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Histopathogenesis of tympanosclerosis

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Tympanosclerosis is an anatomo-clinical entity which can be defined as the irreversible end-result, though not immutable, or any unresolved inflammatory process in the ear that has produced anatomical injury and almost always functional impairment.

Tympanosclerosis is strictly connected with inflammation, either specific or non-specific, of the middle ear. In most cases, it is the end-product of inflammation and only rarely it is iatrogenic or due to trauma (Surján, 1970). Therefore, there is not one specific kind of inflammation leading to tympanosclerosis, but the condition is the consequence of any unresolved inflammatory process in the ear (Sala and Ferlito, 1978). Inflammation is dynamic and evolutionary in nature, whereas sclerosis is the final stage of a process (Ferlito, 1975b). Of course, the sclerotic ear may be subject to a new acute inflammatory process.

The aetiologic agents, the evolutionary steps and the clinical entities leading to tympanosclerosis are numerous, but with a single final stage. It is not always easy to reconstruct the biologic course of the disease until it has reached the final stage expressed by functional impairment, mainly due to fixation of the ossicular chain and involvement of the mastoid. The hearing loss is of the conductive type, but may become mixed if the internal ear becomes involved. An impossible 'restitutio ad integrum' and irreversibility of the lesions give tympanosclerosis its own configuration within the many inflammatory diseases of the middle ear.

An anatomo-histopathologic classification of specific and non-specific inflammatory processes of the middle ear, proposed by the present writer (Ferlito, 1974b), is given overleaf.

Von Tröltsch (1873) first created the term 'Paukensklerose' or 'tympanosclerosis' to describe sclerotic changes in the middle ear mucosa. The term was then revived by Zöllner (1955) and Zöllner and Beck (1955a,b). Zöllner continued his investigation of this ear disease which he later described accurately in his writings (1956, 1963, 1969).

Further pathologic and clinical studies on tympanosclerosis have been conducted by other authors (Goodhill, 1960; House and Sheehy, 1960; Harris, 1961; Harris and Weiss, 1962; Sheehy and House, 1962; Joseph and Gordon, 1963; Beck and Ebert, 1964; Gundersen, 1965; Hybasek, 1966; Chang, 1969; Charachon *et al.*, 1969; Barocci and Nenci, 1970; Igaraschi *et al.*, 1970; Bonnaud, 1971; Friedmann, 1971; Surján and Juhasz, 1971; Karma, 1972; Smyth, 1972; Sørensen and True,

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A) NON-SPECIFIC INFLAMMATORY PROCESSES

- Acute
  - Serous otomastoiditis (°)
  - Mucous otomastoiditis
  - Suppurative otomastoiditis
- Chronic
  - Mucous otomastoiditis
  - Suppurative otomastoiditis
    - simple
    - cholesteatomatous

B) SPECIFIC INFLAMMATORY PROCESSES
- Tuberculous otomastoiditis
- Syphilitic otomastoiditis

C) RESIDUUM OF INFLAMMATORY PROCESSES OF THE EAR

- Tympanosclerosis
  - extensive
  - circumscribed
    - Syndrome of fixation of the head of the malleus
    - Tympanosclerotic pseudo-otosclerosis

Cholesteatomatous tympanosclerosis

(°) Serous otomastoiditis is the only inflammatory process in which lesions are restricted to the mucosal lining, whereas in other processes there is always osteomucosal involvement.

1972; Nobre Leitao *et al.*, 1974; Tos and Bak-Pedersen, 1974; Morgan, 1977).

A basic contribution to the knowledge of tympanosclerosis was given by Bocca *et al.* (1968) who combined their experience with that of other researchers in an Official Report to the Italian Society of Otorhinolaryngology and Cerrico-Facial Pathology. The problem was treated from the aetiologic, diagnostic and therapeutic points of view.

The problems connected with tympanosclerosis are manifold, though most of them are common to inflammatory disease of the middle ear in general, considering that the condition is the result of acute or chronic inflammation, specific or non-specific, of the middle ear.

The elements on which a diagnosis of tympanosclerosis may be established are basically those related to the patient's history, those which may be seen by means of otomicroscopy, and audiometric tests (hearing loss of the conductive type, negative Rinne, prolonged Schwabach, Weber to the side of the hearing impairment, impedance studies of the middle ear, x-ray examination, tomography of the tympanic cavity and mastoid, which is of the ivory type). Transmeatal exporatory tympanotomy may have to be undertaken for diagnosis when other investigations are negative or doubtful.

Tympanosclerosis is an insidious disease and its incidence is higher than that reported in the literature. This is due to the fact that, at times, the diagnosis, though possible clinically in unequivocal cases, may only be made at operation (Sheehy and House, 1962).

Sørensen and True (1972) state that tympanosclerosis has been histologically proven in some cases in which it had not been suspected on gross examination. Tos and Bak-Pedersen (1974) also are of the opinion

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that there are mild, subclinical cases and cases in which the diagnosis is made only by histological examination. This confirms that the incidence of tympanosclerosis is higher than believed, and this is even more evident if we consider the number of patients who, having had an inflammatory process of the middle ear resulting in sclerosis, no longer consult the otologist.

Many inflammatory processes considered 'clinically' cured (those in which after acute inflammation, there is no hearing loss or in which the air-bone 'gap' is minimal) do not finish at 'restitutio ad integrum'. The pathologist may confirm this fact, as did Sørensen and True (1972), by studying the histologic sections from patients in whom tympanosclerosis was not suspected. Friedmann (1971) reported 60 cases of tympanosclerosis investigated between 1966 and 1970 in which the diagnosis had been made clinically in only 32 patients.

Specimens removed from patients with tympanosclerosis are rarely examined and when this happens it is not always easy to reconstruct the pathologic pattern of the disease, though in general it has inflammation or injury as the common denominator.

The severity of lesions and their extent are partly due to the initial inflammation; that is to say, a suppurative inflammatory process without 'restitutio ad integrum' causes more severe lesions than serous or mucous inflammation.

Tympanosclerosis, or sclerosis of the tympanic membrane and tympanic cavity with its contents, is, as said before, a pathologic condition which is morphologically and dynamically exhausted—it is the irreversible end-result of previous middle ear inflammation. It is a post-otorrhoeic sequel, regardless of the kind of otorrhoea which characterized the ear inflammation. This disease, examined by the clinician in one or other of its evolutionary stages, is designated with different, often improper terms, such as fibrous otitis, chronic dry otitis media, sclerotic otitis media, chronic adhesive process, sequelae of chronic suppurative otitis media, post-infective condition, diathetic otitis sicca, sclerotic otitis, cicatricial otitis, catarrhal tympanosclerosis, cicatricial tympanosclerosis, fibrotic otitis media, atrophic otitis media, healed otitis media, etc.

Bocca *et al.* (1968) maintain, and I with them, that the most adequate, most descriptive term is that of tympanosclerosis, as it most effectively describes the anatomo-clinical entity.

In my opinion, however, a distinction should be made between tympanosclerosis 'with an open tympanum' and tympanosclerosis 'with a sealed tympanum', according to whether or not there is a perforation of the tympanic membrane.

There are other circumscribed forms of tympanosclerosis, among which the fixed malleus head syndrome and tympanosclerotic pseudo-otosclerosis should be mentioned.

Pathomorphologic investigations, conducted by means of both light

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and electron microscopy, have established that the basic lesions of tympanosclerosis are found in the submucosa.

The most common pathological changes are hyalinization, necrosis, calcification, fibrosis and ossification. Electron microscopic studies have shown calcified deposits in the mitochondria and lysosomes of fibrocytes (Chang, 1969) and a dense network of typical collagen fibers (Friedmann, 1971). Sørensen and True (1972) have also observed that degenerative processes involve not only the connective tissue (lamina propria and submucosal stratum), but also the epithelium, of the tympanic membrane.

The mastoid, which may be involved in all forms of otitis (Ferlito, 1973a, c; 1974a, b, c,; 1975a, b,; Ferlito and Sala, 1973) can also be affected by tympanosclerosis. In fact, the processes of new bone formation are at times so extensive that the radiologic pattern is one of 'ivory mastoid' or hypopneumatized mastoid air cells.

Tympanosclerosis may be associated with the so-called cholesteatoma, when the condition is called cholesteatomatous tympanosclerosis. This association has been reported in the literature (Harris and Weiss, 1962; Bonnaud, 1971; Friedmann, 1971; Ferlito, 1975b). Figs. 1 and 2 show this association.

As to cholesteatoma, I wish to emphasize that the lesion is actually an epidermoid cyst. (For further details, see Ferlito, 1970, 1972; 1973a, b, d; 1977; Sala and Ferlito, 1974; McCabe *et al*, 1977.)

Tympanosclerosis may also be associated with cholesterol granuloma (Fig. 3) (Harris and Weiss, 1962; Friedmann, 1971; Nobre Leitao *et al*, 1974).

According to Harris (1961), there are two forms of tympanosclerosis: one in which the lesions involve mainly, if not exclusively, the mucosa; and one in which there is involvement of the underlying bony structures. This author refers to the former as 'sclerosing mucositis' and to the latter as 'osteoclastic mucoperiostitis'.

The first stage of tympanosclerosis is effusion in the mastoid air-cells. Biochemically, this effusion is an exudate and has different characteristics according to the type of inflammation. This exudate collects in the tympanic cavity, where recesses and tortuosities which nature seems to have capriciously created favour stagnation. With progression of the inflammatory process, if resorption of the exudate does not take place, either because of local or general conditions or because treatment has not been adequately administered (insufficient dosage, insufficient duration, delay in beginning treatment—Sala and Ferlito, 1973), the characteristics of the exudate change. It is then called, successively, serous, mucous or suppurative exudate. In practice, however, the exudate does not show such clear features; very often it has two components and may be designated as sero-mucous, sero-purulent or muco-purulent, and so on. The least severe form of ear inflammation produces a serous exudate.

Serous otitis, better defined as serous otomastoiditis (Ferlito, 1975b;

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FIG. 1

Specimen from the promontory. Note so-called cholesteatoma associated with tympanosclerosis (Haematoxylin-Eosin, ×16, original magnification). The patient had tympanosclerosis associated with cholesteatoma in both ears.

Sala and Ferlito, 1977), so common in childhood, is to be considered as the least severe form of ear inflammation. Pathogenetically, it is strictly connected with inflammation of the upper airways (common cold, adenoiditis, pharyngo-tonsillitis, etc.)

The dynamics of the pathologic process start with the exudate, and continue through a long series of transitional stages which are in fact consequential in their progression and are recognized by the otologist as the various stages of inflammatory disease of the middle ear. Symptoms,

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FIG. 2

Specimen from the oval window. Cholesteatoma associated with tympanosclerosis may be seen (Haematoxylin-Eosin, ×16, original magnification).

often different in each stage induce the clinician to label the 'dynamic' momentum with various more or less proper terms and to divide the disease into various compartments. On the contrary, the disease is a complex pathologic entity, the variable aspects of which are due partly to its evolution and partly to inadequate treatment, which often apparently 'cures' the disease by masking the clinical symptoms, but actually furthers its progress.

Acute serous otomastoiditis is characterized by the presence of a serous exudate, clear and transparent in appearance, of low viscosity, collecting

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FIG. 3

Cholesterol granuloma composed of cholesterol crystals (Haematoxylin-Eosin, ×40, original magnification).

not only in the tympanic cavity, but also in the antrum and mastoid air-cells. Obstruction of the Eustachian tube follows and the tympanic cavity is no longer aerated. Resorption of pre-existing air occurs and a negative pressure is exerted on the tympanic membrane which objectively appears to be slightly retracted. This inflammatory process may lead to the formation of connective tissue with hyaline degeneration (Sørensen and True, 1972).

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The course of the disease may vary:

(a) it may regress to 'restitutio ad integrum' with resorption of the exudate;
(b) it may change into acute mucous otomastoiditis;
(c) it may, not infrequently, change into a more severe form of ear inflammation—acute suppurative otomastoiditis;
(d) it may remain clinically silent, but organization in the exudate may cause mild tympanosclerosis.

Aute serous otomastoiditis is therefore an ear disease which may lead to tympanosclerosis if not adequately treated.

Serous otomastoiditis, however, is not to be confused with catarrhal or *mucous otitis media*—the glue ear. The mucous form shows an exudate rich in mucin, and thick and gelatinous in consistency. This is why many authors label the condition 'muco-gelatinous otitis' or 'glue ear'. The latter term was first used by Jordan (1949).

The most significant aspects of the two inflammatory processes are listed (Ferlito, 1975b).

SYNOPTIC TABLE OF DIFFERENTIAL PATHOLOGIC CHARACTERISTICS BETWEEN SEROUS OTOMASTOIDITIS AND MUCOUS OTOMASTOIDITIS

	Serous otomastoiditis	Mucous otomastoiditis
Location of the lesion	Mucosal lining	Mucosa and underlying bone
Exudate	Serous	Mucous
Characteristics of exudate	Watery, clear, transparent, slightly viscous	Yellowish, viscous, gluey, homogeneous
Immunoelectrophoretic profile	The ratio lipids–proteins shows higher concentration of lipids	The ratio lipids–proteins shows higher concentration of proteins
Inflammatory cells	A few	Fairly numerous
Serum-secreting cells	A few	Absent
Mucus-secreting cells	A few	Increased in number
Gland-like structures	Absent	Present
Muco-ciliary system	Slightly altered	Severely altered
Evolution	Complete cure	Tendency to become chronic

In my opinion, this form should be called mucous otomastoiditis, since the lesion extends through the aditus ad antrum to the mastoid (Ferlito, 1975b; Smyth *et al.*, 1977), which shows reduced pneumatization (Bradbeer and Jones, 1974). The term 'mucous' defines the pathogenesis of this inflammatory process.

Light and electron microscopic studies (Sadé, 1965, 1966; Kawabata and Paparella, 1969; Lim and Hussl, 1969; Hentzer, 1970a, b; Hilding and Heywood, 1971; Lim and Shimada, 1971; Bak-Pedersen and Tos, 1972, 1973a, b, c,; Brémond and Coquin, 1972; Hiraide and Paparella, 1972; Shimada and Lim, 1972; Lim *et al.*, 1973; Tos, 1973; Lim, 1974,) have demonstrated that, under normal conditions, there are mucus-secreting goblet cells and ciliary structures in the mucosal lining of the tympanic

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cavity. In this inflammatory process, a phenomenon of mucous metaplasia of the epithelium of the tympanic cavity and of the Eustachian tube takes place. Not infrequently, this process of cellular differentiation involves the lining of the mastoid air-cells. Persistence of the inflammation alters the ratio of the mucus-producing cells. As is known, mucus, under normal conditions, has a defensive, protective, physiologically significant action, but 'clearance' of the tympanic cavity is difficult if its composition is altered, and also because the ciliary system is destroyed by the disease (Sala and Ferlito, 1972).

Alteration of the ciliary structures and qualitative and quantitative changes in mucus lead to stagnation of the pathologic mucous exudate, thus favouring processes of organization and sclerosis. All this makes it possible to see later a sclerotic, thickened, retracted tympanic membrane displaying patchy calcification, sometimes attached to the mucosal lining of the promontory.

It is clear, then, how tympanosclerosis may represent the sequelae of acute mucous otomastoiditis and how this post-otorrhoeic pattern may be extensive or circumscribed, according to whether the amount of mucous exudate was abundant or, as rarely happens, restricted to one area of the middle ear owing to the compartmental configuration of the middle ear. Anatomical impairment is greater if the area involved is the epitympanum. Exploratory tympanotomy—or tympanic laparotomy as some authors label it—will show the fixed malleus head syndrome described by Powers *et al.* (1967), Goodhill (1966), Sleeckx *et al.* (1967) and Davies (1968). This syndrome is caused by particular anatomical conditions. In fact, as evidenced by Proctor (1964), there is an inter-attic-tympanic diaphragm allowing communication between the epitympanum and tympanic cavity only through the anterior tympanic isthmus. Occlusion of this isthmus separates the attic from the tympanic cavity, thus sequestering the exudate which has gathered there, and thereby the inflammatory process, in an anatomical site which is extremely delicate in view of its anatomical relationship with neighbouring structures. Also the stapes may be fixed to the oval window following middle ear inflammation. In this case there is otosclerosis secondary to chronic otitis media or pseudo-otosclerosis (Goodhill, 1960) or false otosclerosis (Nicoucar, 1967). These are circumscribed forms of otosclerosis.

Acute suppurative otomastoiditis (commonly called acute suppurative otitis media) is the severest form of ear inflammation. Almost always, it is secondary to inflammatory processes in the rhino-pharynx or paranasal sinuses, and sometimes it is an evolutionary step in inflammation of the middle ear. Discharge from the ear is abundant and may be sero-purulent, muco-purulent or frankly purulent; it is almost regularly associated with perforation of the tympanic membrane through which the exudate flows into the external auditory meatus. When tympanic perforation is not present, the disease is more severe because of stagnation of the exudate.

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Inflammation, then, is never restricted to the tympanic cavity but extends to the antrum and mastoid air cells—hence, a better term is suppurative otomastoiditis.

The exudate is rich in polymorphonuclear neutrophils commingled with fibrin. Leucocytes undergo regressive phenomena involving both cytoplasm and nucleus and, after phagocytosis, they degenerate. Macrophages, not present in the beginning, appear when resorption of the exudate begins and display phagocytic properties. In the purulent exudate, epithelial cells, necrotic debris, cholesterol crystals and fibrin may be seen to be rapidly digested by proteolytic enzymes and by polymorphonuclear leukocytes. If resorption does not take place, the stagnating exudate is the 'ground' for future organization and sclerosis. Later, in fact, a decrease of fibroblasts occurs and the tissue is poorer in cells and blood vessels (unlike granulation tissue), and richer in collagen fibers arranged in bundles.

Acute suppurative otomastoiditis may:

a) regress to 'restitutio ad integrum';

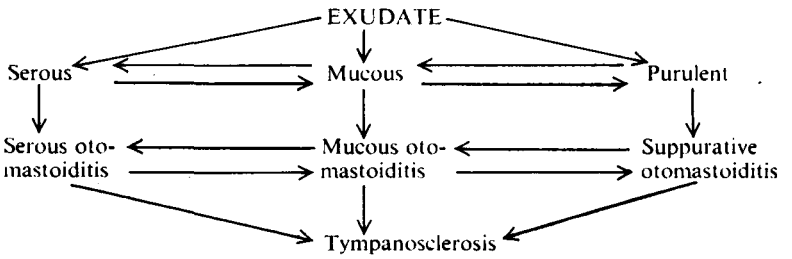
b) become chronic, thus causing chronic suppurative otomastoiditis

c) evolve towards tympanosclerosis.

Mucous otomastoiditis, chronic suppurative otomastoiditis and tubercular or syphilitic otomastoiditis may all lead to severe tympanosclerosis.

It appears that the exudate—regardless of its distinctive features—serous, mucous or purulent, is a common factor in the various inflammatory conditions of the middle ear which may lead to tympanosclerosis; it is the first sign of inflammation which it is necessary to refer to, in order to understand the histopathogenesis of tympanosclerosis.

The following diagram shows the background for the development of tympanosclerosis.



If the general and local conditions are good, and if treatment is early and adequate, any inflammatory process regresses to 'restitutio ad integrum', which means that the organ is anatomically and functionally as it was before the disease. However, owing to a variety of factors (local and constitutional factors, immunologic deficiency, debilitating diseases, inadequate treatment), the body is not always capable of counteracting the invading agent and succumbs to it, perhaps with alternating acute

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episodes of inflammation and regression. This unstable situation at times ends up in a 'cold' pathologic condition, that is, sclerosis of the ear. This final stage is reached through the well-known phenomena of organization: granulation tissue invades and surrounds the exudate, and then resorbs and replaces it by producing fibroblasts and amorphous matter with the appearance of collagen fibers. There then occurs a gradual reduction in fibroblasts, cellular elements and capillaries, but collagen fibers increase considerably in number. At this moment, the inflammatory process has prevailed over the body's tissue responses and has led to an inactive, sclero-hyaline non-functional condition.

Tympanosclerosis, as said before, is the terminal, irreversible stage of a pathologic process, based on inflammation, which has not regressed to 'restitutio ad integrum' and which does not continue as an inflammatory process. It is a non-functional, inert repair phenomenon which is not, however, unchangeable, since a new inflammatory process may occur, particularly if there is persistence of the pathogenetic factors (inflammation of paranasal sinuses, rhino-pharynx, etc.), to which the primary treatment must be directed.

The most valid treatment for tympanosclerosis is prevention, and therefore efforts must be made to understand better the evolutionary steps of this disease and so as to prevent them, thus reducing the incidence of the lesion.

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