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Electron microsopy of anterior pituitary changes following radiothyroidectomy

Vernon F. Garwood
University of Nebraska Medical Center

ELECTRON MICROSCOPY OF ANTERIOR PITUITARY CHANGES FOLLOWING RADIOTHYROIDECTOMY

Vernon F. Garwood

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INTRODUCTION AND REVIEW

Changes in pituitary cytology have been noted for many years following thyroid insufficiency. These changes have been noted to involve both the basophils and acidophils of the pituitary.

Severinghaus et al. (1934) reported that the basophils of thyroidectomized adult male rats were similar to the basophils of castrated animals. They noted that the acidophils were degranulated and diminished in size. Zeckwer et al. (1945) reported stunting of thyroidectomized rats. In this study the pituitaries contained "thyroidectomy" cells and the acidophils were degranulated.

Griesbach and Purves (1945) demonstrated that the basophils respond to slight thyroxin deficiencies while the acidophil changes occur only after complete thyroidectomy and are corrected by small doses of thyroxin. From these facts they concluded that the basophils produce thyrotrophin.

In 1946 Purves and Griebach reported that acidophil degranulation was complete by three weeks after thyroidectomy. The acidophils were thought to have some impaired function after severe thyroxin deficiency as larger doses of thyroxin are necessary to restore granulation than to maintain it if thyroxin is given from the date of thyroidectomy.

The basophils which became thyroidectomy cells have been studied and characterized by several authors as summarized by Purves in 1961. There has been special emphasis on differentiation of these cells from castration cells which are similar in several respects. The details of the light microscope picture are not particularly germane so will not be presented. References will be made to light microscope findings and particularly to certain histochemical aspects as related to protein synthesis.

In 1954 Farquhar and Rinehart described the ultrastructure of thyroidectomy cells. They reported progressive dilatation of vesiculated endoplasmic reticulum cisternae with variation of vesicle size within individual cells, in different thyroidectomy cells, and in various animals, correlated with the degree of thyroidectomy. They also noted fairly prominent Golgi complexes; decreased specific granulation; the occurrence of "T-granules" - small, dense intracisternal granules, as early as the tenth day; and incidentally, degranulation of the acidophils.

Lundin and Schelin (1964) described the ultrastructure of thyrotrophic pituitary adenomas in mice and generally confirmed the above observations. They discussed the ultrastructure as related to protein synthesis and concluded that these cells are well differentiated for their high rate of protein synthesis.

The present study was undertaken with the following objectives:

1. To re-evaluate the secretory status of growth hormone-producing cells after thyroidectomy, utilizing the improved resolution afforded by electron microscopy.
2. To study the degranulation process of the acidophil cells.
3. To further define the ultrastructure of thyroidectomy cells.
4. To identify the type of cells which produce thyrotrophin by comparison of the development and ultrastructure of thyroidectomy cells with cells of euthyroid rats.
5. To evaluate the ultrastructure of thyroidectomy cells as related to protein synthesis.

MATERIALS AND METHODS

Mature male rats were selected for study for the following reasons: (1) Most of the reports regarding the effect of thyroidectomy on the pituitary involve rats as the experimental animals; (2) The pituitaries of males contain only small numbers of prolactin (or luteotrophic hormone) producing cells which resemble growth hormone cells; (3) Mature animals were chosen so the growth hormone cells would be secreting at a minimal basal level to provide a good comparison with any possible stimulation.

Four male rats weighing 400-500 grams were utilized. Three of the rats were radiothyroidectomized by the intraperitoneal injection of 300 microcuries (uc) of carrier-free sodium iodide as I^{131} and the other animal served as a control. The dates of the injections were staggered so as to allow sacrifice at the same time but 37 days in one rat and 45 days post-injection in the other two animals.

Maloof et al. (1952) reported fibrosis of the thyroid 48 days after the intraperitoneal injection of 300 uc of I^{131} in rats. However, there has been a recent trend to larger doses of I^{131}. Indeed, Meyer and Evans (1964) followed surgical thyroidectomy with intraperitoneal injection of 500 uc of I^{131} in 24 hours to destroy possible thyroid remnants.

The animals were maintained in the Department of Radiology with artificial illumination for 10 hours daily (8 AM to 6 PM), approximately the length of daylight in November and December. The animals were fed Purina rat chow and given distilled water ad libitum.

The animals were sacrified under ether anesthesia by opening the cranial vault, removing the brain, and removing the lobes of the anterior pituitary. The material for electron microscopy was placed in 1 per cent phosphate buffered OsO_4 at room temperature with osmolarity adjusted with sucrose. Fixation was carried out for 60 minutes followed by dehydration in a graded

series of ethyl alcohol. Replacement was accomplished with propylene oxide and the material was embedded in Epon 812.

Thin sections were stained with uranyl acetate and viewed with a Phillips EM100B electron microscope. Electron micrographs were taken on 35 mm. film and enlargements made as necessary.

OBSERVATIONS

A. Control Animals

The anterior pituitary gland of rats contains several distinct cell types differentiated on details of fine structure. In fact, most of the cells can be classified in contrast to light microscopy where the heterogeneous class of chromophobes is relatively large. The various cell types will be briefly discussed.

1. Growth hormone cells. - As described by Hymer et al. (1961) these cells contain varying numbers of large 300-400 mu dense, uniformly spherical granules. (Figure 1) There is endoplasmic reticulum arranged in scattered flattened cisternae with ribosomes along the outer surfaces of the membranes. The Golgi complex is generally small and in a juxtanuclear position. There are usually several Golgi vesicles which contain small amounts of material similar to the definitive granules.

Some of the growth hormone cells appear packed with granules and have only meager development of endoplasmic reticulum and Golgi complex. In other cells there are fewer granules and more extensive

endoplasmic reticulum and Golgi complex. This gradation undoubtedly represents varying degress of synthetic activity.

2. Prolactin (or luteotrophic hormone) cells. - In these male rats only infrequent prolactin cells as described by Hymer et al. (1961) are seen. These cells have granules similar to growth hormone cells but differ in being somewhat irregularly shaped. In addition, the endoplasmic reticulum and Golgi complex are generally more extensive.

3. Basophils. - The cells generally considered to correspond to basophils of light microscopy have not been as well characterized. Hence, several fairly distinct types of cells will be described for comparison of results in the experimental animal.

a. There is a group of large, generally rounded cells with relatively large cytoplasmic-nuclear ratios which contain many small 150-250 mu circular granules of variable density. (Figure 1) The endoplasmic reticulum occurs mostly as small circular profiles, studded with ribosomes, and containing a faintly-staining, homogeneous material. Some of the endoplasmic reticulum cisternae tend to be flattened and in concentric stacks. However, most of the cisternae are seen as circular, slightly dilated profiles. The Golgi complex is moderately well developed, well limited, and contains developing granules. Occasional cells are seen in which there is variable dilatation of the isolated endoplasmic reticulum cisternae, and rarely there are very large isolated accumulations of material similar to the contents of smaller endoplasmic reticulum cisternae.

These cells correspond to the gonadotrophs of Farquhar and Rinehart(1954) and Lever and Peterson (1960) and to the follicle stimulating hormone cells of mice as described by Barnes (1962). The occasional cells with large dilated cisternae may represent the small number of "signet-ring" cells which are always present according to Wolfe (1943).

b. There are some cells which resemble the above basophils but which are generally situated away from blood vessels, are smaller, and are angular in outline. (Figures 2 and 3) The granules are slightly less electron dense than those of the above cells and consequently the granulation does not seem as prominent. These cells will be discussed later as possible precursors of the thyroidectomy cells.

c. There is a group of cells which are relatively small and often irregular. They contain granules that are darker than the previous classes of cells. (Figure 1) The granules are of a fairly uniform density. The endoplasmic reticulum tends to be in flattened cisternae and there is minimal development of the Golgi complex. These cells are similar to the cells which Barnes (1962) correlated with luteinizing hormone production in mice.

d. A very few cells have been observed which contain small (100-200 mu), generally smooth vesicles with discrete internal densities. (Figure 8) There are numerous free ribosomes, many in

clusters, and a few scattered small endoplasmic reticulum cisternae with ribosomes. The Golgi complex in these cells does not seem to be remarkable. Similar cells have not been observed in the previous studies involving female mice but there is a good possibility that these cells were overlooked.

Although it is probably risky to do so, it is tempting to speculate on morphological grounds that these cells may secrete a protein of rather low molecular weight and simple structure. It is suggested that these cells may produce adrenocorticotrophic hormone, a relatively small and simple molecule.

B. Thyroidectomy Animals

In this study the pituitaries from rats 37 and 45 days after radiothyroidectomy were examined. The changes observed in the animals were essentially the same so they will be described as a common group.

No appreciable difference in the cells corresponding to the growth hormone and prolactin cells in the control could be consistently identified. (cf. Figures 1, 3, and 12) Hence these cells will not be described again.

A definite group of presumed "thyroidectomy" cells can be identified and will be described. Since this experiment does not include animals subjected to short and intermediate term thyroidectomies, the full development and hence original identity of these

cells can not be defined precisely. However, some cells are seen which seem to be intermediate in their development into "thyroid-ectomy" cells.

The thyroidectomy cells are quite large and the cytoplasm is filled with enlarged endoplasmic reticulum cisternae which contain a faintly staining, generally homogeneous material. The size of the cisternae in individual cells is roughly uniform, however there is considerable variation between even adjacent cells. (Figure 5) In some cells one or more greatly enlarged cisternae are seen which contain material resembling that within the smaller cisternae. (Figure 12)

Occasional cells are observed which have endoplasmic reticulum in several forms, suggesting fragmentation of flattened cisternae and subsequent progressive dilatation of the smaller fragments. (Figure 5) This suggests that the endoplasmic reticulum cisternae in thyroidectomy cells accumulate material, presumably at least related to thyroid stimulating hormone, eventually corresponding to the large "colloid" droplets seen in light microscopy.

The dilated cisternae of the thyroidectomy cells are studded on their external surface by ribosomes, occasionally seen in clusters. (Figure 11) An initially smooth-membraned cisterna could, of course, appear to become studded by ribosomes as it enlarges and encroaches on the total volume occupied by free ribosomes.

However, cells with granular endoplasmic reticulum cisternae ranging from flattened cisternae to enlarged isolated cisternae offer proof that the enlarged cisternae of thyroidectomy cells are derived from the granular endoplasmic reticulum. (Figure 5)

In some thyroidectomy cells the dilated cisternae contain circular condensations with essentially the same density and diameter as the occasional secretory droplets seen in the cytoplasm between cisternae. (Figure 10) It is believed that these droplets correspond to the "T-granules" of Purves and Griesbach (1951) and Halmi (1952) which were thought to reflect long-term thyroid deficiencies. Halmi presented evidence that the granules were not identical with definitive thyroid stimulating hormone. Farquhar and Rinehart (1954) noted these granules as early as the tenth day after thyroidectomy.

The thyroidectomy cells contain prominent nucleoli and apparently in increased numbers. Some of the cells contain several nucleoli. (Figures 5, 6, and 7)

C. General Morphology

The general organization of the anterior pituitary of the control and operated animals is essentially the same. The fine structure of the vasculature is essentially as described by Farquhar (1961). The capillaries have complete endothelial linings and are surrounded by a pair of basement membranes. These membranes are

separated by a variable distance with occasional connective-tissue cells and collagen in the intervening space. (Figure 9)

Occasional cilia are noted as described by Barnes (1961). The distinctive features of these cilia is the absence of the central pair of filaments. No effort is made to tabulate the type of cell from which they arise.

DISCUSSION

Even though no consistent changes were observed in the acidophils, marked changes were readily apparent in some of the basophils. This reconfirms the previously reviewed observations that the basophils respond to lesser degrees of thyroid deficiency than the acidophils. Since no changes occurred in the acidophils it must be concluded that the experimental method did not achieve sufficiently complete thyroid ablation.

A. Origin of Thyroidectomy Cells

Since no observations are available in this study of intervening stages of thyroidectomy it is difficult to precisely define the thyroid stimulating hormone cells of the control animal. In light microscopy these cells are categorized partially by their shape, size, and relation to blood vessels. Hence, they can not be directly compared to the somewhat distorted and expanded thyroidectomy cells.

The ultrastructure of the second type of basophils described earlier does, however, correspond fairly well to the type of cell previously designated as thyroid stimulating hormone cells (see Farquhar and Rinehart, 1954). The descriptions in the literature have been brief with less than fully enlightening illustrations.

The granule content of these basophils does appear similar to the sparse granulation of thyroidectomy cells. The control basophils do not have much development of the endoplasmic reticulum or Golgi complex so that comparison with the thyroidectomy cells is frustrating. These cells are probably the thyroid stimulating hormone cells and respond to thyroid deficiency by enhanced secretion, becoming thyroidectomy cells.

B. Relation to Protein Secretion

The initial synthesis of proteins is known to occur in association with ribosomes and groups of ribosomes (polysomes) in the cytoplasm and involves several types of ribonucleic acids as reviewed by Nirenberg (1963). This arrangement insures the production of protein molecules with precise linear arrangement of the constituent amino acids as genetically directed.

In a number of experiments involving pulse isotope labeling of export proteins, serial sacrifice, and high resolution autoradiography it has been shown that after the initial synthesis the

molecules for export are transported across the cisternal membrane of the endoplasmic reticulum into the intracisternal space. The molecules are then transported to the Golgi complex for further enzymatic modifications and condensation into secretory granules within membranes derived from the Golgi complex. Upon proper stimulation the granule contents are released from the cell by fusion of the membrane surrounding the granule and the cell membrane.

The ribosomes which can be readily identified in the cytoplasm and attached to the external surfaces of the endoplasmic reticulum cisternae are the sites of actual interaction of RNA molecules necessary for the production of polypeptide chains. Among the free ribosomes and where the cisternal membranes are sectioned nearly tangentially (Figure 11) the ribosomes can be seen arranged in groups. These groups possibly are polysomes, or groups of ribosomes associated with a single messenger RNA molecule, presumably improving the efficiency of protein synthesis. Rich (1963) reviews the polysome concept as derived from biochemical observations in relatively simple organisms. Polysomes have not yet been functionally proven in tissues with developed endoplasmic reticulum.

After synthesis on the ribosome the protein for export is thought to be transported across the endoplasmic reticulum cisternal membrane to the intracisternal space (see Hokin and Hokin, 1961). Accumulations of material within the intracisternal space have been occasionally observed.

For instance, Palade (1956) observed small intracisternal granules in the exocrine pancreas of refed guinea pigs. Movat and Fernando (1962) concluded that the Russell bodies in plasma cells are intracisternal granules or crystals probably secondary to enhanced secretion since they occur in hyperimmunized animals. (They could not rule out accumulation of material secondary to stagnation of the secretory product).

Revel and Hay (1963) report occasional dilated endoplasmic reticulum cisternae containing newly synthesized collagen in differentiating cartilage cells. These examples are all presumed to involve conditions of enhanced secretion.

The results of the present study are consistent with the progressive accumulation of thyroid stimulating hormone precursors within intracisternal spaces and coalescence of the resultant dilated cisternae to produce several markedly dilated cisternae. The accumulation of the precursors would correspond to the hyaline material seen in the thyroidectomy cells of light microscopy. The T-granules are probably analogous to the Russell bodies in plasma cells (Movat and Fernando, 1962).

Thus the thyroidectomy cells are another example of the appearance of intracisternal material in conditions of exaggerated protein synthesis. The accumulation is probably due to relative or absolute inadequacy of the usual intracellular transport mechanisms.

This might reflect relative inadequacy of the enzyme systems involved in further modifications of the protein molecule or those responsible for condensation of the final product. The delayed transport might also be stagnation due to impaired release, such as due to insufficiency of possible release factors.

As reviewed, the export protein is conveyed to the Golgi complex from the endoplasmic reticulum. Earlier authors suggested direct connections between the endoplasmic reticulum and the Golgi complex. However, there seems to be meager documentation of such connections.

Zeigel and Dalton (1962) and Garwood and Latta (1963) described several protein secreting tissues with modified endoplasmic reticulum where the cisternae were adjacent to the Golgi complex. These areas appeared to be giving rise to small vesicles resembling the small (50-60 mu) Golgi vesicles which occur throughout the Golgi complex.

These authors interpreted the above as the transport mechanism whereby small quanta of new protein in solution are carried from the endoplasmic reticulum to the Golgi complex. However, in the above reports the endoplasmic reticulum was mostly well segregated and composed of flattened cisternae, whereas in thyroidectomy cells the cisternae occur as dispersed and dilated cisternae. Some cisternae even occur within the area of the Golgi complex.

Additionally, there are relatively few small Golgi vesicles and apparently more ribosomes within the Golgi complex. (Figures 5, 6, and 12) Hence, these are probably not comparable situations and the mechanics of transport of material to the Golgi complex in thyroidectomy cells can not be deduced at present.

The Golgi complex of thyroidectomy cells is relatively prominent with moderate numbers of condensing granules occurring within Golgi vesicles. (Figures 5 and 12) In 1957 Farquhar and Wellings described series of granules within smooth Golgi vesicles suggesting progressive increase of size and density of the granules. They interpreted these findings to represent a process of condensation of secretory product resulting in mature granules completely filling the membranous vesicles. Caro (1961) and other have presented fairly convincing proof of this condensation process utilizing electron microscope radioautography.

Recent studies implicate the parallel stacks of flattened Golgi cisternae in enzymatic modifications of secretory products. (Figures 6 and 12) Lane et al. (1964) show that the sulfation of the mucopolysaccharides of colonic goblet cells occurs in association with the flattened Golgi cisternae. Peterson and Leblond (1964) show that glucose is incorporated into glycoproteins and mucopolysaccharides in the Golgi complex. The present observations do not deal directly with this problem but there is prominent development of these structures in the thyroidectomy cells.

The number of mature specific granules decreases with the extent of the thyroidectomy changes (cf. Figures 2, 4, 5, 6, 7, and 12) This correlates well with the decreased or absent aldehyde fuchsin-positive granules following thyroidectomy since this stain is thought to be specific for thyroid stimulating hormone (Purves and Griesbach, 1951). This finding also supports the above hypothesis that the material within the dilated endoplasmic reticulum cisternae is not thyroid stimulating hormone but probably rather a precursor.

No definite examples of release of either mature granules or of intracisternal material have been observed (see Figure 9). The small size of the mature granules precludes easy recognition of release at the cell membrane and would also undoubtedly mean rather rapid dissolution. The intracisternal material has minimal electron density so would also be difficult to observe in any possible release mechanism.

Cilia lacking the central pair of fibrils are observed frequently. Barnes (1961) suggests that such cilia in some way are adapted for a sensory function such as chemoreceptors. Wilson and McWhorter (1963) describe cilia in human skin, review the pertinent literature, and suggest that these organelles may be important for the initiation of mitosis. However, until concrete evidence of function is presented, it seems more appropriate to consider isolated cilia as random expressions of an inherent cell potential.

The nucleolus has long been implicated in the biosynthesis of proteins. MacRae (1964) has recently briefly reviewed the biophysiology of the nucleolus. Recent evidence supports the thesis that the nucleolus has a role in the production of the cytoplasmic ribosomes and the transfer or soluble RNA molecules. The present observations concerning prominent and multiple nucleoli in thyroidectomy cells are interesting since these cells show general adaptation for rapid protein secretion. However, the electron microscope does not readily lend itself to checking the validity of these observations quantitatively.

As discussed above, the ultrastructure of thyroidectomy cells demonstrates modifications for very rapid protein synthesis. In turn, these modifications shed light on the intracellular mechanisms involved in protein biosynthesis.

CONCLUSIONS

In the present study the ultrastructure of the male rat anterior pituitary is described in a control rat and in three experimental rats which were radiothyroidectomized. The cells of the control animal are described on a morphological basis and an attempt is made to correlate the cell types with the secretion of specific hormones based on reported observations.

The growth hormone cells and prolactin cells have been quite well characterized previously. Very few prolactin cells were seen

in this male tissue. No consistent changes were observed in the acidophils of the experimental animals. Hence, it must be concluded that the experimental design did not achieve sufficiently complete thyroidectomy.

The cells corresponding to the basophils of light microscopy have not been as well characterized. However, several relatively homogeneous classes of cells can be identified and compared to the previous reports. Cells which are thought to secrete follicle stimulating hormone, luteinizing hormone, and thyroid stimulating hormone are described. A small number of cells are speculatively identified as adrenocorticotrophic hormone secreting cells based primarily on morphological criteria.

The experimental design did not include intermediate, shorter term periods of thyroid deficiency. Consequently, it is impossible to describe the early development of thyroidectomy cells from the present observations.

The anterior pituitaries of the experimental animals contain many large cells filled with dilated endoplasmic cisternae containing a light, homogeneous material and occasional small, dense granules. There is variation in the size of the dilated cisternae with occasional enormous accumulations of material. This evidence suggests a progressive dilatation of endoplasmic reticulum cisternae.

The specific granules of thyroidectomy cells resemble those of thyroid stimulating hormone cells of the control animals. The granules are present in reduced numbers in the thyroidectomy cells. There is a prominent Golgi complex which appears quite active. There are prominent and often multiple nucleoli.

The ultrastructure of the thyroidectomy cells is correlated with the synthesis of protein. The initial peptide synthesis occurs in association with ribosomes followed by transport of the protein within the endoplasmic reticulum cisternae to the Golgi complex. The dilated endoplasmic reticulum cisternae are thought to contain thyroid stimulating hormone precursor, reflecting a relatively inadequate transport because of a rapid rate of synthesis.

The Golgi complex contains examples of apparent condensation of granules. It is suggested that the protein may undergo enzymatic modifications and additions in association with the Golgi complex.

Finally, it is believed that the ultrastructure of thyroidectomy cells demonstrates modifications for rapid protein synthesis. In turn, these modifications shed light on the intracellular mechanisms involved in protein biosynthesis.

SUMMARY

1. The literature concerning the effects of thyroidectomy on the hypophysis is briefly reviewed, especially as related to the effects on the acidophil cells and presumably the secretion of growth hormone.
2. Radiothyroidectomies were accomplished by the intraperitoneal injection of 300 microcuries of carrier-free I^{131} into adult male rats.
3. These animals and a control animal were sacrificed after varying durations of hypothyroidism and the pituitaries prepared for electron microscopy.
4. The ultrastructure of the control pituitary is described. An attempt is made to describe morphologically homogeneous cell types and relate them to the secretion of specific hormones, based upon the available information.
5. The ultrastructure of the thyroidectomized rats is described. The cells associated with the secretion of growth hormone showed no consistent changes from those of the normal and it is apparent that complete thyroidectomy was not achieved.
6. The ultrastructure of the thyroidectomy cells is discussed in relation to the secretion of a protein product.

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Figure 1. Magnification 7,500x. Control animal.

This electron micrograph illustrates several types of cells. Along the mid-left border is a portion of a growth hormone cell (GH) containing characteristic large, dense, circular granules.

There are portions of two follicle stimulating hormone cells (FSH) adjacent to a capillary (cap). They have rounded contours and a large cytoplasmic-nuclear ratio. There are many relatively small granules of variable density. The endoplasmic reticulum cisternae are seen as small, slightly dilated profiles.

There is a portion of a small luteinizing hormone cell (LH) in the superior portion of the electron micrograph. It is somewhat angular and contains small, dense granules.

Note: The horizontal bars represents one micron except in the illustrations where it is noted to represent 0.1 micron.

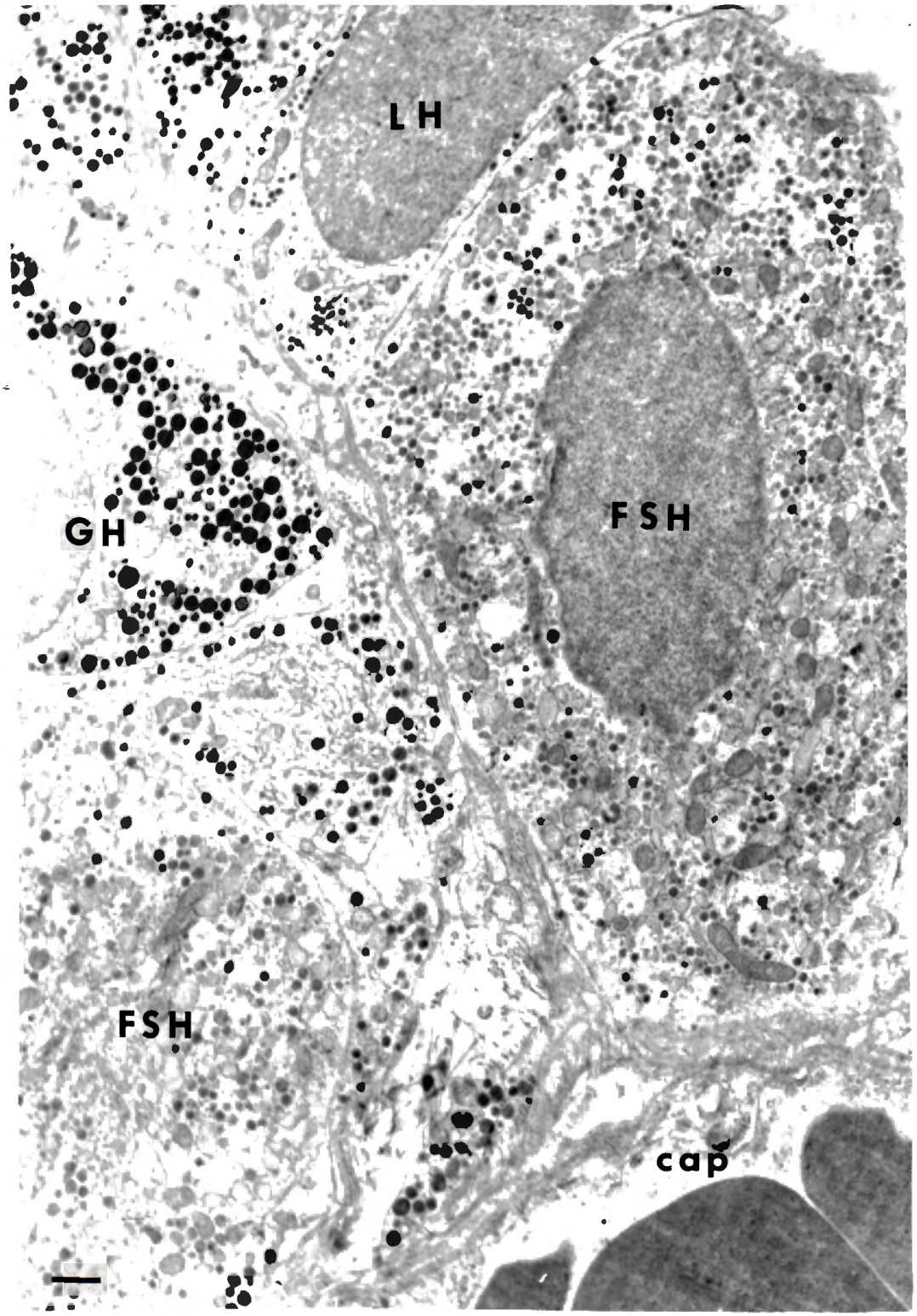
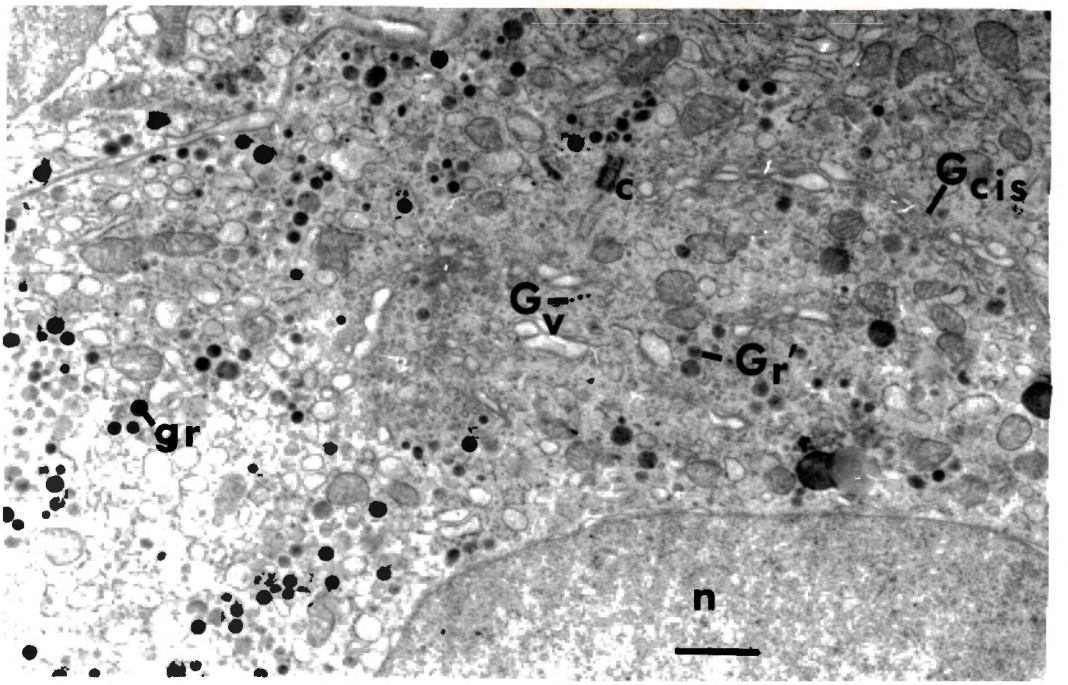

LH
FSH
GH
FSH
cap

Figure 2. Magnification 11,000x. Control animal.

This is a portion of a cell illustrating the second type of basophil and thought to secrete thyroid stimulating hormone. The nucleus (n) is at the lower right corner. There is a relatively large supranuclear Golgi complex generally limited by stacks of flattened Golgi cisternae (G_{cis}). The Golgi complex contains many 50-60 mu Golgi vesicles (G_v), several condensing granules (Gr') within larger Golgi vesicles, and a centriole (c). There are numerous mature specific granules (gr) showing some variability of electron density.

Figure 3. Magnification 11,500x. Control animal.

The cell in the upper left corner is characteristic of growth hormone cells (GH). It contains numerous dense, circular specific granules. The central cell is somewhat angular; has a moderately developed paranuclear Golgi complex (Gc); meager, fragmented endoplasmic reticulum (er); several mitochondria (m); and moderate numbers of specific granules (gr). This cell also illustrates the second type of basophils.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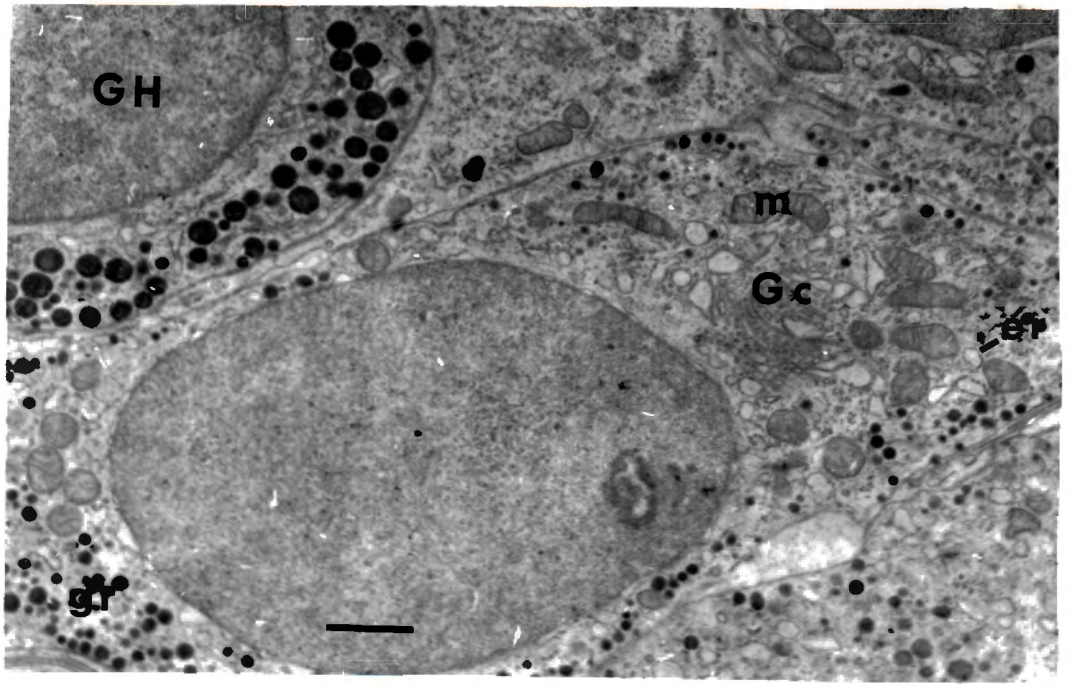

GH
m
Gc
gr
gr

Figure 4. Magnification 12,100x.
Forty-five days post-radiothyroidectomy.

The large cell in the right central area is a typical thyroidectomy cell containing numerous moderately dilated endoplasmic reticulum cisternae (er) which are filled with a light, homogeneous material. A few mitochondria (m) are present and there are only a few mature specific granules (gr).

There is a capillary (cap) along the inferior margin.

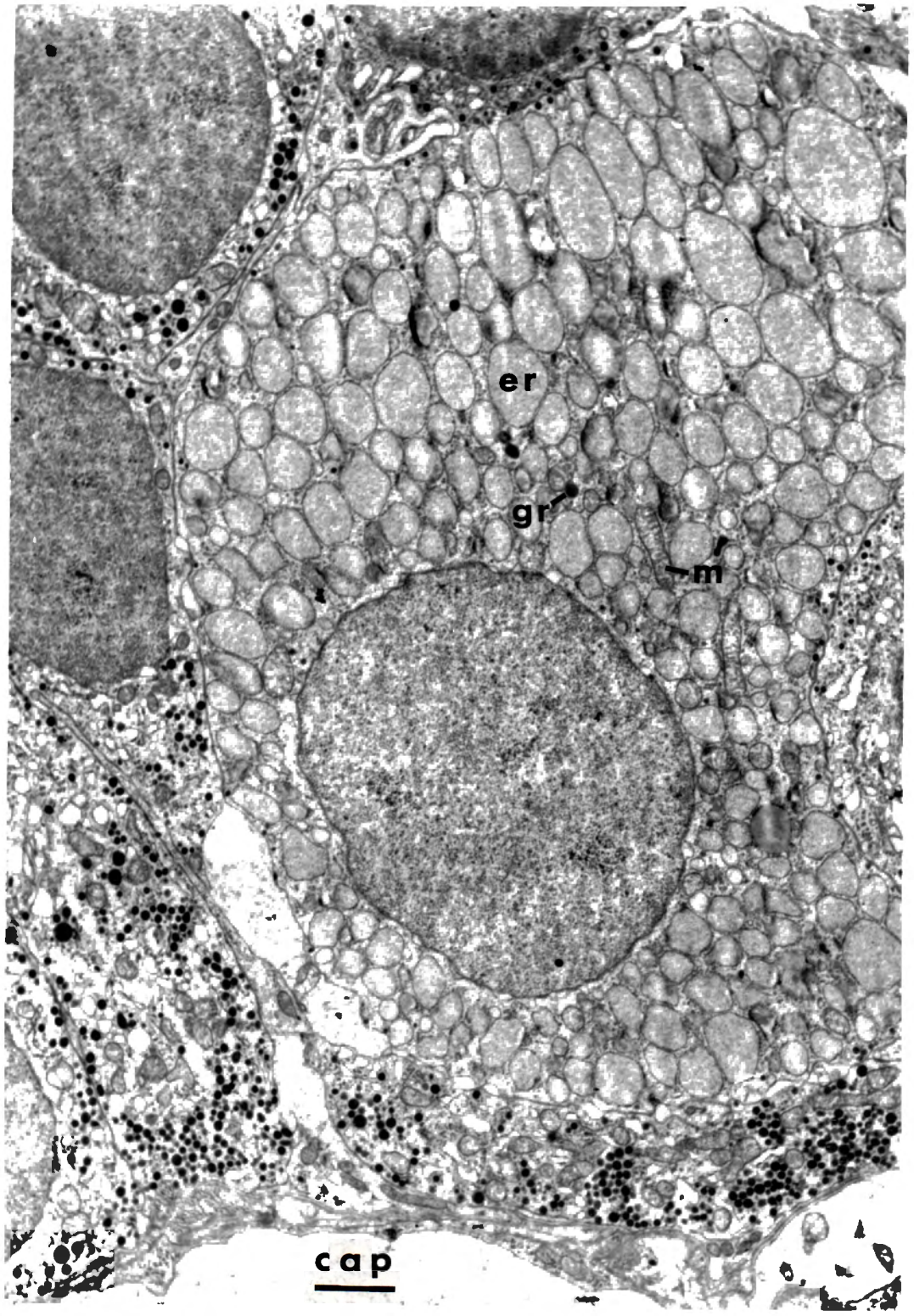

er
gr
m
cap

Figure 5. Magnification 13,500x.
Forty-five days post-radiothyroidectomy.

The central thyroidectomy cell nucleus (n) contains a prominent nucleolus (nu). The abundant endoplasmic reticulum ranges from somewhat flattened cisternae (er_1) in the superior portion of the cell to variable sized, dilated fragments of cisternae (er_2). This suggests evolution of the dilated cisternae by fragmentation from flattened cisternae and then progressive accumulation of light, homogeneous material.

The Golgi complex (Gc) to the left of the nucleolus contains several condensing granules (gr') within Golgi vesicles. There are relatively few mature specific granules (gr).

The thyroidectomy cell in the upper left corner contains endoplasmic reticulum cisternae which demonstrate greater dilatation.

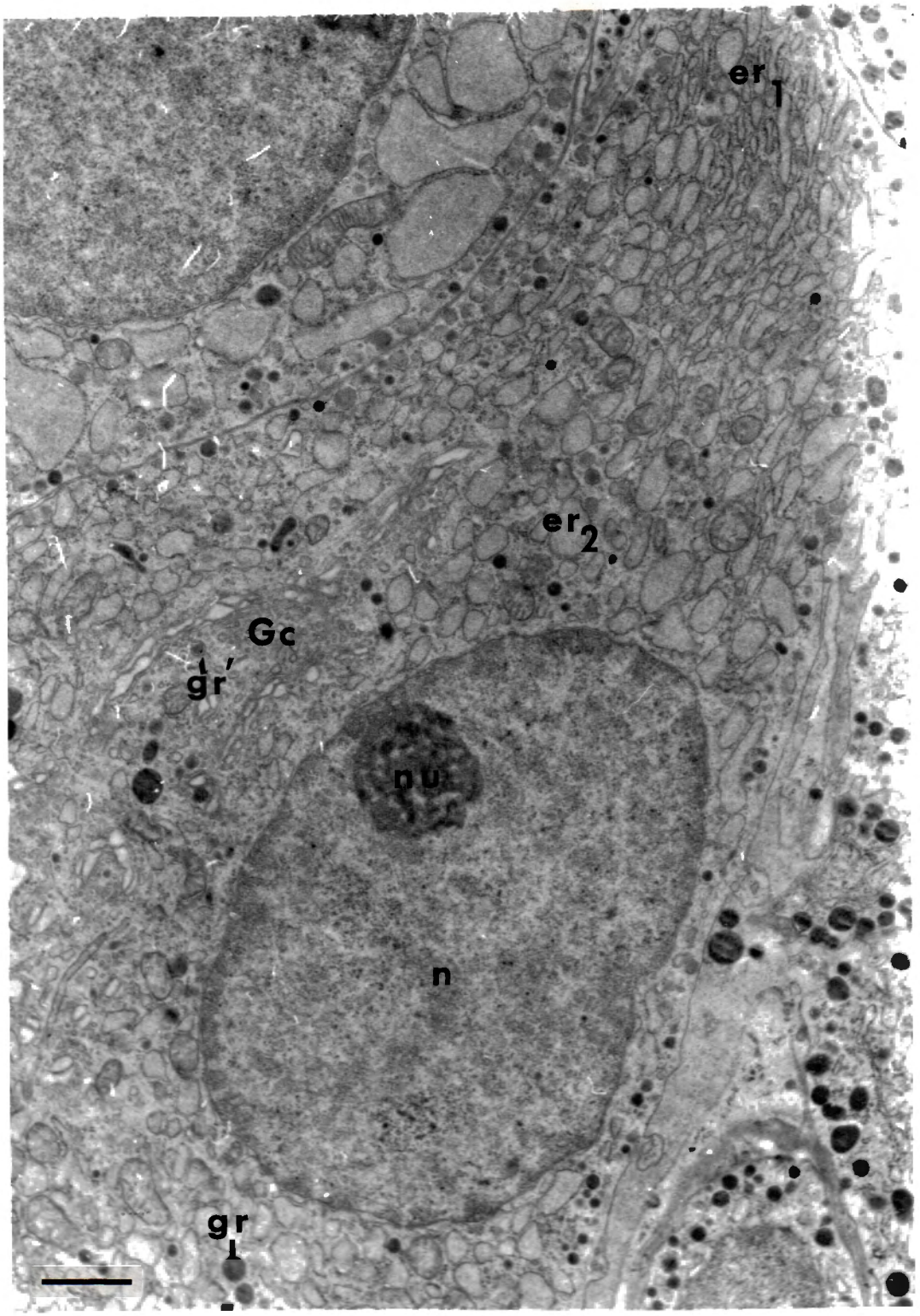
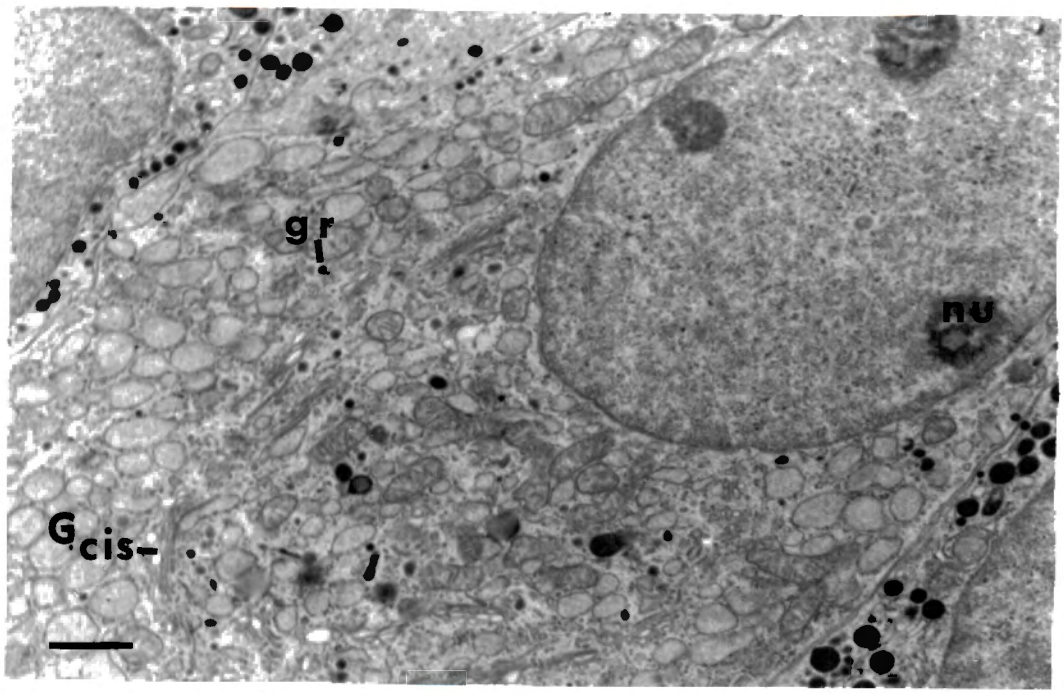

er1
er2
Gc
gr'
nu
n
gr

Figure 6. Magnification 11,000x.
Forty-five days post-radiothyroidectomy.

The central cell is a thyroidectomy cell. The nucleus contains three nucleoli (nu) and the cytoplasm contains Golgi complex components, especially flattened cisternae (G_{cis}) scattered over a wide area adjacent to the nucleus. There are numerous dilated endoplasmic reticulum cisternae which also are seen within the region of the Golgi complex. There are only a few mature granules (gr).

Figure 7. Magnification 9,000x.
Forty-five days post-radiothyroidectomy.

This is a thyroidectomy cell near a narrow capillary (cap). There is a prominent nucleolus (nu). There are many dilated endoplasmic reticulum cisternae and very few granules.


gr
nu
G cis

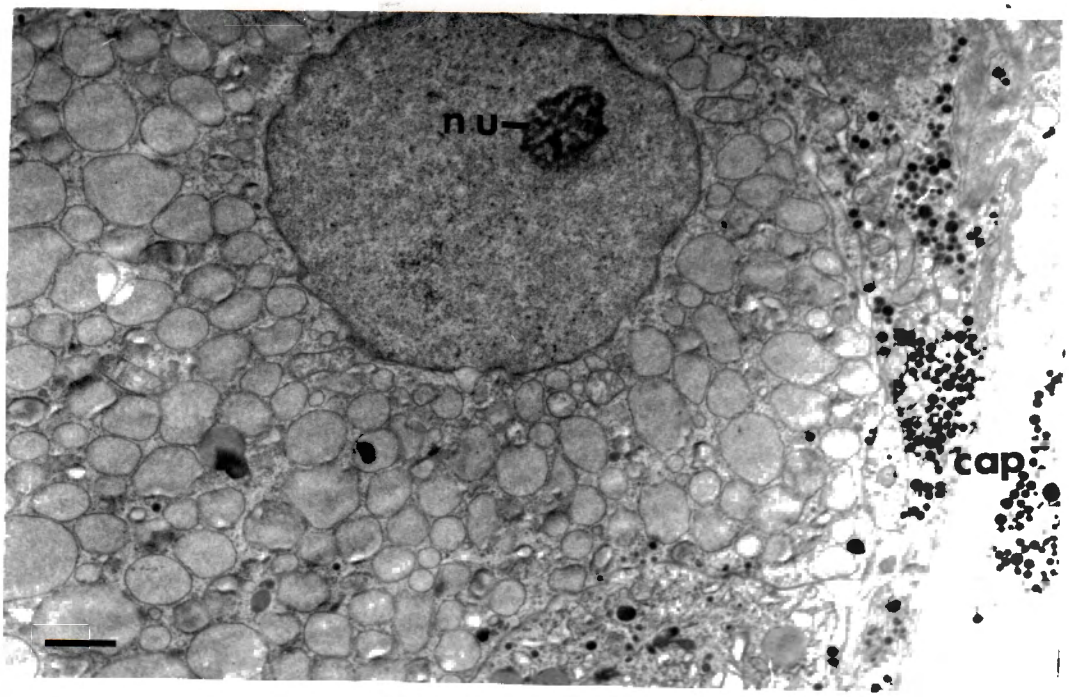

nu
cap

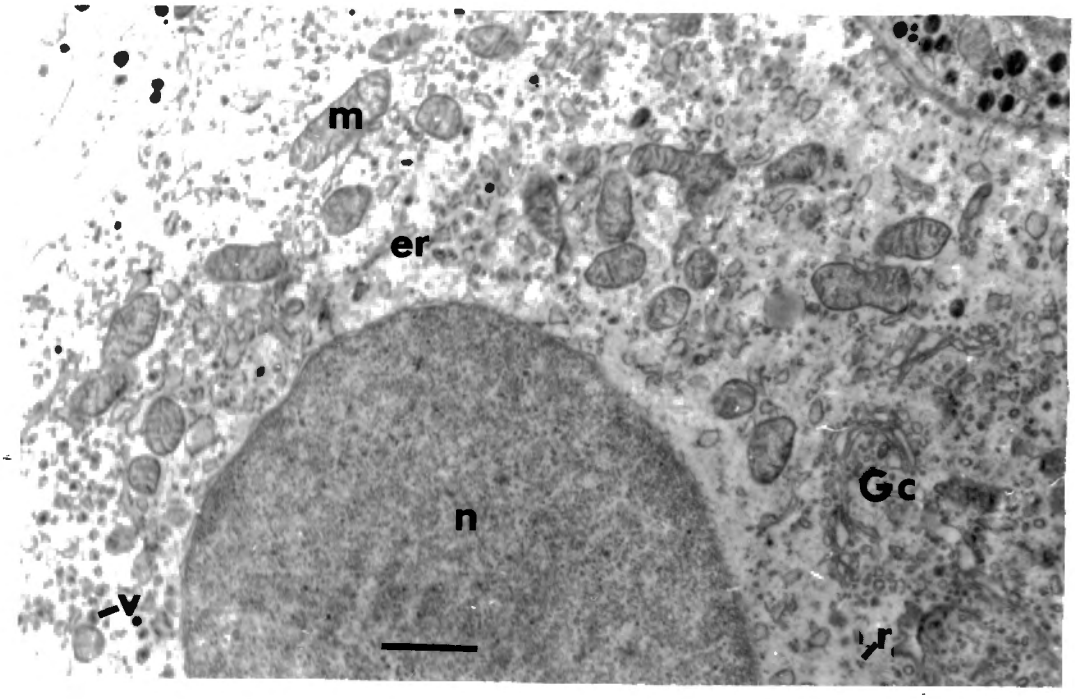
Figure 8. Magnification 12,700x. Control animal.

This cell illustrates the fourth type of basophil which is suggested as the origin of adrenocorticotrophic hormone. There are many mitochondria (m), some Golgi components (Gc) to the right of the nucleus (n), scattered fragments of endoplasmic reticulum (er) with attached ribosomes, free ribosome (r), and numerous small, smooth vesicles (v) containing small granules.

Figure 9. Magnification 22,300x.
Forty-five days post-radiothyroidectomy.

The thyroidectomy cell on the left contains specific granules (gr) aligned near the cell membrane (cm). In several places (arrows) there are suggestions of release of granules. There is a capillary lumen (cap) along the inferior margin containing erythrocytes (eryth) and lined by attenuated endothelium (en). Between the endothelium and the cell membrane are the characteristic pair of basement membranes (bm) separated by a variable space.

Note: The horizontal bar represents 0.1 micron.


m
er
n
Gc
v
r

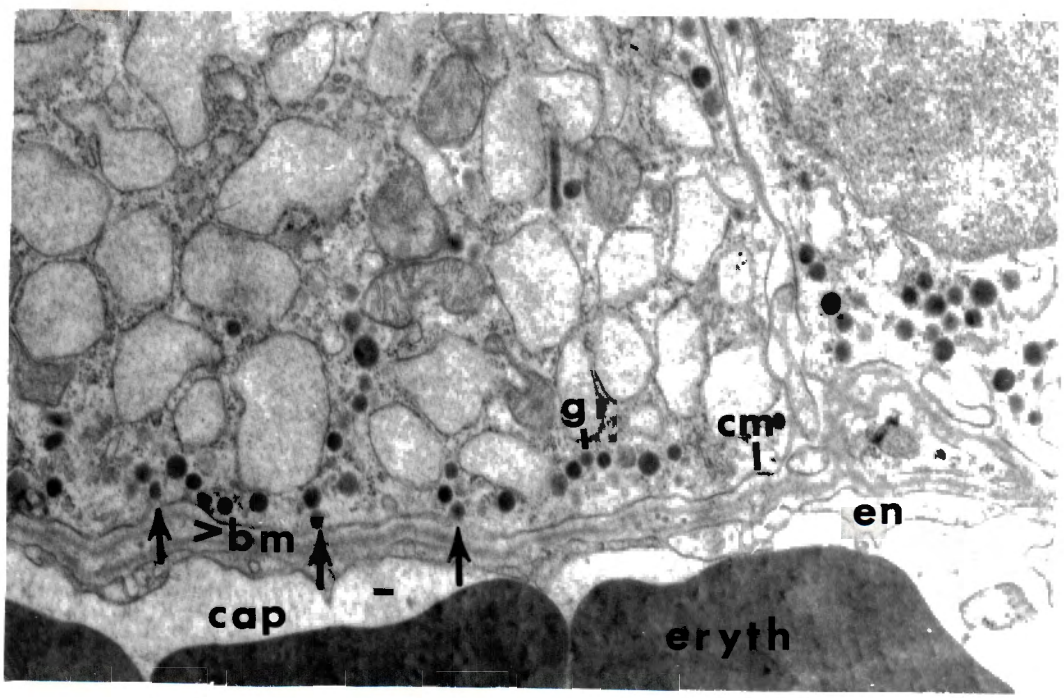

gl
cm
en
bm
cap
eryth

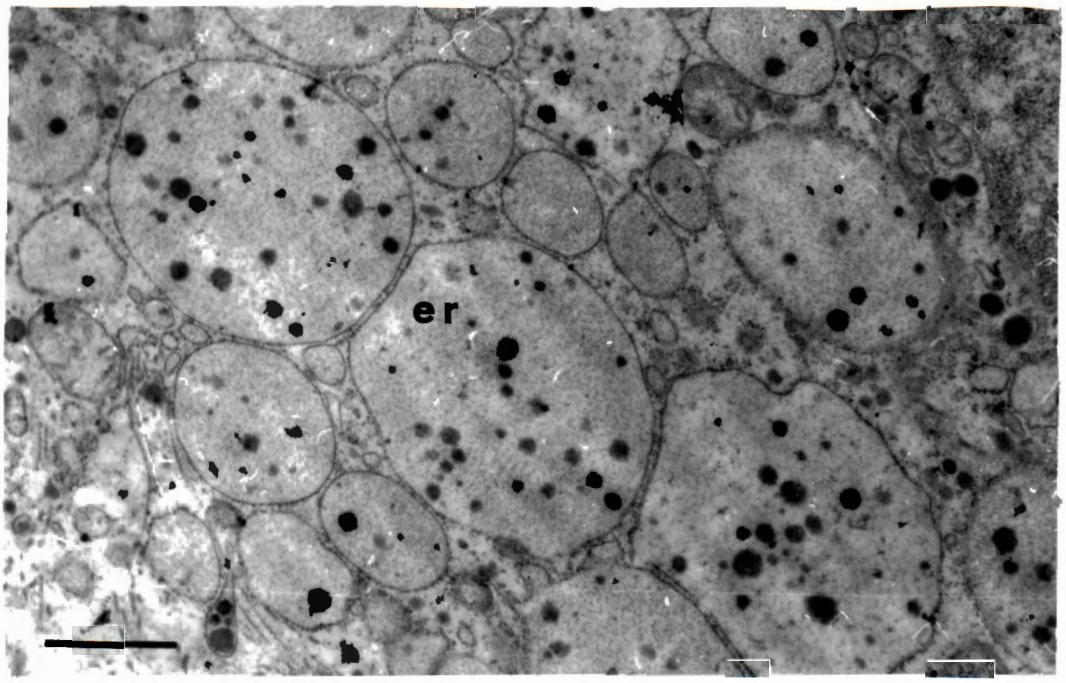
Figure 10. Magnification 17,000x.
Forty-five days post-radiothyroidectomy.

This is a portion of a thyroidectomy cell containing large, dilated endoplasmic reticulum cisternae (er). These cisternae contain relatively dense, circular condensations representing the T-granules. These granules reflect chronic thyroid deficiency.

Figure 11. Magnification 31,000x.
Forty-five days post-radiothyroidectomy.

This cell illustrates clustering of ribosomes, possibly in polysomal formation. Clusters are seen involving ribosomes associated with endoplasmic reticulum (r_1) and free in the cytoplasm (r_2). The mitochondria (m) have characteristic internal structure.

Note: The horizontal bar represents 0.1 micron.


er

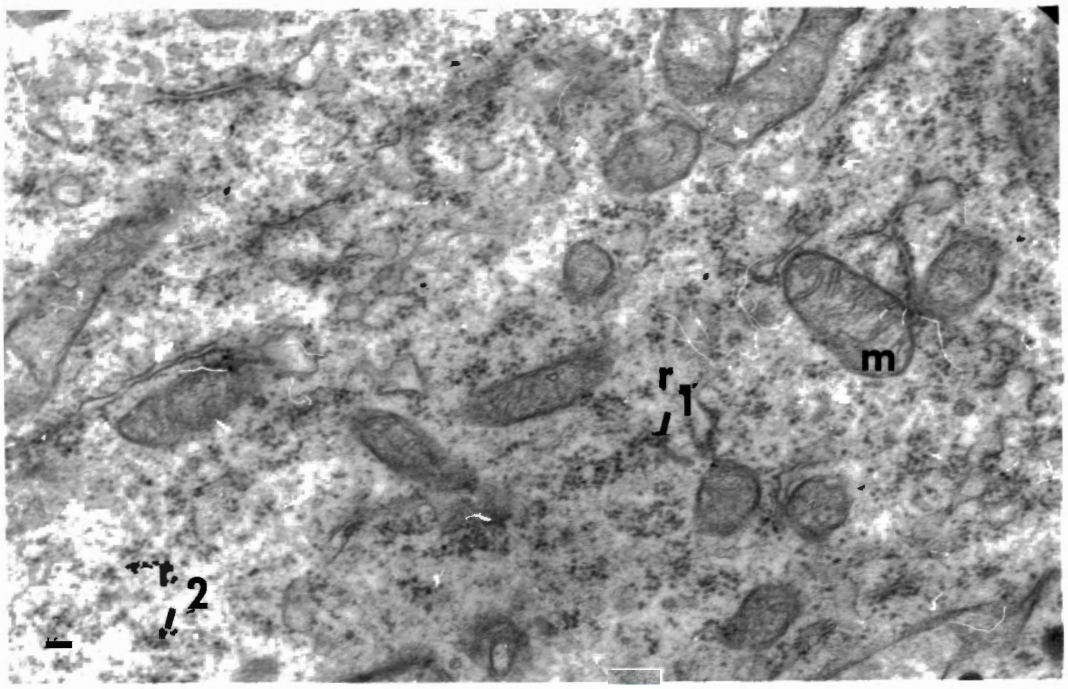
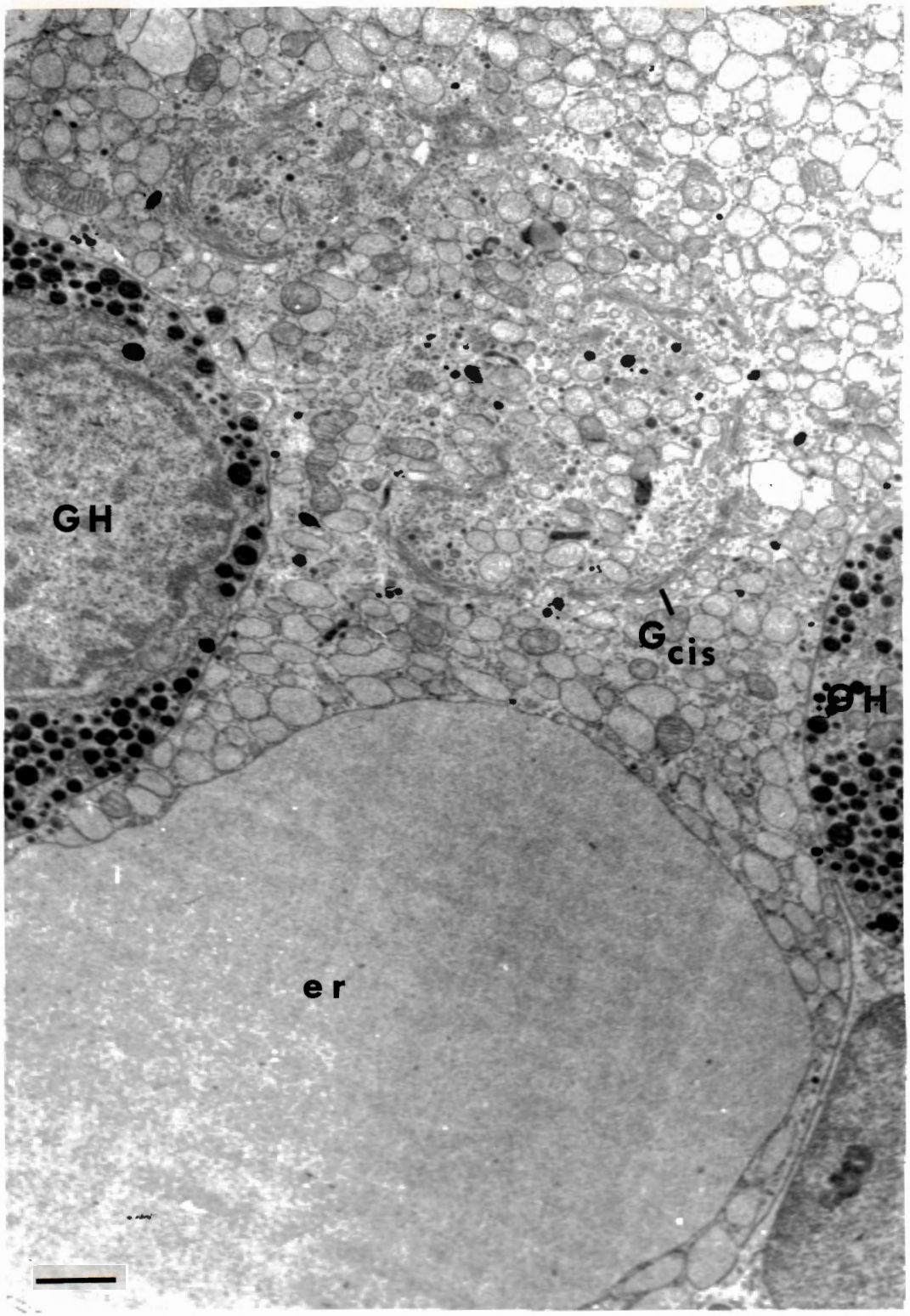

m
r1
r2

Figure 12. Magnification 12,500x.
Forty-five days post-radiothyroidectomy.

The central cell is a thyroidectomy cell with an enormously dilated endoplasmic reticulum cisternum (er). The remainder of the cytoplasm contains numerous smaller cisternae containing similar material. There is a prominent Golgi complex limited by stacks of flattened Golgi cisternae (G_{cis}) and containing most of the visible granules.

On both sides of the thyroidectomy cell are portions of growth hormone cells (GH) with characteristic granulation. These cells illustrate the similarity to the comparable cells of the control animal.


GH
G cis
GH
er