The Fine Structure of the Parathyroid Gland*

BY JERRY STEVEN TRIER, M.D.

(From the Department of Anatomy, University of Washington School of Medicine, Seattle)

PLATES 3 TO 10

(Received for publication, July 29, 1957)

ABSTRACT

The fine structure of the parathyroid of the macaque is described, and is correlated with classical parathyroid cytology as seen in the light microscope.

The two parenchymal cell types, the chief cells and the oxyphil cells, have been recognized in electron micrographs. The chief cells contain within their cytoplasm mitochondria, endoplasmic reticulum, and Golgi bodies similar to those found in other endocrine tissues as well as frequent PAS-positive granules. The juxtanuclear body of the light microscopists is identified with stacks of parallel lamellar elements of the endoplasmic reticulum of the ergastoplasmic or granular type.

Oxyphil cells are characterized by juxtanuclear bodies and by numerous mitochondria found throughout their cytoplasm. Puzzling lamellar whorls are described in the cytoplasm of some oxyphil cells.

The endothelium of parathyroid capillaries is extremely thin in some areas and contains numerous fenestrations as well as an extensive system of vesicles. The possible significance of these structures is discussed.

The connective tissue elements found in the perivascular spaces of macaque parathyroid are described.

INTRODUCTION

It is the purpose of the present paper to report some observations on the fine structure of the parathyroid gland employing the electron microscope and the techniques of thin sectioning. Throughout this study an attempt is made to correlate findings made with the electron microscope with those based on light microscopy.

In 1880 Sandström (32), in a classical paper, described the constant presence of small epithelial glandular organs in or near the thyroid of man and several other mammalian species. Since then many anatomists and cytologists have studied the parathyroid glands of a variety of mammalian species. Welch in 1898 (55) outlined much of the classical histology of human parathyroid as it is generally accepted today and was the first to recognize and describe accurately the oxyphil cells.

* This study was supported in part by grants from the Life Insurance Medical Research Fund and from the United States Public Health Service, Department of Health, Education and Welfare (Grant H-2698.)

Other contributions to the present concepts concerning the human parathyroid can be found in the reports of Bergstrand (7), Morgan (34), Pappenheimer and Wilens (45), Castleman and Mallory (10), and Gilmour (20).

Valuable contributions to the understanding of parathyroid structure of other mammals are contained in the descriptions of the parathyroids of the cat by Kohn (25), the horse by Bobeau (8), the rat by Rosof (51) and by De Robertis (15), the mouse by Foster (17), the dog by Bensley (6), and the macaque monkey by Cowdry and Scott (11) and by Baker (3). An extensive review of the literature regarding parathyroid structure up to 1939 can be found in the report of Bargmann (4).

More recently Lever (29, 30), utilizing the electron microscope, has described some aspects of the fine structure of rat parathyroids.

This present paper confirms many of the observations reported in papers mentioned above, and in addition presents some new findings not yet included in the literature.
Materials and Methods

The macaque monkey was selected as the animal of choice for this study, since the parathyroids obtained from the mature monkey possess both chief cells and oxyphil cells (11, 3). The parathyroids of the more common laboratory animals are said to contain only chief cells.

Mature male and female monkeys of the species, *Macaca mulatta,* were anesthetized by intravenous injection of pentobarbital sodium. The thyroid gland was exposed with a minimum of trauma and the external parathyroids were located on the lateral aspect of each thyroid lobe, embedded within the tissue of the thyroid just below its surface.

In most animals one external parathyroid was prepared for examination with the electron microscope while the other was reserved for study by light microscopy.

The parathyroids used for study with the electron microscope were removed while the animal was still alive and were fixed immediately in a 1 per cent solution of osmic acid buffered with veronal acetate to pH 7.3-7.5 (35). The duration of the fixation was 2/4 to 1 hour.

Attempts were made to perfuse the parathyroids of three animals with the fixative, but there was some doubt as to the success of the perfusions, since, although the thyroid gland darkened immediately on completion of the perfusion, rapid blackening of the external parathyroids was not observed. The parathyroids were removed immediately following the perfusion and were then handled in the same manner as described above for tissue prepared by immersion fixation only. Little difference was noted in the quality of fixation between the perfused tissue and the tissue exposed only to immersion fixation.

Following fixation, the tissue was washed, dehydrated in alcohol, embedded in methacrylate, and sectioned in the usual manner on a Servall microtome originally designed by Porter and Blum (49), with glass knives similar to those described by Latta and Hartmann (28). The sections were examined with an RCA EMU 2C electron microscope equipped with a compensated objective. Either 50 or 100 μ objective apertures were used. Original magnifications of the electron micrographs ranged from 1500 to 7500 diameters, as calibrated with polystyrene latex (2, 19). Further magnification was achieved photographically.

The parathyroids used for study with the light microscope were fixed immediately after extirpation in either Bouin’s or Helly’s solution. The glands were sectioned at 4 μ and a variety of staining techniques were employed, including the Altmann-Kull method for mitochondria (9), the periodic acid Schiff technique (23), toluidine blue, hematoxylin and eosin, and others.

In addition, mounted sections from 2 parathyroids were subjected to hydrolysis by a 0.15 per cent solution of ribonuclease prepared from a commercial preparation of crystalline salt-free ribonuclease and distilled water. The sections were flooded with the enzyme solution and incubated at 37°C for 3 hours. Control sections were handled in exactly the same manner as the experimental sections, except that distilled water was substituted for the enzyme solution. Following the incubation both experimental and control sections were simultaneously stained with various dyes, including iron hematoxylin, gallocyanin-chromalum, and others known to stain intensively structures with a high content of nucleic acids.

Observations

The external parathyroid glands of the macaque monkey are composed of a compact parenchyma containing two basic cell types: chief cells and oxyphil cells. A profuse network of vascular channels, with associated perivascular structures, traverses the dense stroma of the gland.

Chief Cells:

General Features.—The chief cell is by far the predominant cellular element in the parathyroid of the monkey. Only one distinct type, the pale chief cell, can be identified in these preparations, although Baker (3), it should be noted, has described pale and dark chief cells in this same species. The appearance of the pale chief cell as observed here confirms, in general, the description of this cell by Baker (3). Certain cytoplasmic structures can be identified in virtually each chief cell following adequate preparation of the tissue. Numerous small, rod-shaped and filamentous mitochondria are seen which, though distributed diffusely throughout the cytoplasm, have a tendency to be congregated at the vascular pole of the cell (Fig. 1). A distinctive, compact, relatively large, dense, deeply basophilic structure, previously described in the parathyroids of man and the macaque monkey (45, 11, 3) and designated by Pappenheimer and Wilens as the “juxtanuclear body,” is present in each chief cell. Several profiles of juxtanuclear body material are frequently present in a single chief cell (Figs. 2 to 4).

When tissue sections of macaque parathyroid are subjected to hydrolysis with a ribonuclease solution and subsequently stained with basic stains as described above, the juxtanuclear bodies still stain lightly and can be identified, but the basophilia is

1 The ribonuclease enzyme preparation was obtained from General Biochemicals, Inc., Chagrin Falls, Ohio.
strikingly less intense when compared with those in control sections which have not been treated with ribonuclease solution (compare Fig. 4 with Fig. 5). The background basophilia of the cytoplasm is reduced only slightly following hydrolysis with ribonuclease.

In many of the chief cells one can see discrete small granules which stain brightly with the periodic acid Schiff technique (23). These granules are scattered throughout the cytoplasm, often in close relation to the juxtanuclear bodies (Fig. 3). They are here designated the PAS-positive granules.

The dark chief cell described by Baker (3) could not be identified in this study with either the light or electron microscope.

Fig. 6 represents a low power electron micrograph of a group of parathyroid chief cells. The area portrayed is somewhat unusual in that no blood vessels are seen in the relatively large area of parenchyma represented. Chief cells tend to be compactly arranged, each cell usually lying directly adjacent to neighboring chief or oxyphil cells. The appearance of these cells at low power is much as one would anticipate from the structure of macaque parathyroid chief cells as seen with the light microscope. Structures easily identified include the cell nuclei, numerous mitochondria, endoplasmic reticulum, fairly large granules of moderate density, and diffuse fine cytoplasmic granulation. In many places plasma membranes of adjacent chief cells tend to pursue a complex and undulating course; this is discussed in detail later in the paper.

Nuclei.—The chief cell nuclei show characteristic elliptical profiles and contain one or more nucleoli (Figs. 6 and 7). The nuclear matrix appears to contain many very fine densely packed granules, 150 to 250 Å in diameter, which are slightly more numerous at the periphery (Figs. 6 and 7). Favorable sections reveal a double nuclear membrane as described by Hartmann (22) for nerve cells. One may also find nuclear pores (Fig. 7) resembling those reported by Watson (54).

Mitochondria.—The mitochondria of the chief cell, although numerous, are not evenly distributed throughout the cytoplasm (Figs. 6, 7, and 11). Thus various sections of the same cell may show a marked variation in the number of mitochondria seen, depending upon which area of the cell is represented. As mentioned previously, there is a distinct tendency toward congregation of the mitochondria at the vascular pole of the cell (Figs. 11 and 15). The chief cell mitochondria appear as rods or filaments of varying length, as originally described (3). In electron micrographs the profiles may be approximately 0.2 μ in width and up to 1 μ in length. The submicroscopic structure of the mitochondria present in parathyroid chief cells is consistent with Palade's description of mitochondrial structure in other mammalian tissues (36, 37).

Endoplasmic Reticulum.—The endoplasmic reticulum as seen in a variety of cells has been well described by Porter (47, 48), Palade and Porter (41) and Palade (38, 39). Its presence in the chief cells of the rat parathyroid has already been noted by Lever (30). It has also been found to be a component of the cytoplasm of the chief cells of the macaque (Figs. 6 to 8), where it is disposed both diffusely and in well organized masses of oriented lamellae resembling some of the Nissl bodies described in nerve cells by Palay and Palade (42).

The distribution and size of the masses of oriented lamellae as seen with the electron microscope correlates well with the distribution and size of the juxtanuclear body seen with the light microscope in virtually each chief cell. The masses have dimensions of 1 to 3 μ in section and are most frequently found in close relation to the cell nucleus. They may, however, be found in any portion of the cytoplasm (Figs. 2 to 4, 6, 10, and 11). This similarity permits one to conclude that the juxtanuclear body of the light microscopist is characterized by organized stacks of parallel lamellae of the endoplasmic reticulum.

Within a single juxtanuclear body two to fifteen of these membrane pairs may be present in profile in normal or nearly normal sections. The membranes delimit flattened vesicles or cisternae. Occasional anastomoses joining the stacks of parallel flattened vesicles are encountered in favorable profiles. Thus this system of membranes forms a true reticulum (Fig. 8). Numerous small, spherical, or rod-shaped particles 100 to 300 Å in size, as described by Palade (39), are applied to the outer surface of the individual membranes comprising the granular reticulum. This feature permits one to speak of these masses as belonging to the ergastoplasmic or granular portion of the endoplasmic reticulum.

In addition to the granular component of the endoplasmic reticulum described above, small oval and circular agranular profiles 500 to 2000 Å in diameter (and looking like vesicles) are seen throughout the cytoplasm of the chief cells (Figs. 7 and 11).

Golgi Bodies.—The presence of the Golgi complex in chief cells of the parathyroid as seen with the light microscope has been reported in a variety of mammalian species (7, 16, 18, 26, 27). However, Baker was unable to demonstrate this structure in cells of macaque...
parathyroid despite the utilization of specific stains and techniques (3).

In recent years the appearance of Golgi bodies when viewed through the medium of the electron microscope has been well characterized (12, 13, 42, 53). Its presence in rat parathyroid chief cells studied with the electron microscope has been reported (30). Golgi membranes and vesicles can be identified in virtually each macaque parathyroid chief cell adequately prepared for electron microscopic study. They occupy an area of up to 4 µ in favorable profiles and are generally located in the perinuclear zone of cytoplasm (Figs. 7, 8, and 10). The Golgi bodies of the parathyroid are similar in structure to those of the gall bladder epithelium, as described by Yamada (56) and to the "agranular reticulum" described in nerve cells by Palay and Palade (42). They are characterized by a series of paired, parallel agranular membranes intimately associated with many small vesicles. No large vacuoles in close relation to the Golgi substance, as described in pancreatic acinar cells (53) and anterior pituitary cells (16) are seen in parathyroid chief cells.

**PAS-Positive Granules.**—Fairly large granules or vesicles are commonly seen in the cytoplasm of parathyroid chief cells. These granules are filled with homogeneous appearing material of greater density than the surrounding cytoplasm of the chief cells. They are ellipsoidal and measure about 0.5 to 1 µ in their greatest diameter. Several of these granules are commonly encountered in a section of a single chief cell. They may be found in any cytoplasmic area of the cell, but are most commonly seen in close relation to the endoplasmic reticulum (Figs. 6, 7, 11, and 15). These granules are believed to correspond to the PAS-positive granules described above in the paragraph dealing with light microscopic observations (p. 15) (Fig. 3). Similar structures described as ellipsoidal, spherical, or U-shaped vesicles but of greater size have been described previously in macaque parathyroid by Baker (3). Whether or not these granules represent stored secretory product of the parathyroid, perhaps in the form of colloid, is a matter of conjecture. The granules have not been observed in the process of traversing the plasma membrane of the chief cell.

**Cytoplasmic Matrix.**—The background cytoplasmic matrix of parathyroid chief cells contains small, moderately dense granules approximately 100 to 200 A in diameter. In addition larger, irregularly shaped inclusions of homogeneous dense material, thought to represent accumulations of lipide, are encountered in varying quantities in the cytoplasm of chief cells (Figs. 7 and 11).

**Plasma Membrane.**—When visualized through the light microscope, the plasma membrane surrounding the parathyroid chief cell appears as a straight, thin membrane applied directly to the plasma membranes of neighboring parenchymal cells, or, in the case of the vascular pole of the cell, applied directly to a thin basement membrane which stains prominently with the periodic acid Schiff technique (Fig. 3).

With the greater detail revealed by the electron microscope, it is evident that in some areas the apposed plasma membranes of adjacent macaque chief cells tend to pursue complex and undulating courses, with frequent infoldings of the membranes, much as reported in rat parathyroids by Lever (30). As a result, a complex interdigitation of cytoplasmic processes of adjacent cells is seen, reminiscent of the manner in which pieces of an intricate jigsaw puzzle interlock (Figs. 6 and 15). In other areas apposed cell membranes pursue a more or less straight uncomplicated course with only occasional plications and interdigitations (Fig. 11). Generally one sees between the dense portions of the plasma membrane profiles of adjacent chief cells a narrow interval of lesser density about 100 to 200 A in width.

In other areas, portions of plasma membranes of adjacent chief cells are separated by a variable but considerable distance (Fig. 7). The intercellular space located between these plasma membranes may represent a connective tissue or interstitial fluid space. Many finger-like projections of chief cell cytoplasm enclosed by the continuous plasma membrane extend into this interstitial space. A similar intercellular space has been described in rat parathyroid by Lever (29, 30).

It is possible that the plications of the chief cell plasma membranes allow the individual cells to vary their size to some degree, as may be required during different stages of activity, without undue stretching or rupture of the cell membrane.

The portion of the plasma membrane limiting the surface of the chief cell that faces the capillary, pursues essentially a straight course without plications. It is closely applied to a continuous basement membrane, designated as the parenchymal cell basement membrane. This separates the cell from the perivascular structures surrounding the blood vessels of the parathyroid gland. Numerous minute vesicles, from 200 to 400 A in diameter, similar to those described in gall bladder epithelium by Yamada (56), are seen in close relation to this portion of the plasma membrane of the chief cell (Figs. 11 and 12). In addition, tiny cave-like indentations similar to those described along the cell membrane of capillary endothelial cells by Palade (38) and seen in gall bladder epithelial cells by Yamada (56) (who called them *caveolae intracellularis*) are seen along this portion of the cell membrane in favorable sections.

**Oxyphil Cell:**

A second, less abundant basic cell type in the macaque parathyroid parenchyma is the oxyphil
cell. Oxyphil cells as seen with the light microscope have been described in the parathyroid of man (10, 20, 34, 35), cow and steer (31), and macaque monkey (3, 11).

Baker described pale and dark oxyphil cells in macaque parathyroid prepared by the usual techniques. The dark oxyphils were characterized by large numbers of mitochondria and the frequent occurrence of the juxtanuclear body. In the pale oxyphils fewer mitochondria were observed, and the juxtanuclear body was seen infrequently (3).

The light microscope observations made in this study are essentially in accord with those of Baker. Fig. 1 represents a photomicrograph of a portion of monkey parathyroid prepared and stained by the Altmann-Kull technique (9). An oxyphil cell containing numerous mitochondria is seen in the center of the field. Fig. 3 reveals a group of oxyphil cells. One of them displays a prominent juxtanuclear body. It must be emphasized that the number of oxyphil cells present in the parathyroids of the macaque monkey is extremely small. Often none or only one oxyphil can be identified in a cross section measuring four or more mm².

Because of this infrequency, relatively few well fixed oxyphil cells could be studied via the electron microscope. Frequently tissue areas were encountered in which chief cell fixation was considered good by current criteria, but the adjacent oxyphil cells revealed much fragmentation and distortion of cellular contents. No distinction between dark and pale oxyphil cells could be made in tissue studied with the electron microscope. Oxyphil cells were recognized and distinguished from chief cells by their greater size, greater cytoplasm to nucleus ratio, smaller, more dense nuclei, and distinctive cytoplasmic content. They occurred singly or in groups of two or three.

The most striking characteristic of oxyphil cells is the tremendous number of mitochondria present throughout the cytoplasm (Figs. 9 and 10). These cells virtually represent sacs stuffed with mitochondria. The mitochondria are packed so closely that in some instances they indent one another. Their fine structure is similar to that described by Palade (36, 37). These mitochondria differ from those of chief cells in that the former are of larger size (up to 0.35 μ in diameter in contrast to 0.25 μ for chief cell mitochondria). Filamentous forms are less common, while plump, rod-shaped forms predominate.

In favorable profiles small accumulations of the granular endoplasmic reticulum and material suggestive of Golgi membranes are seen. Many small vesicles and fine, dense granules are present in the cytoplasmic matrix. Dense inclusions of irregular shape and size, similar in appearance to those described in the section dealing with chief cells and presumed to be lipide inclusions, are present. No oxyphil cells sectioned so as to show a surface presented to a capillary were observed with the electron microscope, but these were seen with the light microscope (Fig. 3).

In addition to the characteristic oxyphil cells described above, several other large cells of comparable size containing different and peculiar cytoplasmic structures were encountered in macaque parathyroid. The outstanding structural element present in these cells is a whorl-like structure composed of laminated, concentrically arranged, agranular membrane pairs (Figs. 16 and 17), similar in appearance to a structure described in the cytoplasm of sympathetic ganglion cells by Palay and Palade (42). It also appears similar in structure to, but of different dimensions than, developing myelin in peripheral nerves of chick embryos as reported by Geren (18). In favorable profiles as many as nine lamellar, agranular membrane pairs can be identified disposed around a central core of variable density. This central core varies in appearance. It may consist of homogeneous material with a density similar to that of the surrounding cytoplasm; of fine, moderately dense granular material; of uniform, dense material resembling lipide inclusions; or of combinations of the above (Figs. 16 and 17). The individual membranes comprising the lamellar structures are about 50 A thick and the distance between membrane pairs is about 150 A. The individual membrane pairs are in turn separated from each other by larger but variably sized spaces of intervening material of the density of the cytoplasmic matrix. In some profiles, anastomoses between membrane pairs can be seen (Figs. 16 and 17).

Structures up to 0.5 μ in their smallest diameter, here thought to be specialized mitochondria, are seen in intimate association with some of these lamellar whorls. Often these whorls appear to be encircled partially by bodies which might be construed as incompletely formed mitochondria. It is difficult to separate the anatomic limits of these mitochondria from those of the whorl-like structures (Figs. 16 and 17). To state that these elements function in mitochondrial formation would be pure conjecture, since no concrete evidence for this is at hand. However, the dimensions of the
membrane system of mitochondria (36) and the membrane system of these enigmatic structures correlate well. Further information regarding them is desirable.

**Capillaries:**

The macaque parathyroid is generously endowed with an extensive capillary network which courses through the parenchymal substance of the gland. The capillary wall is described by light microscopists as being composed of a single layer of endothelial cells closely applied to a surrounding continuous thin basement membrane (4), (Fig. 3). In most areas this capillary wall is so thin that its total thickness is considerably less than the limit of resolution of the light microscope.

Electron micrographs of parathyroid capillaries confirm the presence of a single cell layer of endothelium closely applied to a thin basement membrane. The endothelial cell is quite thick in the region of the nucleus, but from the nuclear area, sheet-like extensions of cytoplasm, which vary considerably in thickness in different areas of the same cell, spread circumferentially, forming the capillary wall. In some areas the endothelial wall is extremely thin, measuring only about 250 A in its entire thickness (Figs. 11, 12, and 14). In these thin areas, the capillary wall appears to consist only of two cell membranes, one facing the capillary lumen and the other facing the adjacent basement membrane. The only barrier, other than the actual pore itself, to free communication of the capillary lumen with the surrounding perivascular space is the uninterrupted, thin (100 to 150 A) basement membrane, which is closely applied to the outer limits of the capillary endothelium. The possible significance of this is discussed below.

Other portions of the capillary endothelium reveal a much thicker cytoplasmic wall without interrupting pores. In these thick portions are cytoplasmic structures such as mitochondria, endoplasmic reticulum, and Golgi bodies. In addition, in these thicker areas, one sees numerous fine vesicles and caveolae intracellular, similar to those described in capillaries of other tissues (24, 38, 50, 56, 57) (Figs. 11 to 14). Larger, irregularly shaped vesicles or cisterns, identified as part of the endoplasmic reticulum, can also be recognized (Fig. 13). In some areas small, thin, finger-like projections of endothelial cytoplasm can be seen extending into the capillary lumen (Fig. 12).

The intercellular attachments of the endothelial cells lining the capillaries of the parathyroid are similar in structure to the “terminal bars” as described in gall bladder epithelium (56), kidney glomerular endothelial cells (57), and pulmonary endothelium (24).

**Perivascular Space:**

Utilizing the light microscope, Allara (1) described the presence of two thin basement membranes delineating the space between the parenchymal cells and the capillary endothelium of human parathyroid. The presence of collagen fibers and mesenchymal cellular elements including fibroblasts, reticulo-endothelial cells, and mast cells within the confines of this space has been described (27, 32). Lever (29) studied the subendothelial space of the rat parathyroid with the electron microscope and described the presence of an amorphous material applied to, but distinct from, the plasma membrane of both the parenchymal and the endothelial cells.

The present studies with the light microscope demonstrate that this space is present in the macaque. The two basement membranes lining it stain intensely with the periodic acid Schiff technique (Fig. 3). Between these basement membranes is homogeneous material which stains faintly with the periodate Schiff method and which is thought to represent connective tissue ground substance. Many cells which stain metachromati-
cally with toluidine blue are thought to represent mast cells (Fig. 2). Other cells morphologically suggestive of fibroblasts and macrophages are seen within the confines of this perivascular space.

Electron micrographs confirm many of the above findings. The submicroscopic structure of the space is in essence very similar to the fine structure of an analogous space described in the anterior pituitary (50) and the thyroid gland (14). Two distinct, concentric, thin (100 to 150 A thick), homogeneous appearing, uninterrupted, moderately dense basement membranes are seen completely encircling the perivascular space and separating it from neighboring tissues. One membrane is closely applied to the antiluminal cell membrane of the capillary endothelial cells, the other basement membrane is closely applied to the cell membrane limiting the vascular pole of the parathyroid parenchymal cells. These basement membranes follow closely the course of the cell membranes and are separated from them by an irregular space of decreased density usually 250 to 500 A in width (Figs. 11, 12, and 15). However, in some sections, portions of the space between basement membrane and parenchymal cell border may be as much as 1 μ wide.

The width of the space between the two basement membranes shows considerable variation, some of which may be due to shrinkage artifact. The content of this space is also variable. In some sections cellular elements suggestive of fibroblasts, macrophages (Fig. 15), and mast cells are seen together with collagen fibers. In other sections only connective tissue fibers and homogeneous material of medium density, interpreted as being connective tissue ground substance, are visualized.

There is very little connective tissue material between the parenchymal cells of the parathyroid. These cells are generally closely applied to one another and only infrequently is an actual space resolved between these cellular elements. There are, however, sections in which a sizable intercellular space between parenchymal cells can be seen and it is uncertain if this space represents a connective tissue space containing ground substance and fibrillar connective tissue elements (Fig. 7).

DISCUSSION

It is known that cytoplasmic structures containing a high percentage of ribonucleic acid stain intensely with ordinary basic stains. The juxtanuclear body, as seen with the light microscope in the cytoplasm of virtually all macaque parathyroid chief cells, is characterized by intense basophilia (Figs. 2 to 4). This intense basophilia is greatly reduced following enzymatic hydrolysis of tissue sections of parathyroid with ribonuclease (see above, Figs. 4 and 5), and this supports the view that much of the basophilia of the juxtanuclear body can be attributed to ribonucleic acid. It is also now known that the granular component associated with the endoplasmic reticulum is composed largely of ribonucleoprotein, and it has been suggested that these submicroscopic cytoplasmic particles are responsible for much of the cytoplasmic basophilia encountered in active tissue cells (40). The amounts, distribution, and dimensions of the juxtanuclear bodies within parathyroid chief cells as seen with the light microscope and aggregations of granular elements of the endoplasmic reticulum as seen with the electron microscope are essentially identical (Figs. 2 to 4, and 6). Baker (3), in his description of the structure of the juxtanuclear body as observed with the light microscope, states "It frequently appeared to be made up of threads which were somewhat parallel to each other. Usually this organelle was compact and elongated with some lighter internal areas." This description correlates well with the actual observed structure of this portion of the endoplasmic reticulum as seen in parathyroid chief cells with the electron microscope. Thus it is apparent that the juxtanuclear bodies of macaque parathyroid chief cells represent stacks of lamellar elements of the endoplasmic reticulum which are readily recognized with the electron microscope.

The functional cytology of the oxyphil cells of the parathyroid continues to be an enigma. The long standing problem of whether the oxyphil cells have a physiologically important but as yet unrecognized role to play in the function or functions of the parathyroid gland remains unanswered. One can suspect that a cell virtually packed with mitochondria might be an important functional component of the parathyroid gland, but it must be admitted that few other tissue components are currently as incompletely understood as the parathyroid oxyphil cells, and much further work is necessary before the full significance of these cells may be appreciated.

The fine structure of capillary endothelia of endocrine glands other than the parathyroid has been reported. Monroe (33) described areas of discontinuity in the capillary endothelium of the
vesicles and caveolae may also be seen in favorable
sections in association with the parenchymal cell
membrane limiting the vascular pole of the paren-
chymal cell. Thus the mechanism of membrane
vesiculation may also play an important role in the
exchange of material between the parenchymal cell
and the perivascular space.

Thus if the endothelial pores and the mechanism
of membrane vesiculation are both utilized, the
only structures traversed by all materials exchang-
ing between the parenchymal cells and the blood
plasma are the two thin basement membranes and
the perivascular space they delineate.

The author wishes to thank Dr. H. Stanley Bennett
and the other members of the Department of Anatomy
at the University of Washington whose kind advice,
encouragement, and criticism made this study possible.

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Plate 3

Figs. 1 to 5 represent photomicrographs of macaque parathyroid.

Fig. 1. An oxyphil cell, containing many mitochondria which appear bright red in the original preparation, is seen in the center of the micrograph. Although individual mitochondria located within the chief cell cytoplasm are not resolved, the accumulation of mitochondrial substance at the vascular pole of the chief cell can be recognized in the original preparation by the more intense staining (arrow) observed in this region. Altmann-Kull, × 1400.

Fig. 2. Two dark mast cells, staining metachromatically, are present in the perivascular space. The deeply basophilic juxtanuclear bodies (J) of surrounding chief cells are clearly demonstrated. Toluidine blue, × 1400.

Fig. 3. A typical area of parathyroid parenchyma traversed by a profuse capillary network (L). A group of oxyphil cells is seen in the upper right corner. A basophilic juxtanuclear body is shown to advantage in one of the oxyphils (J). Small, dark granules which appear deep magenta in the original preparation are seen in the chief cells in the left half of the micrograph. In the original slide, the perivascular space (S) is a light magenta hue, outlined by the dark magenta basement membranes (B) located at the vascular poles of the chief cells and the antiluminal wall of the capillary endothelium. Periodic acid Schiff, × 1400.

Fig. 4. A group of chief cells representing a control section handled in the same manner as the tissue illustrated in Fig. 5, except that this preparation was incubated with distilled water rather than ribonuclease solution. Note the prominent, deeply basophilic juxtanuclear bodies (arrow). Gallocyanin-chromalum, × 1400.

Fig. 5. A group of chief cells following incubation with a 0.15 per cent solution of crystalline ribonuclease at 37° C. for 3 hours, followed by staining. Note the pale representation of the juxtanuclear body (arrow), which, indeed, is scarcely discernible (compare with Fig. 4). Gallocyanin-chromalum, × 1400.
(Trier: Fine structure of parathyroid gland)
**PLATE 4**

**Fig. 6.** A low magnification survey electron micrograph of a section including a group of chief cells. Numerous mitochondria are scattered throughout the cells. Large granules of moderate density (A), thought to be the same granules which stain intensely with the periodic acid Schiff technique (Fig. 3), are seen throughout the cytoplasm. Often they are in close relation to aggregations of the granular component of the endoplasmic reticulum (Rg). The accumulations of ergastoplasmic endoplasmic reticulum are frequently located in juxtaposition to the chief cell nuclei, and correspond to the juxtanuclear bodies seen with the light microscope (compare with Figs. 2 and 4). Note the complex undulating course of the adjacent cell membranes (W) with the resulting intricate interdigitation of the peripheral cytoplasm of adjacent chief cells. X 6000.
(Trier: Fine structure of parathyroid gland)
Plate 5

Fig. 7. Higher magnification electron micrograph of portions of several adjacent chief cells. The fine, almost homogeneous granularity of the nuclear structure (Nc) is apparent. Pores (Z) in the nuclear membrane can be seen. Golgi membranes and vesicles (G) are located in the perinuclear zone of cytoplasm in the cell in the upper left corner. Mitochondria (M) appear in this figure in less abundance than in most portions of chief cell cytoplasm. Circular agranular profiles (Ra) of variable size are seen throughout the cytoplasm. Lipide accumulations (H) are present. The space (I), seen infrequently between adjacent chief cells, is thought to represent an intercellular connective tissue space. × 15,000.

The insert (lower left) represents the perinuclear cytoplasm of cell at upper left at higher magnification and shows specifically the Golgi bodies (G) in greater detail. × 23,000.
(Trier: Fine structure of parathyroid gland)
FIG. 8. Detail of a portion of chief cell cytoplasm, showing the juxtanuclear body. This body is characterized by parallel oriented lamellae of endoplasmic reticulum of the ergastoplasmic type. The lamellae occur in pairs enclosing flattened cisterns, which are connected by occasional anastamotic membranes (arrow). Numerous small spheroidal particles are applied to the outer surface of the membrane constituting the juxtanuclear body. Mitochondria (M) and Golgi complex (G) can be identified. X 33,000.

FIG. 9. A portion of an oxyphil cell (Oc), adjacent to a chief cell (Cc). Note the numerous typical mitochondria (M) present in the oxyphil cell cytoplasm. In this portion of the cell few other cytoplasmic structures can be recognized, except for lipide accumulations (H) and small ovoid profiles which probably represent part of the endoplasmic reticulum. The adjacent oxyphil and chief cell membranes (W) portrayed in this micrograph pursue a relatively straight, uncomplicated course. X 31,000.
(Trier: Fine structure of parathyroid gland)
Plate 7

Fig. 10. Electron micrograph showing portions of two oxyphil cells (Oc) and a chief cell (Cc). Note that the oxyphil cell cytoplasm is packed with numerous mitochondria (M) which are larger in size than chief cell mitochondria. Some of the Golgi structures (G) and granular endoplasmic reticulum (Rg) can be identified in the oxyphil cells. Lipide inclusions (H) are more numerous than in chief cells. × 15,000.
(Trier: Fine structure of parathyroid gland)
PLATE 8

Fig. 11. A portion of a parathyroid capillary and surrounding chief cells. The capillary lumen (L) contains a polymorphonuclear leukocyte (X) and precipitated plasma. Note the extreme thinness of the endothelial cell (E) in some areas of the capillary wall. Pores (P) are seen perforating the endothelium in some of the thin areas. Mitochondria (M) and the vesicles of Palade (V) can be recognized in the endothelial cytoplasm. Several caveolae intracellulares (C) can be seen along the endothelial cell membrane. Two terminal bars (T) sectioned obliquely are present. The thin, continuous parenchymal cell and capillary basement membranes (B) are demonstrated delineating the perivascular space (S). This space completely surrounds the portion of the capillary portrayed and contains loosely arranged collagen or reticular fibers and connective tissue ground substance. Mitochondria (M), which are most numerous at the vascular pole, lipid inclusions (H), and PAS-positive granules (A), often in close relation to the granular component of the endoplasmic reticulum (Rg), are seen in the chief cell cytoplasm. Minute vesicles (U) in close relation to the chief cell plasma membrane abutting the perivascular space are present. × 15,000.

The insert represents at higher magnification a portion of the above micrograph showing in greater detail the pores (P), vesicles (V), and caveolae (C) of the endothelium. One notes also the parenchymal and endothelial basement membranes (B), and the minute "membrane vesicles" (U) at the vascular pole of the chief cells. × 30,000.

Fig. 12. A portion of a parathyroid capillary seen in cross-section. Fine, finger-like projections (Q) of endothelial cell cytoplasm extend into the capillary lumen. × 23,000.
(Trier: Fine structure of parathyroid gland)
PLATE 9

FIG. 13. Detail of a parathyroid capillary wall. A terminal bar ($T$) is seen sectioned in or near the perpendicular plane. The structures comprising the terminal bar include the dense, adjacent endothelial cell plasma membranes separated by homogeneous appearing material of less density than the membranes, but of greater density than the endothelial cell cytoplasmic matrix or blood plasma. Within the endothelial cell cytoplasm, mitochondria ($M$), cisternal dilatations of endoplasmic reticulum ($Rg$), and Palade's vesicles ($V$) can be recognized. $\times 56,000$.

FIG. 14. Detail of a parathyroid capillary wall. Endothelial pores ($P$), caveolae intracellulares ($C$), Palade's vesicles ($V$), and a terminal bar ($T$) can be identified. The capillary basement membrane ($B$) is evident. $\times 56,000$.

FIG. 15. A portion of the perivascular space surrounding a large parathyroid capillary. In the upper right a portion of the capillary and its lumen ($L$) can be recognized. To the left, cytoplasm of two chief cells is seen. Note the plications and intricate interdigitation of adjacent chief cell plasma membranes. Mitochondria, accumulations of granular endoplasmic reticulum, and PAS-positive granules ($A$) can be identified in the chief cell cytoplasm. The perivascular space ($S$) is quite wide in the area portrayed and is limited by parenchymal and capillary basement membranes. Portions of several perivascular cells ($D$) are seen within the confines of the space. $\times 14,000$. 
(Trier: Fine structure of parathyroid gland)
FIG. 16. A portion of the cytoplasm of a large cell type infrequently found in parathyroid parenchyma and presumed to be a type of oxyphil cell. Whorl-like structures (K), consisting of laminated agranular membrane pairs concentrically disposed about a central core, characterize these cells. In some profiles the central core consists of homogeneous dense material. Two of the central cores pictured consist of a central homogeneous dense area surrounded by a less dense, granular area (arrows). Large mitochondria (M) are seen in close relation to these whorl-like structures. Granular endoplasmic reticulum (Rg) is present, particularly in the peripheral cytoplasm of the cell. X 15,000.

Fig. 17. Higher magnification of a portion of the cell illustrated in the preceding figure. Several of the whorl-like elements are pictured. Their structure is as described in Fig. 16, but, at this higher magnification, anastomotic bridges (arrows) between the concentric membrane pairs can be seen. Note the close relation of the upper whorl-like structure to the large mitochondrion which partially encircles it. It is difficult to separate the limits of the mitochondrion from the whorl-like structure. X 48,000.