CHAPTER II

CELL-DIVISION

"Where a cell exists there must have been a preëxisting cell, just as the animal arises only from an animal and the plant only from a plant. The principle is thus established, even though the strict proof has not yet been produced for every detail, that throughout the whole series of living forms, whether entire animal or plant organisms, or their component parts, there rules an eternal law of *continuous development*."

VIRCHOW.[1]

It is now sixty years since Virchow first adequately stated the principle of genetic continuity of cells by division, which was destined to form the rallying point for all future conceptions of heredity and development. Only a minute fraction of the vast field of cytology and embryology had then been examined, and Virchow's celebrated aphorism *omnis cellula e cellula* [2] was too far in advance of his time to appear in its true proportions. As years passed, it gradually became evident that this terse phrase embodies one of the most important generalizations of modern science. The advance of cytological research still continues day by day to add fresh weight to the demonstration that cells have no other mode of origin than by the division of preëxisting cells. [3] In this respect a fundamental likeness exists between unicellular organisms, the tissue-cells of higher plants and animals, and the germ-cells from which the higher organisms take their origin. Upon cell-division, therefore, depends not alone heredity but the very continuity of life.

The division of cells was probably first seen in the segmentation of the animal egg (Prévost and Dumas, 1824), and soon afterwards in the lower plants by several botanists; [4] but its significance was not fully recognized until after the promulgation of the cell-theory, as a result especially of the work of Kölliker, Remak and Virchow. During the first two decades following Schleiden and Schwann these observers, together with the botanists Mohl, Nägeli and others, were accumulating the proof that cells arise only by the division of preëxisting cells and that the authors of the cell-theory fell into error when they accepted the independent origin of cells

[1] *Cellularpathologie*, p. 25, 1858.

[2] *Cf.* Introduction, p. 11.

[3] Division may be equal (fission), unequal (gemmation or budding) or endogenous (usually multiple).

[4] Brogniart, Meyen, Mirbel, Mohl, 1827–1835.

out of a formative blastema.[1] The mechanism of cell-division was not precisely investigated until long afterward, but Remak and Kölliker showed that the process involves a division of both the nucleus and the cytosome. Remak believed it to be of simple type (Fig. 44) and to proceed from the center outwards, the nucleolus dividing first, next the nucleus and finally the cytosome ("Remak's scheme"); and this was for a time widely accepted, though on wholly insufficient grounds. In the meantime, however, observations were accumulating to show that cell-division is by no means so simple an operation as this.

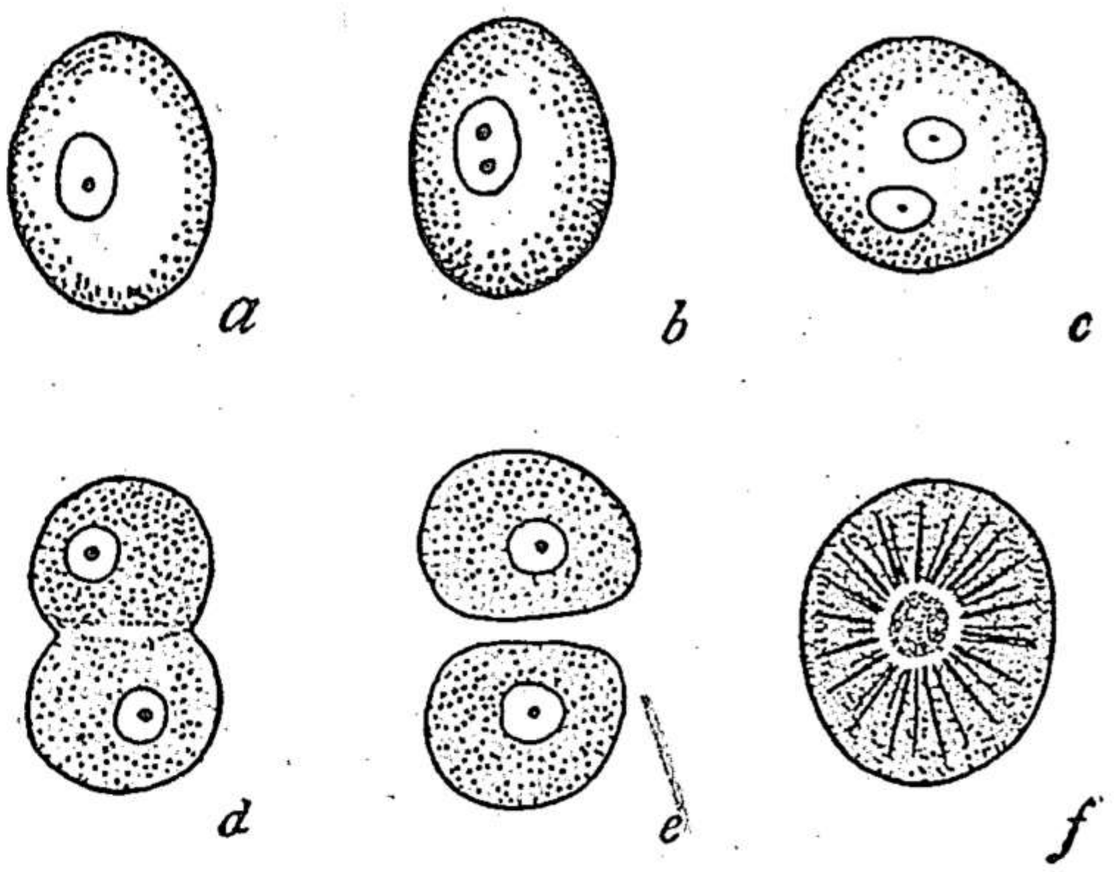


Fig. 44.—Direct division of blood-cells in the embryo chick, illustrating Remak's scheme (REMAK).

a–e, successive stages of division; *f*, cell dividing by mitosis.

Among both plants and animals many cases were found, prior to the seventies, in which the nucleus was lost to view at the onset of cell-division while at the same time star-shaped radiations (asters) were often observed in the protoplasm.[2] These observations, first made especially upon the polar divisions and early cleavages in living animal eggs, led to the conclusion that the nucleus actually disappears at this time by a process of "karyolysis" (Auerbach), to be subsequently formed *de novo* in the daughter-cells; and this was for a short time held even by such observers as Kölliker, Bütschli, Fol, Strasburger and Van Beneden. As soon as the phenomena were examined by means of fixing and staining reagents (acetic and osmic acids, carmine), it was found that the seeming disappearance of the nucleus is illusory, being only the result of a profound transformation of its substance; and that this process, together with the appearance of astral radiations in the cytosome, belong to a mode of nuclear division far more complicated than Remak's traditional scheme. In the end it became evident that nuclear division is of two widely different types, which came to be known as *direct* and *indirect* (Flemming, '79). In the direct and simpler type the

[1] See Introduction, p. 9. For an early historical review of this period see Remak's *Untersuchungen ueber die Entwicklung der Wirbelthiere*, 1855, pp. 164–180. For later reviews see Tyson on the *Cell Doctrine* ('78), Sachs' *Geschichte der Botanik* ('90), Heidenhain's *Plasma und Zelle* (1907) and O. Hertwig's *Generelle Biologie*, 5th ed. ('20). As Heidenhain points out, Kölliker in his celebrated work, *Entwicklungsgeschichte der Cephalopoden* (1844), stated the essential doctrine expressed by Virchow in the phrase *omnis cellula e cellula*.

[2] Such radiations were figured by Remak himself (Fig. 44) and described or figured by other early observers, including von Baer, Virchow, Derbés, and Kowalewsky. They were first carefully studied by Fol ('73–'76) in the eggs of medusæ, and mollusks, and by Auerbach ('74) in those of nematodes.

nucleus, like the cell-body, undergoes a simple mass-division into two parts. In the indirect and more complex type, the nucleus is not destroyed, but is spun out into long threads which *split lengthwise* so that every portion is exactly divided between the daughter-nuclei. Before the separation of their longitudinal halves these threads shorten, and thicken to form more condensed bodies known as *chromosomes* (so named by Waldeyer because of their intense staining-capacity). The products of their fission (daughter-chromosomes) separate, and pass to opposite poles; and from the two groups of daughter-chromosomes are rebuilt two corresponding daughter-nuclei which by reason of the preceding processes are exact duplicates of each other and of the mother-nucleus. In this operation we now recognize one of the most fundamental mechanisms of heredity (p. 667).

By Schleicher (1878) this process was called *karyokinesis*, a term still widely employed for cell-division of this type. Flemming (1882) proposed the more appropriate term *mitosis*, in allusion to the characteristic thread-formation, while the direct mode of division was called *amitosis;* and this usage gradually became firmly established.[1] Strictly speaking, all these terms refer to division of the nucleus, but by an extension of meaning they are often applied to cell-division as a whole. It is often convenient to employ the term *cytokinesis* (Whitman, 1887) to designate the associated changes taking place in the cytoplasmic cell-body, though in practice it is sometimes difficult to draw any definite line of distinction between the nuclear and the cytoplasmic activities, *e. g.*, in the formation of the spindle. Cytokinesis includes not only the division of the cytosome as a whole but also the orderly distribution of smaller elements within it, such as the chondriosomes or the Golgi-bodies; and these processes have received corresponding names (*chondriokinesis*, *dictyokinesis*). The processes of cell-division as a whole may therefore be conveniently, if not quite logically, grouped as follows:

I. *Mitosis* (indirect division).

1. *Karyokinesis* (the nuclear transformation).
2. *Cytokinesis* (the cytoplasmic changes).
   a. Cleavage or Division of the Cytosome.
   b. Meristic division or distribution. Chondriokinesis (chondriosomes), *dictyokinesis* (Golgi-bodies), etc.

II. Amitosis.

Amitotic division was regarded by Remak and his immediate followers as the typical mode. Modern research has, however, demonstrated that it is a relatively rare and secondary process, often unaccompanied by division of

[1] Other terms are *karyodieresis*, *cytodieresis* (Henneguy), *kinesis*, and *akinesis* (Fol, Carnoy), but these are less generally used.

the cell-body, and especially frequent in highly specialized cells, or such as are in the early stages of degeneration; for instance, in glandular epithelia or in the cells of transitory embryonic envelopes. Some writers have maintained that nuclei which once have thus divided have undergone a fatal derangement that renders them incapable of long-continued multiplication, but this view can only be maintained in a qualified sense (p. 222). In any case it is a fact that in all the higher and in many of the lower forms of life mitosis is the usual and typical mode. We may therefore justly regard it as the basic phenomenon that underlies Virchow's "eternal law of continuous development."

I. GENERAL OUTLINE OF MITOSIS

In the course of mitotic division the nucleus usually disappears from view as an individualized body, while in its place appears a complicated structure known as the *mitotic* or *karyokinetic* figure, or, more simply, the *division-figure*. We may distinguish in this structure (Figs. 46, 49, etc.) a *chromatic* and an *achromatic figure*, of which the former is derived solely from the nucleus, the latter often from both nucleus and cytoplasm. The chromatic figure consists of the *chromosomes*, which are most often rod-shaped or V-shaped bodies, originally threads, formed by a transformation of the network of the vegetative nucleus, and staining with great intensity in the "nuclear" or basic dyes. The most constant feature of the achromatic figure as seen in sections is a fibrillar *spindle*, around or in which lie the chromosomes, while in a large class of cases at or near each of its poles is a central body, often double, surrounded by a star-shaped *aster*. When such asters are present the achromatic figure is called an *amphiaster*. This structure is colored only slightly by nuclear dyes and shows on the whole the staining qualities of the cytoplasm. In all higher plants and animals the formation and division of the chromosomes seem to take place essentially in the same way. In the Protista, on the other hand, exist various simpler types of mitosis in some of which it is questionable whether chromosomes are formed in the same sense as in higher forms (p. 210).

In respect to the achromatic figure, two general types may be distinguished, the *amphiastral* and the *anastral*. In the former true asters are present at the spindle-poles, characterized by their definite and sharply focussed astral rays and by the presence of well-marked central bodies at their foci (Fig. 49). Such amphiasters are typical of the mitoses of higher animals generally (though there are some exceptions), are of common occurrence among the thallophytes (Fig. 84), and are found in some Protista (Figs. 85, 90). In the anastral type (Fig. 65, etc.) true asters are wanting and often central bodies also. In many of these forms, it is true, fibrillæ radiate in more or

less irregular fashion from the spindle-poles;[1] but they are not sharply focussed at the spindle-poles, nor are definite central bodies present. Anastral spindles are characteristic of the vegetative mitoses in higher plants

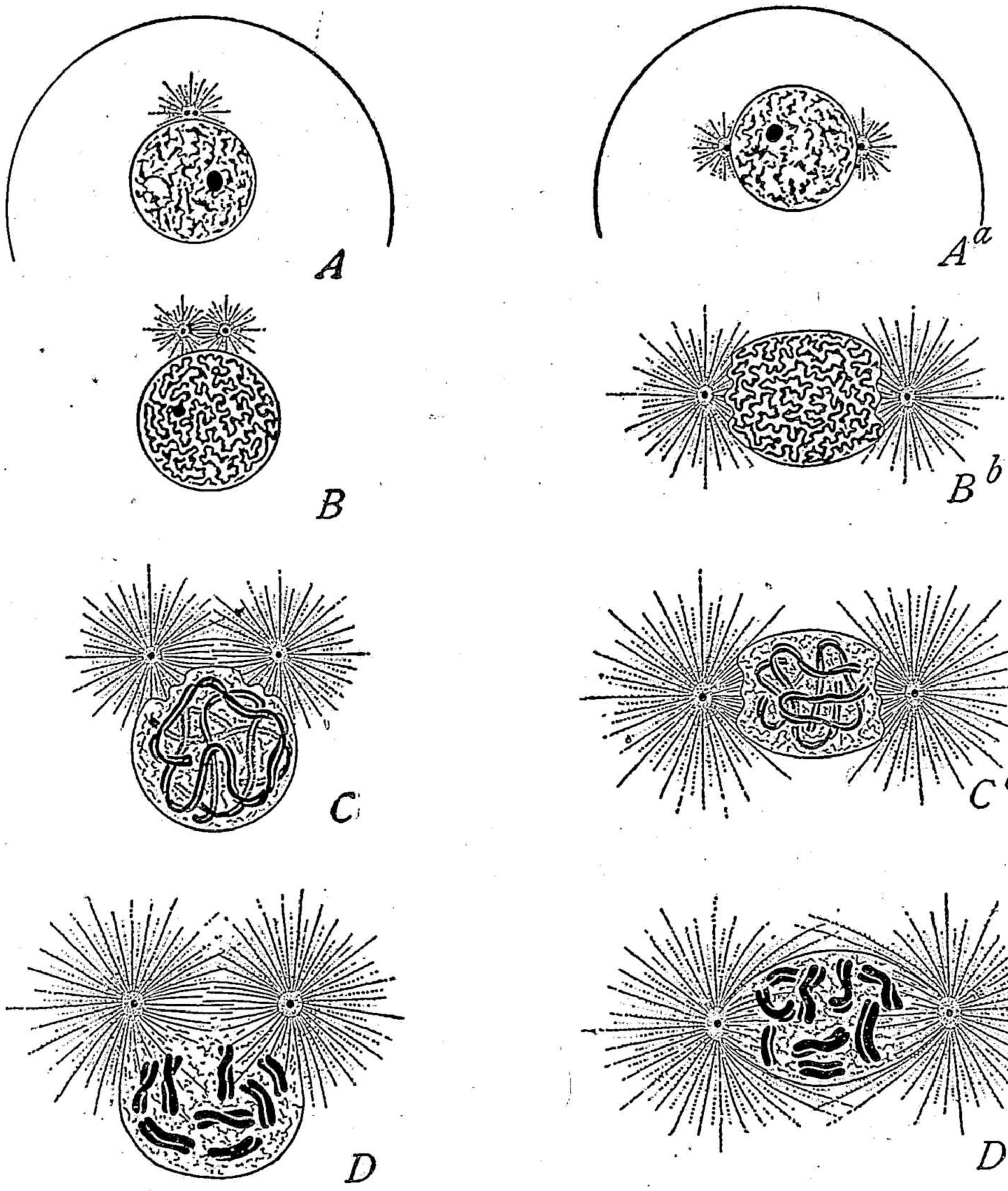


Fig. 45.—Diagram of the prophases of mitosis.

A–D, "Type A," (*Ascaris*); A^a–D^d, Type B (sea-urchin).

A, vegetative nucleus; *B*, fine spireme; *C*, coarse spireme; *D*, late prophase with chromosomes, spindles forming.

(cormophytes) generally, and occur also in the maturation-mitoses of certain animal ova and in many Protista. It now seems nearly certain that in the higher forms the absence of asters has resulted from a secondary sim-

[1] An excellent photograph of such a case is given by Timberlake ('00, Fig. 2), from a dividing pollen-mother-cell of the larch, *Larix*, in which the equatorial crossing of the rays is clearly shown.

plification of the mitotic apparatus. In Protista, on the other hand, many of the anastral forms may represent a primitive condition (p. 213).

Both spindle and asters as seen in sections ordinarily show a beautiful fibrillar structure, consisting of delicate and closely crowded filaments which radiate from the spindle-poles, the astral rays spreading in all directions as they thread their way through the protoplasmic meshwork, and finally branching out in it to lose themselves insensibly. The central body, at the center of the aster (and hence near the pole of the spindle) varies greatly in structure in different kinds of cells and at different stages of development. In its simplest form it is a very minute, intensely staining *centriole*, which is frequently double; and surrounding this may often be distinguished a larger *centrosome* (also called the *centrosphere* or *periplast*), from which the astral rays proceed. When the asters are absent (as in higher plants) centrioles and centrosomes, according to most observers, are also absent. The relations between centriole and centrosome have been the subject of controversy, and both these terms have become somewhat ambiguous. We shall find it convenient to employ the more vague term *central body* (which is historically the older) or *division-center*, without prejudicing the question as to its exact homology in any particular case.[1]

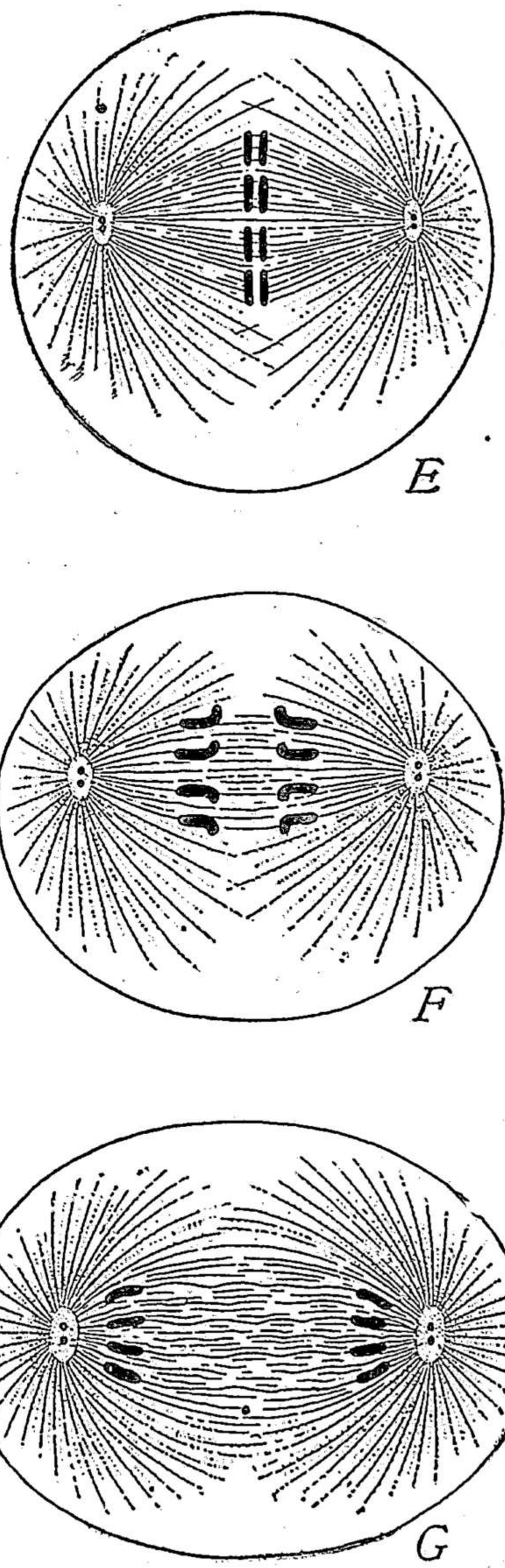


Fig. 46.—Diagram of the middle phases of mitosis.

E, metaphase; *F*, *G*, earlier and later anaphases.

The chromosomes undergo their final division at the equator of the spindle, the daughter-chromosomes then separating and proceeding in opposite directions along the spindle nearly or quite to the poles where each daughter-group of chromosomes gives rise by a complicated process of "reconstruction" to a new nucleus. While this latter process is

[1] See p. 672.

going on the whole cell divides through the equatorial plane of the spindle, so that each daughter-cell contains a daughter-nucleus. At the close of the process the spindle usually disappears and often also the aster; but the central body (centriole), now usually divided into two, frequently persists in the vegetative cell (p. 29), and the same is sometimes the case with the remains of the spindle ("spindle-remnant" or *mitosome*).

Though every detail of mitosis varies more or less widely in different

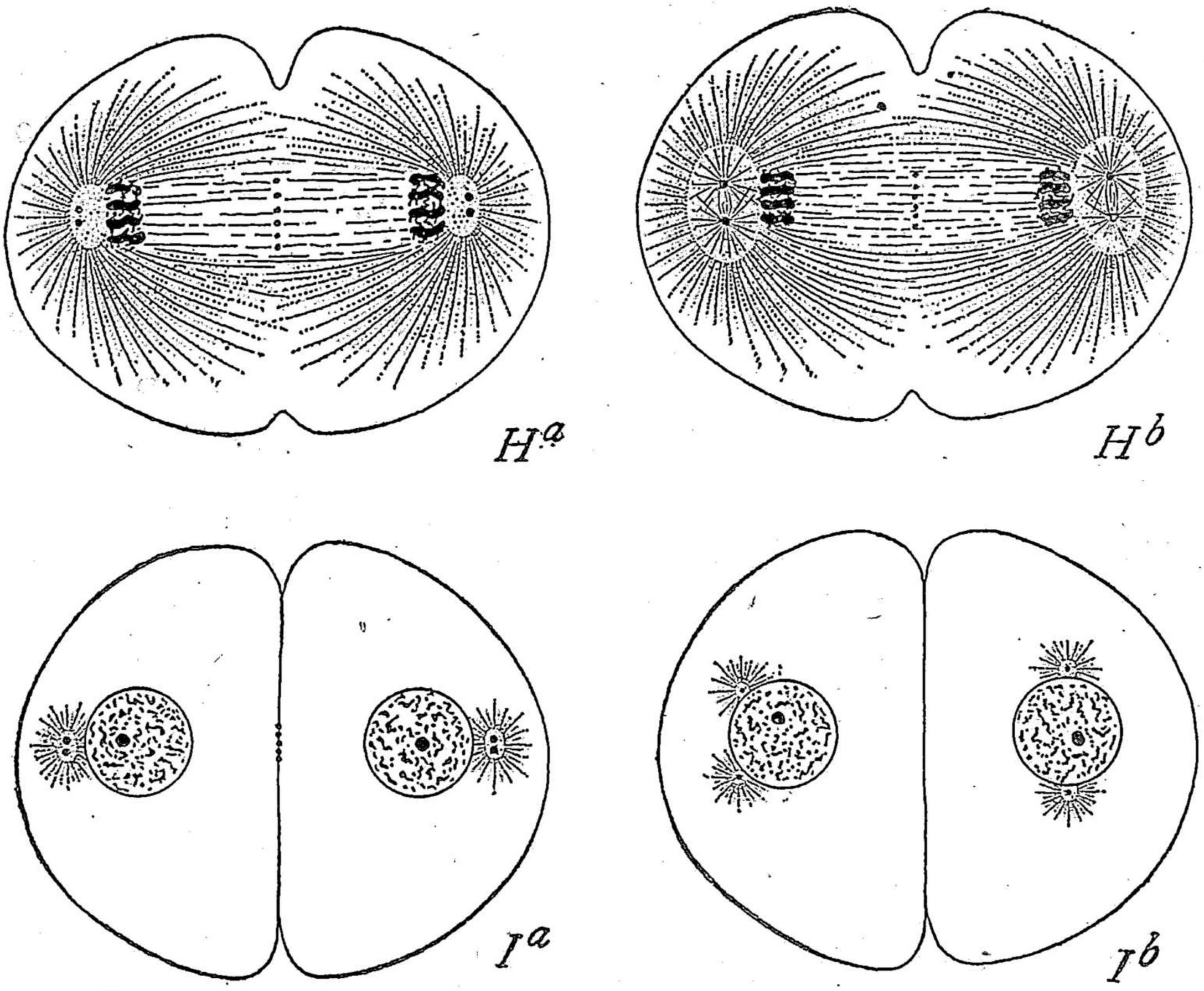


Fig. 47.—Diagram of closing phases of mitosis. H^a and I^a, "Type A"; H^b and I^b, "Type B"; I^b showing two slightly different conditions in the interphase.

forms of cells the process always displays a typical succession of general phases or stages, as follows: [1]

(1) The *prophases*, in which the mitotic figure is formed and the chromosomes become longitudinally split (Figs. 45, 48, etc.).

(2) The *metaphase*, in which the longitudinally divided chromosomes take up a position in the equatorial plane of the spindle to constitute the equatorial plate or metaphase-group. In some cases they lie around the periphery of the spindle, in others within its substance (Figs. 46, 49).

[1] These terms were proposed by Strasburger, 1884.

(3) The *anaphases*, in which the daughter-halves of each longitudinally split chromosome separate, thus giving rise to two sister-groups which pass to opposite poles of the spindle (Figs. 46, 58).

To these terms may be added a fourth, due to Heidenhain (1894), namely,

(4) The *telophases*, in which the daughter-nuclei are reconstructed from the two groups of daughter-chromosomes, and division of the cell-body takes place (Figs. 47, 50). Mitotic nuclear division is, however, not always followed by cell-division. The nucleus may divide, even many times, without cleavage of the cytosome, thus giving rise to multinucleate cells (syncytia or plasmodia). This is of comparatively rare occurrence in higher organisms, though common in lower ones.

The history of the chromatic figure and that of the achromatic are to a considerable extent experimentally separable; for example, a complete amphiaster may be formed in a mass of protoplasm deprived of a nucleus, and conversely a considerable part of the transformation of the nucleus may go forward without the formation of a spindle, possibly without the formation of asters (p. 168). For the purposes of a preliminary account, therefore, we may conveniently treat the history of the chromatic and the achromatic figures as if they were separate, though closely parallel processes. In such a preliminary description many critical questions must be passed over until the general outlines of the phenomena have been made clear.

II. KARYOKINESIS. GENERAL HISTORY OF THE CHROMOSOMES

1. The Prophases

The essential feature of the early prophase is a gradual transformation of the nuclear framework into a thread or *spireme*, sometimes apparently continuous, more frequently segmented into separate pieces, which from an early period is longitudinally double, consisting of two exactly similar halves. The result of this process is remarkably constant throughout nearly all higher plants and animals, but its details vary considerably. In this respect there are two main types of spireme-formation in one of which the threads arise by a direct and gradual transformation of the nuclear framework, while in the other the process is preceded by a condensation of the framework into localized areas each of which resolves itself into a single thread. Even closely related forms, particularly among the higher plants, may differ markedly in this respect.[1] The first of these is exemplified by that classical object the epithelial cells of larval salamanders, which have been minutely examined by many observers (Fig. 52); and the same mode of spireme-formation appears in the presynaptic spireme of these

[1] See for instance Litardière ('21) on mitosis in ferns. Compare also the presynaptic spireme-formation in plants and animals, Chap. VI.

animals (p. 540) and has been described in many plants. In this case the nuclear framework becomes finer and more thread-like, becomes more basophilic and transforms itself into fine and closely convoluted threads which from an early period show here and there a longitudinal cleft and ultimately become longitudinally double.[1] (Fig. 53).

By the earlier observers the spireme was believed to be at first a single, continuous thread; and such in fact it appears to be in some cases, later segmenting transversely to form the separate chromosomes. Examples of this are offered by the somatic and meiotic prophases of *Carex* (Stout, '12) or by the spermatogonial prophases of *Ascaris* as described by Brauer (Fig. 53). In many cases, however, the chromosomes are undoubtedly separate from the very beginning of the spireme-formation. One of the best demonstrations of this is given by the cleavage-cells of *Ascaris* where, as was first described by Van Beneden and Boveri, the free ends of the separate spireme-threads may readily be detected, since they lie from the beginning in separate, pouch-like pockets of the nucleus (Figs. 416–418). A similar conclusion is indicated by many other facts which indicate that a continuous primary spireme is an exceptional occurrence and has only a secondary significance.

In the second type of spireme-formation the process begins by a drawing together of the nuclear framework into localized tracts or areas. At first these have an alveolar or net-like structure, and they may remain in this condition until the thread-formation.[2] The condensation may, however, proceed further, thus giving rise to more massive bodies or chromatin-blocks in which the net-like structure is hardly visible.[3] In such cases these bodies have often been called "prochromosomes" (p. 901). It was supposed by some earlier observers that these more massive bodies might in some cases be directly converted into the chromosomes, but it is now certain that in most cases each mass resolves itself into a fine, convoluted, zigzag or irregularly coiled thread which then unravels or uncoils (Figs. 421, 422) to form a single spireme-thread.[4] In case of the more solid, prochromosome-like bodies this process gives the aspect of a mere regrouping of the original substance,[5] and the coiled appearance is more striking. In case of the alveolized bodies the thread as

[1] The very early duality of the spireme-threads was first emphasized by Flemming and Strasburger (1882–1884). See p. 138.

[2] See Grégoire and Wygaerts, '03, '04, Grégoire, '06, Davis, '08, Sharp, '13, '20, Litardière, '21, Martens, '22, Overton '22, etc.

[3] Especially in the meiotic prophases of many animals (p. 538); but sometimes also in the somatic prophases, *e. g.*, in *Triton*, Janssens, '01.

[4] *Cf. merokinesis*, p. 895.

[5] See Janssens ('01), Bonnevie ('08–'11), Vejdovský ('11), Wilson ('12), etc. For the theoretical interest of these facts, see p. 899.

described by Grégoire, Sharp and Litardière is an irregular zigzag (Fig. 55) which is formed by the partial breaking down of the alveolar walls and

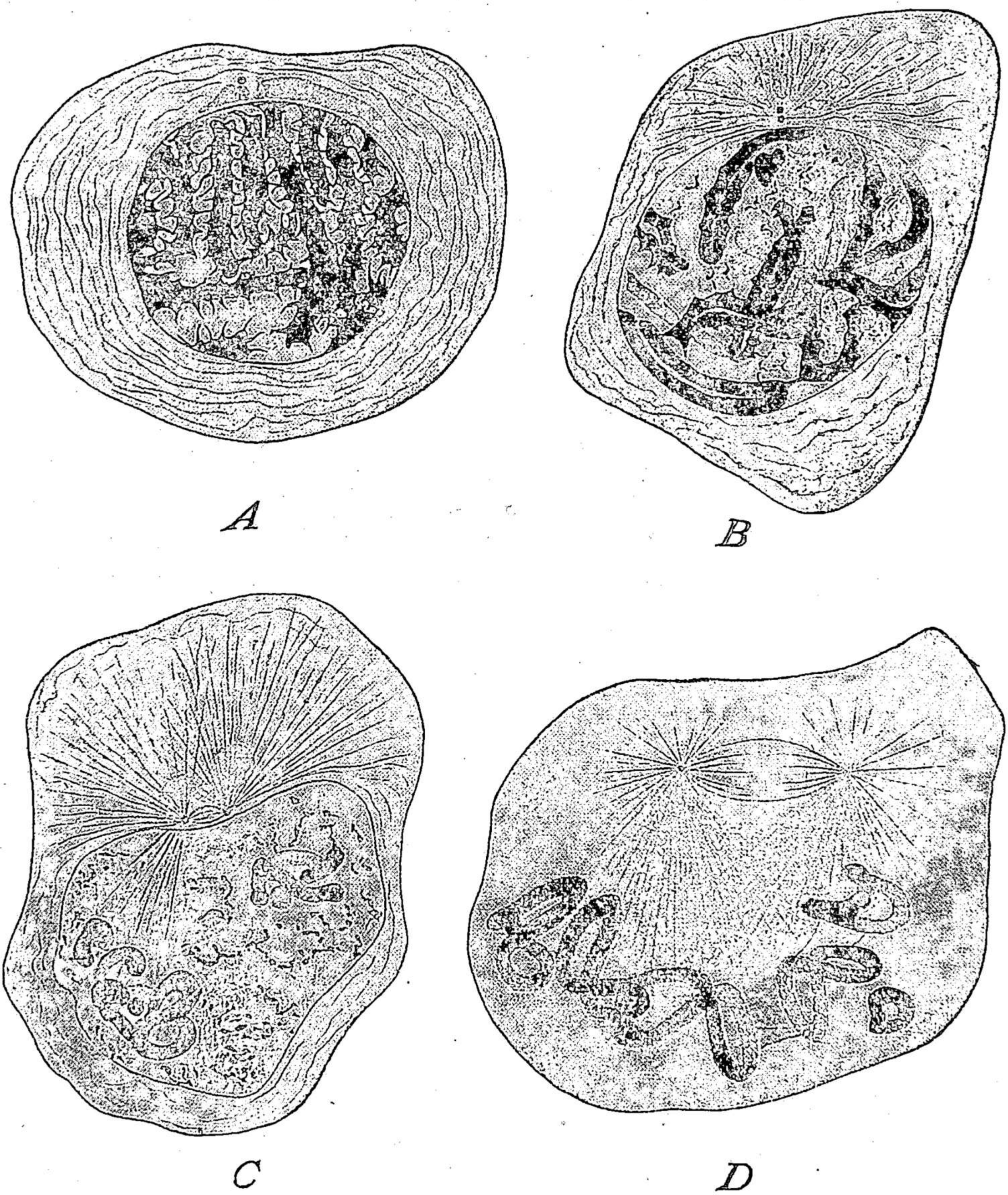


Fig. 48.—The prophases of mitosis (heterotypical form) in primary spermatocytes of *Salamandra* (MEVES).

A, early segmented spireme; two centrioles outside the nucleus in the remains of the sphere or idiozome; *B*, longitudinal doubling of the spireme, appearance of the astral rays, disintegration of the sphere; *C*, early amphiaster and central spindle; *D*, chromosomes in the form of rings, nuclear membrane disappeared, amphiaster enlarging, mantle-fibers developing.

coalescence of the vacuoles, while the remaining substance takes on the form of a continuous irregular thread. The two cases do not seem to differ in principle. In either case the result as usually described is a fine single

thread, which usually retains for some time a more or less wavy course. In this type, the spireme seems always to be segmented from the beginning.

The spireme-threads are at first fine and delicate, rather lightly staining in basic dyes, and crowded so as to give a more or less convoluted appear-

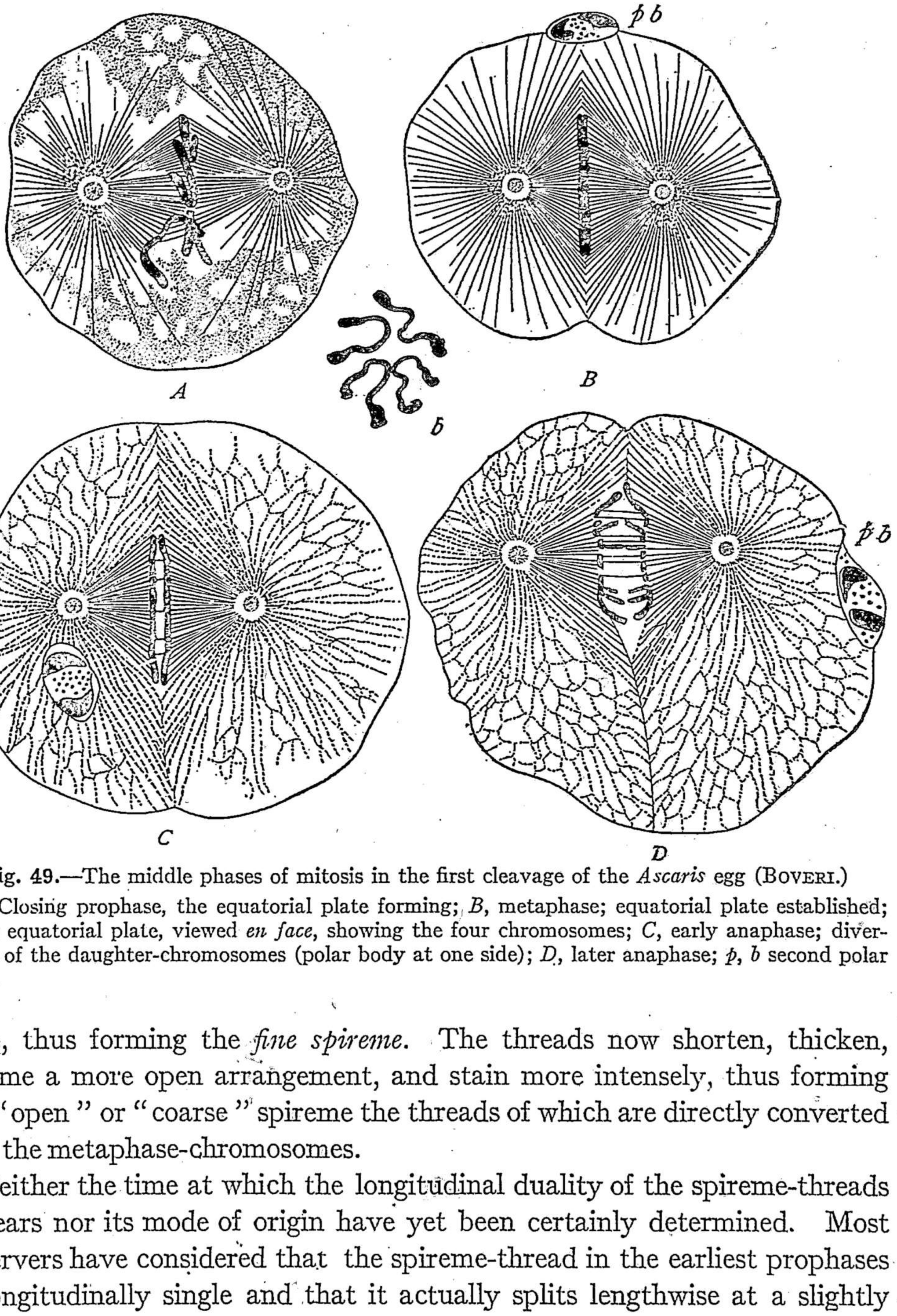


Fig. 49.—The middle phases of mitosis in the first cleavage of the *Ascaris* egg (BOVERI.)

A, Closing prophase, the equatorial plate forming; *B*, metaphase; equatorial plate established; *b*, the equatorial plate, viewed *en face*, showing the four chromosomes; *C*, early anaphase; divergence of the daughter-chromosomes (polar body at one side); *D*, later anaphase; *p*, *b* second polar body.

ance, thus forming the *fine spireme*. The threads now shorten, thicken, assume a more open arrangement, and stain more intensely, thus forming the "open" or "coarse" spireme the threads of which are directly converted into the metaphase-chromosomes.

Neither the time at which the longitudinal duality of the spireme-threads appears nor its mode of origin have yet been certainly determined. Most observers have considered that the spireme-thread in the earliest prophases is longitudinally single and that it actually splits lengthwise at a slightly

later stage, but both these conclusions are still a matter of dispute. A large number of observers, beginning with Balbiani ('76) and Pfitzner ('81) have described the thread as containing a linear series of smaller bodies or *chromomeres* which divide by fission and thus initiate the splitting of the whole thread (p. 908). Others have considered the chromomeres as accidental or at least non-significant bodies;[1] but the most recent and accurate studies on the subject give very strong reason to reject such a view (p. 909). By some observers the so-called splitting is regarded as comparable to the changes seen in the telophase (p. 133) and as arising through the appearance in the thread of a series of axial vacuoles which subsequently fuse. The two

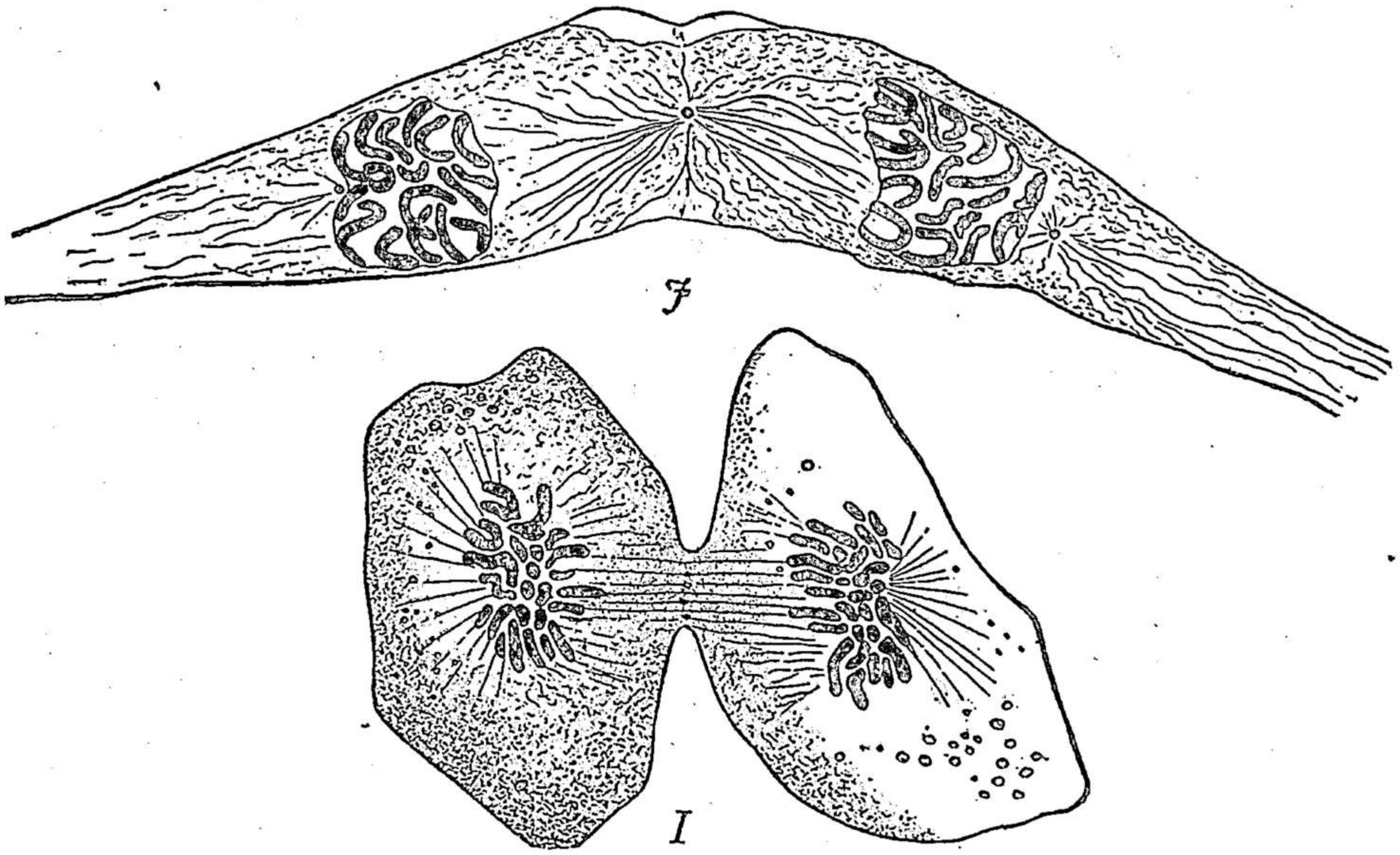


Fig. 50.—Final phases (telophases) of mitosis in salamander cells (FLEMMING).

I, epithelial cell from the lung; chromosomes at the poles of the spindle, the cell-body dividing; granules of the "mid-body" or *Zwischenkörper* at the equator of the disappearing spindle; *F*, connective tissue-cell (lung) immediately after division; daughter-nuclei reforming, mid-body a single granule in the middle of the remains of the spindle.

opposing conceptions are united by Müller ('12) who believes that the thread splits first between adjacent chromomeres (forming the "vacuoles"), the division of the chromomeres following (Fig. 54).[2]

A second group of observers believe the spireme-threads to be longitudinally double from their first appearance, and consider this condition as resulting from a doubling (by splitting or otherwise) that has occurred either during the vegetative stage of the nucleus or still earlier, during the preceding telophases or anaphases; to the writer, however, the evidence for

[1] See Grégoire and Wygaerts ('03), Grégoire ('06, '07), Mano ('04), Maréchal ('04, '07,) Stomps ('10), Lundegårdh ('12), Sharp ('13), etc.

[2] *Cf.* p. 99.

this seems insufficient (p. 139). During the middle prophases the longitudinal split often becomes obscured by close apposition of the longitudinal halves, but always comes clearly into view in the final stages. A noteworthy peculiarity of the spireme sometimes seen is a twisting of the longitudinal halves about each other to form a *strepsinema;* but this is much less common in the somatic mitoses than in meiosis (p. 544). After definite formation of the chromosomes the nuclear membrane usually disappears and the chromosomes, together with the remains of the linin network and enchylema, are set free in the protoplasm while the chromosomes take up their position in the equatorial plane of the spindle. In some cases the nuclear membrane persists throughout the whole process of mitosis, a condition common among the Protista, and sometimes occurring in higher forms.

Since a large part of the nuclear substance may enter into the formation of the spireme-thread, it seems certain that both oxychromatin (linin) and

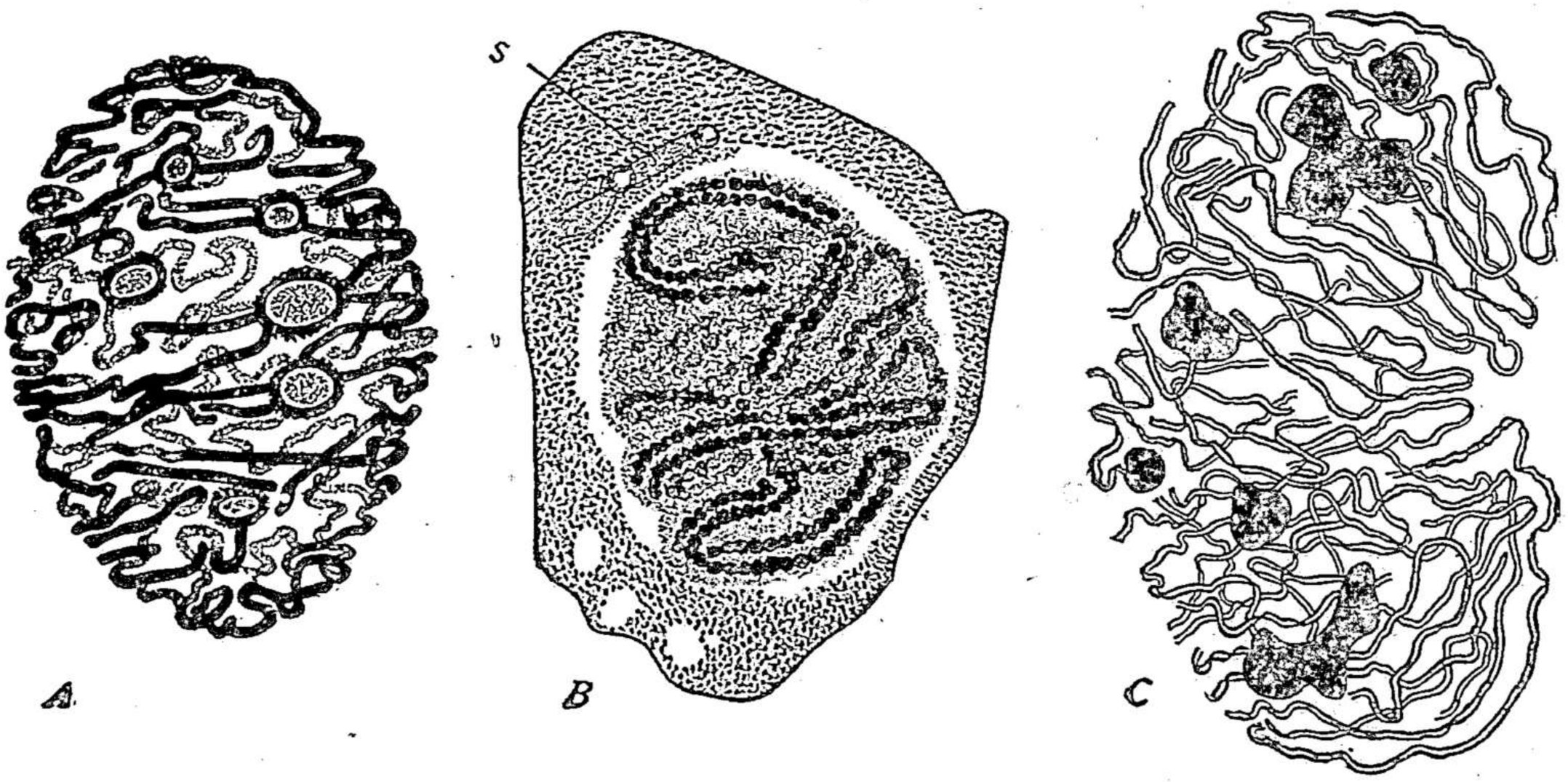


Fig. 51.—Early figures of spiremes.

A, from the endosperm of the lily, showing true nucleoli (FLEMMING); *B*, spermatocyte of salamander; segmented double spireme-thread (diplotene) composed of chromomeres; central bodies and central spindle at *s* (HERMANN); *C*, early spireme-thread completely split, with six nucleolar fragments. Endosperm of *Fritillaria* (FLEMMING).

basichromatin (if these be distinct substances) contribute to the chromosomes; and this is borne out by numerous observations showing that two corresponding substances may often be differentiated in the chromosomes (p. 896). In this respect, however, the chromosomes seem to differ widely in different species and at different periods. In many cases they appear quite homogeneous and intensely basichromatic; in others they seem to consist of a series of basichromatic chromomeres (Figs. 8, 427, 428) suspended in a more lightly staining or even oxychromatic linin or plastin;

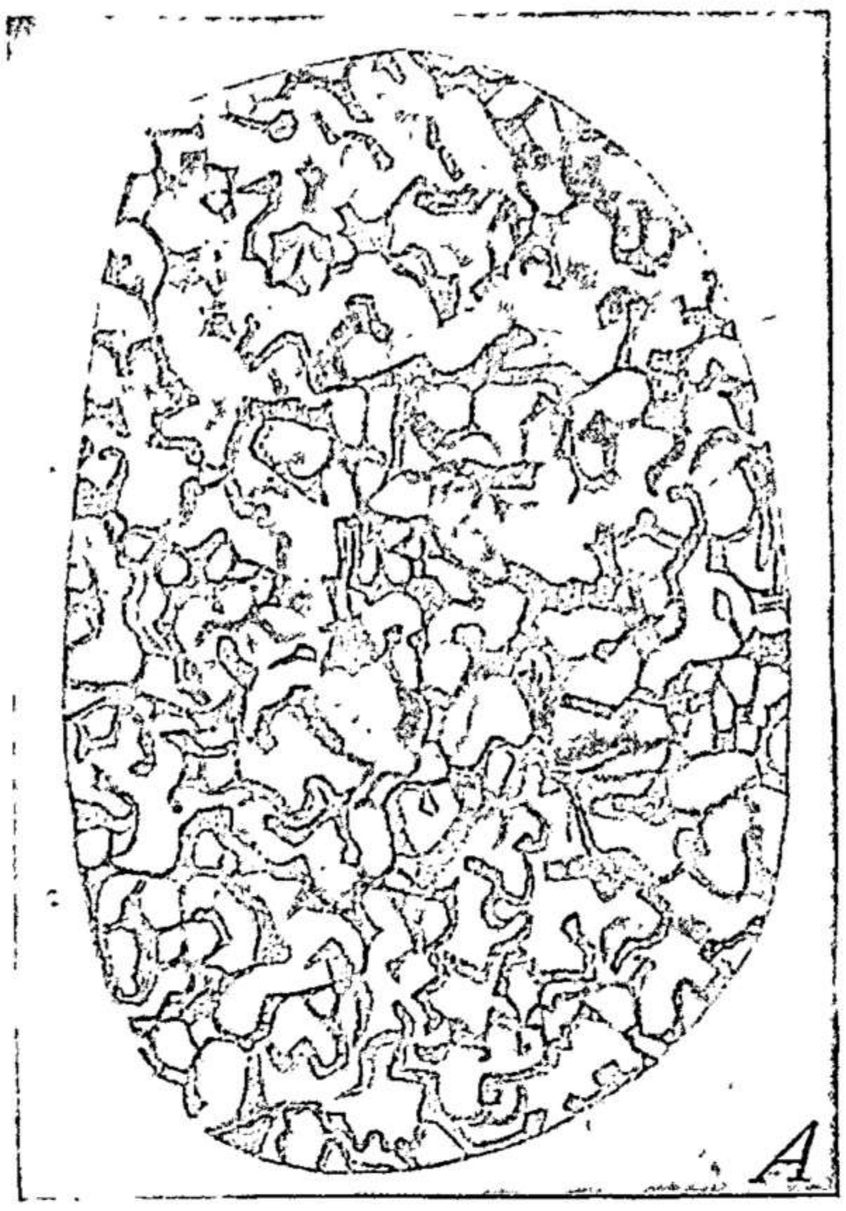
in still other cases they have during the prophases a very loose texture and are but slightly basophilic, or even oxyphilic (*e. g.*, in the oöcyte-nucleus (p. 350). It seems certain also that in some cases a considerable part of the linin-network is converted into spindle-fibers or astral rays (p. 148).

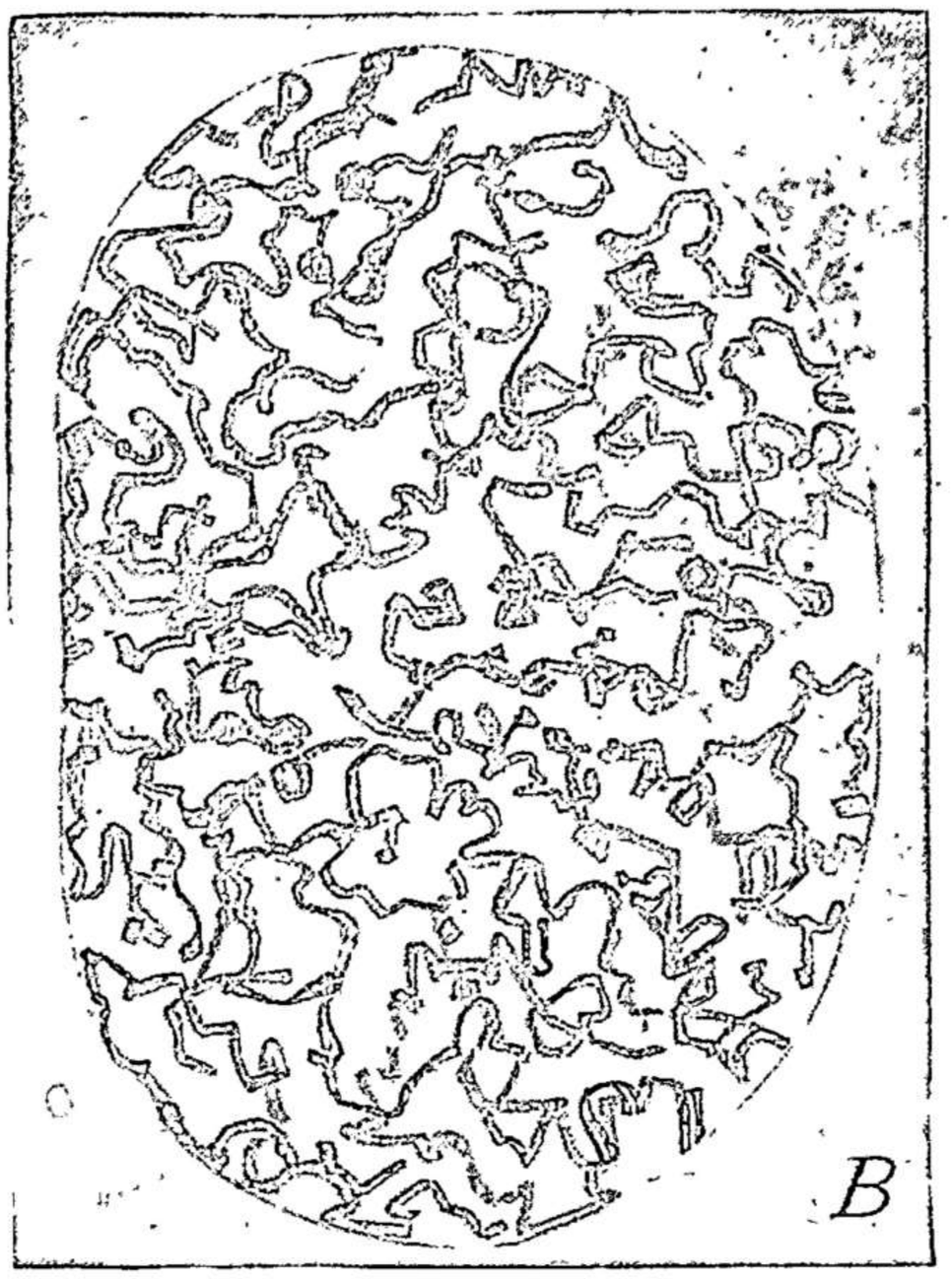
2. The Metaphase

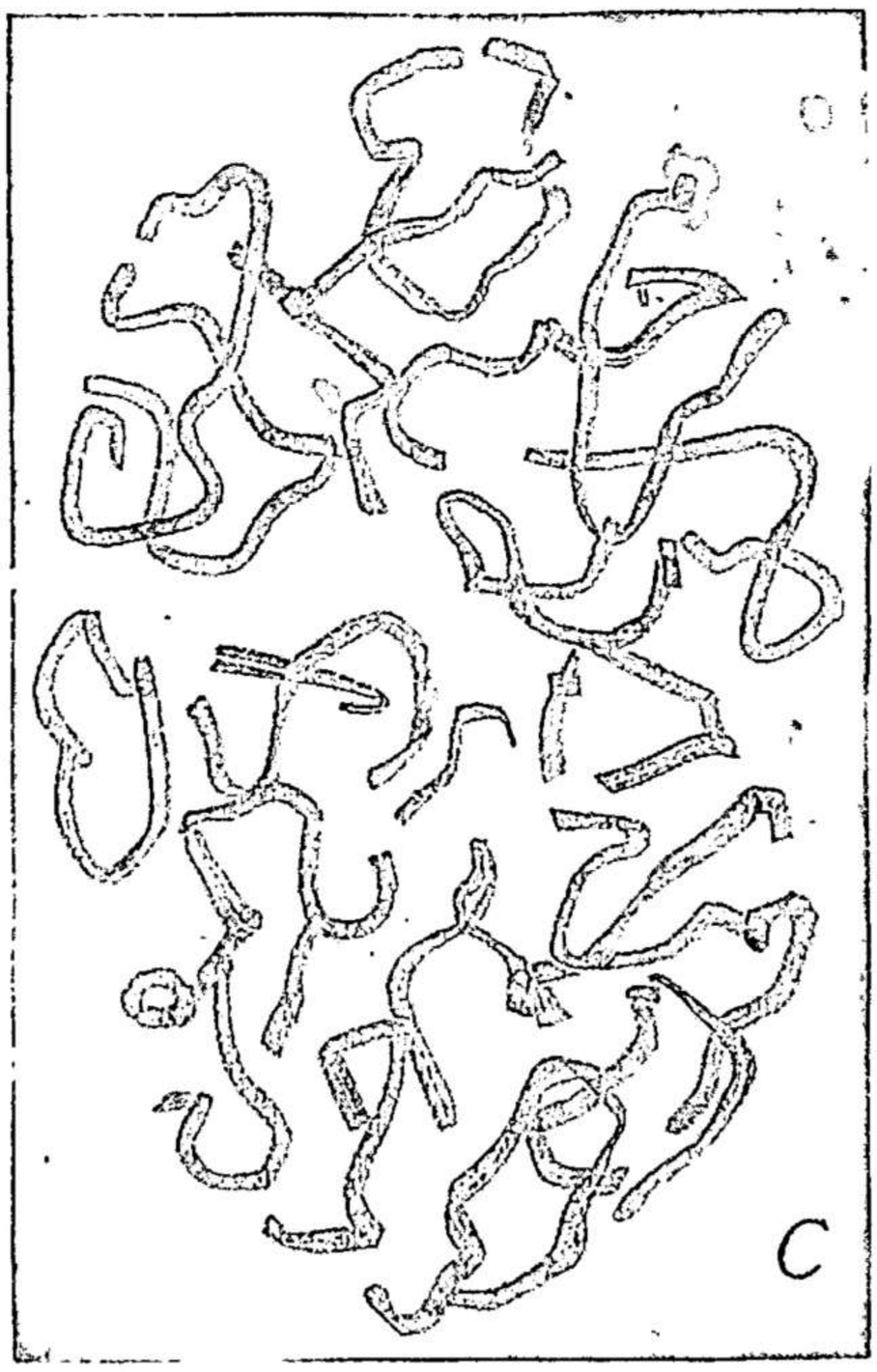
At full metaphase the chromosomes typically lie nearly in a single plane at the equator of the spindle, forming the so-called *equatorial plate* (Figs. 46E, 49). In some cases, of which the epidermal cells of larval salamanders offer a classical example, they are arranged in ring-like fashion around the spindle; and this has very often been figured as the typical case. In point of fact this condition is exceptional; and in most cases the chromosomes actually lie in the spindle, the equatorial plate extending completely through it in the equatorial plane. At this time the chromosomes are plainly double (or quickly become so), always placed with the division-plane lying in the equatorial plane and attached to the spindle-fibers in such a manner that the longitudinal halves of each chromosome are connected by one or more fibers with opposite spindle-poles (Figs. 49C, D). Their basophilic staining-capacity has now reached its climax; and in sections properly stained they are often the most conspicuous objects in the cell.

a. Forms and Arrangements of the Chromosomes. The metaphase-chromosomes show a great diversity of form in different species of plants and animals and often show marked individual differences of form and size in the same cell (Fig. 394). In a general way their number, size and form are characteristic of the species, though within a limited range variations occur. In part, their form is determined by their degree of condensation, which varies widely in different species, in part by their mode of attachment to the spindle, in part by other conditions. In many cases they still retain more or less the form of threads; in others they shorten and thicken to form short rods, sometimes even spheroidal bodies, in which all traces of the original thread-like condition have been lost. To a certain extent these conditions are characteristic of different groups; in arthropods, for example, they are commonly more rounded, in urodeles more thread-like. Nearly related groups may vary in this respect; among insects, for example, the chromosomes are in general more elongated in Orthoptera or Diptera (Figs. 396, 413), shorter and more rounded in Odonata, Coleoptera and Hemiptera (Figs. 354, 366). Many exceptions to this could, however, be mentioned.

In the case of thread-like or rod-shaped chromosomes their transverse diameter is on the whole fairly constant, and the size-differences which they may display are in the main due to differences of length; but







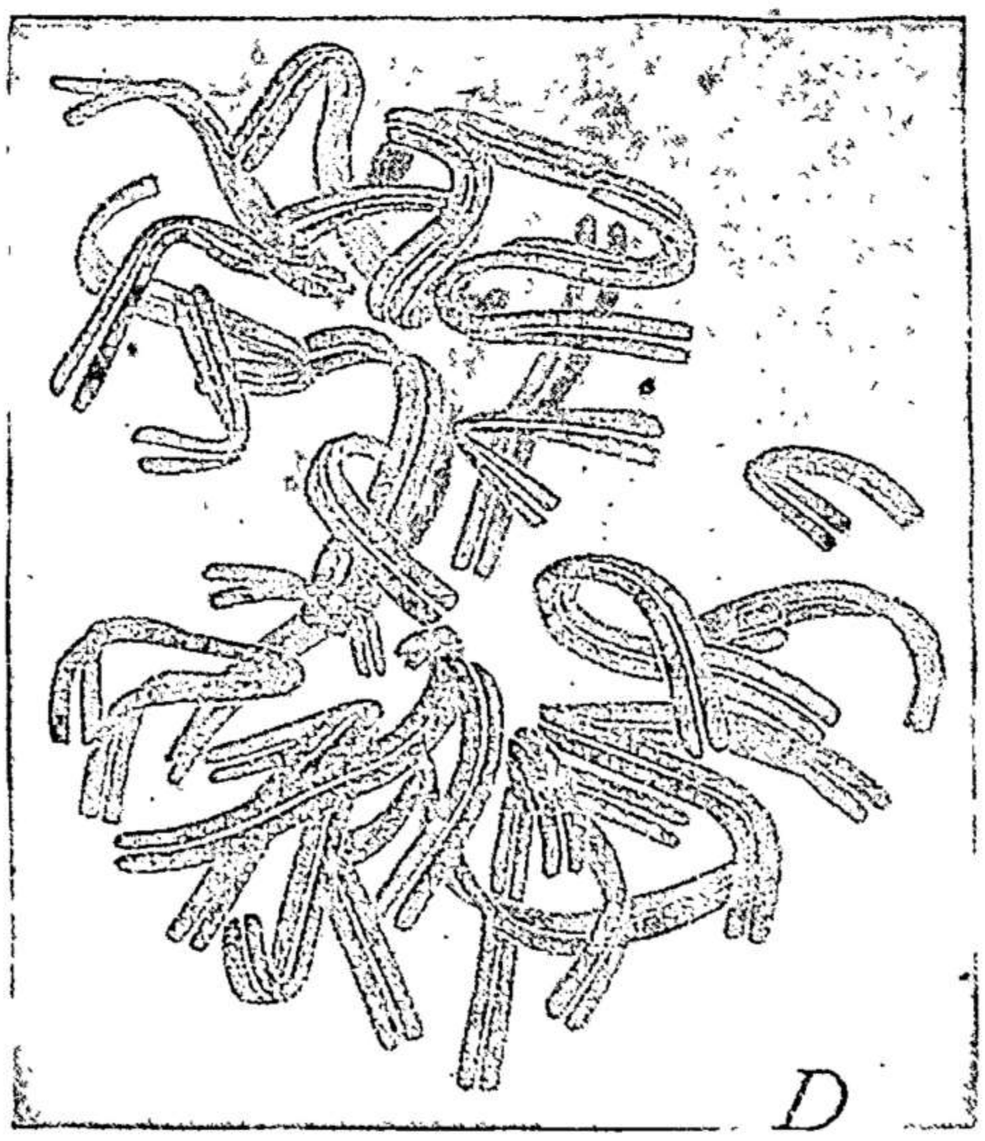


Fig. 52.—Prophases of mitosis in epithelial cells of the salamander accurately represented (HEIDENHAIN).

A, first stages of spireme-formation; *B*, fine spireme, duality here and there apparent; *C*, coarse, segmented spireme; *D*, chromosomes ready to go on the spindle, longitudinally split.

(In *A*–*C* the spireme-threads are still connected by fine "achromatic" bridges, not shown in the figure, so that the whole structure is still in a net-like condition though the spireme is evident.)

many exceptions to this are known (p. 834). When the size-differences are conspicuous the smaller chromosomes often tend to lie towards the center of the group (Fig. 394); but conspicuous exceptions to this exist. There is also a tendency for chromosomes of the same size to lie side-by-

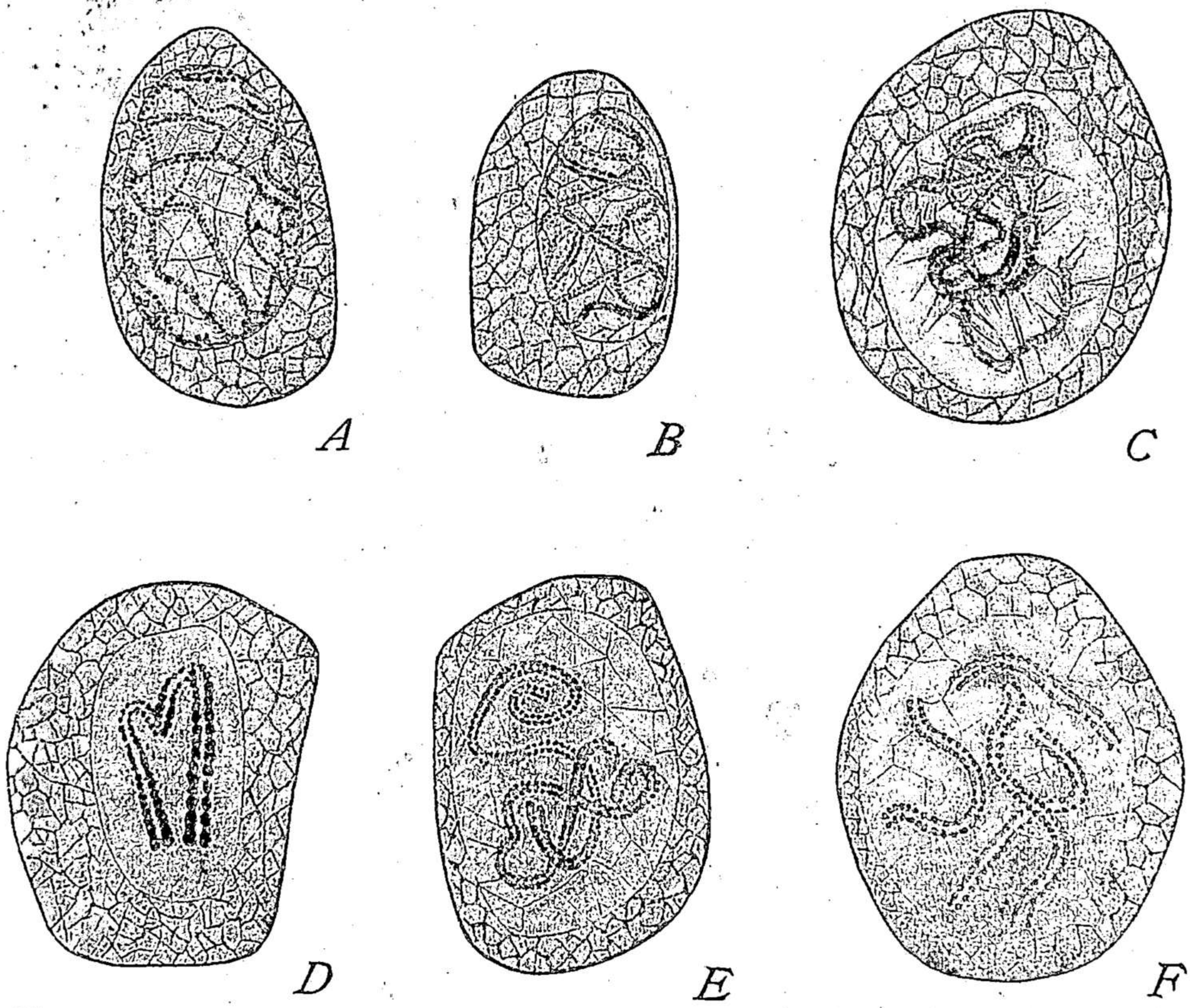


Fig. 53.—Formation of chromosomes and early splitting of the chromatin-granules in spermatogonia of *Ascaris megalocephala*, var. *bivalens* (BRAUER).

A, very early prophase; granules of the nuclear reticulum already divided; *B*, spireme; the continuous chromatin-thread split throughout; *C*, later spireme; *D*, shortening of the thread; *E*, spireme-thread divided into two parts; *F*, spireme-thread segmented into four split chromosomes.

side in pairs. A conspicuous example of this is offered in the Diptera, where all the chromosomes, as a rule, are plainly paired (Fig. 396). In most cases, however, the paired grouping is not clearly evident, or is demonstrably absent (p. 837).[1]

In respect to their form we may distinguish in the somatic mitoses three principal types of chromosomes, connected by various intermediate forms:

(1) Straight rods or threads, which arise directly by shortening of the spireme-threads.

(2) Loops, V's or hook-forms, derived from the rods by a flexure at the middle point or near one end.

[1] For the theoretical interest of these facts, see p. 575.

(3) Ovoidal or spheroidal forms, which arise by extreme shortening of the threads.[1]

All of these forms are double owing to the presence of a cleft or split that may be traced back to the original longitudinal split of the spireme-threads. In case of the rod- and loop-forms the duality still appears as a longitudinal split; but in the ovoidal or spheroidal forms, it often appears as an apparently transverse constriction (the so-called dumb-bell forms), owing to the great shortening which the chromosomes have undergone.

b. Spindle-Attachments of the Chromosomes. The metaphase-chromosomes, considered individually, show marked differences in respect to their modes

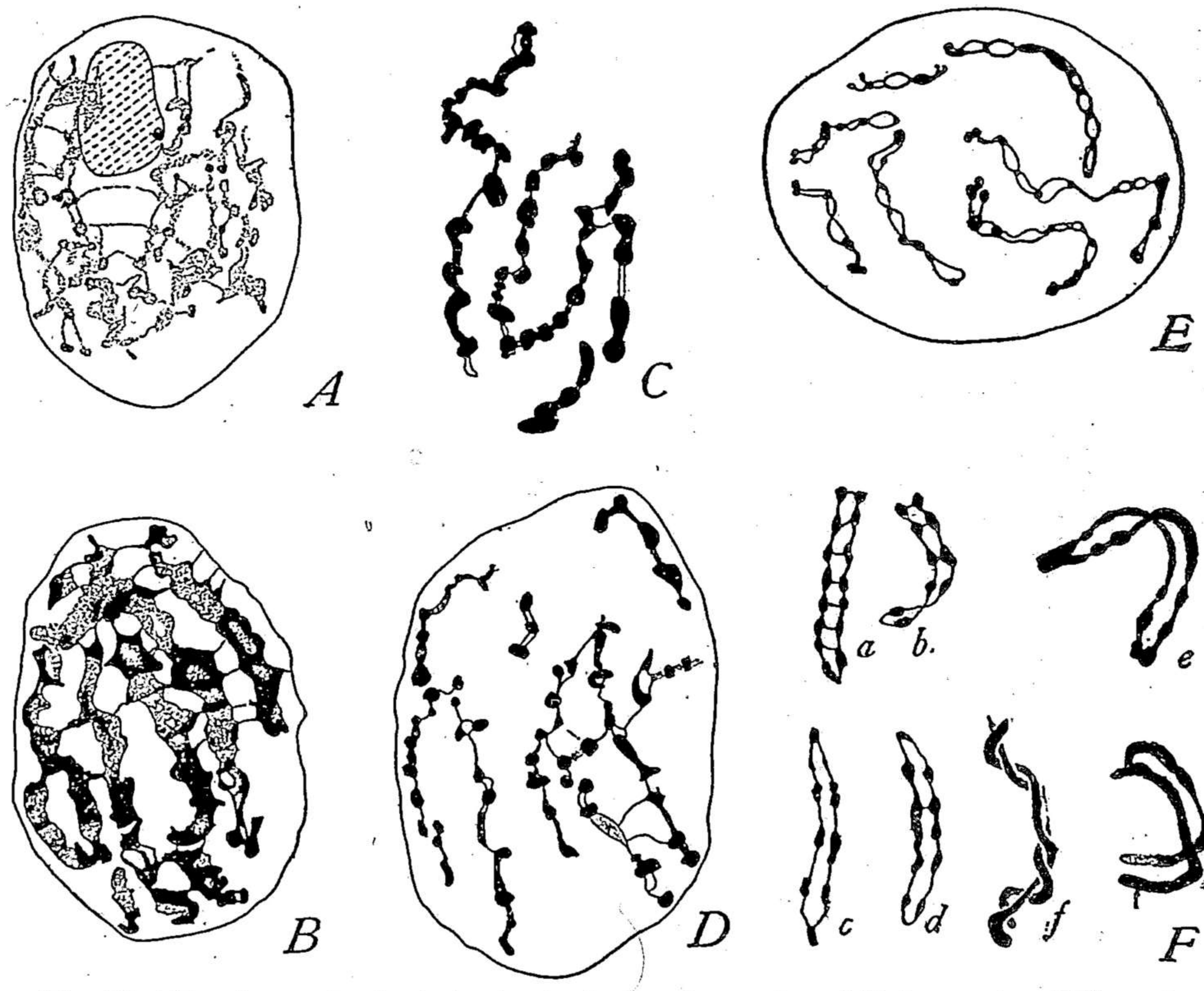


Fig. 54.—Prophases of mitosis in the meristem of root-tips of *Naias marina* (MÜLLER).

A, beginning of the band-like concentration of the nuclear framework; *B*, later stage; *C*, evolution of the chromomeres, *D*, early spireme; *E*, early stage of the splitting; *F*, later stages; *a–d*, fission of the chromomeres, *f–g* later stages, twisting of the halves.

of attachment to the spindle-fibers; and both their form and their history during the anaphases are profoundly influenced thereby. Recent studies have led to the remarkable conclusion that the mode of attachment is approximately constant for each particular chromosome and that it is inherited from generation to generation (p. 834). Attachment of the chro-

[1] In the maturation-mitoses occur many other forms, such as rings, crosses and tetrads, which will be considered in Chapter VI.

mosome to the spindle is commonly limited to a small area, and is of two general types, namely: (1) *terminal* or *telomitic* and (2) *non-terminal* or *atelomitic*, being in the former case at one end, and in the latter at some other point or points. Non-terminal attachment may be at the middle point (*median*) or at an intermediate point (*submedian*, *sub-terminal*). All gradations exist between these various cases; the attachment is sometimes not localized but extends along the whole length of the chromosome (*lateral* attachment). These various attachments show a very definite correlation with the form of the chromosomes (Fig. 56) sometimes evident in the prophases, commonly in the metaphase, and always in the anaphases; with terminal attachment the chromosome is rod-shaped; with median or sub-median usually V-shaped or loop-shaped; with sub-terminal hook-shaped or J-shaped. This correlation becomes more evident when we consider

3. The Anaphases

There is reason to conclude that the metaphase is a condition of relative stability in which the mitotic figure often remains for a considerable time. [1]

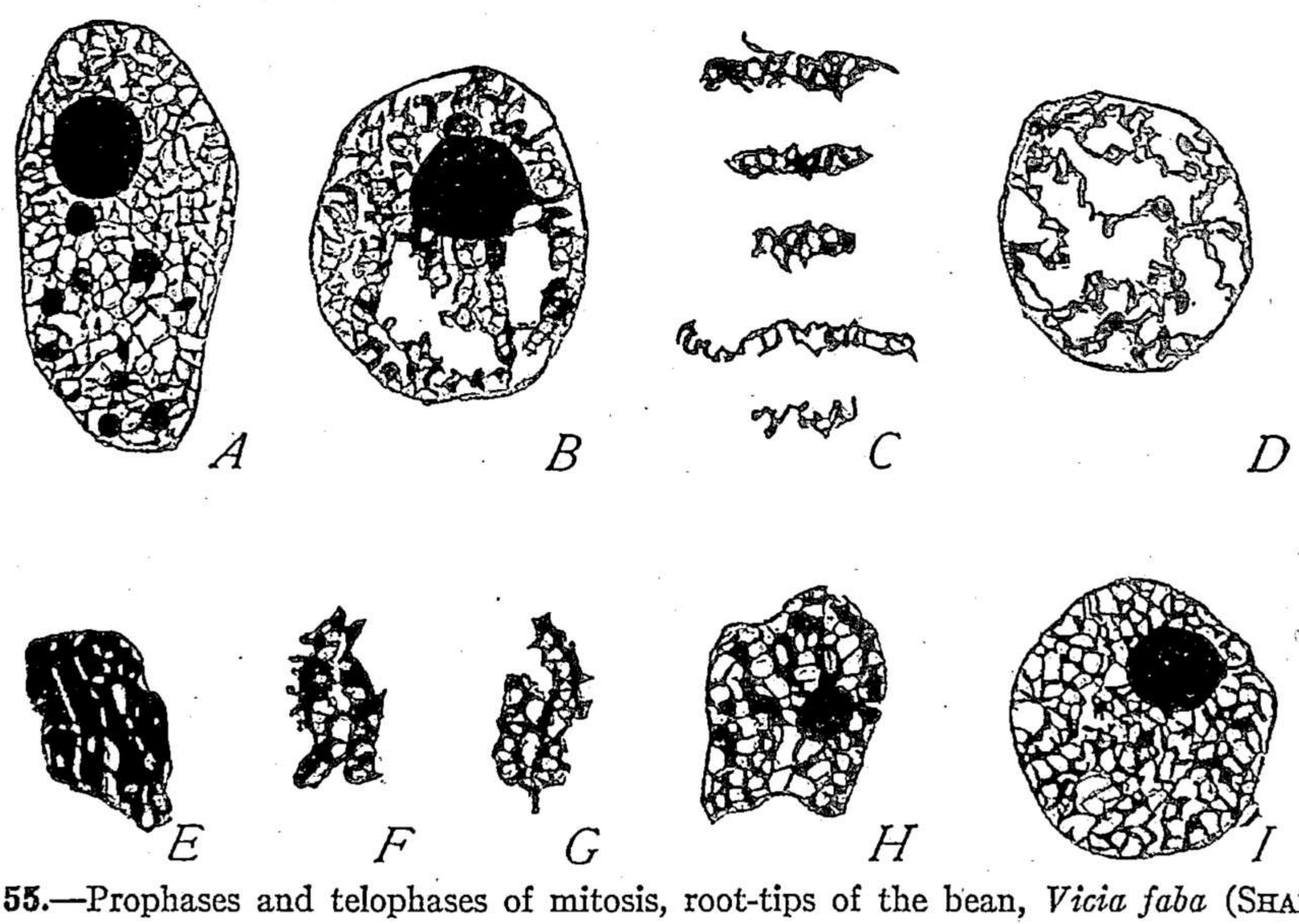


Fig. 55.—Prophases and telophases of mitosis, root-tips of the bean, *Vicia faba* (SHARP).

A, resting nucleus; *B*, early prophase; *C*, early prophase-chromosomes, unravelling of the spireme; *D*, early split spireme; *E*, *F*, telophases, vacuolization and branching; *G*, details of same; *H*, young nucleus.

The anaphases, on the other hand, are passed through rapidly and represent a phase of great activity, during which the daughter-halves of each chromosome move apart and proceed to opposite poles of the spindle. As they separate, their characteristic forms, in so far as they are correlated

[1] A striking example of this is offered in the polar mitoses of many eggs (p. 404).

with their modes of attachment, become more pronounced and often undergo very definite changes. All these appearances, as shown in the diagram (Fig. 56) are explained by the simple fact that whatever be the mode of attachment, the *daughter-chromosomes always begin to separate at the point of attachment* and move as if dragged towards the poles by traction of the spindle-fibers. In the simplest cases, shown by V-shaped chromosomes and by the lateral types of attachment, the chromosomes undergo

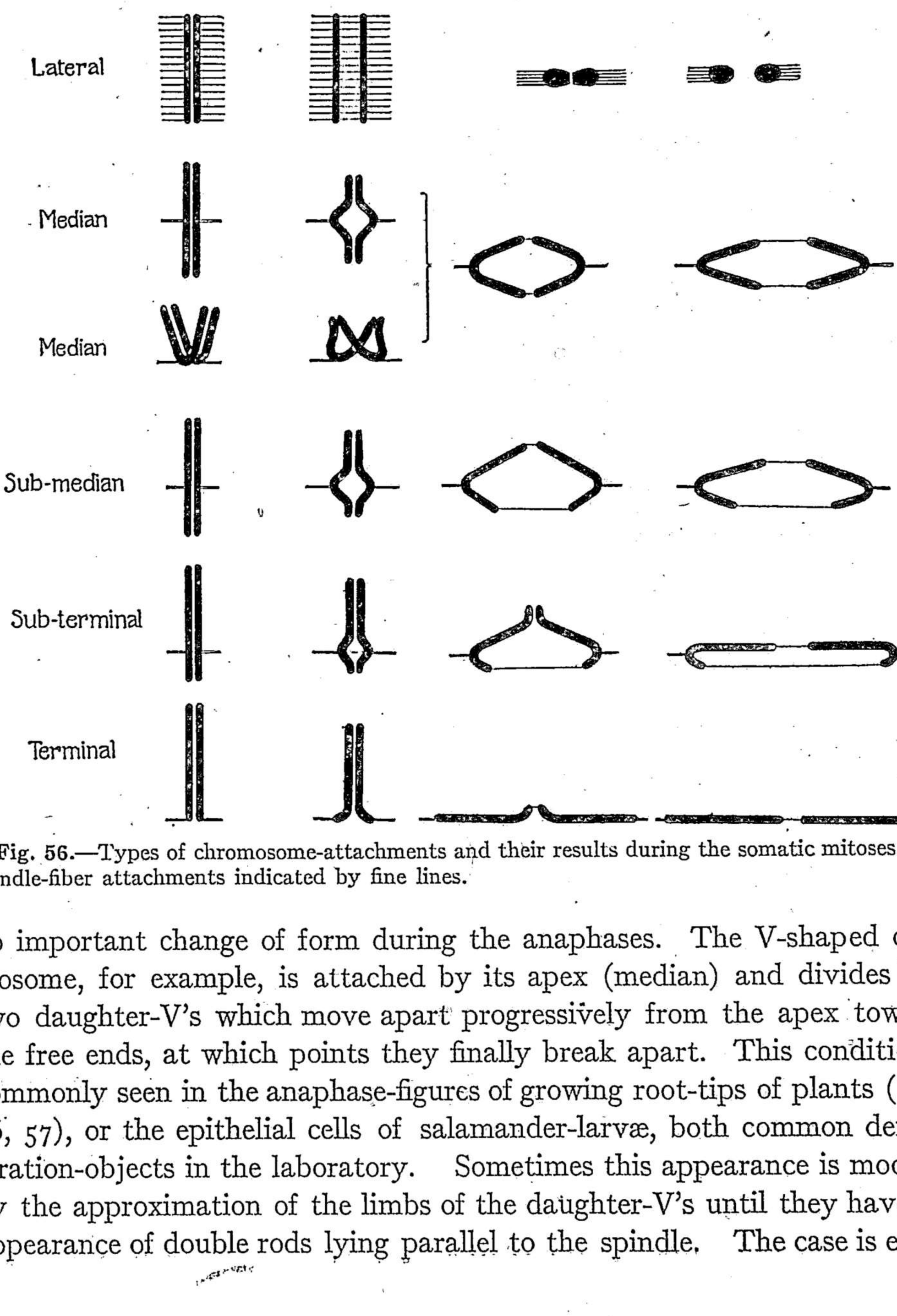


Fig. 56.—Types of chromosome-attachments and their results during the somatic mitoses. The spindle-fiber attachments indicated by fine lines.

no important change of form during the anaphases. The V-shaped chromosome, for example, is attached by its apex (median) and divides into two daughter-V's which move apart progressively from the apex towards the free ends, at which points they finally break apart. This condition is commonly seen in the anaphase-figures of growing root-tips of plants (Figs. 56, 57), or the epithelial cells of salamander-larvæ, both common demonstration-objects in the laboratory. Sometimes this appearance is modified by the approximation of the limbs of the daughter-V's until they have the appearance of double rods lying parallel to the spindle. The case is essen-

tially the same with asymmetrical V's (sub-median attachment) or J-shaped chromosomes (sub-terminal) which differ from symmetrical V's only in the unequal length of the two limbs.

Rod-shaped chromosomes show more striking variations, since they may have any form of attachment. When this is median the daughter-rods are transformed during the early anaphases into V's because the middle point of each longitudinal half is drawn polewards while the ends still remain united (Figs. 56, 57). The double rod thus gives rise to a <>-shaped figure, which breaks apart into daughter V's exactly as in the case of chromosomes that are originally V-shaped. If attachment be sub-median or sub-terminal the daughter-chromosomes are correspondingly drawn out into unequal V's, J's, or hooks (Fig. 56).

With a terminal attachment the two halves of the rod first draw apart from the attached end to form Y-shaped or T-shaped figures and by a continuation of the process come to lie in a straight line along the spindle while still connected at one end. At this point, they finally break apart to form two daughter-rods, lying end to end and parallel to the axis of the spindle (Fig. 58). As seen during the early anaphase this mode of division might readily be mistaken for a transverse division of the rod; and for such it was in fact mistaken by some of the early observers before the importance of the mode of attachment had been recognized.

4. The Telophases

The preceding phases of mitosis are fundamentally important for a study of the mechanics of division. Those which now ensue are equally so for broader questions, including above all the individuality of the chromosomes and the theoretic interpretation of meiosis (pp. 561, 890).

a. Reconstruction of the Daughter-Nuclei. In the final anaphase the chromosomes, often closely crowded together, lie at the extreme end of the spindle (Fig. 50), and in some cases even pass beyond it so as to lie actually within the substance of the centroplasm (*i. e.*, inside the centrosome, Figs. 58, 322). Each daughter-group of chromosomes now gives rise to an ordinary nucleus by a process of "reconstruction"; and during the earlier part of this period the entire cell divides into two across the equator of the spindle. Three principal modes of nuclear reconstruction have been described, as follows:

The simplest and rarest type is by the formation of *chromosomal vesicles*, or *karyomeres*, a process long ago described by Bütschli and Fol in the blastomeres of segmenting eggs and since observed in embryonic cells of many species. In this process each chromosome is converted into a

small vesicle exactly like a minute nucleus, the whole group then fusing together progressively so as to form first an irregular, chambered structure and finally a single nucleus (Figs. 58, 419). From the outer wall of this, apparently, arises the nuclear membrane, while the inner walls of the vesicles break down irregularly to form the nuclear network. The nucleus thus formed is at first small, irregular in outline, and stains lightly. It then rapidly enlarges, becomes spheroidal, and the staining capacity of the network increases. A somewhat similar mode of reconstruction

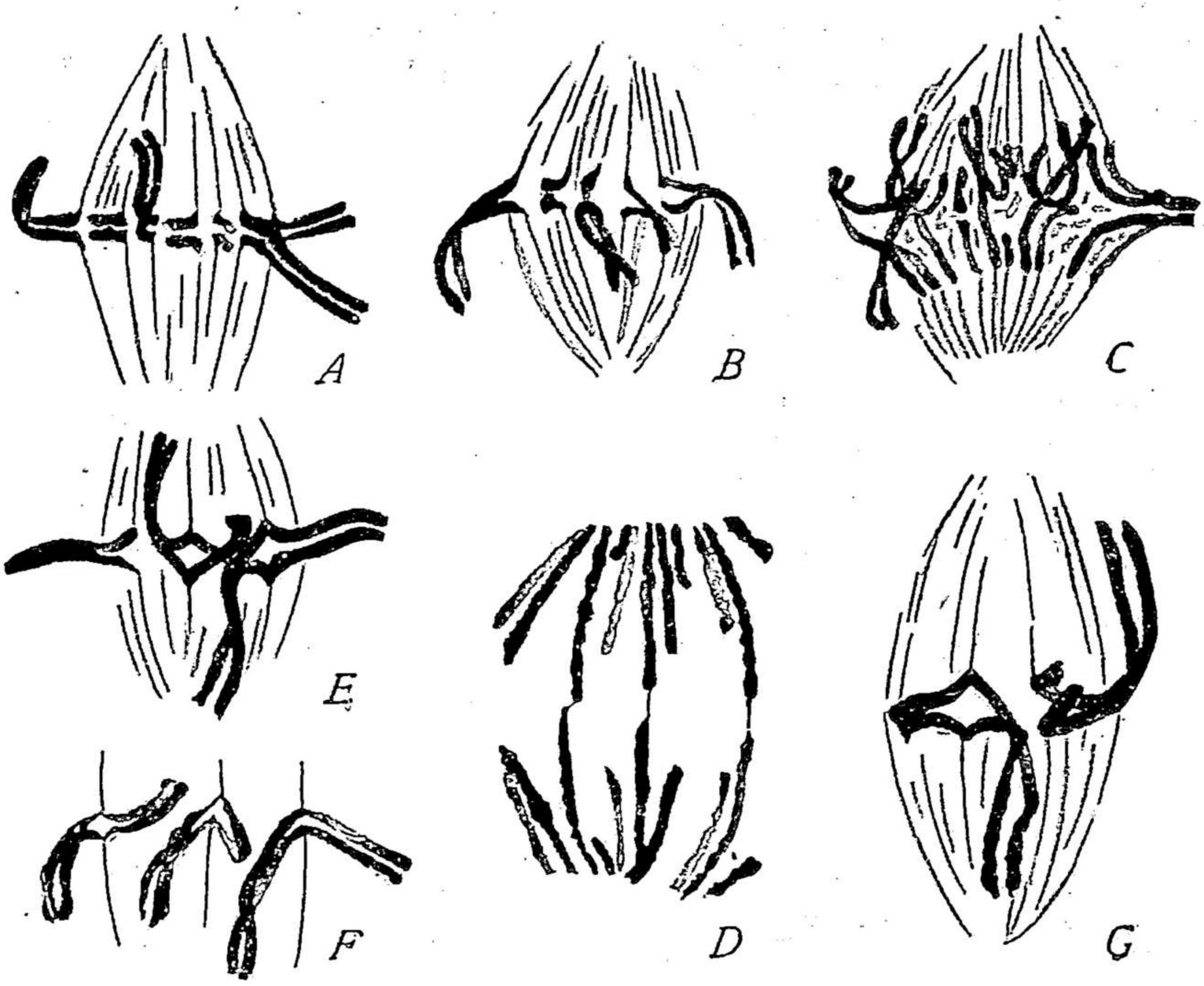


Fig. 57.—Chromosome attachments in mitosis in root-tips (GRÉGOIRE).

A–D, *Galtonia*, terminal attachments; *E*, *F*, *Allium*, terminal median, sub-median; *G*, *Trillium*, sub-terminal, intermediate.

has been described by Sutton, McClung and many others in the spermatogonial divisions of the Orthoptera (Fig. 361). Both in this case and in the cleavage of the ovum, where the divisions rapidly succeed one another, the karyomeres sometimes fail to fuse or fuse but incompletely (Fig. 95), thus giving rise to irregularly lobed "polymorphic nuclei," or nests of more or less separate karyomeres, which might readily be mistaken for stages of amitotic division.[1]

A second and more frequent mode of reconstruction, described in many kinds of cells in both animals and plants, involves a twofold process including a branching of the chromosomes by which they give rise to an irregular

[1] See for instance, Beckwith, '14 (hydroids), Richards '17 (teleosts).

network, and also the development within them of numerous vacuoles which enlarge, crowd together and finally seem to break down more or less so as to form an internal netlike structure. The nucleus thus becomes, in the phrase of Grégoire, a "network of networks," in which the boundaries of the original chromosomes can no longer be distinguished (Fig. 55). In the meantime

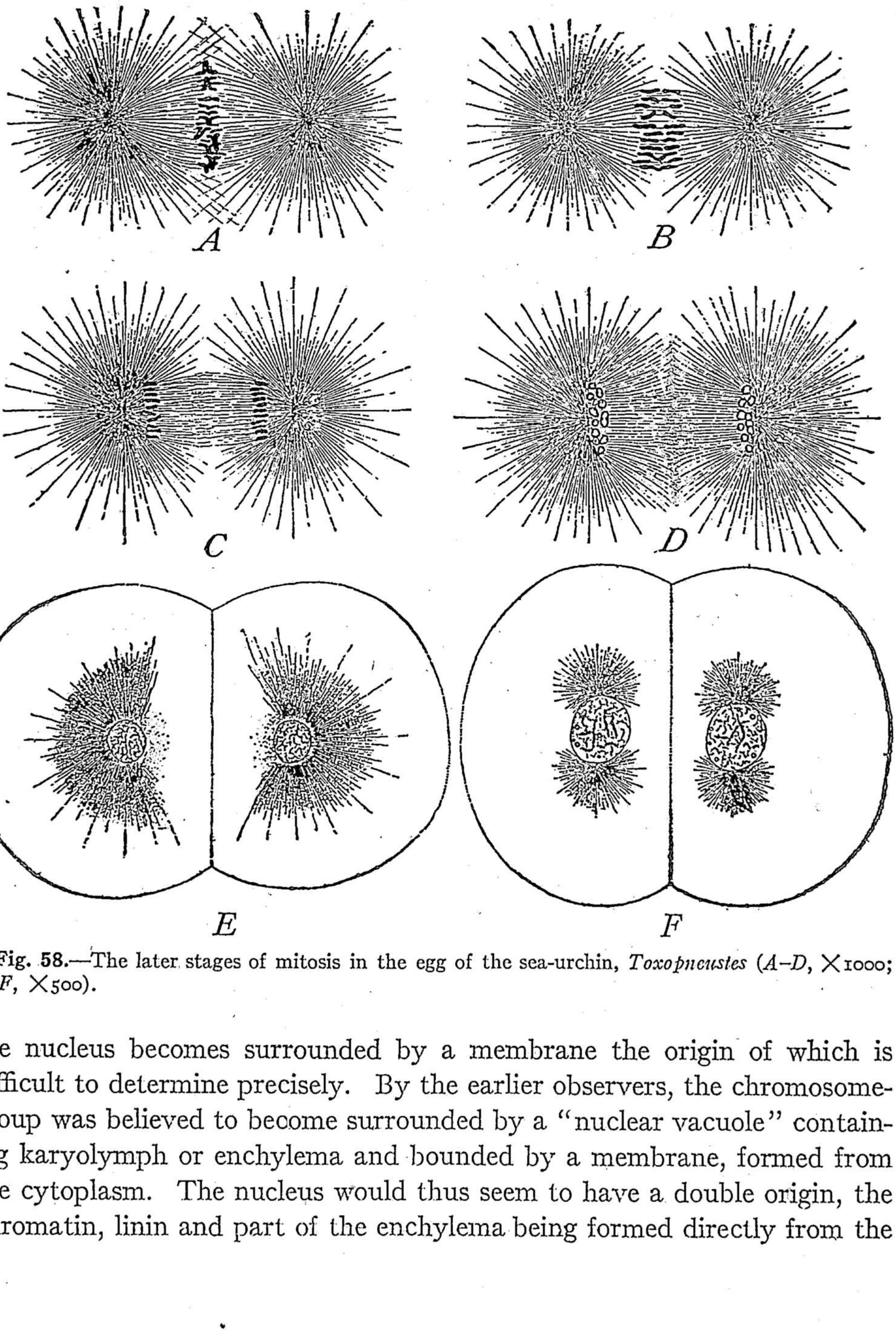


Fig. 58.—The later stages of mitosis in the egg of the sea-urchin, *Toxopneustes* (*A–D*, ×1000; *E–F*, ×500).

the nucleus becomes surrounded by a membrane the origin of which is difficult to determine precisely. By the earlier observers, the chromosome-group was believed to become surrounded by a "nuclear vacuole" containing karyolymph or enchylema and bounded by a membrane, formed from the cytoplasm. The nucleus would thus seem to have a double origin, the chromatin, linin and part of the enchylema being formed directly from the

chromosomes, the membrane and the remaining portion of the enchylema from the surrounding cytoplasm. Strasburger and his followers were thus led to consider the nuclear membrane as essentially a cytoplasmic structure and to designate it as the "inner cell-wall." More recent studies, emphasizing the telophasic vacuolization of the chromosomes, indicate that the membrane is formed by the outer walls of vacuoles that appear in the peripheral regions of the chromosomes, or outside them; and it thus becomes a difficult question whether the membrane is formed from the surrounding cytoplasm, or from the periphery of the chromosomes, as appears to be the case in the first type of reconstruction. Perhaps both processes may take place, as often seems to be the case with the formation of spindle-fibers (p. 148).

Both the telophasic branching and the vacuolization were recognized by the early observers; for instance, Van Beneden ('83–'84, '87) described a sponge-like vacuolization of the chromosomes in *Ascaris*, while the branching was emphasized by many observers, including especially Rabl ('89) and Boveri ('87, etc.), who built on this basis the hypothesis of the individuality and genetic continuity of the chromosomes. "In the objects which I have studied . . . (these phenomena) . . . seem to me to admit of no other interpretation than that the daughter-chromosomes pass over into a network by sending forth branches; and that each new chromosome arises through the contraction of a particular region of this network. A highly important corollary to this is given by the evidence afforded by various forms of nuclei that each region of the network derived from a chromosome draws together again to form a chromosome again" (Boveri, '07, p. 232). The vacuolization has been emphasized by Grégoire and his followers, and has recently been studied with especial care by Sharp in seed-plants, by Litardière, in ferns, and by other observers.[1]

A third type of reconstruction, described by a few observers is by the formation of a *chromonema*,[2] a delicately coiled, convoluted or zigzag thread formed within the late anaphase- or telophase-chromosomes, which is said to uncoil or unravel and branch to form the reticulum; but this appearance, as described especially by Bonnevie in *Ascaris*, *Amphiuma*, and *Allium* and by Vejdovský in *Ascaris* and in certain Orthoptera (Fig. 59) has been variously interpreted. According to Vejdovský the chromonema lies in an achromatic basis by the swelling and liquefaction of which arises the enchy-

[1] See Grégoire and Wygaerts ('03), Kowalski ('04), Berghs ('04), Grégoire ('06), etc., De Smet ('14), Sharp ('13, '20), Litardière ('21). Some observers have found the vacuoles appearing already in the anaphases (Merriman, '04, Nemec, '10, Lundegårdh, '10, 12b) or even in the metaphase (Grégoire and Wygaerts, '03). Most of these observers have accepted the telophasic branching of the chromosomes; but this is questioned by Overton ('22).

[2] Bonnevie ('08, '11), Schneider ('10), Dehorne ('11), Vejdovský ('12), Brunelli ('10, '14), Bolles Lee ('11), Martens ('22).

lema or nuclear sap, while the nuclear membrane is formed from its periphery and the nuclear framework from the chromonema itself.[1] Most recent observers, especially among botanists [2] have failed to find evidence of a definite spiral in the telophase-chromosomes and have considered the so-

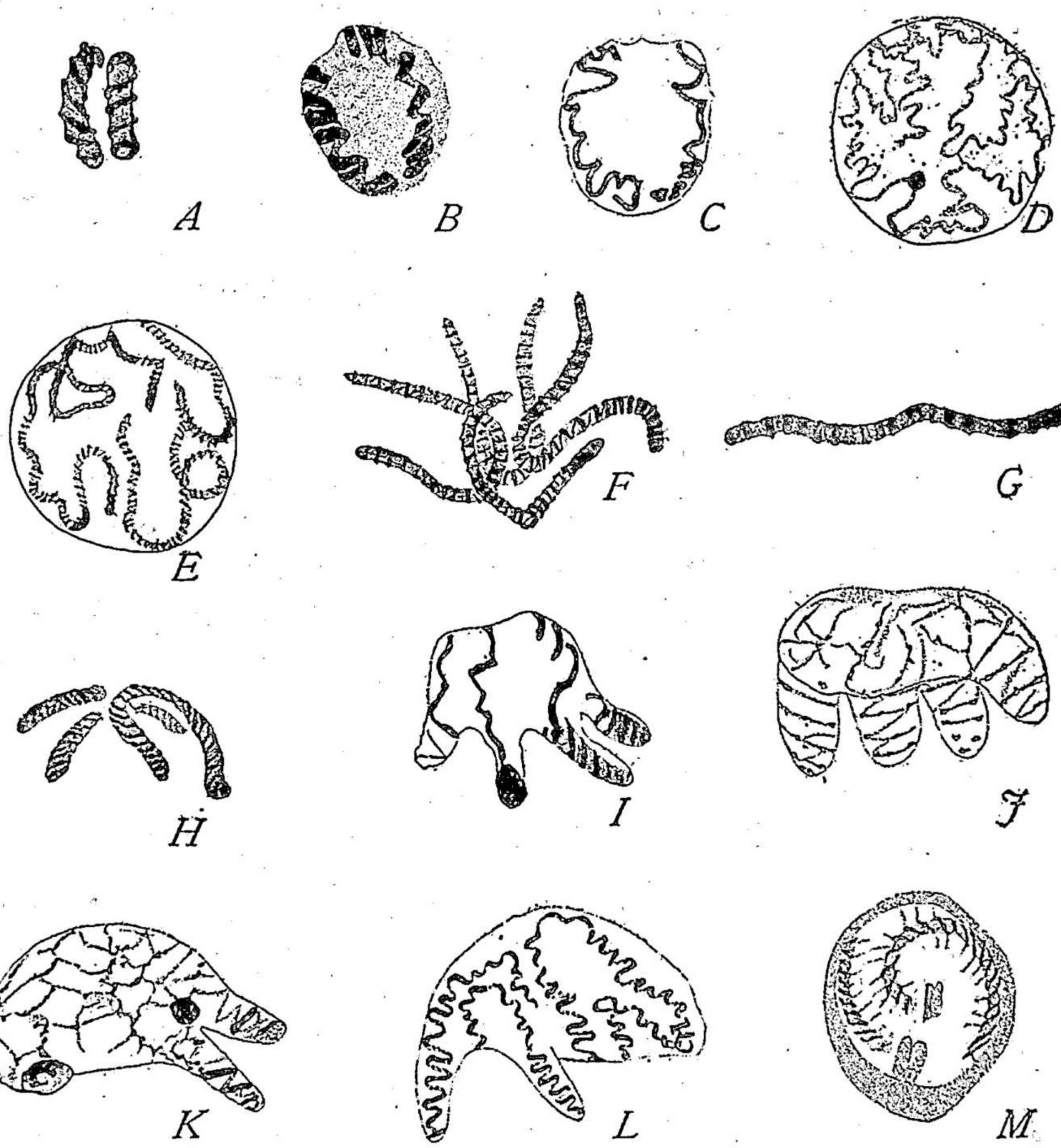


Fig. 59.—The chromonema in *Ascaris megalocephala* (VEJDOVSKÝ).

A, *B*, chromosomes from early gamete-nuclei; *C*, *D*, uncoiling of the thread; *E*, formation of new chromonema within the thread; *F*, late prophase-chromosomes; *G*, metaphase-chromosome; *H*, anaphase-chromosome with chromonema; *I*, telophase; *J*, "resting" stage; *K*, *L*, prophases; *M*, supposed spiral structure of bivalent chromosomes in prophase of spermatocyte-division in the grasshopper *Decticus*.

called chromonema as an illusion due to the vacuolization of elongate telophase-chromosomes which causes the more solid portions to appear as an irregular spiral or zigzag. The author's observations, especially on the spermatogonial divisions of Orthoptera, point to the same conclusion, although in these same cells (*Phrynotettix*, etc.) the contorted spiriform *prophase*-chromonema is very clearly seen (Wilson, '12).

[1] See p. 896.

[2] See especially the works of Grégoire, Sharp and Litardière.

The foregoing types of reconstruction, different in aspect as they are, are closely related. The first or karyomere type represents an extreme form of vacuolization with little or no branching, the second type a vacuolization of different character and complicated by the branching of the chromosomes. The third type, as shown especially by Sharp, is closely connected with the second, but in its original form still awaits adequate confirmation.

b. The so-called Anaphasic or Telophasic Duality. As above stated, a considerable number of observers, beginning with Van Beneden ('83–'84) have described the telophase- or even the anaphase-chromosomes as longitudinally double. Many have believed this duality to persist during the resting-nuclei and to reappear as the longitudinal split of the early spireme in the ensuing mitosis; [1] and this conception has even been applied to some of the Protozoa in an effort to explain the apparent cross-division of the chromosomes in these forms (p. 212). Some observers believe that the anaphasic "split" is already in evidence during the metaphase, the chromosomes having at this time a quadripartite structure analogous to that seen in the heterotypic division (p. 509).[2] A remarkable case is described by Taylor ('22) in the heterotypic division (pollen-mother-cells) of *Gasteria*. As is the rule with this division, the anaphasic chromosomes are longitudinally double here, with widely separated halves, in preparation for the following homeotypic division (p. 519). The remarkable point is that each half-chromosome (or at least the chromomeres which it contains) is itself at first longitudinally double and later (early telophase) longitudinally quadripartite. This may possibly mean that in the closing phases of the heterotypic division preparation has already been made, not alone for the succeeding homeotypic division but also for an additional division, which later takes place in the pollen-grain (p. 496). This latter conclusion, however, has not yet been demonstrated.

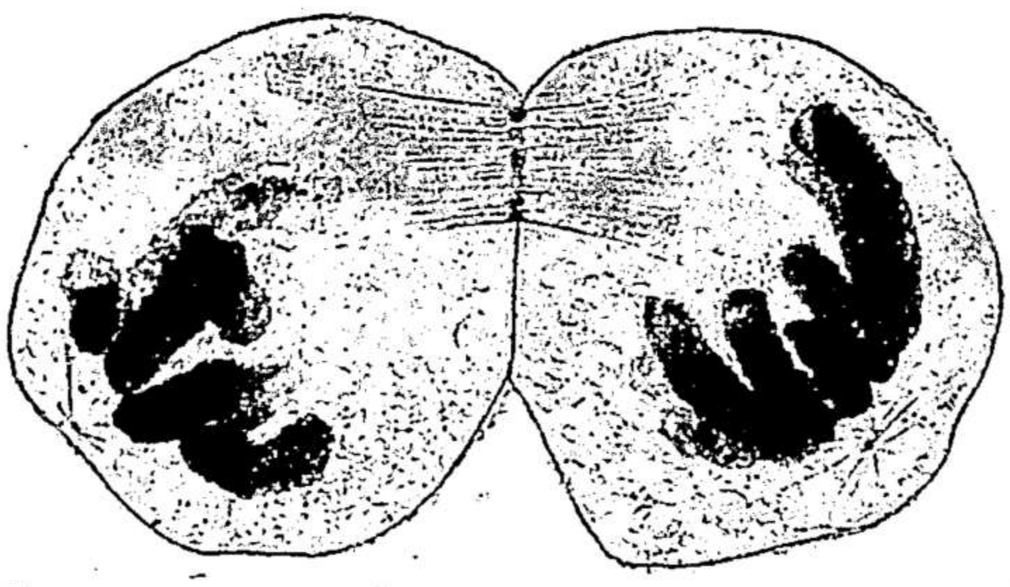


Fig. 60.—Telokinesis in spermatogonial division of the grasshopper *Rhomaleum*.

On the other hand, a considerable group of observers have considered the so-called telophasic split as an illusion due to the vacuolization of the

[1] See Hof ('98), Farmer and Shove ('05), Bonnevie ('08, etc.), Meves ('07), Lundegårdh ('10, '12), Digby ('10, '14, '19), Farmer and Digby ('10), Brunelli ('10), Granier and Boule ('11), Frazer and Snell ('11), Bolles Lee ('11), Schneider ('10), Dehorne ('11), Frazer ('14), Schüstow ('13), Reed ('14), etc.

[2] Merriman ('04), Nawaschin ('10), in the root-tips of plants, Bonnevie ('08) in the eggs of *Ascaris*. See also Sands ('22).

chromosomes at this time.[1] Some advocates of the telophasic split (Lundegårdh, Schüstow, Frazer and Snell, etc.) endeavored to reconcile the contradiction by assuming the telophasic vacuolization to result in a complete longitudinal division, as described by other observers in the prophasic splitting (p. 125). This, however, has been contradicted by some of the most careful recent studies both of the telophases and the prophases, which seem clearly to demonstrate that the telophasic vacuoles are often not in an axial series but quite irregularly disposed (Sharp), and that the prophase-threads are not double but single and subsequently split lengthwise.[2] The work of Sharp, Kuwada and Litardière shows clearly that in the prophases of various plants the fine prophase-spireme is formed from alveolized bands very similar to the alveolized telophase-chromosomes; and that by the confluence of the vacuoles and partial breaking down of their walls arises a single irregular zigzag thread, which later splits lengthwise. This is in accordance with many other observations on the formation of the prophase-spirals in animal mitoses referred to above.

Martens ('22) in a study of *Paris*, has endeavored to harmonize the conflicting interpretations by the conclusion that the anaphasic and telophasic duality, though real, is not the forerunner of the future prophasic split. This observer describes an anaphasic and telophasic chromonema, similar in principle to that of Bonnevie and Vejdovský but less regular, the substance of which is said to concentrate at the periphery and thus produce a transitory appearance of duality, which, however, later disappears (Fig. 420). In the prophases the chromonema reappears as a single zigzag thread, as described by other observers; but this is asserted *not to split lengthwise* but again to concentrate on both sides of the chromosome until the latter becomes longitudinally double. This account confirms the accounts of those who consider the prophasic split to arise already in the preceding anaphases, but also contradicts observers who, like Sharp, Litardière, the writer and others, believe the prophase chromonema to split lengthwise. The contradictions here arising must await further study.[3]

c. Telokinesis. Under this name Heidenhain ('94) characterized certain movements of the mitotic figure, or its remains, that often take place during the later telophases soon after cleavage of the cytosome, and may conveniently be considered here, though they affect particularly the cytoplasmic elements. They involve two principal events, both of which seem to vary widely in different kinds of cells and apparently may fail to take place in

[1] This point is urged by Grégoire, Lundegårdh ('10, 12), Sharp ('13, '20), de Smet ('14), Sakamura ('14), and others, more recently by Litardière ('21), and by Kuwada ('21) whose observations were made in my laboratory. My own observations on Orthoptera indicate the same conclusion.

[2] See especially Wilson, '12, Sharp, '13, Litardière, '21, Kuwada. '21.

[3] *Cf.* p. 896.

some cases. One is a rotation of the daughter-chromosome-groups towards one side of the spindle accompanied by a corresponding movement of the centers and often also by a more or less pronounced bending of the spindle at its middle point (Fig. 60). In extreme cases the spindle is thus flexed almost into the form of a V or U and the nuclear axes form a more or less wide angle with one another or may even become nearly parallel. In the latter case the nuclei have rotated through nearly 90°, and the central bodies,

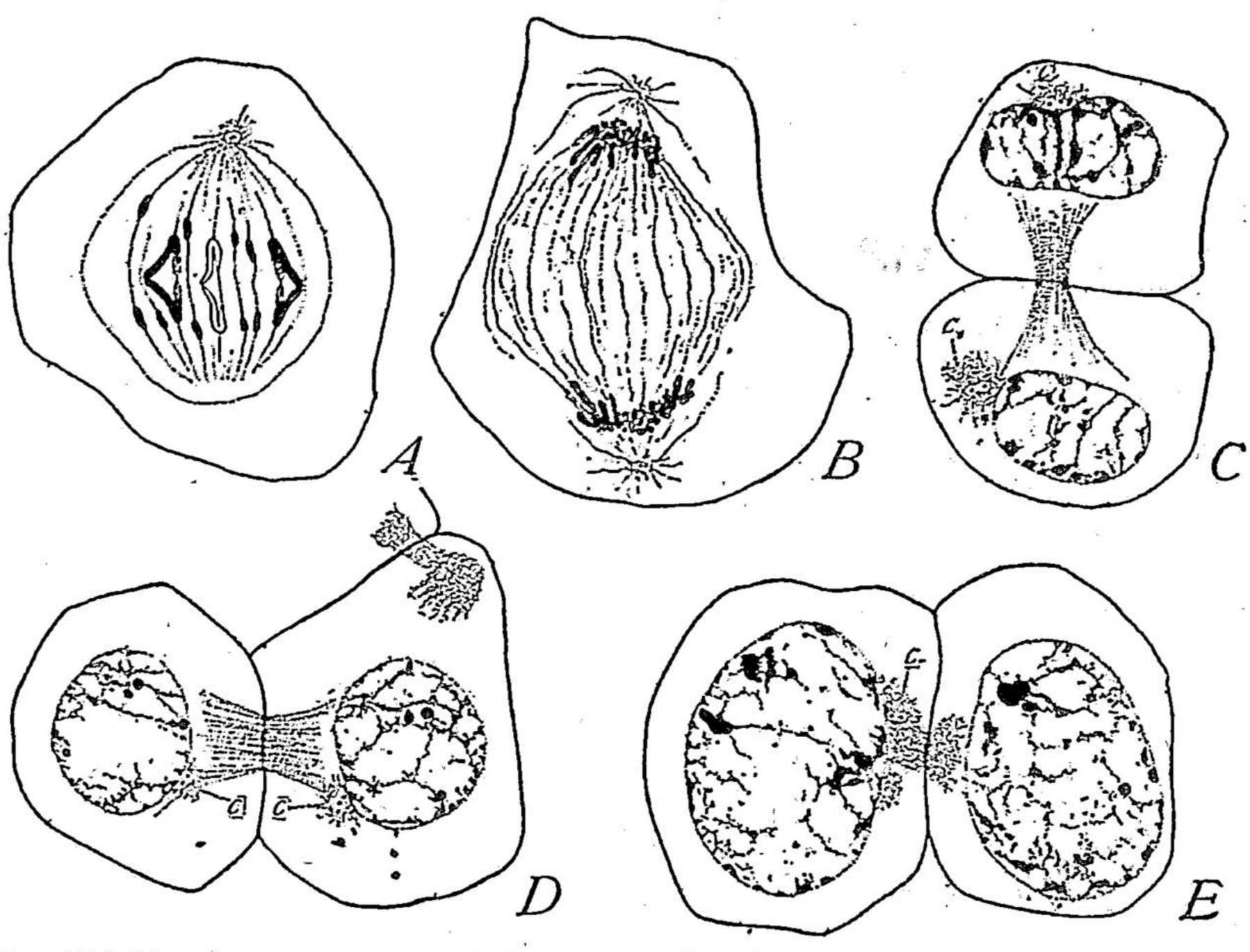


Fig. 61.—Telokinetic movements of the centers in the spermatogonia of the beetle *Blaps* (NONIDEZ).

A, metaphase; *B*, late anaphase; *C*, late telophase; *D*, *E*, still later stages, telokinetic movement completed.

originally at opposite sides of the nuclei, have come to lie nearly side by side. In their more pronounced forms these processes are often well seen in the cleavage of the ovum (Fig. 62), and also in the early spermatids prior to the differentiation of the sperm. In both these cases, further, the nuclei often separate more or less from the spindle so as to lie beside it instead of at its ends (Fig. 167).

Secondly, the centrioles often perform at this time certain definite movements by which their original relation to the nucleus is greatly changed. One is a separation of the two halves of each centriole (each of which becomes double during the metaphase or anaphase) and their migration to opposite poles of the nucleus 90° away from their original position (Figs. 322, 327). This is clearly a preparation for the next division following and might appropriately be reckoned as a prophasic event. In another

type of telokinetic movement, both centrioles, still closely associated, migrate around the periphery of the nucleus until they may come to lie at a position on the spindle side of the nucleus (instead of opposite to it) and nearly 180° away from their original position (Figs. 61, 278). The meaning of this remarkable process is quite unknown.

5. History of the Nucleoli

The history of the nucleoli in mitosis, as in the vegetative or interphasic nucleus, still involves many obscure points. In the prophases the chromatin-nucleoli undoubtedly contribute directly, in one way or another, to the formation of the chromosomes. The smaller net-knots seem to be drawn directly into the spireme-threads; larger blocks, in the form of prochromosomes or the like (p. 899) may be resolved into contorted or coiled threads which then unravel or uncoil to form spireme-threads (Fig. 421). The chromosome-nucleoli, characteristic of the auxocytes (though sometimes found in other cells), are usually likewise drawn out more or less before their longitudinal fission though in some cases this is but slight (p. 761). Karyospheres differentiate into a closely crowded group of basichromatic chromosomes, often imbedded in a more lightly staining or oxychromatic matrix from which the chromosomes break away or escape into the nuclear cavity (Fig. 37). The matrix may thus be left behind in the form of a plasmosome, while the chromosomes may undergo a considerable process of extension before condensing into their final form. A good example of this is offered by the spermatocytes of *Notonecta* (Browne, '13).

True nucleoli or plasmosomes are not known to make any direct morphological contribution to the chromosome-formation. They often persist with only slight change while the spireme forms and in the later stages rapidly diminish in size, fragment and disappear; but there are a few cases in which the plasmosome, or a considerable residue of it, is cast out bodily after completion of the mitotic figure. It is possible, nevertheless, as earlier indicated (p. 95), that these nucleoli may be storehouses of material that is given off in a soluble form and may play some part in the mitotic transformation. We may here again recall the possibility that in their basophilic condition these nucleoli may have stored up some substance, such as nucleic acid, that has been given off from the chromosomes (which have in consequence decreased in basophily) and is given back to them during their increase in basophily in the later prophases. This, however, is a mere conjecture.[1]

[1] The best examples of such changes are offered by the growing oöcytes (p. 354); others are seen in *Zygnema* according to Escoyez ('07) and van Wisselingh ('14) or in *Marsilia* according to Strasburger ('07) and Berghs ('09).

In the telophases the plasmosomes reappear, often very early, in the form of drop-like spheres which commonly flow together to form larger spheroids. Their exact source is still doubtful. Until recently most ob-

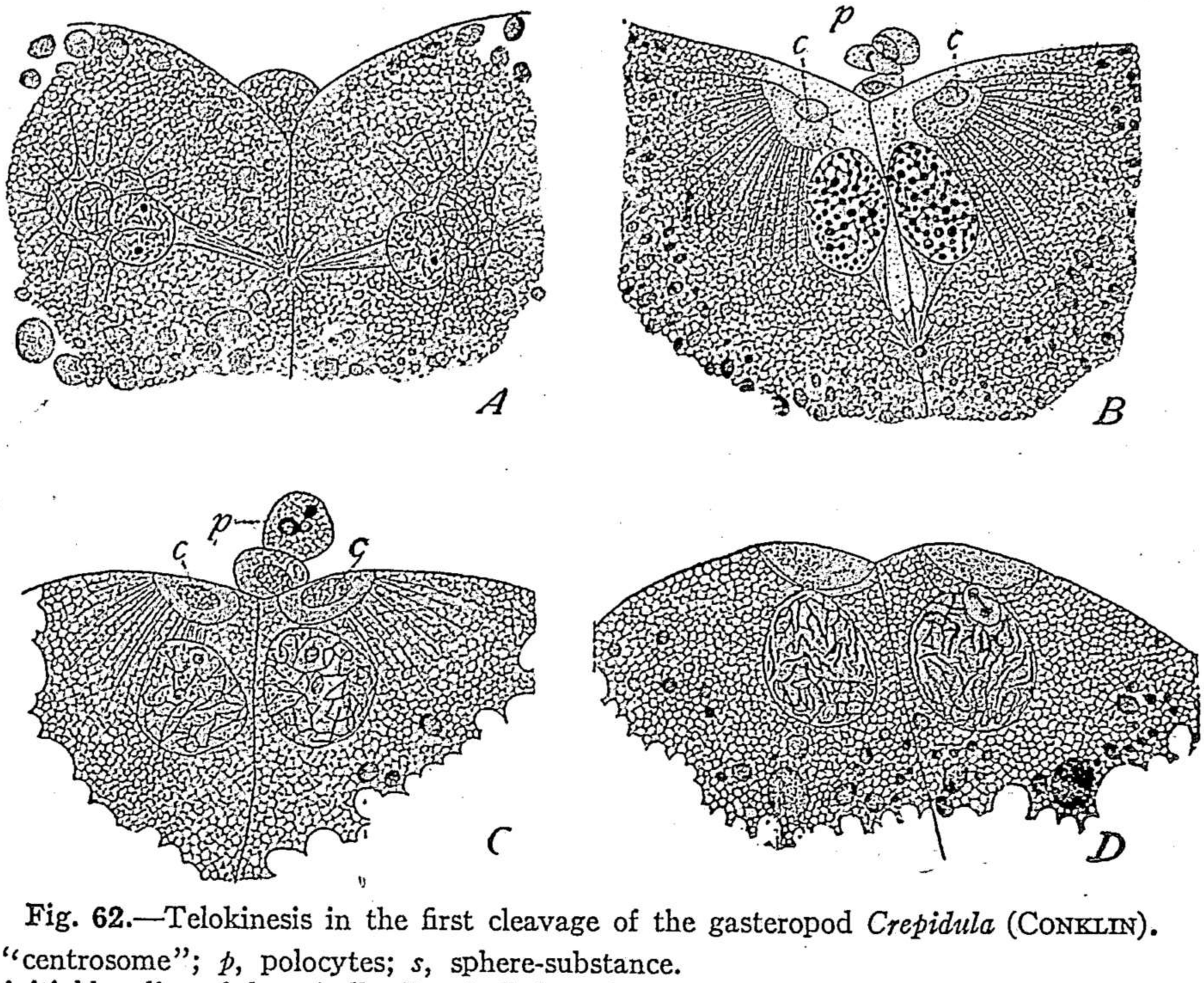


Fig. 62.—Telokinesis in the first cleavage of the gasteropod *Crepidula* (CONKLIN).

c, "centrosome"; *p*, polocytes; *s*, sphere-substance.

A, initial bending of the spindle; *B*, spindle bent into a *V*, nuclei almost in contact; centers above, near the surface; *C*, interphase, after disappearance of the spindle; *D*, early prophase of second cleavage, division of the daughter-centers and formation of the daughter-amphiasters.

servers have found them arising independently of the nuclear framework and apparently *de novo* (see, however, p. 911).

III. CYTOKINESIS. GENERAL HISTORY OF THE ACHROMATIC FIGURE

A. THE AMPHIASTRAL TYPE

The amphiaster may be thought of as two astral systems which jointly give rise to the spindle that lies between them; and the spindle is perhaps comparable to a specially modified group of astral rays, but this is not entirely certain. The spindle is superficially similar to the spindle-shaped area found between the poles in the magnetic or electrostatic field, but it is more than doubtful whether the two cases are really analogous. As viewed in the living object the asters appear as radiating tracts of hyaloplasm, defined by a radial disposition of the alveolar spheres (macrosomes) and

microsomes about the centers. The spindle appears as merely a clear fusiform area between the asters, containing no alveolar spheres, and most commonly showing no trace of spindle-fibers.[1] The question is thus prominently raised as to whether the fibrillar structure of the amphiaster, as seen in sections, may not be a coagulation artifact; and, as has earlier been indicated, the experiments especially of Bütschli, Hardy and Fischer have in fact demonstrated that fine fibrillar aster-like and spindle-like structures (Fig. 24) may be produced by coagulating agents in artificial emulsions, or even in homogeneous colloidal solutions (p. 65).

As seen in sections both asters and spindle are in most cases undoubtedly composed of very distinct fibrillæ, those of the spindle often more sharply marked than astral rays. Both sets of fibrillæ anastomose to some extent, but in well-fixed material this is as a rule hardly noticeable in the spindle until after the metaphase has been passed. The astral rays are unbranched centrally but branch out distally into the protoplasmic framework and are lost to view, though often extending nearly to the periphery of the cell. In many cases the fibrillæ of both spindle and asters seem to consist of a homogeneous basis along which or in which are scattered microsomes; and some writers, for instance Van Beneden, have described the fibrillæ as actually built up as linear series of microsomes.

1. The Spindle

By the earlier observers, such as Van Beneden ('83, '87) and Boveri ('88) the metaphase-spindle was regarded as consisting of two cone-shaped, half-spindles placed base-to-base and separated by the equatorial plate of chromosomes. Subsequently it became evident that, in many cases at least, the spindle consists of two kinds of fibers; and these have been supposed to differ widely in functional significance. One of these includes *half-spindle* fibers, extending from the poles to the chromosomes, as just indicated; these, which are probably concerned in some manner with the movements of the chromosomes towards the poles, are called *traction-fibers*, or *chromosomal fibers*. Secondly, the spindle contains *continuous fibers* which extend without interruption from pole to pole and sometimes constitute a *central spindle* about which the chromosomes are grouped in a ring, attached on either side to the traction-fibers, in this case called, because of their position, "mantle fibers" (Figs. 48, 247). More frequently the two sets of fibers are mingled, and no central spindle can be distinguished. In such cases the chromosomes do not surround the spindle but lie in its substance.

[1] *E. g.*, in echinoderm eggs, Wilson, '99, '01. So-called spindle-fibers may sometimes be seen in the unfixed object (*e. g.*, in the spermatocyte-divisions of insects) but it is doubtful whether this may not be due to a sub-mortem change.

During the anaphases the two diverging groups of daughter-chromosomes are connected by a set of *connecting-fibers* or *interzonal-fibers* ("Verbindungsfasern," "filaments réunissants") which now form the equatorial region of the spindle (Figs. 46, 58). By the early observers these were believed to be spun out from the chromosomes as the latter drew apart, and hence to differ wholly in nature and origin from the true spindle-fibers; some recent observations seem to give this at least partial support. Many cytologists, however, have accepted the conclusion of Hermann ('91) that the connecting fibers are in the main identical with the continuous fibers which are exposed to view as the chromosomes draw apart. The interzonal region of the spindle is at first more or less convex in outline, but as the anaphases advance its boundaries become straighter and in the later anaphases and early telophase nearly parallel, while the connecting fibers become less crowded, more contorted, more granular in structure, and their anastomoses are more readily seen. In many cases they develop, during the early telophase, a series of deeply staining thickenings in the equatorial plane, forming the *cell-plate* or *mid-body*. This structure is conspicuous in the anastral forms of mitosis in the cells of higher plants, where it plays an important part in the division of the cell-body (p. 159). In the amphiastral types (animals generally) the mid-body is less developed and often rudimentary, being represented by only a few granules (Figs. 50, 60).

2. The Asters

The configuration of the astral formations, most conspicuously shown in embryonic cells, varies markedly in different phases of mitosis. In the very small asters of early stages, the rays are straight, simple and relatively few. With advancing development they rapidly elongate in all directions, increase in number, and in many cases those of the two asters intersect so as to *cross one another* at a decided angle in the equatorial region outside the spindle. This condition, of great interest for all general theories of mitosis (p. 186), is often seen in the metaphase or even earlier (Figs. 48, 205) and may persist until the late anaphase or even the early telophase. Sooner or later, however, the crossing of the rays disappears by a readjustment during which those from the two asters curve more and more towards one another and often seem to join in the equatorial plane so as to be continuous from pole to pole, even in the region outside the spindle. This condition is most perfectly seen in the living object during the early telophase just at the time when the cell-constriction appears, when the karykinetic field sometimes closely resembles the polarized magnetic or electrostatic field, the astral rays and spindle fibers following

a course nearly similar to that of the lines of force. This configuration is, however, but temporary and is quickly lost as the constriction cuts through the spindle (Wilson, '01c).

The asters are typically equal, in which case the whole karyokinetic figure is perfectly symmetrical with respect to both chromatic and achromatic elements and cell-division is also equal. The asters are, however, often unequal; and this is always accompanied by a correspondingly unequal division of the protoplasmic cell-body, *though the chromosomes divide equally as before.* In some of these cases the asters only become unequal when the spindle takes up an eccentric position, thus diminishing the field of action of the more peripherally placed aster (*e. g.*, in the polar divisions of the egg, Figs. 183, 189). In a few cases, however, the inequality seems to appear almost from the beginning and before the peripheral movement of the spindle occurs, as shown by Lillie ('12) in the first cleavage of the *Nereis egg* (Fig. 470). In either case we find here additional evidence that the asters are directly concerned with division of the cytoplasmic cell-body (p. 175).

An exceptional feature of the asters is a very distinct spiral twisting of the rays. Such spiral asters were first made known by Mark ('81) in case of the second polar spindles in the egg of the slug, *Limax;* and they have since been described in various other animals of widely separated groups, including echinoderms, nemertines, mollusks, annelids and vertebrates. Conklin ('02) ascribes the origin of spiral asters to vortical protoplasmic currents; and this is borne out by the more recent work of Painter[1] ('16), who concludes that the spiral asters probably are formed as a result of rotational shiftings of the aster subsequent to its formation in the typical manner.

3. The Central Bodies

The intricate questions involved in the relation between centriole, centrosome, aster and spindle, here indicated in only a general way, will be considered more critically at a later point (p. 672). The centriole, always very minute and sometimes almost at the limit of microscopical vision, stains intensely with certain dyes (such as iron hæmatoxylin or crystal violet). In the earliest stages of the asters it is most commonly single but sooner or later divides into two, a process which commonly takes place not later than the metaphase and sometimes even earlier (Figs. 322, 328). In the very young aster the astral rays seem to be given off directly from the centriole. Later the centriole is seen to be surrounded by a mass of *centroplasm* which usually forms a definite body generally known as the *centrosome* (Boveri) a term which has gradually displaced the earlier

[1] This author gives a good review of the literature of the subject.

terms "periplast" (Vejdovský), "attraction-sphere" (Van Beneden) and "centrosphere" (Strasburger).

This body varies greatly in structure in different kinds of cells and in different stages of development of the aster. In its most definite form (*e. g.*, as described by Boveri in *Ascaris*) it is a definite and homogeneous sphere from which the rays take their origin. In other cases, it is transversed by the astral rays, which may be traced into the centriole, as in *Thysanozoön* (Van der Stricht), *Unio* (Lillie) or *Nephelis* (Jörgensen). In such cases the centrosome seems to be merely the innermost zone of the aster, its boundary being formed as a rule by a circle of microsomes (Fig. 321); and this view of the centrosome is sustained by the fact that one or more additional concentric zones may sometimes be distinguished in the aster outside the inmost one.[1] In still other cases, illustrated by the segmenting eggs of *Thalassema* (Fig. 205), *Cerebratulus* (Fig. 322) or *Rhynchelmis* (Fig. 330) the centrosome or "centrosphere" is a larger and less sharply defined mass which is not traversed by the astral rays and shows a fine net-like or alveolar structure. Such centrosomes appear to arise by a breaking down of the inner region of the astral rays, a progressive process which in some cases leads to an enormous growth of the centrosome (Fig. 330). Such cases offer advantages for the study of the division of the centriole and the formation of the new amphiaster within it (p. 680).

4. Origin of the Amphiaster

In all cases the amphiaster is formed about the central bodies (centrioles) as foci; and in a large number of cases the latter undoubtedly arise by the division of a single original body. It is remarkable that division of the original centriole into two, which constitutes the initial step in mitosis, often takes place before completion of the preceding mitosis; the typical procedure, indeed, is its division *not later than the metaphase of the preceding mitosis* and sometimes much earlier.[2] In respect to the later stages we may distinguish two types as follows:

A. In one of these, well shown in the cleavage stages of *Ascaris* (Figs. 45, 48, 63), the formation of the new amphiaster is delayed until cell-division has been completed and the resting stage attained. In such cases the two centrioles, often surrounded by a centrosome or "attraction-sphere" and

[1] See p. 682.

[2] Striking examples of this are offered by the auxocytes of certain animals. In the primary spermatocytes of Lepidoptera and some other insects, for example, not only is the centriole double in the early prophases, but each half has already prepared for the second following mitosis by its double shape and structure. In prophases of the primary oöcytes of the snail *Arion* Lams ('10) found the centrioles already double and widely separated for the ensuing first polar mitosis, with each daughter-centriole also completely divided for the *second* polar mitosis.

sometimes by astral rays, continue to lie side by side during the vegetative phase of the daughter-cell. The ensuing division is initiated by a progressive separation of the centrioles, accompanied by the development of a small aster about each and of a *primary spindle* between them (Figs. 48, 63). As originally described by Van Beneden ('83, '87) and Boveri ('87, '07, etc.), this process takes place in the cytoplasm and the primary amphiaster is entirely extra-nuclear. In such cases the whole structure, at least in its earlier

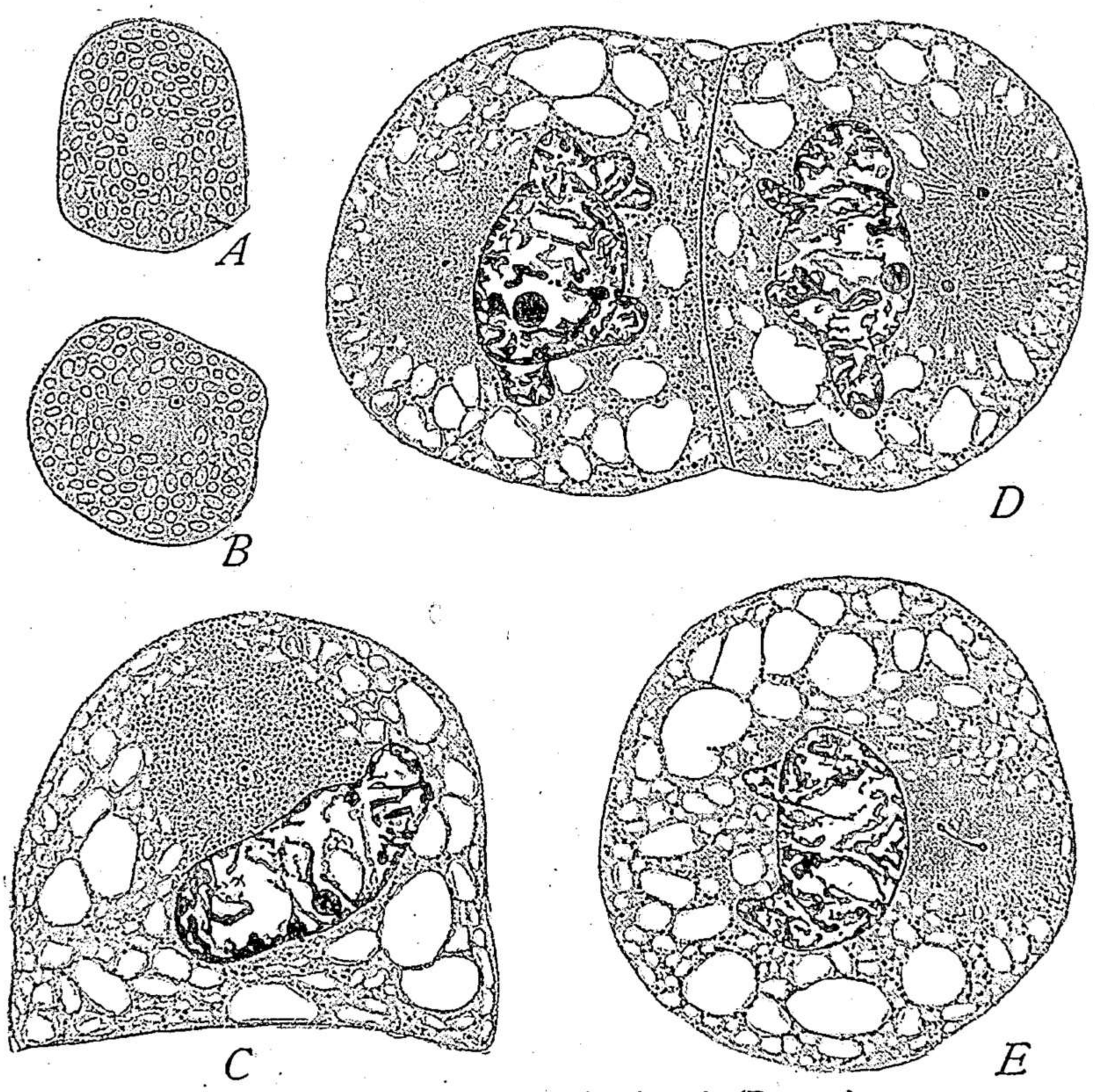


Fig. 63.—Central bodies in *Ascaris* (BOVERI).

A, *B*, early prophases of the spermatocytes; *C*–*E*, early prophases in 2-cell stage of cleavage.

stages, is undoubtedly of cytoplasmic origin. The nature of the primary spindle is, however, a difficult question. Heidenhain ('94) supposed it to arise from a specific substance surrounding the centrioles and forming between them a primary *centrodesmus*. Others have supposed it to arise from the substance of the centrioles, or from hyaloplasm flowing centrifugally from the centers in the region between them (Bonnevie, '10). Once formed the amphiaster rapidly enlarges by elongation of the spindle and extension of the astral rays; and at this time the crossing of the rays from the two astral systems in the equatorial plane outside the spindle is often conspicuously seen.

Where the outgrowing astral rays abut against the nuclear membrane the latter is often *pushed in or thrown into folds* (Fig. 239), a fact difficult to explain unless the rays are of considerable solidity and are actually growing. Sooner or later the wall of the nucleus liquefies and the astral rays grow actively into the interior, apparently by progressive differentiation out of the linin-network. The chromosomes are now quickly drawn upon the spindle, as if pulled into position by the action of the ingrowing astral rays with which they have come into attachment.

In this type of amphiaster-formation it seems clear: (1) that the fibers of the primary spindle may persist to form the continuous fibers of the definitive spindle; (2) that the chromosomal fibers, "traction-fibers," or half-spindle fibers likewise arise, in part at least, from astral rays that grow into the nucleus from outside; (3) that the primary spindle commonly persists as a *central spindle*, with the chromosomes lying in a ring about its equator, and with the half-spindle fibers, attached to the chromosomes, forming an investment of "mantle-fibers" on either side (p. 182).

In a second type the primary amphiaster arises at a much earlier period—already, indeed, during the anaphase or telophase of the preceding division. In such cases, common in the cleavage of the ovum (Figs. 47, 205, 322, 330), the centrioles separate and a new amphiaster forms at each pole of the spindle, inside the old centrosome and from its substance.[1] During this process the two centrioles usually move away from the original spindle-pole towards the periphery of the centrosome, now considerably enlarged, and may even pass outside it into the substance of the degenerating old aster. In the final telophase the two asters finally may pass to opposite poles of the reformed daughter-nucleus; and here the centrioles persist throughout the vegetative period of the cell. Meanwhile the primary spindle seems to disappear completely; though some observers have supposed that it may only have flattened out against the nuclear wall. The asters usually become much reduced or even disappear from view, but the centriole is usually surrounded by at least a portion of the centrosome, which forms the *sphere*.

During the ensuing prophases an aster redevelops about each centriole, the nuclear wall often being pushed in by the rays at each pole. At these two points the wall soon fades, and the ingrowing astral rays enter the nucleus, quickly invading the whole nuclear area and apparently growing at the expense of the linin-network. A new spindle is thus finally built up in

[1] *E. g.*, in *Salmo* (Henneguy, '91), *Thysanozoön* (Van der Stricht, '97), *Diaulula* (MacFarland, '97), *Thalassema* (Griffin '99), *Cerebratulus* (Coe, '99, Yatsu, '10), *Rhynchelmis* (Vejdovský and Mrazek, '03) or *Arion* (Lams, '10).

the nuclear area lying between the two centrioles, the chromosomes being from the first in intimate relation with it. In this case, accordingly, continuous fibers and half-spindle fibers are intermingled, and no central spindle can be distinguished as such. The two foregoing types, are connected by many intermediate gradations due to variations in the time of amphiaster-formation.

The inpushing of the nuclear membrane by the ingrowing astral rays, has been described in many different objects and by many observers who have found (*i. e.*, Van der Stricht, '95, Griffin, '99) that dissolution of the membrane begins at the points most deeply infolded. In certain cases the inpushing fibrillæ seem actually to compress the entire nucleus lying between the bases of the two astral cones and in such cases almost the entire spindle would seem to be of cytoplasmic origin (Vejdovský, '88, Vejdovský and Mrazek, '93). Other observers (Watase, '93) have concluded, on the other hand, that the nuclear wall is penetrated by the ingrowing rays, which then push the whole contents of the nucleus before them as they grow.

Among the many modifications of the foregoing types there are two of especial interest. The fact has earlier been mentioned (p. 29) that in certain cases the division-centers are intra-nuclear and at least the early stages of amphiaster-formation take place within the nucleus. Intra-nuclear centers are common among the Protozoa, though nearly all of these cases are of the anastral type (p. 204); in Metazoa they are of rare occurrence. In the spermatocytes of *Ascaris megalocephala univalens* the primary amphiaster is intra-nuclear, the central bodies only passing out into the protoplasm near the time of the metaphase (Fig. 323).[1] A somewhat similar case is described by Hegner ('08) in the oöcytes of the copepod, *Canthocamptus*. Again, in the oöcytes of the platode *Thysanzoön*, Schockært ('01) describes a remarkable intra-cellular division-center of elongate spindle-shape, which divides into two within the nucleus, the products passing to opposite poles of the germinal vesicle, shortening to a spheroidal form, and becoming the center of two conspicuous protoplasmic asters. These results, in general, are in agreement with earlier conclusions of Van der Stricht ('98) and are substantially confirmed by Kaltenbach ('15).[2] It is a surprising fact that an amphiaster may be formed synthetically by the secondary union or association of two asters or centers originally separate. Apparently no doubt concerning the fact can exist in the case of triasters or tetrasters in double-fertilized eggs (Fig. 79), where one or two of

[1] It is remarkable that in *A. megalocephala* var. *bivalens* the division-centers are extra-nuclear (Hertwig, Boveri, etc.).

[2] A number of others have reached more or less similar conclusions, *e. g.*, Julin ('93) in the spermatocytes of *Styleopsis*, Rückert ('94) in the eggs of *Cyclops*, Mathews ('95) in those of *Asterias;* but outside of the Protozoa none of these are as well substantiated as the foregoing.

the spindles, though indistinguishable from the others, must have had centers of different parental origin.

B. Anastral Types of Mitosis

As far as the history of the chromosomes is concerned the anastral types of mitosis (excepting for the moment those of Protozoa) do not differ in any important way from the amphiastral. The two types differ remarkably, however, in respect to both the structure and the mode of formation of the achromatic figure and often also in the mode of division of the protoplasmic cell-body; for the anastral spindle is not ordinarily formed between two definite focal points and is devoid of central bodies, and division of the cell-body typically does not take place by constriction but by the formation of a cell-plate (p. 159).

Anastral forms of mitosis are of common occurrence among Protista, including both unicellular plants and animals (p. 201). In Metazoa they seem to occur only in the maturation-divisions of the ovum (p. 508). In plants, on the other hand, they are of widespread occurrence and with few exceptions are characteristic of the vegetative divisions in the cormophytes from the bryophytes upwards.

In the seed-plants a number of the earlier observers, particularly Guignard ('91) believed that definite "centrosomes" could be demonstrated at the poles of the spindles and that the spindle-formation was initiated by their division. This result was, however, proved to be erroneous by the work particularly of Belajeff and his followers. It is, however, a very interesting fact that in *Ginkgo* and the cycads (*Cycas*, *Zamia*, etc.) and in some at least of the pteridophytes and bryophytes, the final or semi-final gamete-producing divisions of the male are characterized by the presence of conspicuous asters with central bodies known as *blepharoplasts*, because of their relation to the formation of cilia or flagella (p. 387).

Important questions concerning the nature and origin of anastral spindles have been raised by some of the latest studies in this field.[1] According to most of the current accounts the anastral spindles of higher plants and animals seem to be of two widely different types. The simpler of these occurs in the oöcytes of certain animals (Figs. 238, 243) *and arise wholly from the nucleus*, which is drawn out as a whole to form the spindle, without visible participation of the cytoplasm. The spindle-fibers here seem to arise by a direct transformation of the linin-network, and never to converge to definite foci at the poles as is the case in the amphiastral type.

By some of the earlier observers the absence of asters and centers in these cases was ascribed to defective fixation; but this seems to be excluded

[1] See especially Devisé, '21.

by the fact that the same preparations show conspicuous sperm-centers surrounded by sharply marked astral rays and central bodies.[2] During the cleavage of these forms asters and centers are always present; but here too the spindle seems to be largely of nuclear origin, as in the second

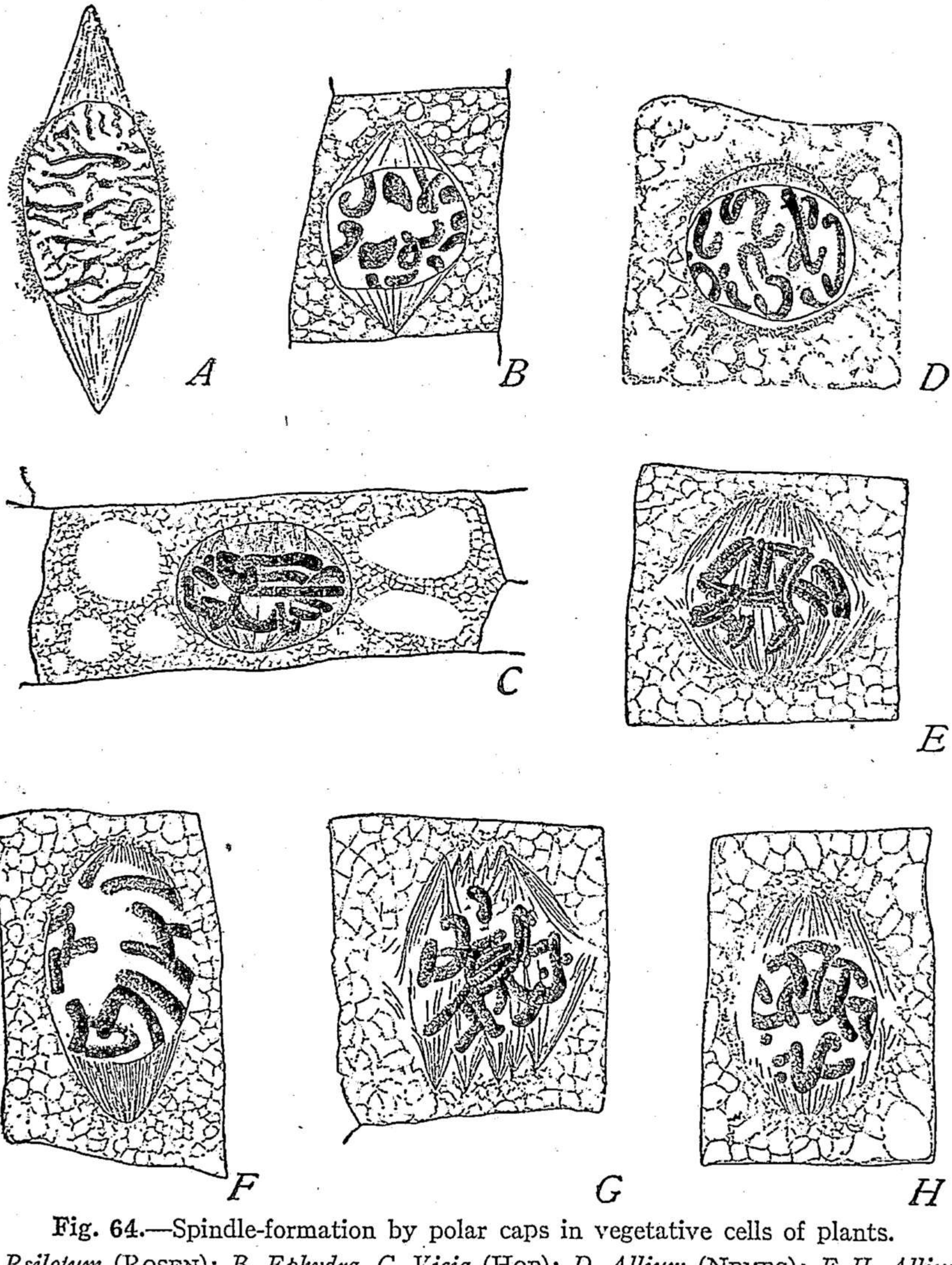


Fig. 64.—Spindle-formation by polar caps in vegetative cells of plants.

A, in *Psilotum* (ROSEN); *B*, *Ephydra*, *C*, *Vicia* (HOF); *D*, *Allium* (NEMEC); *E–H*, *Allium* (MC. COMB); *C* and *G* are multipolar diarch spindles.

or sea-urchin type, as above described (p. 146). When we consider that in lower forms generally (sponges, cœlenterates, platodes, annelids, mollusks or echinoderms) the maturation-spindles of the oöcytes are of typical amphiastral type, with conspicuous asters and centers, it seems probable

[2] *Cf.* Hill, '95, Conklin, '05[a] etc.

that the anastral spindles here in question have resulted from the disappearance of centers and asters that were present in the ancestral forms, the spindle-formation remaining in the main of similar type but simplified by loss of the central structures originally present at the poles.

The second, and more complicated type of anastral spindle is that found in the vegetative and spore-forming divisions of cormophytic plants. According to nearly all existing accounts these are in large part formed from

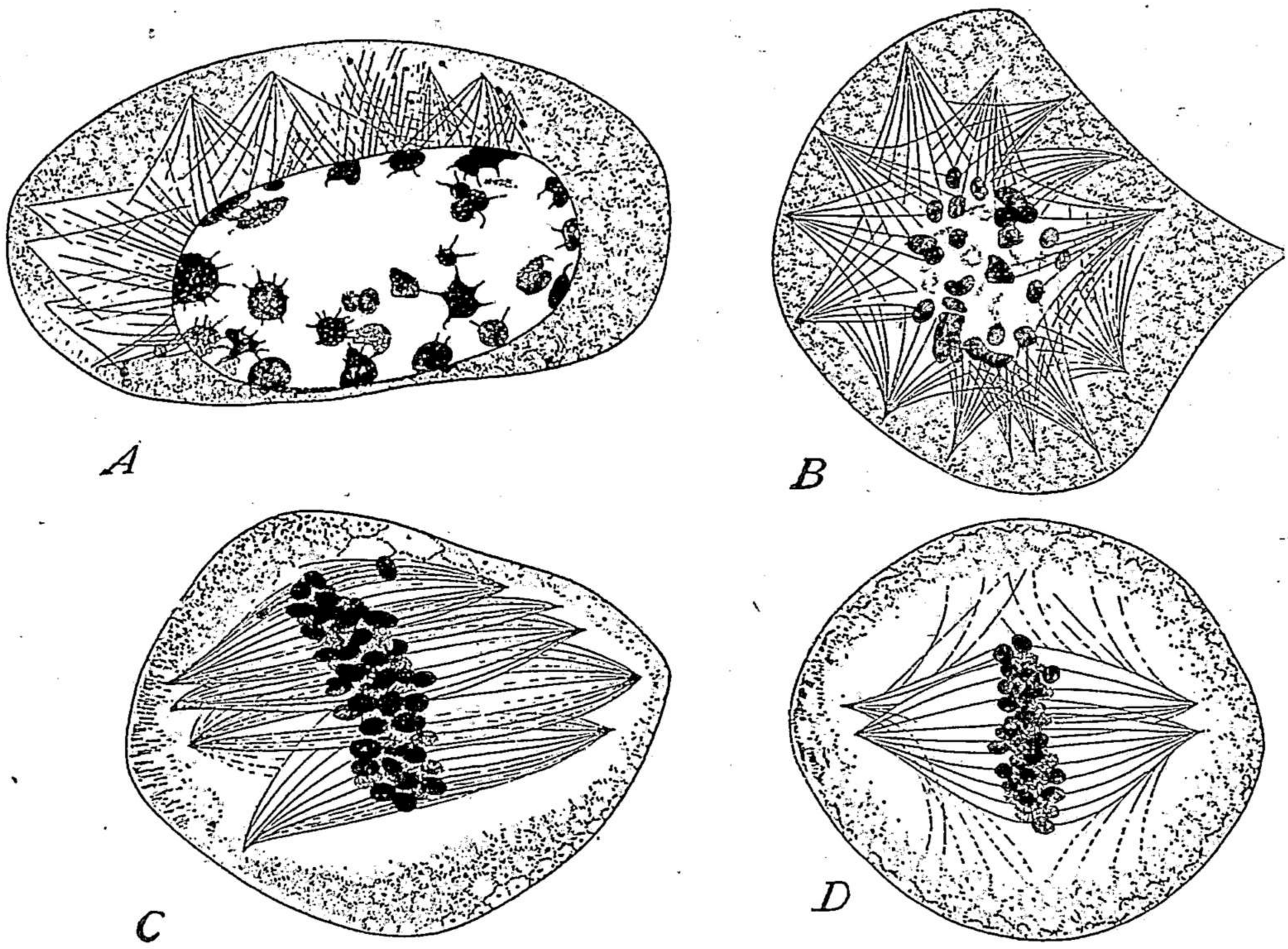


Fig. 65.—Division of spore-mother cells in *Equisetum*, showing anastral multipolar spindle-formation (OSTERHOUT).

A, early prophase, "kinoplasmic" fibrillæ in the cytoplasm; *B*, multipolar fibrillar figure invading the nuclear area, after disappearance of the nuclear membrane; *C*, multipolar spindle: *D*, quadripolar spindle which finally condenses into a bipolar one.

the cytoplasm immediately surrounding the nucleus by a process that seems to have little definite relation to that seen in the first or intra-nuclear type. In respect to their mode of origin they are of two principal types, namely, those that are always *bipolar* and those that are at a certain stage *multipolar*. The latter, in turn, were distinguished by Strasburger ('00) as multipolar *diarchal* and multipolar *polyarchal*, the former showing more or less clearly a bipolar condition from the beginning, while the latter show at the start no trace of bipolarity (Figs. 65, 66). All these various conditions lead to the same final result, a spindle that is strictly bipolar

but devoid of sharply marked polar foci and of definite asters such as are seen in the amphiastral type, though cytoplasmic strands often radiate irregularly from the poles. The simpler or bipolar type is characteristic in general of the vegetative divisions of the higher plants (Fig. 64), the multipolar of the spore-forming divisions.

In all these cases the spindle is said to arise from accumulations of fibrillar cytoplasm or *kinoplasm* near the nuclear wall. In the strictly bipolar forms characteristic of the vegetative mitoses these accumulations are first found at opposite poles of the nucleus, forming the so-called polar or kinoplasmic caps.[1] At first consisting of hyaline cytoplasm (kinoplasm), they later become fibrillar, forming two cones with their bases against the nuclear poles; and as the nuclear membrane disappears invade the nuclear cavity and come into relation with the chromosomes. The two polar caps thus finally give rise to an anastral spindle, often rather sharply pointed but sometimes truncated, in either case devoid of definite central bodies or asters. There is no evidence that the polar caps arise by the division of a single body; nevertheless it is not impossible that they arise from material which originally forms a single mass and later segregates into two polar masses, as is suggested by the facts in certain Protozoa (p. 208).

In the multipolar spindle-formation characteristic of the spore-forming divisions of higher plants [2] the process begins with the appearance of a perinuclear zone of "kinoplasm" which from an early period has a fibrillar structure, the fibrillæ being sometimes at first disposed more or less radially about the nucleus (Figs. 65, 66). Very soon they become contorted and closely aggregated to form a felt-like web closely surrounding the nucleus; and from this the fibrillæ are later drawn out into a variable number of irregular cone-like projections. In the diarchal forms these are from the first more or less polarized, in the polyarch quite irregular. Upon dissolution of the nuclear membrane the fibrillæ quickly invade the nuclear area and thus give rise to the "multipolar spindle." The cones now diminish in number, apparently by progressive fusion, until a bipolar spindle is formed of the same general type as that derived from polar caps.

From an early period considerable differences of opinion existed concerning the origin of the spindle-material. By a considerable group of observers, headed by Strasburger ('95, '00, '08) the spindle was supposed to be derived very largely, if not exclusively from the peri-nuclear cyto-

[1] These were first described by Rosen ('95), Nemec ('97), Juel ('98, '99), later by many others.

[2] This mode of spindle-formation was first carefully studied and figured in the pollen-mother-cells of *Larix* by Belajeff ('94), in *Lilium* by Farmer ('93, '95) and Strasburger ('95), in *Hemerocallis* by Juel ('97), in *Lilium*, by Sargent ('97), and Mottier ('97) and in *Equisetum* (Osterhout, '97); also in the vegetative cells of *Chara* (Debski, '98). The results have repeatedly been confirmed by later observers. Literature in Allen ('03), Davis ('04), Farmer and Digby ('10), Devisé ('12), Overton ('22) etc.

plasm; but others urged that the linin-network also contributes to its formation. For example, Lawson ('98, '00, '03) found in *Cobæa*, *Hedera*, *Gladiolus*, and other forms that the spindle is almost wholly of protoplasmic origin; while the observations of Williams ('99) on *Passiflora* indicated that it receives a large contribution from the linin-network. Still other observers found the spindle to be completely intra-nuclear in origin, *e. g.*, in the early cleavage of the ovum and in the division of the pollen-nuclei in gymnosperms. [1] Such divergences seemed hard to reconcile, but it should

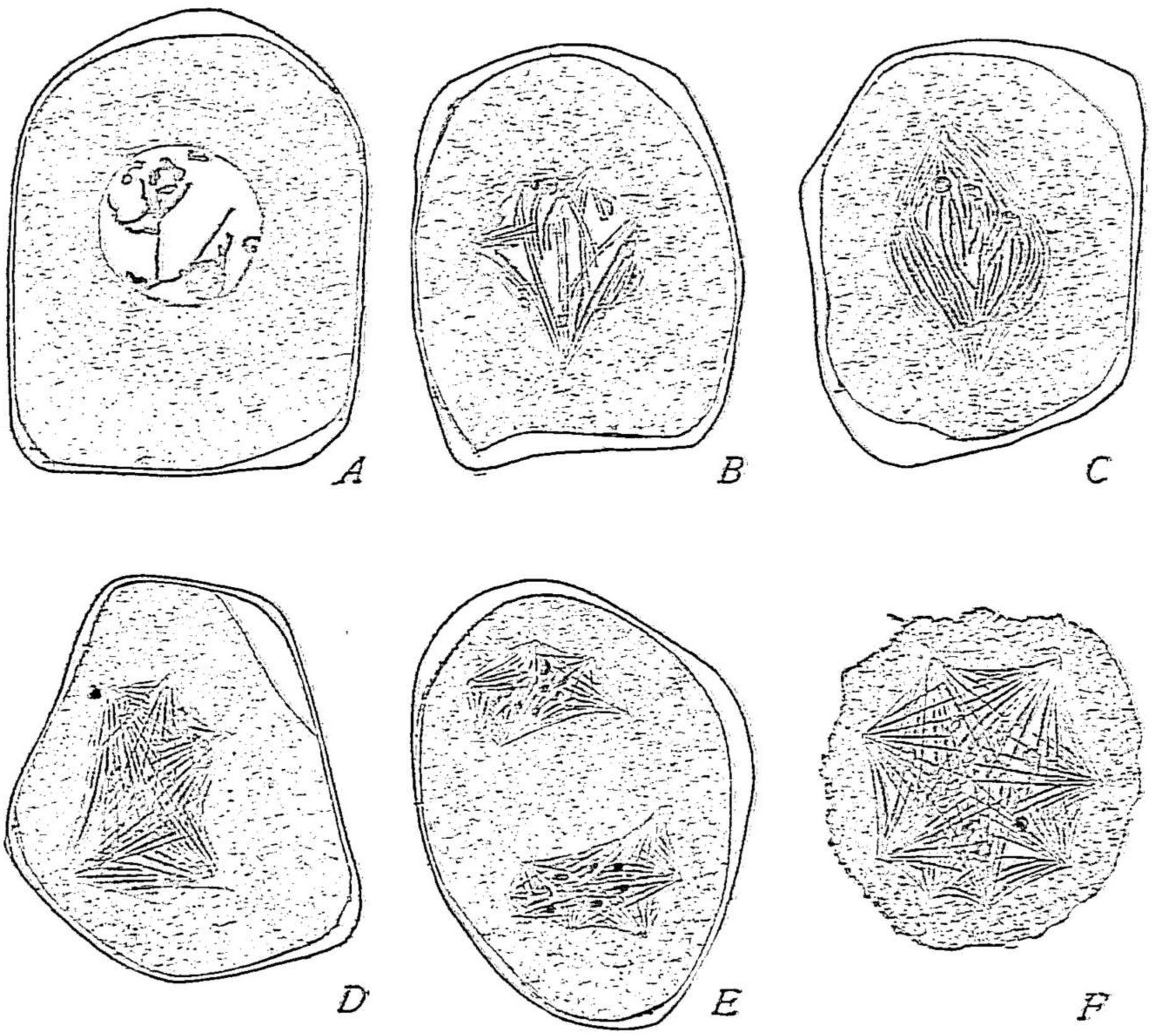


Fig. 66.—Multipolar spindle-formation in pollen-mother-cells of *Cassia* (Hus).

A, appearance of perinuclear zone of "kinoplasm"; *B–D*, various conditions seen in prophase; *E*, multipolar diarch spindles, prophases of second division; *F*, multipolar polyarch spindle.

be recalled that in the amphiastral types, too, the spindle undoubtedly may be either intra-nuclear or extra-nuclear in origin, though the mechanism is here widely different (p. 148).

The whole question is placed in a new light by the recent work of Devisé ('21) from Grégoire's laboratory. These studies were made on the microsporocytes of the larch, *Larix*, the remarkable fine object on which Belajeff's conclusions were originally based, and by the use of the modern

[1] See Chamberlain, '97, Ikeno, '98, Murrill, '00, Ferguson, '01, Webber, '01, Coker, '03.

technique for demonstration of the chondriosomes. The results seem to show that the spindle is in reality strictly intra-nuclear in origin, the so-called multipolar spindle and the perinuclear feltwork and radial stage that precede it being artifacts produced by the destructive action of acetic acid in the reagents (Flemming's fluid) formerly employed. When properly fixed and stained (Benda's method) cells in the "resting" or vegetative stage are found to contain numerous scattered chondrioconts and in the early prophases these become radially disposed, later closely crowded and more or less contorted to form the perinuclear layer or "feltwork" (Fig. 67), which is visible as a granular zone in the living cell. In this

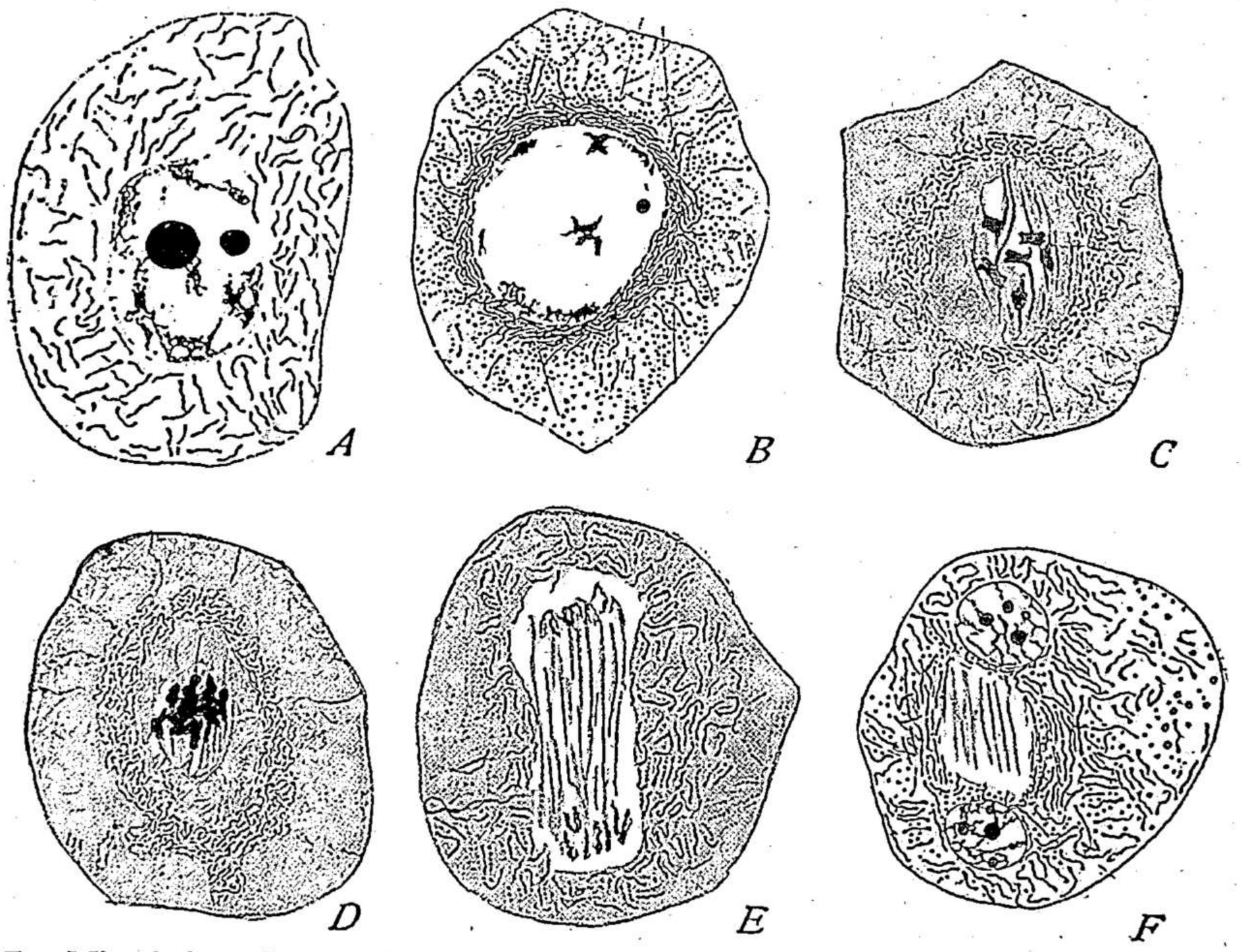


Fig. 67.—Mitosis in pollen mother-cells (primary sporocytes), of the larch, *Larix*, after Benda's fixation for chondriosomes (DEVISÉ).

A, beginning of the prophase, scattered chondrioconts; *B*, perinuclear felt-work of chondrioconts; *C*, disappearance of nuclear membrane, diarch spindle forming in central nuclear area; *D*, later stage of same; *E*, anaphase; *F*, late telophase (second division).

position the chondriocont-layer remains throughout all the succeeding stages of spindle-formation but taking no part in it. Collapse of the nucleus is followed by a concentration of the chromosomes towards the center of the nuclear area, the peripheral part of which forms a clear zone of linin limited externally by the chondriocont layer. Inside the latter, and quite separate from it, is formed the spindle, bipolar from the first, and closely associated with the chromosomes; and during the telophases the chondrioconts, or their products, become again dispersed through the cytosome. In the control material, fixed by Flemming's fluid, the chondrioconts fail

to appear, but the multipolar spindles are shown as described by earlier observers. The observations of Nassonoff (p. 163) on chondriokinesis suggest a possibility that even the polar caps in the vegetative division of plants may represent the disorganized remains of chondriosomes at the poles of the nucleus.

These results must await confirmation by other observers before they can be unreservedly accepted. If well founded they go far towards reconciling the strange mode of mitosis seen in the so-called multipolar spindle-formation with the simpler type that appears in the anastral spindles of the animal ovum, as above described. For all the facts would fall into line under the assumption that in all the higher plants the spindle is intra-nuclear in origin and that the centers and asters, present in lower plants (p. 199), have disappeared, precisely as in case of certain animal ova. What has determined this is unknown. We are tempted to the conjecture that it may be correlated with the more extensive development of the cell-walls and a consequent general substitution of cell-plate formation (p. 159) for constriction in cleavage of the cell-body; but this suggestion is not supported by the anastral polar spindles of the animal egg, which seem to lead to division by constriction. That the anastral type in higher plants has been determined by some such condition is, however, supported by the presence of asters and central bodies (blepharoplasts) in the microgamete-producing mitoses. The central bodies seem here to have been retained because of the part which they play in forming the locomotor apparatus of the spermatozoids (p. 387); and this is supported by the fact that in the higher seed-plants (higher gymnosperms, angiosperms), where motile microgametes are absent, both blepharoplasts and asters are likewise absent. In their relation to the locomotor apparatus (flagella, etc.) the blepharoplasts of plants are obviously closely analogous to those of the sperm-forming cells in animals, and of the flagellated cells of sponges, both of which are known to be identical with centrioles; and the same is true, in many cases, of the blepharoplasts of the flagellated Protozoa which may very well represent the most primitive condition (*cf.* pp. 690, 696). It seems, accordingly, reasonable to assume that the presence of asters and blepharoplasts in the gamete-forming divisions represents the primitive amphiastral mode of mitosis that still exists in many thallophytes, and has persisted in the sperm-producing divisions because of a specific physiological motive. The possibility remains that although true asters seem to have disappeared in the higher plants central bodies may still be present, perhaps very small, so as to have been overlooked, or intra-nuclear in position as is the case in some Protista.

C. Cleavage. Division of the Cytosome

Superficially regarded the process of cytoplasmic division or cleavage of the cell-body offers a much simpler aspect than that of nuclear division; but this appearance may be deceptive. In the main it appears as a mass-division of the cytoplasmic substance; but it is important to bear in mind that the division is often unequal and that it is often accompanied or preceded by the separate division of individual structural elements, such as plastids, centrioles, flagella, and perhaps also of chrondriosomes and other structures. The fact remains that cytoplasmic cleavage is on the whole effected without any systematic general resolution of the cytosome into separately dividing elements comparable to the spireme-threads and chromosomes of the nucleus.

Cleavage is of two types or modes, entirely different in general aspect, namely: by *furrowing* or *constriction*, and by the formation of a *cell-plate*. The first is on the whole characteristic of the amphiastral type of mitosis, the second of the anastral; but there are some exceptions to this and there are also certain conditions intermediate between the two types. Broadly speaking, cleavage by constriction is characteristic of mitosis in higher animals, and cell-plate formation of higher plants. In both cases cleavage takes place in a plane approximately at right angles to the spindle-axis, and primarily across its equatorial plane.

1. Cleavage by Constriction or Furrowing

This mode of cleavage has given rise to many speculations concerning the possible function of the astral rays in mitosis. It is important, therefore, to bear in mind the fact that in some cases constriction occurs in division of the anastral type, as was first noted by Guignard ('97) in the pollen-forming divisions of various dicotyledonous plants; this process has recently been studied with care in the magnolia by Farr ('18).

Cleavage by constriction appears already in the one-celled organisms, both plant and animal, but is studied to greatest advantage in the cells of higher animals and particularly in the cleavage of the animal ovum. It is preceded by a progressive elongation known as the *karyokinetic elongation*, during which the cell, at first typically spheroidal, assumes the form of a prolate spheroid, the long axis of which coincides with (or is parallel to) that of the spindle. This constitutes the *karyokinetic axis;* and across it the cleavage-furrow typically cuts at right angles. The karyokinetic elongation first becomes clearly marked during the anaphases and reaches its climax in the telophase, just before the cell divides.[1] A furrow now makes its

[1] This is clearly shown in the photographs of the author's *Atlas of Fertilization and Karyokinesis* (Wilson, '95); see also '96.

appearance at the periphery, opposite the equator of the spindle and vertical to its long axis, and then progressively deepens until it cuts through the entire cell.

When the spindle-axis lies eccentrically the furrow always first appears on that side of the cell nearest the spindle, and progressively extends itself thence around the periphery to the opposite point (Fig. 47). An extreme case of this is seen in the ctenophore-egg (Fig. 83) where the constriction starts from one pole and travels thence downwards completely through the egg, without the appearance of any furrow at the opposite pole.

The process of constriction is preceded and accompanied by a change of surface-tension at the periphery of the egg that undoubtedly plays an important part in the process of division and may be its immediate cause. All the facts indicate that this change is a relative increase in the equatorial region and a corresponding decrease towards the poles. Evidence of this latter change is the fact that in many cases the polar region shows an outward bulging to form a more or less pronounced lobe, or even a group of lobes, which in some cases give this region an almost amœboid aspect (Figs. 68, 69).[1] To this point we shall return (p. 195). The region of the equatorial furrow is itself often marked out by an accumulation of the peripheral hyaloplasm, sometimes called the "cleavage-head" which in the ctenophore-egg persists during the whole process and travels steadily downward through the egg as the cleavage advances.[2] Even before the furrow actually appears the future cleavage-plane is often clearly foreshadowed by a peculiar structural modification of the protoplasm in the equatorial plane called the *diastem*, commonly a narrow, more lightly staining zone composed of larger alveoli (*e. g.*, in *Crepidula*, Conklin, '02) or in some cases of vacuoles; examples of the latter case have been described especially in lower plants.[3] Cleavage is also preceded and accompanied by vortical streaming movements of the peripheral protoplasm (p. 194).

As the cleavage-furrow advances towards the center of the cell the spindle is usually constricted at its middle point and thus often assumes an hour-glass shape (Fig. 62). When the furrow advances more rapidly from one side the center of the spindle is often bent more or less sharply at this point; but this result is clearly not due merely to the advance of the furrow but also to telokinetic movements of the asters (or spheres) and daughter-nuclei towards the surface (Fig. 62). These movements, which have been studied

[1] The polar bulging was described and figured by Van Beneden ('83) in the *Ascaris* egg; and later by several other observers. See Conklin, '02, '12, Vejdovský, '11–'12, Bowen, '20, etc. Conklin found that in certain cases the polar lobe may be seen even in the resting cell, foreshadowing the future spindle-axis.

[2] Ziegler, '98, Rhumbler, '99.

[3] See, for instance, Harper, '99, on *Synchytrium*, and other fungi, Swingle, '09, in *Phycomyces*. See also Rhumbler, '96, '03, Kostanecki, A. M. A. X.

with especial care by Conklin ('02), probably form part of the more general vortical movement of the protoplasm referred to above, and hence probably are traceable likewise to the equatorial increase of surface-tension at this time.

In or around the narrow neck formed by constriction of the spindle usually appear a series of granules, formed by thickening of the spindle-fibers in the equatorial plane and constituting the so-called *mid-body* (Fig. 50). In animals the mid-body is small and inconspicuous and offers the aspect of a vestigial structure which seems to play no active part in the division. In the end it usually becomes condensed into a single deeply staining body lying between the two cells after the cleavage-furrow has cut completely through. In many cases this body seems to disappear completely; in others it may persist for a considerable time at the boundary between the two cells, sometimes having the form of a very definite, deeply staining ring. The spindle itself usually disappears entirely; but in some cases it breaks down into a granular, often deeply staining mass, which persists for a considerable time and often forms a bridge between the daughter-cells. This body, known as the *spindle-remains* or *mitosome*, often persists to form a permanent protoplasmic connection between the daughter-cells. The best examples of this have been described in the germ-cells, *e. g.*, in the spermatogonia of Amphibia (Fig. 7), or in the nurse-cells of various insects, which thus remain in connection with the oöcyte (Fig. 155). In some of these cases the mid-body also persists for a considerable time in the form of a deeply staining ring lying between the sister-cells and traversed by the spindle-remains. A striking example of this is described by Mrázek in the spermatogonia of Lepidoptera.

Since the equatorial furrow or constriction always appears between two asters, whether in bipolar or in multipolar mitosis, and since the position of the asters (and hence of the furrows) may be artificially shifted by mechanical deformation of the cell (*e. g.*, by pressure), nearly all theories of mitosis have assumed that the astral rays play some definite rôle in the production of the furrow. It is therefore of interest that cleavage may take place by constriction in cells which divide without either asters or central bodies, (p. 157). It nevertheless remains probable that the astral rays, when present, may be concerned in causing an equatorial increase of surface-tension (p. 192).

2. Cleavage by Cell-Plate Formation. The Phragmoplast

This type of cleavage was first observed and carefully studied by Strasburger ('75, '80) in the cells of higher plants and since investigated by numerous observers. With few exceptions these cells (typically surrounded

by firm cellulose walls) divide without the appearance of an equatorial furrow, by the formation of a protoplasmic partition-wall or *cell-plate*, which first appears in the equatorial plane of the spindle and extends itself thence completely across the cell at right angles to the spindle-axis. The cell-plate appears at first to be single, but sooner or later (often before it has reached the cell-periphery) splits into two parallel plates between which appears a new cell-wall which extends across the whole cell and thus cuts it in two.

The origin of the cell-plate is now generally agreed to be essentially as described by Strasburger ('88, '98), Timberlake ('00), and Allen ('01) by

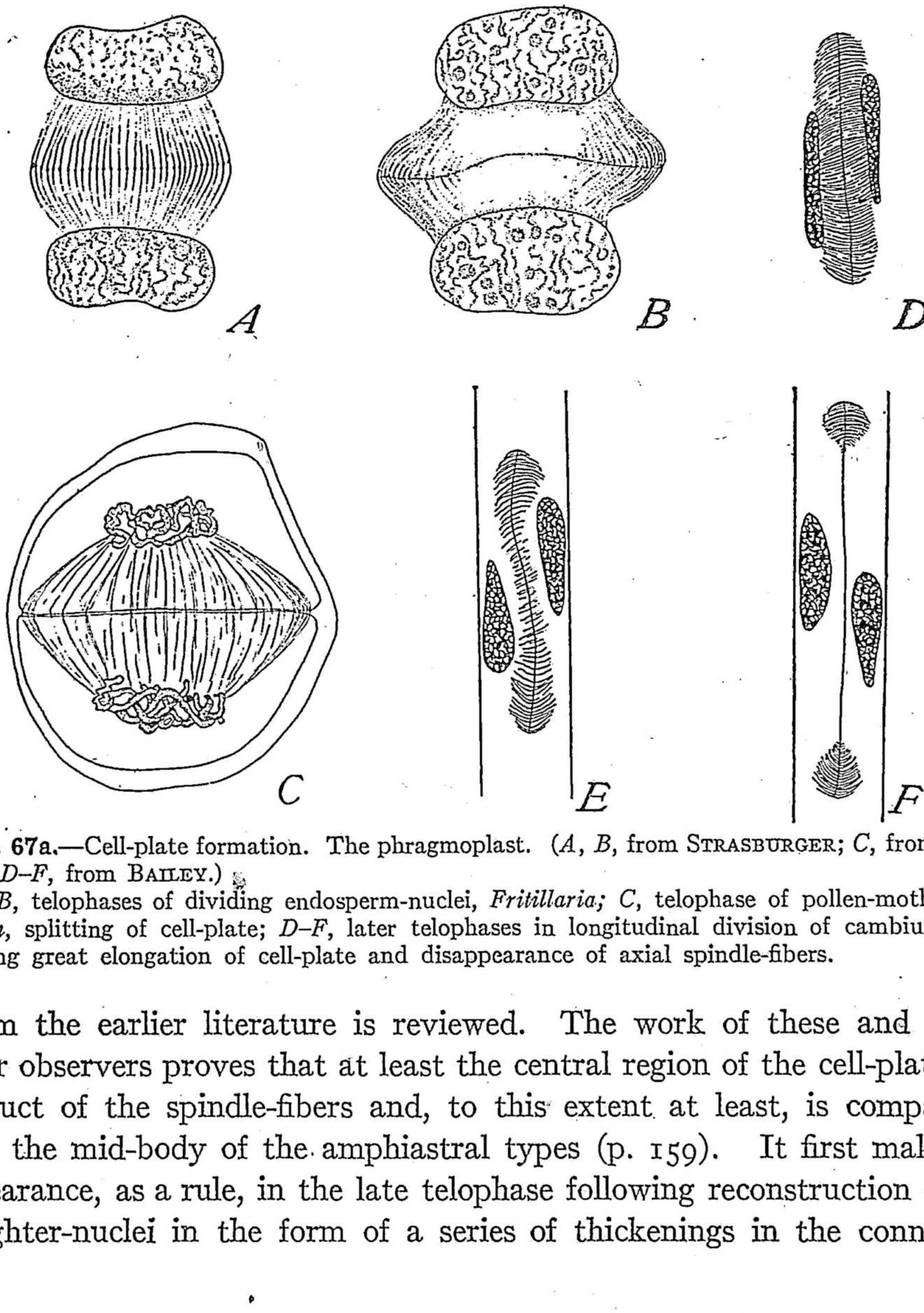


Fig. 67a.—Cell-plate formation. The phragmoplast. (*A*, *B*, from STRASBURGER; *C*, from MOTTIER; *D–F*, from BAILEY.)

A, *B*, telophases of dividing endosperm-nuclei, *Fritillaria;* *C*, telophase of pollen-mother-cell; *Lilium*, splitting of cell-plate; *D–F*, later telophases in longitudinal division of cambium-cells, showing great elongation of cell-plate and disappearance of axial spindle-fibers.

whom the earlier literature is reviewed. The work of these and many other observers proves that at least the central region of the cell-plate is a product of the spindle-fibers and, to this extent at least, is comparable with the mid-body of the amphiastral types (p. 159). It first makes its appearance, as a rule, in the late telophase following reconstruction of the daughter-nuclei in the form of a series of thickenings in the connecting

fibrillæ of the spindle in the equatorial plane (Fig. 67a). At this time the spindle becomes convex in the equatorial region so as to assume more or less of a barrel-shape in which condition it is often called the *phragmoplast*. In later stages the phragmoplast undergoes further lateral extension, apparently by the continual addition of new fibers outside the limits of the original spindle, until it extends completely across the cell in the equatorial plane. The equatorial thickenings of the fibers, at first separate and confined to the axial region of the spindle, extend progressively as the phragmoplast widens, and finally reach the periphery. At the same time they fuse to form a continuous cell-plate, a process which begins in the axial region, before the phragmoplast has reached the periphery, but finally extends across the whole cell. Meanwhile the spindle-fibers begin to disorganize and finally disappear; and this process, too, commonly begins in the axial region and often long before the cell-plate has reached the periphery, while the more peripheral fibers are still intact. This fact is remarkably shown in much elongated cells, as in the cambium, which divide lengthwise. Here the phragmoplast is seen as a continuous plate extending lengthwise for a long distance between the fully formed daughter-nuclei, and with a group of curved fibers at either end (Fig. 67a, D-F) by which the cell-plate is continually extended at its free margins until it finally cuts completely through the cell.[1]

Sooner or later the cell-plate splits into two layers between which a new cell-wall is laid down. It is an interesting fact, described already by the earlier observers (Treub, '78) that this process begins in some cases before the cell-plate has extended completely across the cell. It was believed by Strasburger that the separate spindle-thickenings might divide separately before fusing to form a continuous structure; but later observers have failed to confirm this (see Timberlake, '00).

The cell-wall first appears as a very delicate continuous layer between the two layers into which the cell-plate splits, and according to Allen ('01) is itself at first double. The wall thus formed becomes the middle lamella of the definitive wall, and is composed of pectose, while the two halves of the cell-plate itself form the plasma-membrane on each side.[2] Subsequently additional layers, consisting largely of cellulose, are laid down on each side of the middle lamella to form the secondary and tertiary thickenings of the wall (p. 56).

The process just described seems to have little in common with cleavage by constriction; but the gap seems to be partially bridged by conditions seen in some of the green algæ (*Spirogyra*, *Cladophora*, *Closterium*), where formation of the cell-wall proceeds centripetally in the form of a ring-like

[1] See especially Bailey, '19, '20; also Sharp '11.

[2] Treub ('78), Strasburger ('98), etc.

ingrowth from the lateral walls towards the center. This involves a corresponding infolding of the plasma-membrane which may be considered as a process of constriction and is possibly the cause rather than the result of the ingrowth of the wall.

3. Meristic Division and Segregation in the Cytosome

As earlier indicated (p. 116), mitotic division of the nucleus is essentially meristic, *i. e.*, is not merely a mass-division but one that affects every part of its substance and is always equal, in both respects offering superficially a striking contrast to cleavage of the cytosome, which has the general aspect of a mass division, and one that may show all degrees of inequality. Nevertheless the cytosome may contain differentiated smaller bodies, such as the plastids, that multiply by division; and evidence has accumulated to show that other formed elements are distributed in more or less definitely ordered fashion to the daughter-cells, and may have similar powers of division. The clearest case of this is offered by the centrioles, as earlier described (p. 120), and further possibilities are opened by the behavior during division of the plastids, chondriosomes and Golgi-bodies. It thus becomes possible that the contrast between nucleus and cytosome in respect to mode of division is not in fact as great as it superficially appears; and that cytoplasmic division, too, may at bottom be a meristic process (p. 720).

a. Plastids. In higher plants generally, where the plastids are numerous, the division of these bodies is not known to be accompanied by any definite apparatus of distribution to the daughter-cells, though the distribution appears to be on the whole approximately equal. In this respect these plastids might be compared with the more diffuse types of chondriosomes and Golgi-bodies, considered in the following sections. In lower plants, on the other hand, where the plastids are few in number, a definite correlation often exists between their division and that of the cell as a whole. This commonly occurs among the simple algæ, for example in *Coleochæte*, in which each cell contains a single plastid (Allen, '05), or *Zygnema* in which two are present (Kursanow, '11), and the same is true in some of the mosses as shown by Davis ('99), Scherrer ('14) and Sapĕhin ('15). These facts strikingly illustrate how the division and segregation of purely cytoplasmic formed elements may be synchronized with that of the nucleus and cytoplasm as a whole; and they perhaps indicate that the loss of such coördination in higher forms may represent a secondary condition. Too little is known of this subject, however, to warrant any very far-reaching conclusions. In this direction broader aspects are opened by the chondriosomes (of which plastids may be derivatives, p. 709) and the Golgi-bodies.

b. Chondriokinesis. Benda and his successors emphasized the fact that the chondriosomes are distributed to the daughter-cells with approximate equality, and raised the question whether this process may not be regarded as a final stage in their division. Opinion concerning this question is still divided; and the most careful studies seem to show that wide differences exist between different species in respect to the precision and orderliness of the distribution. In this regard numerous gradations exist, beginning with a condition in which the chondriosomes show no definite orientation in respect to the centers or the spindle-poles and seem to be segregated into two groups passively, without themselves undergoing division during mitosis. Examples of this are offered by the dividing germ-cells of vertebrates, [1] by the cleavage-stages of the ovum, and by many forms of tissue-cells in both plants and animals. In such cases (as often in the division of plastids) there is almost no evidence of definite relation between the division of chondriosomes and that of the nucleus and cytosome as a whole. A good example of this is seen in the spermatocyte-divisions of certain scorpions (*Opisthacanthus*, *Vejovis*, *Hadrurus*) in which the chondriosomes, at first small and numerous, finally condense into a definite number of separate spheroidal chondriosomes, which certainly do not divide but are merely segregated passively into two nearly equal groups. In *Opisthacanthus*, where the number of chrondriospheres is 24 (each secondary spermatocyte receiving 12 and each spermatid 6), the writer ('16) found exact equality of distribution in about 75% out of 200 cases, about 25% having one more or fewer than the expected number (6) (Fig. 168).

In the spermatocytes of *Ascaris*, as described by Hirschler ('13) the numerous slightly elongated chondriosomes show a distinct orientation towards the centrioles, but are not known to divide. In the vegetative divisions of seed-plants (*Vicia*) as described by Nassonov ('18) the chondriosomes (in the form of thick chondrioconts) become segregated, but without evidence of division, into two very definite groups at opposite poles of the nucleus already in the thick spireme-stage and apparently before the nuclear wall breaks down or the spindle is formed. This is an interesting case, since no central bodies or asters are present; but the spindle is said to arise from polar caps (p. 153) about which the chondriosomes aggregate. In none of the foregoing cases is there satisfactory evidence of actual division of the individual chondriosomes. On the other hand, Fauré-Fremiet ('10) produced evidence that in ciliates the numerous scattered mitochondria divide synchronously with the nucleus (Fig. 346[a]).

The transitional conditions from the foregoing type of process to those in which the chondriosomes are actually cut in two during mitosis are most

[1] *Cf.* Benda ('03), or Duesberg ('10) on mammals.

clearly shown in the dividing germ-cells, especially the spermatocytes, which in general show in this respect more highly specialized conditions than either the gonia or the somatic cells. In many of the insects the chondriosomes have the form of numerous elongate rods or threads (chondrioconts) which already in the prophases show a definite orientation with respect to the centers [1] and in the metaphase are placed parallel to the

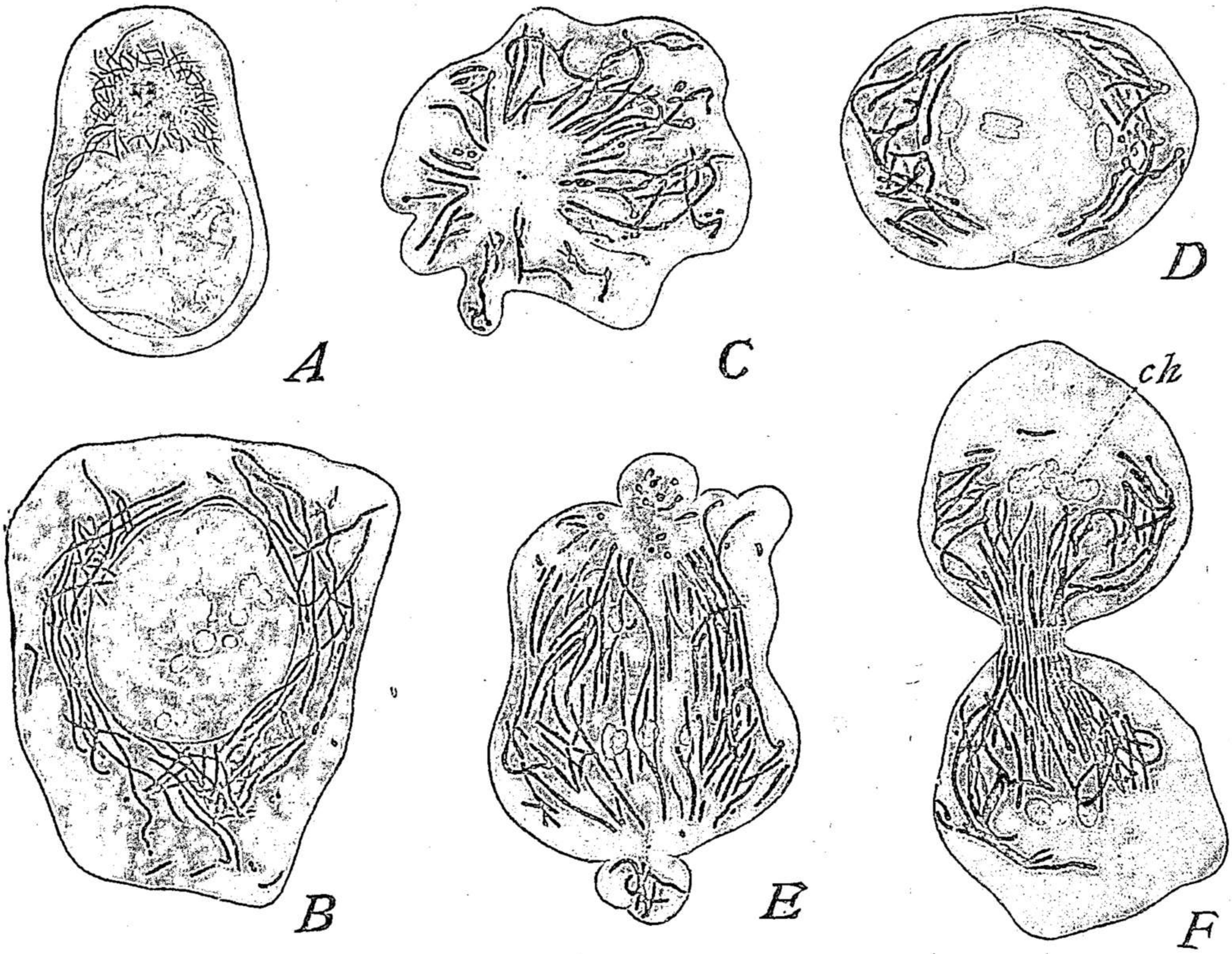


Fig. 68.—Chondriokinesis in the spermatocytes of Hemiptera (BOWEN).

A, early primary spermatocyte of *Euschistus*, with nuclear cap of chondriosomes; *B*, later stage with scattered chondrioconts; *C*, polar view of late prophase; *D*, lateral view of same stage; *E*, anaphase, showing polar lobes; *F*, telophase, separation of the chondriosomes nearly complete.

In all the figures the chondriosomes are black, the chromosomes pale; in the original preparations (Benda method) the former are deep blue, the latter yellowish.

spindle, which they closely surround like a mantle or "palisade" [2] (Fig. 68). There seems to be no doubt that during the ensuing cell-division many or some of these threads are cut across the equator. In many of these cases, nevertheless, it seems probable that at least some of the threads are passively drawn into one cell or the other without division. The process is

[1] On this point see Meves ('07) on the bee, Wilke ('13) on *Hydrometra*, Bowen ('20) on *Euschistus*.

[2] This type of chondriokinesis has been described by many observers, for example in *Coleoptera* by Benda ('03) and Duesberg ('10), Schaffer ('17), Voïnov ('16); in the *Hymenoptera* by Meves ('07); in *Hemiptera* by Fauré-Fremiet ('09), Montgomery ('11), Bowen ('20); and in *Orthoptera* by Gérard ('07), Duesberg ('09), Payne ('16) and (in the living object) by Lewis and Robertson ('16).

more definite in *Paludina* where the chondriosomes assume the form of four to six thick rod-like bodies which place themselves around the spindle and are cut across by the ensuing division.[1] The climax is reached in the scorpion *Centrurus* (Wilson) where all the chondriosome-material aggregates into a single ring-shaped body, which is placed tangentially to the spindle in the first spermatocyte and is cut across transversely by the division accurately into two half-rings. Each half-ring now breaks apart to form two parallel rods (Figs. 169, 170) which in the second mitosis are again cut across transversely into two shorter rods. The original ring thus is divided into eight equal parts, of which each resulting cell (spermatid) receives two, a process comparable in precision with the division of a heterotypic chromosome-ring, though very different in detail.[2]

It is certain from the foregoing that in some cases the chondriosomes are actually divided in the course of mitosis; but on the whole the present evidence points to the conclusion that the division is a passive and mechanical result of the cell-constriction. It must, however, be borne in mind that in many of these cases the larger chondriosomes seen during the actual divisions arise by the growth and aggregation of much smaller bodies; and we should keep clearly in view the possibility that the latter may be capable of division.

c. Dictyokinesis. Recent observations on the Golgi-bodies give substantial reason to extend the foregoing conclusions to them also, though the facts are even less completely known. An increasing number of observers have found that even when the Golgi-apparatus is of the localized or aggregate type, it returns in greater or less degree to a scattered or diffuse condition during mitosis, undergoing a process of *dictyokinesis* in the course of which it breaks up into smaller bodies or *dictyosomes*[3] ("batonettes, Golgi-bodies, etc.) which undergo a process of definite segregation to the daughter-cells.

This process has been most carefully examined in the spermatocytes of insects, mollusks and vertebrates, and shows considerable variation in different forms. In the simplest case, as offered by the scattered or diffuse type of Golgi-bodies, the dictyosomes do not aggregate at the equator of the spindle or near its poles, but are passively distributed, apparently at random,

[1] See Meves ('00), Gatenby ('18).

[2] For further discussion of these cases, see p. 357.

[3] This term is due to Perroncito ('10). The main outlines of the process were clearly described and figured by Platner ('89) in the spermatocytes of *Helix* and by Murray ('98) in those of *Helix* and *Arion*, before the Golgi-apparatus was known as such. Platner derived the dictyosomes from a "Nebenkern," Murray from an "attraction-sphere" the true nature of which as a Golgi-apparatus was established in this case by Sjövall ('06), Weigl ('12), and later by Hirschler ('13, '17) and Gatenby ('17, '18). It was more carefully examined by Deineka ('12) and Cajal ('14) in tissue-cells, and later especially by Hirschler and Gatenby (as above), by Bowen ('20) in insects, and by Ludford and Gatenby ('21) in mollusks and mammals.

to the daughter-cells (Fig. 347). This has been described in only a few cases, excellent examples being offered by the segmenting ova of pulmonates.[1] More commonly the dictyosomes become definitely oriented with respect to the centers and segregate into two approximately equal groups near the spindle-poles.

There seem to be two somewhat different types of this process. In one, recently described by Ludford and Gatenby ('21), in the spermatocyte-

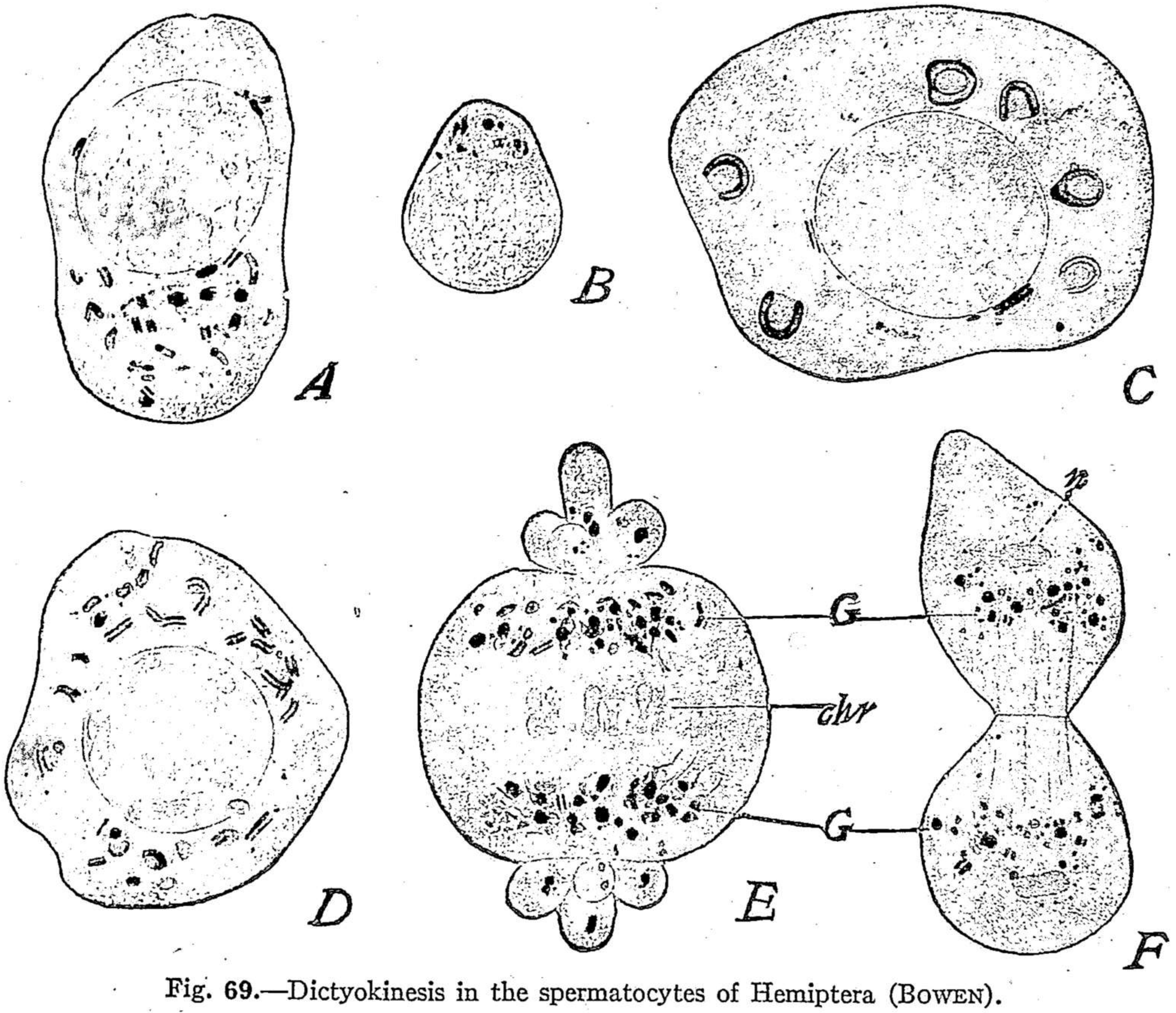


Fig. 69.—Dictyokinesis in the spermatocytes of Hemiptera (BOWEN).

(*A–D, Euschistus; E, F, Brochymena; chr., chromosomes; G, Golgi-bodies* or *dictyosomes.*)

B, late spermatogonium or early spermatocyte, Golgi-bodies aggregated about mitochondrial mass near nuclear pole; *A*, older spermatocyte, spreading of Golgi-bodies; *C*, later stage, growth of Golgi-bodies; *D*, late prophase, Golgi-bodies fragmenting into dictyosomes; *E*, first spermatocyte-metaphase with polar lobes, dictyokinesis completed; *F*, second spermatocyte-telophase with scattered dictyosomes.

divisions of mammals and mollusks, the whole localized apparatus ("archoplasmic mass," "centrosphere," etc.) divides into two parts which pass with the centrioles to opposite poles of the spindle and break up into separate Golgi-bodies or dictyosomes which scatter through the cell during the metaphase and again aggregate into a localized mass in the daughter-cells.

[1] See Hirschler ('13), Gatenby ('18).

In a second type, described by Deineka and Cajal in tissue-cells, and more in detail in the spermatocytes of insects by Bowen, the dictyosomes first scatter through the cell and subsequently aggregate in an equatorial belt surrounding the spindle, which separates into two groups that pass to opposite poles *in advance* of the chromosomes (Fig. 69), and later reaggregate to form a localized structure. Bowen has also shown ('22) that in abnormal tripolar divisions (spermatocytes of *Chlorochroa*) the dictyosomes segregate into three groups towards the poles while the chromosomes are still in metaphase, and before the equatorial constriction has appeared. This clearly indicates that the segregation of these bodies is not a simple mechanical result of cleavage but is oriented with respect to the centers.

In all of these cases the result is an approximately equal partition of the Golgi-elements between the daughter-cells; and this process, obviously, is in some manner closely correlated with the activity of the mitotic figure. Beyond this point little can be concluded with certainty. Platner ('89), probably the first to observe dictyokinesis, believed the dictyosomes to undergo a regular process of longitudinal splitting during division; but this has failed of confirmation by later observers. Bowen ('20) has clearly shown that the so-called longitudinal split of these bodies, though very conspicuous in the prophases, has apparently no connection with their division, and is an illusion produced by the presence of an axial non-staining substance (p. 361).

Fragmentation of the Golgi-bodies prior to division has been described by many observers beginning with Platner and Murray in case of the pulmonates. Gatenby ('19), who describes it carefully in the oöcytes of *Lymnæa*, considers division of the batonettes to be accompanied by that of the clear "archoplasm" sphere by which each is accompanied. Their actual number at the time of mitosis seems to vary widely. In the primary spermatocytes of *Limax* Gatenby ('18) finds but eight, the number being halved at each mitosis, so that the spermatid receives but two. In insects, as shown especially by Bowen ('20, etc.) the number is much greater (Fig. 69); but here too the evidence is that they do not split or otherwise divide during the actual mitosis but are passively sorted out into approximately equal groups.[1]

d. Review. Too little is known of the foregoing phenomena to justify any very far-reaching conclusions; but they do not thus far greatly lessen the wide general contrast that has been drawn between nucleus and cytosome in respect to mode of division (p. 162). In any case it must be admitted that neither chondriokinesis, dictyokinesis nor the phenomena of plastid-division can be compared with karyokinesis in respect to precision

[1] *Cf.* the analogous process demonstrated in the chondriokinesis of scorpions, p. 163.

of division and segregation; it is not certain that plastids always arise by the division of preëxisting bodies of the same kind; and it is much more uncertain whether the same is true of either chondriosomes or Golgi-bodies. Nevertheless the phenomena are significant as expressions of the care so often taken by nature (to use the words of old-fashioned teleology) to ensure the perpetuation and fairly precise segregation of specific formed elements in the daughter-cells. It is impossible to overlook the fact that in these phenomena we see a regrouping of preëxisting, specifically organized material that is preparatory to its definite segregation in the daughter-cells; and one which, if less precise than in case of the nuclear material, is a phenomenon of analogous type. Its broader significance appears in the possible relation of plastids to chondriosomes (p. 709), and that of the formed elements generally to the underlying organization of protoplasm (p. 717).

4. Monocentric Mitosis. The Monaster

It is a fact of much interest for the analysis of mitosis and for many problems connected with the chromosome-cycle that the cell may pass through a nearly complete cycle of mitosis, or even a series of successive cycles, without division of the central body or aster.[1] (Figs. 70–72). The figure thus formed, often spoken of as a *monaster*, shows all of the phenomena observed in a dicentric figure, including the normal formation and division of the chromosomes, with the following exceptions: (1) the daughter-chromosomes do not separate far but remain in a single group which gives rise to a single nucleus; (2) cleavage of the cytosome does not take place. Monocentric mitosis thus leads to a doubling of the chromosomes, without cell-division, the original chromosome-number being increased from the diploid to the tetraploid number or to a still larger number if the egg passes through subsequent monaster-cycles. As many as six such successive cycles have been observed in a single living egg.[2]

After passing through one or more monaster-cycles the cell may resume its normal mode of bipolar division, the increased number of chromosomes being retained. Boveri showed, in the case of sea-urchin-eggs, that monocentric mitoses artificially induced at the time of the first cleavage are often immediately followed by regular bipolar cleavage, and that this may lead to the production of young Pluteus larvæ having the tetraploid number of chromosomes, externally of normal appearance but having cells correspond-

[1] The monasters were first observed by Boveri in 1885–86 in the testis cells of the cray-fish, but not described by him until much later ('01, '05). They were in the meantime described by R. Hertwig ('96) in the eggs of sea urchins treated by strychnine ("half spindles," "fan-nuclei"), by Ziegler ('98) in sea-urchin eggs after mechanical injury (see p. 447), and by Morgan in strychninized eggs (1900). Their history was followed out in some detail by Wilson ('01, 1), M. Boveri ('03), and more recently by Painter ('16, '18).

[2] Wilson ('01a), Hinderer ('14), Herlant ('17).

ingly larger and fewer (p. 730) (Fig. 349).[1] These facts indicate one probable mode by which the normal number of chromosomes as seen in nature may change, whether from species to species, or in the appearance of tetraploid or polypoid chromosome-groups in certain of the tissue-cells (p. 870), or in the production of tetraploid mutants (often giants) (p. 885).

Although there is reason to believe that monocentric mitosis may occur spontaneously under natural conditions, it is no doubt a pathological phe-

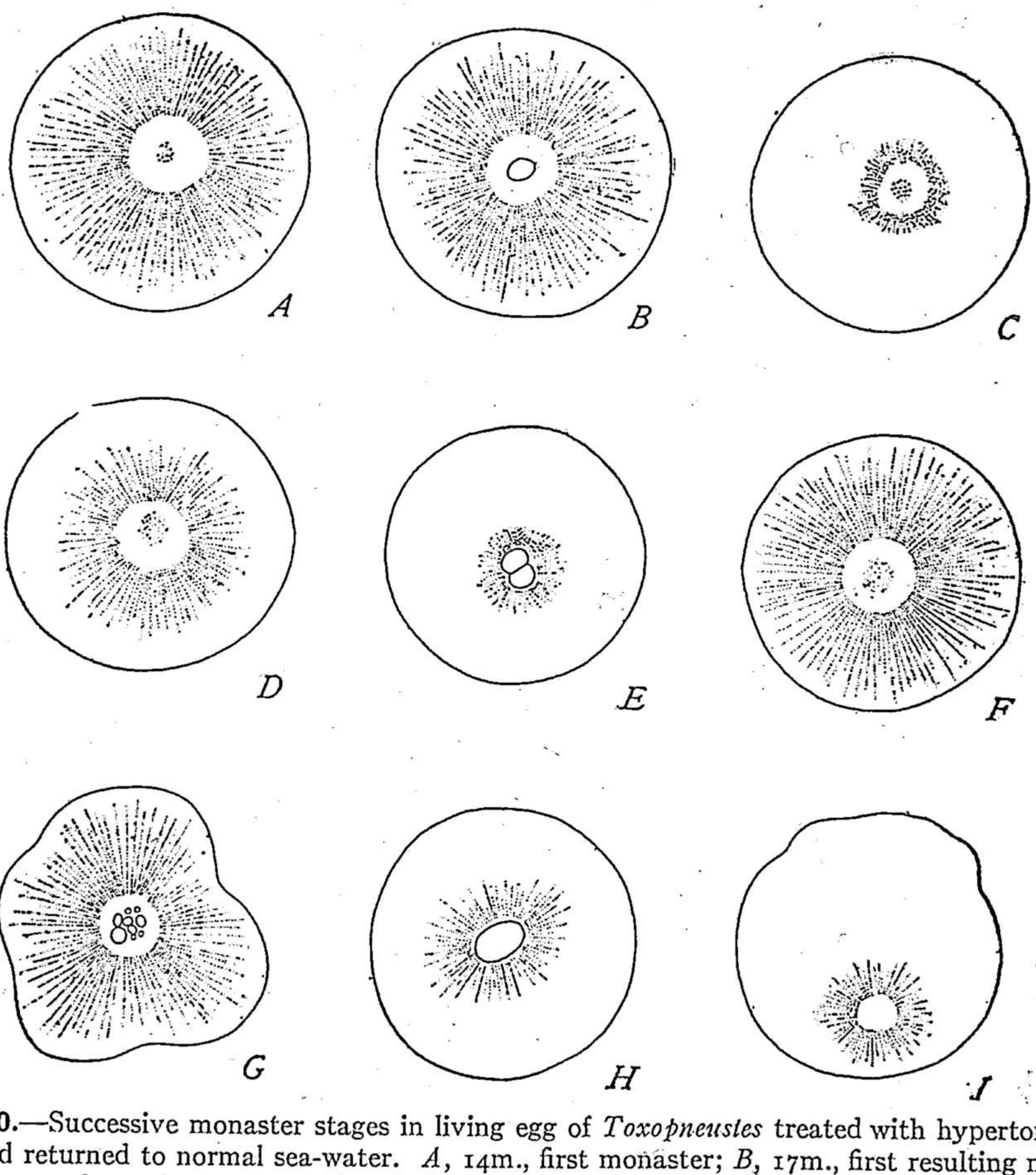


Fig. 70.—Successive monaster stages in living egg of *Toxopneustes* treated with hypertonic sea-water and returned to normal sea-water. *A*, 14m., first monaster; *B*, 17m., first resulting nucleus; *C*, 30m., second prophase, aster reduced; *D*, 37m., second monaster; *E*, 47m., second nucleus; *F*, 59m., third monaster; *G*, 69m., third monaster telophase; *H*, 75m., third nucleus (note increase in size); *I*, 157m., sixth monaster.

nomenon, and one that may be induced by various chemical, physical or mechanical agents. Examples of these are strychnine, or chloral hydrate (Hertwig), CO_2 (Herbst), phenol urethane (Painter), hypertonic sea-water (Morgan, Wilson, Herlant), ether (Wilson) and mechanical agitation or

[1] This has been confirmed by various later observers. (See Herbst, '06, '09, '12, '14, etc.), Hinderer ('14).

injury (Boveri, Ziegler, Painter). The last method was employed by Boveri, who found that monocentric mitosis may be produced by shaking sea-urchin eggs a few minutes after fertilization; and it is of especial practical value, because of the comparative ease with which monasters may thus be obtained, and also because eggs thus treated have not been poisoned by drugs. Monasters are often formed in artificial parthenogenesis (p. 484), either in close association with the nucleus or lying quite apart from it in the cytoplasm, in which case they are variously called "accessory asters," "artificial asters," or more appropriately, *cytasters;* and these may ultimately divide, though no chromosomes are associated with them. These interesting structures will be considered elsewhere (p. 684). The monaster is typically symmetrical, with rays extending in all directions, but in some cases the rays are wanting in a considerable sector on the side opposite to the chromosomes (Fig. 228), thus giving the appearance of a "fan-nucleus," as first described by R. Hertwig ('96).

In its general history the monaster shows a remarkably close parallel to that of a normal amphiaster.[1] In the prophases the astral rays rapidly extend themselves through the cytosome, often giving a very striking appearance; in the telophases they are rapidly reduced and may nearly or quite disappear during the interkinesis (Fig. 70). As the aster approaches its highest development it moves towards the cell-periphery, the centrosome (centrosphere) becomes flattened, elongating parallel to the nearest periphery of the egg and assuming, as seen in side-view, a more or less curved biscuit or lens-shape. This is followed, finally, by a reduction of the rays until they nearly or quite disappear while the nucleus re-forms.

The resemblance extends to other phenomena, both nuclear and cytoplasmic. The chromosomes form in normal fashion, become longitudinally split and attach themselves to the astral rays, forming a group (Fig. 71), which typically lies in one side of the aster (as it likewise does in the amphiaster). This stage, as M. Boveri shows, is of relatively long duration and corresponds to the stage of the equatorial plate in normal mitosis. The chromosomes now draw out along the astral rays and finally divide into two,[2] but the two halves do not move far apart, undergoing the typical telophase-transformations *in situ* and becoming transformed into a common group of karyomeres or chromosonal vesicles, which finally fuse to form a single nucleus (Figs. 70–72).

Meanwhile the peripheral or ectoplasmic layer thickens, most *on the side furthest from the aster*, while in this region the contour of the egg becomes irregular or even amœboid, sometimes to such an extent that rounded pro-

[1] See especially Wilson, '01a, T. Boveri, '03, M. Boveri, '03, Painter, '16, '18, Herlant, '18, '19.
[2] See especially M. Boveri, '03.

toplasmic protuberances are cut off, and the whole egg may assume an irregular form. These changes may lead to the complete destruction of the egg; and Painter's observations ('18) indicate that the severity of the action depends on the distance that the aster retreats from the center of the egg. If it is not too extreme the egg gradually recovers, resumes its spheroidal form as the nucleus re-forms and the aster dies down, and the egg passes into a "resting" condition. As first pointed out by Boveri, the cortical disturbance of the cytoplasm undoubtedly corresponds to the equatorial change of surface-tension and thickening of the ectoplasmic layer which in the normal cell leads to constriction and division. The force of this comparison is shown by Boveri's figure of an abnormally dividing egg that simulates two monaster eggs artificially associated (Fig. 72), which also shows the peripheral movement of the aster, the enlargement and change of shape of the centrosome, and the position of the chromosomes.

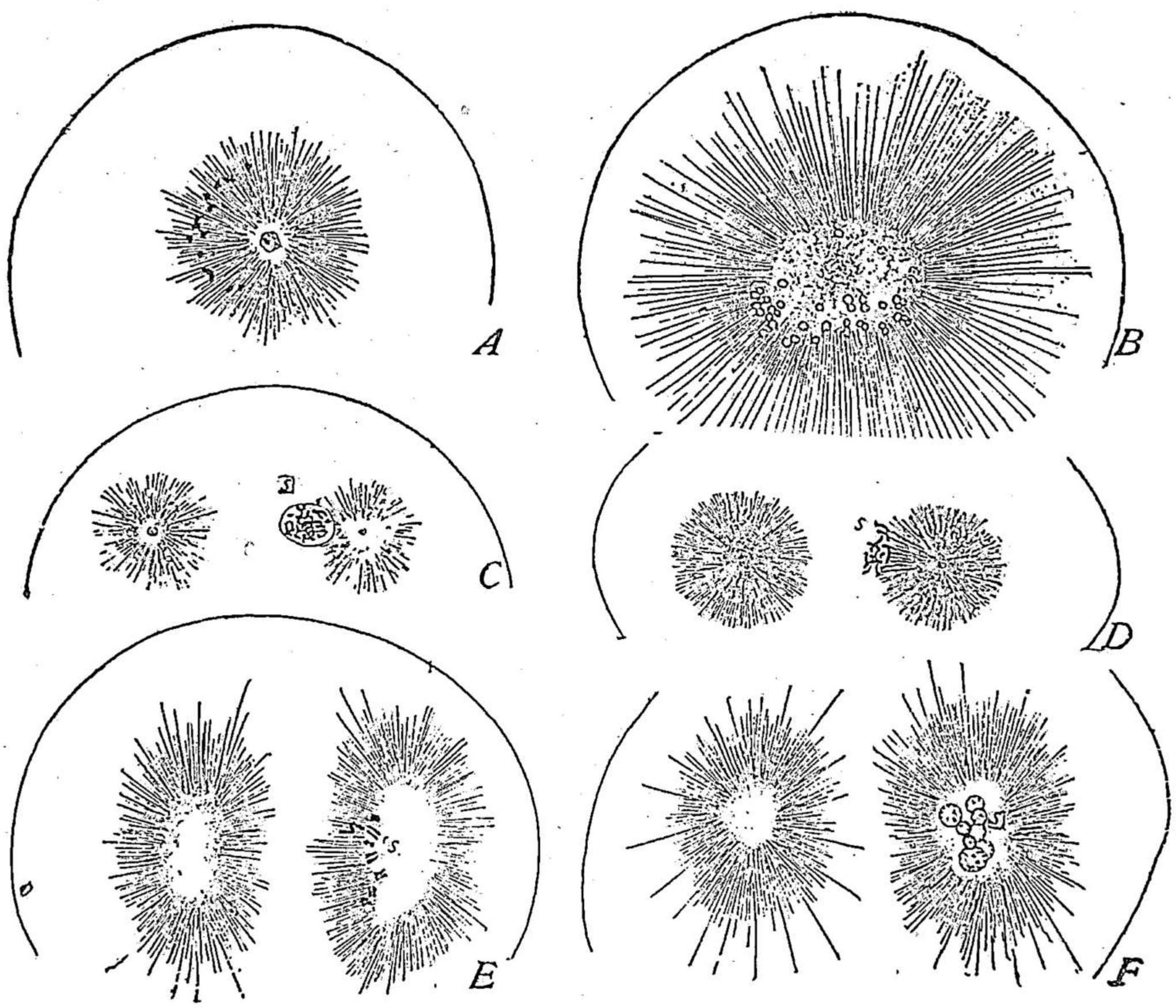


Fig. 71.—Monocentric mitosis in sea-urchins (M. Boveri).

A, monaster-metaphase showing dividing chromosomes (*Paracentrotus*); *B*, telophase, karyomeres; *C–F*, from enucleated fragments of *Echinus* fertilized by sperms of *Paracentrotus*, showing separation of the centers and unipolar chromosome-distribution; the figures show successive stages in the history of the sperm-nucleus (*s*).

The failure (temporary or permanent) of the monaster to divide may be due either to a corresponding failure of the centrioles to divide or to separate

after their division. The centrosome in these monasters is a rather large body within which, as Painter has shown, may in some cases be seen a minute pair of centrioles; and in the later phases of the cycle these may even go so far as to separate and to form a small spindle between them. Such monasters, no doubt, may be succeeded in the succeeding cycle by amphiasters and bipolar division may regularly follow. An interesting detail

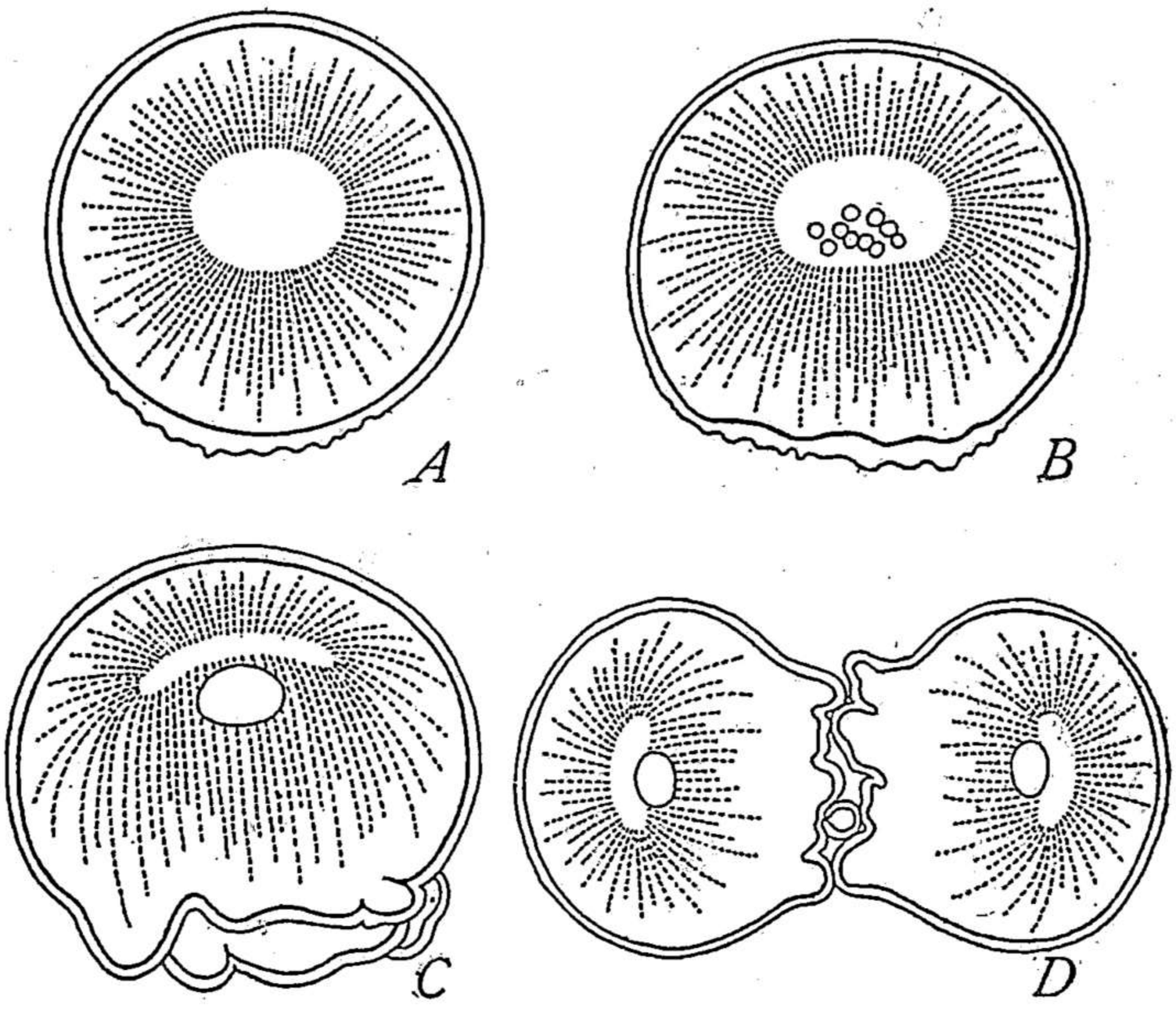


Fig. 72.—Monasters from eggs of the sea-urchin *Paracentrotus* (*Strongylocentrotus*) obtained by shaking (BOVERI).

A, middle period; *B*, early telophase karyomeres; *C*, later telophase with nucleus; *D*, abnormally dividing egg, like two monaster-eggs together.

of these figures noted by Painter is that the formation of the amphiaster is often accompanied by the appearance of spiral asters (p. 145).

5. Multipolar Mitosis

Multipolar or polycentric mitosis, like monocentric, is usually a pathological process and is characterized by the presence of more than two poles or centers. Such multipolar figures may have few or many poles and may be of either the astral or the anastral type, in the former case forming triasters, tetrasters, or polyasters, sometimes of great complexity (Figs. 79, 193). A noteworthy character of such mitoses is the fact that spindles are often formed between non-adjacent as well as adjacent centers. In tetrasters, for example, in addition to four spindles formed between the four centers in square formation, a fifth and even a sixth spindle may appear between diagonally opposite centers (Fig. 79). This fact is fundamentally important for the mechanics of mitosis (p. 186).

Multipolar mitosis may arise in various ways. As first observed by Fol and O. Hertwig in echinoderm-eggs, it is the usual result of pathological polyspermy; and it was shown by O. and R. Hertwig ('87) that this condition may readily be produced by the action of various toxic agents. In such cases the multipolar figure is usually formed synthetically by the union of amphiasters that are originally separate (since each sperm-nucleus is accompanied by a single amphiaster p. 440). Multipolar mitoses are also readily produced in tissue-cells dividing under the influence of poisons as

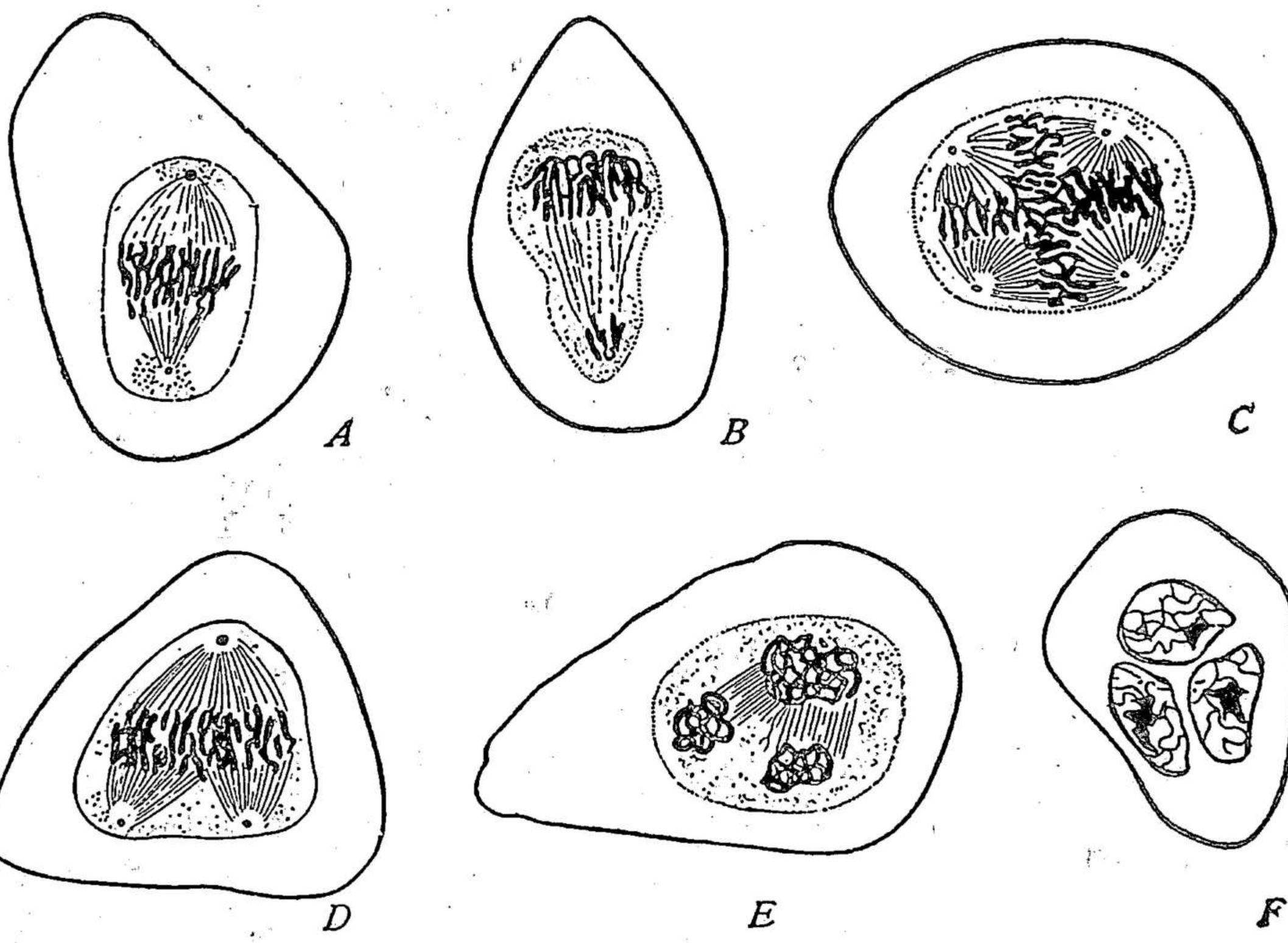


Fig. 73.—Pathological mitoses in human cancer-cells (GALEOTTI).

A, asymmetrical mitosis with unequal central bodies; *B*, later stage, showing unequal distribution of the chromosomes; *C*, quadripolar mitosis; *D*, tripolar mitosis; *E*, later stage; *F*, trinucleate cell resulting.

was long since observed by Galeotti ('93). They also have long been known in abnormal growths, such as tumors or cancers (Fig. 73), and were for a time supposed to be the active cause of such growths. It is now clear, however, that tumors, like normal tissues, grow primarily by typical mitosis, and that the multipolar figures are of secondary origin.

In mitoses of this type the chromosomes are found scattered at random on the spindles and hence undergo an irregular distribution to the poles (Figs. 79, 430). Boveri made effective use of this fact in his masterly analysis of the dispermic eggs of sea-urchin eggs with regard to the nuclear organization (p. 917).

IV. THE MECHANISM OF MITOSIS

We should distinguish clearly between the effect of mitosis and the nature of its mechanism. The effect of mitosis is obvious; it involves not a mere mass-division of the nucleus as a whole but one that is completely meristic and also exactly equal. In both respects the nuclear division shows a marked contrast to cleavage of the cytosome which gives the general appearance of a mass-division, though it can no longer be regarded as strictly non-meristic (p. 162). Division of the cytosome, is often unequal, sometimes extremely so, but nuclear division remains perfectly equal even in the most extreme cases. In the formation of the polocytes, for instance, (p. 493), one of the products may be thousands of times larger than the other, but nuclear division remains exactly equal.

A consideration of the energies at work in mitosis leads us into one of the most difficult and debatable fields of cytological inquiry; the admission must indeed be made that after forty years of investigation we have taken no more than the first steps towards a real solution of the problem. We will here limit our attention to the amphiastral type as the one that has been most thoroughly studied by experimental and analytical methods. The problem is a twofold one, involving the history of the chromosomes on the one hand and that of the amphiaster on the other. Most attempts to solve it have centered in hypotheses concerning the nature and mode of action of the amphiaster and may conveniently be classed as *fibrillar* and *dynamical* (Ziegler, '95), though logically the latter term is not very defensible. To the first group belongs the hypothesis of *fibrillar contractility* and its various modifications (Klein, Van Beneden Boveri, Heidenhain, etc.); to the second group hypotheses, largely based on the study of living protoplasm and on the view that protoplasm has in general the properties of a colloidal, viscid or semi-liquid substance commonly alveolar in structure. Some of these hypotheses have attempted to explain the phenomena as a result of radially disposed lines of diffusion-currents or of protoplasmic flow (Bütschli, Rhumbler), others as a result of electrical polarities in the protoplasmic field (Ziegler, Gallardo, Hartog, R. Lillie). A survey of these various hypotheses will drive us to the conclusion that none of them has yet afforded a satisfactory solution of the problem, though each has contributed interesting suggestions. We first offer a brief preliminary analysis based primarily upon the study of living cells.

1. General Analysis. Separability of the Factors

(1) Division of the nucleus without accompanying division of the cell-body is a common phenomenon in nature, where it leads to the formation of syncytia or plasmodia, as already indicated (p. 24). In some of these

cases the failure of cytoplasmic division is correlated with its overloading by inert matter, such as yolk; which leads to the suspicion that this phenomenon is in general due to a relative lack of energy in the general mass of protoplasm as compared with the nucleus and the cytoplasm within its immediate sphere of influence. [1] This view is sustained by the fact that the same result may be brought about experimentally by various agents which lower the protoplasmic activity, such as lack of oxygen (Demoor, Loeb, Schultze, Samassa, Godlewski), lowered temperature (O. and R. Hertwig), narcotics, such as chloral hydrate (Hertwig) or ether (Demoor, Wilson, Fig. 78), changes in the concentration of the surrounding medium (Hertwigs, Driesch, Loeb, and Norman) or mechanical shock (Boveri).[2] All of these agents cause a diminished development or even a complete suppression of the rays (O. and R. Hertwig, '87). Complete suppression of the rays is followed by complete suppression of division. Partial or complete recovery from the ether is followed by a partial or complete redevelopment of rays leading either to complete division or to the formation of more or less abortive cleavage-furrows, that approach to a complete cleavage in direct ratio to the development of the rays. In such cases, the cleavage-furrows always cut into the cell between the asters, and their depth is directly proportional to the development of the rays (Wilson, '01b, Teichmann, '03),—a result also established by study of the supernumerary asters or cytasters which often appear in the course of artificial parthenogenesis (p. 481).

The conclusion is irresistible that the central bodies are centers of cytoplasmic division, and that the astral rays are somehow concerned in the process, a result originally reached from a study of the normal phenomena by Van Beneden, Rabl, Boveri and their successors.

(2) The same experiments also demonstrate that the division of both the cell-body and of the nuclei as such may be suppressed while that of the chromosomes and the central bodies steadily proceeds. When the cytoplasmic activity is sufficiently reduced by the action of ether, etc., only slight separation of the daughter-chromosomes occurs, and they may give rise together to a single nucleus or to two closely approximated nuclei which finally fuse. By continuation of this process the number both of chromosomes and of centers continually increases, while the nucleus increases in size at each step. Thus arises a giant nucleus surrounded by many centers; and from it at each mitosis arises a polyaster having a large number of chromosomes scattered among the spindles.

(3) Progressive division of the chromosomes may take place without division of either the centers, the nuclei or the cell-body, as is seen in mono-

[1] *Cf.* Wilson, '83, p. 742.

[2] Literature in Wilson, '01b.

centric mitosis (p. 168). This clearly indicates that both the separation of the daughter-chromosomes and the division of the cell-body are dependent upon the presence of a spindle.

(4) Of great interest is the fact, discovered by Boveri ('96) in sea-urchin eggs that *progressive multiplication of the centers, accompanied by the periodic formation of perfect amphiasters, may take place in the entire absence of nucleus or chromosomes.* Such enucleated masses of protoplasm containing a central body and aster are not uncommonly

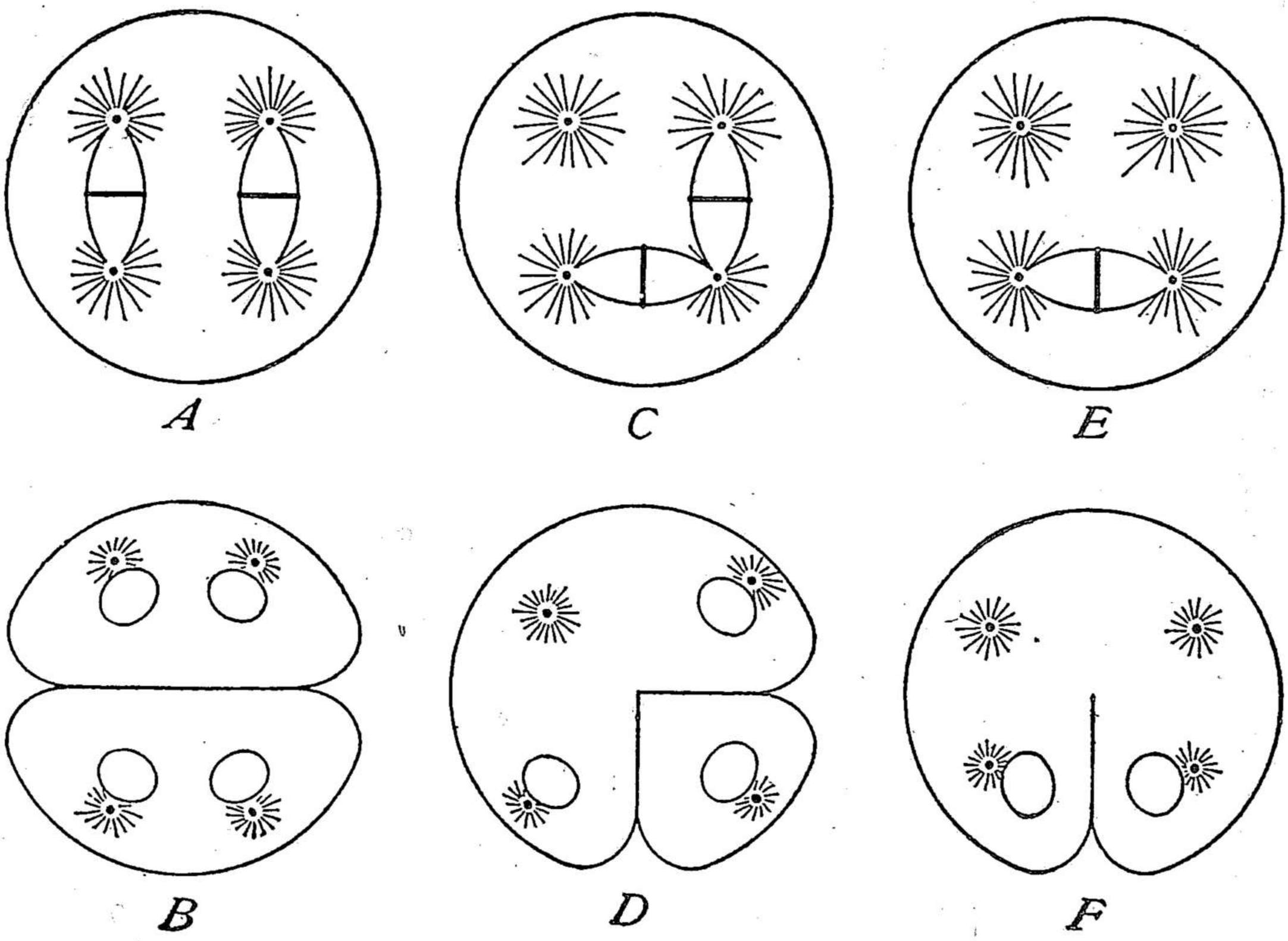


Fig. 74.—Division of dispermic eggs in sea-urchin eggs, schematic (BOVERI).

A, *C*, *E*, eggs before division, showing various connections of the asters; *B*, *D*, *F*, resulting division in the three respective cases, showing cleavage only between centers connected by a spindle.

formed by the passage of all the chromosomes to one pole of the spindle, so that each of the resulting cells contains an aster, but only one of them a nucleus.[1] Boveri, whose results have been confirmed by Ziegler, Wilson, Teichmann, Yatsu, McClendon and others, found that in later stages the central body and aster thus isolated continue to divide progressively and synchronously with the mitotic activity in the products of the nucleated blastomere. At each such division a perfect amphiaster is formed, later dividing into two separate asters which become much reduced in the

[1] This abnormality may be artificially induced by shaking of the eggs during their division (Boveri), by treatment with hypertonic solution or by etherization (Wilson), by sucking out the nucleus with a fine pipette (McClendon), and in other ways.

ensuing period of rest, quite as in the normal cleavage. Step by step the enucleated blastomere thus becomes filled with a constellation of asters.[1]

(5) These facts evidently constitute strong evidence in favor of the genetic continuity of the central bodies in successive mitoses. Another important fact is that the non-nucleated blastomere rarely divides at all, though the periodic formation of asters is followed by the appearance of cleavage-furrows between them. As a rule, such furrows soon disappear; or, if they cut completely through the cell, are subsequently obliterated.

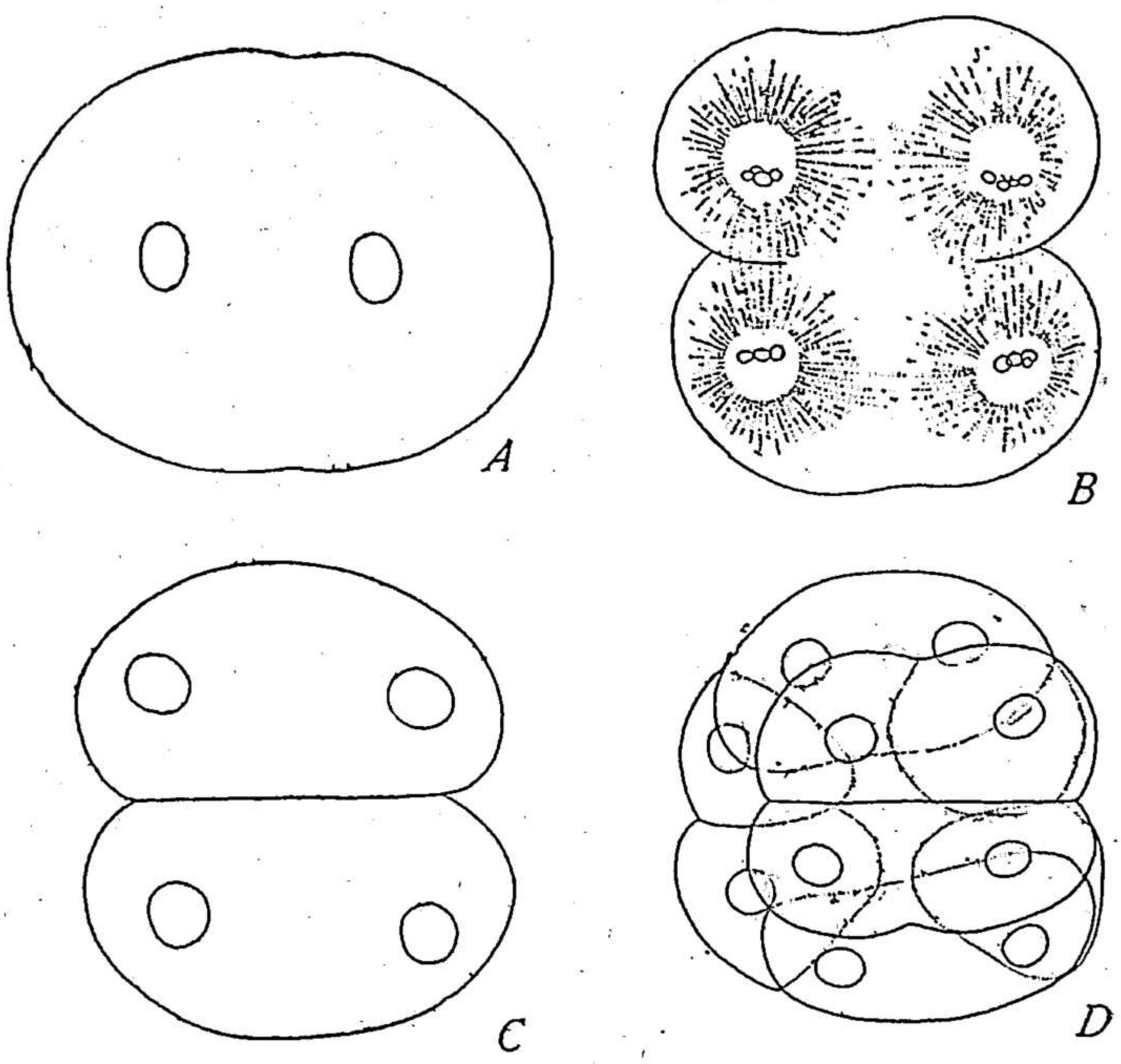


Fig. 75.—Mitosis in binucleate egg of the sea-urchin *Toxopneustes*, produced by obliteration of first cleavage as a result of shaking during first cleavage; from life.

A, rest-stage; *B*, next cleavage; *C*, product; *D*, 16-nucleus stage, 12 cells.

Boveri likewise found in the tetrasters of dispermic sea-urchin eggs, also in eggs in which the first cleavage-plane is suppressed by means of pressure, lowered temperature or shaking (Fig. 75), that complete and permanent cleavage only occurs across the chromosome-bearing spindles. Boveri concluded from this that the presence of chromosomes on the spindle is somehow necessary for complete and permanent division.

In respect to the last conclusion, later work has given somewhat contradictory results, that of Teichmann ('03) supporting Boveri's conclusions,

[1] M. Boveri ('03) has demonstrated that in such cases the two asters separate more rapidly and are cut apart sooner than in the chromosome-bearing amphiasters (the same is true of mitosis in which all of the chromosomes pass to one pole). The facts indicate that the centers (or asters) repel one another, but are held together by the spindle, and that the latter action is more effective in the case of nuclear spindles.