STUDIES ON THE DYNAMICS OF MORPHOGENESIS AND INHERITANCE IN EXPERIMENTAL REPRODUCTION

II. PHYSIOLOGICAL DOMINANCE OF ANTERIOR OVER POSTERIOR REGIONS IN THE REGULATION OF PLANARIA DOROTOCEPHALA

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TWENTY-ONE FIGURES

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INTRODUCTION

It has long been recognized by the botanists that the apical region is physiologically dominant over other regions to a greater or less extent in higher plants. In Tubularia (Child, '07) and various—perhaps all other—hydroids the hydranth region is dominant over more proximal regions so far as they are not beyond the limit of effectiveness for the given conditions. In the present and following papers data will be presented which establish, I think, beyond a doubt that in Planaria dorotocephala a relation of the same sort exists between anterior and posterior regions. The head region dominates and controls all regions posterior to it, though the degree of this dominance differs at different levels and under different conditions.

It is primarily the processes in the anterior region of the body which determine the localization and differentiation of more posterior parts and the formation of a second zoöid and often of additional zoöids at the posterior end of the body is due to the fact that the correlative factors originating in the anterior region are effective only within a certain distance, the effective distance, i.e., they lose in energy or effectiveness with transmission from the point of origin, so that if increase in length beyond a certain point occurs certain regions become in greater or less degree physiologically isolated from the dominant region and begin to react in much the same way as when physically isolated.

In short, we shall find that if a head is formed in regulation, the development of other organs follows necessarily, so far as nutritive material is available. On the other hand, the regulatory formation of a head in Planaria is not due to any 'inherent tendency' of any sort whatever of the piece to form a new whole. So far is this from being the case that we find that new heads form more frequently in pieces from old than in pieces from young animals and under certain conditions we can even increase the capacity of a piece to produce a new head by decreasing the rate of dynamic processes in it by means of alcohol and various other anesthetics, by low temperature and by various other means. The data to be presented in this and following papers will show that the formation of a new head in an isolated piece of Planaria is to a certain extent opposed to rather than correlated with other activities of the piece.

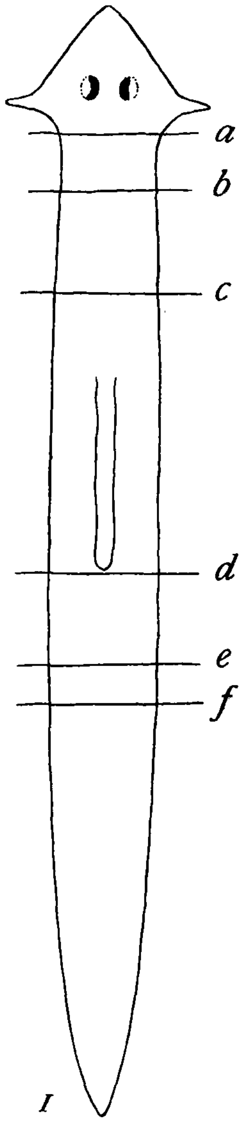
When once the process of head formation is well under way then the remodelling and redifferentiation of the other parts into a new whole begins. In general no piece of Planaria is able to give rise to structures characteristic of regions of the body anterior to that which it originally occupied, *unless a new head region forms or begins to form first.* The new whole arises from the piece in such cases not by a process of 'restitution' of the missing parts, but in a manner rather closely comparable to the formation of a new bud and a new axis from a region of differentiated tissue in a plant. We may say that in general the conditions which favor the regulatory development of a dominant part are opposed in character to those which favor the development of subordinate parts. Under certain conditions weakness or depression of the old system constitutes one of the most favorable factors for the development of a new dominant part, while vigor, i.e., a high rate or intensity of reaction favors the formation of subordinate parts. In other words, physiological isolation (Child, '11a) is the essential factor in the formation of a new dominant part, while the formation of subordinate parts is determined by correlation. That correlative factors are not entirely without influence in the formation of dominant parts is shown by the fact that the frequency of head formation in Planaria varies with the length of the piece (Child, '11b), but it is also a fact that short pieces of Planaria from any region will give rise to heads alone, provided only that the rate of reaction is sufficiently high. In the same way isolated short pieces of Tubularia and Corymorpha stems give rise to hydranths alone or even to only the distal portions of hydranths. Manifestly then the dominant part is capable of forming without any correlation with other parts, though correlative factors may increase or decrease the rate of its formation.

The data obtained in the course of my experiments which bear upon this problem are in part morphological in part physiological: the presentation of the morphological data precedes that of the physiological because the former concern visible features of the processes of regulation while the latter afford a physiological basis for their interpretation.

EXPERIMENTAL DATA

1. *Regional differences in head formation along the axis*

These regional differences were discussed at some length in the preceding paper and need be only briefly referred to here. If we compare pieces of the same length and within certain limits of length in sequence from the anterior end posteriorly, we find first



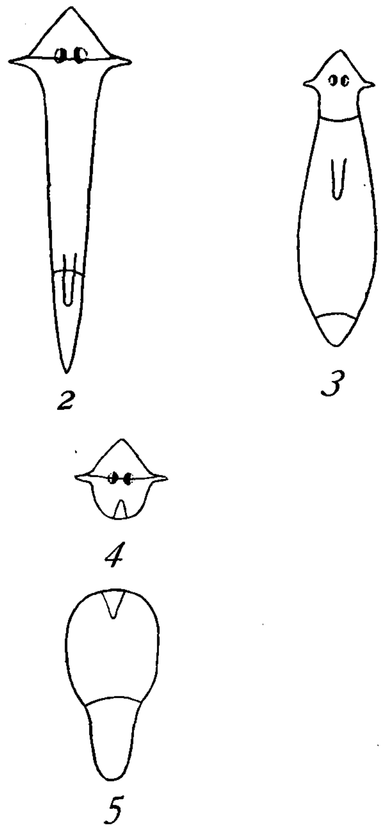


Fig. 1 Outline of Planaria dorotocephala, showing various levels of section.

Figs. 2–5 Pieces of different length from different regions, showing the different methods and results of regulation. Fig. 2, regulation in pieces above a certain length from the anterior region of the body: head large, pharynx near posterior end. Fig. 3, regulation in pieces above a certain length from the posterior region of the first zoöid: head small, pharynx anterior to middle. Fig. 4, one type of regulation in very short pieces from the anterior region; a 'tailless head.' Fig. 5, usual type of regulation in short pieces from posterior region of first zoöid; 'headless.'

that the rate of head formation and the size of the head formed decrease with increasing distance of the level concerned from the anterior end. Fig. 2, an anterior piece including the region *ac*, fig. 1, and fig. 3, a piece from the posterior region of the first zoöid (*df*, fig. 1) illustrate the extreme terms of these differences. But these regional differences, which in longer pieces are merely quantitative become in the shorter pieces qualitative, i.e., in the morphological sense, and we often find very short pieces from the extreme anterior end giving rise to tailless heads (fig. 4), while short pieces from the extreme posterior end of the first zoöid, developing under the same conditions as the others, may give rise to completely headless forms (fig. 5).

In addition to these differences which concern the head as a whole, we find that teratophthalmic[1] (Child, '11b) and teratomorphic heads (Child, '11d) show a similar relation to the main axis: not merely the capacity to form a head but the capacity to form a 'normal' head decreases posteriorly when pieces are compared under uniform conditions. These and other data cited in the pre-

[1] In my earlier experiments I distinguished only three types of anterior regulation in the reconstituted pieces: 'normal,' with two equal eyes symmetrically placed; 'teratophthalmic,' with unequal, unsysmmetrically placed, partially fused or single eyes; 'headless,' including all cases without eyes and auricles whether a distinct outgrowth was present or not. In the preceding paper (Child, '11b), which was almost wholly concerned with my earlier work, only these three types of anterior regulation were distinguished. As my work went on, however, it became evident that different kinds of teratophthalmic heads occurred and that many of the pieces which failed to form eyes and auricles were nevertheless not strictly speaking headless. I found it particularly desirable to distinguish those cases in which only the eyes were abnormal from those in which the form of the head was also abnormal. The term 'teratophthalmic' was therefore used for the former type and the term 'teratomorphic' for those cases in which the anterior median region of the head was reduced in size or failed to develop so that the auricles were brought close together or fused on the front of the head. Similarly the cases where eyes did not appear were grouped under two heads, the 'anophthalmic' pieces in which a distinct outgrowth of new tissue developed at the anterior end, and 'headless' in which the growth of new tissue was limited to closure of the wound. For most purposes this grouping of the results is sufficient, but in certain cases where a more extended analysis of the conditions determining the formation of eyes is the object in view the teratophthalmic type must be still further subdivided.

In a recent summary of certain parts of my work (Child, '11d) the five types mentioned above are described and figured.

ceding paper constitute the basis for the conclusion that a dynamic gradient of some sort exists along the chief axis of the planarian body.

2. Regional differences in the position of the pharynx

The pharynx serves as a visible landmark for a region of the body which possesses certain functional characteristics. In the contraction and extension of the planarian body the prepharyngeal and postpharyngeal regions behave differently. In the former contraction occurs in such a manner that the intestinal contents are in general forced posteriorly, while in the latter the intestinal contents move anteriorly as contraction occurs. In extension the contents move in the reverse directions in the two regions. In other words, the pharynx appears at the posterior end of a characteristic region, the prepharyngeal region. The longer this region, the farther from the head does the pharynx appear and vice versa.

When we compare pieces of the same length from different regions of the body, we find that the prepharyngeal region is longest and the new pharynx farthest from the head in the most anterior pieces (fig. 2) and that the length of the prepharyngeal region decreases and the pharynx becomes more anterior in successive pieces from the anterior regions of the body backward (fig. 3). In general then, there is a very definite relation between the rate of head formation, the length of the prepharyngeal region and the position of the pharynx; the greater the rate of head formation the longer the prepharyngeal region and the more posterior the pharynx and vice versa.

3. The later course of regulation

It has commonly been stated that pieces of Planaria gradually acquire in the course of regulation the proportions of the original animal. Such a statement can be accepted as true only in a very general sense. For example, the proportions of young small worms are different in various ways from those of old large animals. In general, the shorter the piece the more closely do its proportions after regulation approach those of the young animal and vice versa.

But the point of chief importance in the present connection is that the change in proportions which occurs during the later stages of regulation is a very different process in pieces from the old prepharyngeal region from that in pieces from the old postpharyngeal region. Under anything approaching natural conditions the change in proportions in the postpharyngeal piece is rapid (figs. 10 and 11). The head increases in size rapidly after its first appearance and the pharynx seems to migrate posteriorly because of the elongation of the new prepharyngeal region at the expense of the postpharyngeal region. Sooner or later the animal cannot be distinguished from a normal worm of medium size. Changes of this character occur in pieces from the postpharyngeal region whether food is given or not, but in the presence of agents which decrease the rate of metabolism and consequently the rate of formation of the head the changes in proportions are also retarded and in extreme cases are limited to the newly formed prepharyngeal region of the piece (figs. 13, 18).

In pieces from the old prepharyngeal region on the other hand, whether they retain the old head or develop a new one, we find that the short new postpharyngeal region (fig. 2) grows very slowly when no food is given. If such pieces are not fed, we usually find, that even after months the head is disproportionately large and the prepharyngeal region disproportionately long.

Briefly stated then the facts are these: a new prepharyngeal region formed in pieces arising from the old postpharyngeal region attains full size even in starving animals, but a new postpharyngeal region formed in pieces from the old prepharyngeal region remains indefinitely of relatively small size unless an excess of nutritive material is present.

These facts seem to me to indicate that in growth as well as in localization and differentiation the prepharyngeal region is dominant over the postpharyngeal. If we carry the experiments of this character farther and compare different parts of the prepharyngeal region with respect to the degree of their dominance over more posterior regions, we shall find that the more anterior prepharyngeal regions are more completely dominant than others over newly formed postpharyngeal regions. In other words, the growth of the new postpharyngeal region at the expense of the old prepharyngeal region proceeds more slowly and ceases at an earlier stage in pieces from the most anterior region than in pieces farther from the old head.

My observations upon these points include hundreds of pieces and a large number of measurements. I have not attempted to give the data in full because I believe that all who are familiar with the course of regulation in Planaria and related forms will be able to confirm my statements. Morgan observed this relation between prepharyngeal and postpharyngeal regions in his earlier work on Planaria (Morgan, '00, pp. 62–3) but merely recorded the fact without attempting to interpret it or to connect it with other facts.

4. The dominance of anterior regions in the regulatory developmen. of pharynx and intestine

The facts to be considered under this head are briefly these: pieces from the postpharyngeal region of the first zoöid of Planaria never develop a new pharynx or prepharyngeal region except in cases where some approach to the formation of a head occurs at the anterior end. On the other hand, pieces containing any part of the original pharyngeal or prepharyngeal region always develop a new pharynx—or retain the old—whether a head develops or not.

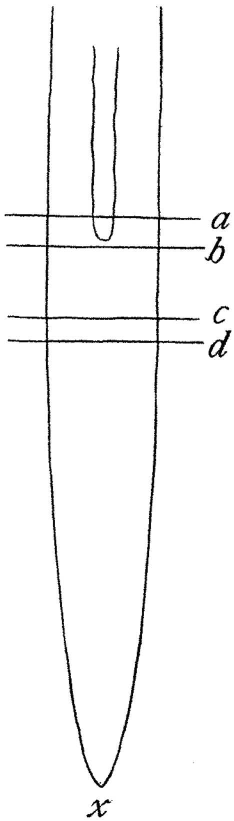
All who have worked with Planaria are familiar with the fact that under the usual conditions of experiment in all pieces where regeneration of a head occurs a pharynx also develops except in cases where the piece retains the old pharynx, or when it is so small that it produces a 'tailless head.' The differences in such pieces as regards rate of development of the head and the length of the prepharyngeal region have been noted above.

But the pieces which fail to produce a head differ widely in their ability to produce a pharynx. During 1905 I made an extensive study of short pieces in which large individuals were cut into from ten to twenty-four pieces, a record being kept of the approximate region of the body from which each piece came and of the history of each individual piece. These experiments established the fact considered briefly in the preceding paper (Child, '11b), viz., that the capacity for forming a new head depends to some extent upon the length of the piece and that this factor in head formation becomes increasingly important with increasing distance of the pieces from the anterior end of the original worm back to the region of fission. In addition to this evidence for the existence of an axial gradient of some sort, the experiments established the important fact the pieces which fail to produce a head do not produce any regions of the body anterior to their original level. My records show that in every case where pieces from the prepharyngeal or pharyngeal region remain headless they nevertheless develop a new pharynx, or the old pharynx remains: even pieces which include at the anterior end only the old mouth and a very small part of the pharyngeal region such, for example, as *ac*, fig. 6, are capable of developing a new pharynx whether a head develops or not. But pieces from a region slightly farther posterior than this which includes no part of the pharyngeal region (*bd*, fig. 6) *never produce a new pharynx when they remain headless*. If, however, some slight approach to head formation occurs a new pharynx always appears in such pieces. Further experiments in later years confirmed these results. My earlier records concerning this point include some fifty pieces.

During the present year I prepared a series of pieces for a further test concerning this point. Well-fed worms 15 to 18 mm. in length were used and from these pieces like *bd*, fig. 6, were cut, 50 such pieces being prepared. The results are given in percentages in the following table:

	NORMAL	TERATOPHTHALMIC	TERATOMORPHIC	ANOPHTHALMIC	HEADLESS
With pharynx.....	4	8	10	26	0
Without pharynx.	0	0	0	6	46
	4	8	10	32	46

The table shows that all of the normal, teratophthalmic and teratomorphic pieces developed new pharynges. Of the 50 pieces



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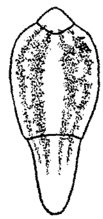
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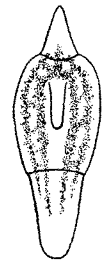
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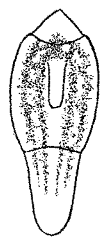
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Fig. 6 Outline of pharyngeal and postpharyngeal region showing various levels of section.

Figs. 7–9 'Anophthalmic' pieces from posterior region of first zoöid. Fig. 7, anterior outgrowth small, no pharynx formed and no anterior regulation of the alimentary tract. Figs. 8 and 9, anterior outgrowth larger, new pharynx present, short prepharyngeal intestine formed.

16, 32 per cent, are anophthalmic, i.e., they show some outgrowth at the anterior end but do not develop eyes. The amount of the anterior outgrowth differs widely in different pieces. Of these anophthalmic pieces 13, 26 per cent of the whole series and more than three-fourths of this type, developed new pharynges, while only 3 pieces, 6 per cent, remained without pharynges. Moreover, my records show that in every case where a pharynx failed to develop in these anophthalmic pieces the anterior outgrowth was small like that in fig. 7 or even smaller, while in all but two cases where a pharynx was formed the outgrowth was visibly greater and of the types shown in figs. 8 and 9. In short it was evident from examination of the pieces that in general those which developed pharynges were less completely headless than those which did not.

The regulatory changes in the intestine run parallel with the other changes: in those cases where a new pharynx is formed a short median prepharyngeal intestinal axis is formed, while in those pieces which do not give rise to a pharynx no appreciable regulatory changes in the intestinal tract occur. Figs. 8 and 9 show the intestinal structure in pieces which develop a pharynx and fig. 7 that in pieces without a pharynx. It is sufficiently clear that the development of a pharynx is associated with the presence or new formation of a prepharyngeal region.

The strictly headless pieces of the series, twenty-three in number, 46 per cent of the whole series, did not in a single case give rise to a new pharynx. The alimentary tract in these pieces is essentially similar to that in fig. 7. It should perhaps be added that in the examination to determine the presence or absence of a pharynx each piece, after it had been kept long enough for regulation to proceed as far as it it would go—twenty days at 20° C.—was subjected to compression under the microscope. By this means it is possible to detect the pharynx even when it is very minute and otherwise quite invisible. My records also include hundreds of headless pieces from the pharyngeal and prepharyngeal regions and in no single case among them where the old pharynx was not retained has a pharynx failed to develop.

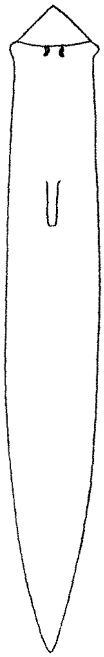
These facts seem to me to be of great importance in connection with the question of dominance of anterior over posterior regions. They show that where a part of the pharyngeal or prepharyngeal region is present a new pharynx develops whether a head forms or not, while in the postpharyngeal region of the first zoöid no new pharynx appears unless at least a start toward head formation occurs. Evidently the process of head formation determines at a very early stage the localization of a new prepharyngeal and so of a pharyngeal region. In short a new pharynx appears in an isolated piece only when some part of the original pharyngeal or prepharyngeal region is included in the piece or is formed anew in the course of regulation. And furthermore, the formation of a new prepharyngeal and pharyngeal region is dependent on the formation of a head or something which approaches a head in physiological character. Discussion of the question as to the nature of this capacity of the head region to determine the development of other regions and of the capacity of regions at any level to determine regions posterior to them, in short, the question as to the nature of antero-posterior physiological dominance, requires the consideration of other data of different character from those presented here and must therefore be postponed.

5. The position of the pharynx under experimental conditions

A. In pieces from the old postpharyngeal region. The relation described above between the region of the body from which the piece is taken, the size and rate of development of the head and the position of the pharynx is by no means fixed in character, and can be altered very readily by a great variety of experimental conditions.

In describing a few experiments of this character we may consider first pieces from the original postpharyngeal region: in such pieces the process of regulation involves the formation of a prepharyngeal and pharyngeal region from the anterior part of the old postpharyngeal region. In such pieces we can alter the size and rate of development of the head, the length of the prepharyngeal region and the position of the pharynx almost at will.

For experimental purposes pieces including the whole postpharyngeal region (*bx*, fig. 6) afford the most striking results, though shorter pieces from the posterior region of the first zoöid may be used. As a basis for comparison I have used in my experiments the postpharyngeal regions isolated from worms 15 to 18 mm. in length which have been sufficiently well fed to keep them from either decreasing or increasing in size to any marked extent. Regulation of these control pieces occurred at a temperature of about 20° C. in water containing an excess of oxygen for the requirements of the animals. The results from such pieces are uniform in high degree. The pieces produce a large head with normal eyes and the pharynx appears at about



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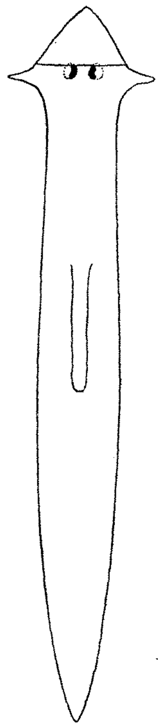

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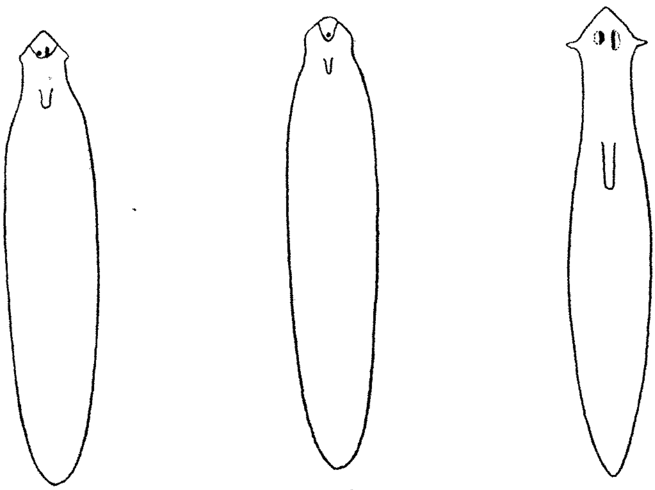
Figs. 10 and 11 Postpharyngeal pieces showing regulation in water at temperature of 20° C. Fig. 10, early, fig. 11, later stage.

one-third of the length of the piece from the anterior end. Fig. 10 shows an earlier, fig. 11 a later stage in the regulation of such a piece. The only appreciable variation from this result which I have observed, when material and conditions are as above stated, is the very rare occurrence of partly fused eye spots. In ten series of 50 pieces each, a total of 500, 497 pieces were essentially similar to fig. 11, while 3 pieces (0.6 per cent) differed only in possessing partly fused eye spots. It is evident from these data that these pieces under constant conditions give a very definite characteristic result.

Similar pieces from worms in similar condition which undergo regulation in alcohol or ether or other anesthetics at the same



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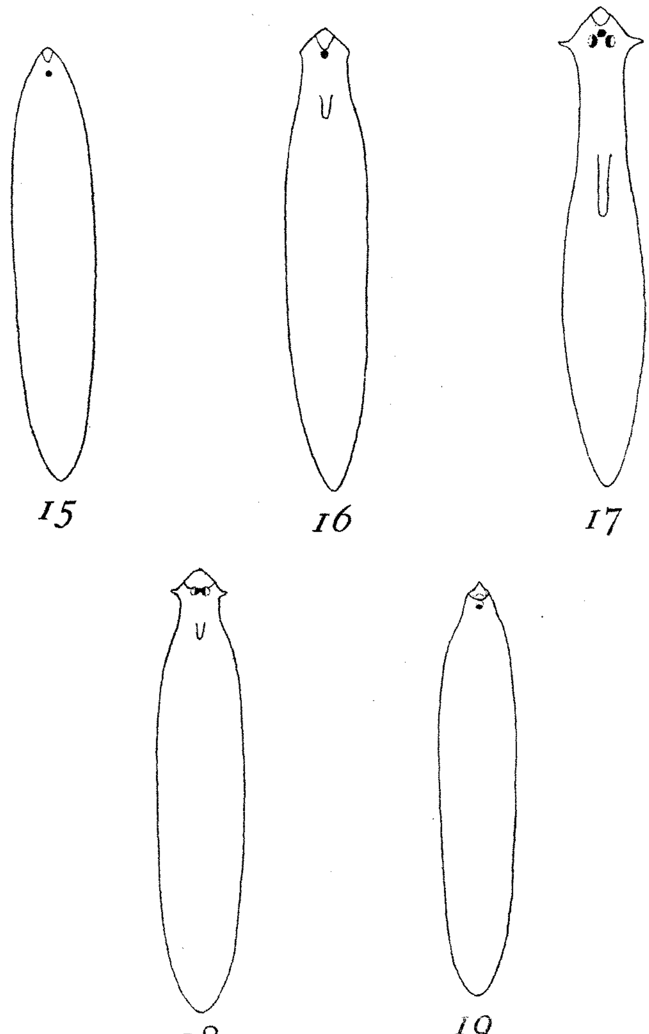
Figs. 12–14 Postpharyngeal pieces showing relation between regulation and external conditions. Figs. 12 and 13, regulation in alcohol 1.5 after twelve days. Fig. 14 shows the changes in these pieces after return to water.

temperature as the controls give strikingly different results. My records include more than a hundred such pieces and show uniformly that the head is always smaller, develops more slowly than in the controls, and is very commonly teratophthalmic and often teratomorphic: in most cases also redifferentiation plays a larger part in the formation of the head than in the controls. The pharynx is also small and *is always much nearer the anterior end* than in the controls. Figs. 12 and 13 show two characteristic pieces after twelve days in 1.5 per cent alcohol. In fig. 12 the head is more nearly normal and a small pharynx is present: in fig. 13 the head is almost entirely the result of redifferentiation and possesses only a single eye in the median line and the pharynx is even smaller and nearer the anterior end than in fig. 12. It should also be noted that the changes in proportion in these pieces extend posteriorly only a short distance from the head. If these pieces are kept in alcohol they remain in approximately the condition figured until death. If, however, they are returned to water the development of the head proceeds, it becomes larger, the prepharyngeal region becomes longer and the elongation and decrease in width gradually extend posteriorly (fig. 14).

The intestinal regulation in these pieces occurs only in the region anterior to the pharynx, whether this region is long or short. In cases like figs. 12 and 13, for example, we find a prepharyngeal median axial intestine in the short prepharyngeal region and with the elongation of this region after the return to water (fig. 14) the prepharyngeal axial intestine also elongates. The pharynx is then an excellent morphological and physiological landmark.

Pieces which regulate in ether give very similar results. A series of postpharyngeal pieces after eighteen days in five-tenths per cent ether showed forms ranging from the type of fig. 12 to that of fig. 15. In the extreme type of fig. 15 anterior regeneration is limited to the extreme tip of the head region, other parts of the head being the result of redifferentiation. No auricles are visible, only a single eye is present, there is no elongation and change in proportions and no pharynx is present. In such pieces no intestinal regulation occurs and no prepharyngeal axial intestine is formed from the union of the lateral postpharyngeal branches in the anterior region of the piece. When a pharynx appears the prepharyngeal axial intestine is always present, though it may be short. In cases like fig. 15 it is evident that practically all regulation except the redifferentiation of the head region has been inhibited by the ether. The fact that this can go on under conditions which stop all other regulatory processes is itself suggestive. Its bearing will be discussed later.

If such pieces are returned to water extensive changes occur. During the first four or five days the head region enlarges and a pharynx appears near the anterior end of the piece (fig. 16), but the prepharyngeal region soon begins to elongate and becomes more slender as the activity of the head increases. After eight days in water the pieces resemble fig. 17. The postpharyngeal region is not yet under complete control and drags along behind the rest of the worm like a dead mass, except when the animal is very strongly stimulated. The prepharyngeal region, on the other hand, resembles that of the pieces in water. Incidentally it may be noted that when the piece develops only one median



Figs. 15–19 Postpharyngeal pieces showing the effect of ether and metabolic products on regulation. Fig. 15 regulation in ether 0.4%. Fig 16, four days in water after ether. Fig. 17, eight days in water after ether. Figs 18 and 19, regulation in water from planarian cultures.

eye in alcohol or ether it usually develops two more in the normal position (fig. 17) after its return to water.

These cases of regulation in alcohol and ether show very clearly that when the formation of a head at the anterior end of a piece is retarded by external conditions the length of the prepharyngeal region is decreased and the pharynx arises nearer the head: in extreme cases regulation is confined to the head region alone and neither pharynx nor prepharyngeal region appear. On returning these pieces to water we can see that the regulatory changes proceed in the posterior direction.

It is possible to alter the rate of formation and the size of the head and the position of the pharynx by various other means. For example CO_2 and other products of metabolism in the water in which the pieces are kept are very efficient factors in altering the course of regulation. The following series will serve as an example: 50 postpharyngeal pieces (*bx*, fig. 6) were placed in old culture water in which a stock of several hundred worms had been kept for nine days. Since this experiment was merely preliminary, no attempt was made to determine whether the CO_2 or other substances were the more important factors in determining the results: more exact data will appear in a later paper. As a control 50 similar pieces were placed in fresh, well aërated water at the same temperature. The results in percentages, so far as they concern our present purpose, are as follows:

	HEADS	NORMAL EYES	PHARYNGES
In old culture water	54	6	48
In fresh water	100	100	100

The differences are evident at once. Certain features of the results however are not apparent from the table. In no case did a pharynx appear in a piece which did not form a head and some of the pieces which formed the smallest and most abnormal heads did not produce pharynges at all. In all cases where a head formed it was relatively small and was commonly teratophthalmic or teratomorphic and the pharynx when present was only a short distance posterior to it. Fig. 18 shows a characteristic piece from this series and fig. 19 a more extreme case with single median eye, teratomorphic head and without a pharynx.

Differences which are similar in character though less extreme may be obtained with different temperatures. At high temperatures postpharyngeal pieces produce large heads with normal eyes and relatively long prepharyngeal regions. At lower temperatures the heads are smaller and more frequently teratophthalmic and the prepharyngeal regions shorter, i.e., the pharynges are further anterior.

As regards still other methods by which similar results may be obtained, further data will be presented at another time.

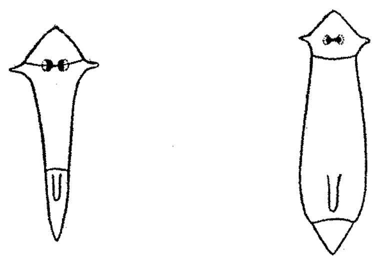
The important point for present purposes is that in a piece from the original postpharyngeal region *the rate of development and the size of the head, the length of the new prepharyngeal region and consequently the position of the new pharynx all vary with the rate of the dynamic processes concerned with the formation of the new head and can be controlled experimentally.*

B. In pieces from the old prepharyngeal region. Internal conditions are very different in the pieces from the original prepharyngeal region from those existing in the postpharyngeal pieces. In prepharyngeal pieces the greater portion remains prepharyngeal in structure and function and only a short posterior portion becomes postpharyngeal. At the posterior end of the newly determined prepharyngeal region the new pharynx appears (fig. 20). Here then a prepharyngeal region exists from the beginning and it is merely a question as to how much of it shall become postpharyngeal.

A superficial consideration of this case might perhaps lead us to expect from analogy with postpharyngeal pieces that a decrease in the rate or intensity of the dynamic processes in the head region would result here also in a decrease in length of the new prepharyngeal region or more strictly speaking in the determination of a shorter prepharyngeal region and the consequent localization of the pharynx more anteriorly. This result would occur if the head region alone were dominant over all other regions and these latter coördinate in character. But as a matter of fact each level of the body is dominant in some degree over the levels posterior to it so far as they are within the effective distance.

It was shown in the preceding section that in the pieces from the original prepharyngeal region the formation or presence of a head is not necessary as it is in postpharyngeal pieces for the development of a new pharynx. The presence of any part of the original prepharyngeal or pharyngeal region is sufficient to determine the formation of a new pharynx whether a head forms or not. In such pieces the localization of the new pharynx will depend on the length of the region which undergoes redifferentiation to form the missing posterior regions, for the new pharynx appears on the boundary between the region which retains its original prepharyngeal character and that which becomes postpharyngeal in character. Since the prepharyngeal region is dominant over regions posterior to it, pieces from the prepharyngeal region develop the new pharynx near their posterior ends (fig. 2) and the new postpharyngeal region is formed almost wholly by regeneration and remains short for a long time unless the animal is fed. But when we compare prepharyngeal pieces from different levels we find that as the level of the pieces approaches the level of the old pharynx, i.e., the posterior end of the prepharyngeal region, the degree of dominance of the anterior regions of the piece over its more posterior regions decreases, a fact that will appear more clearly later, and in the course of regulation the new postpharyngeal region becomes longer and the pharynx appears more anteriorly in the piece.

In P. dorotocephala the degree of dominance of the prepharyngeal over the postpharyngeal region is such that the formation of a new postpharyngeal region in a prepharyngeal piece occurs slowly, is limited to the extreme posterior region of the piece and is almost wholly a process of regeneration in the stricter sense. Consequently in all pieces from the prepharyngeal region the new pharynx arises at or very near the posterior end of the old tissue. As a matter of fact its level does differ somewhat according to the level of the piece. In pieces from the extreme anterior region of the body (*ab*, fig. 1) the new pharynx may appear in the posterior new tissue (fig. 20), i.e., in such cases not only the postpharyngeal region but the pharyngeal region also is the product of regeneration. As the level of the piece becomes more posterior the new



Figs. 20 and 21 pieces from different parts of the prepharyngeal region to show the position of the pharynx. Fig. 20, from the region immediately behind the old head. Fig. 21, from the region just anterior to the old pharynx.

pharynx appears more anteriorly until at a level just anterior to the old pharynx the new pharynx appears in the old tissue somewhat anterior to its posterior end (fig. 21). In P. maculata the corresponding differences in the level of the new pharynx are somewhat greater since the axial gradient in this species differs in certain respects, as will appear later, but in both cases the principle involved is the same.

In general these differences in the level at which the new pharynx appears in the prepharyngeal pieces are merely expressions of the different degrees of stability of different prepharyngeal levels. The most anterior levels of the prepharyngeal region are more fixedly prepharyngeal than other levels and a new postpharyngeal and pharyngeal region arise only from their most posterior parts. In fact, if we isolate very short pieces from just behind the old head they give rise in most cases under standard conditions, i.e., when taken from large well fed worms and allowed to regulate in well aërated water at a temperature of 20 C., to 'tailless heads' (fig. 4) in which neither pharyngeal nor postpharyngeal regions are formed, the new tissue at the posterior end ofthe piece being limited to closure of the wound, while anteriorly such pieces produce large heads. At more posterior levels the pharyngeal and postpharyngeal regions are formed and as the level of the piece in the original body becomes more and more posterior they become larger and the new head becomes smaller.

The question as to why a new postpharyngeal region should arise at all in such a piece was discussed in connection with the analysis of regulation in another form (Child, '05). In that form, Cestoplana, almost no regeneration occurs posteriorly and the new postpharyngeal region arises from the old prepharyngeal region by redifferentiation and its length differs at different levels in the same way as in Planaria. In my account of regulation in that form I called attention to the fact that the first visible change in the process of formation of a postpharyngeal region from a part of the original prepharyngeal region is not a change in structure but a change in function, in the motor reactions of the part. The visible structural changes follow this functional change and they occur, as I believe, in consequence of the altered dynamic conditions in this region of the piece.

In Planaria, however, where the new postpharyngeal region is formed largely or wholly by regeneration conditions are somewhat different and we must consider the question as to why a new postpharyngeal region should arise by regeneration at the posterior end of a prepharyngeal piece.

In the first place a cut surface, a new terminal region, has been formed by the operation and that means that certain characteristic metabolic conditions and functional conditions in the stricter sense must exist or arise in the posterior region of the piece. These result first of all in dedifferentiation, i.e., loss of the old structural characteristics and renewed or accelerated growth of the cells near the wound. In this way a small region of more or less 'embryonic' tissue is formed. The later fate of this tissue depends mainly upon its correlation with parts anterior to it, for if the law of the dominance of anterior over posterior levels holds good in this case, and I shall show later that it does, this region is subordinate to the regions anterior to it and the course of its development is determined chiefly by those more anterior regions. The correlative factors to which this region is subjected are essentially similar to those to which the old postpharyngeal region was subjected and it develops into a postpharyngeal region in consequence of the influence upon it of these factors. The rate of metabolism of the dedifferentiated cells which form the starting point of regeneration is accelerated by the process of dedifferentiation which is essentially a process of rejuvenescence (Child, '11c) and in consequence of this acceleration of metabolism these cells are able to grow and divide for a time at the expense of the regions anterior to them. This growth continues until in the course of redifferentiation the cells again grow physiologically older and their rate of metabolism decreases to such an extent that they can no longer grow at the expense of more anterior regions and there regeneration ceases unless the piece contains an excess of nutritive material. In short the conditions which determine the regeneration of a postpharyngeal region in a prepharyngeal piece are: first, the dedifferentiation of the cells in reaction to the wound and the resulting increase in capacity for metabolism and growth; second the correlative factors to which they are subjected in consequence of their physiological continuity with more anterior regions and which determine that growth and redifferentiation shall actually occur. In consequence of all these conditions a new postpharyngeal region arises at the posterior end of the prepharyngeal piece, while other parts of the piece remain almost unchanged structurally and functionally. The growth of the postpharyngeal region after its determination as such is then essentially a process of 'functional' growth and the final cessation of growth is the result of an equilibration in the rate of metabolism between the new part and the old.

The occurrence of 'tailless heads' in very short pieces from extreme anterior regions, in other words, the failure of such pieces to form pharyngeal and postpharyngeal regions depends upon the fact which will be demonstrated later that a higher rate of metabolism is concerned in the formation of a head than in that of a posterior part: in these short pieces the posterior regions do not form because the process of head formation with its higher rate of reaction uses up the available material so rapidly and to such an extent that the formation of a posterior end is inhibited or rather prevented. With the aid of proper experimental conditions it is possible to produce tailless heads in longer pieces as well as in pieces from other regions of the body. In Planaria the dominant morphogenic reaction, i.e., the morphogenic process with the highest rate of metabolism is that of head formation, just as in Tubularia the dominant morphogenic reaction is that of hydranth formation—moreover, in Tubularia the distal hydranth regions are dominant over the proximal—and whenever this dominant reaction begins in a piece the other reactions are controlled by it and if the amount of material available as a source of energy is insufficient the subordinate reactions are decreased or completely inhibited. In short pieces of the Tubularia stem, particularly in those from the more distal regions, the product of regulation is more and more exclusively distal in character, the shorter the piece. Similarly in the anterior regions of Planaria the product of regulation becomes more and more exclusively anterior as the length of the piece decreases. Certain apparent exceptions to this law, e.g., the formation of headless pieces and biaxial 'heteromorphic' tails in Planaria and other forms will be considered later and will be shown to be only apparent exceptions.

The origin of a new dominant part like the head from any subordinate part, i.e., any region posterior to the head is a problem of somewhat different nature and one which has not been considered in any of the attempts at analysis of the process of form regulation which have been made, because the dominance of this region has not heretofore been recognized. My experiments have led me to the conclusion that the formation of the head in Planaria, the hydranth in Tubularia, etc., are in no sense restorations of missing parts, restitutions or anything of that kind, but rather that the new head or the new distal region as the starting point of a new individual arises from the mass of old tissue in a manner closely comparable to the formation of a new bud from differentiated tissue in a plant The new individual, which is at first merely a head, lives at the expense of the old parts and at the same time makes them over into parts of a new worm or uses the energy which it obtains through their destruction in the development of new parts. The new individual simply forms and grows head first out of the old mass. In Planaria the position of the new head commonly shows a definite relation to the old axis, though this is not always the case, but in various coelenterates, e.g., Corymorpha (Child, '11a, pp. 112–119) and Harenactis

(Child, '09, '11a) the new axes may arise 'adventitiously.' In other words, if the original axial gradient is sufficiently obliterated or if external conditions are sufficiently powerful to overcome its influence new gradients, i.e., new axes may arise without definite relation to it.

CONCLUSION AND SUMMARY

Although the consideration of the question as to the nature of the dominance of anterior over posterior regions in Planaria must be deferred until further facts have been presented, we may at this time consider briefly the significance of such dominance.

The dominance of one region over another is of course relative rather than absolute. To say that a given region is dominant over others means merely that it influences and determines the processes and conditions in them to a greater extent than it is influenced by them. This, as will appear in later papers of this series, is the case in Planaria.

In the present paper certain of the facts of regulation in Planaria have been presented which indicate that the head region controls and determines the development of regions posterior to it to a very large extent and that each level of the body is to a certain extent dominant over more posterior levels. This, however, is only the first step in the presentation of evidence.

If the head region of Planaria and the distal region of Tubularia and various other forms are dominant over other regions as I have maintained, it follows that these regions develop more independently than any other part of the body. The formation of the head in Planaria, of the distal region in Tubularia, is the most fundamental, the most characteristic morphogenic reaction of the protoplasm of those species. Other reactions depend upon this to a much greater extent than it depends upon them. In general the first morphogenic regulatory change in an isolated mass of planarian or tubularian protoplasm is the formation of a head or a distal region or the initiation of this process. This fact will become more and more apparent as further experimental data are presented. As we know from numerous experiments, many isolated pieces of the planarian body appear to be incapable of producing heads. In such pieces I have been able to induce head formation experimentally by simply subjecting them to conditions which increase the rate of metabolism (Child, '11d) and can demonstrate that in these pieces the absence of the head under the usual conditions is due, not to absence of the necessary 'organization' or to lack of certain 'formative substances' or anything of that character, but merely to an insufficiently high rate of metabolism in the region concerned. By increasing the rate sufficiently in any way heads appear on pieces which would not otherwise produce them. By altering the conditions in the opposite direction it is also possible to induce the formation of teratophthalmic in place of normal heads or to inhibit head formation completely.

But little attention has been paid to the matter of rate of reaction as a factor in ontogenetic and regulatory morphogenesis. When pieces fail to regenerate certain parts it has usually been taken for granted that the necessary 'organization' is lacking. This, however, is by no means always the case. The formation of a new whole from a piece or the failure to form such a whole, as well as the character of the whole formed, e.g., normal, teratophthalmic and teratomorphic wholes in Planaria may be the result of differences which are fundamentally purely quantitative rather than qualitative in nature. Undoubtedly differences in organization do exist and do play a part in many cases, but they are certainly not the only nor the chief factors in many other cases.

In the absence of the head region the most anterior regions present are dominant over more posterior regions within a certain distance and to a certain degree. In general we find that while any region is a very important factor in determining what shall go on in regions posterior to it, it has but little influence, though it can be shown to possess a certain amount, in determining what goes on in regions anterior to it. The morphological characteristics of Planaria are determined chiefly by the correlative influence of more anterior upon more posterior regions.

It is evident that this point of view gives a very different conception from that generally held of the process of formation of a new whole from a piece of a planarian body. Instead of being a process which shows almost infinite possibilities of adjustment to the conditions existing in a particular case, it is essentially one and the same reaction in all cases. In pieces where the head is present the posterior parts arise in consequence of correlation with more anterior parts. Where the head is absent a new head arises from the region involved in reaction to the wound, provided merely that the rate of reaction in this region becomes sufficiently rapid. When the process of head formation attains a certain stage the new head region begins to dominate the rest of the piece and makes it over according to certain definite and unchanging laws. All that is necessary for the formation of a planarian is first a cell or a group of cells capable of initiating a characteristic series of reactions which result in what we call a head and second an excess of nutritive material as a source of energy for growth.

To put the matter in still another form, it is not too much to say that the capacity for head formation is all that exists in the planarian egg, all that is inherited. Given this, together with an excess of nutritive material, which in the case of Planaria exists in the yolk cells and the characteristic form of Planaria must result.

And this brings us to the question as to how far similar relations obtain in regulatory and the ontogenetic development of other forms. At present I desire only to call attention to certain points in this connection. Tubularia and Corymorpha are essentially similar to Planaria as regards the axial gradient. In the first place it has been shown by various investigators that if a tubularian stem is cut into a series of pieces of equal length the oral hydranth develops most rapidly and is largest in the most distal piece and its size and rate of development decrease with each successive piece from the distal end proximally. These differences are similar in character to the differences in head formation at different levels of the first zoöid in Planaria.

Secondly, as regards the dominance of distal over proximal regions Tubularia likewise resembles Planaria. In asexual reproduction in nature the factor of distance is apparent, i.e., the tip of the stolon gives rise to a new hydranth when it has reached a certain distance, varying with conditions, from the original distal region and has become to some extent physiologically isolated from the latter (Child, '11a, pp. 95–96, 101–112). When pieces are cut from the stem only vigorous pieces give rise to stolons at their proximal ends (Child, '07) and as the piece becomes less and less vigorous the terminal region of the stolon, or the proximal end of the stem if a stolon was not formed, becomes physiologically isolated from the dominant distal region and gives rise to a hydranth. Axial heteromorphosis in long pieces of the stem is merely the result of physiological isolation of the proximal region of the piece in consequence of increasing weakness, i.e., decreasing rate of metabolism and therefore decrease in length of the stem over which the distal region is dominant (Child, '11a, pp. 101–112).

Furthermore, as the length of the piece cut from the stem of Tubularia decreases the parts to which the piece gives rise become more and more exclusively distal: the longer pieces produce hydranths and stems, somewhat shorter produce hydranths alone, still shorter only manubrium and distal tentacles and so on, until finally the shortest pieces give rise only to the distal region of the manubrium with the distal tentacles (Child, '07). These facts demonstrate that the distal region is able to form without correlation with other parts, but the more proximal regions have never been seen to arise except in connection with considerable regions distal to them.

Corymorpha is essentially similar to Tubularia in all these respects except that it does not reproduce asexually by transformation of the end of the stolon into a hydranth. This difference is probably due to the fact that the proximal region of the stem of Corymorpha is a much more highly specialized region than in Tubularia. So far as data are available, the relations seem to be similar in many if not in all other hydroids.

Rand ('11) has recently stated that in Hydra the peristome region controls morphogenesis and I have found in Cerianthus and Harenactis an axial gradient of the same character as in Tubularia and Planaria and in these forms also the peristome region appears to be dominant in regulation. The distance factor is more difficult to demonstrate in these actinians since the rate of metabolism at the proximal end is so low that reproduction does not occur under ordinary conditions even when these regions are physically isolated.

As regards plants, it is a well-known fact that in at least most forms the apical region of the axis is to a very large extent dominant over more proximal regions and I have endeavored to show (Child, '11a) that the factor of distance is in many cases a factor of great importance in reproduction in plants as well as in animals.

These facts as well as many others which might be cited show very clearly that an axial gradient exists in a large number of organisms and that in many cases at least the apical or anterior region is dominant in regulation.

Turning now to normal ontogeny, we find that in most if not in all animals the visible phenomena of development begin in the region of the so-called animal pole of the egg and that this region in most if not in all cases becomes the anterior, distal or apical region of the resulting organism. I believe that these facts in themselves are highly suggestive when taken in connection with the facts concerning the dominance of the distal and anterior regions in the regulation of various forms. In fact it seems probable that dominance of anterior or distal over posterior or proximal regions is a very general law of organic development, not only in animals but in plants as well. A more extended consideration of this question will be undertaken elsewhere.

Critics of such a conclusion will at once cite those cases in which different parts of the developing egg appear to be almost wholly independent of each other, e.g., the annelid and mollusk and the amphibian. It seems at least probable that in such cases the characteristics of the different parts once determined through correlation at a very early stage are stable to a high degree and do not change when the parts are isolated. Even in such cases the 'animal' region of the egg may be dominant over other regions at some stage in the history of the egg. The experiments of recent years on the nemertean egg afford strong evidence in favor of the view that independence of parts in later stages is preceded by a condition in which at least certain parts are determined correlatively. According to this view the eggs which show the extreme mosaic type of development are merely cases of early differentiation or of absence of regulatory capacity due to one cause or another, rather than a type of constitution fundamentally different from the extreme correlative type.

In regulatory reproduction we find all stages between the two extremes. For example, in Planaria simplicissima the first formation of the tail region depends as in P. dorotocephala upon connection with more anterior regions, but when it is once formed this region is more definitely determined as a tail region than in P. dorotocephala and when isolated often gives rise, as Morgan first observed (Morgan, '04), to a tail at its anterior end. Somewhat similar conditions exist in the earthworm, except that there the 'tail region' includes the greater part of the body length.

In Stenostomum, on the other hand, posterior regions remain posterior in structure only so long as they are under the complete control of the dominant head region. When this control decreases below a certain limit, either in consequence of increase in length of the animal or other conditions (Child, '11a) a new head begins to develop in the posterior region of the body, even though organic continuity with the original head region is not interrupted.

It seems probable then that we shall find in ontogenetic as well as in regulatory development that anterior or distal regions are very generally dominant over posterior or proximal regions, at least at some stage, and that the egg as well as the piece capable of regulation represents primarily the anterior or distal region, together with an excess of nutritive material or some means of obtaining such an excess as a source of energy for growth.

The most important facts of the paper and the conclusions to which they point may be summarized as follows:

1. As was shown in the first paper of this series, the most important regional differences in the course of regulation in pieces of Planaria taken in sequence along the axis from the anterior end posteriorly consist first, of decrease in the size of the head, the rate of its formation and the frequency of normal eyes; second, of decrease in the length of the prepharyngeal region and therefore the formation of the pharynx at a more anterior level of the piece. These differences indicate the existence of an axial gradient of

some kind and their character suggests that this gradient concerns, at least in part, the rate or intensity of certain processes along the axis.

2. A head or prepharyngeal region is capable of growing or of maintaining itself at the expense of more posterior regions in the absence of other food to a much greater extent than posterior regions can grow or maintain themselves at the expense of more anterior regions. These facts also suggest differences in the rate or intensity of certain processes at different levels.

3. In pieces of Planaria dorotocephala which contain a part of the original prepharyngeal or pharyngeal region and in which the old pharynx is not present or does not persist, a new pharynx develops whether a new or old head is present or not. In pieces from the postpharyngeal region, on the other hand, a new pharynx or a new prepharyngeal region never forms unless a head region begins to form first.

In general no piece of the planarian body is capable of giving rise to structures belonging to levels anterior to that which the piece originally occupied in the body, unless the formation of a head or the first stages of this process occur first. But a piece can give rise to parts characteristic of levels posterior to that which it originally occupied, whether a head region is present or not.

4. The formation of a head at the anterior end of a piece may be retarded or inhibited by various agents and conditions, e.g., alcohol, ether and other anesthetics, CO_2 and other products of metabolism, KCN and even by low temperature and insufficient nutrition. In all pieces from the postpharyngeal region of the body in which the formation of a head is thus retarded the length of the new prepharyngeal region is less than in pieces under the usual conditions and the pharynx appears nearer the head. When the depressing agents or conditions are used in higher concentration or intensity so as to produce the more extreme effects, or when the animals are in such physiological condition as to be more sensitive to their effects, the regulatory changes may be limited to the early stages of head formation, all regulatory changes being completely inhibited in regions posterior to the head. The fact that the regulatory processes concerned in head formation are

able to go under conditions which completely inhibit all other morphogenic regulatory processes is of great importance. It constitutes very strong evidence in support of the conclusion that regulation at the anterior end of a piece is initiated by the process of head formation or by the beginning of this process.

In general we find that *in pieces from the original postpharyngeal region the size of the head the length of the new prepharyngeal region and in extreme cases its presence or absence, and consequently the position or presence or absence of the pharynx are all very closely correlated with the rate of the dynamic processes or certain of them which are concerned in head formation.*

5. In pieces from the original prepharyngeal region a new postpharyngeal region develops much more slowly, is much shorter and is to a much larger extent a product of regeneration in the stricter sense than is a new prepharyngeal region developing in a postpharyngeal piece. The new pharynx in pieces from the prepharyngeal region appears near the posterior end of the old tissue. Only when excess of nutrition is present does the new postpharyngeal region grow to the proportions characteristic of animals in nature.

6. The facts point to the conclusion that the regulatory formation and development of the head in Planaria, as well as the hydranth in Tubularia and the anterior or distal regions of various other forms are not in any sense a restoration of missing parts, a 'restitution' a return to a condition of wholeness or anything of that sort. Such a process consists rather in the formation of a new individual, beginning with the head or distal region: this new individual simply grows out of the mass of old tissue head first and as it grows either uses the old tissue as a source of energy or brings about its redifferentiation until the dynamic equilibrium characteristic of the specific system and the existing conditions is attained. The regulatory changes at the anterior end in such cases begin in the region of the developing head and proceed posteriorly. By means of external factors we can determine the distance from the new head to which they shall proceed and where they shall produce certain results.

7. Attention is called to the fact that this dominance of anterior or distal over posterior or proximal parts is similar in character to the relations between parts which exist in most if not in all plants. The regulatory formation of a new head in Planaria or of a new hydranth in Tubularia or Corymorpha, together with the effects of such a process on other parts is not essentially different in character from the formation of a new apical cell or vegetative tip in a plant and the resulting development of the new axis. In the plant, however, the new dominant region is in most cases unable to bring about to so great an extent as occurs in many animals the redifferentiation of masses of old tissue adjoining it, consequently the new plant axis remains short and small except when excess of nutrition is present. A considerable degree of redifferentiation of the old tissue under the influence of the new vegetative tip does occur, however, in many cases.

If my conclusions are correct the processes of form regulation in the animal and in the plant follow the same law and this law finds a general expression in the statement that any given region along the axis in which dynamic processes are occurring dominates more or less completely regions proximal or posterior to it and is dominated by regions anterior to it.

8. The very general if not universal formation of the distal or anterior region of the organism from the animal pole of the egg or from some region near it and the fact that many larvae consist essentially of only the most anterior regions of the body, together with the fact that it is the animal pole which initiates ontogenetic development in those cases where a difference in time along the axis can be observed in the earliest stages, and finally the very general progression of morphogenesis in the posterior direction, all these facts as well as many others suggest that the dominance of anterior or distal over posterior or proximal regions is a very general law of organic life. When we review the facts now at hand it appears probable that all organisms, except perhaps the simplest, are fundamentally systems of this character. Moreover, such a conception affords a most satisfactory and logical basis for a physico-chemical theory of development. Undoubtedly in many cases secondary isolations of parts occur, new correl-

ative factors arise and many other conditions combine to alter the original condition. But even in the adult organism the fundamental fact appears in the dominance of the apical region of the plant and in the functional dominance of the head region in animals.

9. It follows further, if the above conclusions are correct that in all cases where development is of this type the process of inheritance concerns primarily the anterior or distal regions. An isolated mass of protoplasm of a given species which is capable of continued existence and synthesis, no matter whether it is a mass of cells from the soma or an egg, represents primarily the dominant distal or anterior region, i.e., its specific type of reaction results always in the formation of this region and then if excess of nutritive material is present or obtainable so that growth may occur other parts arise in consequence of growth and of the correlative influence of the dominant region. In such cases the reproductive element, whether germ cell, somatic cell or mass of cells may represent merely a single specific reaction complex from which others arise as continued metabolism brings about the establishment of certain characteristic internal and external conditions.

So far as the formation of new distal or anterior regions is concerned, the process of form regulation in such cases consists essentially first in the return or approach of somatic cells or cell masses to the specific type of reaction in consequence of isolation from a dominant part which had previously determined some modification of this type of reaction in these cells, second of the formation of a new dominant region in consequence of this change, and finally of the development of subordinate parts under the control of the new dominant region so far as material or energy is available for such development.

In cases where only the formation of proximal or posterior parts is concerned form regulation consists first in the local reaction of cells to the absence of other parts, i.e., to altered correlative conditions, and second in the renewed growth and differentiation of such cells under the influence of more distal or anterior regions which dominate them.

Experimental data which throw light upon the problem of the nature of the dominance of certain regions over others will be presented in a later paper.

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