

of the upper hemisphere represent the "animal layer," outer germ-layer or ectoblast from which arise the epidermis, the nervous system, and the sense-organs. This fact, afterward confirmed in a very large number of animals, led to the designation of the two poles as *animal* and *vegetative, formative* and *nutritive*, or *protoplasmic* and *deutoplasmic*, the latter terms referring to the fact that the nutritive deutoplasm is mainly stored in the lower hemisphere, and that development is therefore more active in the upper. The polarity of the ovum is accentuated by other correlated phenomena. In every case where an egg-axis can be determined by the accumulation of deutoplasm in the lower hemisphere the egg-nucleus sooner or later lies eccentrically in the upper hemisphere, and the polar bodies are formed at the upper pole. Even in cases where the deutoplasm is equally distributed or is wanting — if there really be such cases — an egg-axis is still determined by the eccentricity of the nucleus and the corresponding point at which the polar bodies are formed.

In vastly the greater number of cases the polarity of the ovum has a definite promorphological significance; for the egg-axis shows a definite and constant relation to the axes of the adult body. It is a very general rule that the upper or ectodermic pole, as marked by the position of the polar bodies, lies in the median plane at a point which is afterward found to lie at or near the anterior end. Throughout the annelids and mollusks, for example, the upper pole is the point at which the cerebral ganglia are afterward formed; and these organs lie in the adult on the dorsal side near the anterior extremity. This relation holds true for many of the Bilateralia, though the primitive relation is often disguised by asymmetrical growth in the later stages, such as occur in echinoderms. There is, however, some reason to believe that it is not a universal rule. The recent observations of Castle ('96), which are in accordance with the earlier work of Seeliger, show that in the tunicate *Ciona* the usual relation is reversed, the polar bodies being formed at the vegetative (*i.e.* deutoplasmic or entodermic) pole, which afterward becomes the dorsal side of the larva. My own observations ('95) on the echinoderm-egg indicate that here the primitive egg-axis has an entirely inconstant and casual relation to the gastrula-axis. It may, however, still be possible to show that these exceptions are only apparent, and the principle involved is too important to be accepted without further proof.

(b) *Axial Relations of the Primary Cleavage-planes.* — Since the egg-axis is definitely related to the embryonic axes, and since the first two cleavage-planes pass through it, we may naturally look for a definite relation between these planes and the embryonic axes; and if such a relation exists, then the first two or four blastomeres must likewise have a definite prospective value in the development. Such

relations have, in fact, been accurately determined in a large number of cases. The first to call attention to such a relation seems to have been Newport ('54), who discovered the remarkable fact that *the first cleavage-plane in the frog's egg coincides with the median plane of the adult body*; that, in other words, one of the first two blastomeres gives rise to the left side of the body, the other to the right. This discovery, though long overlooked and, indeed, forgotten, was confirmed more than thirty years later by Pflüger and Roux ('87). It

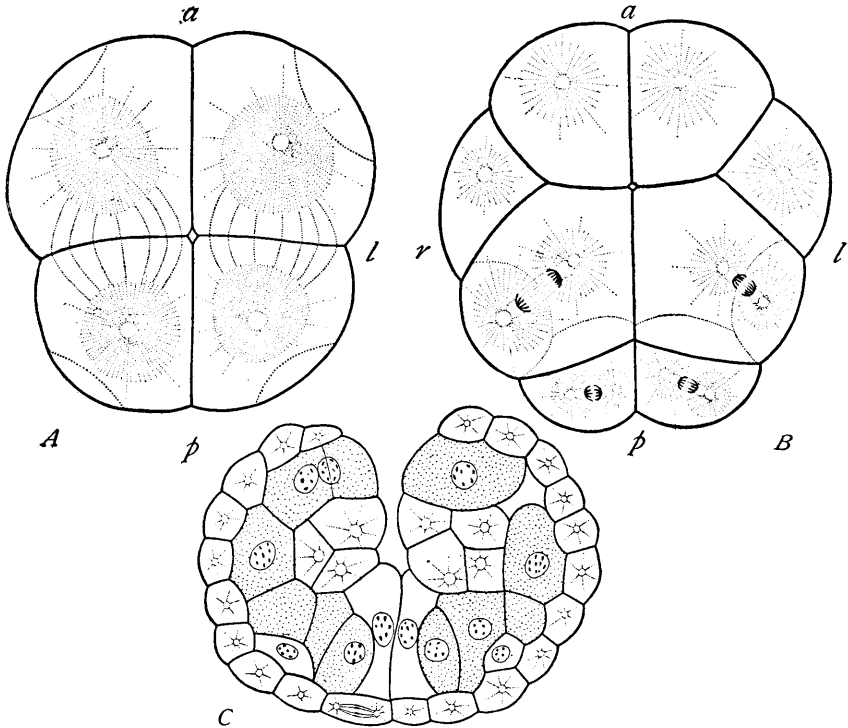


Fig. 177. — Bilateral cleavage of the tunicate egg.

A. Four-celled stage of *Clavelina*, viewed from the ventral side. B. Sixteen-cell stage (VAN BENEDEEN and JULIN). C. Cross-section through the gastrula stage (CASTLE); a, anterior; p, posterior end; l, left, r, right side. [Orientation according to CASTLE.]

was placed beyond all question by a remarkable experiment by Roux ('88), who succeeded in killing one of the blastomeres by puncture with a heated needle, whereupon the uninjured cell gave rise to a half-body as if the embryo had been bisected down the middle line (Fig. 182).

A similar result has been reached in a number of other animals by following out the cell-lineage; e.g. by Van Beneden and Julin ('84)

in the egg of the tunicate *Clavelina* (Fig. 177), and by Watasé ('91) in the eggs of cephalopods (Fig. 178). In both these cases all the early stages of cleavage show a beautiful bilateral symmetry, and not only can the right and left halves of the segmenting egg be distinguished with the greatest clearness, but also the anterior and posterior regions, and the dorsal and ventral aspects. These discoveries seemed, at first, to justify the hope that a fundamental law of development had been discovered, and Van Beneden was thus led, as early as 1883, to express the view that the development of all bilateral animals would probably be found to agree with the frog and ascidian in respect to the relations of the first cleavage.

This cleavage was soon proved to have been premature. In one series of forms, not the first but the second cleavage-plane was found

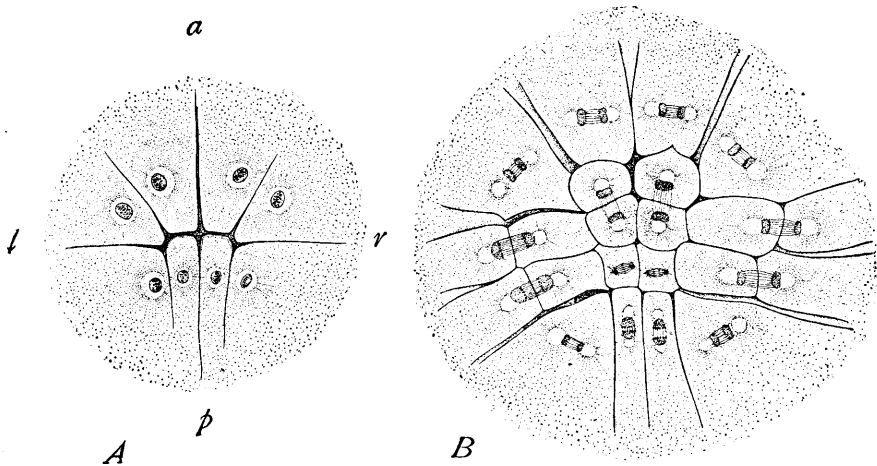


Fig. 178. — Bilateral cleavage of the squid's egg. [WATASÉ.]

A. Eight-cell stage. B. The fifth cleavage in progress. The first cleavage (*a-p*) coincides with the future median plane; the second (*l-r*) is transverse.

to coincide with the future long axis (*Nereis*, and some other annelids; *Crepidula*, *Umbrella*, and other gasteropods). In another series of forms neither of the first cleavages passes through the median plane, but both form an angle of about  $45^\circ$  to it (*Clepsine* and other leeches; *Rhynchelmis* and other annelids; *Planorbis*, *Nassa*, *Unio*, and other mollusks; *Discocaelis* and other platodes). In a few cases the first cleavage departs entirely from the rule, and is equatorial, as in *Ascaris* and some other nematodes. The whole subject was finally thrown into apparent confusion, first by the discovery of Clapp ('91), Jordan, and Eycleshymer ('94) that in some cases there seems to be no constant relation whatever between the early cleavage-planes and the adult axes, even in the same species (teleosts, urodeles); and even in

the frog Hertwig showed that the relation described by Newport and Roux is not invariable. Driesch finally demonstrated that the direction of the early cleavage-planes might be artificially modified by pressure without perceptibly affecting the end-result (*cf.* p. 375).

These facts prove that the promorphology of the early cleavage-forms can have no fundamental significance. Nevertheless, they are of the highest interest and importance; for the fact that the formative forces by which development is determined may or may not coincide with those controlling the cleavage, gives us some hope of

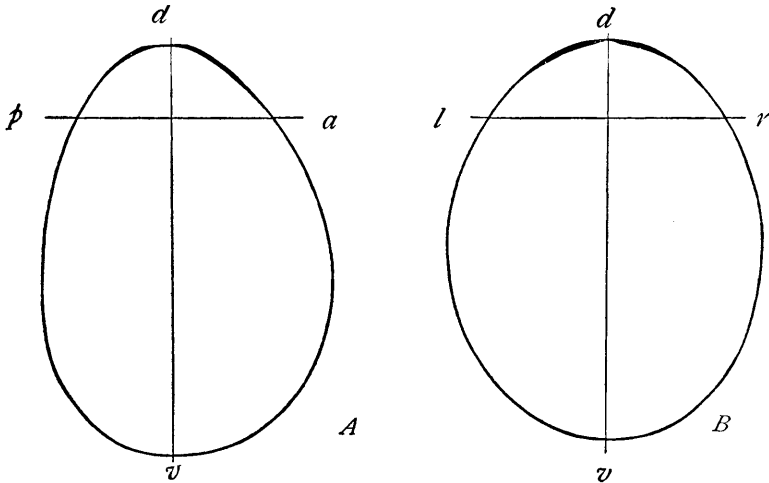


Fig. 179. — Outline of unsegmented squid's egg, to show bilaterality. [WATASÉ.]

*A.* From right side. *B.* From posterior aspect.

*a-p.* antero-posterior axis; *d-v.* dorso-ventral axis; *l.* left side; *r.* right side.

disentangling the complicated factors of development through a comparative study of the different forms.

(*c*) *Other Promorphological Characters of the Ovum.* — Besides the polarity of the ovum, which is the most constant and clearly marked of its promorphological features, we are often able to discover other characters that more or less clearly foreshadow the later development. One of the most interesting and clearly marked of these is the bilateral symmetry of the ovum in bilateral animals, which is sometimes so clearly marked that the exact position of the embryo may be predicted in the unfertilized egg, sometimes even before it is laid. This is the case, for example, in the cephalopod egg, as shown by Watasé (Fig. 179). Here the form of the new-laid egg, before cleavage begins, distinctly foreshadows that of the embryonic body, and forms as it were a mould in which the whole development is cast. Its general shape is that of a hen's egg slightly flattened on one side,

the narrow end, according to Watasé, representing the dorsal aspect, the broad end the ventral aspect, the flattened side the posterior region, and the more convex side the anterior region. *All the early cleavage-furrows are bilaterally arranged with respect to the plane of*

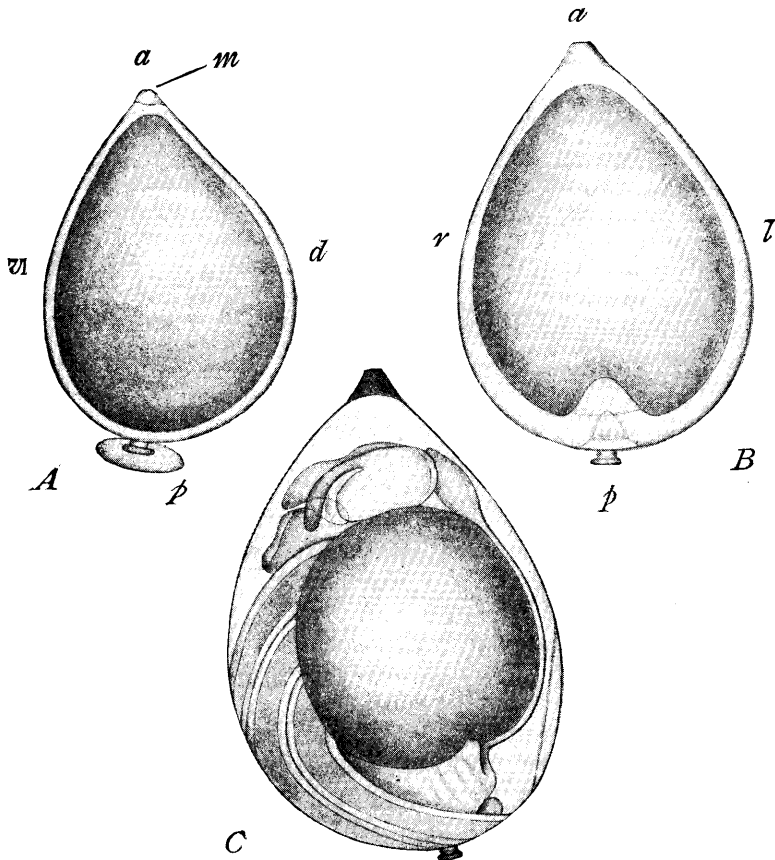


Fig. 180.—Eggs of the insect *Corixa*. [METSCHNIKOFF.]

*A.* Early stage before formation of the embryo, from one side. *B.* The same viewed in the plane of symmetry. *C.* The embryo in its final position.

*a.* anterior end; *p.* posterior; *l.* left side, *r.* right; *v.* ventral, *d.* dorsal aspect. (These letters refer to the *final* position of the embryo, which is nearly diametrically opposite to that in which it first develops); *m.* micropyle; near *p.* is the pedicle by which the egg is attached.

*symmetry in the undivided egg*; and the same is true of the later development of all the bilateral parts.

Scarcely less striking is the case of the insect egg, as has been pointed out especially by Hallez, Blochmann, and Wheeler (Figs. 62, 180). In a large number of cases the egg is elongated and

bilaterally symmetrical, and, according to Blochmann and Wheeler, may even show a bilateral distribution of the yolk corresponding with the bilaterality of the ovum. Hallez asserts as the results of a study of the cockroach (*Periplaneta*), the water-beetle (*Hydrophilus*), and the locust (*Locusta*) that "the egg-cell possesses the same orientation as the maternal organism that produces it; it has a cephalic pole and a caudal pole, a right side and a left, a dorsal aspect and a ventral; and these different aspects of the egg-cell coincide with the corresponding aspects of the embryo."<sup>1</sup> Wheeler ('93), after examining some thirty different species of insects, reached the same result, and concluded that even when the egg approaches the spherical form the symmetry still exists, though obscured. Moreover, according to Hallez ('86) and later writers, the egg always lies in the same position in the oviduct, its cephalic end being turned forwards toward the upper end of the oviduct, and hence toward the head-end of the mother.<sup>2</sup>

## 2. *Meaning of the Promorphology of the Ovum*

The interpretation of the promorphology of the ovum cannot be adequately treated apart from the general discussion of development given in the following chapter; nevertheless it may briefly be considered at this point. Two widely different interpretations of the facts have been given. On the one hand, it has been suggested by Flemming and Van Beneden,<sup>3</sup> and urged especially by Whitman,<sup>4</sup> that the cytoplasm of the ovum possesses a definite primordial organization which exists from the beginning of its existence even though invisible, and is revealed to observation through polar differentiation, bilateral symmetry, and other obvious characters in the unsegmented egg. On the other hand, it has been maintained by Pflüger, Mark, Oscar Hertwig, Driesch, Watasé, and the writer that all the promorphological features of the ovum are of secondary origin; that the egg-cytoplasm is at the beginning isotropous — *i.e.* indifferent or homaxial — and gradually acquires its promorphological features during its preëmbryonic history. Thus the egg of a bilateral animal is at the beginning not actually, but only potentially, bilateral. Bilaterality once established, however, it forms as it were the mould in which the cleavage and other operations of development are cast.

I believe that the evidence at our command weighs heavily on the side of the second view, and that the first hypothesis fails to

<sup>1</sup> See Wheeler, '93, p. 67.

<sup>2</sup> The micropyle usually lies at or near the anterior end, but may be at the posterior. It is a very important fact that the position of the polar bodies varies, being sometimes at the anterior end, sometimes on the side, either dorsal or lateral (Heider, Blochmann).

<sup>3</sup> See p. 298.

<sup>4</sup> *Cf.* pp. 299, 300.

take sufficient account of the fact that development does not necessarily begin with fertilization or cleavage, but may begin at a far earlier period during ovarian life. As far as the *visible* promorphological features of the ovum are concerned, this conclusion is beyond question. The only question that has any meaning is whether these visible characters are merely the expression of a more subtle pre-

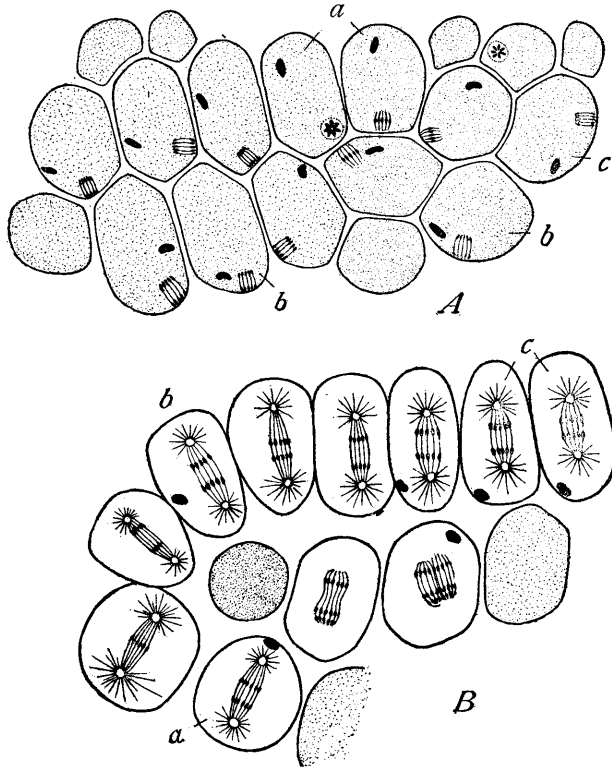


Fig. 181. — Variations in the axial relations of the eggs of *Cyclops*. From sections of the eggs as they lie in the oviduct. [HÄCKER.]

A. Group of eggs showing variations in relative position of the polar spindles and the sperm-nucleus (the latter black); in *a* the sperm-nucleus is opposite to the polar spindle, in *b*, near it or at the side. B. Group showing variations in the axis of first cleavage with reference to the polar bodies (the latter black); *a*, *b*, and *c* show three different positions.

existing invisible organization of the same kind. I do not believe that this question can be answered in the affirmative save by the trite and, from this point of view, barren statement that every effect must have its preëxisting cause. That the egg possesses no fixed and predetermined cytoplasmic localization with reference to the adult parts, has, I think, been demonstrated through the remarkable

experiments of Driesch, Roux, and Boveri, which show that a fragment of the egg may give rise to a complete larva (p. 353). There is strong evidence, moreover, that the egg-axis is not primordial but is established at a particular period; and even after its establishment it may be entirely altered by new conditions. This is proved, for example, by the case of the frog's egg, in which, as Pflüger ('84), Born ('85), and Schultze ('94) have shown, the cytoplasmic materials may be entirely rearranged under the influence of gravity, and a new axis established. In sea-urchins, my own observations ('95) render it probable that the egg-axis is not finally established until after fertilization. These and other facts, to be more fully considered in the following chapter, give strong ground for the conclusion that the promorphological features of the egg are as truly a result of development as the characters coming into view at later stages. They are gradually established during the preëmbryonic stages, and the egg, when ready for fertilization, has already accomplished part of its task by laying the basis for what is to come.

Mark, who was one of the first to examine this subject carefully, concluded that the ovum is at first an indifferent or homaxial cell (*i.e.* isotropic), which afterward *acquires* polarity and other promorphological features.<sup>1</sup> The same view was very precisely formulated by Watasé in 1891, in the following statement, which I believe to express accurately the truth: "It appears to me admissible to say at present that the ovum, which may start out without any definite axis at first, may acquire it later, and at the moment ready for its cleavage the distribution of its protoplasmic substances may be such as to exhibit a perfect symmetry, and the furrows of cleavage may have a certain definite relation to the inherent arrangement of the protoplasmic substances which constitute the ovum. Hence, in a certain case, the plane of the first cleavage-furrow may coincide with the plane of the median axis of the embryo, and the sundering of the protoplasmic material may take place into right and left, according to the preëxisting organization of the egg at the time of cleavage; and in another case the first cleavage may roughly correspond to the differentiation of the ectoderm and the entoderm, also according to the preorganized constitution of the protoplasmic materials of the ovum.

"It does not appear strange, therefore, that we may detect a certain structural differentiation in the unsegmented ovum, with all the axes foreshadowed in it, and the axial symmetry of the embryonic organism identical with that of the adult."<sup>2</sup>

This passage contains, I believe, the gist of the whole matter, as far as the promorphological relations of the ovum and of cleavage-

<sup>1</sup> '81, p. 512.

<sup>2</sup> '91, p. 280.



forms are concerned, though Watasé does not enter into the question as to how the arrangement of protoplasmic materials is effected. In considering this question, we must hold fast to the fundamental fact that the egg is a cell, like other cells, and that from an *a priori* point of view there is every reason to believe that the cytoplasmic differentiations that it undergoes must arise in essentially the same way as in other cells. We know that such differentiations, whether in form or in internal structure, show a definite relation to the environment of the cell—to its fellows, to the source of food, and the like. We know further, as Korschelt especially has pointed out, that *the egg-axis, as expressed by the eccentricity of the germinal vesicle, often shows a definite relation to the ovarian tissues*, the germinal vesicle lying near the point of attachment or of food-supply. Mark made the pregnant suggestion, in 1881, that the primary polarity of the egg might be determined by “*the topographical relation of the egg (when still in an indifferent state) to the remaining cells of the maternal tissue from which it is differentiated,*” and added that this relation might operate through the nutrition of the ovum. “It would certainly be interesting to know if that phase of polar differentiation which is manifest in the position of the nutritive substance and of the germinal vesicle bears a constant relation to the free surface of the epithelium from which the egg takes its origin. If, in cases where the egg is directly developed from epithelial cells, this relationship were demonstrable, it would be fair to infer the existence of corresponding, though obscured, relations in those cases where (as, for example, in mammals) the origin of the ovum is less directly traceable to an epithelial surface.”<sup>1</sup> The polarity of the egg would therefore be comparable to the polarity of epithelial or gland-cells, where, as pointed out at page 57, the nucleus usually lies toward the base of the cell, near the source of food, while the centrosomes, and often also characteristic cytoplasmic products, such as zymogen granules and other secretions, appear in the outer portion.<sup>2</sup> The exact conditions under which the ovarian egg develops are still too little known to allow of a positive conclusion regarding Mark’s suggestion. Moreover, the force of Korschelt’s observation is weakened by the fact that in many eggs of the extreme telolecithal type, where the polarity is very marked, the germinal vesicle occupies a central or sub-central position during the period of yolk-formation and only moves toward the periphery near the time of maturation.

Indeed, in mollusks, annelids, and many other cases, the germinal vesicle remains in a central position, surrounded by yolk on all sides, until the spermatozoon enters. Only then does the egg-nucleus move

<sup>1</sup> '81, p. 515.

<sup>2</sup> Hatschek has suggested the same comparison (*Zoölogie*, p. 112).

to the periphery, the deutoplasm become massed at one pole, and the polarity of the egg come into view (*Nereis*, Figs. 60 and 97).<sup>1</sup> In such cases the axis of the egg may perhaps be predetermined by the position of the centrosome, and we have still to seek the causes by which the position is established in the ovarian history of the egg. These considerations show that this problem is a complex one, involving, as it does, the whole question of cell-polarity; and I know of no more promising field of investigation than the ovarian history of the ovum with reference to this question. That Mark's view is correct in principle is indicated by a great array of general evidence considered in the following chapter, where its bearing on the general theory of development is more fully dealt with.

### C. CELL-DIVISION AND GROWTH

The general relations between cell-division and growth, which have already been briefly considered at page 58 and in the course of this chapter, may now be more critically examined, together with some account of the causes that incite or inhibit division. It has been shown above that every precise inquiry into the rate form, or direction of cell-division, inevitably merges into the larger problem of the general determination of growth. We may conveniently approach this subject by considering first the energy of division and the limitation of growth.

All animals and plants have a limit of growth, which is, however, much more definite in some forms than in others, and differs in different tissues. During the individual development the energy of cell-division is most intense in the early stages (cleavage) and diminishes more and more as the limit of growth is approached. When the limit is attained a more or less definite equilibrium is established, some of the cells ceasing to divide and perhaps losing this power altogether (nerve-cells), others dividing only under special conditions (connective tissue-cells, gland-cells, muscle-cells), while others continue to divide throughout life, and thus replace the worn-out cells of the same tissue (Malpighian layer of the epidermis, etc.). The limit of size at which this state of equilibrium is attained is an hereditary character, which in many cases shows an obvious relation to the environment, and has therefore probably been determined and is maintained by natural selection. From the cytological point of view the limit of body-size appears to be correlated with the total *number* of cells formed rather than with their individual size. This relation has been carefully studied by Conklin ('96) in the case of the gastero-

<sup>1</sup>The immature egg of *Nereis* shows, however, a distinct polarity in the arrangement of the fat-drops, which form a ring in the equatorial regions.

pod *Crepidula*, an animal which varies greatly in size in the mature condition, the dwarfs having in some cases not more than  $\frac{1}{25}$  the volume of the giants. The eggs are, however, of the same size in all, and their *number* is proportional to the size of the adult. The same is true of the tissue-cells. Measurements of cells from the epidermis, the kidney, the liver, the alimentary epithelium, and other tissues show that they are on the whole as large in the dwarfs as in the giants. The body-size therefore depends on the total number of cells rather than on their size individually considered, and the same appears to be the case in plants.<sup>1</sup>

A result which, broadly speaking, agrees with the foregoing, is given through the interesting experimental studies of Morgan ('95, 1, '96), supplemented by those of Driesch ('98), in which the number of cells in normal larvæ of echinoderms, ascidians, and *Amphioxus* is compared with those in dwarf larvæ of the same species developed from egg-fragments (Morgan) and isolated blastomeres (Driesch). Unless otherwise specified, the following data are cited from Driesch.

The normal blastula of *Sphærechinus* possesses about 500 cells (Morgan), of which from 75 to 90 invaginate to form the archenteron (Driesch). In half-gastrulas the number varies from 35 to 45, occasionally reaching 50. In the same species, the normal number of mesenchyme-cells is 54 to 60, in the half-larvæ 25 to 30. In *Echinus* the corresponding numbers are  $30 \pm$  and 13 to 15. In the ascidian larvæ — a particularly favourable object — there are 29 to 35 (exceptionally as high as 40) chorda-cells; in the half-larvæ, 13 to 17. While these comparisons are not mathematically precise, owing to the difficulty of selecting exactly equivalent stages, they nevertheless show that, on the whole, the size of the organ, as of the entire organism, is directly proportional to the number and not to the size of the cells, just as in the mature individuals of *Crepidula*. The available data are, however, too scanty to justify any very positive conclusions, and it is probable that further experiment will disclose factors at present unknown. It would be highly interesting to determine whether such dwarf embryos could in the end restore the normal number of cells, and, hence, the normal size of the body. In all the cases thus far determined the dwarf gastrulas give rise to larvæ (*Plutei*, etc.) correspondingly dwarfed; but their later history has not yet been sufficiently followed out.

The gradual diminution of the energy of division during development by no means proceeds at a uniform pace in all of the cells, and, during the cleavage, the individual blastomeres are often found to exhibit entirely different rhythms of division, periods of active division being succeeded by long pauses, and sometimes by an entire cessa-

<sup>1</sup> See Amelung ('93) and Strasburger ('93).

tion of division even at a very early period. In the echinoderms, for example, it is well established that division suddenly pauses, or changes its rhythm, just before the gastrulation (in *Synapta* at the 512-cell stage, according to Selenka), and the same is said to be the case in *Amphioxus* (Hatschek, Lwoff). In *Nereis*, one of the blastomeres on each side of the body in the forty-two-cell stage suddenly ceases to divide, migrates into the interior of the body, and is converted into a unicellular glandular organ.<sup>1</sup> In the same animal, the four lower cells (macromeres) of the eight-cell stage divide in nearly regular succession up to the thirty-eight-cell stage, when a long pause takes place, and when the divisions are resumed they are of a character totally different from those of the earlier period. The cells of the ciliated belt or prototroch in this and other annelids likewise cease to divide at a certain period, their number remaining fixed thereafter.<sup>2</sup> Again, the number of cells produced for the foundation of particular structures is often definitely fixed, even when their number is afterward increased by division. In annelids and gasteropods, for example, the entire ectoblast arises from twelve micromeres segmented off in three successive quartets of micromeres from the blastomeres of the four-cell stage. Perhaps the most interesting numerical relations of this kind are those recently discovered in the division of teloblasts, where the number of divisions is directly correlated with the number of segments or somites. It is well known that this is the case in certain plants (*Characeæ*), where the alternating nodes and internodes of the stem are derived from corresponding single cells successively segmented off from the apical cell. Vejdovský's observations on the annelid *Dendrobæna* give strong ground to believe that the number of metamericly repeated parts of this animal, and probably of other annelids, corresponds in like manner with that of the number of cells segmented off from the teloblasts. The most remarkable and accurately determined case of this kind is that of the isopod crustacea, where the number of somites is limited and perfectly constant. In the embryos of these animals there are two groups of teloblasts near the hinder end of the embryo, viz. an inner group of mesoblasts, from which arise the mesoblast-bands, and an outer group of ectoblasts, from which arise the neural plates and the ventral ectoblast. McMurrich ('95) has recently demonstrated that the mesoblasts always divide exactly sixteen times, the ectoblasts thirty-two (or thirty-three) times, before relinquishing their teleoblastic mode of division and breaking up into smaller cells. Now the sixteen groups of cells thus formed give rise to the sixteen respective somites of the post-naupliar region of the embryo (*i.e.* from the second maxilla backward). In other

<sup>1</sup> This organ, doubtfully identified by me as the head-kidney, is probably a mucus-gland (Mead).

<sup>2</sup> Cf. Fig. 171.

words, each single division of the mesoblasts and each double division of the ectoblasts splits off the material for a single somite! The number of these divisions, and hence of the corresponding somites, is a fixed inheritance of the species.

The causes that determine the rhythm of division, and thus finally establish the adult equilibrium, are but vaguely comprehended. The ultimate causes must of course lie in the inherited constitution of the organism, and are referable in the last analysis to the structure of the germ-cells. Every division must, however, be the response of the cell to a particular set of conditions or stimuli; and it is through the investigation of these stimuli that we may hope to penetrate farther into the nature of development. The immediate, specific causes of cell-division are still imperfectly known. In the adult, cells may be stimulated to divide by the utmost variety of agencies — by chemical stimulus, as in the formation of galls, or in hyperplasia induced by the injection of foreign substances into the blood; by mechanical pressure, as in the formation of calluses; by injury, as in the healing of wounds and in the regeneration of lost parts; and by a multitude of more complex physiological and pathological conditions, — by any agency, in short, that disturbs the normal equilibrium of the body. In all these cases, however, it is difficult to determine the *immediate stimulus* to division; for a long chain of causes and effects may intervene between the primary disturbance and the ultimate reaction of the dividing cells. Thus there is reason to believe that the formation of a callus is not directly caused by pressure or friction, but through the determination of an increased blood-supply to the part affected and a heightened nutrition of the cells. Cell-division is here probably incited by local chemical changes; and the opinion is gaining ground that the immediate causes of division, whatever their antecedents, are to be sought in this direction. That such is the case is indicated by nothing more clearly than the recent experiments on the egg by R. Hertwig, Mead, Morgan, and Loeb already referred to in part at pages 111 and 215. The egg-cell is, in most cases, stimulated to divide by the entrance of the spermatozoon, but in parthenogenesis exactly the same result is produced by an apparently quite different cause. The experiments in question give, however, ground for the conclusion that the common element in the two cases is a chemical stimulus. In the eggs of *Chaetopterus* under normal conditions the first polar mitosis pauses at the anaphase until the entrance of the spermatozoon, when the mitotic activity is resumed and both polar bodies are formed. Mead ('98) shows, however, that the same effect may be produced without fertilization by placing the eggs for a few minutes in a weak solution of potassium chloride. In like manner R. Hertwig ('96) and Morgan ('99) show that unfertilized

echinoderm-eggs may be stimulated to division by treatment with weak solution of strychnine, sodium-chloride, and other reagents, the result being here more striking than in the case of *Chaetopterus*, since the entire mitotic system is formed anew under the chemical stimulus. The climax of these experiments is reached in Loeb's artificial production of parthenogenesis in sea-urchin eggs by treatment with dilute magnesium chloride. Beside these interesting results may be placed the remarkable facts of gall-formation in plants, which seem to leave no doubt that extremely complex and characteristic abnormal growths may result from specific chemical stimuli, and many pathologists have held that tumours and other pathological growths in the animal body may be incited through disturbances of circulation or other causes resulting in abnormal local chemical conditions.<sup>1</sup>

But while we have gained some light on the immediate causes of division, we have still to inquire how those causes are set in operation and are coördinated toward a typical end; and we are thus brought again to the general problem of growth. A very interesting suggestion is the resistance-theory of Thiersch and Boll, according to which each tissue continues to grow up to the limit afforded by the resistance of neighbouring tissues or organs. The removal or lessening of this resistance through injury or disease causes a resumption of growth and division, leading either to the regeneration of the lost parts or to the formation of abnormal growths. Thus the removal of a salamander's limb would seem to remove a barrier to the proliferation and growth of the remaining cells. These processes are therefore resumed, and continue until the normal barrier is re-established by the regeneration. To speak of such a "barrier" or "resistance" is, however, to use a highly figurative phrase which is not to be construed in a rude mechanical sense. There is no doubt that hypertrophy, atrophy, or displacement of particular parts often leads to compensatory changes in the neighbouring parts; but it is equally certain that such changes are not a direct mechanical effect of the disturbance, but a highly complex physiological response to it. How complex the problem is, is shown by the fact that even closely related animals may differ widely in this respect. Thus Fraisse has shown that the salamander may completely regenerate an amputated limb, while the frog only heals the wound without further regeneration.<sup>2</sup> Again, in the case of coelenterates, Loeb and Bickford have shown that the tubularian hydroids are able to regenerate the tentacles at both ends of a segment of the stem, while the polyp *Cerianthus* can regenerate them only at the distal end of a section (Fig. 194).

<sup>1</sup> Cf. p. 97. For a good discussion of this subject, see E. Ziegler, '89.

<sup>2</sup> In salamanders regeneration only takes place when the bone is cut across, and does not occur if the limb be exarticulated and removed at the joint.

In the latter case, therefore, the body possesses an inherent polarity which cannot be overturned by external conditions. A very curious case is that of the earthworm, which has long been known to possess a high regenerative capacity. If the posterior region of the worm be cut off, a new tail is usually regenerated. If the same operation be performed far forward in the anterior region, a new head is often formed at the front end of the posterior piece. If, however, the section be in the middle region the posterior piece sometimes regenerates a head, but more usually a tail, as was long since shown by Spallanzani and recently by Morgan ('99). Why such a blunder should be committed remains for the present quite unexplained.

It remains to inquire more critically into the nature of the correlation between growth and cell-division. In the growing tissues the direction of the division-planes in the individual cells evidently stands in a definite relation with the axes of growth in the body, as is especially clear in the case of rapidly elongating structures (apical buds, teloblasts, and the like), where the division-planes are predominantly transverse to the axis of elongation. Which of these is the primary factor, the direction of general growth or the direction of the division-planes? This question is a difficult one to answer, for the two phenomena are often too closely related to be disentangled. As far as the plants are concerned, however, it has been conclusively shown by Hofmeister, De Bary, and Sachs that *the growth of the mass is the primary factor*; for the characteristic mode of growth is often shown by the growing mass before it splits up into cells, and the form of cell-division adapts itself to that of the mass: "Die Pflanze bildet Zellen, nicht die Zelle bildet Pflanzen" (De Bary).

Much of the recent work in normal and experimental embryology, as well as that on regeneration, indicates that the same is true in principle of animal growth. Among recent writers who have urged this view should be mentioned Rauber, Hertwig, Adam Sedgwick, and especially Whitman, whose fine essay on the *Inadequacy of the Cell-theory of Development* ('93) marks a distinct advance in our point of view. Still more recently this view has been almost demonstrated through some remarkable experiments on regeneration, which show that definitely formed material, in some cases even the adult tissues, may be *directly moulded into new structures*. Driesch has shown ('95, 2, '99) that if gastrulas of *Sphærechinus* be bisected through the equator so that each half contains both ectoderm and entoderm, the wounds heal, each half forming a typical gastrula, in which the enteron differentiates itself into the three typical regions (fore, middle, and hind gut) correctly proportioned, though the whole structure is but half the normal size. Here, therefore, the formative process is in the main independent of cell-division or increase in size. Miss Bickford

('94) found that in the regeneration of decapitated hydranths of tubularians the new hydranth is primarily formed, not by new cell-formation and growth from the cut end, but by direct transformation of the distal portion of the stem.<sup>1</sup> Morgan's remarkable observations on *Planaria*, finally, show that here also, when the animal is cut into pieces, complete animals are produced from these pieces, but only in small degree through the formation of new tissue, and mainly by direct remoulding of the old material into a new body having the correct proportions of the species. As Driesch has well said, it is as if a plan or mould of the new little worm were first prepared and then the old material were poured into it.<sup>2</sup>

Facts of this kind, of which a considerable store has been accumulated, give strong ground for the view that cell-formation is subordinate to growth, or rather to the general formative process of which growth is an expression; and they furnish a powerful argument against Schwann's conception of the organism as a cell-composite (p. 58). That conception is, however, not to be rejected *in toto*, but contains a large element of truth; for there are many cases in which cells possess so high a degree of independence that profound modifications may occur in special regions through injury or disease, without affecting the general equilibrium of the body. The most striking proof of this lies in the fact that grafts or transplanted structures may perfectly retain their specific character, though transferred to a different region of the body, or even to another species. Nevertheless the facts of regeneration prove that even in the adult the formative processes in special parts are in many cases definitely correlated with the organization of the entire mass; and there is reason to conclude that such a correlation is a survival, in the adult, of a condition characteristic of the embryonic stages, and that the independence of special parts in the adult is a secondary result of development. The study of cell-division thus brings us finally to a general consideration of development which forms the subject of the following chapter.

#### LITERATURE. VIII

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<sup>1</sup> Driesch suggests for such a process the term *reparation* in contradistinction to true regeneration.

<sup>2</sup> '99, p. 55. It is mainly on these considerations that Driesch ('99) has built his recent theory of vitalism (*cf.* p. 417), the nature of the formative power being regarded as a problem *sui generis*, and one which the "machine-theory of life" is powerless to solve.  *Cf.* also the views of Whitman, p. 416.



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