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# Odontogenic jaw cysts: light and electron microscopical investigations

**L. Domenici-Lombardo[1], F. Amunni[2], M. Bergamini[2] and P. Romagnoli[1]**

[1]Department of Human Anatomy and Histology and [2]Institute of Odontognathostomatology, University of Florence, Florence, Italy

**Summary.** Light and electron microscopy were used to analyze the epithelial lining of odontogenic cysts excised from edentulous regions of the jaws. Clinically, three cases were identified as keratocysts, and 21 cases as cysts other than keratocysts («non-keratocysts»). The epithelium of the former was found to achieve keratinization over most of the surface and to never contain mucus secreting cells. The epithelium of the latter appeared to be in part stratified squamous, with cells loosely connected to each other, and in part stratified columnar, with superficial cells connected to each other by tight junctions and secreting mucus. The results suggest that cysts arising from edentulous regions of the jaws may be either keratocysts or cysts with heterogeneous, non-keratinizing epithelium; the content of keratocysts can be formed mainly by shedding of cornified epithelial layers, and that of non-keratocysts by mucus secretion from columnar epithelium associated to fluid filtration through non-keratinizing squamous epithelium.

**Key words:** Epithelium, Keratinization, Keratocysts, Langerhans cells, Mucous secretion

## Introduction

Several types of cysts may arise in the jaws from residues of the odontogenic epithelium (Shear, 1983; Lucas, 1984; Waldron, 1988). These cysts may also occur in areas where teeth have been extracted previously. Among these cysts, keratocysts are characterized by a dense, cheese-like content and a stratified squamous epithelial lining which undergoes keratinization, either complete (orthokeratinization) or incomplete (parakeratinization) (Lucas, 1984). The other odontogenic cysts which arise in edentulous areas are characterized by a fluid content and their epithelial lining may differentiate along different lines, i.e. columnar or squamous, keratinizing or, more frequently, non-keratinizing (see review by Lucas, 1984). Despite several light microscopy reports (Shear, 1983; Lucas, 1984; Waldron, 1988), very little is known about the histochemical and electron microscopical features of these epithelia (Fritiof and Hagglund, 1966; Wilson and Ross, 1978; Meurman and Ylipaavalniemi, 1984; Fujiwara and Watanabe, 1988), which achieve terminal differentiation in an environment other than skin or mucosae and which do not communicate, even indirectly, with the exterior of the body.

More detailed knowledge of the epithelial lining of these cysts may help us to understand the differentiation potentials of odontogenic epithelia and the mechanisms of production of cyst content. To address this issue, we have analyzed the epithelial lining of a series of jaws cysts by light microscopical histochemistry and electron microscopy, which allow for a better resolution than that achieved by conventional light microscopy.

*Offprint requests to:* Dr. Lola Domenici, Department of Human Anatomy and Histology, Section «E. Allara», Viale Pieraccini 6, I-50139 Firenze, italy

## Materials and methods

For this research, we used 24 cysts excised from edentulous regions of the jaws. Three of these cysts were diagnosed as keratocysts on the basis of clinical information and aspect at surgery. The others were collectively identified as cysts other than keratocysts; from now on indicated as non-keratocysts. These have been reported on first in the results, since they were more numerous. The cysts were excised from 19 males and 5 females, aged between 22 and 84 years (mean, 36 years). Part of each specimen was fixed in 10% formol in 0.1 mol/L phosphate buffer, pH 7.4, and embedded in paraffin. Sections were stained with hematoxylin and eosin, periodic acid-Schiff (PAS), diastase-PAS, alcian blue, pH 2.6, and alcian blue, pH 1 (Pearse, 1968; Kapur, 1986).

Part of 15 specimens was fixed in 4% glutaraldehyde in 0.1 mol/L cacodylate buffer, pH 7.4, postfixed in 1% osmium tetroxide in 0.1 mol/L phosphate buffer, pH 7.4, dehydrated in graded acetone, passed through propylene oxide and embedded in epon 812. Flat moulds were used to orientate the specimens so that they were always sectioned perpendicular to the epithelial surface.

Sections were stained with uranyl acetate followed by alcaline bismuth subnitrate or lead citrate and examined in a Siemens Elmiskop 102 electron microscope, at 80 kV.

## Results

### *Non-keratocysts*

The 21 cysts other than keratocysts were lined by a non-keratinizing stratified squamous epithelium. In many instances (10 cysts), the lining included limited areas of short, or tall columnar epithelium. In these cases the superficial columnar cells contained apical cytoplasmic granules, which were PAS-positive, diastase resistant and stained by alcian blue at pH 2.6, not at pH 1.0.

The electron microscopical features of the epithelium of these cysts will be described separately for the squamous and columnar varieties.

**Fig. 1.** Non-keratocyst. Cubic suprabasal cells of non-keratinizing stratified squamous epithelium contain thin tonofibrils (arrow) and are joined to each other by small desmosomes (arrowheads). Intercellular spaces between desmosomes are wide (asterisks). Electron microscopy. x 15,000

Non keratinizing stratified squamous epithelium

A basal, an intermediate and a superficial layer could be recognized in these areas (Figs. 1, 2). All cells contained thin tonofibrils and were joined to each other by few, small desmosomes; the basal ones were also joined to basement membrane by hemidesmosomes.

The shape was cubic or columnar for basal cells, spinous for intermediate ones, and disc-like for superficial ones. Intercellular spaces were wide up to the epithelial surface, except for desmosomes.

Stratified columnar epithelium

Four cell layers were recognized in this epithelium; namely a basal, a suprabasal, an intermediate and a superficial layer.

Basal and suprabasal cells were similar to the basal and intermediate cells, respectively, of non-keratinizing squamous epithelium. Intermediate cells were wide, polyhedrical, rich in tonofilaments arranged in a loose mesh and contained filamentous mitochondria located

**Fig. 2.** Non-keratocyst. Wide intercellular spaces (asterisks) can also be found between superficial squamous cells. Electron microscopy. x 9,000

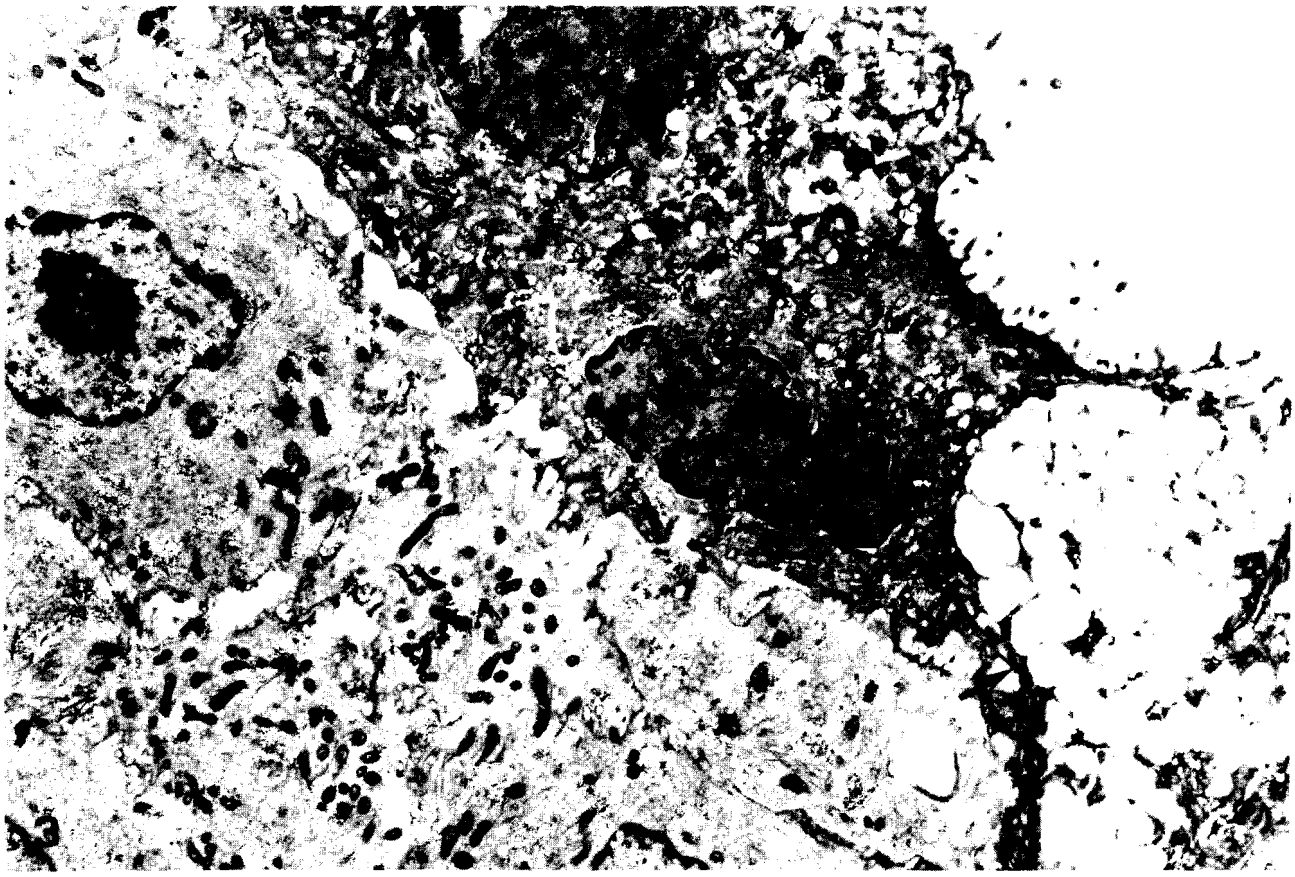
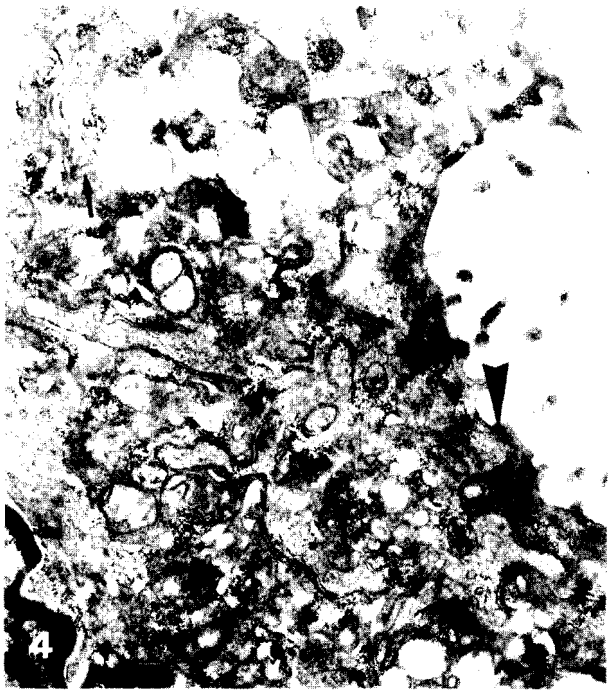


**Fig. 3.** Non-keratocyst. In stratified columnar epithelium, intermediate polyhedrical cells contain a mesh of tonofilaments, not arranged into fibrils, and columnar superficial cells contain variable numbers of mucous secretion granules (arrow). Electron microscopy. x 7,000



mainly at the cell periphery; these cells were joined to each other by few, small desmosomes (Fig. 3).

Superficial cells were short or tall columnar, rich in organelles (mitochondria, rough endoplasmic reticulum and Golgi apparatus), and poor in tonofilaments. The apical cytoplasm contained membrane-bound electron lucent secretion granules 0.2-1.0 μm in diameter, sometimes fixed while in exocytosis (Fig. 3). The apical cell surface expanded in short microvilli, with a thick cell coat (glycocalix). A terminal bar, including a tight and an intermediate junction and desmosomes, was found on the lateral cell surfaces close to their apical border (Fig. 4); small desmosomes were also found all over the cell surface facing other cells.

Intercellular spaces were wide up to the intermediate layer and narrow between superficial cells, and apparently sealed off at the terminal bar.

**Fig. 4.** Non-keratocyst. Superficial cells of non-keratinizing epithelium are joined to each other by junctional complexes which occlude intercellular spaces (arrowhead). Short microvilli with a relatively thick cell coat project from the apical cell surface. Note the formation of mucous secretion granules from the apical surface of the Golgi complex (arrow). Electron microscopy. x 18,000

### *Keratocysts*

The three cysts diagnosed as keratocysts were lined by a stratified squamous epithelium which keratinized over the whole surface, or part of it. Keratinization was complete (orthokeratinization) in two cases and incomplete (parakeratinization) in the third case. PAS-positive, diastase-sensitive granules, i.e. glycogen, were contained within the cells of the intermediate, spinous layer in these three cases.

Two of these cysts were available for electron microscopical analysis; in both cases, the epithelium was orthokeratinizing (Fig. 5). Basal, spinous, granular and cornified cell layers were easily identified. Spinous cells contained Odland granules with usually amorphous, sometimes in part lamellated content. Granular cells contained keratohyalin granules with a smooth surface and superficial cells were filled with tonofilaments organized with a keratin pattern and connected to each other by modified desmosomes, as is typical of such a layer in the keratinizing oral epithelia (Fig. 5). They did not contain organelles or nuclei and were wrapped in a cornified envelope. Intercellular spaces were wide (except for desmosomes) among cells of basal and spinous layers and narrow among cells of more superficial layers. Langerhans cells, dendritic in shape, rich in rough and smooth endoplasmic reticulum, with wide Golgi apparatus, few primary lysosomes and some typical Birbeck granules, were found between keratinocytes (Fig. 6).

In some areas, the epithelium lining these cysts appeared as non keratinizing; basal, spinous and superficial cell layers were recognized in these areas (Fig. 7). Basal and spinous cells looked similar to those of keratinizing areas, including the presence of well-developed tonofibrils and some Odland granules; superficial cells were flat, contained tonofibrils and were connected to each other by desmosomes. Dendritic cells, similar to those described for keratinizing areas, but devoid of Birbeck granules, were found between keratinocytes of non-keratinizing areas (Fig. 8).

### *Intraepithelial infiltrate*

Variable numbers of lymphocytes, neutrophils and mast cells with immature secretion granules were found within the epithelial lining of both types of cysts (i.e., non-keratocysts and keratocysts).

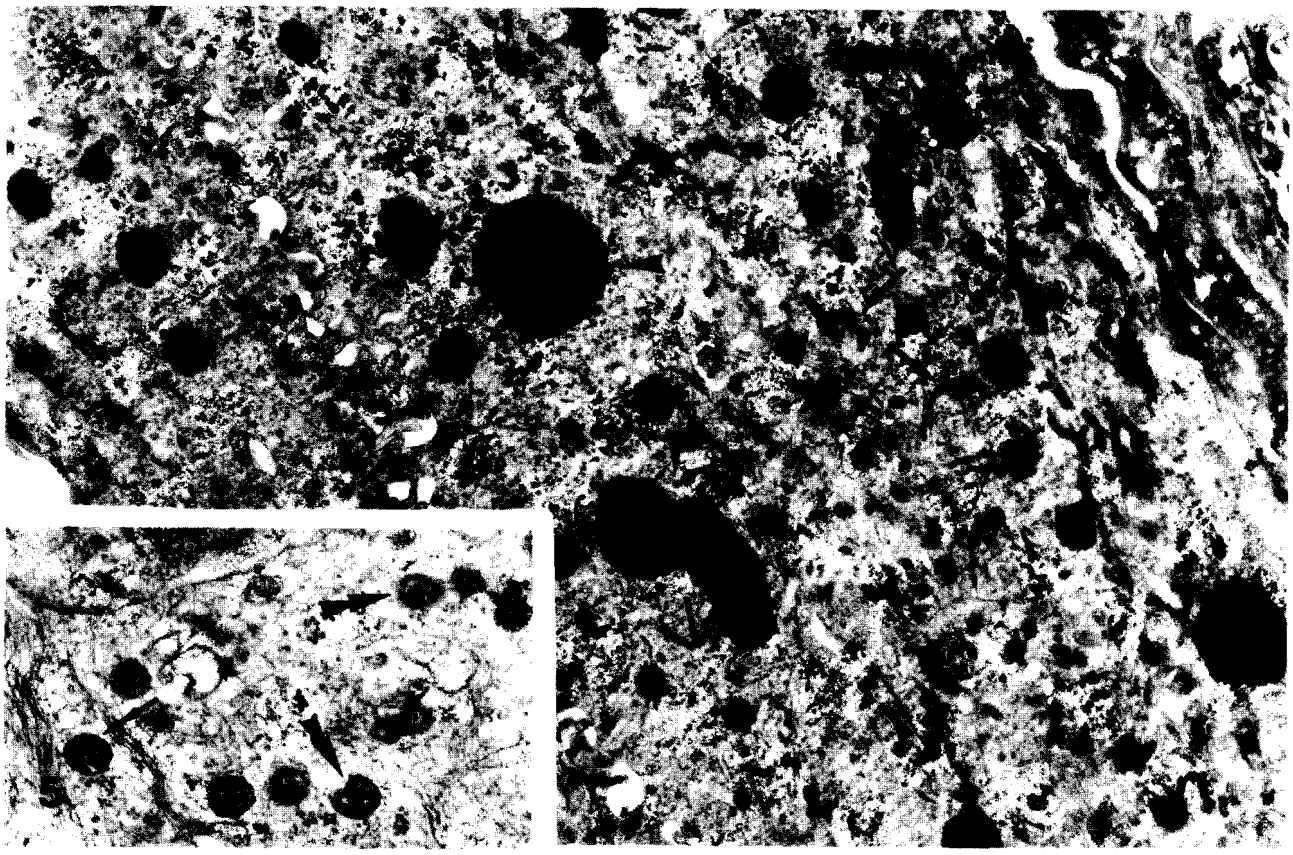


**Fig. 5.** Keratocyst. Tonofibrils (arrows) and keratohyalin granules with a smooth surface (arrowheads) are present in the granular cell layer and superficial cells are fully keratinized. The inset shows Odland granules with lamellated (arrow) or amorphous content; the latter sometimes include a central dense core and a peripheral paler halo (arrowheads). Electron microscopy. x 10,000; inset, x 31,000

## Discussion

In this research, a detailed description of the epithelial lining of jaw cysts has been provided. The two types of cysts recognized on the basis of clinical and surgical findings corresponded to two different types of epithelial linings; keratocysts were lined by ortho- or para-keratinizing squamous epithelium, non-keratocysts were lined by non-keratinizing squamous epithelium.

The epithelium of about one half non-keratocysts included patches of columnar secretory epithelium. The frequency of this finding may have been understimated, because the patches of columnar epithelium were often small and serial sectioning of the whole cysts was not completed. In these areas, the structure of the various cell layers was peculiar if compared with what is described for normal human columnar epithelia (Hay, 1977; Ham and Cormack, 1979; Vidic, 1986). In particular, there was a layer of intermediate cells characterized by abundant tonofilaments arranged in a mesh (instead of fibrils), many filamentous mitochondria at the cell periphery and very a poor development of all other organelles. The transition between these cells and suprabasal ones (rich in organelles and containing well-organized - although thin - tonofibrils) on one side, and between them and superficial columnar ones was abrupt. Superficial cells had common features of mucus-secreting cells. On the basis of alcian-blue staining, their secretion product appeared to contain sialomucins, but not histochemically-detectable sulphomucins (Pearse, 1968; Kapur, 1986). The formation of the content of these cysts seemed to depend on both active secretion by columnar cells and filtration of fluids among the intercellular spaces of squamous, non-keratinizing epithelium; these spaces seemed to be open towards the cyst cavity, whereas they were sealed off between columnar cells. Although microscopical evidence of areas of columnar epithelium only showed the glycoprotein component of the mucus, it is reasonable to assume that water too was secreted here, since the surface epithelium was similar to that of typical mucus-secreting surfaces in all respects. We cannot answer, on the basis of microscopical findings, whether different epithelial linings within single non-keratocysts derive from multiple differentiation pathways of a single germinative layer or by fusion of originally independent epithelial remnants - each with its own differentiation ability - into a single cyst.

**Fig. 6.** Keratocyst. A Langerhans cell with Birbeck granules (arrows) is included in the prickle cell layer. Electron microscopy. x 11,000

Keratocysts were characterized by the presence of a cornified layer on most of the epithelial surface. In two cases, this layer achieved full differentiation, as indicated by the lack of nuclei and organelles, the presence of a keratin pattern and a cornified envelope, and the aspect of desmosomes. A typical spinous and a granular cell layer were also recognized and the cells of the former produced typical Odland granules (Landmann, 1988), which were transiently stored in the cytoplasm and eventually secreted in the granular cell layer. The complete differentiation achieved by this keratinizing epithelium reflected also its ability to induce full differentiation into Langerhans cells, including the formation of Birbeck granules, of intra-epithelial dendritic cells of the immune system. This differentiation depends on the epithelial micro-environment and is hampered in areas of epidermal atrophy (Mori et al., 1994). In these cysts, some epithelial areas were non-keratinizing; however, these areas contained a well-developed spinous layer of cells, similar to that found in keratinizing areas. Therefore, differentiation along the pathway of keratinizing epithelia was typical of the lining of these cysts, even if full keratinization was not always achieved. The formation of cyst content in these cases seemed to depend primarily on shedding of surface epithelial cells and to a minor extent on filtration of fluid among cells of non keratinizing areas. The material shed from the surface of keratinized areas consisted of tonofilament-rich, dehydrated cells and a lipid-rich intercellular substance deriving from Odland granules, like in a normal keratinization process (Montagna and Parakkal, 1974; Fuchs, 1990; Wertz et al., 1992).

In both keratocysts and non-keratocysts, some

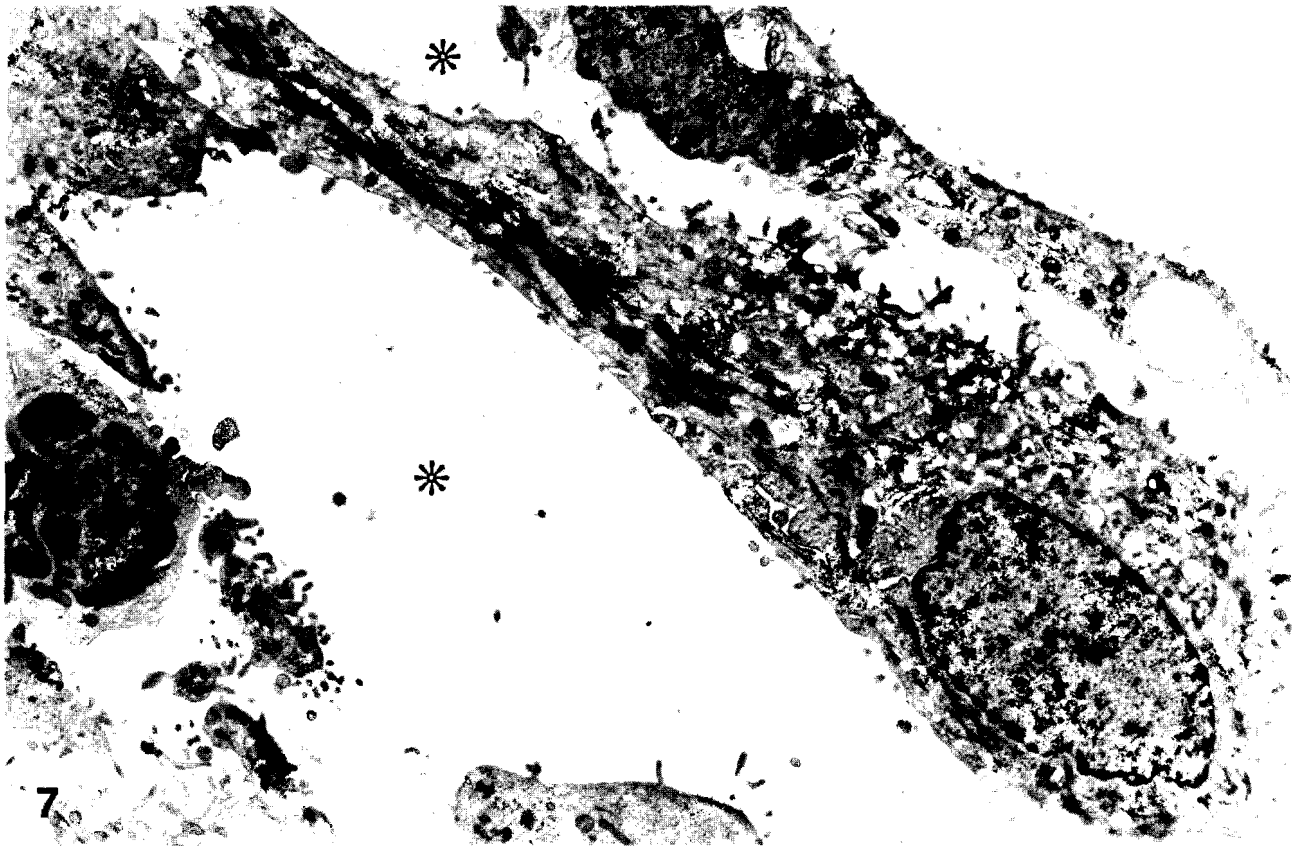



**Fig. 7.** Keratocyst. In this area, the epithelium is non-keratinizing and the intercellular spaces are wide (asterisks). Electron microscopy. x 7,000

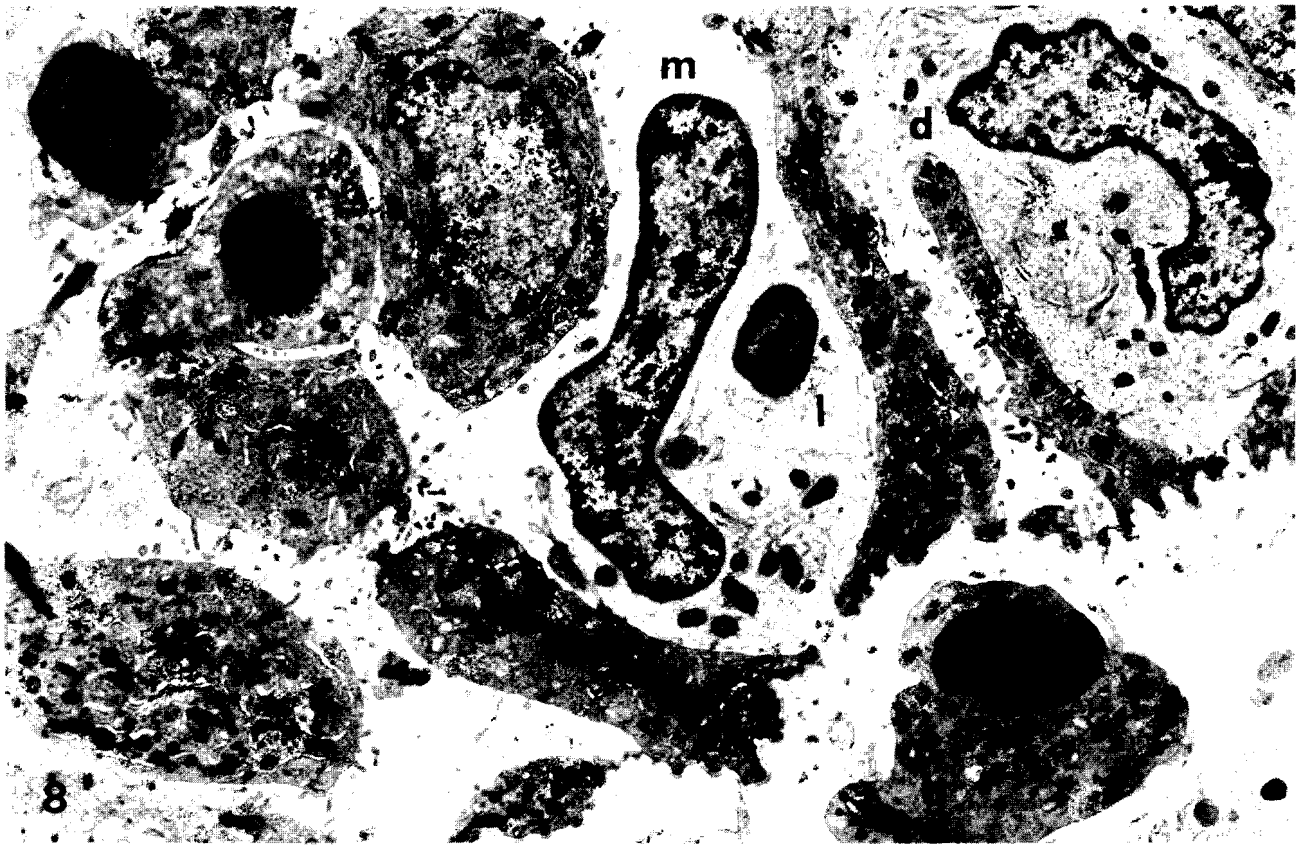



**Fig. 8.** Keratocyst. The epithelium is infiltrated by monocytoid cells (m), dendritic cells of presumable Langerhans lineage, but devoid of Birbeck granules (d), lymphocytes (l) and granulocytes (g). Electron microscopy. x 7,000

inflammatory cell infiltration was demonstrated - in a limited amount - within the epithelium. This leads to the suggestion that inflammation may contribute to giving rise to the content of both types of cysts.

In non-keratocysts, both squamous non-keratinizing and columnar secretory epithelium may differentiate, even close to each other. Cells with a peculiar structure appear to differentiate into an intermediate layer of columnar epithelium. This fact may hint to the formation of a peculiar microenvironment in the wall of these cysts, possibly depending on the lack of communication with the exterior and leading to the activation of a differentiation pattern apparently distinct from that of the columnar, secretory epithelium of airway mucosae.

The epithelial lining of keratocysts appears incapable of giving rise to secretory cells. Although the degree of keratinization may differ from point to point of the cyst lining, the cell types present do not show any derangement from the differentiation pathway of similar epithelia in the oral cavity (Stern, 1986). Therefore, the apparently more aggressive clinical behaviour of these cysts is not coupled to any sort of dysplasia.

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