STUDIES ON THE HUMAN CORPUS LUTEUM

II. Observations on the Ultrastructure of Luteal Cells During Pregnancy

ELEANOR C. ADAMS and ARTHUR T. HERTIG

From the Department of Pathology, Harvard Medical School, Boston, Massachusetts 02115 and the New England Regional Primate Research Center, Southborough, Massachusetts 01772

ABSTRACT

The ultrastructure of human corpora lutea obtained during the 6th, 10th, 16th, and 35th week of pregnancy is reported. Differences between the established luteal cell of pregnancy and the transitory luteal cell of the menstrual cycle are noted. In pregnancy the luteal cell is more compartmentalized into a peripheral mass of ER (endoplasmic reticulum) and a central area where mitochondria and Golgi complexes are concentrated. The latter area extends to a cell surface where microvilli face on a perivascular space. Long bundles of filaments are prominent within the luteal cell cytoplasm and, in contiguous cells, appear to arise from adjacent desmosomal regions. Bilateral subsurface cisternae of granular ER at lateral cell borders appear to be areas of specialized junctional surfaces. Certain luteal cells with irregular nuclear membranes are also characterized by vesicular aggregates enclosed within a single membrane. These aggregates are found within the peripheral nucleoplasm or the perinuclear cytoplasm. Their single limiting membrane often appears continuous with either the inner or outer leaflet of the nuclear membrane.

INTRODUCTION

In contrast to our preceding paper on the development and regression of luteal cells in the transitory corpus luteum of the menstrual cycle (1), this study examines these same steroidogenic cells after they have become established as the corpus luteum of pregnancy. Within a few weeks (not precisely determined) after the implantation of the fertilized ovum, the corpus luteum is no longer essential to the maintenance of pregnancy. Nevertheless the present ultrastructural study of the relationship of organelles in luteal cells from the sixth through the 35th week of pregnancy indicates that massive regression in this tissue in the later months of pregnancy does not take place. Green et al. (7) likewise concluded in their electron microscopic study that luteal cells from term pregnancies could be capable of secretion. In a study of the incorporation of acetate-1-^{14}C into progesterone in corpora lutea from the luteal phase of the cycle and from the eighth and 40th weeks of pregnancy, Savard et al. (16) reported high rates of incorporation in specimens from pregnant patients and in those from patients at days 15–21 of the menstrual cycle. They further reported that the specimens from pregnant patients form less progesterone in vitro in terms of micrograms of steroid than do cyclic corpora lutea. They conclude that the corpus luteum undergoes profound metabolic changes throughout its lifespan.

MATERIALS AND METHODS

Five corpora lutea from human pregnancies have been studied (Table I) by the same methods of

TABLE I
Clinical Age of the Five Human Corpora Lutea of Pregnancy Used in This Study

Case no.	Stage of Pregnancy in weeks
H51	6
H49	10
H42	16
H53	16
H43	35 (Caesarean section)

preparations reported in the preceding paper on cyclic human luteal cells (1).

OBSERVATIONS

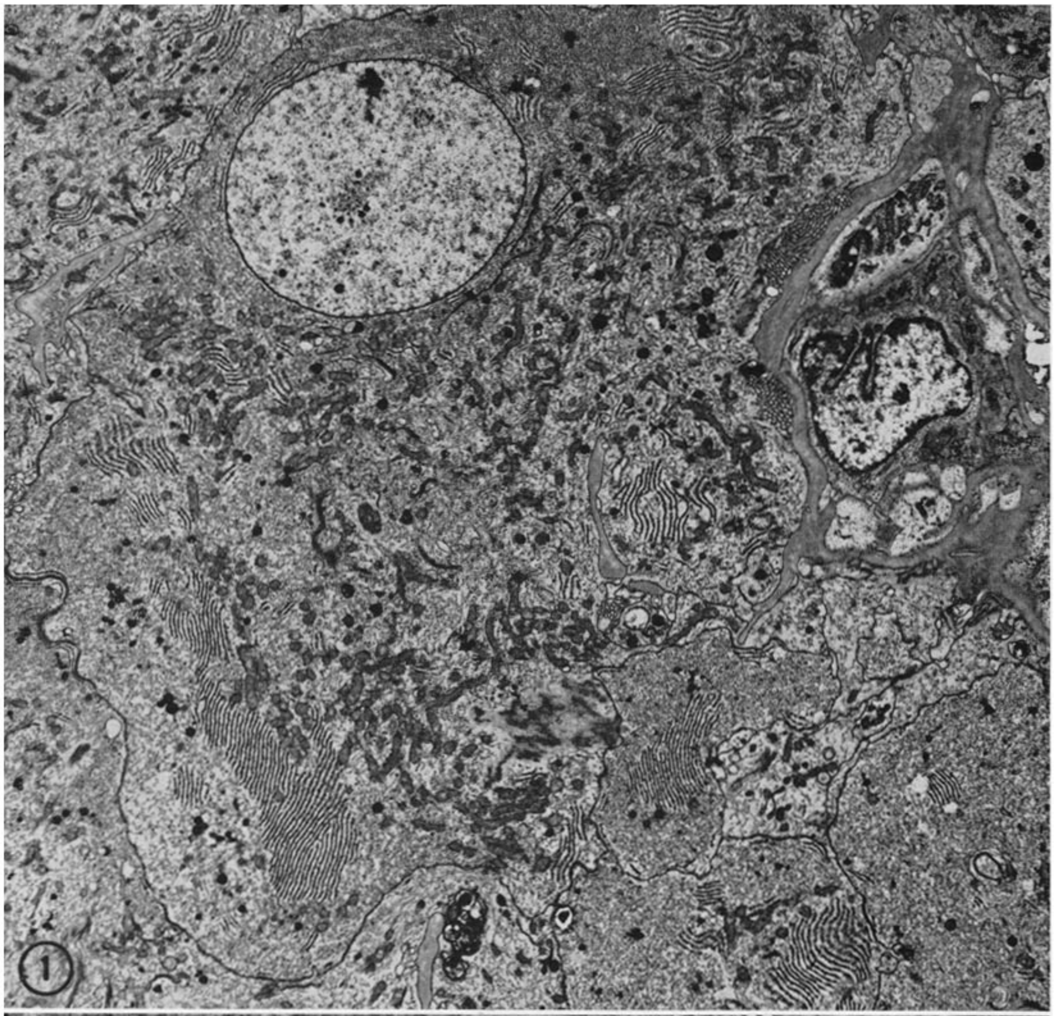
Throughout pregnancy the predominant type of luteal cell is very irregularly shaped and large lobules of its peripheral cytoplasm are closely enveloped by adjacent cells (Fig. 1). Extensive portions of the extremely peripheral cytoplasm are filled with tubular endoplasmic reticulum (ER), a few small, very osmiophilic lipid droplets, small vesicles containing a flocculent electron-opaque material, and only sparsely distributed mitochondria (Fig. 3). As pregnancy progresses, the relative volume of this type of cytoplasm in each cell appears to decrease somewhat. In what may be optimal planes of section these peripheral areas of the cytoplasm appear to be connected to the more central cytoplasm by parallel arrays of cisternae of granular ER. The central cytoplasm contains a concentration of mitochondria and Golgi complexes both of which are surrounded by tubular ER that is closely associated with mitochondria (Fig. 3). The central cytoplasm containing multiple Golgi complexes, membrane-bounded dense bodies, mitochondria, and agranular ER extends to a cell surface whose microvilli face on a perivascular space (Figs. 1 and 2). Closely adjoining cells which lie in the perivascular channel and appear to be phagocytic (Fig. 2) become more prominent as pregnancy progresses. In a corpus luteum from the 35th week of pregnancy, some of these phagocytic cells contain large electron-opaque deposits of crystalline material which may represent calcium.

The Golgi complex of these luteal cells is a crescentic, glomerulus-shaped structure with many small vesicles in the matrix between the saccules (Fig. 4). As pregnancy approaches term the saccules become interdigitated and show elaborate crescentic configurations associated with a variety of vesicles (Fig. 5). Frequently, a granular sphere surrounded by a halo of small vesicles lies near the Golgi complex (Fig. 4). Homogeneous dense bodies and other dense bodies of irregular shape and containing vesicles of a variety of sizes are prominently associated with the Golgi complex (Fig. 33) and accumulate in the cytoplasm near perivascular spaces. The structure of the vesicular dense bodies differs from that of the vesicular granules in the active cyclic luteal cell by the presence of a homogeneous electron-opaque matrix and by the absence of a halo of surrounding small, uniform vesicles (1) (Fig. 6). In addition, the granule-containing cytoplasmic projections or blebs that are so prominent in the intercellular spaces or attached to the surface of developing cyclic luteal cells are not observed in pregnancy.

Mitochondria are, for the most part, elongate with both tubular and lamellar cristae (Fig. 3). (Many mitochondrial cristae in the term corpus luteum seem to be more lamellar than tubular.) Other mitochondria within any one cell are irregular in shape, while still others contain large, spherical, amorphous electron-opaque deposits (Fig. 15). Some cells contain many mitochondria with these deposits or with cristae of unusual contours (Fig. 7).

The electron-opacity of adjoining cells differs (Fig. 15), as may that of the cytoplasm of various areas within any one cell (Fig. 1). This variation appears to be related to the dilation and/or close-packing of the tubular ER as well as to the density of the cytoplasmic matrix. Folded membrane complexes (Fig. 13) and a few spherical inclusions similar to those described in the cyclic luteal cell (1) are present in the peripheral cytoplasm. Peripheral whorled membranes that often enclose a large lipid droplet become prominent in a few cells toward term (Fig. 9).

Extensive bundles of intracytoplasmic filaments, some of which are associated with dense regions (Fig. 13), are present in the 6-week corpus luteum and become more prominent as pregnancy progresses. In many instances they appear to form a network that compartmentalizes the cell into a peripheral mass of agranular and granular ER and a central mass of mitochondria, agranular ER, and Golgi complexes (Fig. 10). These long bundles of filaments may traverse the entire cell cytoplasm, and in contiguous cells may arise from adjacent desmosomal regions (Fig. 12). Other filamentous



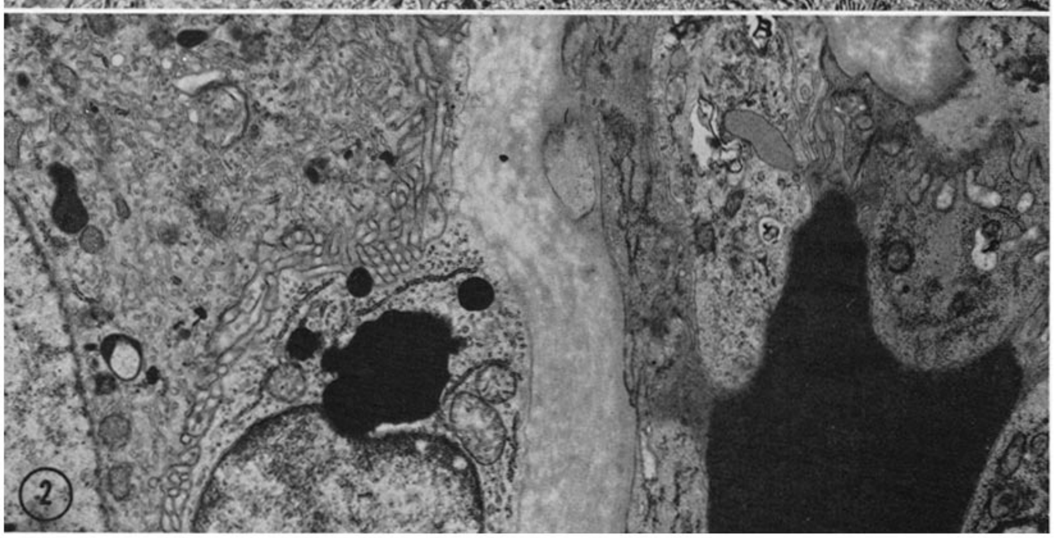


FIGURE 1 A survey view of a luteal cell from the sixth week of pregnancy. Note peripheral cytoplasmic masses of agranular ER, parallel cisternae of granular ER, and a large central area where mitochondria and Golgi complexes are concentrated. This area extends to a cell surface containing microvilli that face a vascular space. H51. × 3800.

FIGURE 2 A luteal cell surface at a vascular channel from a 16-week pregnancy. Phagocytes become closely apposed to the luteal microvilli and accumulate electron-opaque deposits. A collapsed vascular channel is present at right. H42. × 10,000.

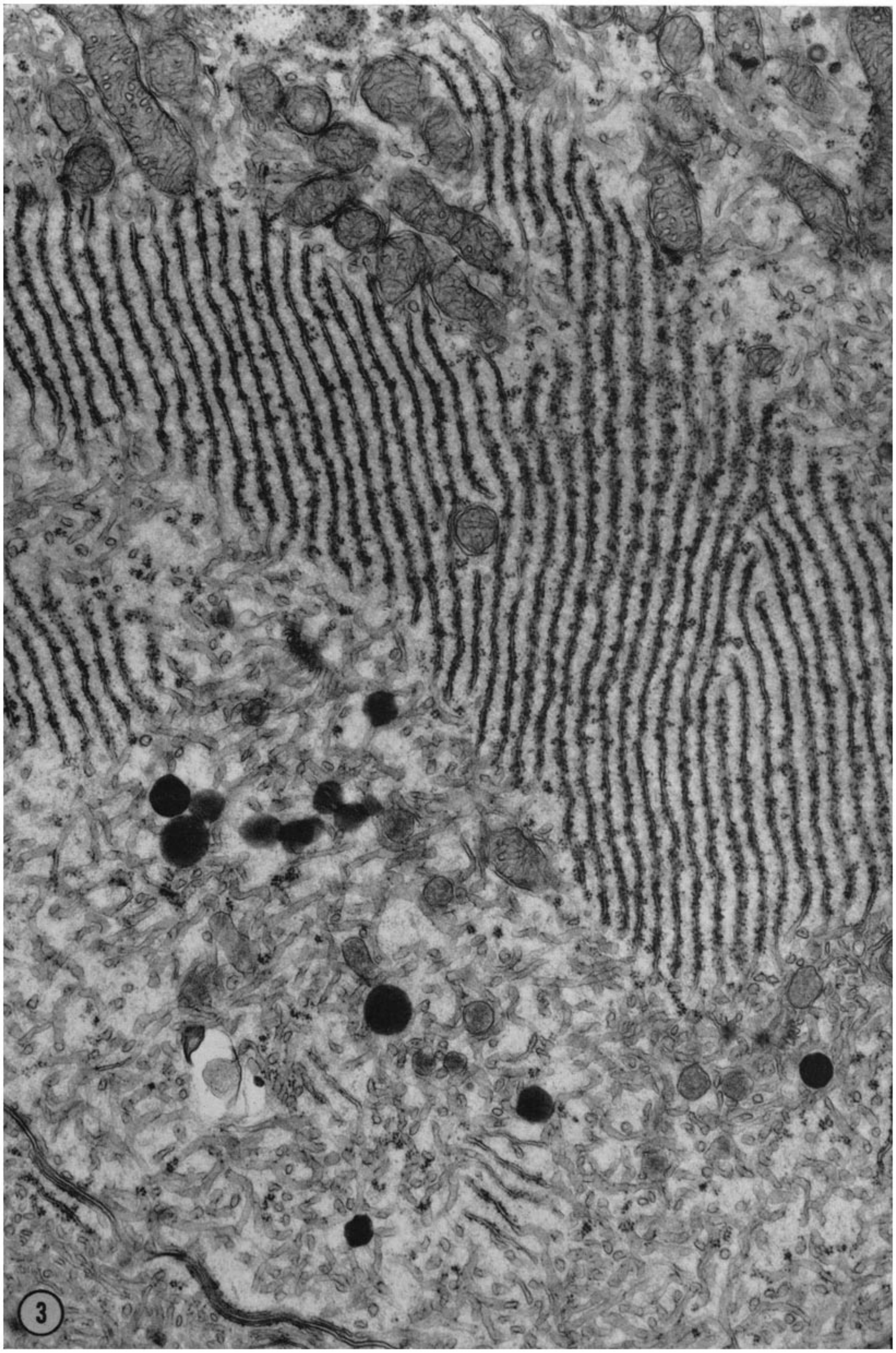


FIGURE 3 A higher magnification of the peripheral cytoplasm of the luteal cell seen in Fig. 1. Note subsurface cisternae of granular ER at lower left, peripheral mass of agranular ER whose membranes are often in continuity with granular ER, and, at top, the more central agranular ER that is closely associated with mitochondria. H51. × 22,000.

bundles terminate in microvilli, either at the cell surface (Fig. 11) or in those surfaces seen near the nucleus at the terminal end of a deep fold of the lateral cell membrane. The bundles of filaments usually are surrounded by an organelle-free, fibrillar matrix which merges with the matrix throughout the cytoplasm.

Hyalin (colloid) bodies, histologically characteristic of luteal cells of pregnancy, and/or large vacuoles are seen within occasional cells. The hyalin bodies contain an electron-opaque homogeneous material with occasional needle-like crystals (Fig. 8) or vesicular structures. The apparently intracellular vacuoles, often large enough to distort the entire luteal cell, are lined by attenuated microvilli and contain an electron-translucent material.

Where luteal cells are closely adjoined, segments of their cell membranes often are bilaterally associated with subsurface cisternae of granular ER (Fig. 3). These cisternae have ribosomes only on the membrane at the cytoplasmic side (Fig. 14). The other membrane which is agranular is separated by only 60–70 A from the cell surface. Adjoining luteal cells also have agranular ER in close apposition to the cell surface facing a narrow intercellular space (Fig. 16). Elsewhere along such narrow spaces, which apparently are freely continuous with the perivascular spaces (Fig. 15), there are patches of microvilli (Fig. 18). These microvilli often surround an intercellular space or channel containing vesicular or foamy material (Figs. 19 and 20). In early pregnancy, these lateral margins form deep, narrow folds into the luteal cell cytoplasm which terminate in microvilli situated near a paranuclear Golgi complex with associated vesicular dense bodies (Fig. 17). Within the intercellular space surrounded by these microvilli, granular and vesicular material also can often be seen.

Another type of luteal cell present in all stages of pregnancy is characterized by an irregular nuclear membrane, ER that is usually vesicular, and variable forms of mitochondria (Figs. 21–23). This cell is also distinguished by the presence within the nucleus or the perinuclear cytoplasm of multiple aggregates of vesicles enclosed within a single smooth membrane (Figs. 21 and 24). Such vesicular aggregates were never seen within similar cells in active corpora lutea of the menstrual cycle (1) but are prominent in most cells of this type during pregnancy. Small vesicles are often present either singly or in aggregates within the perinuclear space. These vesicles are similar in size to those clustered within a single smooth membrane either apparently free in the peripheral nucleo-

FIGURE 4 A crescentic Golgi complex from a 16-week pregnancy. Note the small vesicles between Golgi saccules and the associated two granular spheres at top. H42. × 22,000.

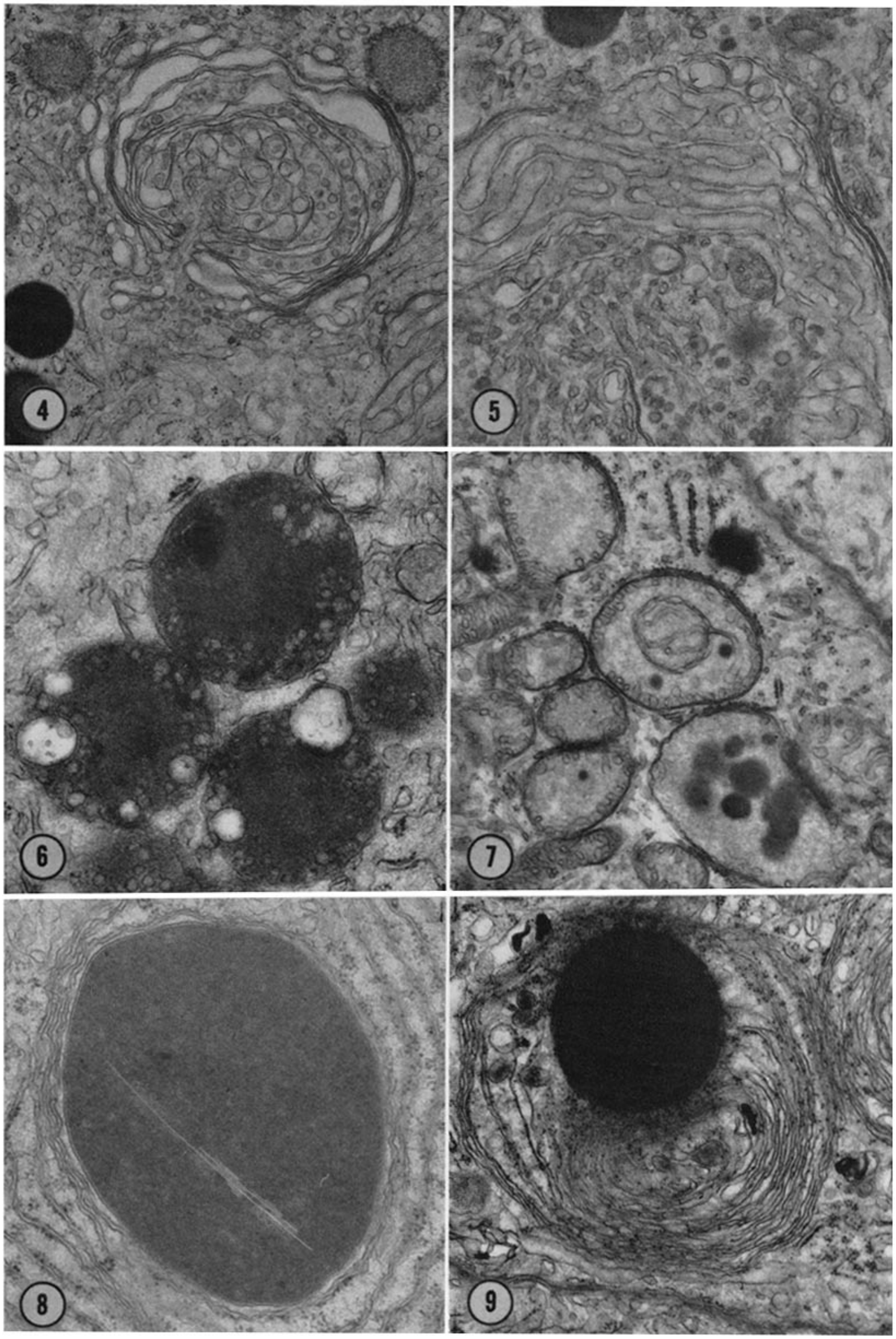
FIGURE 5 A portion of an elaborate Golgi complex from a 35-week pregnancy. Note interdigitation of expanded Golgi saccules and the variety of associated vesicles. H43. × 22,000.

FIGURE 6 Dense bodies containing vesicles of a variety of sizes from a 6-week pregnancy. H51. × 34,000.

FIGURE 7 A few luteal cells contain clustered mitochondria with electron-opaque deposits in their matrix and short or distorted cristae. From a 10-week pregnancy. H49. × 22,000.

FIGURE 8 A hyalin (colloid) body in a luteal cell from a 16-week pregnancy. Note needle-like crystals within the homogeneous, electron-opaque material. Some smaller hyalin bodies such as this one are surrounded by granular ER, but other larger ones are not. H42. × 28,000.

FIGURE 9 A whorled membranous structure in the peripheral cytoplasm of a 35-week pregnancy. H43. × 22,000.


4
5
6
7
8
9

plasm or attached to the inner leaflet of the nuclear membrane. Many cells with nuclear vesicular aggregates also have similar structures either in the convoluted perinuclear cytoplasm or attached to the outer leaflet of the nuclear membrane (Fig. 24). In some instances these single membrane-bounded vesicular aggregates resemble structures associated with nearby Golgi complexes, but many others within the same section do not appear to be related to Golgi areas (Fig. 24). In some of the more electron-opaque cells with nuclear vesicular aggregates, vesicular ER that is sparsely granular and that contains an inner small vesicle can be seen to be in continuity with the outer leaflet of the nuclear membrane (Fig. 25). Many nuclei of this type of luteal cell contain one or more spheroidal bodies, in addition to the nuclear or perinuclear vesicular aggregates (Figs. 24 and 29). Occasional spheroidal bodies have a large granular core and a halo of granular or fibrillar material (Fig. 30), whereas others are formed of irregular concentric rings of granular or fibrillar material (Figs. 29, 31, and 32). Only very rarely are such structured nuclear bodies seen in the more prevalent type of luteal cell containing a spherical nucleus and tubular ER (Fig. 31).

Clumps of the luteal cells with irregular nuclear membranes can be seen along the larger vascular channels and in the basal layer of the corpus luteum. Other such luteal cells are seen singly and surrounded by luteal cells of the more prevalent type. Toward term they form a plaque along vascular channels where they are associated with large extracellular vacuoles, luteal debris, and red blood cells (Fig. 23). Some of these luteal cells are very electron-opaque with clumped, apparently pycnotic nuclear elements, a dense cytoplasmic matrix, and mitochondria of various sizes and shapes (Fig. 22). Their projections appear to engulf and/or invade the peripheral cytoplasm of neighboring luteal cells whose tubular ER is often in close apposition to the cell membrane (Figs. 22 and 28). Other cells with nuclear vesicular aggregates have mitochondria and vesicular ER dispersed in a cytoplasmic matrix that is no more electron-opaque than that of neighboring cells (Figs. 21 and 33). Granular ER which is often dilated to form vacuolar structures and which is associated with clumps of ribosomes in the surrounding matrix is prominent in the peripheral cytoplasm (Fig. 27). Where the surface membrane of these cells borders a perivascular space, it often appears incomplete or indistinct and vesicles appear to be liberated into the extracellular space (Fig. 26).

A thecal layer is prominent in our specimens obtained during the first half of pregnancy but was not observed in the 35-week specimen. Cells in the thecal layer can be distinguished by their smaller size, their cuboidal shape, their closely apposed straight membranes, and their greater electron-opacity. Their cytoplasm contains closely packed agranular ER, a few peripheral parallel arrays of granular ER, elongate mitochondria with both tubular and lamellar cristae, and conspicuous dense bodies (Fig. 34). Lipid droplets are not present in any thecal cell we observed.

DISCUSSION

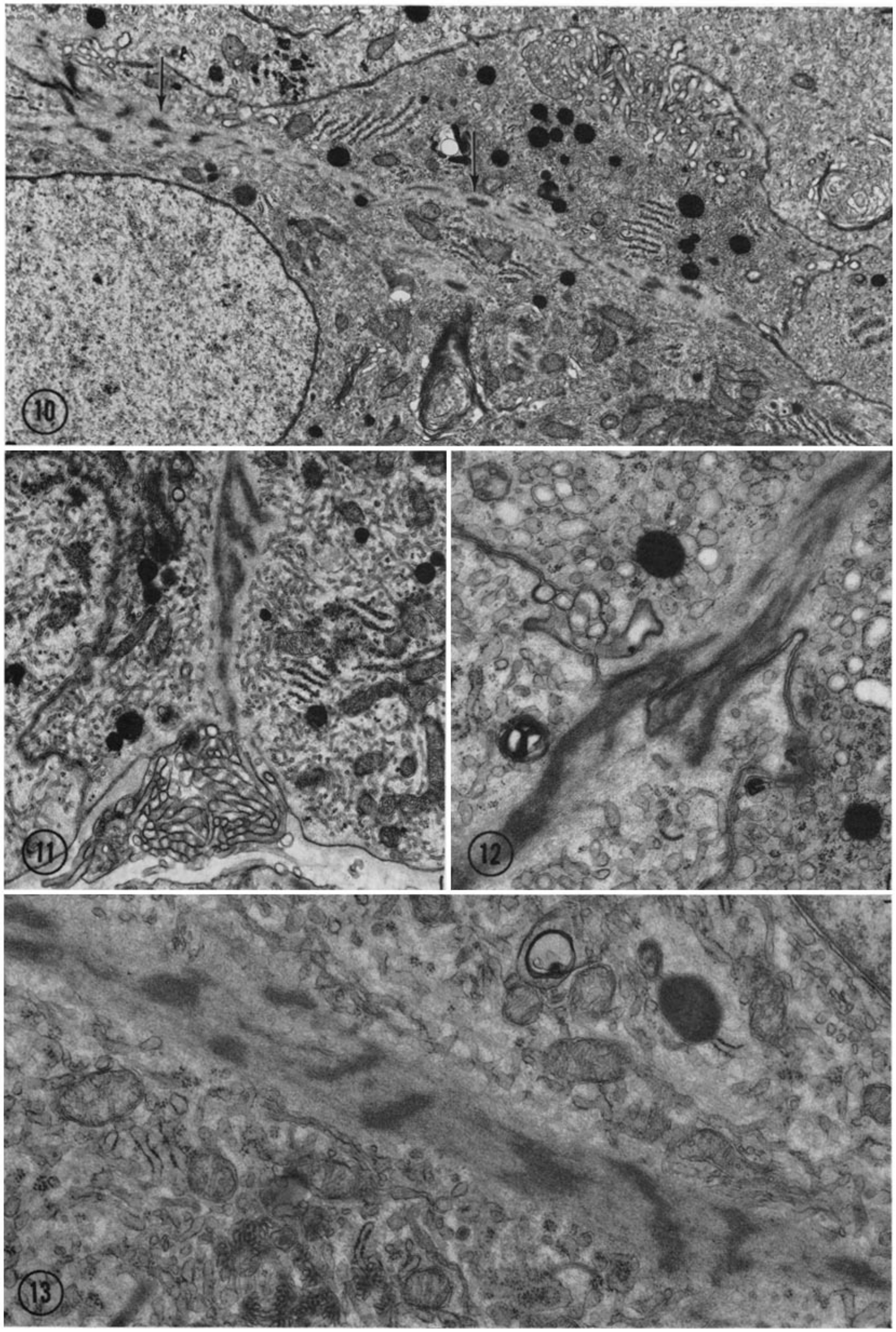
Soon after the implantation of the fertilized ovum, on about its fifth or sixth day of development (10), the immature trophoblast begins to secrete chorionic gonadotropin (9). This secretion directly or indirectly supports the maintenance of the

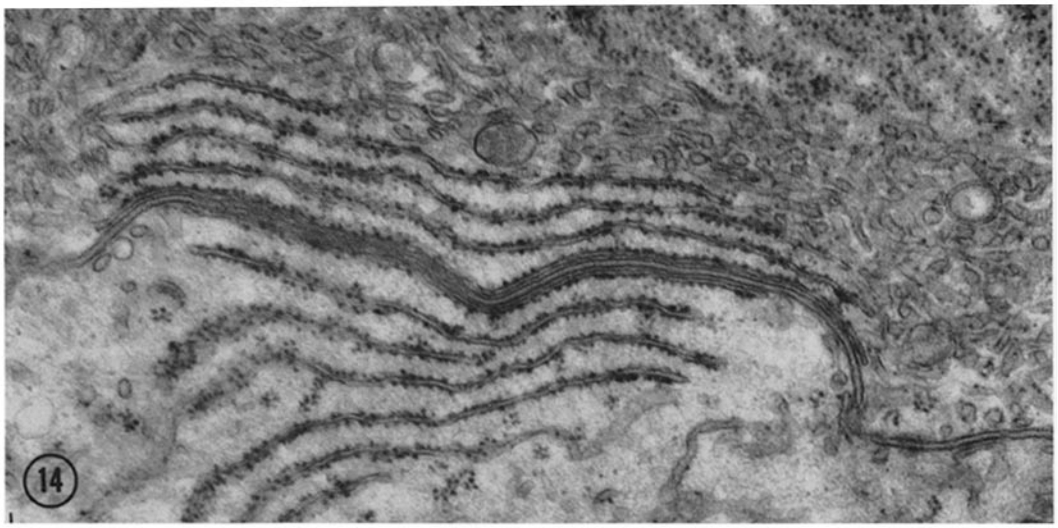
FIGURE 10 Long bundles of filaments (↑) traverse the cytoplasm of luteal cells and often appear to separate the peripheral ER from the central region of mitochondria and Golgi areas. From a 16-week pregnancy. H42. × 7400.

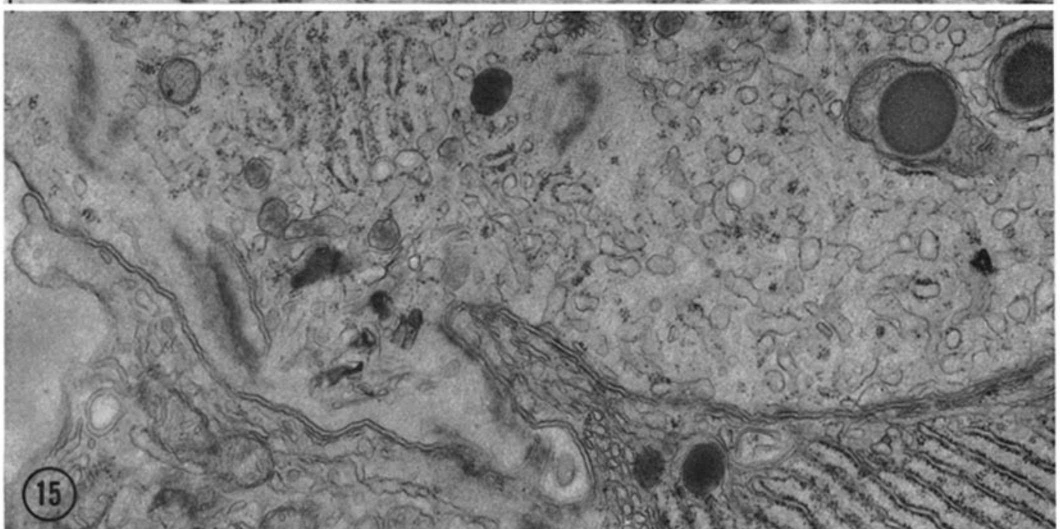
FIGURE 11 Some filamentous bundles terminate at microvilli as in this 6-week pregnancy. H51. × 10,000.

FIGURE 12 Bundles of filaments in contiguous cells may arise from adjacent desmosomal regions. H42. × 22,000.

FIGURE 13 The bundles of filaments often show irregular dense regions as in this luteal cell from a 35-week pregnancy. H43. × 22,000.


10
11
12
13





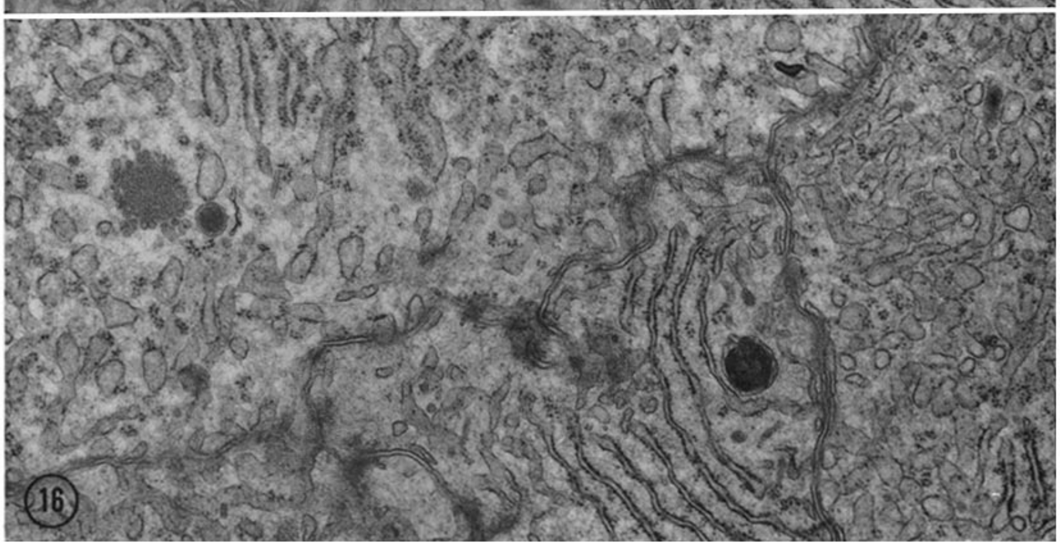


FIGURE 14 Bilateral subsurface cisternae of granular ER are frequently found in closely adjoined luteal cells from this 6-week pregnancy. Granules are present only on the cisternal membrane that faces the cytoplasm. H51. × 34,000.

FIGURE 15 Note that the intercellular space between these two luteal cells opens freely into perivascular space at left. Also, note mitochondrion with spherical electron-opaque deposit in its matrix at right. H42. × 22,000.

FIGURE 16 The tubular ER is very closely apposed to the luteal cell surfaces along a narrow intercellular space. H43. × 22,000.

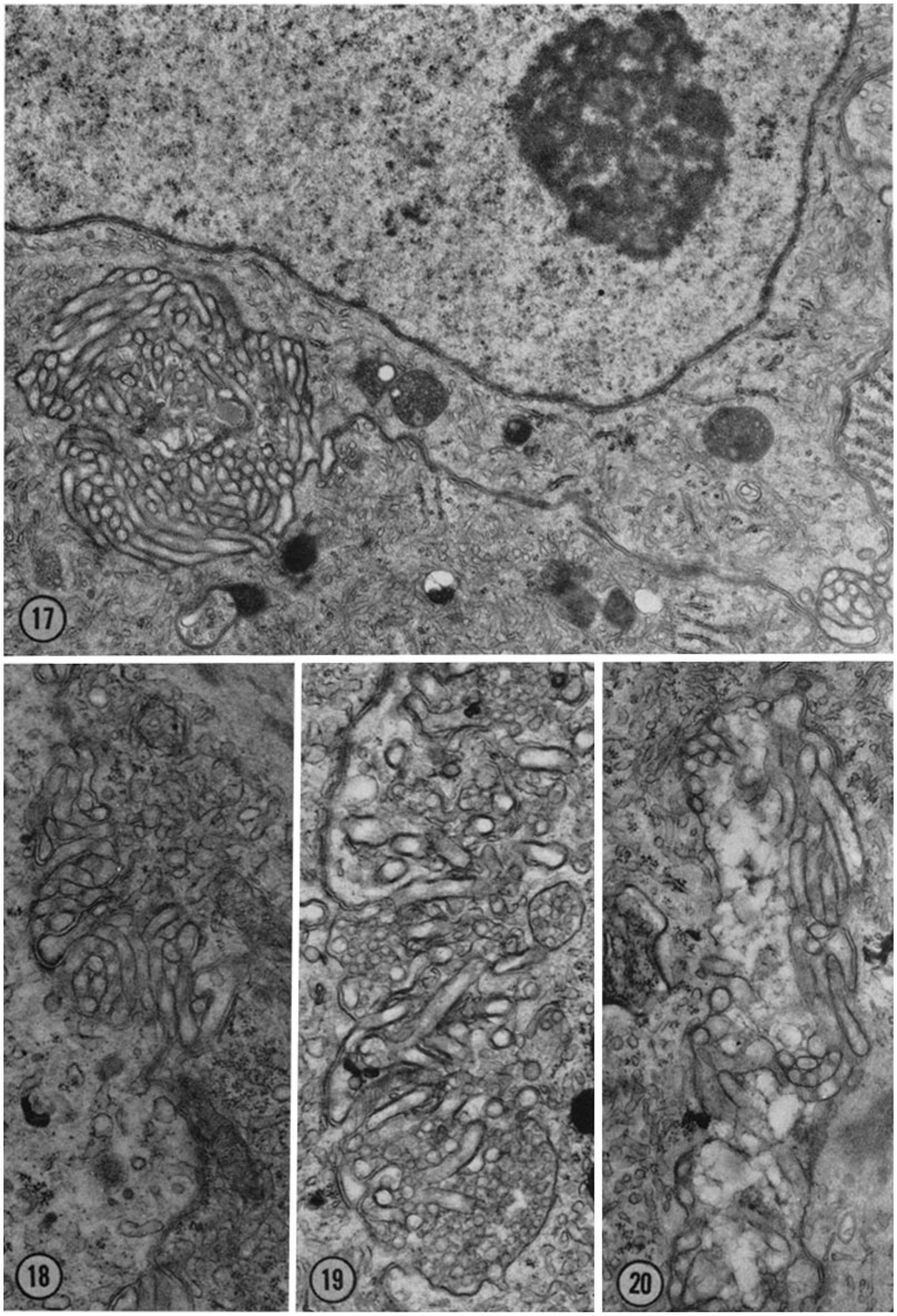


FIGURE 17 In this luteal cell from a 6-week pregnancy, a deep narrow fold of its lateral surface terminates in paranuclear microvilli associated with dense bodies near a Golgi complex. H51. × 15,000.

Figure 18 Microvilli on the closely adjoined surfaces of two luteal cells. H42. × 22,000.

FIGURE 19, 20 Microvilli on the lateral cell surfaces frequently enclose an intercellular space containing vesicles or foamy material. Fig. 19, H42; Fig. 20, H51. X 22,000.

otherwise transitory steroidogenic properties of the cyclic luteal cell and results in the establishment of the corpus luteum of pregnancy. Therefore, it is not surprising that the ultrastructure of luteal cells of pregnancy closely resembles that of luteal cells seen in our study of the active phase of the menstrual cycle before the regressive cellular changes of the late luteal phase and menstruation begin (1). The cellular changes that do occur in pregnancy may reflect either a cellular organization not fully established in the brief period between differentiation and regression of the menstrual cycle luteal cells or the effect of placental vs. pituitary gonadotropic hormone.

The cytoplasm of the typical luteal cell of pregnancy is more clearly compartmentalized into a peripheral mass of tubular ER with only scattered mitochondria and small lipid droplets which merges into a central area where mitochondria and Golgi complexes surrounded by tubular ER are concentrated. Multiple parallel arrays of granular ER often appear to lie in a position intermediate between these peripheral and central areas of cytoplasm. The intimate association of tubular ER with the lateral cell borders of closely adjoined cells, the close topographic relationship of tubular ER and mitochondria (organelles known to be associated with steroidogenesis in many steroid cells), and the prominent central Golgi complexes were also observed and discussed in our preceding paper on the active cyclic luteal cell. These relationships again suggest the possibility that substrate may enter the cytoplasm via the lateral cell border and be converted to and stored as cholesterol in the peripheral tubular ER (4). Such material may pass through the cisternae of granular ER to an area of close association between tubular ER and mitochondria, where biosynthetic pathways of steroidogenesis are determined, and then enter the Golgi areas perhaps for conversion to substances suitable for secretion at the cell border facing the vascular channel. In the luteal cell of pregnancy these borders develop prominent microvilli that are present in addition to the patches of microvilli along the lateral borders of luteal cells of both pregnancy and the menstrual cycle. Green et al. (7) noted that the patches of microvilli along the borders of contiguous luteal cells have a structure similar to that of bile canaliculi and suggested that they may serve as channels to carry steroids to the vascular bed.

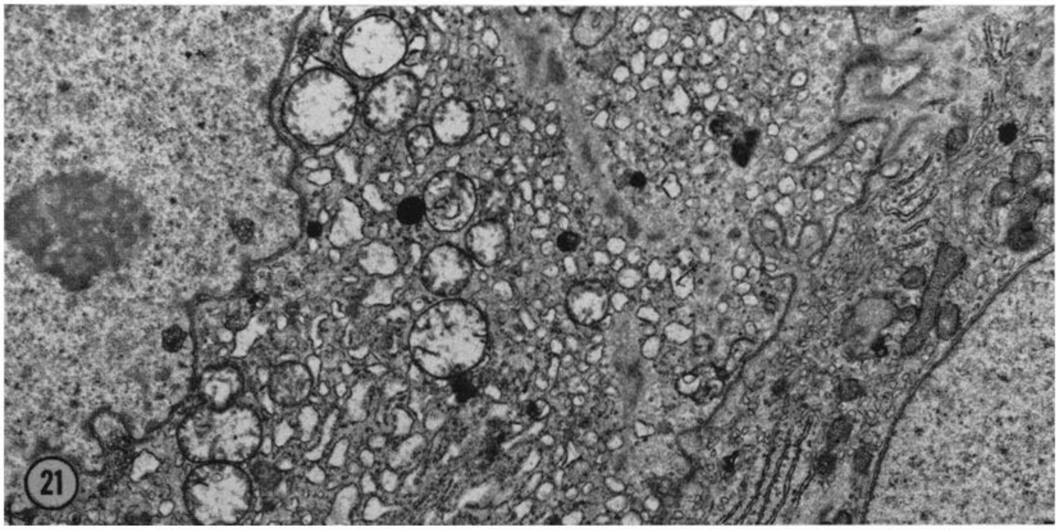
Segments of subsurface cisternae of granular ER at the lateral cell borders were observed only rarely in active luteal cells of the menstrual cycle but are striking and usually bilateral in the luteal cells of early pregnancy and remain prominent thereafter. Similar structures, but unilateral and usually lacking ribosomes, have been described in neurons by Rosenbluth (14). He discussed their probable electrical or chemical effect on the plasma membrane and reported that they appear to be most prominent in various cell types which engage in the generation or conduction of electrical potential changes. The subsurface cisternae in the luteal cell of pregnancy appear to be areas of specialized junctional surfaces and may serve a function similar to that suggested for the tight junctions and their derivatives and for the spherical inclusions which are present in the cyclic luteal cell. These pentilaminar structures, i.e. tight junctions and spherical inclusions, are present in luteal cells of pregnancy but are not nearly so prominent as in the cyclic cells. We have postulated that in the cyclic luteal cells these structures are areas of cell conductivity possibly related to the coordination of cell function (1).

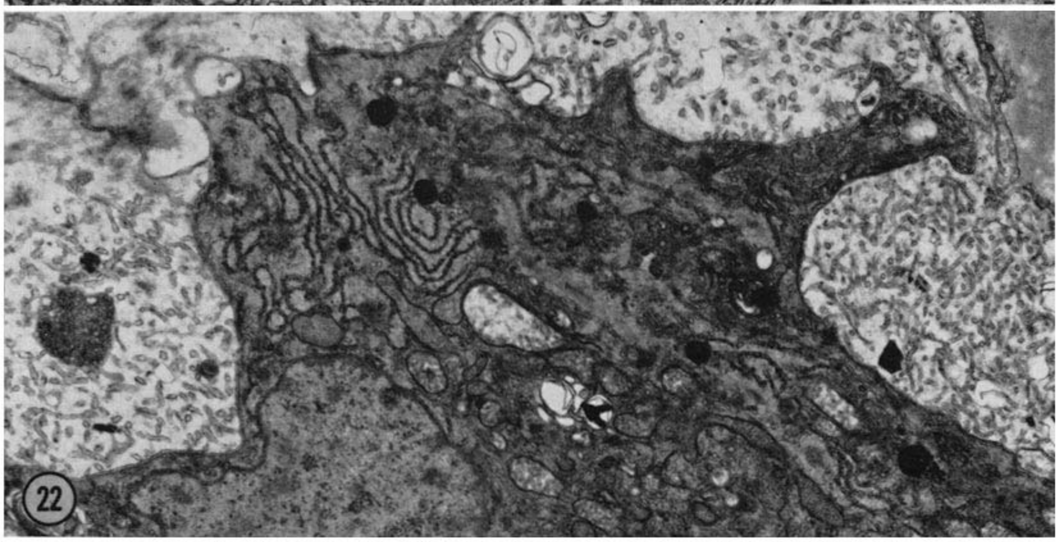
The long bundles of filaments which become

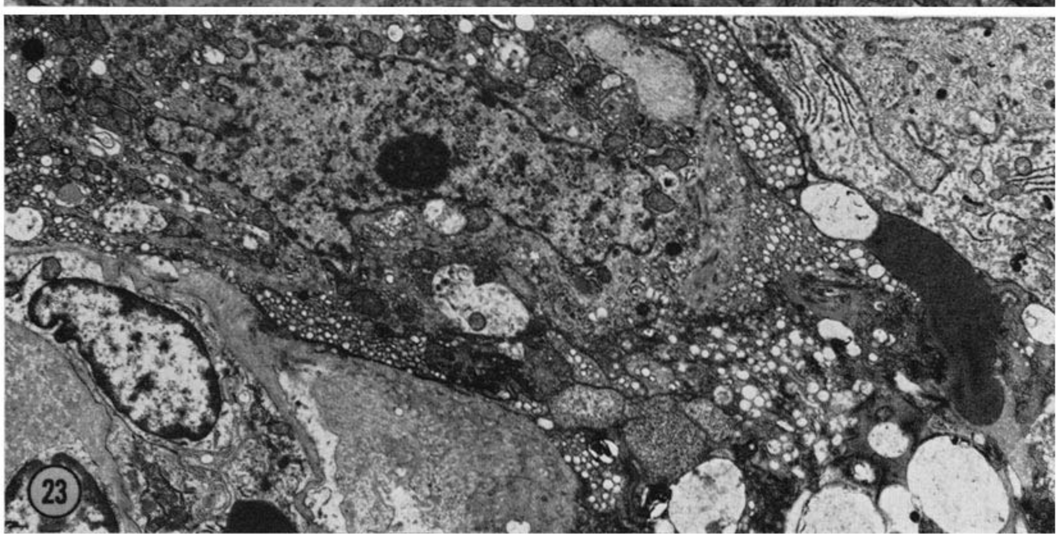
FIGURE 21 The luteal cell at left has an irregular nuclear membrane, dilated mitochondria, and vesicular ER. Note vesicular aggregates in nucleus and perinuclear cytoplasm. Some luteal cells of this type are no more electron-opaque than the more prevalent type with a spherical nucleus and tubular ER (right). H42. × 10,000.

FIGURE 22 Many of these luteal cells containing nuclear vesicular aggregates are electron-opaque and show evidence of nuclear pycnosis and cellular death. Their cytoplasmic projections appear to invade the surrounding cells. H49. × 10,000.

FIGURE 23 In the corpus luteum of a 35-week pregnancy, the cells with irregular nuclear membranes are found in plaques along vascular channels. H43. × 5400.


21


22


23

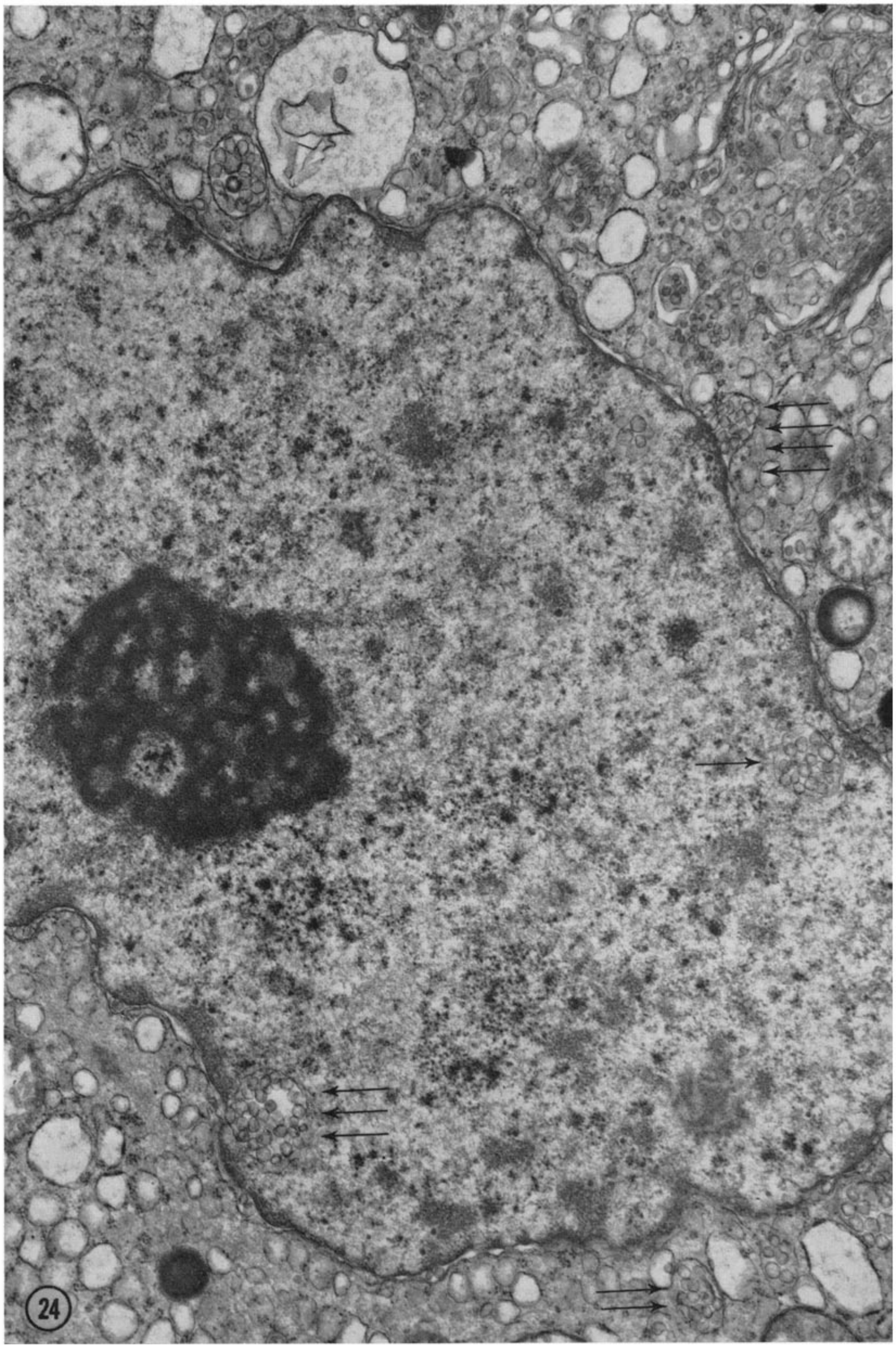


FIGURE 24 The cells with irregular nuclear membranes usually contain vesicular aggregates enclosed within a single membrane. These structures are found in the nucleus (↑) and perinuclear (two arrows) cytoplasm. Their limiting membrane may be formed by the inner (three arrows) or outer leaflets (four arrows) of the nuclear membrane. A few single vesicles can be seen within the perinuclear space. A structure reminiscent of a spheroidal body is seen in lower right of nucleus. H42. × 22,000.

prominent in luteal cells of pregnancy were beginning to form in occasional cells of the late luteal phase of the menstrual cycle. Strands of filaments have been previously reported in luteal cells from a human term pregnancy by Green et al. (7) but have not been noted in luteal cells from other mammalian species. Conspicuous masses or bundles of filaments have been observed in the interstitial cells of the bird testis (5) and in the fusiform interstitial cells of the human testis (6). In the human luteal cell the conspicuous bundles of filaments may function as cellular supports but, since they frequently lie between the peripheral ER and the more central mitochondrial–Golgi areas, it is also possible that in some way they may control or direct the intracellular flow of substances.

The luteal cell of pregnancy that is characterized by vesicular aggregates in the nucleoplasm or in the perinuclear cytoplasm may be a functionally specialized type of cell, but this characteristic ultrastructure could also represent an effect of some specific form of regression or inhibition in the more prevalent type of luteal cell. Their counterparts, in the active phase of the menstrual cycle were the cells with irregular nuclear membranes, vesicular ER, and variable mitochondrial forms. The cyclic cell, however, consistently lacked the nuclear or cytoplasmic vesicular aggregates so prominent in pregnancy but did on occasion contain spheroidal nuclear bodies. In both the menstrual cycle and in pregnancy these cells are often associated with vascular channels and show a variable electron-opacity, the most electron-opaque cells apparently being dehydrated, dead or dying cells with pycnotic nuclei. It was suggested (1), on the basis of position and increased density, that these cells may represent at least a part of the population of thecal cells which invade and become incorporated into the corpus luteum of menstruation. Histologically, a distinct thecal layer is present in the early corpus luteum of pregnancy but is absent in corpora lutea of term pregnancy. This could mean that thecal cells continue to migrate into the corpus luteum of pregnancy and are a possible source of the cells containing nuclear or perinuclear vesicular aggregates. Cells histologically comparable to the more electron-opaque luteal cells with irregular nuclear membranes have been noted by White et al. (18) and by Hertig (8) who reported their presence in the early active cyclic corpus luteum as well as in the corpus luteum of pregnancy and suggested their thecal origin. The steroidogenic importance of thecal cells of the corpus luteum of pregnancy or of the menstrual cycle is unknown. Ryan and Petro (15) have shown that, during the follicular phase, these cells produce estrogen, a substance known to be formed in the human corpus luteum.

The physiologic implications and the site of production of the vesicular aggregates in the cells with irregular nuclear membranes are unknown. The single membrane that encloses them appears to derive from or attach to either the inner or the outer leaflet of the nuclear membrane. If they are formed in the cytoplasm they may be related to vesicles associated with Golgi complexes or to the vesicular form of ER usually characteristic of this type of cell. Intranuclear cisternae resembling structures of the Golgi complex have been reported in cells in intracranial Rous sarcoma by Bucciarelli (3). The vesiculation of the agranular ER together with the dilation of the granular ER may be an artifactitious response to fixation in particular cells whose agranular ER is more labile than that of adjoining cells with tubular ER. The variable structure of the mitochondria together with an unusual lability of the ER in these cells could reflect either a cell with a different physiologic activity or one whose cytoplasmic integrity has already been affected by some regressive change.

The frequent finding of spheroidal bodies within the nuclei of the same type of luteal cell that usually contains vesicular aggregates—nuclear or cytoplasmic—suggests a possible correlation between these structures. Furthermore, the possibility that the vesicular aggregates are formed initially within the nucleus should be considered in view of the studies by Weber et al. (17) on the nuclear bodies of the adrenal zona fasciculata of the calf treated with adrenocorticotropic hormone (ACTH). These authors reported that these nuclear bodies showed structural and positional changes, apparently in specific response to ACTH, leading to the development of a multilocular body enclosed in a single membrane. Subsequently, this multilocular body moved from the nucleolar area toward the nuclear membrane and in some instances became contiguous with it. Weber et al. suggest that these changes in the nuclear body may be associated either with the nucleolar organizer or with degenerative change, but they speculate that the nuclear body may be a receptor center for tropic hormones of the pituitary. Although a variety of forms of spheroidal nuclear bodies was observed in our material, no structure indicating a transition to vesicular aggregates was found. Spheroidal nuclear bodies in liver cell nuclei in rats with subacute ethionine intoxication have been reported by Miyai and Steiner (13) and in hamster liver cells by Jones and Fawcett (11). The distribution of nuclear bodies has been the subject of two recent reports. The ultrastructural variations in these bodies in human disease have been classified by Bouteille et al. (2). They conclude that nuclear bodies are related to cellular hyperactivity, the cause of which may be physiological, hormonal, drug-induced, viral, or tumoral. Nuclear bodies in hamster tissues and in a variety of human tumors also have been described by Krishan et al. (12) whose preliminary histochemical studies indicate that fibrous nuclear bodies do not contain DNA or RNA but may have proteins in their structure.

In view of all of these reports, the luteal cell of pregnancy that contains nuclear vesicular aggregates and/or spheroidal bodies may represent a cell that has been subject to a prolonged (and possibly particular) stimulation and shows variable evidence of secretory exhaustion which ultimately results in the electron-opaque, dehydrated-appearing stellate cell with a pycnotic nucleus.

This work was supported largely by grant HD 00137, Division of Human Development and Child Health, formerly C-2451 of the National Institutes of Health and supplemented by the Proctor and Milton Funds of Harvard University. Grateful thanks are due to Mrs. Barbara Barton and Miss Harriet Jopson for their skilled technical assistance, to Miss Audrey Hadfield for the preparation of the micrographs, and to Mrs. Nancy Cote and Miss Mary Gethin for typing the manuscript. The authors are greatly indebted to members of the staff of the Boston Hospital for Women for their cooperation in providing us with these human ovaries.

Please address reprint requests to the authors at the New England Regional Primate Research Center, Southborough, Massachusetts 01772.

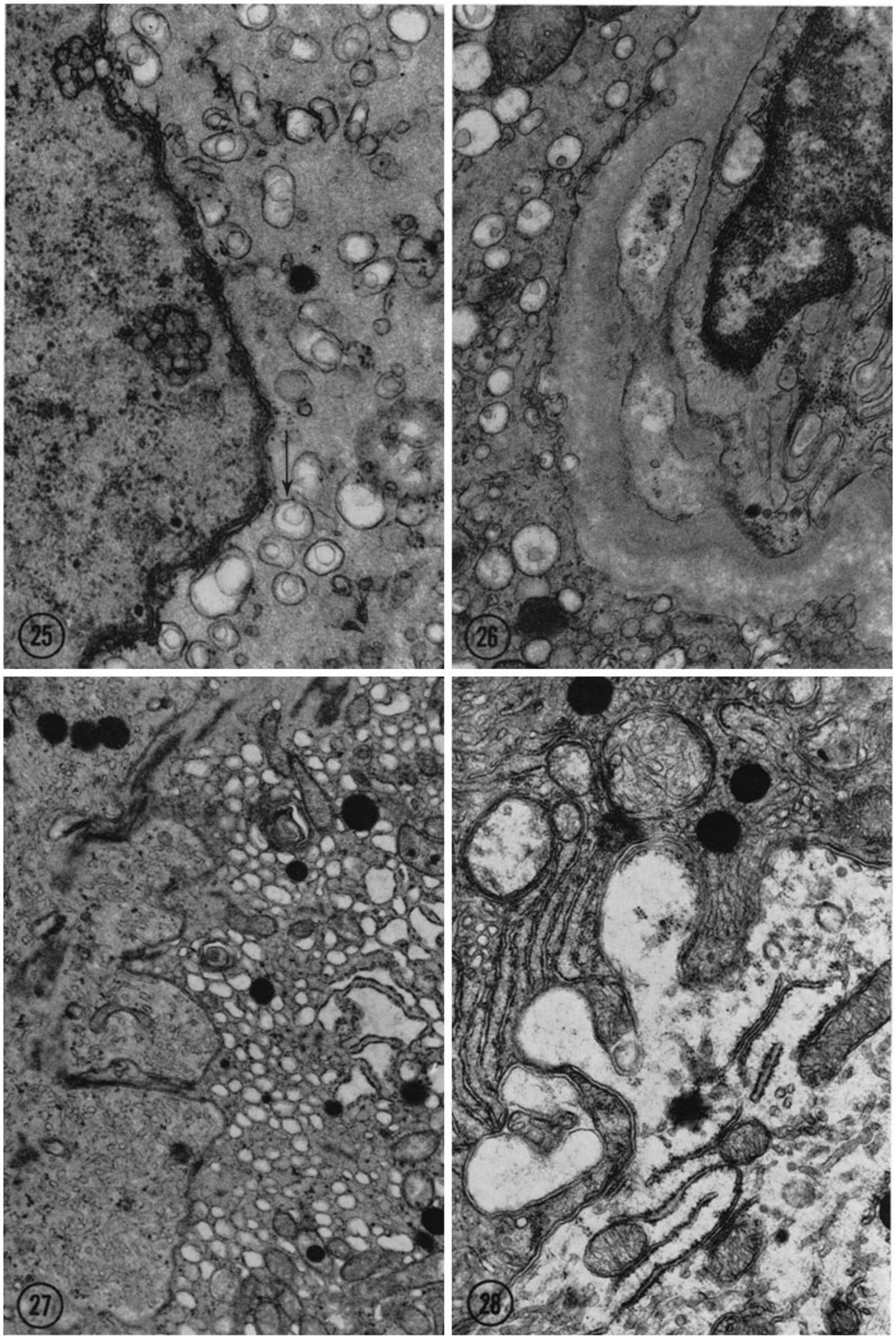
Received for publication 14 May 1968 and in revised form 10 January 1969.

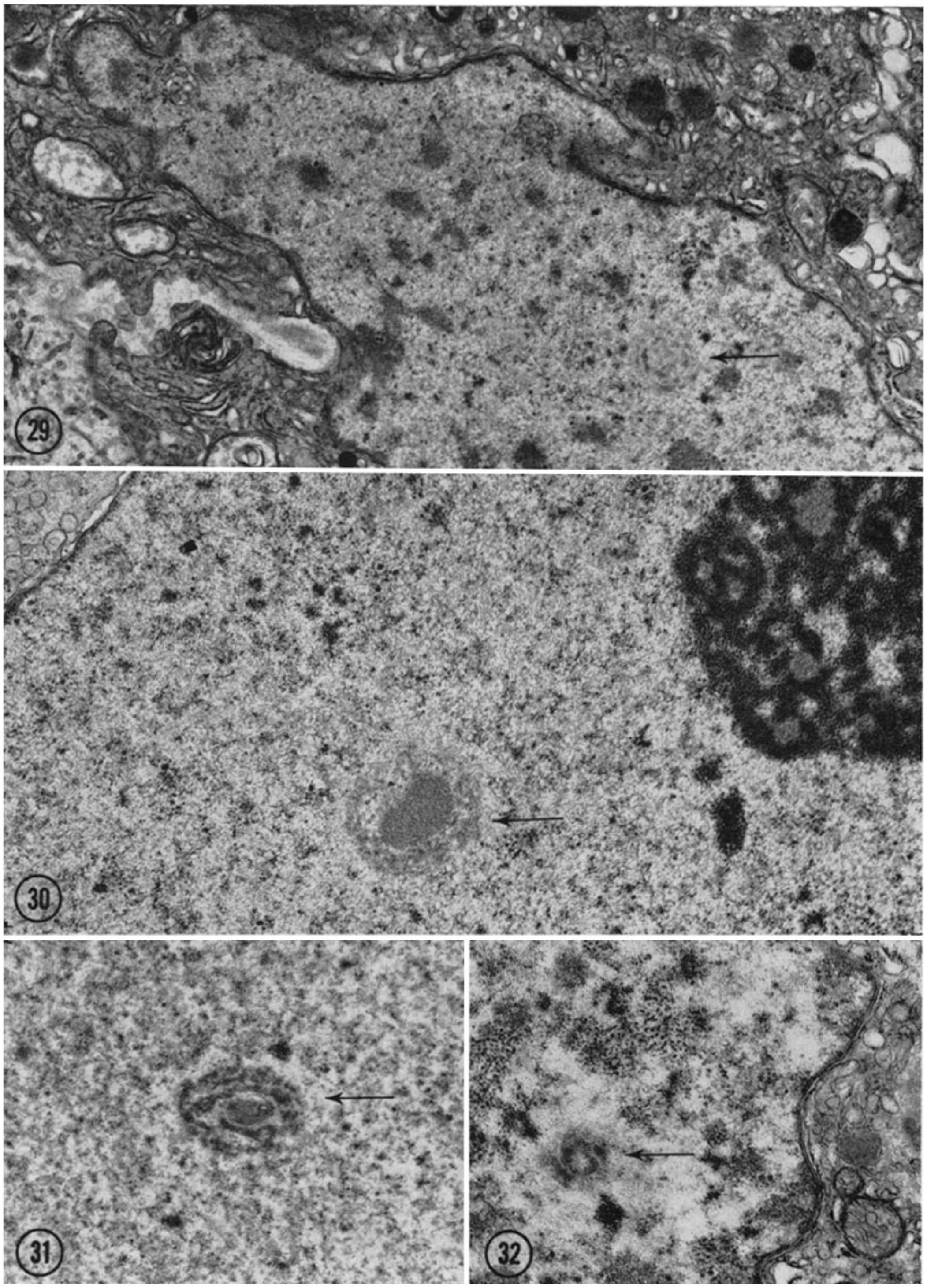
FIGURE 25 In some of the more electron-opaque cells with nuclear vesicular aggregates, the sparsely granular vesicular ER containing an inner vesicle appears to be continuous with the outer leaflet of the nuclear membrane (↑). H51. × 34,000.

FIGURE 26 The surface of these altered cells often appears incomplete, and vesicles similar to the cytoplasmic ER appear to be extracellular. H43. × 22,000.

FIGURE 27 At right is the peripheral cytoplasm of a cell with an irregular nucleus. Note vacuolization of its granular ER. H42. × 10,000.

FIGURE 28 The cytoplasm of this electron-opaque luteal cell at top left appears to invade and engulf the cytoplasm of another cell. H49. × 22,000.


25
26
27
28



FIGURES 29–32 Spheroidal nuclear bodies (↑) are also frequently found in the cells with irregular nuclei but only rarely in luteal cells with spherical nuclei and tubular ER. Note presence of nuclear vesicular aggregates in Fig. 29. Fig. 29: H49, × 15,000. Fig. 30: H42, × 22,000. Fig. 31: H53, × 15,000. Fig. 32: H49, × 22,000.

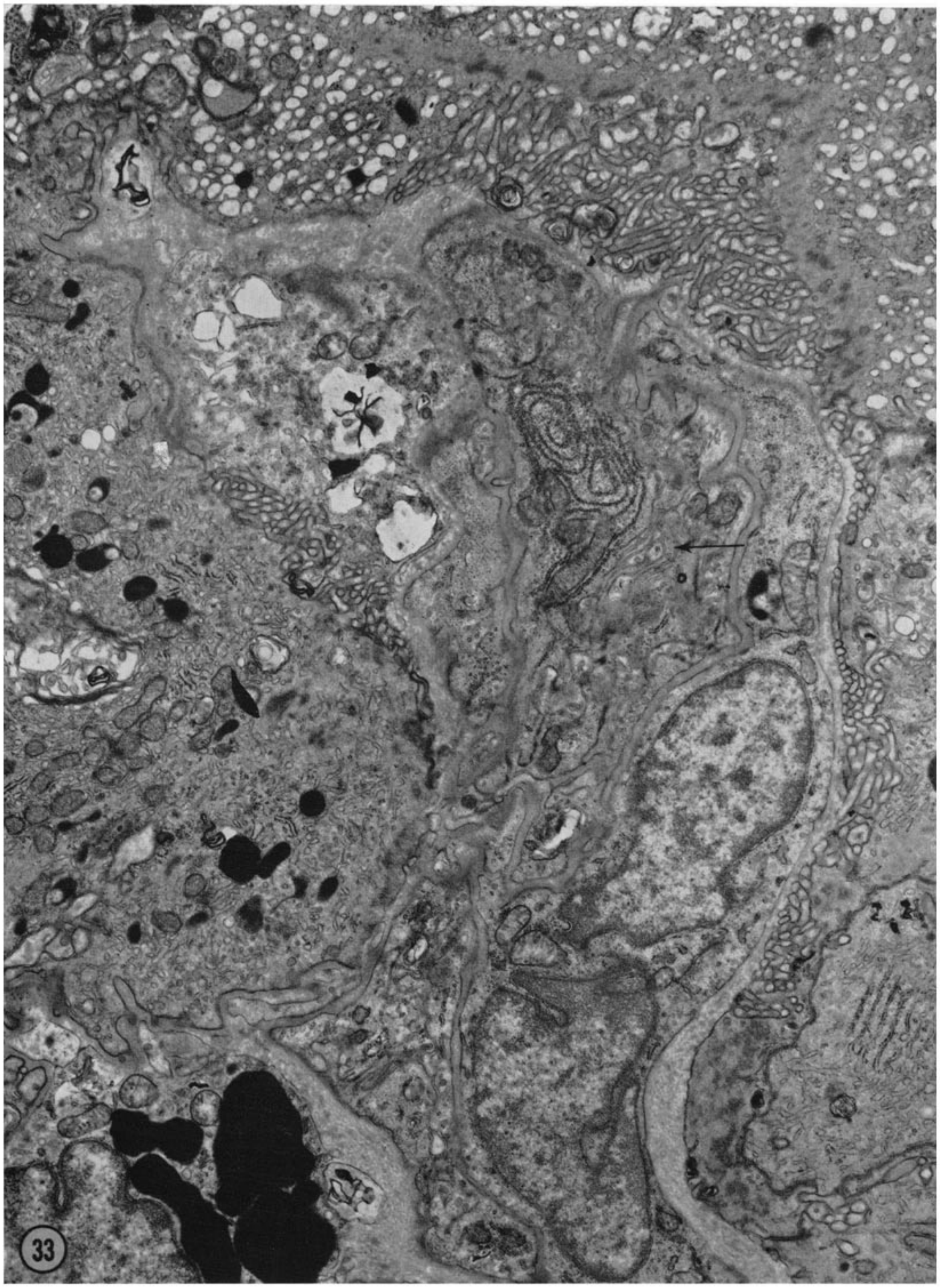


FIGURE 33 A vascular channel with a collapsed lumen (↑) surrounded by luteal cells, one of which (top) is of the type with vesicular ER. H42. × 10,000.

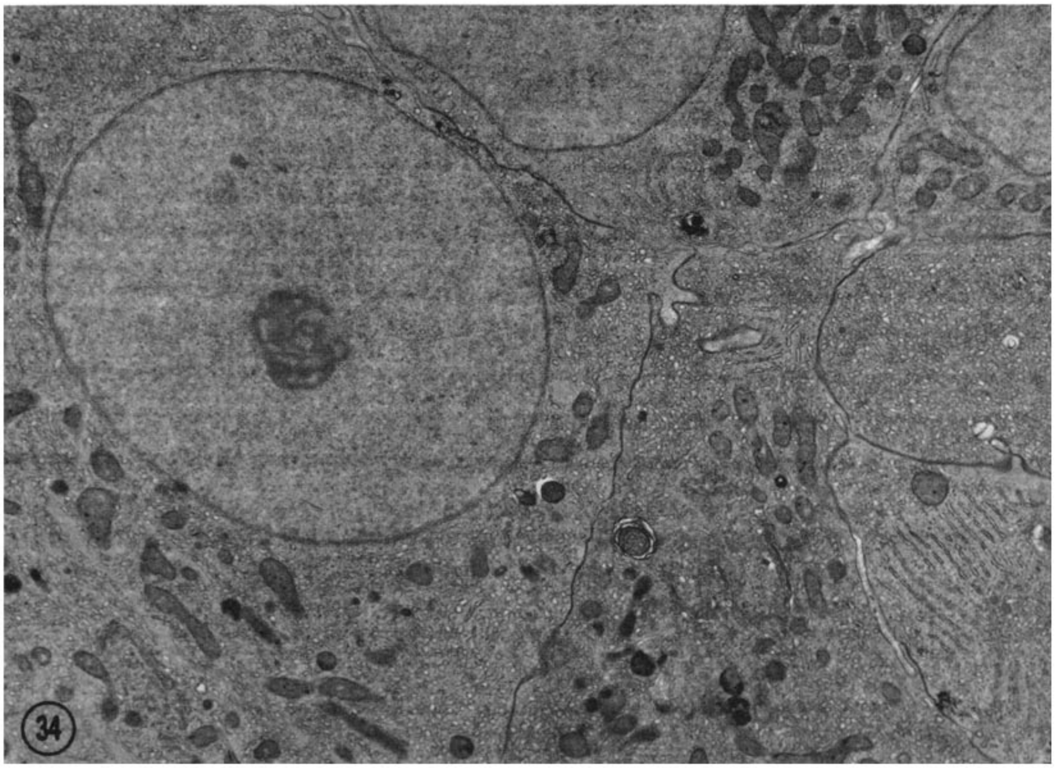


FIGURE 34. Cells of the thecal layer are closely packed, smaller, and more electron-opaque than the luteal cells of the corpus luteum. H53. × 7400.

REFERENCES

1. ADAMS, E. C., and A. T. HERTIG. 1969. Studies on the human corpus luteum. I. Observations on the ultrastructure of development and regression of the luteal cells during the menstrual cycle. *J. Cell Biol.* **41**:000.
2. BOUTEILLE, M., S. R. KALIFAT, and J. DELARUE. 1967. Ultrastructural variations of nuclear bodies in human diseases. *J. Ultrastruct. Res.* **19**:474.
3. BUCCIARELLI, E. 1966. Intranuclear cisternae resembling structures of the Golgi complex. *J. Cell Biol.* **30**:664.
4. FAWCETT, D. W. 1965. Structural and functional variations in the membranes of the cytoplasm. *In* Intracellular Membranous Structure. S. Seno and E. V. Cowdry, editors. Japan Society for Cell Biology, Okayama.
5. FAWCETT, D. W. 1966. An Atlas of Fine Structure: The Cell; Its Organelles and Inclusions. W. B. Saunders Co., Philadelphia, Pa.
6. FAWCETT, D. W., and M. H. BURGOS. 1960. Studies on the fine structure of the mammalian testis. II. The human interstitial tissue. *Amer. J. Anat.* **107**:249.
7. GREEN, J. A., J. A. GARCILAZO, and M. MAQUEO. 1967. Ultrastructure of the human ovary II. The luteal cell at term. *Amer. J. Obstet. Gynecol.* **99**:855.
8. HERTIG, A. T. 1964. Gestational hyperplasia of endometrium. A morphologic correlation of ova, endometrium and corpora lutea during early pregnancy. *Lab. Invest.* **13**:1153.
9. HERTIG, A. T., and J. ROCK. 1941. Two human ova of the pre-villous stage, having an ovulation age of about eleven and twelve days respectively. *Contrib. Embryol.* **29**:127.
10. HERTIG, A. T., J. ROCK, and E. C. ADAMS. 1956. A description of 34 human ova within the first 17 days of development. *Amer. J. Anat.* **98**:435.
11. JONES, A. L., and D. W. FAWCETT. 1966. Hypertrophy of the agranular endoplasmic reticulum in hamster liver induced by phenobarbital (with a review of the function of this organelle in liver). *J. Histochem. Cytochem.* **14**:215.

12. KRISHAN, A., B. G. UZMAN, and E. T. HEDLEY-WHYTE. 1967. Nuclear bodies: A component of cell nuclei in hamster tissues and human tumors. *J. Ultrastruct. Res.* **19**:563.

13. MIYAI, K., and J. STEINER. 1965. Fine structure of interphase liver cell nuclei in subacute ethionine intoxication. *Exp. Mol. Pathol.* **4**:525.

14. ROSENBLUTH, J. 1962. Subsurface cisternae and their relationship to the neuronal plasma membrane. *J. Cell Biol.* **13**:405.

15. RYAN, K. J., and Z. PETRO. 1966. Steroid biosynthesis by human ovarian granulosa and theca cells. *J. Clin. Endocrinol. Metab.* **26**:46.

16. SAVARD, K., J. M. MARSH, and B. F. RICE. 1965. Gonadotropins and ovarian steroidogenesis. *Recent Progr. Hormone Res.* **21**:285.

17. WEBER, A., S. WHIPP, E. USENIK, and S. FROMMES. 1964. Structural changes in the nuclear body in the adrenal zona fasciculata of the calf following the administration of ACTH. *J. Ultrastruct. Res.* **11**:564.

18. WHITE, R. F., A. T. HERTIG, J. ROCK, and E. C. ADAMS. 1951. Histological and histochemical observations on the corpus luteum of human pregnancy with special reference to corpora lutea associated with early normal and abnormal ova. *Contrib. Embryol.* **34**:55.