Zoology. — *"On the Thyroid Glands and on the Phylogeny of the Perennibranchiate and Derotremous Salamanders"*. By Prof. J. VERSLUYS.

(Communicated at the meeting of June 27, 1925).

In the latest decennia it has become more and more evident that hormones are highly instrumental to the growth of the animal body, and to the development of several of its chief qualities. But then it is most likely that some of the modifications the animals underwent during their phylogenesis, were associated with changes in the production of the hormones. The factors that brought about the evolution of animals need not have affected the structure of the organs in a direct way only; this may have occurred also indirectly through their influence upon the organs that form the hormones and upon the production of hormones. So the rate of development, which may be of great importance for the acclimatization and consequently for the propagation of a species, is at least sometimes under the control of the hormone-forming organs. Hereby a new point of view was brought forward for the study of evolution. It is of special importance that the production of hormones depends on the climate and probably also on the food; changes of climate or food can through the agency of hormones modify the structure and the psychical properties of an animal. When in course of time the modifications increase, they can be either deleterious, immaterial, or useful to the animal; consequently they can be conducive to the propagation or the extinction of the species. Perhaps in this way, an explanation can be given of the occurence of some useless properties or of such properties as are even noxious on account of their exorbitancy (DENDY 1911).

Not a few investigators have already pointed out the probable significance of hormones for evolution, e.g. CUNNINGHAM (1908, 1921), BOURNE (1911), DENDY (1911, 1923), TANDLER (1913), MAC BRIDE (1914, 1917), NOPCSA (1917, 1923), KEITH (1919), HART (1920), BOLK (1921A, 1921B, 1922) and GRAHAM KERR (1924). For Man this problem derives additional interest from BOLK's conception that the modified hormone-production played an important part in the descent of Man from Primates, and from KEITH's theory that the differentation of Man into racial types is associated above all with a different production of hormones. It will, therefore, be undoubtedly of great importance to test these conceptions of the part played by hormones in phylogeny.

The first question we have to answer is whether any modifications in the hormone-forming organs can be found that are correlated with

evolution. As far as I am aware, there is only one example of it on record, viz. that given by NOPCSA (1917). This scientist pointed to the fact that among the fossil *Dinosaurs* there exists a parallelism between an excessively enlarged groove for the hypophysis in the base of the skull (which implies an abnormally large hypophysis) and the gigantism of many of these animals, some of which are the largest of all land-animals. He compares this gigantism with the well-known pathological overgrowth in Man, designated by the name of acromegalia. This disease is very probably a direct consequence of an affection of the hypophysis, which is thereby enlarged and imparts an unusual amount of hormone to the body. It is notorious that the hormone of the hypophysis stimulates the growth. Hence NOPCSA correlates the gigantism of the *Dinosaurs* with an anomalous hypertrophy of their hypophysis.

However the assumption of such a correlation between evolution and hormone-producing organs requires additional evidence, the more so as NOPCSA's example concerns fossil-forms, of which we cannot examine the hormone-producing organ itself; we know only the groove in which it laid, and which it need not have filled up entirely. Now I believe to have found an additional case in the thyroid of the *Urodela*. Its hormone is largely instrumental in the metamorphosis of these animals, as was first demonstrated by GUDERNATSCH (1912A, 1912B, only for *Frogs*) and corroborated by a number of researchers (e.g. by HERINGA, 1922, 1924 and notably for *Salamanders* by JENSEN, 1916, HART, 1917, WINTREBERT, 1908, UHLENHUTH, 1921, 1922, HUXLEY and HOGBEN, 1922, and SWINGLE, 1923, 1924).

The administration of thyroid hormone calls forth the metamorphosis even in very young larvae, whereas withholding it through extirpation of the thyroid body prevents the metamorphosis. Now, in a number of *Urodeles*, in the *perennibranchiate* and the *derotremous Salamanders*, the metamorphosis is either completely suppressed or does not attain completion, so that the development of the animals comes to a standstill in metamorphosis: they are *neotenous*. It appears that in all these forms the thyroid deviates more or less from the normal [1]). Some reports in the literature point in this direction. So SCHMIDT, GODDARD and VAN DER HOEVEN (1862, fig. 3, see page 32) give a picture of a surprisingly large thyroid of the *Giant Salamander* Megalobatrachus maximus; the authors add the following remark: "These glands are an assemblage of blind folliculi, measuring 1—2 mm., which are filled with a colloid mass. On the whole these glands reminded us of diseased glandulae thyreoideae in Man with incipient colloid degeneration" [2]) BOLAU (1899) found in a specimen of the *Giant Salamander*, of the length of 132 cm., very large thyroids 6 cm. in length and 1½ cm. in breadth. It is also of interest that

[1]) For the structure of the normal thyroid gland in non-neotenous *Salamanders* see BOLAU 1899, LIVINI 1902, THOMPSON 1911; and for Rana ADLER 1916.

[2]) Translated from the dutch.

VON EBNER (1877) has described a neotenous specimen of Triton cristatus 13 cm. long, of which the thyroids were excessively enlarged, measuring on either side : length 5, breadth 5, thickness 2½ mm., while the normal dimensions of the thyroid in this animal, in individuals of the same bodylength, are about long 1½ to 2, broad ¾ to 1, thick ½ mm. We see then that the thyroids of VON EBNER's larva are about 70 times the normal size. In every respect this animal possessed the structure of a larva with external gills, but it was sexually mature, and of the size of a full-grown animal. This gives reason to assume that there is in this case a correlation of neotony with the hypertrophied thyroids (VON EBNER, of course, did not think of this). Neotenous specimens of normal *Salamander*-species, especially Tritons are not rare, but EBNER's case is the only one in which some information is given on the thyroid. Presumably it is not so anomalous in other neotenous Tritons, otherwise this would have been noticed before (see MAREES VAN SWINDEREN 1925).

Opposed to these reports that point to enlarged thyroids in neotenous Salamander-forms are some others mentioning very small dimensions of these glands. So for instance the thyroid of the *perennibranchiate Salamander* Proteus is described by LEYDIG in 1863 as an extremely small, unpaired, median organ, made up of 15 to only 3 follicles of 0.12—0.15 mm. diameter (however, he has not found the paired thyroid, also present). And concerning the perennibranchiate form Typhlomolge Rathbuni miss EMERSON reports that she could not find a thyroid in a series of sections. A detailed investigation has proved that here, indeed, the thyroids are very rudimentary and are even lacking in some individuals. A normally functioning thyroid is not present here (UHLENHUTH, 1923 ; SWINGLE, 1922).

The present writer examined a number of specimens of *perennibranchiate* and *derotremous Salamanders* for the size and the structure of their thyroid glands, and compared with them the thyroids of a number of normal *Salamanders* and of a few *Axolotls,* i.e. neotenous individuals of Amblystoma mexicanum. We had some difficulty in procuring the necessary material, and the conservation also fell short. Only one individual of Siren was at my disposal. Typhlomolge I was not in a position to examine, but this is entirely made up for by UHLENHUTH's paper (1923). However, the results of my inquiry seemed sufficiently complete to justify their publication. Already in 1923 a short preliminary communication on my researches was published.

In the first place I examined the size of the thyroids in relation to the body-volume. In a number of specimens of various forms I measured the lenght, the breadth and the thickness of the thyroid which was most often paired, occasionally with accessory thyroids ; by multiplying these numbers and adding up the separate values of the two glands I obtained a number expressing the amount of thyroid-tissue present. This number I divided by the volume of the animal ; the quotient constituted the index by which

forms could be intercompared, that furnished a standard to judge of the relative size of the thyroid glands.

It goes without saying that this index varies rather much individually for normal *Salamanders*, with nutritive conditions, with outward circumstances; the amount of colloid [1]) present in the thyroid is also of great importance. In my limited material I could not establish a great influence of the age of the animals. In order to get some idea of the normal relation of the size of the thyroids to that of the body in typical *Salamanders*, that is a normal index, I added up the indices of 3 specimens of Triton cristatus, 2 of Triton taeniatus and 4 of Salamandra maculosa, and divided the sum bij the number of specimens, 9. The normal index thus obtained is 0.00016921 [2]).

In this connection it should be remembered that the nature of the colloid present in the follicles influences the contraction of the thyroid when conserved in alcohol. Generally the thyroid contains a colloid so consistent as to contract little in alcohol, and to fill up the follicles almost entirely; but sometimes the thyroids in the preparations contain very little colloid, presumably because the colloid was less consistent and has contracted considerably in alcohol. Such is the case with the specimens D and C of Megalobatrachus, with Amphiuma B and with Siren, and here the thyroid has probably contracted more in alcohol than could possibly be the case with a normal consistence of the colloid. In life the thyroids of these specimens were probably larger than is expressed by the indices.

The text-figures A and B represent the thyroids of some of the forms examined; figure B, in which all the heads have been reduced to the same length, gives a good idea of the marked differences in the size of the thyroids.

For a number of neotenous forms and for some specimens of Amblystoma I found the indices given in the table page 833.

When surveying this table we see that in some of the neotenous forms the thyroids are enlarged, in others more or less reduced, and that these differences do not occur in a disorderly way: a hypertrophy of the thyroid is found in all specimens of *Derometremata* examined and in Siren; a reduction is observed in all the other *Perennibranchiates*. This is very evident in Proteus and according to UHLENHUTH also in Typhlomolge. In these two forms the thyroids are not only very

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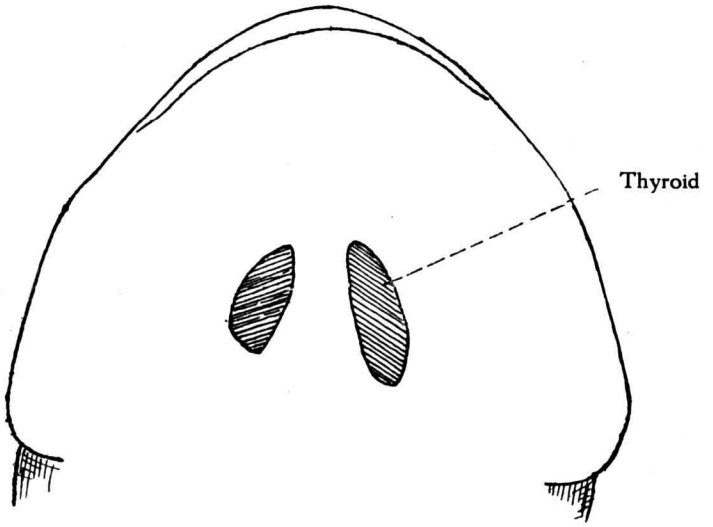
[1]) On the difference in the size of the thyroids in Rana temporaria from various regions, see ADLER, 1916.

[2]) The indices were for Triton cristatus: spec. A, long 125 mm., 0.0003947; spec. C, long 128 mm., 0.000109; spec. B, long 148 mm., 0.0001688; for Triton taeniatus: spec. B, long 86 mm., 0.0001732; spec. D, long 85 mm., 0.0002142; for Salamandra maculosa: spec. B, long 166 mm., 0.00017; spec. A, long 168 mm., 0.0001213; spec. C, long 161 mm., 0.0000931; spec. D, long 141 mm., 0.0000786. Specimen A of Triton cristatus exceeds the normal.

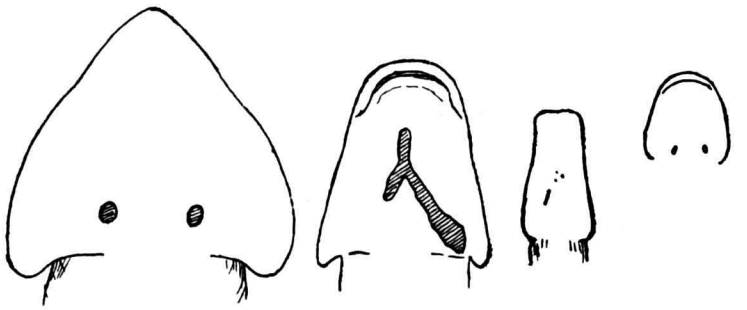
Indices of the Thyroid Glands in some neotenous Urodela and in an Amblystoma tigrium, adult.

Species	Length mm	Body volume cm^3	Index	Size of the Thyroids
Necturus spec. C	168	21	0.000107	about $^2/_3$ normal
„ spec. A	255	83	0.000189	normal
„ spec. B	408	552	0.000065	$^2/_5$ normal
Proteus spec. A	150	5	0.000025	$^1/_6$ normal
„ spec. B	215	15	0.000028	$^1/_6$ normal
„ spec. C	240	20	0.000012	$^1/_{14}$ normal
Siren spec. A	514	297	0.000469	± 3 × normal
Megalobatrachus maximus spec. A	175	28	0.000342	2 × normal
„ spec. B	380	260	0.000785	nearly 5 × normaal
„ spec. D	600	2880	0.000433	rather more than $2^1/_2$ × normal
„ spec. C	790	4400	0.000231	nearly $1^1/_2$ × normal
Cryptobranchus alleghaniensis spec. B	250	65	0.000343	rather more than 2 × normal
Amphiuma spec. B	550	162	0.000355	„ „ „ 2 × normal
„ spec. A	710	380	0.000326	„ „ „ 2 × normal
Amblystoma larve *(Axolotl)* spec. D	186	50	0.00121	„ „ „ 7 × normal
„ spec. C	234	63	0.00054	3 × normal
Amblystoma tigrinum spec. A	230	40	0.000343	2 × normal

small, but they also display an aberration in their development. Whereas the normal *Urodela* have a paired thyroid (see fig. A, 5), a third, more forward, median, unpaired thyroid is present in Typhlomolge as described bij UHLENHUTH. Most often one of the three thyroids is lacking, sometimes no thyroid could be detected at all. In Proteus I found a similar condition, only the reduction is less marked, and I could always find thyroids, though in two specimens one of the paired thyroids was absent (fig. A 4), once on the left, and once on the right. I find the follicle-epithelium in Proteus distinctly flattened, which is suggestive of a feeble function. In Necturus the reduction of the thyroid is much less pronounced, but the follicles are very large, their mean diameter being twice that in the normal adult *Salamanders* (I compared Salamandra maculosa and Onychodactylus japonicus), so their volume is 8 times larger. It follows, then, that the surface of the follicle epithelium in Necturus must be proportionately smaller than in normal *Salaman-*

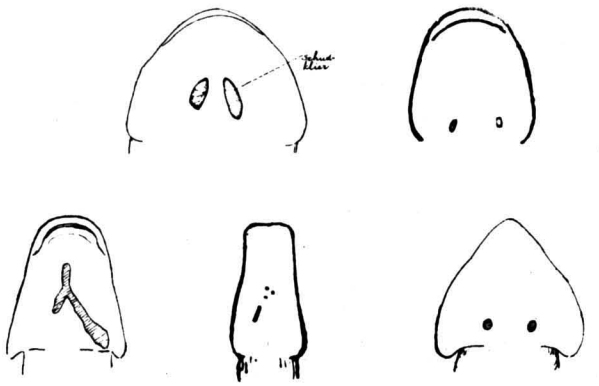


1. Megalobatrachus maximus (spec. D).



2. Necturus maculatus (spec. B). 3. Siren (spec. A). 4. Proteus (spec. B). 5. Salamandra maculosa (spec. D)

Text-figure A,
Thyroids of some *Urodeles* in situ. All figures $^2/_3$ nat. size.



Text-figure B.
The same figures as in fig. A, but all reduced to the same length.

ders; the considerable amount of colloid in the follicles has caused the thyroid to expand, but its productive surface is smaller than normal (about half). So we find in three forms of the *perennibranchiate Salamanders* a thyroid that is reduced and there is *hypofunction.* The reduction of the thyroid is most pronounced in Proteus and Typhlomolge, which also display the greatest anomaly, the more pronounced secondary adaptations, in their bodystructure. In Necturus the reduction of the thyroids is much less, while their histological structure is still normal, with a slightly flattened cubic epithelium of the follicle wall; this form in its body structure deviates little or not at all from a normal larva of *Urodeles.*

Quite different is the transformation of the thyroids in the *Derotremes* and the *Perennibranchiate Siren* (in so far as we may form an estimate of the relations in the latter form from one individual). The thyroids are not reduced, but enlarged, as a rule two or three times. This is also the case, when only a small part of the follicles in the alcohol-material is filled with colloid, so that the thyroids are contracted more than is the case with a normal consistence of the colloid (see page 832). Indeed, in some of the specimens examined the dimensions of the follicles are larger than in normal *Salamanders,* but at the same time the consequent diminution of the secreting surface is mostly more or less compensated by a folding of the follicle-wall (in a very marked degree in Amphiuma, spec. B; see fig. 3, plate) or by the irregular shape of the follicles (as in Amphiuma A, fig. 4, plate). In other specimens, i.a. in Megalobatrachus, spec. A, 175 mm. long, (which has almost entirely lost the external gills, except a few remains, but which still has an open gill-slit) the follicles are smaller than normally, so that the secernent surface is still more enlarged than would follow from the hypertrophy of the whole thyroid. In Siren the follicles appear to be as large as in normal *Salamanders.* It is, however, of special importance that in the *Detotremes* and Siren I invariably found the follicle-epithelium highly cylindrical (fig. 8, 9, plate), for this points to *hyperfunction.* The occasional formation of papillae by the epithelium (fig. 9) also points in this direction. The figures given us by the *Derotremes* bear some resemblance to those of the human thyroid in BASEDOW's disease, in struma parenchymatosa, which is also attended with a hyperfunction of the thyroid (see KOCHER 1912, BREITNER 1924); there we often meet with cylindrical epithelium, with papillae-growth and hypertrophied follicles of very irregular shape with folded wall, like the preparation of Amphiuma spec. B., represented by fig. 3.

The thyroid of the *Derotremata* and of Siren apparently functions vigorously. In this process we must assume the product to be supplied to the body [1]); anyhow the follicles only exceptionally contain colloid of

[1]) The colloid is probably not identical with the thyroid hormone which, however, is decidedly present in the colloid.

more viscous consistence, which displays the typical breaking up in columns in the preparations of alcohol material (e.g. in a specimen of Megalobatrachus, of which Mr. DE FREMERY furnished the material (see plate fig. 5). Most often the follicles in the preparations are for the greater part empty, just as with struma parenchymatosa. This strikes us all the more, when we compare the thyroid of the *Axolotl*. This is pretty much enlarged (see table p. 833), chiefly in consequence of an accumulation of colloid, through which the follicles are considerably distended and their epithelium is completely flattened (fig. 6, 10, plate). Here the colloid is detained in the thyroid and in consequence the function of the epithelium decreases as is evident from the intense flattening. It can be concluded from the non-appearance of the metamorphosis that there is a hypofunction though the thyroids are enlarged, a condition which, if it should become pathological, would be comparable to colloid goitre (VON EBNER's larva with its 70 times enlarged thyroids, shows that goitre is possible also in *Urodeles.*)

It follows from the above observations that the thyroid of the *perennibranchiate* and the *derotremous Salamanders* is developed abnormally and that two types are to be distinguished :

a. The reduced to rudimentary type with hypofunction of the *perennibranchiate Salamanders* Necturus, Proteus and Typhlomolge.

b. The enlarged type with hyperfunction of the *derotremous Salamanders* and of the *perennibranchiate* Siren.

With regard to the second type, however, the question may be asked whether the secretion of the thyroid contains sufficient normal hormone, whether there is perhaps a dysfunction. It would seem to me that dysfunction is no less probable than an overproduction of normal hormone. I am led to think so in virtue of the interesting researches by ADLER (1916). In his cultures of larvae of Rana temporaria first at a high temperature (30°—32° C.), and then at low temperature (8°—10°) he obtained numerous larvae that did not metamorphose or were late and tardy in doing so. The thyroid of these larvae appeared to be hypertrophied, grew strongly and exhibited in preparations the typical aspect of a *Basedow-thyroid :* the form of the follicles is irregular, many new follicles are formed, the follicle-epithelium is cylindrical; the colloid in the follicles shows less and less affinity to stains, and grows less and less viscous. So it is clear that the thyroid functions vigorously ; the non-appearance or the retardation of the metamorphosis cannot be due to a feeble functioning of the thyroid, it must be ascribed to the quality of the product, which is insufficient. As the thyroid of the *derotremous Salamanders* and of Siren reveals a similar transformation and the very tardy metamorphosis implies a lack of hormone, there is some reason to assume a dysfunction also here.

Now, in this connection it is of paramount significance that, just as there are two types of transformation of the thyroid, there are also two

types of neoteny among the permanently neotenous forms of the Urodeles (VERSLUYS 1909, 1912, 1923) and that these two coincide.

Necturus, Proteus and Typhlomolge are completely in the developmental stage of an Urodele-larva, just before the metamorphosis. They correspond in their structure with *Axolotls* and the not unfrequent neotenous, perennibranchiate specimens of Triton and other *Salamanders*. Like these they must have originated suddenly, because the metamorphosis stayed away, yet the animals became sexually mature and could propagate. That this neoteny is hereditary, we know from the Axolotl and has been demonstrated by DE FREMERY and VAN SWINDEREN for a neotenous race of Triton taeniatus (DE FREMERY 1924; VAN SWINDEREN 1925). The neoteny of Megalobatrachus, Cryptobranchus, Amphiuma, Siren, and the related Pseudobranchus however is a quite different one; these animals do not make a halt before the metamorphosis; they commence it, indeed, but they do not finish it. It cannot be that the metamorphosis is here quite suppressed; it is only retarded and not completed. This transformation may have been reached very gradually; the metamorphosis was then at first still almost completed [1]), subsequently more and more incomplete [2]), until even the external gills were retained in Siren. On the other hand in several respects the structure of Siren is not purely larval, but resembles that of a full-grown animal or anyhow of a *Salamander* in its metamorphosis, which is evident from the well-developed lungs, from the auditory ossicle, from the interruption of the larval palatinum-quadrate bone-junction, from the structure of the olfactory organ with JACOBSON's organ, and from the occurrence of an independent coracoidbone in the shoulder-girdle. In consideration of this combination of larval structure with that of adult *Urodeles* Siren cannot be conceived to have originated suddenly through suppression of the metamorphosis, but only through a gradual slowing and retrogression of the metamorphosis which was lengthened out, just as in the derotremous forms. Although Siren and Pseudobranchus possess external gills like the *perennibranchiate Salamanders* Necturus, Proteus and Typhlomolge, the type of their neoteny is not that of these forms, but is completely the same as that of the *Derotremata*. Now it is remarkable that also the transformation of the thyroid in Siren resembles that of the *derotremous Salamanders* and is unlike that of the other *Perennibranchiates*.

The specimen of Siren examined by me has peculiarly shaped thyroids which extend forward to a considerable distance and unite there to an unpaired median part, corresponding to the processus pyramidalis of the human thyroid (fig. A 3).

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[1]) As still is the case in the *Giant-Salamander*, that does not only shed the external gills, but also shuts its gill-clefts, though it be only after years.

[2]) *Cryptobranchus* and *Amphiuma* in which the gill-clefts are always open, and the skeletal gill-arches remain larval.

In the typical *perennibranchiate Salamanders* Necturus, Proteus and Typhlomolge, the larval structure is retained completely; so their neoteny is a *complete* one, and the thyroid is reduced to rudimentary, with hypofunction. *Derotremata* and Siren retain the larval form only in part; their neoteny is *incomplete*, and the thyroid of these forms is enlarged with hyperfunction, which probably goes hand in hand with a dysfunction. Here we should bear in mind that the various neotenous forms must have originated independently: they are not interrelated except Siren and Pseudobranchus, and perhaps also Megalobatrachus and Cryptobranchus. *Three times the complete neoteny arose independently in* Necturus, Proteus *and* Typhlomolge, *and in this process the transformation of the thyroid invariably went in the same direction: hypofunction and reduction. The incomplete neoteny also arose at least three times; once in* Amphiuma, *a second time in* Megalobatrachus *and* Cryptobranchus, *and a third time in* Siren *and* Pseudobranchus; *in this case there is always enlargement of the thyroid with hyperfunction.* This points to a correlation of the way in which the thyroid is modified and the type of the neoteny.

What conclusion can we now deduce from these observations with respect to the causes of the neoteny of perennibranchiate and derotromous Salamanders?

There is reason to look for the cause of the neoteny in a shortage of hormone, which brings about retardation or total absence of the metamorphosis. In the completely neotenous *Axolotl* the metamorphosis can be elicited by the administration of a larger amount of hormone [1]), so that in this form the neoteny can be unreservedly ascribed to a shortage of hormone (see SWINGLE 1924). This also affords a plausible explanation for the neoteny of Necturus, Proteus and Typhlomolge with their reduced thyroids. However, another explanation also suggests itself, viz. that for some reason or other the body no longer reacts with metamorphosis on the thyroid-hormone (UHLENHUTH 1921). SWINGLE (1924) believes that this must be somewhat the case in the *Axolotl*. Neither do Necturus and Proteus [2]) react any more on the administration of thyroid hormone (JENSEN, 1916; SWINGLE, 1924). The degeneration of the thyroids then would result from the suppression of the metamorphosis. But just this is very improbable, for if the normal development of the thyroid were really so closely bound up with the metamorphosis, we might also expect in normal *Salamanders* after the metamorphosis an atrophy of the thyroids. The two cases are comparable.

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[1]) Here the thyroid produces rather much hormone but retains too much of it, instead of supplying the hormone to the body.

[2]) Since the fourth arterial arch has disappeared here these forms could not metamorphose completely, nevertheless this process might commence for all that (see BOAS, 1881).

Now, since an atrophy of the thyroid after the metamorphosis does not appear in these animals, and since on the other hand the thyroids continue to grow considerably, keeping pace with the growth of the body, we can neither assume that the degeneration of the thyroids in the neotenous Salamander forms results from the neoteny. The relation must be the reverse, viz. the neoteny resulted from the dysfunction of the thyroids, because the body did not receive sufficient hormone. That the two forms of neoteny, the complete and the incomplete form, present either of them a type of transformation of the thyroid of their own also speaks for a far closer correlation than would exist with a passive degeneration of the thyroids as a result of the suppression of the metamorphosis.

For an explanation of the occurrence of the neoteny let our starting point be a shortage of hormone. Then there are still two possibilities to be considered : 1^0 this shortage may result from an insufficient production of normal hormone, 2^0 it may also be that the thyroids do not impart an adequate amount of hormone to the body, but retain it and deposit it in the colloid. The latter is probably the case with the *Axolotl* (UHLENHUTH, 1919, 1923 ; SWINGLE 1922, 1923 A, 1924). There the thyroid resembles that of Man in colloid-goitre (p. 836), which is a consequence of an inhibited emission of secretion to the body (BREITNER 1924). A factor is missing, which makes the thyroids deliver their hormone ; this factor may be a nerve stimulus, or an hormone from the anterior lobe of the hypophysis, or it may arise from a deficient circulation, or lack of oxygen (on the latter factor see BREITNER 1924, p. 4, after MANSFELD-MÜLLER). In this way the complete neoteny of Necturus, Proteus and Typhlomolge can readily be interpreted. By some cause or other the thyroids no longer emitted their hormone, hence they lost their signifiance and ultimately they became smaller and degenerated. Owing to the retention of the hormone all at once a complete neoteny was engendered, as is typical of these animals.

This interpretation does not apply to the *derotremous forms* and Siren, as in them hormone is indeed imparted to the body, which is obvious from the fact that metamorphosis commences. Besides this we have already observed that the structure of the thyroid here points to a hyperfunction and quick emission of the secretion to the body. Most likely we have to do here with a dysfunction, so that the thyroids, although functioning vigorously, and emitting their secretion, yet cannot supply the normal quantity of hormone required by the body (p. 836). The phylogeny of these forms may be imagined to be as follows : The increasing dysfunction of the thyroids retarded the metamorphosis, which began ever later and lasted longer ; the animals became sexually mature in their metamorphosis and did not accomplish their metamorphosis. This was gradually lengthened out, it was still gone through entirely, or partly for some points of their anatomy, for others only for a small part or not at all. Here accommodation to outward circumstances can have been of great influence. The thyroids

tried to make up for the shortage of hormone bij enlarging, but they did not succeed in filling up the deficiency.

Thus the two types of neoteny as well as the associated types of transformation of the thyroids can be explained and correlated. We think that we have to look for the cause of the neoteny, for the origin of the *perennibranchiate and derotremous Salamanders* in the thyroid. Either a change in the hormone production or in the supply of hormone to the body was the cause of the origin of these forms, which could develop to quite new types among the *Urodeles*. This transformation was achieved in the open air, and inadequate forms could not survive; only those forms persisted that were suited to their environment or could soon adapt themselves to it. For the ancestors of the *Derotremata* and of Siren an evolution from a more terrestrial life to a permanent aquatic existence can in this connection have been of influence, because the metamorphosis lost part of its importance for the animal by this change.

Lastly the question may be raised what might then have been the cause or the causes of the irregular function of the thyroids. All sorts of factors can have come into play here. It may have been want of iodin or an influence of the changes in the vascular system during the metamorphosis. It cannot be said whether this supposition is right or not.

Summary.

1. The neoteny of the *perennibranchiate* and *derotremous Salamanders* goes hand in hand with an abnormal development of their thyroids. As the hormone of the thyroid controls the metamorphosis, a case is given here in which the phylogenesis of entirely new animal forms is associated with a change in an endocrine organ closely related with it.

2. Among *Urodeles* there are two types of neoteny: that of the *perennibranchiate forms* proper Necturus, Proteus and Typhlomolge, which in their structural development persist in the stage of the full-grown *Urodele*larvae, before the metamorphosis, and that of the *derotremous forms* Megalobatrachus, Cryptobranchus, Amphiuma and of Siren and Pseudobranchus, which begin their metamorphosis, but do not accomplish it. An entirely different transformation of the thyroids coincides with this. In the first type the thyroids are small to rudimentary, and there is apparently a hypofunction of the thyroids. In the second type the thyroids are enlarged, and there is apparently a hyperfunction of the thyroids, probably associated with a dysfunction. Since the two types of neoteny have originated several times independently of each other, and yet the transformation of the thyroids in each type always went in the same direction, a close relation must needs be assumed between the neoteny and the mode of transformation of the thyroids.

3. The cause of the complete neoteny of the *perennibranchiate forms* is probably to be found in the retention of the hormone in the thyroid, which induced a complete suppression of the metamorphosis. The thyroids lost much of their significance, when they could no longer supply their hormone, or for a small part only.

4. The *derotremous forms* and S i r e n, with their incomplete neoteny, do not retain the hormone in the thyroid. Here the cause of the neoteny is to be looked for in a dysfunction which induced a chronic deficiency of normal hormone, and a marked retardation and final arrest of the metamorphosis. The thyroids tried to supply the deficiency of hormone by an augmented production and increased in size.

5. The *perennibranchiate forms* with their complete neoteny abruptly retained their larval stage ; this transformation was not an accommodation to their environment, and after the change the animals had to make the most of their condition as permanent inhabitants of the water. The development of the *derotremous forms* and S i r e n has been very gradual, because their ancestors gradually retained a more and more larval stage ; so this transformation could take place under the influence of the claims of their surroundings, and could coincide with adaptations.

6. Nothing is known regarding the cause of the irregular function of the thyroids. It might be ascribed to want of iodin or changes in the circulation during the metamorphosis, or want of oxygen. There is no reason to assume that the cause was the same in all cases.

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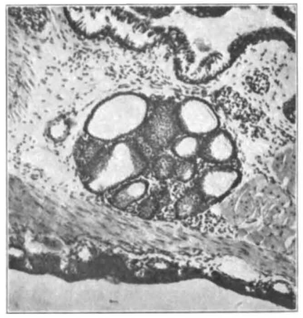

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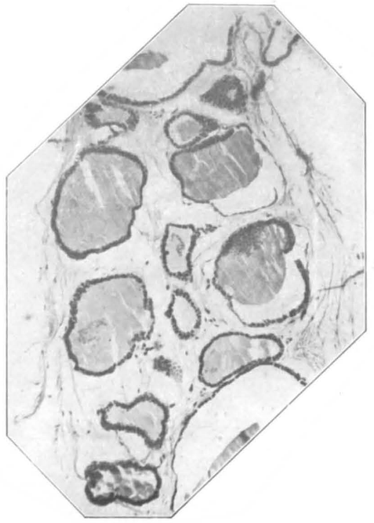

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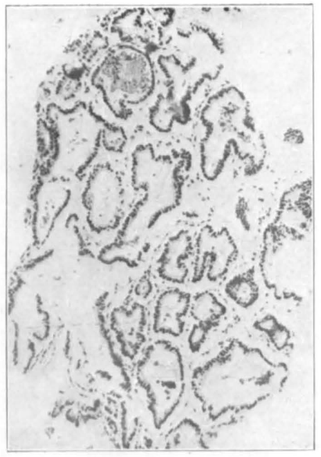

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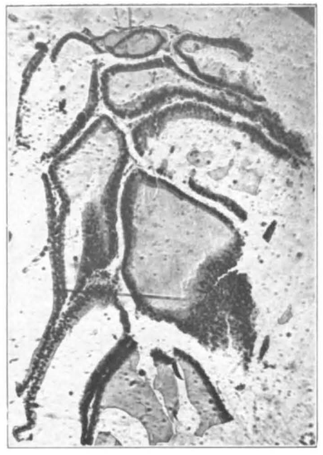

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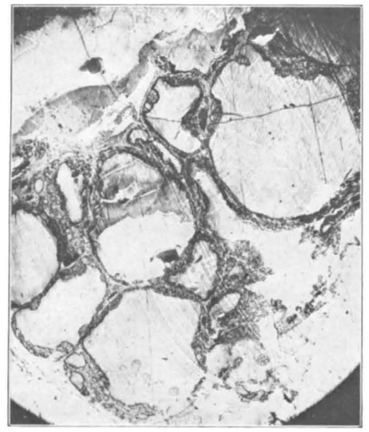

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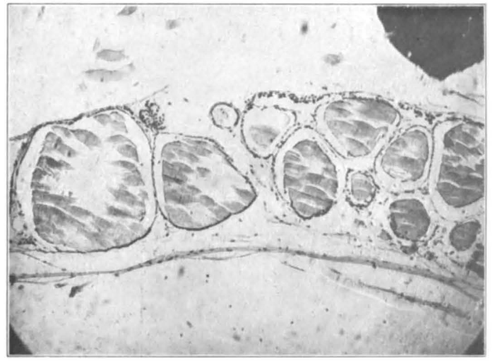

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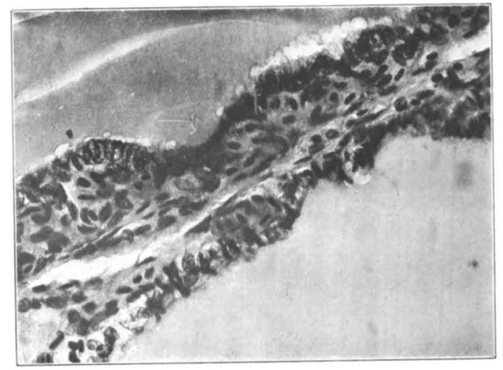

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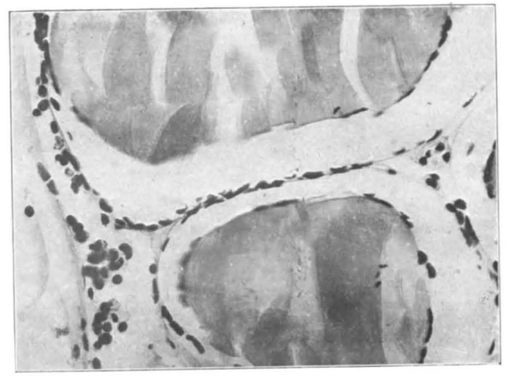

Fig. 10.

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EXPLANATION OF THE PLATE.

Fig. 1. Section through the thyroid of a normal adult *Salamander*, Onychodactylus japonicus; hematoxilin. × 40.

Fig. 2. The same of Necturus (spec. B); hematoxilin, eosin. × 40.

Fig. 3. The same of Amphiuma (spec. B); hematoxilin, eosin. × 40.

Fig. 4. The same of Amphiuma (spec. A); hematoxilin × 40.

Fig. 5. The same of Megalobatrachus maximus, of a specimen, examined by Mr. DE FREMERY. Body-length ± 110 cm. The thyroids were about 5 cm. in length, that is very large. Staining with hematoxilin and eosin. × 18.

Fig. 6. Section through the thyroid of Amblystoma mexicanum (ex. D), neotenous larva (axolotl). Staining with hematoxilin, eosin. × 40.

Fig. 7. The same of Necturus (spec. B); follicle epithelium greatly magnified; hematoxilin, eosin. × 190.

Fig. 8. The same of Amphiuma (spec. B); hematoxilin, eosin. × 190.

Fig. 9. The same of Megalobatrachus maximus (ex. DE FREMERY). Between the follicles very numerous bloodvessels filled with red blood corpuscles; hematoxilin, eosin. × 190. See fig. 5.

Fig. 10. The same of Amblystoma mexicanum (spec. D), Axolotl; hematoxilin, eosin. × 190.