**Paparella: Volume II: Otology and Neuro-Otology**

**Section 3: Diseases of the Ear**

**Part 3: Middle Ear and Mastoid**

# Chapter 37: Otosclerosis

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## Preface

The original of this chapter of the book was written by the late Dr. John Lindsay, one of the world's pioneers in histopathologic studies of the temporal bone and a major contributor to our present knowledge on the subject of otosclerosis. It has been an honor for me to be asked to update this chapter. In his memory, I have maintained his basic organization and many of the original pictures from his chapter.

Since otosclerosis is a universal disease, it was my intention for the sake of completeness to obtain information from important areas of the world where data published in the English literature is scarce. Study groups from Bolivia, Brazil, Chile, Colombia, Mexico, Panama, and Puerto Rico have provided carefully scrutinized information specially for this chapter. These groups are listen in a special section preceding the references and are quoted in the text by country (eg, "Bolivia, 1987"). The groups from Minnesota and Alaska are also quoted as, for example, "Alaska, 1987".

In addition, in an effort to enhance the completeness of this chapter, I have incorporated some of the data of a forthcoming publication (Hueb et al, in press) that comprises the 144 temporal bones with otosclerosis from the temporal bone collection of the Otopathology Laboratory of the University of Minnesota. This collection of human temporal bones consists of 1464 bones from 752 individuals, of which 144 temporal bones from 82 individuals have otosclerotic changes. These bones have not been previously reported.

## Introduction

Otosclerosis is a primary and exclusive disease of the otic capsule (bony labyrinth) and the ossicles that is known to affect spontaneously only humans. The term literally means "hardening of the ear" (Gr, *ous,* ear; *skleros,* hard; *osis,* a condition) and is applied because there are evidences of one or more localized areas in which abnormal bone is deposited. If the location of bony changes and/or their secondary effects is such that clinical manifestations are evident, the term "clinical otosclerosis" is used. The most classical manifestation is conductive hearing loss secondary to stapedial fixation due to otosclerotic changes in the area of the oval window. On the other hand, if the bony changes are not translated into clinical manifestations, the term used is "histological otosclerosis". Obviously, this can only be determined by serial sectioning and microscopic examination of temporal bones.

## Historical Aspects in Histopathology

The first description of ankylosis (Gr, *ankuloun,* to stiffen) of the stapes to the margins of the oval window, found on postmortem examination of a deaf patient, has been credited to Antonio Valsalva in 1735 (Valsalva, 1741, 1742). Subsequently, many other authors in the eighteenth century described ankylosis of the stapes at the autopsy of deaf persons. However, it was not until 1857, when Toynbee, on the basis of 35 positive findings out of 1659 dissected temporal bones, related that "osseous ankylosis of the stapes to the fenestra ovalis was one of the common causes of deafness" (Toynbee, 1860).

The term "sclerosis" was first used by von Tröltsch (1881) to describe these changes, believed at the time to be chronic interstitial middle ear catarrh. This belief persisted until Politzer in 1894 described histologic findings in 16 cases of stapedial fixation and suggested that this was a "primary disease of the bony labyrinthine capsule"; hence, the term "otosclerosis". The first microscopic proof of stapedial ankylosis has been credited to Katz in 1890 (Bezold and Siebermann, 1894), and it was Haberman (1894) who, accordingt to Mayer (1917), first demonstrated that more than one focus may occur.

In the years following Politzer, many descriptions helped increase knowledge of this subject. The presence of otosclerotic foci without associated stapedial ankylosis was described, and the association of otosclerosis, labyrinthine atrophy, and sensorineural hearing loss was suggested. These and other findings revealed that the term otosclerosis was inadequate and did not truly describe the histopathologic changes that occur (to be described). Several terms have been suggested, among them "chronic metaplastic otitis" (Mayer, 1917), and "progressive otospongiosis" (Siebenmann, 1911). In spite of the fact that a more accurate term would be better, the universal use of the term "otosclerosis" has prevailed, with the understanding that it is not adequately descriptive of the changes that occur.

With the improvement of histologic techniques, and with a better knowledge of descriptive morphology (mainly at the level of light microscoy), our current concepts have evolved. In the last two decades this knowledge has increased, thanks to the incorporation of electron microscopy and immunologic and histochemical techniques. Stagnation in research has been in part due to the small size and limited quantity of specimens available for study, the lack of availability of animal models, and the lack of expertise needed to undertake multidisciplinary research efforts (Lim et al, 1987). Currently, new information is being obtained in part through three areas:

1. Biochemical and tissue culture techniques have made available cultured bone-cells from otosclerotic bones, allowing a better evaluation of bone-cell function, leading to a better understanding of the molecular basis for this disorder (Paludetti et al, 1983; Maurizi et al, 1986, 1987, 1988a and b; Lim et al, 1987).

2. Clinical and experimental immunological methods suggest that type II (cytotoxic) and/or III (immune complex) immune responses are underlying mechanisms for the pathogenesis of otosclerosis (Yoo et al, 1982, 1983, 1987; Yoo, 1984; Lim et al, 1987). The bony lesions obtained experimentally are not otosclerotic, and there are reports that are not supportive of some of the observations leading to this theory (Harris et al, 1986; Solvsten Sorensen et al, 1988).

3. It has been observed that inbred LP/J mice develop abnormal bony lesions in the ossicles and otic capsule that are similar grossly and histologically to the lesions in human otosclerosis. This observation is the first known occurrence of spontaneous otosclerosis-like lesions in animals. They develop in the middle and inner ear, are inherited, and produce progressive hearing loss. Moreover, these lesions seemingly develop during early childhood and progress gradually, as in human otosclerosis. It is also suggestive that there is a possible immunologic injury in the pathogenesis of these lesions. In spite of their histologic appearance being similar to (not identical to) human otosclerosis, the use of this animal model should be valuable in the understanding of human otosclerosis (Chole and Henry, 1983; Chole and Tingling, 1985; Cramer and Chole, 1986; Brodie and Chole, 1987; Henry and Chole, 1987).

These three approaches constitute new avenues for research toward a better understanding of otosclerosis. It should be clearly stated, however, that regardless of how valuable they are, the hypotheses derived from them will have to be tested. To date, the etiology and pathogenesis of this all too common disease remains largely unknown.

In spite of the wealth of reports there is limited definite information. Both clinical and histologic studies of prevalence have their limitations. This is important to bear in mind when studying these reports. Clinical studies of otosclerosis generally represent adequate numbers; they are, however, of selected cases that again do not usually represent true prevalence. Audiological data are, more often than not, not compared with data from equivalent clinical populations who do not have otosclerosis. The reported evidence is, in practice, that of the classical manifestation of stapedial fixation. This is not the exclusive form of clinical otosclerosis, and clinical otosclerosis itself does not represent true prevalence, since it does not describe clinically undetected histologic otosclerosis, which appears to be far more prevalent than clinical otosclerosis.

Histologic studies are in general more selective than clinical studies. Most such studies are of a small number of cases, and on some occasions the same temporal bone collections, in part or in total, have been the basis of publications by different authors, sometimes with different observations. In this respect it is worth mentioning that comprehensive studies are possible through the National Temporal Bone Bank Program which, with the help of otologists, can obtain meaningful information for a better understanding of this disease. With the understanding that there is a lack of definite data available and that the author has his own biases in selecting literature, the available reports are described and discussed here. There are literally hundreds of publications on this subject, and the author apologizes to those authors whose studies are not quoted. This is because of reasons of space and not because of lack of significance.

## Etiology

The etiology of otosclerosis is unclear; thus, multiple theories are available. None of them has established a definite cause. Suggested causes include hereditary, endocrine, biochemical, metabolic, and vascular factors. Infection and trauma, as well as anatomic and histologic anomalies of the otic capsule, have also been considered as causes. Space here, and lack of definite evidence, does not permit an extensive discussion of these theories; the references, however, provide this information.

A theory that has enjoyed considerable support is the one of Siebenman's (DeJuan, 1960) that relates an intimate association of early otosclerotic lesions with remnants of embryonic cartilage (Bast and Anson, 1949). Cawthorne (1959) suggested an interaction between unstable cartilage and substances circulating in blood that produce bony growth. Ogilvie and Hall (1962) considered otosclerosis a local manifestation of osteogenesis imperfecta. Bone-cell dysfunction leading to abnormal production of enzymes and bone matrix, including collagen, has also been considered as a cause (Reydon and Smith, 1968; Chevance et al, 1970; Holdsworth, 1973), as has bone-cell dysfunction leading to abnormal calcium metabolism (Paludetti et al, 1983; Maurizi et al, 1986, 1987).

Changes in vascularity have been suggested as a cause; interestingly, some authors have considered increase and others decrease in blood supply to be a factor (Bruhl, 1926; Mayer, 1920, 1931; Wittmaack, 1930; Wolff, 1950; Mendoza and Ruis, 1966; Gussen, 1968, 1969). Intrinsic mechanical stresses as a consequence of erect posture have also been considered as a cause. Otosclerosis has also been believed to be a regional manifestation of a clinically and genetically heterogeneous group of generalized connective tissue disorders (Arslan and Ricci, 1963; Thalmann et al, 1987). Support toward implication of disorders of connective tissue has come from studies by Bentzen (1961), Stadil (1961), Soifer and colleagues (1965), Zechner and Moser (1987), and Yoo and associates (1982), whose findings suggest a possible role for type II collagen autoimmunity in the etiology of otosclerosis, as a genetically linked cellular response to collagen.

## Hereditary Factors

Hereditary factors have long been recognized in otosclerosis and are well documented; such studies, however, have been limited to the heredity of clinical otosclerosis and describe the prevalence of stapedial ankylosis. Again, stapedial ankylosis does not represent the true prevalence of otosclerosis.

Familial predisposition was first noted by Toynbee in 1860. In Shambaugh's series of 2100 patients who underwent fenestration operations, a positive family history of progressive deafness was found in 54.5 per cent (Shambaugh, 1949). Other studies have demonstrated 64 per cent (Panama, 1987), 58 per cent (Nager, 1939), 54 per cent (Cawthorne, 1955), 40 per cent (Wullstein, 1949), 37 per cent (Minnesota, 1987), 22 per cent (Brazil, 1987), and 16 per cent (Puerto Rico, 1987). Studies of large family trees, from three to five generations, have been reported and discussed by various authors (Albrecht, 1932; Davenport, 1933; McGregor, 1940; Chumlea, 1942; Schwarz and Becker, 1964; Gregoriadis et al, 1982). Hereditary predisposition in identical twins has been reported by Albrecht (1932), Shambaugh (1935), and Fowler (1947); there are reported cases, however, in which only one twin has developed stapedial fixation (Fowler, 1947; Juers, 1950). Again, these studies only report clinical otosclerosis, and it is not known if the nonsymptomatic twins in these cases had histologic otosclerosis.

The mode of inheritance of otosclerosis has not been definitely established. Morrison (1967), in a study of 150 patients with otosclerosis and their families, suggested an autosomal dominant inheritance, manifest in 40 per cent of the individuals. Similar suggestions were made by Schwarz and Becker (1964) and by Rüedi (1963) who, quoting Larsson (1960), suggested a monohybrid autosomal inheritance with a penetrance of the

gene of 25 to 45 per cent. Again, this low prevalence is supported by the evidence that many people can have histologic otosclerosis without stapedial fixation. Polygenic multifactorial inheritance in a group of patients has been reported by Mendlowitz and Hirschorn (1976). Gapany-Gapanavicius (1975) suggested an autosomal dominant transmission with incomplete penetrance and variable expressivity. He ruled out the hypothesis for sex-linked recessive or dominant inheritence.

An interesting hereditary finding is that in spite of otosclerosis being very uncommon in certain races, it becomes common when gthere is a racial mixture. In Panama (Panama, 1987) otosclerosis was found to be highly prevalent in whites, prevalent to a much lesser degree in blacks, and nonexistent in pure Indians. However, 29 per cent of the last 103 stapedectomy cases in this series were on white-and-Indian mixed individuals, 10 per cent in white-and-blacks, and 3 per cent in black-and-Indians. In Brasilia, no cases of otosclerosis were found in pure Indians or blacks, but in 83 stapedectomy cases (representing 9.6 per cent of the last 700 otologic procedures), 22 per cent were in white-and-black mixed individuals (so-called mulattos) and 6 per cent in white-and-Indian mixed individuals (so-called mamelucos) (Brazil, 1987). Aguilar-Paz (1964) in Honduras found no cases among pure Indians in a 4-year study. In this study, he found 12 cases of otosclerosis - ten in whites and two in white-and-Indian mixed individuals. These observations are supportive of Tato and Tato's suggestion (1967) that "Otosclerosis is prevalent in those areas where the white race has become widespread and bred with the other two rares, yellow and black, among whom the incidence is null or low". It is likely that genetic studies in these mixed groups may provide additional information on the modes of inheritance of otosclerosis.

In spite of its manifesting a definite genetic pattern, there is no definite evidence of any association between otosclerosis and known genetic markers. There is no association of heritage between otosclerosis and the ABO MnRh blood-group, but there is a statistically significant association with the ability to taste phenylthiocarbamide (Morrison, 1967). Gregoriadis and colleagues (1982) found a significantly increased frequency of $A_1B_{14}$ and Bw35 antigens in a group of patients, suggesting a possible role of HLA antigens in otosclerosis. Chromosomal studies in otosclerosis have demonstrated karyotypes (Nitze, 1967), which is to be expected, since autosomal transmission is not related to chromosomal abnormalities.

## Age of Onset

The age of onset is determined by noting clinical otosclerosis based on symptoms of conductive hearing loss, the magnitude of which is directly related to the fixation of the stapedial footplate. It is thus difficult to determine the true onset, since the development of histopathologic changes is gradual. Clinical otosclerosis is more frequent between the ages of 20 and 30 (Nager, 1969). Some cases become evident as early as six or seven, but majority manifest between ages 15 and 35, with a few cases as late as 54 years old (Shambaugh, 1961). Average age of onset has been reported to be 33 (Panama, 1987), 29 (Minnesota, 1978), 24 (Chile, 1987), and 23 (Brazil, 1987). A review of the clinical charts in our series of 144 temporal bones (Hueb and Goycoolea, in press) yielded a mean age of onset of 33.5 years; the range was from 10 to 48 years of age. DeJuan (1960) reported the onset of clinical otosclerosis to be 28 per cent between the ages of 18 and 21, 40 per cent between 21 and 30, and 22 per cent between 31 and 40.

In the development of stapedial fixation, the otosclerotic focus becomes enlarged and then involves the cartilage at the margins of the oval window and replaces it. Fibrotic thickening then occurs in the adjacent annular ligament. Otosclerotic changes appear in the footplate and involve the stapes, to varying degrees. New bone then makes its appearance in the fibrous tissue of the annular ligament and eventually produces bony ankylosis of the stapes (Nager, 1969). Once the hearing loss reaches its maximum in the third decade of life, there is little further change in the air/bone gap (Glorig and Gallo, 1962).

## Race

There is a definite racial predisposition in otosclerosis, its being more common in Caucasians. The prevalence is estimated to be around 10 per cent histologically, and there is no evidence that there are significant differences between white individuals in Europe and North America. Clinical otosclerosis has been reported to be present in 1 per cent of the population of the UK (Hinchcliffe, 1961); moreover, among white individuals, Cawthorne (1952) has found that otosclerosis has a prevalence 2.5 times higher in fair-haired than in dark-haired individuals. Hall (1974) reported 0.3 per cent prevalence of clinical otosclerosis in the Norwegian population. Guild (1944) reported histologic evidence of otosclerosis in 18.5 per cent of middle-aged white women, 9.7 per cent of adult white men and only 1 per cent of adult blacks. The low prevalence in blacks also has been suggested by Brobby (1986), who observed only two cases of otosclerosis in 650 cases of hearing loss (excluding otitis, external diseases, and trauma) in blacks in Ghana. In our temporal bone collection from 644 white individuals (excluding infants), the temporal bones of 82 individuals had histopathologic evidences of otosclerosis; this represented 12.7 per cent (Hueb and Goycoolea, in press).

The prevalence is low in Japanese (Horiguchi, 1953; Goto and Omori, 1957; Takahara et al, 1959; Nakamura, 1968), Chinese (Altmann and Kornfeld, 1965), and Indonesians (Nizar, 1960). In a comparative study done in Honolulu, Hawaii, otosclerosis was found to be twice as common in Caucasians as in Japanese (Joseph and Frazer, 1964). In another comparative multiracial study, Ponniah and Chin (1976) on the Malayan Peninsula observed that otosclerosis was more prevalent in Indians than in Chinese or Malay patients. In Easter Islanders of Polynesian ethnic background, the author (1986) found no clinical cases or family history of otosclerosis. Rosen and coworkers (1962), in a study of the Maban tribe in the Sudan, did not find clinical cases of otosclerosis there either.

An exception seems to exist in Todas, India, where the estimated prevalence of otosclerosis is 17 per cent. The authors (Kapur and Patt, 1966), however, make a point in establishing that as many as 34 per cent of the marriages in this region are consanguineous, and if marriages between distant relatives are included, consanguineous marriages rise to 40 to 45 per cent. Consanguinity definitely influences the data and makes comparisons difficult. The consanguinity is not described in other reports; it is not unlikely, however, that it may play a role in various communities, although probably not to the degree that it does for the people of Todas, India.

The prevalence of otosclerosis in American Indians seems to be extremely low all across the continent. In the Amerindian population of British Columbia, Canada, otosclerosis has been found to be exceedingly rare (Cambon et al, 1965). At the Alaska

Native Medical Center in Anchorage, Alaska, stapedectomies constituted 0.85 per cent of 2574 otological procedures performed between 1979 and 1985 (Alaska, 1987). In the Indians of the Great Planes in the USA, studies by Gregg and colleagues (1965) and Holzhueter and coworkers (1965) revealed that it is virtually nonexistent. In the southwestern USA, in an extensive review of Navajos, Jaffe (1969) found only three documented cases of otosclerosis. In a 5-year study in the same geographical area, Wiet (1979) evaluated a large number of Indian groups including Apache, Pima, Maricopa, Papago, Hopi, Paiute, Shoshone, Mohave, Chemehuevi, and some Navajos. He found that tend individuals had been subjected to stapedectomy procedures, three of whom had confirmed otosclerosis, representing a minute fraction of the population with ear disease. De la Guardia, in Panama (Panama, 1987), Oliveria in Brasilia (Brazil, 1987), and Aquilar-Paz (1964) in Honduras found no cases of otosclerosis among pure Indians.

Toward the center of South America, there is an area shared by several countries (Argentina, Bolivia, Brazil, Paraguay, and Peru) where there are distinct Indian groups. They have been the subjects of a number of studies of otosclerosis. Central in this area is Bolivia. In that country there are three different geographical environments: (1) the antiplanic area, located in the Andes Mountains, where 70 per cent of the population lives; Indians in this area are Aymaras (Andino Indians); (2) the area of the valleys, inhabited by Quechua Indians; and (3) the oriental valleys (pre-Amazonic jungle), inhabited by smaller tribes, usually nomads with various dialects.

These smaller tribes are the Ayores, Chiquitanos, Chiriguanos, Guarayos, and Matacos. In a special study conducted for this chapter, Aguilera (Bolivia, 1987a) evaluated the tribes in this group and found no cases of otosclerosis. Interestingly, genetically pure Indians are without exception Rh-positive. All patients with otosclerosis operated upon in Santa Cruz, Bolivia, in the last 23 years (Bolivia, 1987b) have occurred in Caucasian or mixed individuals. In one case, in whom all physical characteristics of the patient were suggestive of his being a genetically pure Indian, the was was found to be Rh-negative. Tracing the family revealed Caucasian ancestry (Bolivia, 1987b).

Tato and colleagues (1961) and Tato and Tato (1964, 1967, 1969) have conducted extensive and thorough international studies including various Indian groups, trying to establish the prevalence (if any) of otosclerosis. They evaluated 6500 Andinos (Peru and Bolivia), Pampidos (Argentina and Paraguay), and Silvidos or Amazonidos (Paraguay) and found only two unilateral cases of what was presumably otosclerosis in Aymaras (Andinos). The geographical areas and ways of life of these various Indian groups are strikingly different. While studying Indians in Paraguay (1918 Indians, with no cases of otosclerosis), these investigators were asked (not as part of the study) to evaluate groups of German-Russian Mennonites living in the area; among 157 such persons examined, four cases of typical bilateral otosclerosis were found (Tato and Tato, 1967, 1969).

Studies conducted in Chile (southern tip of the American continents) by Riffo (Tato and Tato, 1967) in 5000 Araucano Indians revealed no cases of otosclerosis. The evidence presented herein confirms from north to south that the prevalence of clinical otosclerosis is extremely low for American Indians all across the continents. In Colombia, Penaranda (Colombia, 1987) evalued eight groups of Colombian Indians from various areas of the country - Tukanos, Cubeos, Desanos (Amazon area, Colombia, and Brazil), Arhuacos, Koguis (Sierra Nevada and northern Colombia), Kamsas, Inyas (Amazon area,

Colombia, and Ecuador) and Negros (Isla Providencia, Caribbean Sea) - and found no cases of otosclerosis among them.

**Sex**

The prevalence of clinical otosclerosis has been reported by many investigators to be higher in women: 72.5 per cent (Schmidt, 1933), 68 per cent (Shambaugh, 1952), 67 per cent (Cawthorne, 1955), 64 per cent (Nager, 1947; Chile, 1987), 60 per cent (Minnesota, 1987), 58.5 per cent (Brazil, 1987), 56 per cent (Panama, 1987), 51.25 per cent (Bolivia, 1987b), and 51 per cent (Puerto Rico, 1987). Histologic otoslerosis as reported by Guild (1944) revealed a prevalence of approximately one in eight middle-aged white women, and one in 15 adult white men. In the temporal bones or out 82 individuals (Hueb et al, in press), 46 were from males (56 per cent) and 36 from females (44 per cent). Goto and Omori (1957) did not find a difference in prevalence between sexes, among the Japanese. Since otosclerosis is not a genetically sex-linked characteristic, one would expect a sex ratio prevalence of 1:1. This has prompted some authors to believe that clinical otosclerosis is more prevalent among women because women are more likely than men to seek medical advice.

On the other hand, because of the higher prevalence in women, endocrinologic factors have been suspected. Pregnancy has been thought to stimulate activity in otosclerosis. Otosclerosis, however, usually becomes evident during the childbearing period of life, so it is difficult to separate fact from coincidence. Schmidt (1933) reported that 19 of 25 women who were pregnant and had conductive hearing loss noticed it for the first time during pregnancy. Cawthorne (1955) reported that 63 per cent of 419 female patients with otosclerosis had onset of aggravation of hearing loss during pregnancy.

Shambaugh (1967) studied 475 mothers who had fenestration operations. Fifty per cent did not observe noticeable effects on hearing during pregnancy. Interestingly, repeated pregnancies in the same women did not have the same effect on hearing. Worsening during pregnancy has been reported in 60 per cent of women with this condition (Panama, 1987), and clinical onset during pregnancy has been reported in 16.6 per cent (Brazil, 1987), 14 per cent (Puerto Rico, 1987), and 10 per cent (Minnesota, 1987). On the other hand, Nager (1947) found the same frequency of otosclerosis in married and unmarried women, and Walsh (1954) was unable to establish a relationship between hearing loss, pregnancy, and otosclerosis.

Having a large number of temporal bones with histologic evidence of otosclerosis (Hueb et al, in press) gave us an opportunity to look into this question. From our 144 temporal bones with otosclerosis, 46 belonged to males (56 per cent) and 36 to females (44 per cent). These results are within the range to be expected for a disease that is non-genetically sex-linked. If endocrinologic factors stimulated activity in otosclerosis, we would expect women to have a higher prevalence of stapedial fixation (clinical otosclerosis). The 36 bones from males had a distribution of 34 (45 per cent) with clinical and 42 (55 per cent) with histologic otosclerosis. These bones beloning to males, however, had bilateral otosclerosis in 65 per cent and unilateral in 35 per cent, whereas bones belonging to females had a distribution of 32 (47 per cent) with clinical and 36 (53 per cent) with histologic otosclerosis, bilateral otosclerosis in 89 per cent and unilateral in 11 per cent. These observations suggest that the higher incidence of bilateral otosclerosis in

females may be another explanation for the fact that women seek medical assistance more often than men.

## Sites of Involvement

An otosclerotic focus is found most often in the area of the otic capsule in front of the oval window. This location has been reported in 80 per cent (Guild, 1944), 90 per cent (Rüedi, 1957), 95 per cent (Schuknecht and Barber, 1985), and 90 per cent (Nylen, 1949) of temporal bones with otosclerosis. In our series (Hueb et al, in press), we observed 81 per cent involvement in front of the oval window. The second most common site is the round window, uncommonly causing complete closure. Complete closure of the round window has been reported by Rüedi (1957) to have a prevalence of 2 per cent. In our series (Hueb et al, in press), obliteration of the round window niche was noted in nine cases (6 per cent). Reports of involvement of the round window range from a prevalence of 30 to 50 per cent (Guild, 1944; Rüedi, 1957; Nylen, 1949; McLay, 1956; Nager, 1969; Hueb et al, in press). In spite of being in close proximity to the oval window, these lesions merge only in about 12 per cent of cases (Nager, 1969). In our series (Hueb et al, in press), we noted merging in 16 cases (11 per cent). Closure of the round window is an uncommon complication of advanced otosclerosis. It has been reported clinically in 1 per cent of 30.000 stapedectomy cases by Shea and Farrior (1987).

Schuknecht and Barber (1985) reported involvement of the round window in 30.1 per cent of cases in clinical otosclerosis and 17.1 per cent of cases of histologic otosclerosis; other sites of occurrence in cases of clinical otosclerosis are, in decreasing order of frequency, the apical medial wall of the cochlea, posterior to the oval window, the osterior internal auditory canal, the cochlear aqueduct, the semicircular canals, and the primary footplate. In the same report, involvement anterior to the oval window as the only focus was seen in 51.2 per cent of cases of clinical otosclerosis. The rest of the sites were mostly involved as one of multiple foci.

Occasional foci have been described in the carotid canal, tegmen, cochleariform process, malleus, and incus (quoted by Nager, 1969). Involvement of the malleus and incus is relatively rare. The osseous fixation of the head of the malleus to the tegmen, found in exploratory tympanotomy for otosclerosis, is not related to the disease (Mayer, 1917). Locations of foci in our series of 144 temporal bones with otosclerosis (Hueb et al, in press) were as follows: anterior to the oval window in 117 temporal bones (TB), 81 per cent, 117 foci; round window in 52 TBs, 36 per cent, 53 foci; apical/medial cochlear wall in 31 TBs, 22 per cent, 34 foci; anterior to the internal auditory canal in 27 TBs, 19 per cent, 27 foci; posterior to the oval window in 20 TBs, 14 per cent, 20 foci; stapedial in 18 TBs, 13 per cent, 18 foci; semicircular canals in 15 TBs, 11 per cent, 28 foci; cochlear aqueduct in 5 TBs, 3 per cent, 5 foci; malleus (3) and incus (1) in 4 TBs, 3 per cent, 4 foci; posterior to the internal auditory canal in 3 TBs, 2 per cent, 3 foci; cochleariform process in 2 TBs, 1 per cent, 2 foci; endolymphatic duct in 2 TBs, 1 per cent, 2 foci; and facial canal in 1 TB, 1 per cent, 1 focus.

Otosclerosis is usually a bilateral disease. Histologically, in 70 to 85 per cent of cases, both ears are involved with otosclerosis, with a certain tendency toward symmetry in locatioon (Nylen, 1949). Nager (1947) found otosclerosis to be histologically unilateral in 10 per cent of serially sectioned temporal bones and in 10.7 per cent (1939) of clinical

cases. Cawthorne (1955) found unilateral otosclerosis clinically in 3.5 per cent, and Hoople (1952) found this in 10 per cent. In our series of temporal bones (Hueb et al, in press), we found unilateral otosclerosis in 24 per cent of 82 individuals with otosclerosis. In the 62 temporal bones with bilateral otosclerosis (76 per cent), there was symmetry in 25 (40 per cent) and asymmetry in 37 (60 per cent), as seen in horizontal sections.

## Anatomy and Histology

The fact that otosclerosis is confined to a small bony region has raised important questions, such as whether there are peculiarities in the structure of the otic capsule and ossicles that distinguish them from other bones, and whether the structure itself provides any explanation of why otosclerosis develops here. The capsule is derived from the mesenchyme surrounding the otic vesicles (Bast and Anson, 1949). The mesenchymal layer enters a precartilaginous stage and, at approximately 8 weeks, cartilage begins to form. The cartilaginous capsule increases in size to week 16, when vascularization increases, absoprtion of cartilage occurs, and ossification begins. Ossification proceeds from 14 centers of ossification, and the bony capsule is formed by fusions of the various centers. A times, these centers of ossification have indistinct boundaries and are different both in spatial distribution and sequence of occurrence. Moreover, on occasion in the same individual, the extent and localization of the process of ossification is asymmetric, ie, different on the left and right-sides (Pedziwiatr, 1967). It is peculiar that this single osseous capsule, during its development, acquires the form of the inner ear spaces.

Cartilage persists throughout life in certain areas of the capsule, notably alongthe margin and vestibular aspect of the stapedial footplate. Bast and Anson (1949) have described seven regions where residual cartilage has been regularly noted: (1) fissula ante fenestram, (2) fossula post fenestram, (3) intracochlear area (endochondral layer), (4) cochlear area (round window), (5) semicircular canals, (6) petrosquamous suture and capsule beneath, and (7) base of styloid process. The modiolus develops separately from membranous bone. The ossicles develop independently of the inner ear, their origin being in the first and second branchial arch (described elsewhere).

Within the labyrinthine (otic) capsule, three layers of bone can be recognized: endosteal, periosteal, and endochondral. *The endosteal layer* is thin and dense and surrounds the periotic space. It is formed by the internal perichondrium, which then becomes the endosteum. It remains unchanged in size throughout life, limiting expansion of the periotic space. It does not grow in bulk or strength.

*The endochondral layer* is located lateral to the endosteal and medial to the periosteal layer. It contains areas of calcified cartilaginous matrix and occasional cartilage cells remain. The calcified areas have capillary buds nearby. Osteoblasts appear and deposit bone in the lacunae, forming small, bony globules, a unique feature termed "globuli ossei" by Manassé (1897) and called intrachondral bone by Bast and Anson (1949). These remnants are found throughout life and are characteristic of the endochondral layer. The remnants of calcified cartilaginous matrix and an occasional cartilage-cell have been termed "interglocular spaces" by Manassé. Even those spaces show little or no change in the adult stage, there are evidences of constant rebuilding of bone throughout life (Rüedi and Spoendlin, 1957).

The primitive perichondrium (Bast and Anson, 1949) becomes the periosteum, or *the periosteal layer*. This is the layer that provides growth and adds bulk to the otic capsule.

*The fissula ante fenestram* is located anterior to the oval window and has received special attention since it is a common site for the appearance of otosclerotic bone. The belief that the otosclerotic process starts in such an area is not consistently sustained histologically. Even if the area is most frequently involved, in many cases it is normal in spite of otosclerotic changes elsewhere in the capsule. In 70 to 90 per cent of cases, the otosclerotic lesions may replace the fissula ante fenestram, but they do not necessarily originate there (Nager, 1969). Our observations (Hueb and Goycoolea, in press) are suggestive of this description.

The fissula forms a fibrous connection between the periotic tissue and the tissues of the middle ear. This fibrous tissue is encased in primary cartilage that later is replaced by bone. From the fissula, the bone acquires a connective tissue lining, which then becomes the perichondrium. The fissula is then reduced in size by the production of new secondary cartilage from the perichondrium. The secondary cartilage remains throughout life. The form, size, and frequency of appearance vary considerably.

*The fossula post fenestram* is an evagination of the periotic tissue into the cartilaginous capsule just posterior to the oval window. Its origin is comparable to that of the fissula, but it is not located in a region where otosclerosis originates. The fossula post fenestram has been found in 67 per cent of fetal and adult ears examined, and it extends through the capsule to the tympanic surface in 15 per cent (Bast and Anson, 1949). The anatomy and histology of the oval window and ossicles are described elsewhere in this book.

## Histopathology

The circumscribed area of pathologic (otosclerotic) bone is clearly demarcated from normal bone. These slowly irregular progressive changes in the otic capsule occur without overall changes in its architecture. The elements involved in these changes are: cells (osteocytes, osteoblasts, osteoclasts, and so forth), blood vessels, vascular spaces, and the intercellular or ground substance. The various changes observed are a reflection of the interactive quantity and activity of these elements.

Early phases are characterized by resorption of bone around blood vessels, with an increase in space and size around vascular channels. Vascular spaces (marrow spaces) become wider. Electron microscopic observations have revealed microfoci occurring in the vicinity of the larger, more evident foci, and the lesion appears to enlarge by fusion of these microfoci (Chevance et al, 1969). The gaps increase in space and the disease seems to expand or "splash out" from these active centers. There is at this time an initial decalcifying process related to the lacunar system and osteocytes. The initial stages are characterized by diffuse or patchy demineralization that coincides with "preotosclerotic lesions" in light microscopy (Lim, 1970; Lim and Saunders, 1977).

The blood vessels in the marrow spaces are increased and become dilated. Vascularity is related to the size of the lesion. If the active focus reaches the periosteal

surface of the promontory, dilated vessels may cause reddish-pink color, which may be seen through the tympanic membrane (Schwartze's sign). According to Rüedi (1969), Schwartze's sign represents vascular shunts between vessels in the foci and submucosal vessels of the promontory. The presence of this sign has been reported in 10 per cent of cvaases (DeJuan, 1960). Clinically active lesions bleed easily at surgery, whereas inactive, hard, poorly vascularized lesions have no bleeding at surgery.

Osteocytes become active, losing their normally elongated shape. There is an increase in deposit of immature basophilic bone rich in ground substance and deficient in collagen, with active resorption and remodeling occurring continuously within a focus. The large amount of ground substance with few collagen fibers is basophilic, hence its blue color when stained with hematoxylin and eosin. The woven pattern of collagen fibrils runs in an irregular criss-cross fashion, with sharply defined boundaries between normal and abnormal bone. At the electron microscopic level, Chevance and colleagues (1970) verified disruption of collagen bundles that caused loss of characteristic striations and reaffirmed the light microscopic impression that the advancing front seems to be caused by osteocyte-mediated resorption of ground substance.

As the activity decreases, there are fewer cellular elements and more fibrils, and less ground substance is produced. There is a tendency then to acidophilia, hence the red color when stained with hematoxylin and eosin. The deposition of bone becomes dominant; thus the area is described as sclerotic, having a weblike fibrillar structure or lamellar arrangement. The vascular spaces narrow. After the initial alteration of one mineralization seen in both early and active stages of otosclerosis, the later stages of the so-called sclerotic lesion do become well mineralized; however, electron microscopic and x-ray analytic investigations have failed to confirm the notion that the sclerotic lesion is hypermineralized (Lim, 1970; Lim and Saunders, 1977). Evaluations of otosclerotic stapes by light microscopy, histochemistry, immunochemistry, and electron microscopy by Lim (1987) have verified (and expanded) these observations.

Within the same area, different rates of activity can be occurring at the same time. These changes have been classified in stages (Schuknecht and Kirschner, 1974), phases (Friedmann, 1974), grades, and so forth. These different areas of activity are represented not only in different foci, but also occasionally in one and the same lesion (Nager, 1969).

Blue mantles (of Manassé) are nonspecific histologic changes characterized by plexus-like projections. They are formed by resorptive spaces in the otic capsule surrounding vascular spaces, which stain markedly with the blue of hematoxylin (Manassé, 1922; Weber, 1933; Nylen, 1949; Lindsay, 1974) and have a "mantle-like" appearance, hence their name. Ultrastructural and histochemical studies (Lim, 1985) have suggested that blue mantles are areas in which collagen is greatly reduced, in contrast to the increase of amorphous ground substance (glycosaminoglycans and glycoproteins). Weber (1960) believed that the otosclerotic foci may be formed through a fusion of blue mantles. These are, however, uncommon in mastoiditis and other bone diseases (Friedmann, 1974).

Hinojosa (1985) has pointed out that in his studies of 700 temporal bones (with different pathologic conditions), about 90 per cent of them show blue mantles in different localizations. Surprisingly, in 1 per cent or less, blue mantles were found in the oval window. Blue mantles may be found not only in continuity with otosclerotic foci but also

in other areas of the otic capsule of ears with otosclerosis, particularly around the semicircular canals. In our series (Hueb and Goycoolea, in press), blue mantles were present in 74 (51 per cent) of 144 temporal bones with otosclerosis, and in two cases (four temporal bones) there were blue mantles in both sides but otosclerotic lesions in only one side.

We found blue mantles in 39 (59 per cent) of 66 temporal bones with clinical otosclerosis and in 35 (45 per cent) of 78 temporal bones with histologic otosclerosis. In agreement with Hinojosa (1985), we found blue mantles mainly around the semicircular canals, and in some instances anterior to the internal auditory canal and to the cochlea. In a review of 60 temporal bones from 30 individuals without otosclerosis and with ages matching those of the group from which we had bones with otosclerosis, blue mantles were found in 12 (20 per cent). It is to be mentioned that even though a high prevalence of blue mantles is found in the presence of otosclerosis (as described), their exact significance is unknown.

Histologic studies have been invaluable in defining morphologic changes characterizing the disease process and in describing the microscopic appearance. Electron microscopy combines ultrastructural detail and allows histochemical confirmation. Using this method, Chevance and colleagues (1969) reported on the role of lysosomes in the active process of lysis during the "extension" stage of the otosclerotic focus. Histochemical and biochemical studies of enzymes, bone matrix, hormones, and inorganic components of bone have shown that otosclerotic foci are metabolically active, particularly during the stages of growth and invasion (Albernaz and Covell, 1961; Alberti and Tarkannen, 1963; Maurer, 1961-1962; Soifer et al, 1969a and b; Chevance, 1962; Causse et al, 1972, 1973; Sziklai et al, 1985; Ribári and Sziklai, 1988).

Several lysosomal enzymes that play an important role in the process of depolymerization of bone matrix have been shown to exhibit increased activity in otosclerotic bone and perilymph. These are acid phosphatase, trypsin, alpha-chymotrypsin, and ribonuclease, Ribári and associates (1987) also demonstrated an increase in cathepsin D and a collagen-like peptidase in otosclerotic stapedial footplates; they called attention to the facts that these enzymes are osteoblastic in origin and that osteoblasts are not only involved in formation of bone but also inthe process of resorption. Cathepsin D breaks down noncollagenic proteins and is involved in the processing of procollagen. Increase in activity of this enzyme and also in $C_1$ peptidase demonstrates an increase in turnover of collagen in otosclerosis. These authors suggested that "as the osteoblast osteoid synthesis is reduced in otosclerosis and these enzymes are of osteoblastic origin, osteoblasts seem to be the signal-transducing cells in otosclerosis". The end products of digestion by cathepsin D of acidic proteoglycans, acidic glucosaminoglycans have beenshown to cause advanced calcium binding (Kogaya and Furuhashi, 1985) resulting in a disturbance of the mineralization. Lim (1985) could demonstrate by transmission electron microscopy that in lesions in which there is concurrent osteoblastic and osteoclastic activity these cells show close contact suggestive of an interaction between them.

It is important to bear in mind that these studies only represent metabolic activity without providing a clear idea of pathogenesis. No single enzyme is responsible for the production of the otosclerotic lesion; moreover, the physiologic inhibitors of these enzymes have not been commonly evaluated. These studies only suggest a disturbance of

the enzymatic balance as a characteristic of the disease (Alberti and Tarkannen, 1963). When evaluating different reports by different methods and techniques, we must always keep in mind the overall picture of the disease and of the temporal bone, and remember that all methods are supplemental of each other in providing an overall picture.

## Tinnitus

Tinnitus is a frequent and sometimes extremely annoying symptom of otosclerosis, especially in patients with considerable sensorineural hearing loss combined with stapedial fixation. The exact mechanism is not clear. Tinnitus in patients with otosclerosis has been reported to be present in 79 per cent (Panama, 1987), 67 per cent (Nager, 1947), 65 per cent (Puerto Rico, 1987), 43 per cent (Brazil, 1987), and 37 per cent (Minnesota, 1987). In Cawthorne's series of 2000 patients with otosclerosis (1955), 1570 patients (78.7 per cent) had tinnitus. Interestingly, the symptom was not disturbing to 79 per cent of these patients with tinnitus.

## Sensorineural Hearing Loss and Otosclerosis

The mechanism of conductive hearing loss in "stapedial otosclerosis" is clearly established, but the mechanism of sensorineural hearing loss is not clearly defined. Moreover, the degree, significance, and even the existence of sensorineural loss by itself in otosclerosis (without stapedial fixation) have been questioned. From a general standpoint it should be established that the otosclerotic focus by itself does not cause deafness, and that what is evaluated are the secondary effects of such focus, be they direct or indirect.

Different mechanisms causing conductive and sensorineural hearing loss have been suggested. Lack of space allows only a general overview of such mechanisms. Fixation of the stapes and obstruction of the round window have anatomic, histologic, and audiologic evidence that makes them clear and definite mechanisms. The possible mechanisms (if any) for the occurrence of sensorineural hearing loss are unclear. The relevant literature offers some major mechanisms by which sensorineural hearing loss might occur in otosclerosis. These studies offer hypotheses with some physiopathologic basis, but these have not been substantiated to date.

Liberation of toxic metabolites (by or as a consequence of the otosclerotic focus) into fluids of the inner ear was suggested as early as 1911 (Siebenmann, 1911). This was further suggested by Nager (1969), and the presence of proteolytic enzymes in the perilymh and footplate of otosclerotic ears was demonstrated by Chevance and colleagues (Chevance et al, 1970; Chevance, 1976), Causse and Chevance (1978), and Ribári and coworkers (Ribári et al, 1987; Ribári and Sziklai, 1988). Since neither the normal metabolism nor the normal constituents of the inner ear are clearly understood, this evidence is hard to substantiate at the present time.

Vascular compromise and hypoxemic lesions of the structures of the inner ear were proposed by Rüedi (1963) and Rüedi and Spoendlin (1966), who demonstrated the presence of venous shunts between the otosclerotic focus and vessels of the inner ear that caused venous congestion and, as a result, cochlear hypoxemia. Extension of the otosclerotic focus beyond the limits of the otic capsule (either in the basal turn or lateral

wall of the cochlear duct), with or without formation of non-otosclerotic new bone, has been demonstrated. It is unclear, however, whether there is a vascular compromise and/or direct destruction of cochlear structures. Alteration of the mechanisms of motion in the cochlear duct, causing loss of amplitude in the traveling waves, was proposed by Linthicum and associated (1975), who suggested that this could occur in relaxed and atrophic parts of the basilar membrane of cochleas with endosteal involvement of the otosclerotic focus.

In this possible association of otosclerosis and sensorineural hearing loss, there are two main alternatives. One is in association with stapedial otosclerosis ("apparently" more frequent) and one (less accepted) without stapedial otosclerosis. The latter has been termed cochlear otosclerosis, and it would be an independent form of clinical otosclerosis; obviously, it is difficult to establish clinically. The main problem with establishing a cause-and-effect relationship between otosclerosis and sensorineural hearing loss has been the lack of definite evidence, associated with the lack of comprehensive studies and perhaps the passion of the investigators for one-sided views. It is difficult to encounter studies correlating clinical and histopathologic observations with audiometric findings matched and correlated with averages of the general population exposed to the same conditions except otosclerosis.

Lindsay and Beal (1966) found sensorineural hearing loss only in temporal bones with extensive and multifocal otosclerosis. Elonka and Applebaum (1981) found an increase in bone conduction levels only in ears with two or more sigtes of endosteal involvement. Schuknecht and Barber (1985) found no correlation between the magnitude of sensorineural hearing loss and endosteal involvement or the size, activity, and location of the otosclerotic focus. On the other hand, Linthicum (1967) showed a relationship between the degree of cochlear endosteal involvement, with hyalinization of the spiral ligament, and sensorineural hearing loss; also, Balle and Linthicum (1984) reported the presence of sensorineural hearing loss in some selected cases of otosclerosis without stapedial fixation. Schuknecht and Kirschner (1974), however, in a survey of more than a thousand temporal bones, demonstrated that the presence of cochlear otosclerosis is not common. In our study (Hueb and Goycoolea, in press), we found that on many occasions the otosclerosis lesion expands from the anterior margin of the oval window toward the apex of the cochlea, involving the endosteum of the upper half of the basal turn, sometimes with true stapedial fixation, sometimes with a thin bony fixation, and sometimes without stapedial fixation.

Since many of the temporal bones in our collection were obtained from elderly patients and therefore favor the presence of lesions of long duration, we believe that it is possible that in some instances the stapedial fixation can occur later in this common pattern of expansion, rendering the entity "cochlear otosclerosis" histopathologically more common than has been believed. In most of these bones, the cochlear endosteum was involved only in the area of the basal turn, sometimes with atrophy and hyalinization of the spiral ligament and atrophy of the stria vascularis. Johnsson and colleagues (1978) called attention to the point that this area of the basal turn becomes a target for possible toxic substanes released by the otosclerotic focus, to cause sensorineual hearing loss when there is an active lesion involving the endosteum of the scalae.

In our study, the average bone conduction thresholds for patients with one site of endosteal involvement by the otosclerotic focus was 33.75 dB, and for patients without endosteal involvement by the otosclerotic focus it was 28.26 dB, when frequencies of 0.5, 1, 2, and 4 kHz were used for calculation, after exclusion of those patients with other causes for their hearing losses. In temporal bones with two or more sites of endosteal involvement, the average bone conduction threshold was 62 dB, and in all those cases the stapedial footplate was fixed by the otosclerotic focus. This is in agreement with Elonka and Applebaum (1981), who suggested that "cochlear endosteal involvement alone may not be sufficient explanation for the sensorineural hearing loss found in otosclerosis with the exception of the most severely involved ears (with two or more sites of endosteal involvement)." In our series, all eight temporal bones that satisfied the pathologic criteria for cochlear otosclerosis had only one site of endosteal involvement.

Our observations are in agreement with Schuknech (Schuknecht and Kirschner, 1974; Schuknecht, 1979) and Guild (1944) in that "an otosclerotic lesion large enough to cause sensorineual hearing loss invariably fixes the stapes", at least in the vast majority of cases. In the temporal bones with active otosclerotic lesions, the mean bone conduction thresholds were significantly worse, compared with losses in bones with inactive lesions, but we could not find consistent results in terms of worsening of bone conduction levels in different age groups, with the exception of those aged 60 to 68 years and those aged 69 years and older when compared with air conduction levels of the worse ear, in a survey conducted by Davis et al (1983). In these age groups, the bones with otosclerosis had significantly worse bone conduction levels. This is in agreement with Browning and Gatehouse (1984), who suggested a small, progressive elevation of the bone conduction thresholds in older patients with otosclerosis when compared with control subjects. We believe that bone conduction thresholds become worse in cases of active lesions, and that there is a tendency toward worsening of these thresholds in elderly patients, in whom it is not uncommon to find active otosclerotic lesions. Since in our collection all eight temporal bones that satisfied the pathologic criteria for cochlear otosclerosis had only one site each of endosteal involvement, we believe that if cochlear otosclerosis does cause an elevation in bone coduction levels, this is not severe.

In summary, in association with stapedial otosclerosis the evidence accumulagted is suggestive of a definite relationship of otosclerosis with sensorineural hearing loss, especially for the higher frequencies of hearing, in older age groups when compared adequately with the general population. In cochlear otosclerosis, descriptions of selected temporal bones with far-advanced otosclerosis, representing a small percentage of the population of otosclerotics, have a definite relationship between otosclerosis and sensorineural hearing loss. The true prevalence and significance seem low, based on histopathologic findings of the large numbers of temporal bones available in the various temporal bone collections. Since space does not permit a detailed description of such studies, the reader is referred to the references (Lindsay, 1966; Kelemean and Linthicum, 1969; Schuknecht, 1979, 1983; Elonka and Applebaum, 1981; Causse, 1983; Hinojosa and Marion, 1983, 1987; Parahy and Linthicum, 1983; Balle and Linthicum, 1984).

## Otosclerosis and Vestibular Involvement

With otosclerosis compromising the otic capsule, it is reasonable to assume that in some cases there should be involvement of the vestibular system as well. The clinical

association between otosclerosis and vestibular imbalance has been reported (Seligman and Shambaugh, 1951; Cohen, 1959; Richards, 1964; Paparella and Chasin, 1966; Cole and Funkhauser, 1972; Cody and Baker, 1978; Parnes et al, 1978; Freeman, 1980; Sismanis et al, 1986). Clinical evidence has shown otosclerotic patients to have vestibular involvement in 27 per cent (Rasmussen, 1949), 30 per cent (Hulk and Jongkees, 1950; Felisati, 1958), 24 per cent (Cawthorne, 1955), 25 per cent (Reinecken, 1960), 26 per cent (Profazio et al, 1963), 7 per cent (Puerto Rico, 1987), 3 per cent and 35 per cent (Meurman et al, 1969). Fisch (1965) found a 28.8 per cent prevalence using electronystagmographic studies and reported that these patients had evidences of cochlear dysfunction as well.

These types of studies were discussed and extended by Morales-Garcia (1972) who, using caloric testing as per Fitzgerald and Hallpike, found a prevalence of vestibular disturbances of 27.7 per cent in 202 otosclerotic patients. He reported that patients with sensorineural compromise had a greater vestibular involvement, but that the increase in sensorineural hearing loss with age occurred both in patients with and those without vestibular compromise. The prevalence of vestibular symptoms was greater in the group with sensorineural hearing loss, but neither the prevalence nor the severity of these symptoms was directly related to age or degree of hearing loss. An important observation was that cochlear involvement is not necessarily accompanied by vestibular compromise and that vestibular compromise can occur in the absence of cochlear involvement. In our series (Hueb and Goycoolea, in press), the vestibular endosteum was involved by the otosclerotic focus anterior to the oval window or by the focus in the footplate or around the semicircular canals in 90 (63 per cent) of 144 temporal bones with otosclerosis. The distribution was as follows: 66 out of 66 (100 per cent) temporal bones with clinical otosclerosis, and 24 out of 78 (31 per cent) temporal bones with histologic otosclerosis. In some instances we noted the presence of hyalinization of the supporting ligament of the semicircular ducts when the otosclerotic lesion surrounded the semicircular canals but without atrophy of sensory elements.

The present evidence is clearly suggestive of an association of otosclerosis and vestibular symptoms. These vestibular symptoms described do not necessarily represent a full symptomatic rotational vertigo, characteristic of endolymphatic hydrops. This association has been the subject of many publications, and as is the case with sensorineual hearing loss and otosclerosis, the subject is under discussion. In this case, however, the lack of evidence is more noticeable at present. The association of otosclerosis and rotational vertigo has been suggested by Shambaugh (1959, 1966) who described 10 per cent of his patients who had fenestration operations and subsequently developed endolymphatic hydrops. Paparella and Chasin (1966) also described the association between episodic attacks of vertigo and otosclerotic conductive deafness, and McCabe (1966) suggested the term "otosclerotic inner ear syndrome" to describe this association. Prevalence of such a syndrome has been found to be 3 per cent (McCabe, 1966), 15 to 25 per cent (Causse et al, 1972), and 10 per cent in cases of histopathologic otosclerosis and 10.2 per cent of retrospective clinical cases (Ghorayeb and Linthicum, 1978). However, it must be mentioned that it is not that easy to clearly distinguish this syndrome as such.

Otosclerotic foci involving the vestibular labyrinth have been noted during fenestration procedures (Seligman and Shambaugh, 1951); on the other hand, Bouche and coworkers (1968) and Martin (1968) have reported typical otosclerotic stapedial ankylosis during surgery in patients with Ménière's disease. Histopathologic association of

otosclerosis and endolymphatic hydrops has been described (Mayer, 1917; Wolff, 1950; Altmann and Kornfeld, 1965; Black et al, 1968; Igarashi et al, 1982; Sando et al, 1974; Ghorayeb and Linthicum, 1978; Johnsson et al, 1978, 1982; Keleman and Linthicum, 1969; Liston and Paparella, 1984); however, there is no definite evidence available to establish a cause-and-effect relationship. Moreover, some studies have suggested this association to be a rare event, possibly coincidental (Schuknecht, 1979, 1983).

Different mechanisms have been suggested for the association of otosclerosis and vestibular imbalance. These vary from foci producing end-organ and/or neural degeneration (Gussen, 1973; Sando et al, 1974) to biochemical changes in the perilymph (Sando et al, 1974; Ghorayeb and Linthicum, 1978; Johnsson et al, 1978), and even to extensive capsular otosclerosis causing labyrinthine hydrops (Johnsson et al, 1982; Liston and Paparella, 1984). Again, however, as mentioned earlier, the evidence for these associations is not at all sufficient and does not allow any definite statements and/or conclusions. We are at present in an early phase of obtaining information. There is no doubt that during the next few years this will become a subject as controversial and fascinating as the association of otosclerosis and sensorineural hearing loss.