

Chapter 163: Systemic Disease Manifestations in the Middle Ear and Temporal Bone

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Several systemic diseases, including granulomatous and infectious processes, tumors, disorders of bone, storage diseases, collagen vascular and autoimmune diseases, and immunodeficiency disorders, may involve the middle ear and temporal bone (see box). In some, the initial clinical symptoms may occur in the temporal bone and be confused with other diseases limited to the middle ear and mastoid, such as chronic otitis media.

Granulomatous and Infectious Diseases

Chronic otitis media with otorrhea, inflammation, and granulation of the middle ear and mastoid is one of the most common entities the otolaryngologist - head and neck surgeon treats. However, several more generalized disease entities, such as the histiocytoses, tuberculosis, Wegener's granulomatosis, mycotic diseases, and syphilis, may closely mimic the symptoms of chronic suppurative otitis media.

Histiocytosis X

Histiocytosis X refers to a group of disorders of the reticuloendothelial system characterized by a proliferation of cytologically benign histiocytes. The term was proposed by Lichtenstein (1953), who considered eosinophilic granuloma, Hand-Schüller-Christian disease, and Letterer-Siwe disease to be related disorders because of the similarity in pathologic lesions. However, their severity and hence prognosis and treatment differ greatly. The etiology remains obscure; recent studies have suggested an immunologic basis (Leikin, 1987), but no consistent pattern of abnormality has been identified.

Unifocal eosinophilic granuloma occurs in children and young adults and demonstrates a male predominance. It appears as a solitary osteolytic lesion in the femur, pelvis, scapulae, vertebrae, ribs, mandible, maxilla, or skull, including the temporal bone. The lesion may be asymptomatic or cause pain, local swelling, and even pathologic fracture. There are no systemic manifestations. Histopathology of the lesion demonstrates benign histiocytes and eosinophils. The clinical course is typically benign with an excellent prognosis, and spontaneous regression may occur. Local curettage and low-dose irradiation (~600 cGy) (Smith et al, 1973) is curative. Temporary splinting or casting may be necessary in weight-bearing bones. Follow-up examination with radiographic skeletal survey should be performed to detect lesions at other sites, which almost always occur within 1 year.

Hand-Schüller-Christian disease may be best understood as multifocal eosinophilic granuloma. It usually occurs before 5 years of age and is characterized by multifocal osteolytic lesions with limited extraskelatal involvement of skin, lymph nodes, and viscera. Multiple lesions are evident at diagnosis or develop within 6 months after a unifocal lesion appears. Systemic manifestations include fever, anorexia, recurrent upper respiratory infections, anterior cervical lymphadenopathy, otitis media, and hepatosplenomegaly. The classic triad of osteolytic skull lesions, exophthalmos secondary to orbital bone involvement, and diabetes insipidus due to pituitary disease may be seen in up to 25% of patients

(Cunningham et al, 1989). The chest radiograph may demonstrate diffuse pulmonary infiltration, particularly in central and perihilar areas; hilar lymphadenopathy is rare. Diagnosis requires biopsy of an accessible lesion. Spontaneous regression may occur, but the disease is typically chronic, and low-dose chemotherapy may be required to control systemic manifestations.

Letterer-Siwe disease is a disseminated histiocytosis that occurs in children under 3 years of age and presents with diffuse multiorgan involvement. Manifestations include fever, seborrheic or eczema-like rash, oral lesions, lymphadenopathy, hepatosplenomegaly, multiple bony lesions, diffuse replacement of marrow with resulting blood dyscrasias, and pulmonary infiltration with respiratory failure. The disease is virulent, with a poor prognosis and a high mortality rate. Treatment consists of varying combinations of corticosteroids and cytotoxic drugs such as methotrexate, 6-mercaptopurine, vincristine, vinblastine, chloambucil, cyclophosphamide, and etoposide (Starling, 1987).

Middle ear and temporal bone manifestations

The mastoid is a common site of involvement. When small, the lesion is asymptomatic. As it expands, it may manifest itself in several ways: by erosion of the posterior bony canal wall; by erosion through the cortex of the mastoid, zygomatic or squamosal portions; or by secondary infection (Schuknecht and Perlman, 1948). The otic capsule and facial nerve are relatively resistant; sensorineural hearing loss, vertigo, and facial nerve paralysis can occur, but are infrequent. Similarly, extension beyond the temporal bone to involve the jugular fossa and skull base is rare.

The reported incidence of otologic manifestations in cases of histiocytosis X varies from 15% to 61% (Cunningham et al, 1989) and may be the initial presentation of the disease. The most common symptom is otorrhea, followed by postauricular swelling, hearing loss, and vertigo (McCaffrey and McDonald, 1979; Tos, 1966). The most common sign is granulation tissue or aural polyps in the external auditory canal. However, the disease may present with perforation of the tympanic membrane, otitis media, otitis externa, a fistula between the mastoid and the external canal, or nontender postauricular swelling. Occasionally, inner ear symptoms and a positive fistula test will be found in the presence of an intact tympanic membrane. The disease often mimics chronic otitis media, and mastoid surgery is often performed before the diagnosis is made (Schuknecht and Perlman, 1948).

The diagnosis is suggested by an inflammatory disorder of the middle ear and mastoid that does not respond to routine antibiotic therapy, bilateral destructive ear disease, an elevated erythrocyte sedimentation rate in the absence of acute infection, exuberant granulation tissue after mastoid surgery with a persistently draining cavity, and associated skin and systemic lesions. Radiographs show destructive lesions in the mastoid and temporal bones (Hudson and Kenan, 1969; Schuknecht and Perlman, 1948; Tos, 1966) (Figs. 163-1 and 163-2). Definitive diagnosis is established by biopsy; the surface of the granulation tissue often shows infection, necrosis and fibrosis; hence, it is necessary to acquire tissue from deeper parts of the lesion (Schuknecht and Papaspyrou, 1980).

Microscopic findings include sheets of histiocytes with a variable number of eosinophils, plasma cells, polymorphonuclear leukocytes, and multinucleated cells (Figs. 163-3

to 163-5). Areas of hemorrhage and necrosis are common. The histiocytes may be vacuolated and accumulate cholesterol. Electron microscopy may show rod-shaped cytoplasmic inclusion bodies, which are thought to be characteristic of histiocytosis X (Favara, 1981).

Tuberculosis

The occurrence of tuberculin otitis media has fallen dramatically. In the early part of this century, the reported incidence of chronic otitis media due to tuberculosis varied from 1.3% to 18.6%, whereas more recent studies report rates of 0.05% to 0.9% (Skolnik et al, 1986). *Mycobacterium tuberculosis* is the offending organism in most cases; occasionally, atypical mycobacteria (such as *Mycobacterium avium* and *Mycobacterium fortuitum*) are responsible (Wardrop and Pillsbury, 1984).

Tuberculosis of the middle ear and mastoid may occur as a result of hematogenous or lymphatic spread or by extension to the middle ear cleft through the eustachian tube. Direct inoculation via a tympanic membrane perforation is also possible. Middle ear involvement in the absence of active pulmonary disease is rare but may occur.

In the early stages of tuberculous otitis media, the tympanic membrane become thickened and the otoscopic landmarks obliterated. A conductive hearing loss is attributable to purulent effusion, thickening of the tympanic membrane and middle ear mucosa, and early destruction of the ossicles. Characteristically there is no pain or tenderness, but lymphadenomegaly in the high jugular chain occurs early. Multiple small perforations of the tympanic membrane occur with seropurulent drainage. The perforation quickly coalesce to cause loss of the tympanic membrane. Likewise, a myringotomy site in an intact tympanic membrane will quickly enlarge.

The middle ear mucosa appears hyperemic with polypoid granulation. Osseous involvement results in sequestration of bone and destruction of the inner ear or facial nerve, or both. Destruction of the mastoid tip may result in an asymptomatic, nontender Bezold's abscess, that is, a "cold" abscess.

The diagnosis of tuberculous involvement of the middle ear is usually delayed. The characteristic signs and symptoms of multiple perforations of the tympanic membrane which quickly coalesce to form total loss of the tympanic membrane, nontender cervical lymphadenopathy, intractable otitis media with polypoid granulation, or bony sequestration should alert the clinician to this possible diagnosis. Unfortunately, involvement of the otic capsule with resultant loss of auditory and vestibular function may be the first symptoms, indicating a process unlike the more typical chronic otitis media. Multiple perforations of the tympanic membrane, exuberant polypoid granulation within the middle ear, and early loss of inner ear function are also seen in Wegener's granulomatosis. The two diseases are distinguished on the basis of skin tests for tuberculosis and histologic demonstration of acid-fast organisms of tuberculosis in granulation tissue, cultures of the middle ear, the presence of serum antibodies to neutrophil cytoplasmic antigens (ANCA) in Wegener's granulomatosis, and the systemic manifestations of each process (see also Chapter 162).

Early involvement of the middle ear and mastoid begins histologically with edema and infiltrations of the mucous membrane with lymphocytes and the characteristic giant cells of

Langhans. The polypoid mucosa then ulcerates; exuberant granulation tissue is formed; and destruction of the middle ear, mastoid, or ossicular bone quickly follows (Figs. 163-6 and 163-7).

The mainstay of treatment of tuberculosis of the middle ear and mastoid is systemic use of standard antituberculous chemotherapy (Skolnik et al, 1986). However, mastoid surgery may be required to remove sequestered bone. Reconstructive surgery of the ossicles and tympanic membrane is feasible once the infection is controlled.

Wegener's granulomatosis

Wegener's granulomatosis is a granulomatous inflammatory process with necrotizing vasculitis. It primarily affects the upper and lower respiratory tract and kidneys, but the vasculitis may be detected anywhere in the body.

Wegener's granulomatosis is considered to be an "autoimmune" disease mediated either by cellular immune mechanisms or by immune complex deposition. The disease demonstrates a 2:1 male predominance, and the mean age of onset is 40 years. Common presenting symptoms include headache, sinusitis, rhinorrhea, otitis media, fever, and arthralgias. The sinus cavities and kidneys are involved in over 90% of patients. Pulmonary manifestations include cough, pleuritic chest pain, hemoptysis, and nodular or cavitary infiltrates on chest radiograph. Approximately 50% of patients have ocular findings of conjunctivitis, iritis, or scleritis, and dermatologic findings of necrotic ulcerations, vesicles, or petechiae.

Laboratory findings in Wegener's granulomatosis may include a normochromic normocytic anemia, thrombocytosis, positive rheumatoid factor, and hyperglobulinemia, particularly IgA. The erythrocyte sedimentation rate is almost always elevated. Renal involvement is demonstrated by evidence of glomerulonephritis or renal insufficiency. Presence of serum ANCA has been used as a diagnostic marker for Wegener's granulomatosis; the antibody titer also parallels disease activity (van der Woude et al, 1985).

Middle ear and temporal bone manifestations

The usual presenting symptom of Wegener's granulomatosis is an upper respiratory tract infection in the nose or sinuses, commonly involving the middle ear. Otitis media and hearing loss can occur and may be the initial symptoms in some patients (Blatt et al, 1959). The granulomatous process may cause obstruction of the eustachian tube (Fig. 163-8) and resultant serous otitis media and conductive hearing loss. Perforation, sometimes multiple, of the tympanic membrane may mimic tuberculosis. Invasion of the inner ear will result in profound loss of auditory and vestibular function.

The histopathologic hallmark of Wegener's granulomatosis is the presence of both granulomas and necrotizing vasculitis (Fig. 163-9). Polyarteritis nodosa does not demonstrate granulomas, and tuberculosis and sarcoidosis demonstrate granulomas, but not vasculitis.

Treatment has traditionally been with cyclophosphamide or other chemotherapeutic agents and corticosteroids (Fauci et al, 1983). Trimethoprim-sulfamethoxazole also has been reported to be efficacious in treating this disorder (DeRemee, 1988).

Sarcoidosis

Sarcoidosis is a chronic, multisystem disorder of unknown etiology, characterized by the presence of noncaseating granulomas. It most frequently affects the lungs, although almost all parts of the body can be affected. A consistent immunologic feature is alteration of cellular immune responses. The disease demonstrates a female predominance and is 10 times more common in blacks than in whites. The onset of disease is usually in the third or fourth decade of life.

Common presenting manifestations include bilateral hilar adenopathy on chest radiograph, cough, and granulomatous skin rash. Other malformations include iridocyclitis, keratoconjunctivitis, peripheral lymphadenomegaly, hepatosplenomegaly, cardiac failure, myalgia, and arthralgia. Neurologic involvement includes both central and peripheral manifestations. The facial and optic nerves are the most commonly affected cranial nerves. Either peripheral mononeuritis or polyneuritis may be seen.

Laboratory findings may include the hilar adenopathy on chest radiograph (Fig. 163-10), hypercalcemia, and elevated serum angiotensin-converting enzyme (ACE). The histopathologic feature of the sarcoid lesion is noncaseating epithelioid granulomas (Fig. 163-11).

Spontaneous resolution occurs in the majority of patients. For those patients with progressive symptoms or with ocular, cardiac, or central nervous system involvement, corticosteroids are beneficial. Serum ACE assay and gallium-67 lung scanning are helpful indicators of disease activity for use in follow-up.

Middle ear and temporal bone manifestations

The facial nerve is the most commonly affected cranial nerve, usually as part of the triad of uveoparotid fever of Heerfordt: uveitis, parotiditis, and cranial nerve palsy (Cohen et al, 1983).

Involvement of the temporal bone may include facial, auditory, or vestibular nerve dysfunction. The pathophysiologic basis for these lesions is not known, as there have been no reported temporal bone studies. However, direct involvement of the nerves by the granulomatous process within the temporal bone or in the posterior cranial fossa is suspected (Hybels and Rice, 1976).

Syphilis

Both congenital and acquired syphilis may affect the middle ear in late latent and tertiary forms (Chapter 155). In the late latent form, the middle ear and mastoid may be affected by rarefying osteitis with leukocytic infiltration of the ossicles and mastoid bone (Figs. 163-12 and 163-13). A similar but larger lesion of tertiary syphilis, the gumma, demonstrates obliterative arteritis and central necrosis. A gumma of the ear canal or middle ear may result in perforation of the drum and a granulomatous appearance of the middle ear mucosa. Definitive diagnosis of syphilis of the middle ear requires a positive serologic test and histologic demonstration of *Treponema pallidum*. Syphilitic involvement of the tympanic

membrane and middle ear may mimic tuberculosis, and superinfection may result in chronic otitis media.

Inner ear involvement may occur in the absence of macroscopic changes in the tympanic membrane or middle ear. Hennebert's sign, the induction of ocular deviation with positive or negative pressure in the external auditory canal, was believed to indicate a true fistula between the middle and inner ear because of rarefying osteitis of the otic capsule. However, the more probable cause is fibrous adhesions between the stapes footplate and the membranous labyrinth secondary to endolymphatic hydrops (Nadol, 1974). Combined antibiotic and corticosteroid therapy is beneficial in treating sensorineural hearing loss (Zoller et al, 1979).

Lyme disease

Lyme disease is a multisystem inflammatory disorder affecting primarily the skin, nervous system, heart, and joints. It is caused by a spirochete - *Borrelia burgdorferi* - and transmitted to humans by certain Ixodes ticks that are part of the *Ixodes ricinus* complex. The known primary reservoirs of the disease are the white-footed mouse and white-tailed deer. The disease was recognized initially in 1975 because of clustering of patients with arthritis in Lyme, Conn, but it is now known that it has been present for several decades in Europe, where it is known as Bannwarth's syndrome.

Infection is usually acquired in the summer months. People of all ages and both sexes are affected. Three clinical stages can occur that are similar to those in syphilis (Steere, 1989). The first stage (early infection, localized) begins 3 to 33 days after a tick bite with a characteristic skin lesion, erythema migrans. This lesion occurs in 60% to 80% of patients and may be accompanied by minor constitutional symptoms.

The second stage (early infection, disseminated) occurs within days or weeks of inoculation of the organism from the site of inoculation and begins with hematogenous dissemination of the organism from the site of inoculation. The symptoms mimic a systemic viral illness with fever, migratory arthralgia, myalgia, headache, meningismus, generalized lymphadenopathy, malaise, fatigue, and secondary annular skin lesions. After hematogenous spread, *B. burgdorferi* seems to be able to sequester itself in certain niches and cause localized inflammation in the nervous system, heart, or joints. Neurologic involvement is manifested by meningitis, encephalitis, cerebrospinal fluid (CSF) lymphocytosis, peripheral neuropathy, myelitis, or cranial neuropathy (including facial nerve paralysis). Cardiac manifestations include atrioventricular block, other arrhythmias, myocarditis, and pericarditis. Joint disease manifests as brief attacks of asymmetric oligoarticular arthritis, primarily in large joints, especially the knee.

The third stage (late infection, persistent) occurs more than a year after onset and can result in chronic, prolonged arthritis, chronic encephalomyelitis, chronic axonal peripheral polyradiculoneuropathy, keratitis (similar to syphilis), acrodermatitis chronica atrophicans, and localized scleroderma-like lesions. A patient may have one or all of the stages, and the infection may not become symptomatic until stage 2 or 3. Affected tissues show infiltration by lymphocytes and plasma cells. Mild vasculitis and hypercellular vascular occlusion can occur. There is generally no tissue necrosis. Unlike syphilis, Lyme disease has not been

associated with granulomas, gummas, multinucleated giant cells, or fibrinoid necrosis (Duray and Steere, 1988).

The diagnosis is based on clinical features, especially erythema migrans, and exposure to an endemic geographic area. Detection of a specific antibody to *B. burgdorferi* is a useful confirmatory test. The specific IgM antibody response appears first, peaking 3 to 6 weeks after infection and gradually waning thereafter (Duffy et al, 1988). Gradually, specific IgG antibody develops, and almost all patients with stage 2 or stage 3 disease have elevated titers. False-negative results (up to 70%) occur primarily during stage 1. False-positive results (particularly with IgM, but uncommonly with IgG) may occur with syphilis, rickettsial diseases, autoimmune diseases, and neurologic disorders. In addition, 5% to 10% of subjects in the USA have apparently asymptomatic *B. burgdorferi* infection. If these patients have symptoms caused by another disease, the symptoms may be attributed erroneously to Lyme borreliosis (Steere, 1989).

The spirochete is highly sensitive to tetracycline, but only moderately sensitive to penicillin. Other effective antibiotics include ampicillin, amoxicillin, erythromycin, ceftriaxone, and imipenem. Steroids have been used for severe carditis and arthritis. Among patients treated early in the disease, the specific antibody response usually disappears within months and patients may become reinfected in the future. Among those with late manifestations such as arthritis, titers have declined after successful treatment, but patients have remained seropositive.

Middle ear and temporal bone manifestations

Facial nerve paralysis is the most common otologic manifestation, with a reported incidence of 3% to 11% (Clark et al, 1985; Petersen et al, 1989). Paralysis may be bilateral in up to 25% of cases and affects patients of all ages and both sexes; it is seen in stage 2. The onset is acute, the duration is from weeks to a few months, and return of function is spontaneous and almost always complete. There may be a history of preceding otalgia or ipsilateral facial pain or paresthesiae (Pachner and Steere, 1985). Other neurologic features of stage 2 may sometimes, but not always, be manifest; facial nerve paralysis can occur as the sole neurologic abnormality (including normal CSF). Antibiotics and steroids do not appear to influence the duration or outcome of facial paralysis (Clark et al, 1985), but are recommended to treat concurrent symptoms and to prevent the more serious late complications. There is no role for surgery.

There have been no reports of electrophysiologic (for example, electroneurography, (ENoG)) or histopathologic (for example, temporal bone) studies of the facial nerve in Lyme disease. The cause of the paralysis and site of lesion have not been elucidated. Histology from other involved peripheral nerves shows perineural and perivascular infiltration by lymphocytes and plasma cells. In chronic and severe neuropathies, demyelination and loss of nerve fibers similar to Wallerian degeneration does occur (Duray and Steere, 1988). It is not clear whether neural lesions are the result of an inflammatory response to the spirochete or due to an immune-mediated epiphenomenon.

A well-documented otologic manifestation is an unusual skin lesion called a *lymphocytoma*; intensely red and violet nodules occur on the ear lobe in stage 2 (Steere, 1989). The lesion consists of benign but hyperplastic lymphocytic follicles in the dermis (Duray and Steere, 1988).

Auditory and vestibular manifestations such as sensorineural hearing loss, sudden hearing loss, positional vertigo, and Meniere-like symptoms have been described (Fox et al, 1990; Hanner et al, 1989; Logigian et al, 1990; Rosenhall et al, 1988). More clinical data and temporal bone studies are required to substantiate these preliminary observations.

Mycotic diseases

Fungi are ubiquitous in the environment and are of low intrinsic virulence. Systemic invasive clinical disease reflects some defect in host defenses, such as in diabetic ketoacidosis, chemotherapy for malignancy, corticosteroid therapy, or acquired immunodeficiency syndrome (AIDS). Aspergillosis, mucormycosis, candidiasis, cryptococcosis, coccidioidomycosis, and histoplasmosis are systemic mycoses that can cause disseminated disease, including involvement of the temporal bone. Diagnosis is made by biopsy and culture. Treatment consists of control of the underlying predisposing condition, surgical debridement of necrotic tissues, and systemic chemotherapy, usually with amphotericin B.

Middle ear and temporal bone manifestations

The middle ear and mastoid can be involved as a result of ascending infection along the eustachian tube and tensor tympani (often seen in mucormycosis (Fig. 163-14) or via superinfection of existing chronic otitis media (Stanley et al, 1988). Destruction of the middle ear cleft ensues, often with extension to surrounding structures, including thrombosis or rupture of the internal carotid artery (Gussen and Canalis, 1982). Other routes of infection include embolic hematogenous dissemination, which can result in multiple granulomata throughout the temporal bone, and via cryptococcal involvement of the central nervous system, which can cause invasion and degeneration of the nerve trunks in the internal auditory canal (McGill, 1978).

Neoplastic Diseases

Although neoplasms of the middle ear and temporal bone are discussed elsewhere (Chapter 192), four neoplasms - multiple myeloma, leukemia, metastatic tumors, and paraganglioma - deserve mention here because temporal bone manifestations are common or, in the case of paraganglioma, may have systemic implications.

Multiple myeloma

Multiple myeloma is a malignancy of plasma cells that are derived from B lymphocytes, the major feature of which is the demonstration of an abnormal monoclonal protein (M component) in blood, urine, or both. There is a slight male predominance and the median age of onset is 60 years. Clinical manifestations are the result of multiple plasma cell tumors and consist of severe bone pain, pathologic fractures, failure of the bone marrow, renal failure, hypercalcemia, and recurrent infections.

Laboratory findings include demonstration of the M component on serum or urine electrophoresis, normochromic, normocytic anemia, hypercalcemia, and elevated blood urea nitrogen levels. Typical radiographic findings include punched-out osteolytic lesions, particularly well seen on the lateral skull radiograph. Bone marrow aspirates show infiltration by plasma cells.

Management involves symptomatic control of complications. Chemotherapy with alkylating agents and corticosteroids is also used to control the progression of myeloma (Bergsagel et al, 1979).

Occasionally, only one plasma cell tumor, without marrow plasmacytosis, can be found. These lesions can occur in bone (*solitary bone plasmacytoma*) or soft tissue (*extramedullary plasmacytoma*), including the temporal bone. Both lesions may affect younger individuals, are associated with an M component in less than 30% of the cases, and have an indolent course with survival of 10 years or more. Local radiotherapy in a dose of 4000 cGy is usually sufficient treatment. Periodic evaluation of serum and urine globulins and a skeletal radiographic survey should be performed to detect conversion to multiple myeloma.

Middle ear and temporal bone manifestations

The temporal bone is frequently involved in multiple myeloma. Radiographs may demonstrate rounded lytic lesions of the calvarium and temporal bone (Figs. 163-15 and 163-16). At a microscopic level, the marrow spaces of the petrous bone are commonly replaced by myeloma cells, and discrete lytic bone lesions may be seen in the otic capsule (Fig. 163-17). Symptoms referable to temporal bone involvement are usually overshadowed by manifestations of diffuse disease. On occasion, however, these symptoms may be the presenting feature of myeloma (Lavine et al, 1979) or may be the only evidence of disease (plasmacytoma of the temporal bone) (Noorani, 1975).

Leukemia

Leukemic infiltrates may occur in the temporal bone. They are common in the submucosa of the pneumatized areas of the middle ear and mastoid, including the tympanic membrane (Fig. 163-18) and in the bone marrow of the petrous apex (Fig. 163-19) (Paparella et al, 1973; Zechner and Altmann, 1969). Secondary bacterial infection of the middle ear and mastoid is often seen as a result of an immunocompromised state, either due to the disease itself or due to chemotherapy. Hemorrhages commonly occur in association with infiltrates and can occur in the middle ear, mastoid, or inner ear. Clinical manifestations include middle ear effusion, acute and chronic suppuration in the middle ear and mastoid, thickening of the tympanic membrane, conductive hearing loss, sensorineural (including sudden) hearing loss, vertigo, facial paralysis, and skin lesions in the auricle or external auditory canal (Druss, 1945; Gotay, 1976).

Granulocytic sarcoma or chloroma is a localized, extramedullary tumor composed of immature myeloid cells. It is related to acute or chronic myelogenous leukemia and its appearance may precede, coincide with, or follow the diagnosis of leukemia. Such a lesion can occur in the temporal bone (Levy et al, 1989; Todd and Bowman, 1984), and otologic manifestations can constitute the initial presentation. Treatment is by local irradiation and

systemic chemotherapy.

Metastatic neoplasms

Secondary malignant tumors usually involve the temporal bone via hematogenous dissemination. The most common sites of origin, in order of decreasing frequency, are breast, lung, kidney, stomach, and larynx (Hill and Kohut, 1976). The lesions are usually destructive and osteolytic (Fig. 163-20); but some, such as from the prostate or breast, may be osteoblastic. The petrous apex and internal auditory canal appear to be sites of predilection for metastases, although any part of the temporal bone may be involved (Fig. 1630-21). The otic capsule appears to be relatively resistant to neoplastic invasion (Schuknecht et al, 1968).

Although otologic manifestations can infrequently present as the first evidence of malignant disease, more often, they are preceded by other systemic symptoms. Involvement of the external canal, middle ear cleft, or eustachian tube may cause conductive hearing loss and pain. Involvement of the otic capsule may produce sensorineural hearing loss, vertigo, and facial paralysis. In meningeal carcinomatosis, rapidly progressive unilateral or bilateral sensorineural hearing loss is a common presenting symptom (Berlinger et al, 1980). This loss may mimic a cerebellopontine angle tumor if unilateral, and immune-mediated inner ear disease if bilateral. Diagnosis is made by cytology of the CSF.

Paraganglioma (glomus tumor)

The symptoms and evaluation of paragangliomas of the ear and adjacent skull base are present elsewhere (Chapter 192). However, up to 10% of patients with nonfamilial paragangliomas in the head and neck will have at least one additional lesion (Alford and Guilford, 1962; Spector et al, 1975). Among patients with a hereditary tendency for developing paragangliomas, multiple tumors will be found in up to 35% (Bogdasarian and Lotz, 1979; Cook, 1977; Rush, 1963).

The possibility of multiple tumors, therefore, should be considered in the radiographic evaluation of such tumors. During transfemoral carotid arteriography, the opposite carotid circulation can be evaluated quickly for contralateral tumor. Digital subtraction angiography and radionuclide scintiangiography may be used as a noninvasive screening and surveillance methods (Veldman et al, 1980).

A few paragangliomas, both benign and malignant, may secrete catecholamine in clinically significant amounts (Farrior et al, 1980; McGuirt and Harker, 1975; Seda and Snow, 1972; Strauss et al, 1983). A history of headaches, hypertension, and flushing should alert the clinician to the possibility of catecholamine secretion, which can be evaluated by a 24-hour urine collection for vanillylmandelic acid, metanephrine, and 5-hydroxyindolacetic acid.

Diseases of Bone

Several generalized diseases of bone affect the middle ear and temporal bone, and occasionally the initial symptoms of the disease will occur in the temporal bone. Paget's disease, osteogenesis imperfecta, and osteopetrosis can sometimes mimic the features of otosclerosis.

Paget's disease (osteitis deformans)

Paget's disease of bone is a chronic, sometimes progressive disease of unknown etiology characterized by osteolytic and osteoblastic changes mainly affecting the axial skeleton. It is genetically influenced, but it is not known whether the gene is autosomal dominant or X-linked.

Paget's disease affects 3% of the population over 40 years of age and as much as 11% over 80 years (Davies, 1968). Men are affected more commonly than women. The onset of clinical manifestations, including enlarging skull, progressive kyphosis, and deformities of the pelvis, femur, and tibia, is usually in the sixth decade. Radiographic findings (Figs. 163-22 and 163-23) include a thickened skull table, patchy, ill-defined densities of the skull, and poor definition of the cortical margins of the inner ear and internal auditory canal, particularly in the lytic phase of the disease.

The etiology is uncertain; endocrine, metabolic, vascular, autoimmune, and neoplastic causes have been postulated, but without convincing evidence. Recent electron microscopic and immunohistochemical studies indicate that it may be caused by a slow virus infection (Mills and Singer, 1976; Mirra, 1987), perhaps with an underlying genetic predisposition.

Middle ear and temporal bone manifestations

The histopathologic appearance of pagetic bone is somewhat variable, depending on the relative osteoclastic and osteoblastic activity. Typical findings include osteoclastic resorption of marrow-containing bone, with an increase in vascularity and formation of fibrous tissue. New bone formation occurs in an irregular manner, producing the typical mosaic pattern because of irregular and curved cement lines (Fig. 163024). Pagetic bone changes occur in three phases, with an initial osteolytic phase, a mixed (or combined) phase, and then an osteoblastic, or "burnt-out", phase. In the temporal bone, a fourth phase can be identified, that of remodeling of inactive pagetic bone into normal-appearing lamellar bone (Khetarpal and Schuknecht, 1990). The disease usually begins in periosteal bone and then extends to involve enchondral and endosteal bone.

Clinical manifestations include hearing loss, tinnitus, and mild vestibular dysfunction. The facial nerve is spared. Hearing loss occurs in 5% to 44% of cases (Davies, 1968) and may be sensorineural, mixed, or, rarely, only conductive. Most often, it is a mixed loss with a descending pattern for bone conduction and relatively flat air conduction thresholds. The losses are progressive and greater than those of age-matched control subjects. Distinguishing features of Paget's disease (when compared with otosclerosis, the most common differential diagnosis) include a later age of onset (sixth decade), greater sensorineural hearing loss (with a descending pattern), an enlarged calvarium, enlargement and tortuosity of the superficial temporal artery and its anterior branches (Davies, 1968), elevated serum alkaline phosphatase, and radiographic evidence of pagetic changes in the temporal bones. Numerous clinical and histologic studies have been reported, but none have clearly identified a consistent pathologic basis for these hearing losses (Khetarpal and Schuknecht, 1990); specifically, conductive loss is not caused by ossicular chain fixation, and sensorineural hearing loss is not caused by compression of cochlear nerve fibers. Hence, attempts at surgical correction of conductive loss is not generally considered worthwhile.

Osteogenesis imperfecta (van der Hoeve-deKleyn syndrome)

Osteogenesis imperfecta (OI) is a genetically determined disorder of connective tissue that is characterized clinically by fragile bones that break with minor trauma. The older terms osteogenesis imperfecta *congenita* and *tarda* have been replaced by a classification system (OI types I to IV) based on clinical features, radiologic criteria, and mode of inheritance (Rowe, 1988). OI type I, the mildest form, has an autosomal dominant mode of inheritance and is associated with blue sclerae, nondeforming fractures, and normal stature. Hearing loss is common and is estimated to occur in about 50%. OI type II is the most severe form, with multiple fractures occurring in utero, often resulting in stillbirth. This type is usually acquired as a sporadic new mutation but can also be autosomal recessive. OI type III is characterized by multiple fractures, progressive bone deformity during childhood and adolescence, and gray (normal) sclerae. Hearing loss occurs, but its incidence is unknown. The long bones may be slender and bowed with abrupt widening near epiphyses. Kyphoscoliosis, pectus excavatum, weak joints, dental abnormalities, and wormian bone in the skull table are common (Figs. 163-25 and 163-26). The mode of inheritance varies and may be autosomal dominant, autosomal recessive, or due to a new mutation. OI type IV is a dominantly inherited form, similar to type I except that the sclerae are gray (normal). Hearing loss is less common than in type I.

Middle ear and temporal bone manifestations

Both conductive and sensorineural hearing loss occur in osteogenesis imperfecta. Severe sensorineural hearing loss is estimated to occur in approximately 40% of patients and has a high correlation with gray or white sclerae.

Conductive hearing loss usually accompanies blue sclerae, first becoming apparent by ages 20 to 25, and is severe enough to cause the patient to seek medical attention 15 to 20 years later, by the early 40s (Armstrong, 1984). There is no relationship between hearing loss and frequency or severity of fractures (Morrison, 1979). Some patients with a mild form of the disease present with conductive hearing loss similar to otosclerosis. An early age of onset of hearing loss, very high compliance values on tympanometry (Morrison, 1979), a history of fractures after minor trauma in childhood that ceased after puberty, a family history of osteogenesis imperfecta, and blue sclerae are helpful diagnostic clues.

The conductive loss reflects structural changes in the ossicles. Microfractures of the manubrium (Berger et al, 1985), fragility of the long process of the incus, and fracture or resorption of the crurae of the stapes have been reported (Armstrong, 1984; Nager, 1988; Zajtchuk and Lindsay, 1975). The stapedial footplate is typically described as thick, soft and chalklike or granular and is usually, but not always, fixed (Patterson and Stone, 1970). An abnormally thick endosteum has also been observed. A few patients have coexistent otosclerotic foci as the cause of their conductive hearing loss (Armstrong, 1984; Nager, 1988, Sando et al, 1981; Zajtchuk and Lindsay, 1975). Rehabilitation can be accomplished by amplification or surgery. A stapedectomy can produce similar results to those achieved to treat otosclerosis, but the procedure is extremely delicate. Other important surgical findings in some patients include increased vascularity and softening of the bone of the tympanic sulcus. Crimping the prosthesis around the incus may cause a pathologic fracture, and a platinum ribbon is preferred to stainless steel wire (Armstrong, 1984).

The histopathology of osteogenesis imperfecta demonstrates that cortical bone consists of a thin, spongy layer with small and irregular spicules of bone. The osteoid matrix seems to be decreased. The underlying disorder has been shown to be a defect in the biosynthesis of type I collagen (Rowe, 1988). In the temporal bone, the enchondral and periosteal layers of the otic capsule show finely trabeculated, feathery-appearing bone with an abnormal amount of fibrous tissue and vascular spaces (Figs. 163-27 and 163-28). The endosteal layer remains intact, as does the cochlear and vestibular labyrinth.

Fibrous dysplasia

Fibrous dysplasia is a benign, chronic, slowly progressive bone disorder of unknown etiology characterized by replacement of normal bone by a variable amount of fibrous tissue and woven bone. It is not heritable. It may occur as part of Albright's syndrome, characterized by multiple bone lesions, abnormal pigmentation, endocrine dysfunction, and precocious puberty in females; or it may exist alone either as the monostotic or polyostotic form. The monostotic form is the most common and usually occurs in the skull, ribs, proximal femur, or tibia. In the polyostotic form skull lesions are seen in over 50% of patients.

Clinical manifestations of fibrous dysplasia include bony deformity, pathologic fractures, and cranial nerve palsies. The disease starts early in life, usually in childhood; the monostotic form usually comes to an arrest at puberty, whereas the polyostotic form can continue to progress. Sarcomatous transformation can occur with an estimated incidence of 0.4% (Schwartz and Alpert, 1964). Laboratory findings include elevated serum alkaline phosphatase in 30% of patients with polyostotic fibrous dysplasia, whereas serum calcium and phosphorus levels are usually normal. The typical radiographic findings include a radiolucent area with a well-defined, smooth or scalloped edge and a "ground-glass" appearance. Areas of increased radiodensity may also occur (Figs. 163-29 and 163-30).

The histopathology of fibrous dysplasia consists of replacement of normal cancellous bone by a fibrous stroma arranged in a whorled pattern. A variable amount of irregularly arranged spicules of woven bone cause the ground-glass radiographic changes (Fig. 163-31).

Middle ear and temporal bone manifestations

While reviewing the world literature of fibrous dysplasia affecting the temporal bone, Nager found 69 reported cases and added 4 more (Nager et al, 1982; Nager and Holliday, 1984). The temporal bone occasionally may be the site of monostotic or polyostotic disease. All parts can be involved, but the process generally begins as a painless, slowly progressive swelling involving the mastoid or squama. Progressive narrowing of the external auditory canal with conductive hearing loss is a frequent manifestation. This may be mistaken for exostoses, but fibrous dysplasia is encountered early in life during the second or third decade; and at surgery, it is vascular with a characteristic soft, spongy, and gritty consistency. Entrapment of keratin debris medial to a stenotic canal can cause an external canal cholesteatoma. Involvement of the middle ear and ossicles or obstruction of the eustachian tube can also cause conductive hearing loss. Erosion of the fallopian canal with facial nerve paralysis or of the otic capsule with sensorineural hearing loss and vertigo are seen occasionally. An isolated lesion of the mesotympanic bone can stimulate a glomus tympanicum tumor and present as a reddish mass behind an intact tympanic membrane with

pulsatile tinnitus and hearing loss.

The treatment of fibrous dysplasia is symptomatic. Operative procedures should be limited to biopsy and relief of functional deficits. Stenosis of the external canal often requires surgical removal with canalplasty and meatoplasty. Restenosis as a result of regrowth of fibrous dysplasia does occur, and multiple procedures are sometimes needed. Radiotherapy is contraindicated because of an increased rate of malignant degeneration (Schwartz and Alpert, 1964).

Osteopetrosis (Albers-Schönberg disease, Marble bone disease)

Osteopetrosis is a rare, generalized dysplasia of bone inherited as either an autosomal dominant or recessive disorder and characterized by greatly increased bone density. It results from defective osteoclast function with failure of normal bone resorption, while normal bone formation by osteoblasts continues and results in the deposition of excessive mineralized osteoid and cartilage.

The autosomal recessive form (osteopetrosis congenita) is rapidly progressive, with encroachment of bone marrow leading to anemia, thrombocytopenia, hepatosplenomegaly, increased susceptibility to infection, and encroachment of neural foramina causing neural atrophy. Optic atrophy, facial paralysis, sensorineural hearing loss, hydrocephalus, and mental retardation are common, and death usually occurs by the second decade. Bone marrow transplantation has been used successfully with reversal of anemia and regression of osteosclerosis (Coccia et al, 1980).

The autosomal dominant form (osteopetrosis tarda) is associated with normal life expectancy and may be asymptomatic. Clinical manifestations include an increased incidence of fractures (the osteopetrotic bone is fragile despite its solid appearance), osteomyelitis of the mandible from dental infection, progressive enlargement of the head and mandible, and clubbing of long bones. Cranial neuropathies, such as progressive optic atrophy, trigeminal hypesthesia, recurrent facial paralysis, and sensorineural hearing loss may also occur. Syndactyly and abnormal finger nails can occur and aid in making the clinical diagnosis. Radiographic evaluation reveals a great increase in density of all bones. The serum acid phosphatase level is increased in some patients.

Middle ear and temporal bone manifestations

The enchondral layer of the otic capsule and ossicles in temporal bones of infants and children suffering from the recessive form of the disease consists mainly of dense calcified cartilage (Myers and Stool, 1969). The mastoid is nonpneumatized, and the stapes persists in fetal form (Figs. 163-23 and 163-33). The inner ears appear normal. Dehiscence of the tympanic segment of the facial nerve, often with herniation of the nerve into the oval window niche, has been a consistent finding (Hawke et al, 1981; Myers and Stool, 1969; Suga and Lindsay, 1976). However, there appears to be no observable compression of the nerve. These children often suffer from recurrent episodes of acute otitis media, serous otitis media, conductive or sensorineural hearing loss, and unilateral or bilateral facial nerve paralysis (Wong et al, 1978).

In the more benign adult form, the temporal bone is markedly sclerotic with obliteration of the mastoid air cells and narrowing of the eustachian tube and external and internal auditory canals. Exostotic overgrowth of the periosteal bone surrounding the tympanic cavity can occur (Fig. 163-24), with ankylosis of the ossicles and obliteration of the oval and round window niches (Fig. 163-35). These changes explain the common finding of conductive hearing loss. Sensorineural hearing loss also occurs, but the inner ears appear normal. Narrowing of the eustachian tube predisposes to serous otitis media (Milroy and Michaels, 1990). Recurrent acute facial nerve paralysis, similar to Bell's palsy, involving one or both sides is a frequent manifestation. There is a tendency toward progressive residual weakness with each episode. Radiographic studies should be performed in any child or young adult with recurrent facial nerve paralysis to determine the possibility of osteopetrosis. Total decompression of the facial nerve has been advocated to ameliorate recurrent palsies (Hamersma, 1973).

Osteitis fibrosa cystica (von Recklinghausen's disease of bone)

Osteitis fibrosa cystica is a bone lesion caused by excess parathormone and is characterized in classic cases by osteoclastic resorption of bone, fibrosis of marrow, bone cysts, bone pain, and fractures. It is caused, in most cases, by primary hyperparathyroidism, which is usually due to an adenoma. Other manifestations relate to hypercalcemia and hypercalciuria.

Affection of the temporal bone in this disorder can occur (Lindsay and Suga, 1976; Rüedi, 1968) but is very rare in clinical practice. The otic capsule is related by abnormal bone made up of loosely arranged trabeculae of varying size and shape interspersed with marrow spaces containing fibrous tissue. Sensorineural hearing loss has been attributed to osteitis fibrosa involving the temporal bone.

Storage Diseases

Mucopolysaccharidoses

The mucopolysaccharidoses (MPS) are a group of diseases caused by an inherited deficiency of one of several lysosomal enzymes that degrade mucopolysaccharides. As a result, undergraded mucopolysaccharides accumulate intracellularly, giving rise to large cells with vacuolated cytoplasm. Ten enzyme deficiencies have been identified and are classified into seven types or syndromes. They are all transmitted as autosomal recessive traits except for Hunter's syndrome (MPS II), which is X-linked recessive. Diagnosis is made by assay of the specific enzyme in plasma or serum, or in tissue culture using fibroblasts or leukocytes. Management is mainly supportive and symptomatic. However, the MPS are potentially amenable to enzyme replacement therapy by procedures such as bone marrow transplantation or gene transfer (Neufeld and Muenzer, 1989).

Hurler's syndrome (MPS IH) is caused by deficiency of alpha-L-iduronidase leading to accumulation of heparan sulfate and dermatan sulfate. Clinical manifestations include corneal clouding, abnormal facies, hepatosplenomegaly, mental retardation, dysostosis multiplex, stiffness of joints, and hernias.

Radiographic features include broadening and shortening of long bones, hypoplasia and fractures of lumbar vertebrae causing kyphosis, and enlargement of the sella turcica. Death usually occurs in the first decade.

Hunter's syndrome (MPS II) results from deficiency of iduronate sulfatase leading to accumulation of heparin sulfate and dermatan sulfate. The syndrome is similar to Hurler's, but corneal clouding is not seen. Survival to adulthood may occur.

Morquio's syndrome (MPS IV) is attributable to a deficiency of N-acetylgalactosamine 6-sulfatase or of beta-galactosidase. Clinical manifestations include spondyloepiphyseal dysplasia. Spinal cord compression caused by hypoplasia of the odontoid process and cervical dislocation is common and may be the cause of death.

Middle ear and temporal bone manifestations

Hearing loss in the MPS is usually both conductive and sensorineural. The conductive component is attributable to serous otitis media secondary to dysfunction of the eustachian tube and chronic thickening of the mucosa of the middle ear (Fig. 163-26). Unresorbed mesenchyme has been described in the middle ear and mastoid in Hurler's syndrome (Schachern et al, 1984). Large cells with vacuolated cytoplasm have been described in the middle ear mucosa in Hunter's (Zechner and Altmann, 1968) and Hurler's (Friedmann et al, 1985) syndromes. The cause of the sensorineural hearing loss is unknown but has been attributed to abnormal metabolism within neural elements (Friedmann et al, 1985; Wolff, 1942; Zechner and Altmann, 1968).

Collagen Vascular and Autoimmune Diseases

The ear may be a target organ in several systemic (non-organ specific) diseases thought to be "autoimmune" in nature (such as polyarteritis nodosa, relapsing polychondritis, Cogan's syndrome, see box on p. 2907), or it may be the sole target in an immune-mediated (organ-specific) inner ear process that causes progressive sensorineural hearing loss with or without vestibular dysfunction. The latter kind was first described by McCabe (1979), although the theoretical concept was first espoused by Lehnhardt in 1958 (Lehnhardt, 1986). Histopathologic findings in the temporal bone in both groups of disorders are similar and include destruction and degeneration of the inner ear tissues, scattered infiltrates of lymphocytes, plasma cells and macrophages, focal or diffuse proliferation of fibrous tissue and bone, and a variable degree of endolymphatic hydrops (Schuknecht, 1991). The otologic manifestations of these diseases are discussed in Chapter 164, and by Stephens et al (1982).

Immunodeficiency Disorders

Infections of the middle ear and mastoid can occur as part of the clinical spectrum of both congenital and acquired immunodeficiency disorders, and, occasionally, otologic manifestations may constitute the presenting feature of the disease.

Primary or congenital immunodeficiency disorders

These disorders comprise a diverse group of conditions that can be subdivided into four broad categories.

Humoral immune deficiency disorders are characterized by an inability to produce antigen-specific antibodies. Patients commonly suffer from recurrent and chronic respiratory infections due to high-grade extracellular bacteria such as *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Streptococcus pyogenes*. Diagnosis is based on analysis of immunoglobulin subtypes and assessment of specific antibody production. Treatment is symptomatic with appropriate antibiotics, as well as replacement therapy with immune human serum globulin. Individual syndromes within the group are classified according to the type of immunoglobulin deficiency, mode of genetic transmission, and specific clinical features and include X-linked infantile agammaglobulinaemia (Bruton's), autosomal recessive agammaglobulinemia, acquired agammaglobulinemia (common variable immunodeficiency), X-linked immunodeficiency with Hyper-IgM, and selective IgA deficiency.

Cellular immune deficiency disorders demonstrate partial or severe deficiencies in functioning of T lymphocytes, and patients typically suffer from recurrent infections due to intracellular, low-grade, opportunistic pathogens such as viruses, fungi, protozoa, and some bacteria. Diagnosis is based on quantitative and qualitative tests of T-cell function. There is often an associated deficiency of antibody production. Syndromes include thymic hypoplasia (DiGeorge syndrome), Wiskott-Aldrich syndrome, ataxia-telangiectasia, chronic mucocutaneous candidiasis, hyperimmunoglobulinemia E (Job's syndrome), and severe combined immunodeficiency.

Disorders of phagocyte function are primarily disorders of neutrophils that leave patients vulnerable to pyogenic bacterial or fungal infections of varying severity and chronicity. This group includes neutropenia, which may be inherited or acquired, and if severe can cause fulminant sepsis; chemotactic defects resulting in pyogenic respiratory infections; and microbicidal disorders such as chronic granulomatous disease and Chédiak-Higashi syndrome. Therapy includes antibiotics, neutrophil transfusions, and bone marrow transplantation.

Complement system defects include deficiencies of the individual components or of the regulatory proteins. Clinical features vary with the type of defect and include recurrent *Neisseria* infections (C5, C6, C7, and C9 deficiency), recurrent staphylococcal infections (C3b inactivator deficiency), lupuslike syndromes (C1, C4, and C2 deficiency), and angioedema (C1 esterase inhibitor deficiency). All complement defects are inherited (generally autosomal recessive); treatment is symptomatic and supportive.

Middle ear and temporal bone manifestations

Otologic disease has been described in all four categories of immune deficiency disorders. Humoral immune defects result in recurrent and persistent acute and serous otitis media. Chronic suppurative otitis media (with all its attendant complications) may develop and is often refractory to medical and surgical therapy (Harris and South, 1982; Sasaki et al, 1981). A subgroup consists of children with selective IgG subclass 2 deficiency who have

been shown to be susceptible to recurrent episodes of otitis media (Oxelius, 1984). DiGeorges syndrome (T-cell deficiency due to thymic hypoplasia) can manifest varying degrees of anomalies of the external, middle, and inner ears with conductive, sensorineural, or mixed hearing losses (Ohtani and Schuknecht, 1984). There is also a high incidence of Mondini dysplasia in these ears. Recurrent episodes of acute otitis media and chronic otitis media have also been described in neutrophil chemotactic defects (Hill et al, 1977), microbicidal disorders (chronic granulomatous disease (Blayney and Bunch, 1984), and complement system defects (Alper et al, 1970).

Acquired immunodeficiency syndrome

AIDS, first recognized in 1981, is caused by the human immunodeficiency virus (HIV). The virus is lymphotropic and attacks primarily T-helper lymphocytes, rendering the patient susceptible to numerous opportunistic infections (Chapter 15).

Middle ear and temporal bone manifestations

Otologic manifestations are infrequent in patients with AIDS, except in the pediatric age group where serous otitis media is common (Smith and Canalis, 1989). When otologic disease does occur, the microbiology is similar to that of the non-AIDS population, with the addition of unusual opportunistic organisms (protozoa, fungi, viruses, and mycobacteria).

Middle ear and mastoid manifestations include acute otitis media, acute mastoiditis, serous otitis media, and bullous myringitis. These infections are of varying severity, depending on the immune status of the patient. External ear disease such as otitis externa and Kaposi's sarcoma can also occur. Tissue diagnosis by biopsy or tympanocentesis is indicated in identifying the causative agent before initiating therapy.

Pneumocystis carinii is an unusual opportunistic protozoan that is a common cause of middle and external ear disease in AIDS. Subcutaneous masses in the external canal or aural polyps arising from the canal, tympanic membrane, or mesotympanum can occur, resulting in conductive hearing loss, otorrhea, and otalgia. Presumed routes of infection include hematogenous spread from another source (for example, pulmonary), ascending infection via the eustachian tube from pharyngeal colonization, or airborne transmission of the aerosolized organism directly to the external canal (Breda et al, 1988; Gherman et al, 1988). Biopsy shows the characteristic organism. The infection responds to treatment with oral trimethoprim-sulfamethoxazole. It is noteworthy that otologic disease due to *P. carinii* may be the only and initial presenting symptom of AIDS (Breda et al, 1988; Gherman et al, 1988; Kohan et al, 1988).

Inner ear symptoms such as sensorineural hearing loss, (including fluctuating and sudden hearing loss), vertigo, and tinnitus can occur. Sensorineural hearing loss is ascribed to a variety of causes including otosyphilis, cryptococcal meningitis, tuberculous meningitis, CNS toxoplasmosis, and ototoxic medication (Kohan et al, 1988). It is interesting to note that the HIV is neurotrophic and may possibly itself be the primary cause of sensorineural hearing loss. The facial nerve can be involved by herpes zoster (Ramsay Hunt syndrome). The spectrum of otologic manifestations and their pathophysiologic mechanisms in AIDS will undoubtedly expand as more clinical and histopathologic data is accrued.