

CHAPTER VIII

CELL-DIVISION AND DEVELOPMENT

“Wir können demnach endlich den Satz aufstellen, dass sämtliche im entwickelten Zustande vorhandenen Zellen oder Aequivalente von Zellen durch eine fortschreitende Gliederung der Eizelle in morphologisch ähnliche Elemente entstehen, und dass die in einer embryonischen Organ-Anlage enthaltenden Zellen, so gering auch ihre Zahl sein mag, dennoch die ausschliessliche ungegliederte Anlage für sämtliche Formbestandtheile der späteren Organe enthalten.”

REMAK.¹

SINCE the early work of Kölliker and Remak it has been recognized that the cleavage or segmentation of the ovum, with which the development of all higher animals begins, is nothing other than a rapid series of mitotic cell-divisions by which the egg splits up into the elements of the tissues. This process is merely a continuation of that by which the germ-cell arose in the parental body. A long pause, however, intervenes during the latter period of its ovarian life, during which no divisions take place. Throughout this period the egg leads, on the whole, a somewhat passive existence, devoting itself especially to the storage of potential energy to be used during the intense activity that is to come. Its power of division remains dormant until the period of full maturity approaches. The entrance of the spermatozoon arouses in the egg a new phase of activity. Its power of division, which may have lain dormant for months or years, is suddenly raised to the highest pitch of intensity, and in a very short time it gives rise by division to a myriad of descendants which are ultimately differentiated into the elements of the tissues.

The divisions of the egg during cleavage are exactly comparable with those of tissue-cells, and all of the essential phenomena of mitosis are of the same general character in both. But for two reasons the cleavage of the egg possesses a higher interest than any other case of cell-division. First, the egg-cell gives rise by division not only to cells like itself, as is the case with most tissue-cells, but also to many other kinds of cells. The operation of cleavage is therefore immediately connected with the process of differentiation, which is the most fundamental phenomenon in development. Second, definite relations may often be traced between the planes of division and the structural axes of the adult body, and these relations are

¹ *Untersuchungen*, 1855, p. 140.

sometimes so clearly marked and appear so early that with the very first cleavage the position in which the embryo will finally appear in the egg may be exactly predicted. Such "promorphological" relations of the segmenting egg possess a very high interest in their bearing on the theory of germinal localization and on account of the light which they throw on the conditions of the formative process.

The present chapter is in the main a prelude to that which follows, its purpose being to sketch some of the external features of early development regarded as particular expressions of the general rules of cell-division. For this purpose we may consider the cleavage of the ovum under two heads, namely:—

1. *The Geometrical Relations of Cleavage-forms*, with reference to the general rules of cell-division.

2. *The Promorphological Relations* of the blastomeres and cleavage-planes to the parts of the adult body to which they give rise.

A. GEOMETRICAL RELATIONS OF CLEAVAGE-FORMS

The geometrical relations of the cleavage-planes and the relative size and position of the cells vary endlessly in detail, being modified by innumerable mechanical and other conditions, such as the amount and distribution of the inert yolk or deutoplasm, the shape of the ovum as a whole, and the like. Yet all the forms of cleavage can be referred to a single type which has been moulded this way or that by special conditions, and which is itself an expression of two general rules of cell-division, first formulated by Sachs in the case of plant-cells. These are:—

1. *The cell typically tends to divide into equal parts.*
2. *Each new plane of division tends to intersect the preceding plane at a right angle.*

In the simplest and least modified forms the direction of the cleavage-planes, and hence the general configuration of the cell-system, depends on the general form of the dividing mass; for, as Sachs has shown, the cleavage-planes tend to be either vertical to the surface (*anticlines*) or parallel to it (*periclinal*). Ideal schemes of division may thus be constructed for various geometrical figures. In a flat circular disc, for example, the anticlinal planes pass through the radii; the periclinal are circles concentric with the periphery. If the disc be elongated to form an ellipse, the periclinal also become ellipses, while the anticlines are converted into hyperbolas confocal with the periclinal. If it have the form of a parabola, the periclinal and anticlines form two systems of confocal parabolas intersecting at right angles. All these schemes are *mutatis mutandis*, directly convertible into the corresponding solid forms in three dimensions.

Sachs has shown in the most beautiful manner that all the above ideal types are closely approximated in nature, and Rauber has applied the same principle to the cleavage of animal-cells. The discoid or spheroidal form is more or less nearly realized in the thalloid growths of

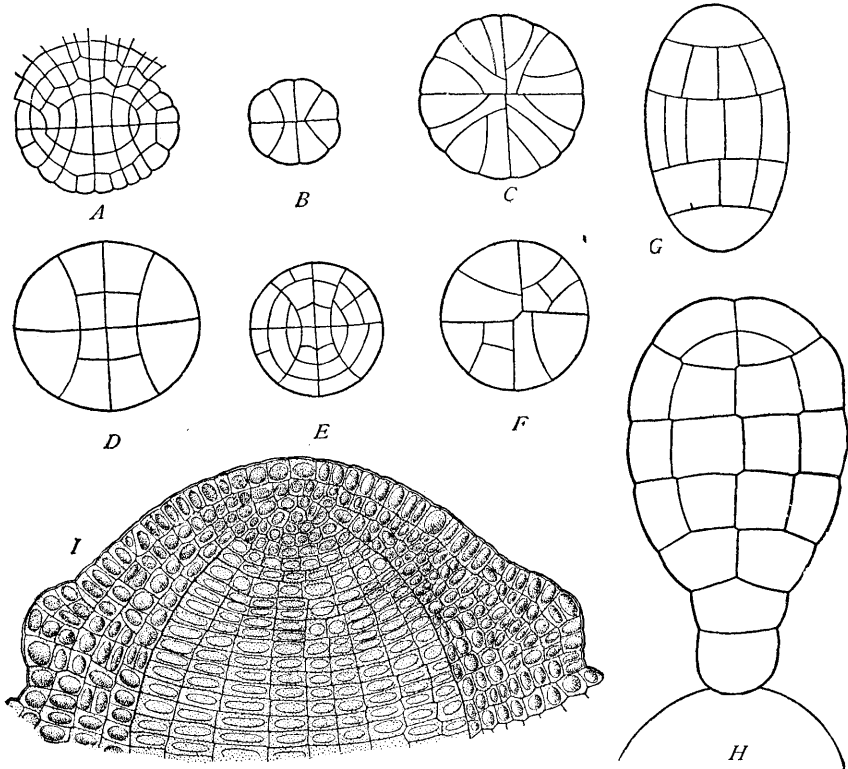


Fig. 168. — Geometrical relations of cleavage-planes in growing plant-tissues. [From SACHS, after various authors.]

A. Flat ellipsoidal germ-disc of *Melobesia* (Rosanoff); nearly typical relation of elliptic periclinal and hyperbolic anticlinal. B. C. Apical view of terminal knob on epidermal hair of *Pinguicula*. B. shows the ellipsoid type, C. the circular (spherical type), somewhat modified (only anticlines present). D. Growing point of *Salvinia* (Pringsheim), typical ellipsoid type; the single pericline is, however, incomplete. E. Growing point of *Azolla* (Strasburger); circular or spheroidal type transitional to ellipsoidal. F. Root-cap of *Equisetum* (Nägeli and Leitgeb); modified circular type. G. Cross-section of leaf-vein, *Trichomanes* (Prantl); ellipsoidal type with incomplete periclinal. H. Embryo of *Alisma*; typical ellipsoidal type, pericline incomplete only at lower side. I. Growing point of bud of the pine (*Abies*); typical paraboloid type, both anticlines and periclinal having the form of parabolas (Sachs).

various lower plants, in the embryos of flowering plants, and elsewhere (Fig. 168). The paraboloid form is according to Sachs characteristic of the growing points of many higher plants; and here, too, the actual form is remarkably similar to the ideal scheme (Fig. 168, I).

For our purpose the most important form is the sphere, which is the typical shape of the egg-cell; and all forms of cleavage may be related to the typical division of a sphere in accordance with Sachs's rules. The ideal form of cleavage would here be a succession of rectangular cleavages in the three dimensions of space, the anticlines passing through the centre so as to split the egg in the initial stages successively into halves, quadrants, and octants, the periclinal cleavages being parallel to the surface so as to separate the inner ends of these cells from the outer. No case is known in which this order is accurately followed throughout, and the periclinal cleavages are of comparatively rare occurrence, being found as a regular feature of the early cleavage only in those cases where the primary germ-layers are separated by delamination. The simplest and clearest form of egg-cleavage occurs in eggs like those of echinoderms, which are of spherical form, and in which the deutoplasm is small in amount and equally distributed through its substance. Such a cleavage is beautifully displayed in the egg of the holothurian *Synapta*, as shown in the diagrams, Fig. 169, constructed from Selenka's drawings. The first cleavage is vertical, or *meridional*, passing through the egg-axis and dividing the egg into equal halves. The second, which is also meridional, cuts the first plane at right angles and divides the egg into quadrants. The third is horizontal, or *equatorial*, dividing the egg into equal octants. The order of division is thus far exactly that demanded by Sachs's rule and agrees precisely with the cleavage of various kinds of spherical plant-cells. The later cleavages depart from the ideal type in the absence of periclinal divisions, the embryo becoming hollow, and its walls consisting of a single layer of cells in which anticlinal cleavages occur in regular rectangular succession. The fourth cleavage is again meridional, giving two tiers of eight cells each; the fifth is horizontal, dividing each tier into an upper and a lower layer. The regular alternation is continued up to the ninth division (giving 512 cells), when the divisions pause while the gastrulation begins. In later stages the regularity is lost.

Hertwig's Development of Sachs's Rules. — Beside Sachs's rules may be placed two others formulated by Oscar Hertwig in 1884, which bear directly on the facts just outlined and which lie behind Sachs's principle of the rectangular intersection of successive division-planes. These are:—

1. *The nucleus tends to take up a position at the centre of its sphere of influence, i.e. of the protoplasmic mass in which it lies.*
2. *The axis of the mitotic figures typically lies in the longest axis of the protoplasmic mass, and division therefore tends to cut this axis at a right angle.*

The second rule explains the normal succession of the division-

planes according to Sachs's second rule. The first division of a homogeneous spherical egg, for example, is followed by a second division at right angles to it, since each hemisphere is twice as long in the plane of division as in any plane vertical to it. The mitotic figure of the second division lies therefore parallel to the first plane, which forms the base of the hemisphere, and the ensuing division is vertical to it. The same applies to the third division, since each quadrant is as long as the entire egg while at most only half its diameter. Division is therefore transverse to the long axis and vertical to the first two planes.

Taken together the rules of Sachs and Hertwig, applied to the egg, give us a kind of ideal type or model, well illustrated by the

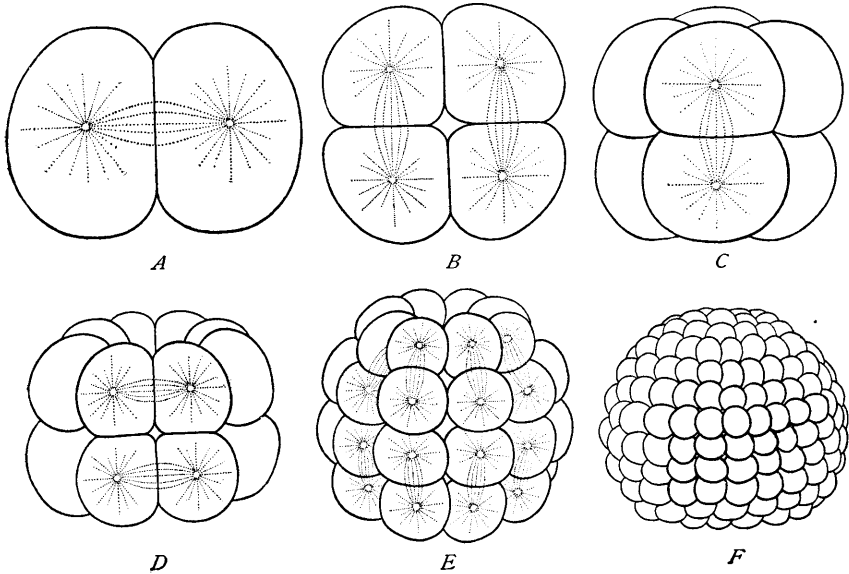


Fig. 169. — Cleavage of the ovum in the holothurian *Synapta* (slightly schematized). [After SELENKA.]

A-E. Successive cleavages to the 32-cell stage. F. Blastula of 128 cells.

cleavage of *Synapta*, described above, to which all the forms of cleavage may conveniently be referred as a basis of comparison. Numerous exceptions to all four of these rules are, however, known, and they are of little value save as a starting-point for a closer study of the facts. Cleavage of such schematic regularity as that of *Synapta* is extremely rare, both the form and the order of division being endlessly varied and in extreme cases showing scarcely a discoverable connection with the "type." We may conveniently consider these modifications under the following three heads:—

1. *Variation in the rhythm of division.*
2. *Displacement of the cells (including variations in the direction of cleavage).*
3. *Unequal division of the cells.*

Nothing is more common than a departure from the regular rhythm of division. The variations are sometimes quite irregular, sometimes follow a definite rule, as, for instance, in the annelid *Nereis* (Fig. 171), where the typical succession in the number of cells is with great constancy 2, 4, 8, 16, 20, 23, 29, 32, 37, 38, 41, 42, after which the order is more or less variable. The factors that determine such variations in the rhythm of division are very little understood. Bal-four, one of the first to consider the subject, sought an explanation in the varying distribution of metaplastic substances, maintaining ('75, '80) that the rapidity of division in any part of the ovum is in general inversely proportional to the amount of deutoplasm that it contains. The entire inadequacy of this view has been demonstrated by a long series of precise studies on cell-lineage, which show that while the large deutoplasm-bearing cells often do divide more slowly than the smaller protoplasmic ones the reverse is often the case, while remarkable differences in the rhythm of division are often observed in cells which do not perceptibly differ in metaplastic content.¹ All the evidence indicates that the rhythm of division is at bottom determined by factors of a very complex character which cannot be disentangled from those which control growth in general. Lillie ('95, '99) points out the very interesting fact, determined through an analysis of the cell-lineage of mollusks and annelids, that the rate of cleavage shows a direct relation to the period at which the products become functional. Thus in *Unio* the more rapid cleavage of a certain large cell ("d. 2"), formed at the fourth cleavage, is obviously correlated with the early formation of the shell-gland to which it gives rise, while the relatively slow rate of division in the first ectomere-quartet is correlated with reduction of the præ-trochal region. The prospective character shown here will be found to apply also to other characters of cleavage, as described beyond.

When we turn to the factors that determine the direction of cleavage or the displacement of cells subsequent to division, we find, as in the case of the division-rhythm, obvious mechanical factors combined with others far more complex. The arrangement of tissue-cells usually tends toward that of least resistance or greatest economy of space; and in this regard they have been shown to conform, broadly speaking, with the behaviour of elastic spheres, such as soap-bubbles when massed together and free to move. Such bodies, as Plateau

¹ Cf. Wilson, '92, Kofoid, '94, Lillie, '95, Zur Strassen, '95, Ziegler, '95, and especially Jennings, '97.

and Lamarle have shown, assume a polyhedral form and tend toward such an arrangement that *the area of surface-contact between them is a minimum*. Spheres in a mass thus tend to assume the form of interlocking polyhedrons so arranged that three planes intersect in a line, while four lines and six planes meet at a point. If arranged in a single layer on an extended surface, they assume the form of

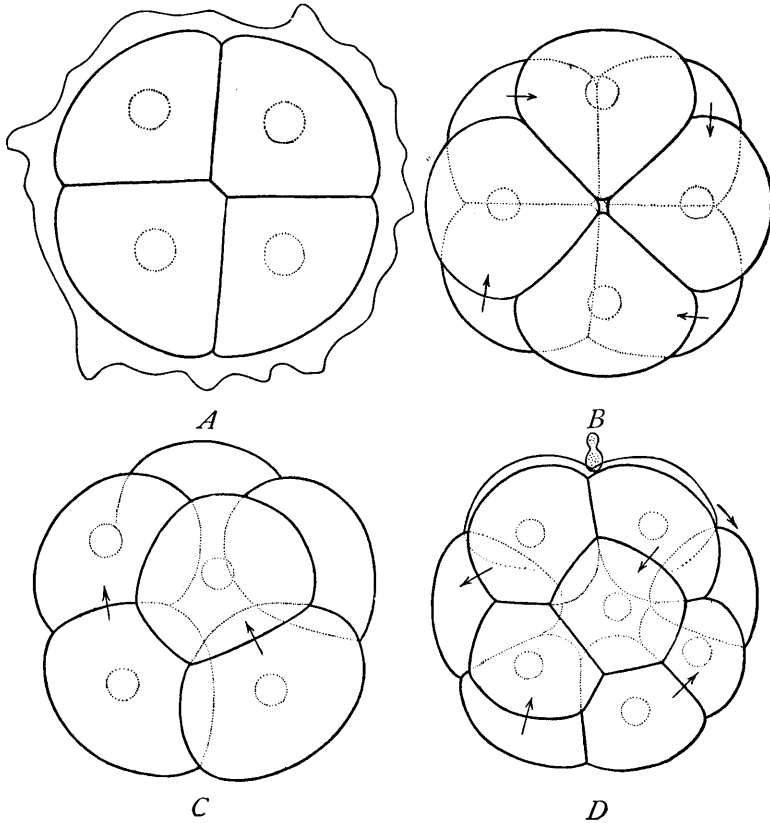


Fig. 170. — Cleavage of *Polygordius*, from life.

A. Four-cell stage, from above. B. Corresponding view of eight-cell stage. C. Side view of the same (contrast Fig. 169, C). D. Sixteen-cell stage from the side.

hexagonal prisms, three planes meeting along a line as before. Both these forms are commonly shown in the arrangement of the cells of plant and animal tissues; and Berthold ('86) and Errera ('86, '87), carefully analyzing the phenomena, have endeavoured to show that not only the form and relative position of cells, but also the direction of cell-division, is, partially at least, thus determined.

It is through displacements of the cells of this type that many of

the most frequent modifications of cleavage arise. Sometimes, as in *Synapta*, the alternation of the cells is effected through displacement of the blastomeres after their formation. More commonly it arises during the division of the cells, and may even be predetermined by the position of the mitotic figures before the slightest external sign of division. Thus arises that form of cleavage known as the spiral, oblique, or alternating type, where the blastomeres interlock during their formation and lie in the position of least resistance from the beginning. This form of cleavage, especially characteristic of many worms and mollusks, is typically shown by the egg of *Polygordius* (Fig. 170). The four-celled stage is nearly like that of *Synapta*, though even here the cells slightly interlock. The third division is, however, oblique, the four upper cells being virtually rotated to the right (with the hands of a watch) so as to alternate with the four lower ones. The fourth cleavage is likewise oblique, but at right angles to the third, so that all of the cells interlock as shown in Fig. 170, *D*. This alternation regularly recurs for a considerable period.

In many worms and mollusks the obliquity of cleavage appears still earlier, at the second cleavage, the four cells being so arranged that two of them meet along a "cross-furrow" at the lower pole of the egg, while the other two meet at the upper pole along a similar, though often shorter, cross-furrow at right angles to the lower (*e.g.* in *Nereis*, Fig. 171). It is a curious fact that the direction of the displacement is quite constant, the first or upper quartet in the eight-cell stage being rotated to the right, or with the hands of a watch, the second quartet to the left, the third to the right, and so on. Crampton ('94) has discovered the remarkable fact that in *Physa*, a gasteropod having a reversed or sinistral shell, the whole order of displacement is likewise reversed, and the same has recently been shown by Holmes ('99) to be true of *Ancylus*.

The spiral or alternating type of cleavage beautifully illustrates Sachs's second rule as affected by modifying conditions; for, as may be seen by an inspection of Figs. 170, 171, each division-plane is approximately at right angles to the preceding and succeeding (whence the "alternation of the spirals" described by students of cell-lineage), while they are so directed that each cell as it is formed is placed at once in the position of least resistance in the mass, *i.e.* in the position of minimal surface-contact. It is impossible to resist the conclusion that one of the factors by which the position of the cells (and hence the direction of cell-division) is determined is a purely mechanical one, identical with that which determines the arrangement of soap-bubbles and the like.

Very little acquaintance with the facts of development is however

required to show that this purely mechanical factor, though doubtless real, must be subordinate to some other. This is strikingly shown, for example, in the development of annelids and mollusks, where the spiral cleavage, strictly maintained during the earlier stages, finally gives way more or less completely to a bilateral type of division in which the rule of minimal surface-contact is often violated. We see here a tendency operating directly against, and finally overcoming,

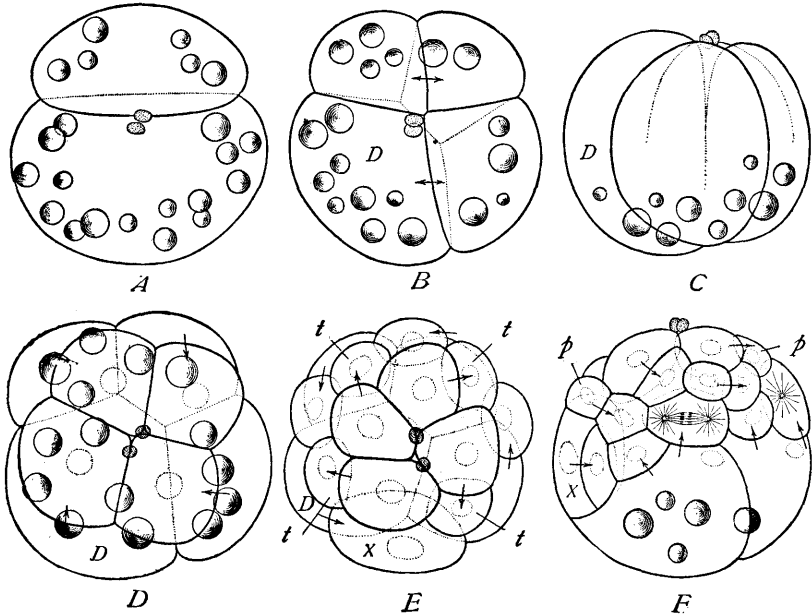


Fig. 171. — Cleavage of *Nereis*. An example of a spiral cleavage, unequal from the beginning and of a marked determinate character.

A. Two-cell stage (the circles are oil-drops). B. Four-cell stage; the second cleavage-plane passes through the future median plane. C. The same from the right side. D. Eight-cell stage. E. Sixteen cells; from the cells marked *t* arises the prototroch or larval ciliated belt, from *X* the ventral nerve-cord and other structures, from *D* the mesoblast-bands, the germ-cells, and a part of the alimentary canal. F. Twenty-nine-cell stage, from the right side; *p*. girdle of prototrochal cells which give rise to the ciliated belt.

the mechanical factor which predominates in the earlier stages; and in some cases, *e.g.* in the egg of *Clavelina* (Fig. 177) and other tunicates, this tendency predominates from the beginning. In both these cases this "tendency" is obviously related to the growth-process to which the future bilateral embryo will owe its form;¹ and every attempt to explain the position of the cells and the direction of cleavage must reckon with the morphogenic process taken as a whole. The blastomere is not merely a cell dividing under the stress of rude

¹ Cf. Wilson ('92, p. 444).

mechanical conditions; it is beyond this "a builder which lays one stone here, another there, each of which is placed with reference to future development."¹

The third class of modifications, due to unequal division of the cells, not only leads to the most extreme types of cleavage but also to its

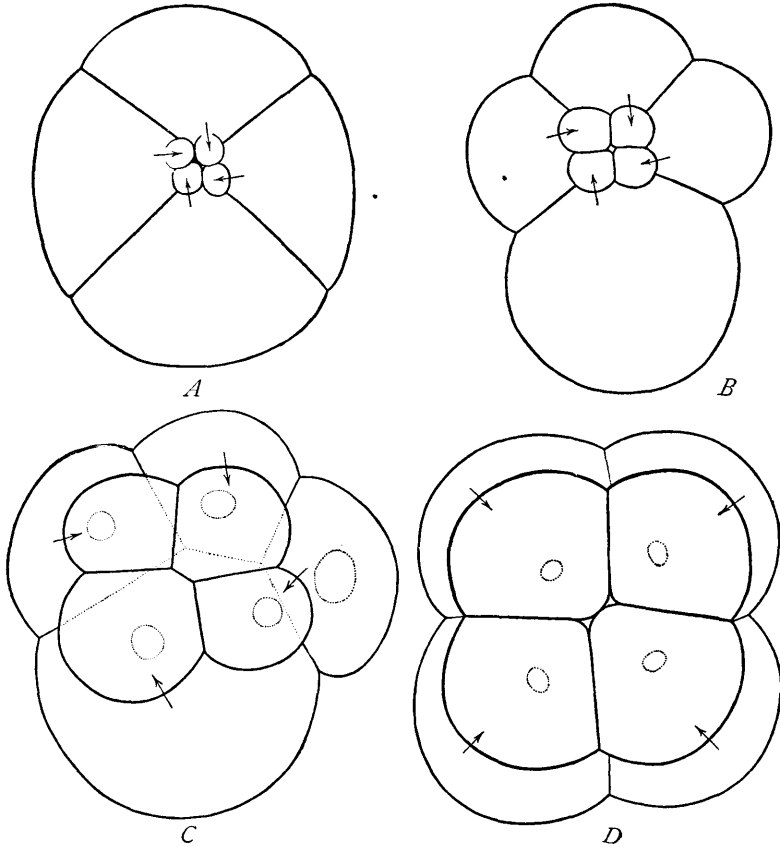


Fig. 172. — The eight-cell stage of four different animals showing gradations in the inequality of the third cleavage.

A. The leech *Clepsine* (Whitman). B. The chaetopod *Rhynchelmis* (Vejdovský). C. The lamellibranch *Unio* (Lillie). D. *Amphioxus*.

most difficult problems. Unequal divisions appear sooner or later in all forms of cleavage, the perfect equality so long maintained in *Synapta* being a rare phenomenon. The period at which the inequality first appears varies greatly in different forms. In *Polygordius* (Fig. 170) the first marked inequality appears at the fifth cleavage;

¹ Lillie, '95, p. 46.

in sea-urchins it appears at the fourth (Fig. 3); in *Amphioxus* at the third (Fig. 172); in the tunicate *Clavelina* at the second (Fig. 177); in *Nereis* at the first division (Figs. 60, 171). The extent of the inequality varies in like manner. Taking the third cleavage as a type, we may trace every transition from an equal division (echinoderms, *Polygordius*), through forms in which it is but slightly marked (*Amphioxus*, frog), those in which it is conspicuous (*Nereis*, *Lymnæa*, polyclades, *Petromyzon*, etc.), to forms such as *Clepsine*, where the cells of the upper quartet are so minute as to appear like mere buds from the four large lower cells (Fig. 172). At the extreme of the series we reach the partial or meroblastic cleavage, such as occurs in the cephalopods, in many fishes, and in birds and reptiles. Here the lower hemisphere of the egg does not divide at all, or only at a late period, segmentation being confined to a disc-like region or blastoderm at one pole of the egg (Fig. 173).

Very interesting is the case of the *teloblasts* or *pole-cells* characteristic of the development of many annelids and mollusks and found in some arthropods. These remarkable cells are large blastomeres, set aside early in the development, which bud forth smaller cells in regular succession at a fixed point, thus giving rise to long cords of cells (Fig. 175). The teloblasts are especially characteristic of apical growth, such as occurs in the elongation of the body in annelids, and they are closely analogous to the apical cells situated at the growing point in many plants, such as the ferns and stoneworts.

Still more suggestive is the formation of *rudimentary cells*, arising as minute buds from the larger blastomeres, and, in some cases, apparently taking no part in the formation of the embryo (Fig. 174).¹

We are as far removed from an explanation of unequal division as from that of the rhythm and direction of division. Inequality of division, like difference of rhythm, is often correlated with inequalities in the distribution of metaphasic substances—a fact generalized by Balfour in the statement ('80) that the size of the cells formed in cleavage varies inversely to the relative amount of protoplasm in the region of the egg from which they arise. Thus, in all telolecithal ova, where the deutoplasm is mainly stored in the lower or vegetative hemisphere, as in many worms, mollusks, and vertebrates, the cells of the upper or protoplasmic hemisphere are smaller than those of the lower, and may be distinguished as *micromeres* from the larger *macromeres* of the lower hemisphere. The size-ratio between micromeres and macromeres is on the whole directly proportional to the ratio between protoplasm and deutoplasm. Partial or discoidal cleavage occurs when the mass of deutoplasm is so great as entirely to prevent cleavage in the lower hemisphere. This has been beautifully con-

¹ See Wilson, '98, '99, 2.

firmed by O. Hertwig ('98), who, by placing frogs' eggs in a centrifugal machine, has caused them to undergo a meroblastic cleavage through the artificial accumulation of yolk at the lower pole, due to the centrifugal force.

While doubtless containing an element of truth, this explanation is, however, no more adequate than Balfour's rule regarding the relation between deutoplasm and rhythm (p. 366); for innumerable cases are known in which no correlation can be made out between the distribution of inert substance and the inequality of division. This is the case, for example, with the teloblasts mentioned above, which contain no deutoplasm, yet regularly divide unequally. It seems to be inap-

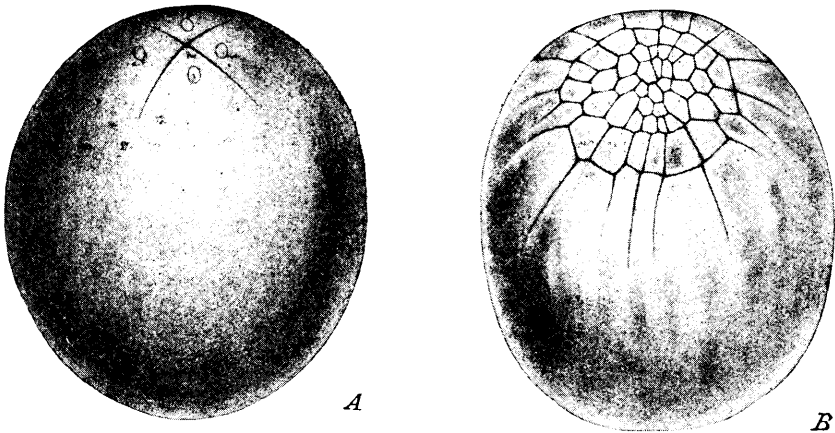


Fig. 173.— Partial or meroblastic cleavage in the squid *Lolligo*. [WATASÉ.]

pliable to the inequalities of the first two divisions in annelids and gasteropods. It is conspicuously inadequate in the history of individual blastomeres, where the history of division has been accurately determined. In *Nereis*, for example, a large cell known as the first somatoblast, formed at the fourth cleavage (*X*, Fig. 171, *E*), undergoes an invariable order of division, three unequal divisions being followed by an equal one, then by three other unequal divisions, and again by an equal. This cell contains little or no deutoplasm and undergoes no perceptible changes of substance.

The collapse of the rule is most complete in case of the rudimentary cells referred to above. In some of the annelids, *e.g.* in *Aricia*, where they were first observed,¹ these cells are derived from the very large primary mesoblast-cell, which first divides into equal halves. Each of these then buds forth a cell so small as to be no larger than a polar body, and then immediately proceeds to give rise

¹ *Cf.* Wilson, '92, '98.

to the mesoblast-bands by continued divisions, always in the same plane at right angles to that in which the rudimentary cells are formed (Fig. 174). The cause of the definite succession of equal and unequal divisions is here wholly unexplained. No less difficult is the extreme inequality of division involved in the formation of the polar bodies. We cannot explain this through the fact that deutoplasm is collected in the lower hemisphere; for, on the one hand, the succeeding divisions (first cleavages) are often equal, while, on the other hand, the inequality is no less pronounced in eggs having equally

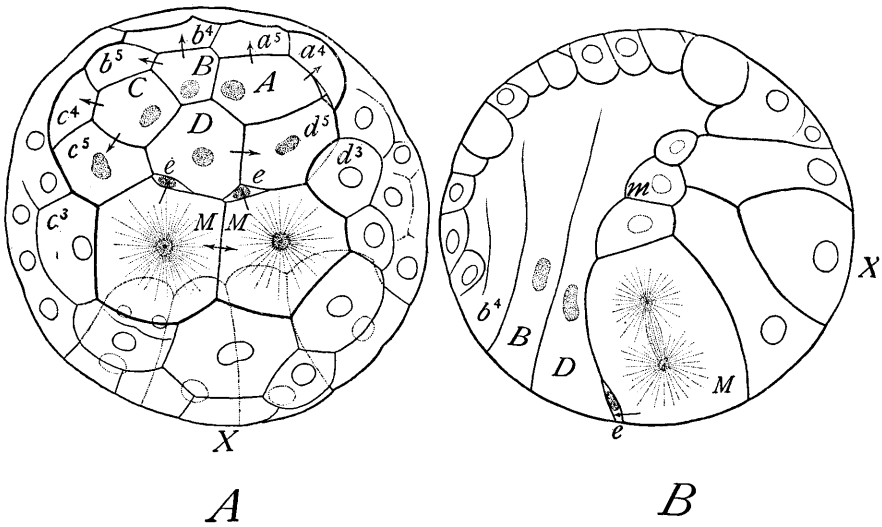


Fig. 174.— Rudimentary blastomeres in the embryo of an annelid, *Aricia*.

A. From lower pole; rudimentary cells at e , e ; the heavy outline is the lip of the blastopore.
 B. The same in sagittal optical section, showing rudimentary cell (e), primary mesoblast (M), and mesoblast-band (m).

distributed deutoplasm, or in those, like echinoderm-eggs, which are "alecithal."

Such cases prove that Balfour's law is only a partial explanation, being probably the expression of a more deeply lying cause, and there is reason to believe that this cause lies outside the immediate mechanism of mitosis. Conklin ('94) has called attention to the fact¹ that the immediate cause of the inequality probably does not lie either in the nucleus or in the amphiaster; for not only the chromatin-halves, but also the asters, are exactly equal in the early prophases, and the inequality of the asters only appears as the division proceeds. Probably, therefore, the cause lies in some relation between the mitotic figure and the cell-body in which it lies.

¹ In the cleavage of gasteropod eggs.

I believe there is reason to accept the conclusion that this relation is one of position, however caused. A central position of the mitotic

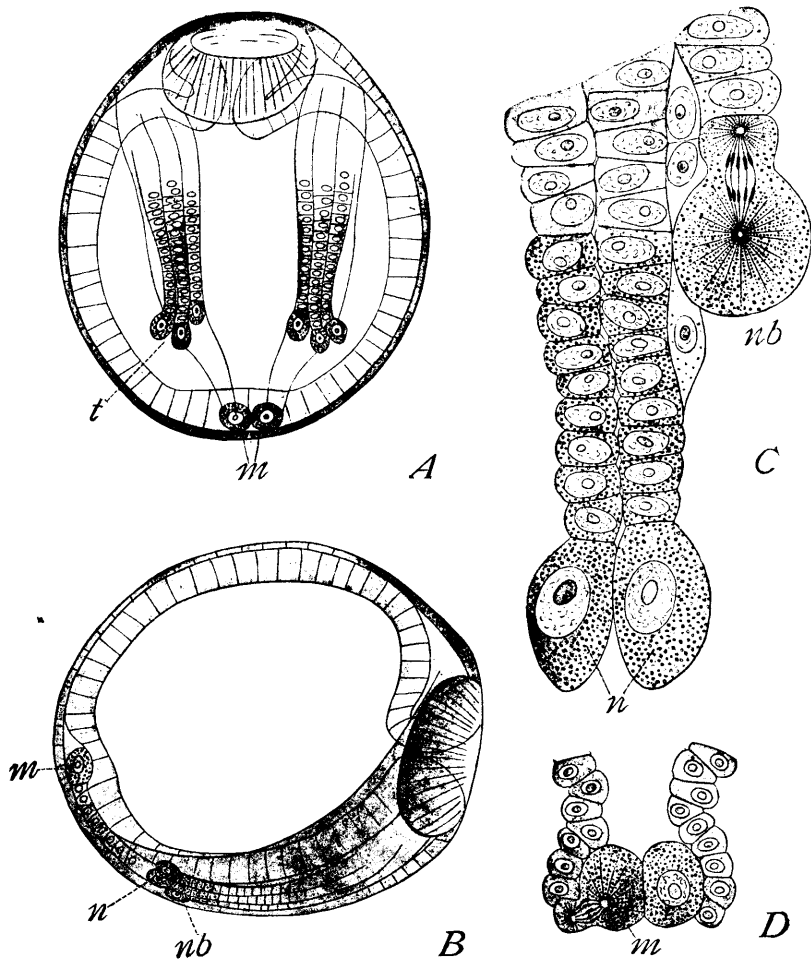


Fig. 175.—Embryos of the earthworm *Allolobophora fatida*, showing teloblasts or apical cells.

A. Gastrula from the ventral side. *B.* The same from the right side; *m.* the terminal teloblasts or *primary mesoblasts*, which bud forth the mesoblast-bands, cell by cell; *t.* lateral teloblasts, comprising a *neuroblast*, *nb*, from which the ventral nerve-cord arises, and two *nephroblasts*, *n*, of somewhat doubtful nature, but probably concerned in the formation of the nephridia. *C.* Lateral group of teloblasts, more enlarged, the neuroblast, *nb*, in division; *n.* the nephroblasts. *D.* The primary mesoblasts enlarged; one in division.

figure results in an equal division; an eccentric position caused by a radial movement of the mitotic figure, in the direction of its axis toward the periphery, leads to unequal division, and the greater the

eccentricity, the greater the inequality, an extreme form being beautifully shown in the formation of the polar bodies. Here the original amphiaster is perfectly symmetrical, with the asters of equal size (Fig. 97, *A*). As the spindle rotates into its radial position and approaches the periphery, the development of the outer aster becomes, as it were, suppressed, while the central aster becomes enormously large. *The size of the aster, in other words, depends upon the extent of the cytoplasmic area that falls within the sphere of influence of the centrosome*; and this area depends upon the position of the centrosome. If, therefore, the polar amphiaster could be artificially prevented from moving to its peripheral position, the egg would probably divide equally.¹

This leads us to a further consideration of the attempts that have been made to explain the movements of the mitotic figure through mechanical or other causes.² Highly interesting experiments have been made by Pflüger ('84), Roux ('85), Driesch ('92), and a number of later investigators which show that the direction of cleavage may be determined, or at least modified, by such a purely mechanical cause as pressure, through which the form of the dividing mass is changed.

Thus, Driesch has shown that when the eggs of sea-urchins are flattened by pressure, the amphiasters all assume the position of least resistance, *i.e.* parallel to the flattened sides, so that the cleavages are all vertical, and the egg segments as a flat plate of eight, sixteen, or thirty-two cells (Fig. 186). This is totally different from the normal form of cleavage; yet such eggs, when released from pressure, are capable of development and give rise to normal embryos. This interesting experiment makes it highly probable that the disc-like cleavage of meroblastic eggs, like that of the squid or bird, is in some degree a mechanical result of the accumulation of yolk by which the formative protoplasmic region of the ovum is reduced to a thin layer at the upper pole; and it indicates, further, that the unequal cleavage of less modified telolecithal eggs, like those of the frog or snail, are in like manner due to the displacement of the mitotic figures toward the upper pole.

The results of Pflüger's and Driesch's pressure experiments obviously harmonize with Hertwig's second rule, for the position of least resistance for the spindle is obviously in the long axis of the protoplasmic mass which is here artificially modified; and it harmonizes further with Drüner's hypothesis of the active elongation of the spindle in mitosis (p. 105). There are, however, a large number of facts which show that neither the form of the protoplasmic mass nor

¹ Cf. Francotte on the polar bodies of Turbellaria, p. 235.

² For a good review and critique, see Jennings, '97.

the distribution of metaplastic materials is sufficient to explain the position of the spindle, whether with reference to the direction or the inequality of the cleavage.

As regards the direction of the spindle, Berthold ('86) long since clearly pointed out that prismatic or cylindrical vegetable cells, for instance, those of the cambium, often divide lengthwise; and numerous contradictions of Hertwig's "law" have since been observed by students of cell-lineage with such accuracy that all attempts to explain them away have failed.¹ In some of these cases the position of the spindle is not that of least but of greatest resistance,² the spindle ac-

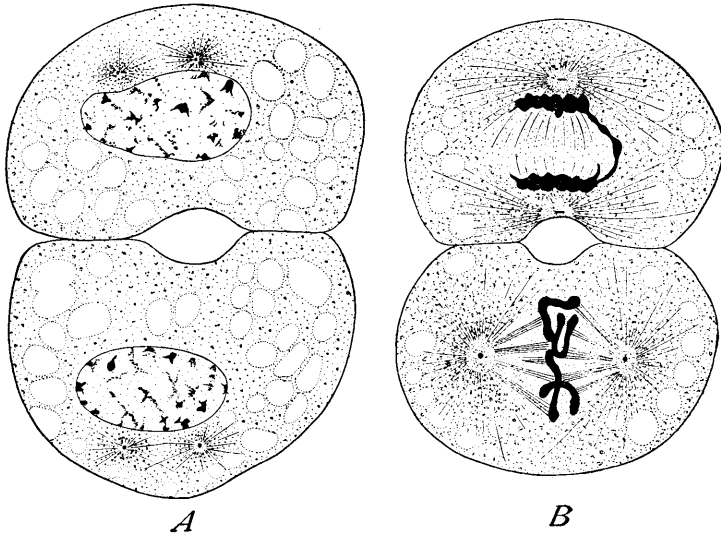


Fig. 176. — Segmenting eggs of *Ascaris*. [KOSTANECKI and SIEDLECKI.]

A. Early prophase of second division, showing double centrosomes. B. Second cleavage in progress; upper blastomere dividing parallel to long axis of the cell.

tually pushing away the adjoining cell to make way for itself. Similar difficulties, some of which have been already considered (p. 372), stand in the way of the attempt to explain the eccentricity of the spindle in unequal division. All these considerations drive us to the view that the simpler mechanical factors, such as pressure, form, and the like, are subordinate to far more subtle and complex operations involved in the general development of the organism, a conclusion strikingly illustrated by the phenomena of teloblastic division (p. 371), where the constant succession of unequal divisions, always in the

¹ Cf. Watasé ('91), Mead ('94, '97, 2), Heidenhain ('95), Wheeler ('95), Castle ('96), Jennings ('97).

² See especially the case observed by Mead ('94, '97, 2), in the egg of *Amphitrite*.

same plane, is correlated with a deeply lying law of growth affecting the entire formation of the body. *We cannot comprehend the forms of cleavage without reference to the end-result*; and thus these phenomena acquire a certain teleological character so happily expressed by Lillie (p. 370). This has been clearly recognized in various ways by a number of recent writers. Roux ('94), while seeking to explain many of the operations of mitosis on a mechanical basis, holds that the position of the spindle is partly determined by "immanent" nuclear tendencies. Braem ('94) recognizes that the position of the spindle is determined not merely as that of least resistance for the mitotic figure, but also for that of the resulting products. I pointed out ('92) that the bilateral form of cleavage in annelids must be regarded as a "forerunner" of the adult bilaterality. Jennings ('97) concludes that the form and direction of cleavage are related to the later morphogenetic processes; and many similar expressions occur in the works of recent students of cell-lineage.¹

The clearest and best expression of this view is, however, given by Lillie ('95, '99), who not only correlates the direction and rate of cleavage, but also the size-relations of the cleavage-cells with the arrangement of the adult parts, pointing out that in general the size, as well as the position, of the blastomeres is directly correlated with that of the parts to which they give rise, and showing that on this basis "one can thus go over every detail of the cleavage, and knowing the fate of the cells, can explain all the irregularities and peculiarities exhibited."² Of the justice of this conclusion I think any one must be thoroughly convinced who carefully examines the recent literature of cell-lineage. It gives no real explanation of the phenomena, and is hardly more than a restatement of fact. Neither does it in any way lessen the importance of studying fully the mechanical conditions of cell-division. It does, however, show how inadequate have been most of the attempts thus far to formulate the "laws" of cell-division, and how superficially the subject has been considered by some of those who have sought for such "laws."

We now pass naturally to the second or promorphological aspect of cleavage, to a study of which we are driven by the foregoing considerations.

¹ Conklin ('99) believes that many of the peculiarities of cleavage may be explained by the assumption of protoplasmic currents which "carry the centrosomes where they will, and control the direction of division and the relative size and quality of the daughter-cells," *l.c.*, p. 90. He suggests that such currents are of a chemotropic character, but recognizes that their causation and direction remain unexplained.

² *Cf.* ('95), p. 39.

B. PROMORPHOLOGICAL RELATIONS OF CLEAVAGE

The cleavage of the ovum has thus far been considered in the main as a problem of cell-division. We have now to regard it in an even more interesting and suggestive aspect; namely, in its morphological relations to the body to which it gives rise. From what has been said above it is evident that cleavage is not merely a process by which the egg simply splits up into indifferent cells which, to use the phrase of Pflüger, have no more definite relation to the structure of the adult body than have snowflakes to the avalanche to which they contribute.¹ It is a remarkable fact that in a very large number of cases a precise relation exists between the cleavage-products and the adult parts to which they give rise; and this relation may often be traced back to the beginning of development, so that from the first division onward we are able to predict the exact future of every individual cell. In this regard the cleavage of the ovum often goes forward with a wonderful clocklike precision, giving the impression of a strictly ordered series in which every division plays a definite *rôle* and has a fixed relation to all that precedes and follows it.

But more than this, the apparent predetermination of the embryo may often be traced still farther back to the regions of the undivided and even unfertilized ovum. The egg, therefore, may exhibit a distinct promorphology; and the morphological aspect of cleavage must be considered in relation to the promorphology of the ovum of which it is an expression.

1. *Promorphology of the Ovum*

(a) *Polarity and the Egg-axis.*—It was long ago recognized by von Baer ('34) that the unsegmented egg of the frog has a definite *egg-axis* connecting two differentiated poles, and that the position of the embryo is definitely related to it. The great embryologist pointed out, further, that the early cleavage-planes also are definitely related to it, the first two passing through it in two meridians intersecting each other at a right angle, while the third is transverse to it, and is hence equatorial.² Remak afterward recognized the fact³ that the larger cells of the lower hemisphere represent, broadly speaking, the "vegetative layer" of von Baer, *i.e.* the inner germ-layer or entoblast, from which the alimentary organs arise; while the smaller cells

¹ ('83), p. 64.

² The third plane is in this case not precisely at the equator, but considerably above it, forming a "parallel" cleavage.

³ '55, p. 130. Among others who early laid stress on the importance of the egg-polarity may be mentioned Auerbach ('74), Hatschek ('77), Whitman ('78), and Van Beneden ('83).