosis in many species; correlated with the first molt is a loss of the large Leydig cells, and the development of a thicker stratum corneum. On the other hand, *Necturus* may molt naturally or be induced to molt; but there are no changes in the Leydig cells of the stratum corneum (35). Complete reduction of the gills is evidence of metamorphosis in many salamanders, but not in *Siren* (80).

When Kollman coined the term "neoteny" in 1884, he applied it in the most general way to those amphibia in which the larval period is extended beyond the normal time. Versluys (132) recognized two grades of neoteny. He said that *Necturus, Proteus*, and *Typhlomolge* retain their larval structures completely, and so exhibit complete neoteny; in these he found the thyroid "rudimentary, with hypofunction." The Derotremata and *Siren*, retaining the larval state only in part, were said to exhibit incomplete neoteny; their thyroids were described as "enlarged with hyperfunction, which probably goes hand in hand with hypofunction." Versluys said complete neoteny arose three times independently in *Necturus, Proteus, and Typhlomolge*; incomplete neoteny also arose three times independently in *Amphiuma,*
in *Megalobatrachus* and *Cryptobranchus*, and in *Siren* and *Pseudobranchus*.

Schreiber (95) described neoteny as an inequilibrium between the somatic line and the germinal line of development due to thyroid dystrophy directly affecting the soma. Schreiber recognized three grades of neoteny — *partial*, as in some of the frogs; *total*, as in the axolotl; and *absolute*, as in the perennibranchiates (96).

Schreiber's classification of the grades of neoteny has much of merit. His use of the terms "partial" and "total" apparently coincides with the original intent of Kollman. His third category, *absolute* neoteny, is well recognized and has been described by de Beer (19) and others as permanent neoteny.

Although there are many slightly varied meanings conveyed by the term, I believe it is correct to say that neoteny normally implies an extension of a young or "larval" period beyond the normal time, after which a normal "adult" may be produced. If this meaning is accepted, *Necturus*, *Proteus*, and *Typhlonolge* should not be considered truly neotenous, for they have lost the capacity to transform (though the inductor is present) either naturally or in response to experimental treatment involving pituitary and thyroid. Neoteny will account for the original establishment of the reproductive state in young developmental stages. Such a young stage, now sexually mature, may supplant the former adult stage, which will disappear in subsequent ontogenies. To describe this process of introduction into the adult descendant of some of the characters which were youthful in the ancestor, Gregory (52) and de Beer (19) have used the term *paedomorphosis*. It seems to me the adjective *paedomorphic* describes very accurately the developmental stage of *Necturus* and other non-metamorphic Urodela.

**GENERAL SUMMARY**

1. The thyroid glands of the Urodela (with the possible exception of *Typhlonolge*) are functional in regulating many activities, including metamorphosis.

2. Failure of metamorphosis is due to a loss of capacity on the part of the tissues concerned. The inductor (thyroxin) is present, and the tissues are sensitive to it, but they cannot respond by metamorphosis.

3. The term "paedomorphic" is proposed, better to describe the condition of "absolute neoteny" in *Necturus* and the other perennibranchiate Urodela.

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**Botanical Notes**

**Astragalus nuttallianus** DC. var. **zapatanus** Barneby, var. nov. Var. **trichocarpo** T.&G. legumine hirsutulo carinaceo acuta similis sed foliolis omnibus cuneatis oblongo-cuneatis retusis, necnon caulis cum foliorum rachi laxe hirsutulis aberrans. Prostrate, stems 1.5-20 cm. long; stems and herbage hirsutulous with rather stiff ascending and incurved hairs up to 0.4-0.75 mm. long, the leaflets thinly pubescent or glabrous above; leaves 1.5-4 cm. long, with (7-) 9-17 cuneate or oblong-cuneate retuse leaflets 2-6 mm. long. Peduncles 2-17 mm. long, 1-2-flowered; calyx 3.0-3.7 mm. long, the teeth 1.2-1.6 mm. long; petals whitish, lavender-tinged; banner (4.0-) 4.7-6 mm., wings (4.0-) 4.6-5.9 mm., keel 3.9-5.7 mm. long, blades of keel petals obliquely triangular, shortly acuminate into a sharply triangular slightly porrect apex. Pod 13-18 mm. long, 2.6-3.2 mm. in diameter, very gently and evenly curved, loosely pilosulous with ascending hairs.