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Undifferentiated cells in gastric mucosa

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INTRODUCTION

In 1953, Stevens & Leblond published their classical paper on the cell types of the gastric mucosa. Epithelial cells of the mucosa of the fundus were divided, on the basis of their staining reaction with PAS, into surface epithelial cells, mucous neck cells, parietal cells and zymogenic cells. Since then, all these cell types, with the addition of argentaffin cells, have been described in detail with the electron microscope (see, for example, Helander & Ekholm, 1959; Sedar, 1961*a*, *b*; Ito & Winchester, 1963; Helander, 1964; Lillibridge, 1964).

During an investigation of the gastric mucosa in dog and man a cell has been noted which has certain ultrastructural characteristics differing from those already described. The present authors believe that it represents yet another cell type which has many characteristics of an undifferentiated cell and which may function in a reserve capacity. A preliminary report of this work has already been made (Johnson & Young, 1967).

MATERIALS AND METHODS

Pieces of mucosa from the greater curvature of dog stomach were carefully removed under intravenous Nembutal anaesthesia. Similar material from human stomachs was obtained from patients undergoing surgical treatment for peptic ulceration and in this instance care was taken to select mucosa from regions showing no pathological involvement. Small blocks of tissue from both sources of material were immediately fixed for 2 h in ice-cold 1 % osmium tetroxide, buffered with veronal acetate (Palade, 1952). The blocks were then dehydrated in alcohol and embedded in Araldite (Luft, 1961). Ultrathin sections were cut on a Porter–Blum microtome and mounted on carboned-formvar grids. The sections were stained with uranyl acetate (Stempak & Ward, 1964) before viewing in a Siemens Elmiskop I.

RESULTS

The cells described in this paper are found in the isthmus and neck of the gastric gland in both man and dog. They appear to be more common in the neck but since counts were not undertaken this impression may be misleading. They occur singly and may lie adjacent to either mucous neck cells, parietal cells or surface epithelial cells.

They are usually ovoid in shape and occupy the full thickness of the epithelium. Their long axis lies roughly at right angles to the basement membrane and their free

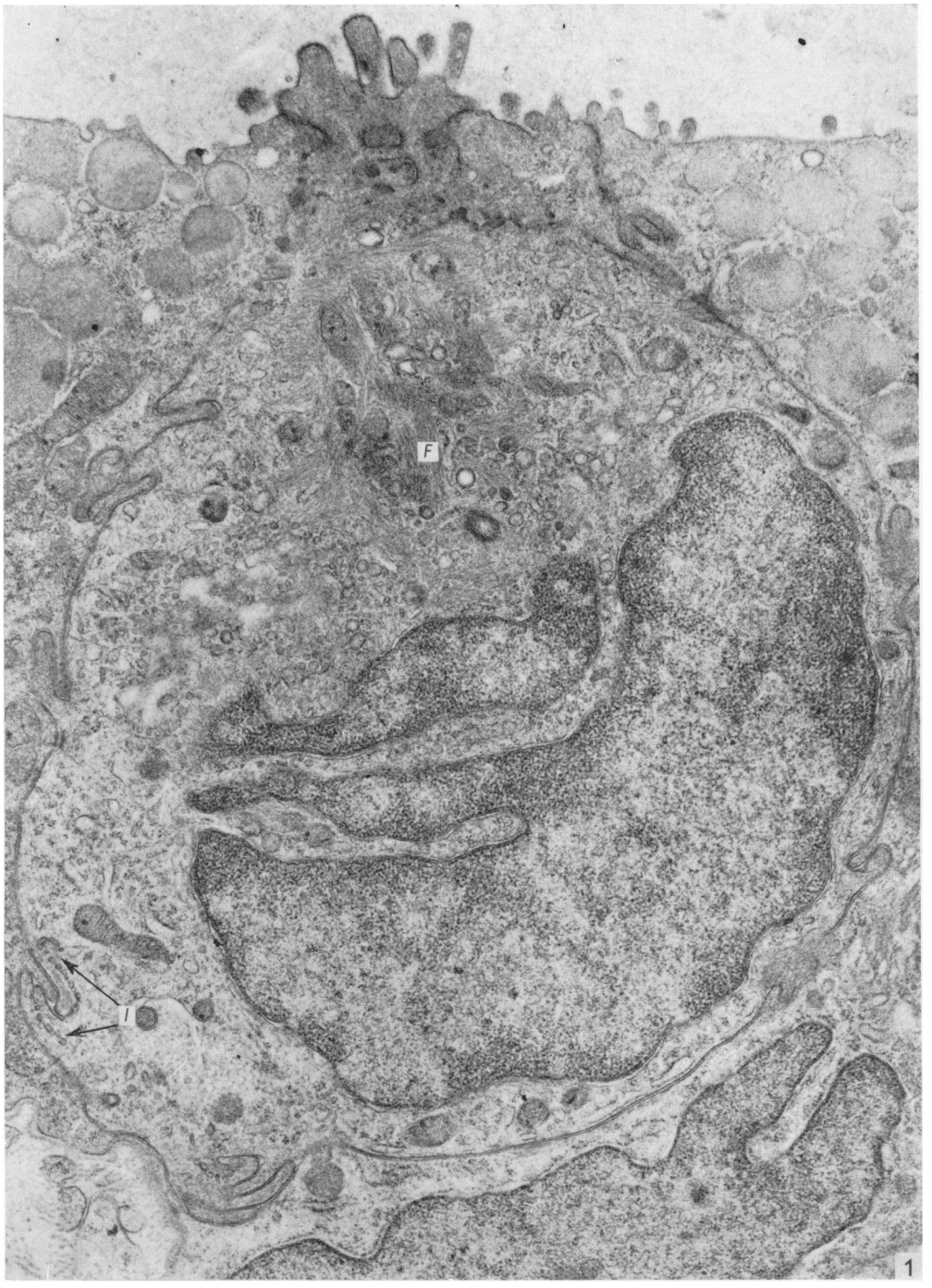

Fig. 1. Undifferentiated cell from gastric mucosa of the dog with portions of mucous neck cells on each side. The thick microvilli protrude above the level of the surrounding cells. The nucleus is deeply indented. Invaginations of the plasma membrane with associated vesicles are present (*I*). The apical cytoplasm contains much fibrillar material (*F*). × 19500.

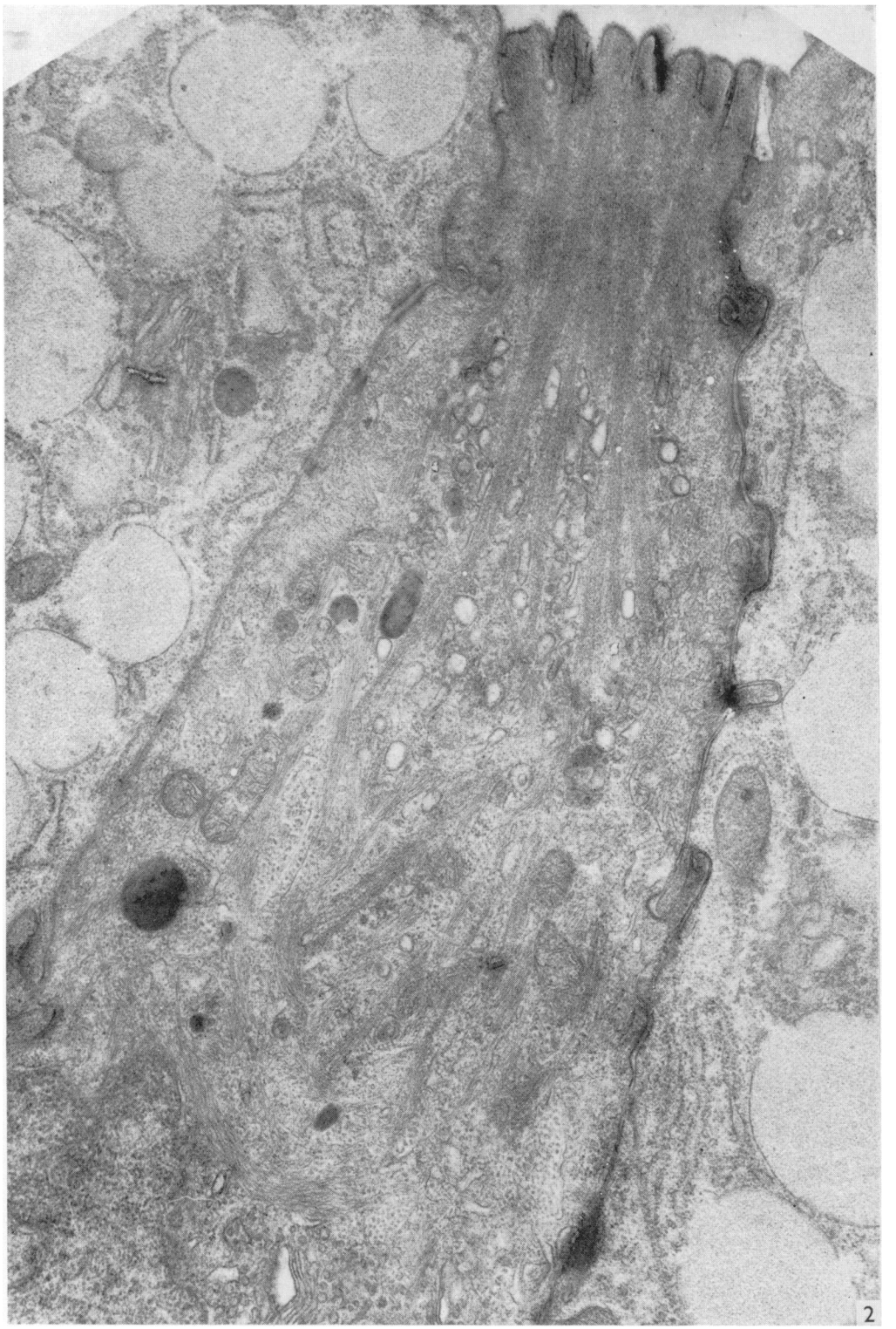

Fig. 2. Cell from dog mucosa showing characteristic arrangement of bundles of filaments in the cytoplasm. Vacuoles, lysosome-like structures and several desmosomes can be seen. ×26000.

surfaces tend to be less extensive than those of adjacent cells. The free surfaces frequently bulge into the lumen of the gland and carry prominent microvilli. These vary in size but are characteristically longer and thicker than those of surface epithelial or mucous neck cells. Apparent fusion over part or all of the lengths of neighbouring microvilli is common. Each microvillus is surrounded by plasma membrane and contains a dense core of fibrillar material which extends into the cytoplasm of the cell (Figs. 1, 2).

The intercellular space surrounding the cells is relatively constant and measures 200–300 Å in most regions. The lateral plasma membranes invaginate and evaginate to form frequent finger-like processes. In regions where the plasma membrane is invaginated small rows of vesicles may be seen to 'stream' into the subjacent cytoplasm; these create an impression of pinocytosis (Fig. 1). The lateral surfaces of these cells are attached to those surrounding them by desmosomes and at their apical extremities the plasma membranes form tight junctions (Fig. 2); these structures are similar to those described in other epithelial sites (Farquhar & Palade, 1963).

The nuclei of the cells are large and basally situated. They have extensive indentations which may give them a multilobed appearance (Fig. 1). Apart from this there is little that is peculiar to them; in their density and distribution of chromatin they most closely resemble the nuclei of mucous neck cells. All of the nuclei examined are in interphase.

The cytoplasm is of moderate density. Its apical half contains considerable masses of fine filaments which are continuous with those forming the central cores of the microvilli (Figs. 2, 3). The filaments, grouped into bundles, turn back on themselves in the supranuclear regions; the directions of the filaments in successive bundles differ and this further emphasizes their presence within the cytoplasm. In regions where the filaments are sectioned longitudinally they are often seen to lie parallel to each other and resemble longitudinally sectioned microtubules. However, examination of regions in which the plane of section lies at right angles indicates that they are true filaments. A terminal web is not seen within these cells.

In addition to the bundles of filaments, the cytoplasm of the apical halves of the cells contains numerous vacuoles surrounded by single smooth unit membranes (Figs. 2, 3). These vary in shape, being either spherical, oval or tubular in outline. Many of them appear entrapped between the bundles of filaments, and their orientation appears to reflect that of the filaments. Their contents are of low to moderate electron density and in this respect, as well as in their size, the vacuoles resemble the vesicles of parietal cells more closely than either mucous granules or zymogen granules.

The Golgi apparatus is disposed laterally to the nucleus (Fig. 2). It consists of small vesicles filled with a material of moderate electron density, flattened cisternae with varying degrees of dilatation at their extremities and round or oval vacuoles. While the vacuoles of the Golgi apparatus appear to be related to the dilated extremities of the cisternae there is no unequivocal evidence that they are directly related to the vacuoles of the apical cytoplasm. However, the similarity in size and contents of the two makes such a possibility probable.

Moderate numbers of mitochondria are present throughout the cytoplasm. They

are small, oval or elongated in shape, of moderate electron density and contain transversely orientated cristae (Figs. 1, 2).

Electron dense bodies, of variable diameter, are also present within the cytoplasm. They are bound by membranes and, although confirmatory enzyme studies have not been undertaken, they have an appearance similar to the lysosomes found in other cells (Novikoff, 1961).

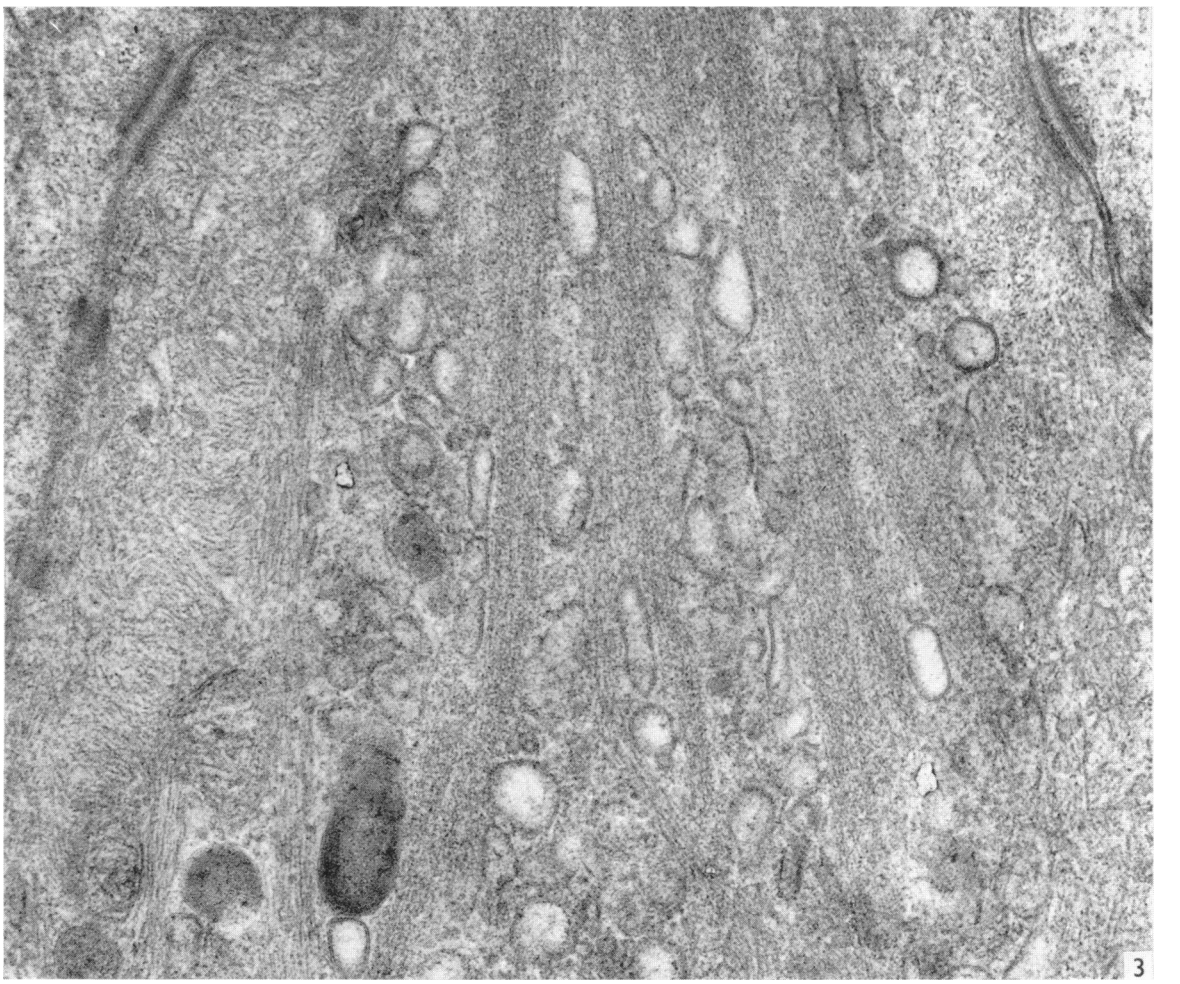

Fig. 3. Photographic enlargement of Fig. 2. The structure of the desmosome is apparent. The cytoplasm contains bundles of filaments which at this level are orientated mainly in a longitudinal direction. The vacuoles between the bundles of filaments can be seen to be surrounded by a unit membrane. × 59000.

Sparse profiles of rough endoplasmic reticulum with varying degrees of dilatation are present. The contents of the profiles have a moderate density which is similar to that present in the elements of the Golgi apparatus.

Other organelles present in these cells include considerable amounts of free ribo-

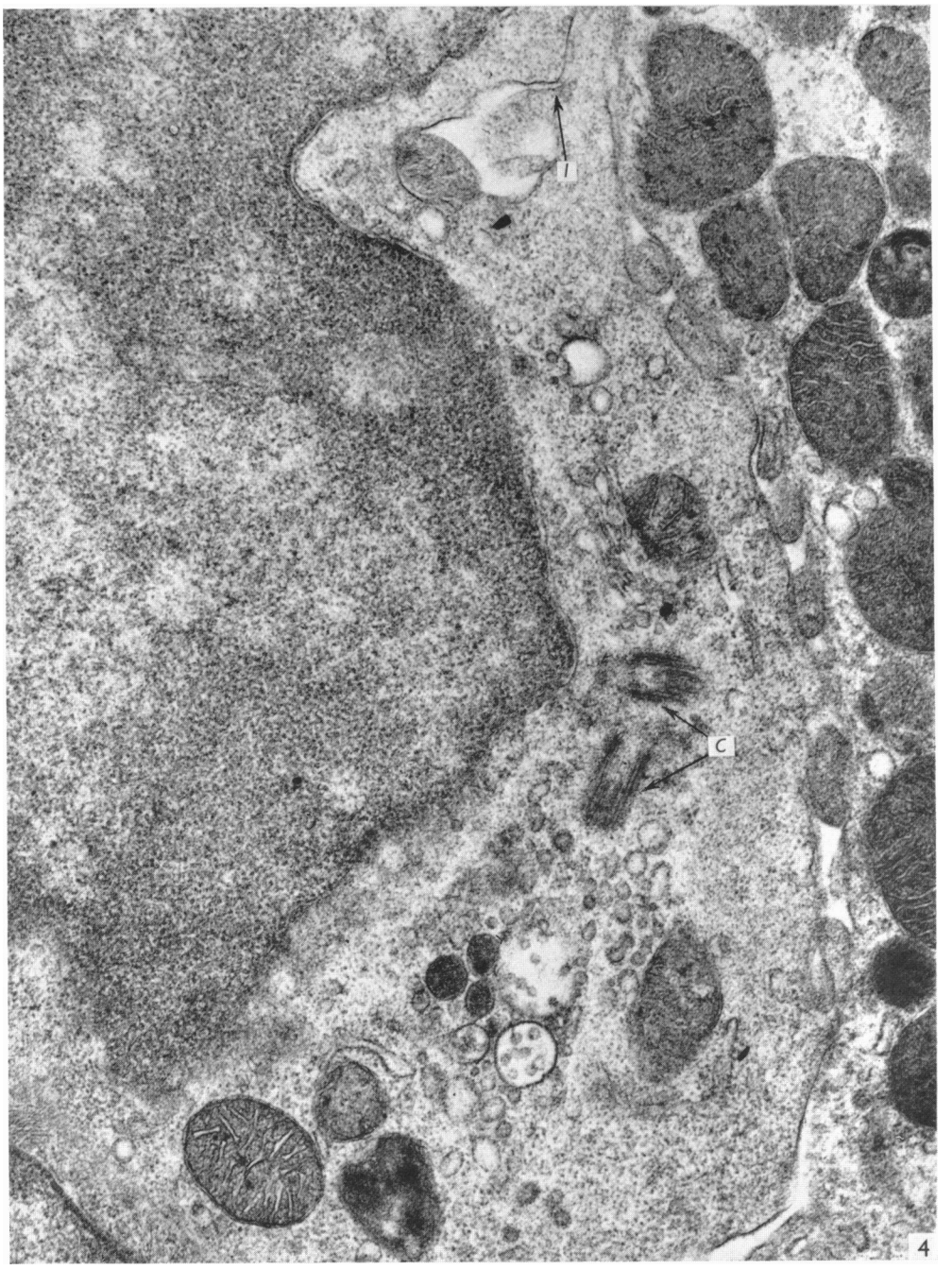

Fig. 4. Undifferentiated cell lying adjacent to a parietal cell. A pair of centrioles (*C*) are present and the plasma membrane is invaginated (*I*). Note the similarity between the mitochondria of this cell and those of the parietal cell. × 32000.

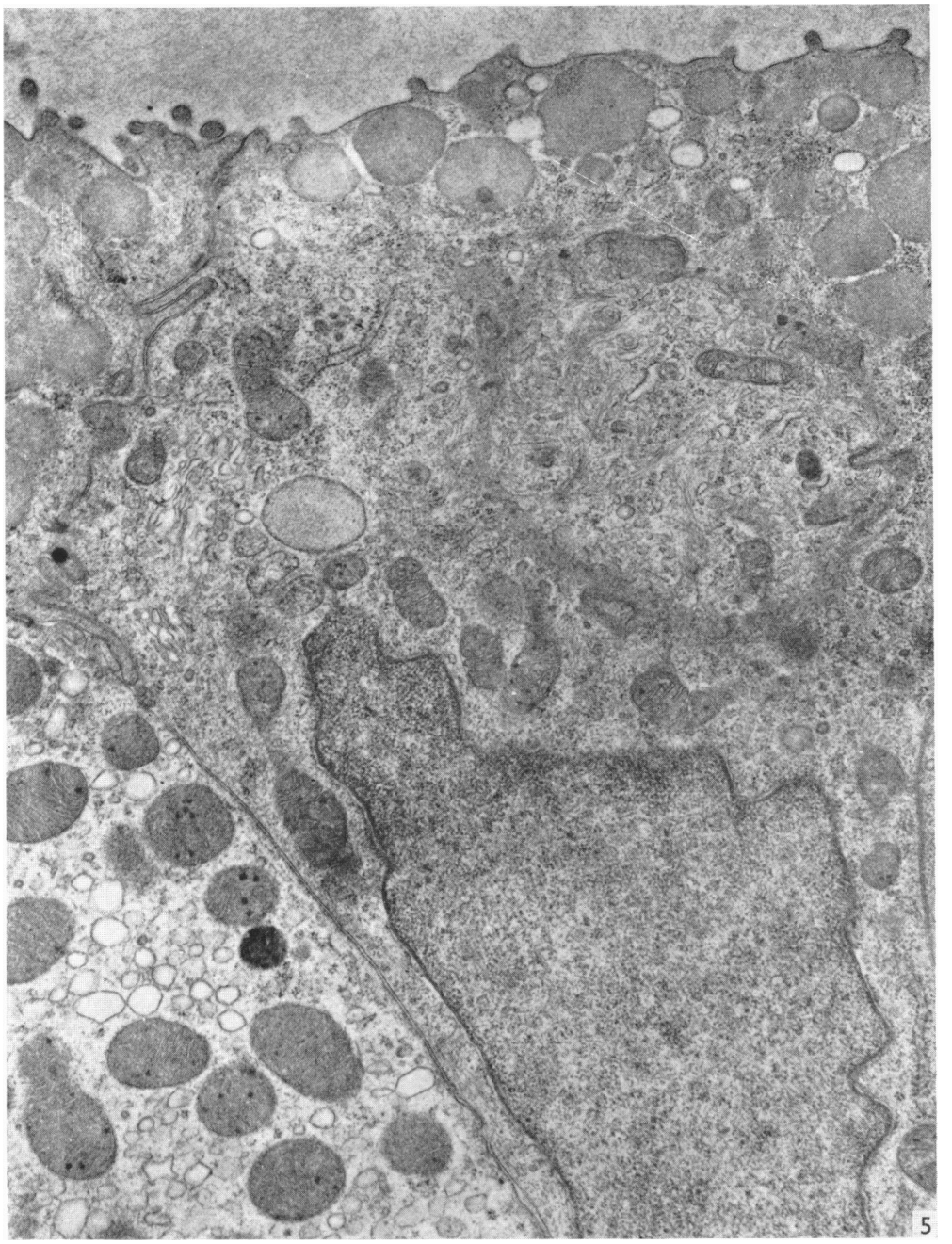

Fig. 5. The cell in this electron micrograph contains secretion granules similar to those in mucous neck cells. It also contains vacuoles with contents of low electron density. The nucleus is moderately indented and the cytoplasm contains much filamentous material. × 19500.

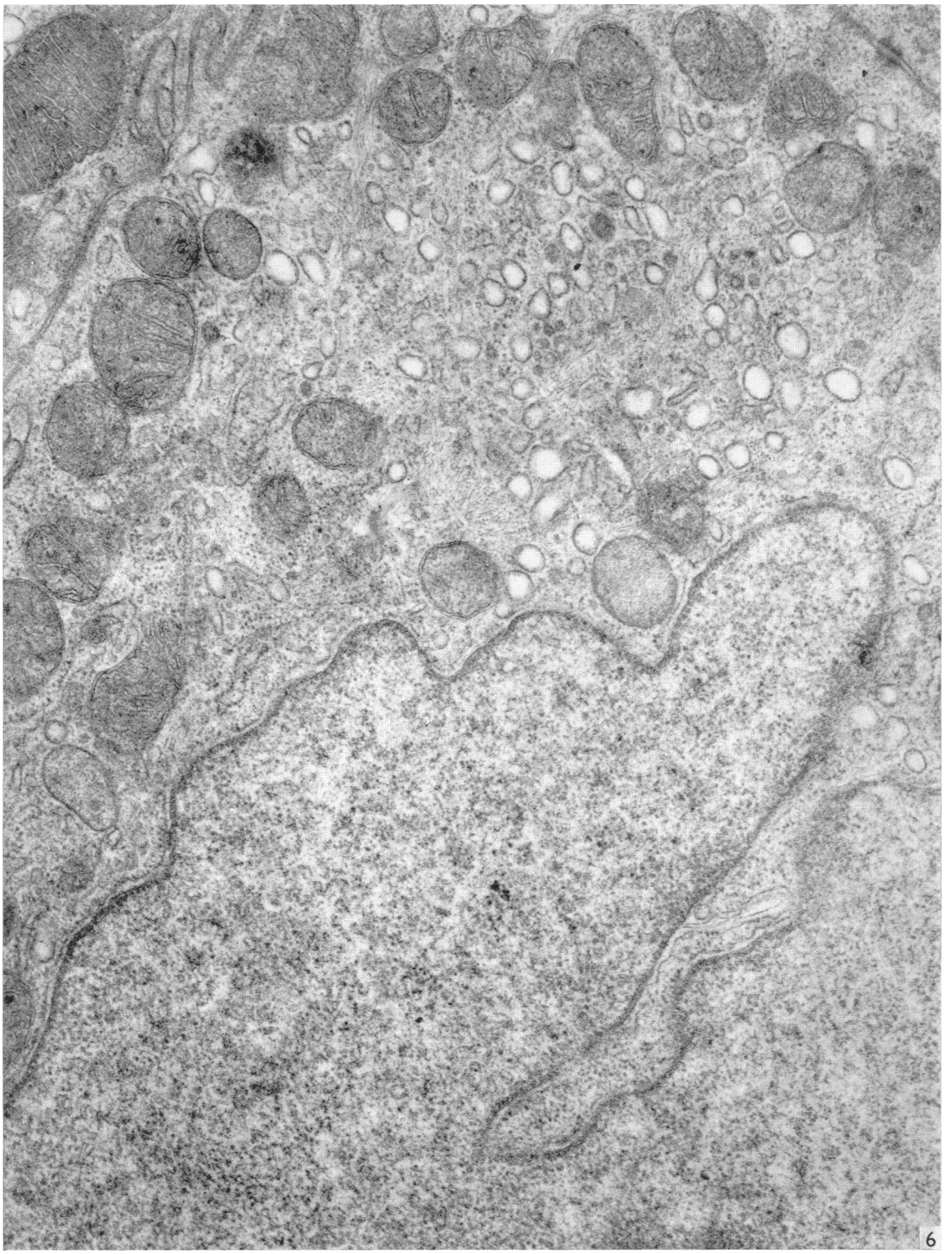

Fig. 6. The nucleus of this cell is indented, and the cytoplasm contains many vacuoles with contents of low density. There are numerous mitochondria and free ribosomes. ×29500.

somes arranged as small clumps or chains, multivesicular bodies, and centrioles. The latter structures are frequently seen as pairs situated in the Golgi zone and with the long axis of one perpendicular to the long axis of the other (Fig. 4).

In addition to these characteristic features occasional cells may contain structures which give them a resemblance to other recognized cell types of the gastric mucosa. The most common additional feature is the presence of large membrane-bound vacuoles filled with a homogenous material of moderate density (Fig. 5). The vacuoles occupy the apical cytoplasm and differ markedly from the vacuoles already described, in that they are larger and their contents are more electron dense. They resemble the mucous granules of adjacent mucous neck cells. Other cells sometimes show additional features which give them a resemblance to parietal cells. These include one or more extensive invaginations of the plasma membrane, increased numbers of mitochondria with a density similar to those of parietal cells and increased numbers of the smooth walled vacuoles. (Figs. 4, 6).

DISCUSSION

The cell described in this work has a combination of features which distinguishes it from the recognized cell types of gastric mucosa. They include short, anastomosing microvilli with prominent central cores extending to the level of the nucleus, scanty rough endoplasmic reticulum, a moderately developed Golgi apparatus, smooth-surfaced vacuoles filled with a material of low electron density, indented nuclei, centrioles and free ribosomes.

Corpron (1966) described a 'non-differentiated cell' in the stomach of the rat in which the cytoplasm and nucleoplasm were of low electron density, the endoplasmic reticulum was poorly developed and free ribosomes were scattered throughout the cytoplasm. It would seem probable that the cell found in the gastric mucosa of man and dog in the present investigation is similar in type to that reported by Corpron in rat and that it also should be classified as an undifferentiated cell.

Cells, resembling in some respects those described in gastric mucosa, have also been reported in the small and large intestines. Trier (1963) described a cell, which he considered to be undifferentiated, in the crypt of Lieberkühn in the small intestine of man. It carried short, wide microvilli with distinctive filamentous cores, and had a lobulated nucleus, poorly developed endoplasmic reticulum, many unattached ribosomes and membrane-bound secretory granules. Silva (1966) reported the presence of 'multivesicular cells' both in the surface epithelium and in the epithelium of the glands of the colon in the mouse. These cells were characterized by microvilli which had approximately twice the dimensions of surrounding epithelial cells and contained fibrillar material which extended into the supranuclear cytoplasm for considerable distances. They also contained large numbers of vacuoles and vesicles, particularly in the apical region of the cell, sparse endoplasmic reticulum and large numbers of ribosomes lying free in the cytoplasmic matrix.

The question arises as to whether or not these cells, from three different regions of the alimentary canal, are related. Their embryological derivation is compatible with such a relationship. All three occur in regions of mucosa noted for mitotic activity; all three show a lack of specialization relative to that of other cells of the

mucosa and can therefore be justifiably called undifferentiated. Thus there appears to be grounds for suggesting that in the alimentary canal the mucosa contains cells, with many common features, whose function is to give rise to other differentiated cells.

Apart from this relationship there is the question, in the gastric mucosa, of the relationship of the undifferentiated cell to those in the immediate vicinity. The interpretation, in this situation, is made difficult by the variety of cells present. In addition to surface epithelial, mucous neck, parietal, zymogen and argentaffin cells, gastric mucosa contains immature surface cells (Corpron, 1966) and neck parietal cells (Lawn,1960). The last two and the mucous neck cells show certain structural characteristics which suggest that they are transitional in type and therefore represent intermediate stages in the development of some of the mature cells already noted. For instance, it has been argued that immature surface cells differentiate to form surface epithelial cells, and neck parietal cells form mature parietal cells (see Corpron, 1966, for fuller discussion). The place of the undifferentiated cell in the hierarchy cannot be unequivocably defined in a study such as this. Nevertheless, its differentiation appears, on morphological grounds, to be less highly advanced than either immature surface, neck parietal, or mucous neck, cells and it would seem possible therefore that it forms a precursor of these cells. This contention is supported by the occasional finding, within it, of features characteristic of the other cell types such as invaginations of the plasma membranes, electron dense mitochondria and mucous-like granules.

SUMMARY

The isthmus and neck of the gastric gland in man and dog contain cells with prominent microvilli. The filaments of the cores of the microvilli pass uninterruptedly into the apical cytoplasm in bundles which form arcades in the supranuclear region. The cells have basally situated, indented nuclei and many vacuoles bounded by smooth membranes. The contents of these vacuoles are of low to moderate density. A well-developed Golgi apparatus is present and there are many free ribosomes. Some of these cells show characteristics of either parietal or mucous neck cells and it is suggested that they are undifferentiated cells which may act as precursors of these two cell types.

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