5 Normal Histology of the Eustachian Tube, Middle Ear, and Mastoid Complex: The Mucoperiosteum Concept

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Introduction

The middle ear, mastoid, and Eustachian tube constitute a continuous, irregular, three-dimensional pneumatic cavity located within the temporal bone, between the tympanic membrane laterally and the petrous portion of the temporal bone medially. It is in this pneumatic space that otitis media occurs.

The middle ear, mastoid, and Eustachian tube are lined by a continuous mucosa of endodermal origin that originates in the nasopharynx. Through the opening of the Eustachian tube, this complex is exposed to the nasopharyngeal space and, in turn, to the environment. The purpose of the mucosa is to maintain an air-filled cavity so that the middle ear can perform its function of sound transmission and amplification. This mucosal lining consists of an epithelium and an underlying connective tissue. In addition, in the bony cavities (middle ear and mastoid), it has a periosteal layer (Fig. 5.1).

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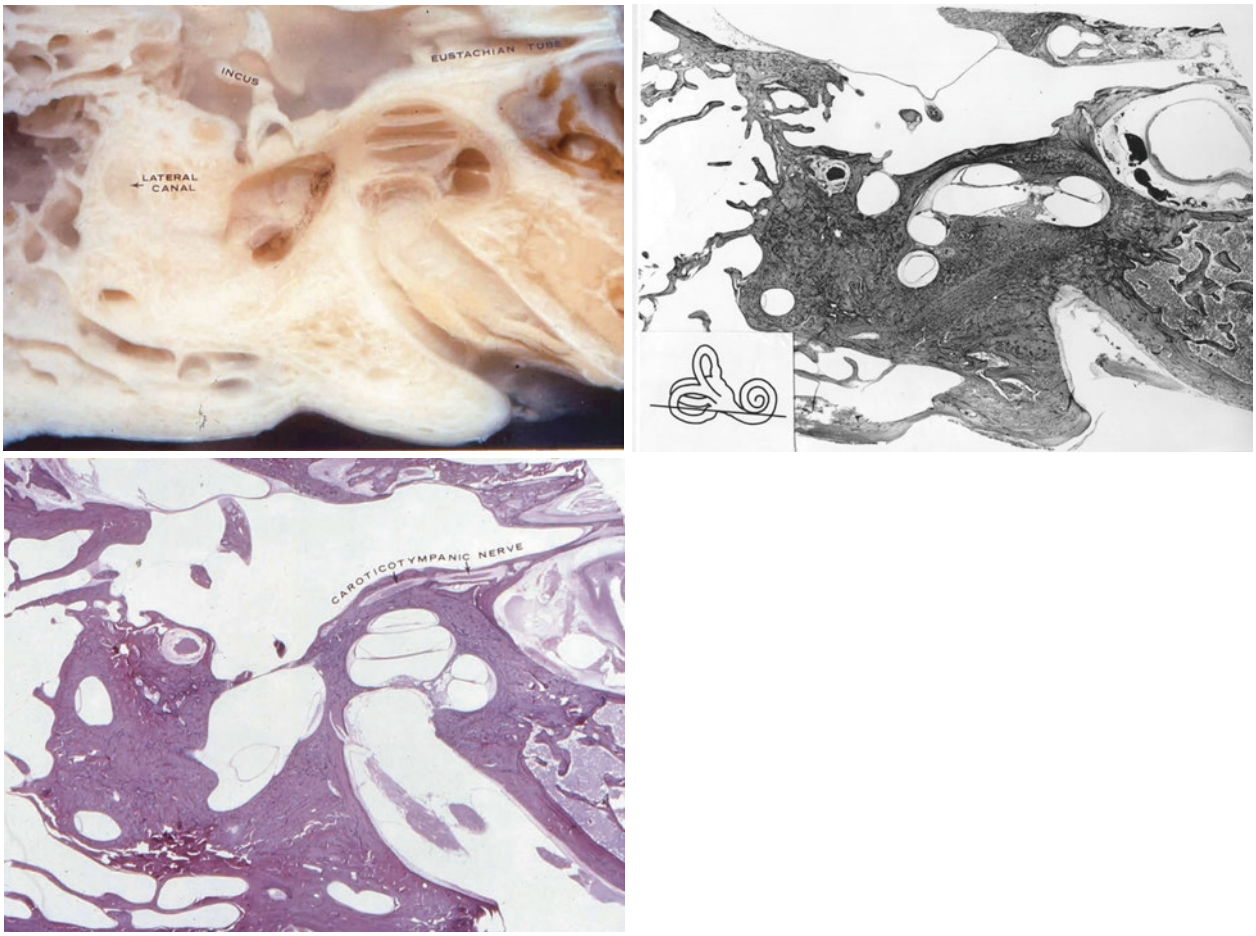


Fig. 5.1 Horizontal section of a temporal bone used as orientation to the different sites of the mucosal lining to be described in the middle ear, mastoid, and Eustachian tube. The Eustachian tube is located in the anterior wall and the mastoid cavity is posterior. The caroticotympanic nerve is over the promontory. (© Marcos Y. Goycoolea 2023; all rights reserved)

The Epithelium

The epithelium is continuous, and the types of cells will depend on their location in the mucosal lining of the middle ear and mastoid. Anteriorly, toward the Eustachian tube opening, there is a respiratory epithelium (Fig. 5.2). As it turns back toward the promontory, it gradually becomes cuboidal, with occasional glands (Fig. 5.3). The hypotympanum has tall ciliated columnar cells with some goblet cells and underlying basal cells, whereas toward the epitympanum, it has cuboidal ciliated cells with interposed small numbers of non-ciliated cells. As it extends towards the posterior wall and towards the aditus and antrum there is a gradual (Fig. 5.4a, b) flattening of epithelial cells with occasional ciliated cells toward the antrum initially, to become a simple squamous epithelium toward the mastoid (Fig. 5.5). In the mastoid the epithelium consists of flat non-ciliated cells devoid of glands and goblet cells. In other words, the mas-

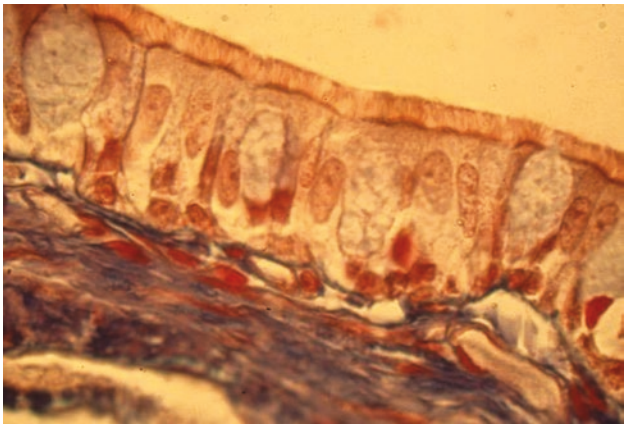


Fig. 5.2 A light micrograph of the Eustachian tube. A respiratory epithelium. Collagen fibers are stained blue with Azan stain. (© Marcos Y. Goycoolea 2023; all rights reserved)

toid cavity is covered by a simple squamous epithelium with occasionally scattered ciliated cells (Fig. 5.5). The ossicles are almost entirely lined by flat non-ciliated cells.

A respiratory epithelium refers to a ciliated, pseudostratified columnar epithelium with goblet cells. Pseudostratified means that all cells are in contact with the basal lamina. The epithelium provides a moist surface because of mucus production that is constantly moving toward the nasopharynx by the beating of the cilia of the ciliated cells. This has been termed "the mucociliary transport system" of the ear. The cells that form this epithelium are ciliated cells, goblet cells (mucus-secreting cells), intermediate cells, and basal cells. Basal cells are stem cells from which the other cells develop (Figs. 5.6 and 5.7).

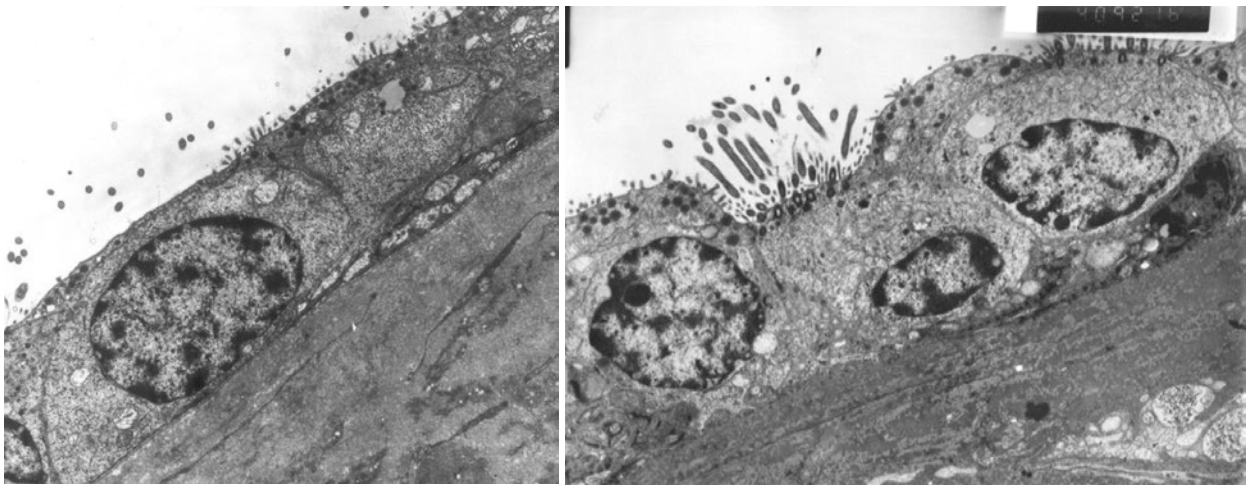


Fig. 5.3 A cuboidal ciliated epithelium at the promontory level. (© Marcos Y. Goycoolea 2023; all rights reserved)

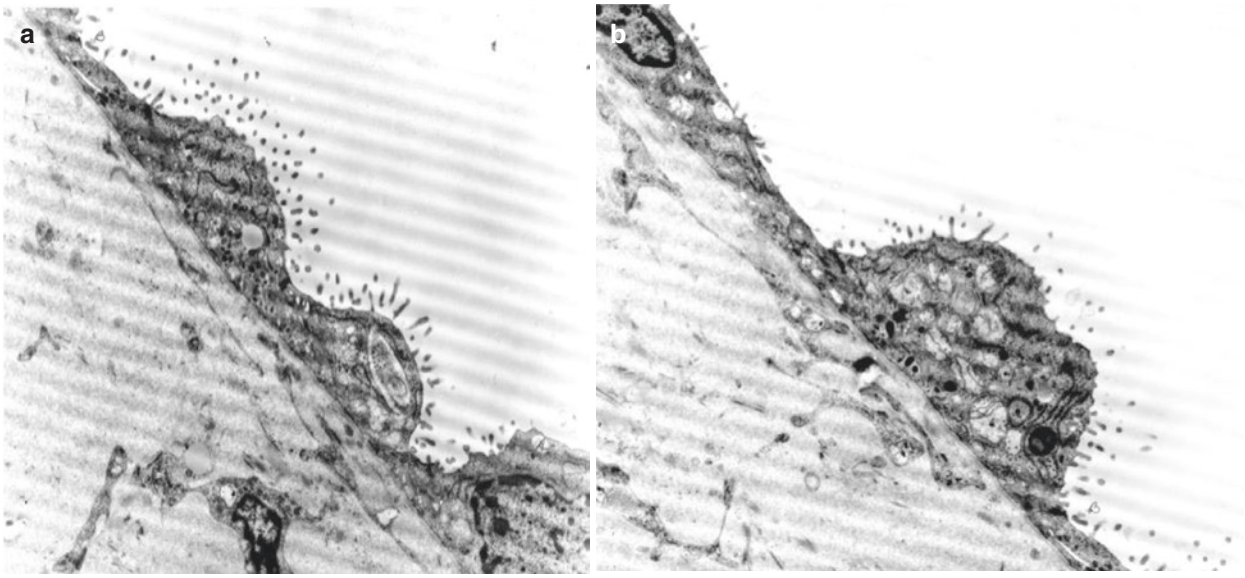


Fig. 5.4 (**a**, **b**) Gradual flattening of epithelial cells with occasional ciliated cells toward the aditus ad antrum initially, to become a simple squamous epithelium toward the mastoid (Fig. 5.5). (© Marcos Y. Goycoolea 2023; all rights reserved)

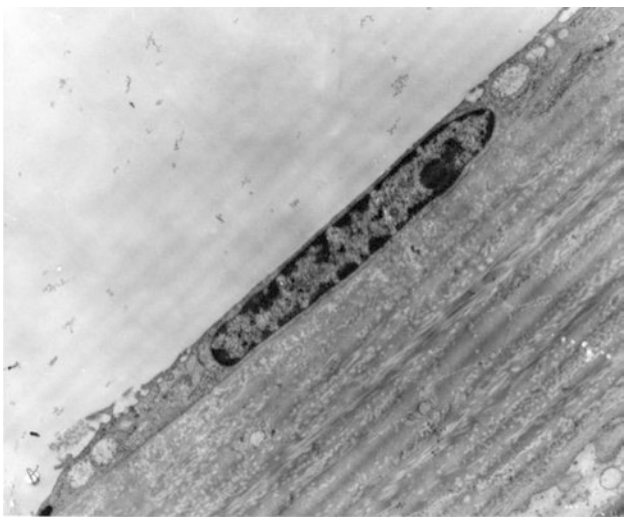


Fig. 5.5 A simple squamous epithelium in the mastoid. (© Marcos Y. Goycoolea 2023; all rights reserved)

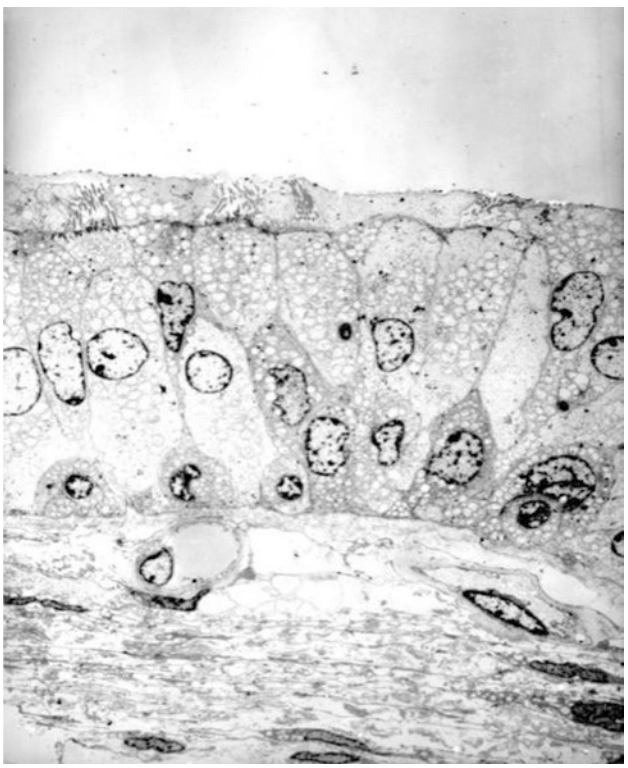


Fig. 5.6 An electron micrograph of a respiratory epithelium. (© Marcos Y. Goycoolea 2023; all rights reserved)

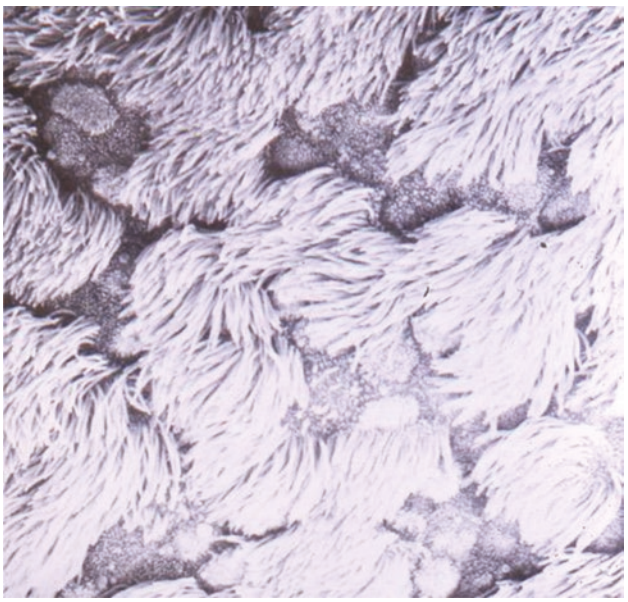


Fig. 5.7 A scanning electron micrograph of the cilia of the mucociliary transport system. (© Marcos Y. Goycoolea 2023; all rights reserved)

The Connective Tissue

The connective tissue of the middle ear and mastoid is continuous. In fact, the connective tissue of the entire body is continuous. Being of mesodermal origin, the connective tissue mechanically joins the different elements of the mucoperiosteum, establishes a fluid space, and contains vessels, nerves, and cells (Figs. 5.2 and 5.8). The most common cells are the fibroblasts that maintain the fiber system and are seemingly capable of performing other functions. Most other cells are those of the defense system such as neutrophils, macrophages, lymphocytes, and plasma cells. Mast cells containing histamine and serotonin are also found. Capillaries are also found in this layer. Forming a definite layer around the endothelium are the basement membrane and pericytes. There are also nerve fibers (myelinated and unmyelinated).

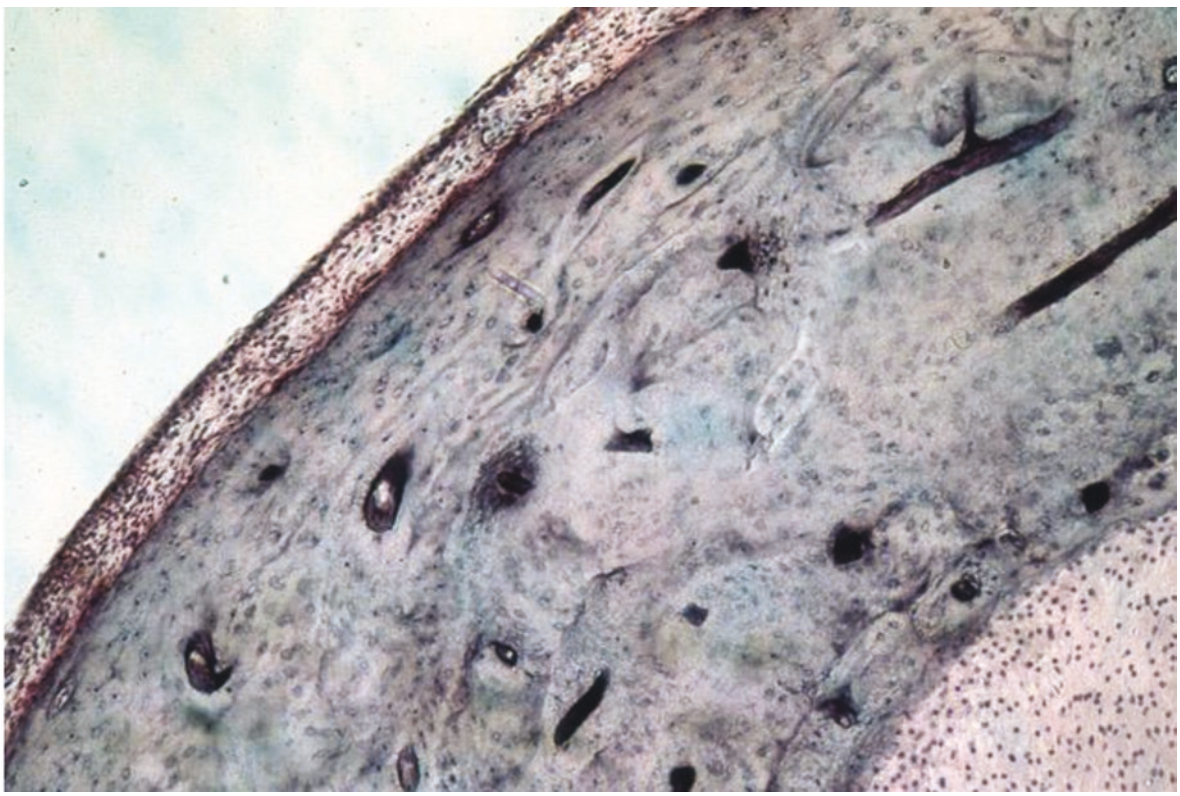


Fig. 5.8 A light micrograph of the promontory lined by the mucoperiosteum. (© Marcos Y. Goycoolea 2023; all rights reserved)

The Periosteum

With the exception of the tympanic membrane, Eustachian tube, and round-window membrane, the middle ear and mastoid are surrounded by a bone with its periosteum facing the connective tissue layer (Figs. 5.3, 5.5, and 5.8).

The Tympanic Membrane

The tympanic membrane is a thin, elliptically shaped membrane situated between the medial end of the external meatus and the middle ear cavity. Structurally, the membrane consists of three layers that are approximately 0.1 mm thick (combined): These layers include:

1. An outer cutaneous layer of thin skin, which is continuous with the skin of the external canal
2. A middle layer of connective tissue consisting of the following:
   (a) A radiate fibrous layer, made up of fibers radiating peripherally from the umbo and manubrium of the malleus
   (b) A circular fibrous layer, made up of concentrically arranged fibers that are most prominent peripherally, where they thicken to form a fibrocartilage ring or annulus, attaching the membrane to the tympanic sulcus of the temporal bone
3. An inner layer of the mucous membrane continuous with that of the middle ear cavity

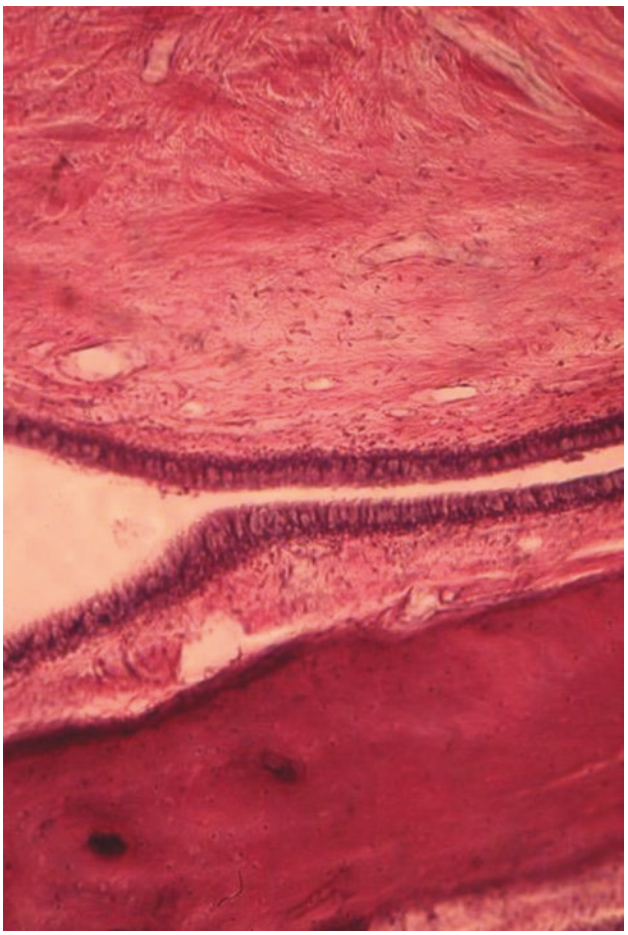


Fig. 5.9 Middle ear opening of the Eustachian tube. (© Marcos Y. Goycoolea 2023; all rights reserved)

The Eustachian Tube

The Eustachian tube extends from the anterior wall of the tympanic cavity to its nasopharyngeal opening just posterior to the dorsal end of the inferior nasal concha. Structurally, the auditory tube consists of both cartilaginous and bony components. The bony portion makes up approximately two-thirds of the tube; it is widest at the tympanic orifice and gradually narrows throughout its length, with its anterior extremity (the isthmus) being the most constricted portion of the entire tube. The cartilaginous portion of the tube extends from the isthmus to the nasopharynx. It is not totally cartilaginous. Its lower lateral and inferior walls consist of a fibrous connective tissue overlying the tensor veli and levator veli palatini muscles.

The lumen of the auditory tube, in the resting state, is a closed, slit-like cavity. The pharyngeal end of the tube strongly resists passage of air from the pharynx to the middle ear. Passage from the tympanic cavity to the pharynx is much easier.

The Eustachian tube is lined by a respiratory epithelium, and, in addition to the opening function of the tensor veli palatini muscle, there is seemingly some role of a surfactant. The respiratory epithelium with its cilia and mucus secretion are the basis of the mucociliary transport system of the middle ear (Figs. 5.6, 5.7, and 5.9).

The Round-Window Membrane

The round-window membrane is located in the medial wall of the middle ear, within the round-window niche. It consists of three layers: an outer epithelium facing the middle ear, a core of connective tissue, and an inner ear epithelium bordering the inner ear. The outer epithelium consists of a single layer of cells that are continuous with that of the promontory. The

cells are low cuboidal. Tight junctions are present near the surface, and there is a continuous underlying basement membrane. The connective tissue layer contains fibroblasts, collagen, and elastic fibers as well as blood and lymph vessels and nerve fibers. The inner epithelium is lined by squamous cells with long lateral extensions that overlap each other. Histological descriptions of the round-window membrane are provided in this chapter of this book that discusses the use of topical treatment and middle inner ear interaction (Chap. 31).

The Otitis Media Process

Once aggression occurs, the ear responds with histopathological defensive factors that are gradual, systematic and universal, and have variations, which are adaptations to the different forms of insults. Their forms of presentation and severity will depend on the balance between the aggression and defense, with a direct influence of the environment, the genetic predisposition of the host, and the general defensive conditions at the time of occurrence.

The result of the response of the ear to aggression is the universal reaction of inflammation. This is the starting point of the sequential steps to be described. This inflammatory process involves all the walls, cavities, and anatomical structures that these contain as well as the mucoperiosteum that lines these cavities and structures (Fig. 5.10). With the understanding that the reaction is simultaneous at all levels, for practical reasons, the epithelial changes will be initially described.

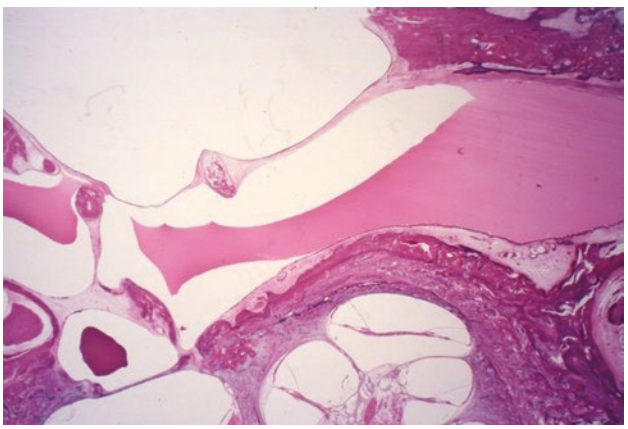


Fig. 5.10 Middle ear cavity with middle ear effusion. The inflammatory process involves all the walls, cavities, and anatomical structures that these contain as well as the mucoperiosteum that lines these cavities and structures. (© Marcos Y. Goycoolea 2023; all rights reserved)

Epithelial Changes

The epithelial cells participate in the inflammatory reaction by themselves and also as part of the mucociliary system. The cells become taller and have increased secretion (Figs. 5.11 and 5.12). There is also new gland formation and an increase in goblet cells.

Cells secrete different defensive substances such as lysozymes. The epithelial cells also have the capacity to synthesize the secretory piece of immunoglobulin (Ig)A (secretory IgA) just like the intestine since both epithelia are of the endodermal origin (Fig. 5.13).

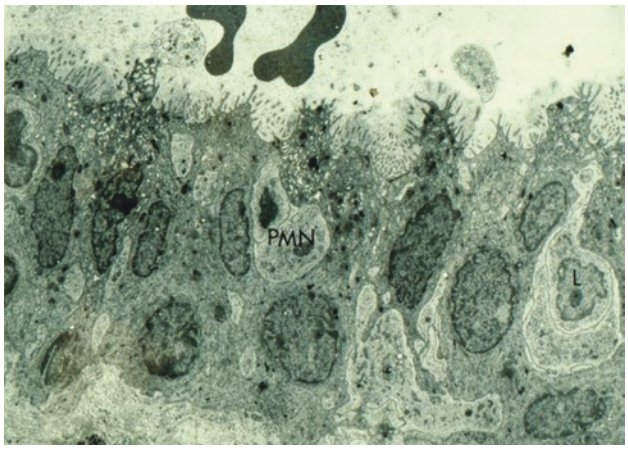


Fig. 5.11 An electron micrograph of the respiratory epithelium in acute otitis media. Secretory granules and migration of polymorphonuclear cells toward the middle ear cavity. (© Marcos Y. Goycoolea 2023; all rights reserved)

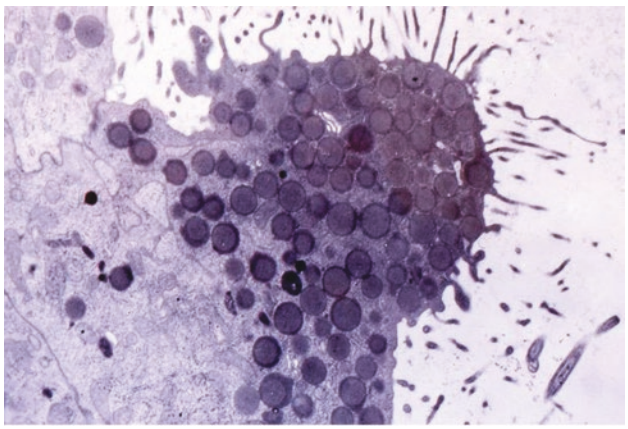


Fig. 5.12 An epithelial cell full of secretory granules and secreting toward the middle ear cavity. (© Marcos Y. Goycoolea 2023; all rights reserved)

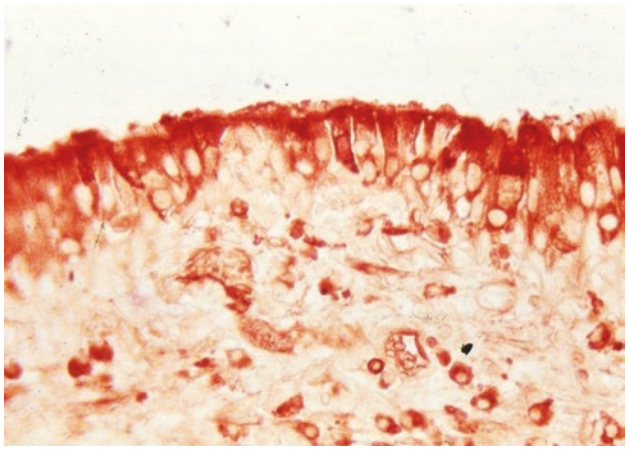


Fig. 5.13 Plasma and epithelial cells staining positive for IgA. (© Marcos Y. Goycoolea 2023; all rights reserved)

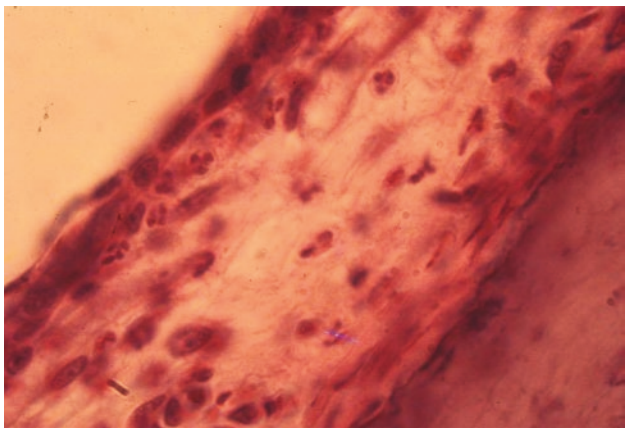


Fig. 5.14 Polymorphonuclears in the connective tissue of the promontory. (© Marcos Y. Goycoolea 2023; all rights reserved)

All these secretions plus the cellular elements in the middle ear cavity develop middle ear effusion. In some areas and depending on the degree of aggression, epithelial ruptures occur. Cholesteatomas seem likely to develop because of migration of the squamous epithelium of the tympanic membrane (and/or ear canal) rather than as a result of metaplastic changes of the inflamed epithelium (Goycoolea et al. 1999).

The Connective Tissue and Periosteal Changes

These are characterized as (Fig. 5.10) follows:

1. Thickening, edema, and increased vascularity
2. Cellular changes: Gradual cellular infiltration, changes in the types and numbers of cells
3. Changes in the shape and numbers of fibers
4. Inflammatory reaction of the periosteum
5. Inflammatory reaction of the underlying bone (osteitis)

In the early stages of the inflammatory process, the initial infiltration is based on polymorphonuclears that respond rapidly and traverse the capillaries toward the connective tissue (Fig. 5.14). From there, some migrate through the epithelium to the middle ear cavity (Fig. 5.11). Their primary function is engulfment of particles and microorganisms. The majority are neutrophils, but there are occasional eosinophils. The second cells to appear active are macrophages (Fig. 5.15) and abundant and active fibroblasts. Macrophages, despite being nonspecific, mark the starting point toward a specific immunological reaction mediated by T and B lymphocytes. Macrophages play a role in processing antigens and interacting with B lymphocytes (humoral immunity), which are the cells with a capacity for specific recognition. B cells develop toward antibody-secreting cells (plasma cells) (Figs. 5.13 and 5.16).

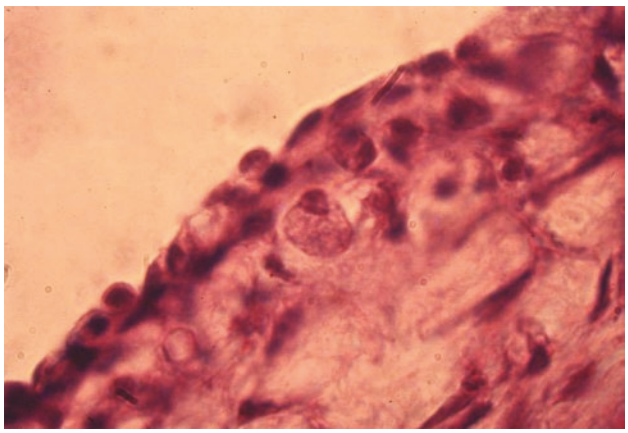


Fig. 5.15 Macrophages and active fibroblasts in the connective tissue of the promontory. (© Marcos Y. Goycoolea 2023; all rights reserved)

The middle ear mucosa also has a local immunological system via secretory IgA in which IgA is secreted by the plasma cells (B cells) and the epithelial cells add the secretory piece. Both IgG and IgM are also synthesized by the plasma cells and are secreted toward the mucosal surface. Fibroblasts are also active since the early stages.

The middle ear defense system consists of:

1. An epithelium that is continuous, regenerative, and constitutes a mechanical barrier
2. A mucociliary transport system (mucus, lysozymes, ciliated and secretory cells)

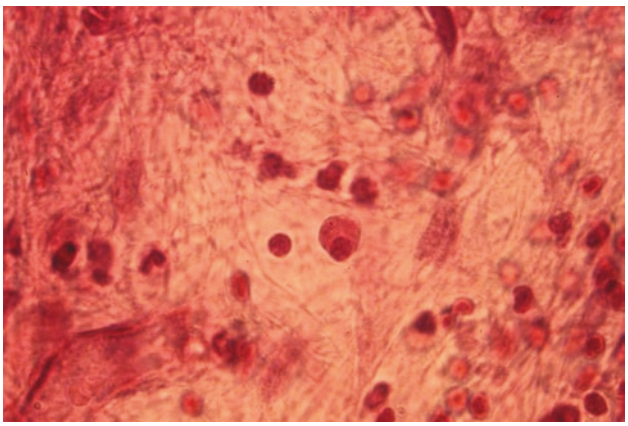


Fig. 5.16 Plasma cells in the connective tissue. (© Marcos Y. Goycoolea 2023; all rights reserved)

3. A patent and functional Eustachian tube
4. An inflammatory reaction of the connective tissue
5. Edema
6. Fibroblasts, collagen, and amorphous substance
7. Polymorphonuclear cells
8. Lymphocytes (small and large T and B cells, respectively).
9. Plasma cells: immunoglobulins (IgA, IgG, IgE, IgM)
10. A complement system.

Effusion Formation

Effusion formation is dynamic and reflects what is going on in the mucoperiosteum in terms of the phase and type of an inflammatory process. Samples will eventually be helpful for deciding treatments accordingly.

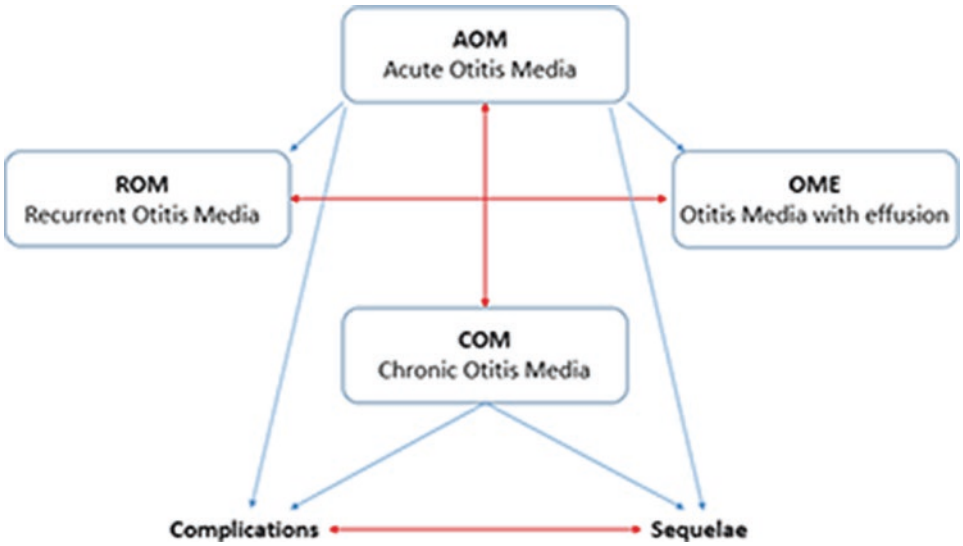
Changes in the Mucosa as a Whole

The middle ear develops polypoidal changes with areas that are prominent and areas that are depressed. Gland and blood vessel formation occur.

All structures are involved in the inflammatory process. The inflammatory process is dynamic and so is the middle ear effusion that tends to follow the histopathological changes that occur in the middle ear mucosa. The different forms of presentation of the otitis media process are therefore moments or instants of this dynamic process.

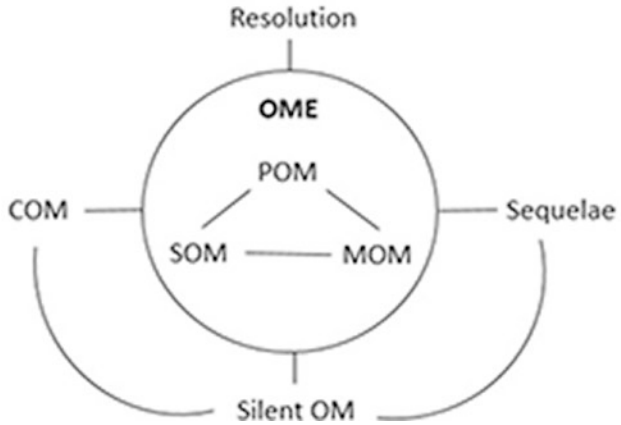
If otitis media is understood in this manner, it is much more than classifications and/or middle ear fluid and an inflammatory process. The changes described are in reality a reflection of the stage of confrontation between the aggression and the defensive factors. Thus, one form may lead to others in a dynamic way (Tables 5.1 and 5.2).

Table 5.1 Forms of otitis media



The form of presentation described in this table and the severity of the otitis media process will depend on the balance between two opposing forces, namely, the aggressive factors and the defensive factors of the middle ear. These are directly influenced by environmental factors, genetic predisposition, and the status of the defensive system of the host at the moment of aggression

Table 5.2 Classification and continuum of otitis media with effusion (OME)



POM, purulent otitis media; *SOM*, serous otitis media; *MOM*, mucoid otitis media; *COM*, chronic otitis media; *OM*, otitis media

Complications and Sequelae

In addition to the involvement of the mucoperiosteum of the middle ear and mastoid as well as the Eustachian tube, there are potential complications and sequelae in this disease process. A complication is a secondary disease or condition developing in the course of a primary disease without being part of it. It occurs when the inflammatory process extends beyond the mucoperiosteum. A sequela is an after effect of a disease or injury. Herein, the term "sequela" refers to processes that remain within the mucoperiosteum (mucoperiosteal changes) and that have the capacity or potential to develop a complication (Goycoolea and Jung 1991) [1, 2]. The line between complications and sequelae is at times extremely tenuous. For example, the granulation tissue is a sequela (active sequela), but erosion of bone by the granulation tissue is a complication. In addition, the overall consequences of a localized problem (e.g., ossicular disruption causing conductive hearing loss) can have significant effects on a person and on their relationships with others (lack of communication, isolation, learning problems, and so forth).

At the level of the epithelium, ruptures occur in some areas of the mucosa (the degree of which will depend on the magnitude and type of aggression).

These ruptures allow:

Pockets with serous content

The inflamed connective tissue without epithelial covering (granulation tissue) can migrate through these openings. This tissue can persist or disappear. When it persists, it can erode the neighboring bone (with or without an associated cholesteatoma) and cause complications. It can disappear or be covered with an epithelium and cause adherences, which at times can serve as bridges for cellular migration as is the case of cholesteatomas (Goycoolea et al. 1999).

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[1]This chapter is a summary of many of our previous reports that are concentrated in two chapters of our *Atlas of Surgical Otology*.

[2]All the figures are my own and represent some of my best in more than 40 years of histological studies of temporal bones.

The references include some of the classic reports of the otitis media leaders, who, together with Michael Paparella and Steve Juhn, inspired my work. I had the privilege of knowing those whose reports are quoted and of learning from all of them—initially as a resident—and then in many symposia of otitis media through the years.

My coauthors are young staff members who have contributed—as I did initially—and, hopefully, they will also become inspired and improve by far these studies to which all of us have contributed.