Introduction

Labyrinthitis is a generalized term referring to an inflammatory process that involves the inner ear. This process may be circumscribed, or limited, to one part of the labyrinth, such as the bony vs. membranous labyrinth or the cochlea vs. vestibular organs. Conversely, it may diffusely and uniformly affect all of the inner ear structures. The etiology of otitis interna can be broadly categorized as infective or noninfective. The non-infectious inflammatory reactions such as autoimmune labyrinthitis will not be covered in this discussion. The infective causes of labyrinthitis are what this grand rounds will focus on and include bacterial, viral, protozoal and fungal invasion of the inner ear. Infection may occur in utero thereby producing a congenital abnormality present in the immediate postnatal period or infection may be acquired with presentation at any age. Labyrinthitis may be an isolated process involving only the inner ear, or it could be just one manifestation of a systemic infection.

Pathogenesis

Infection of the labyrinth occurs via spread of the pathogenic organism through one of three pathways--the meninges, the middle ear space, or the bloodstream. Meningogenic labyrinthitis occurs through either the internal auditory canal (IAC), the cochlear aqueduct, or both. This mechanism of spread appears to be more common in the pediatric population. This may be related to both immunologic and anatomical factors. The immature immune system of the infant is ill equipped to prevent spread from a meningo-encephalitis to the nearby inner ear. The anatomical factor relates to patency of the cochlear aqueduct, which decreases with age. It is estimated that the cochlear aqueduct remains patent in only 30% of the population over 60 years of age. In contrast, as many as 82% of children less than 16 years old will have an open aqueduct. Post-mortem temporal bone studies in both animals and humans have demonstrated invasion of leukocytes and bacteria through the subarachnoid space in the IAC and along perineural and perivascular spaces following the eighth cranial nerve. The ganglion canal and modiolar spaces also become involved with eventual penetration of the perilymphatic scalae. Additionally, marked inflammation and fibrosis was found to involve the cochlear aqueduct and that region of the scala tympani adjacent to the cochlear aqueduct.

Tympanogenic labyrinthitis results from extension of infection from the middle ear, mastoid air cells, or petrous apex. The most commonly reported of these is otitis interna following an acute or chronic otitis media via passage of infection through the round or oval windows. Both human
and animal studies have indicated that the round window is much more significant in this pathologic process. The round window membrane, like the tympanic membrane, consists of three layers. The outer epithelial layer is contiguous with the lining of the middle ear and consists of a single layer of primarily nonciliated squamous cells. The middle layer lies beneath a basement membrane and is made up of fibroblasts, nerve cells, granulated cells, collagen and elastic fibers and large intercellular spaces. Long thin cells with cytoplasmic processes make up the inner layer and there is no basement membrane between the middle and inner layers. The large intercellular spaces are the hypothesized route of spread from the middle to the inner ear. Temporal bone studies have demonstrated thickening of the round window membrane with inflammatory cell infiltration and formation of serofibrinous precipitate in the perilymph adjacent to the round window. Tympanogenic labyrinthitis may also occur in association with cholesteatoma causing bony erosion and penetration of the perilymphatic spaces. This process most commonly involves the horizontal semicircular canal.

Hematogenic labyrinthitis involves a seeding of the inner ear spaces from pathogens in the bloodstream. This is the least commonly documented route of spread to the labyrinth.

**Bacterial Infections**

Two types of labyrinthitis are associated with bacterial infection of the temporal bone--toxic and suppurative labyrinthitis. Toxic labyrinthitis is a sterile inflammation of the inner ear seen with acute or chronic otitis media and early bacterial meningitis. Bacterial toxins penetrate the round window, IAC or cochlear aqueduct and cause an inflammatory reaction in the perilymphatic space. This condition typically produces mild high frequency hearing loss or, less commonly, mild vestibular dysfunction. Early recognition and treatment of the precipitating otitis media or meningitis with appropriate antibiotics and possibly myringotomy usually leads to resolution of the otitis interna with no permanent sequelae.

Suppurative labyrinthitis involves direct bacterial invasion of the inner ear. This can occur in association with bacterial otitis media or meningitis. Meningogenic labyrinthitis often produces bilateral symptoms while tympanogenic labyrinthitis is unilateral. The inflammation typically involves both the cochlea and vestibular organs. Four pathologic stages have been identified along which an episode of suppurative otitis interna typically progresses. The serous or irritative stage is characterized by the production of immunoglobulin rich exudate within the perilymph. This leads to biochemical changes in the fluids and likely alters the endocochlear potential that exists between the perilymph and endolymph. The second, acute, or purulent stage involves bacterial and leukocyte invasion of the perilymphatic scala. Progression of exudate formation with high protein content further alters fluids in the inner ear and predisposes to the formation of hydrops. Blood vessel dilation and thrombosis as well as end organ degeneration and necrosis are seen in this stage. The fibrous or latent stage follows with the proliferation of fibroblasts and granulation tissue within the perilymph. Finally, the osseous or sclerotic stage occurs and involves new bone deposition throughout the involved labyrinth. Fibrous changes in the labyrinth may be seen within 2 weeks post-infection and the process of bony obliteration may begin as early as 2 months after onset of illness.

Purulent labyrinthitis is a medical emergency warranting prompt evaluation and institution of treatment. These patients are obviously ill, have severe vertigo with nausea and vomiting, and profound hearing loss. Symptoms of associated meningitis (nuchal rigidity, headache, altered mental status) or otitis media (otalgia, otorrhea) should be sought during the evaluation. Appropriate management includes hospitalization, hydration, vestibular suppressants, and parenteral antibiotics with an agent with good CSF penetration. Patients with signs of meningeal inflammation should undergo lumbar puncture and culture of CSF to identify the causative agent and direct antibiotic therapy. Patients presenting with associated acute otitis media benefit from
myringotomy to facilitate adequate drainage of the infection. Chronic otitis media, with or without cholesteatoma, may necessitate mastoid surgery. Most often this is undertaken if there is minimal improvement after 24-48 hours of appropriate antibiotic therapy or if signs of meningitis develop in a patient who did not have these signs at presentation.

Bacterial Meningitis

The incidence of postmeningitic hearing loss reported in the literature generally varies between 10-20%. The most common pathogens causing bacterial meningitis are the encapsulated organisms H. influenzae type B, N. meningitidis, and S. pneumoniae. These three organisms account for about 80% of cases of bacterial meningitis worldwide. Prior to the development of the Hib vaccine, H. influenzae was the most prevalent among the three, causing 70% of infections, while N. meningitidis was associated with only 20% and S. pneumoniae 13%. A study in 1995 revealed a significant reduction (55% decrease) in the overall number of cases of bacterial meningitis and a shift in the predominant causative agent to pneumococcus (47%) with N. meningitidis in second place (31%).

The hearing loss caused by meningogenic labyrinthitis seems to occur early in the illness. This loss may be recognized during the acute infection or not until months or years after the event, especially in prelingual children or those who suffer other post-meningitic neurologic sequelae. Hearing loss is most often bilateral, severe to profound, and permanent. Small numbers of patients have been found to have fluctuation, improvement, or progression of their hearing loss over time. Treatment in the acute phase of the illness includes antibiotic coverage of the infecting agent. Some studies have shown a beneficial effect of steroid therapy with bacterial meningitis in reducing the incidence of post-meningitic hearing loss.

Accurate audiologic diagnosis is essential in these patients and begins during the acute infection if possible. Optimally, individual ear testing of the full range of frequencies is obtained. If this is not possible, or not feasible for the patients age, testing should begin with ABR. Patients who exhibit normal ABR early in the course of meningitis, after institution of antibiotic therapy, are unlikely to have subsequent deterioration but should still have a follow up behavioral audiogram. Abnormal ABR testing necessitates behavioral audio as soon as possible to confirm the findings. Persistently abnormal audiogram findings warrant follow up testing every three months until thresholds are stabilized. Patients who are left with a severe to profound loss at this time should be evaluated for amplification.

Syphilis

Labyrinthine involvement may be seen with both congenital and acquired syphilis. Transplacental transmission of Treponema pallidum results in congenital syphilis, which may be apparent at birth (infantile form), or may not manifest until later in life (tardive form). Vertical transmission is most likely to occur with primary maternal infection, which carries a 70-100% transmission rate. Early congenital syphilis is associated with a high fetal and infant mortality rate and systemic symptoms that outweigh vestibulocochlear symptoms. Late congenital syphilis may present as a sudden sensorineural hearing loss (SNHL), often in association with vestibular symptoms. It is estimated that about 37% of cases will demonstrate a SNHL by age 10, 51% between 25-35 years old, and 12% after age 35. Audiologic findings in early congenital syphilis are a symmetrical, profound, flat SNHL. Conversely, the SNHL of late congenital syphilis may be asymmetric, fluctuating, or progressive and is associated with low speech discrimination scores out of proportion to the pure tone average. Acquired syphilis may present with SNHL, most often in association with secondary or tertiary disease. Its presentation is similar to that of late congenital syphilis. Additional findings may include Hennebert's or Tulio's sign, abnormal ABR.
with increased interpeak latency and diminished wave V, or an abnormal ENG indicating a peripheral vestibular disorder and/or unilateral weakness.

Diagnosis of T. pallidum infection is with serologic testing of non-specific (RPR, VDRL) and specific (FTA-ABS) antibodies. Confirmation of a positive screening test can then be performed using a T. pallidum specific microhemagglutination assay or western blot assay to detect IgG and IgM.

High dose parenteral penicillin is the treatment of choice for otosyphilis. Duration of therapy is dictated by the stage of illness. Primary acquired syphilis may be adequately treated with a one-time dose of 2.4 million units of Penicillin G. Alternatively, the replication time of T. pallidum in late congenital syphilis may be as long as 90 days thereby necessitating antibiotic therapy for at least 3 months. The addition of systemic steroids has been shown to have a beneficial effect. In particular, speech discrimination scores improved in 50% of cases with syphilitic hearing loss treated with steroids. Alternate-day, long-term maintenance steroid therapy may sustain this improvement.

The histopathology of the temporal bone in congenital and acquired syphilis is essentially identical. Early congenital and acute secondary and tertiary syphilis are characterized by a meningo-neuro-labyrinthitis. This process involves round cell invasion of CN VIII, with resultant degeneration of the organ of Corti, spiral ganglion, and nerve fibers. Round cell infiltration of the labyrinth leads to deposition of fibrinous exudate and hemorrhage. Late congenital and late latent or tertiary syphilis demonstrates an obliterative endarteritis, gumma formation, and a round cell osteitis of the otic capsule and ossicles.

Viral Infections

Viral labyrinthitis may occur in one of three presentations: 1) congenital infection, 2) as part of a systemic viral illness, or 3) as isolated involvement of the inner ear. Acquired viral infection of the labyrinth, whether isolated or systemic, most often presents with sudden sensorineural hearing loss or vestibular neuritis. Much of the evidence linking viral agents to labyrinthitis is circumstantial, as it is very difficult to prove a causal relationship with this illness. Definitive causality is established by fulfilling Koch's three postulates. First, there must be a clinical association between a specific infectious agent and a distinct inner ear disease. Second, the infectious agent must be identified in or isolated from the affected labyrinth. And third, a similar disease is seen in experimental animals infected with the agent. These criteria have been met only with CMV and mumps labyrinthitis. Based on circumstantial evidence, such as an association with viral upper respiratory infection or seroconversion to acute stage antibody production, numerous other viruses have been implicated in labyrinthine infections. These suspect pathogens include rubella, rubeola, influenza, varicella-zoster, EBV, poliovirus, RSV, adenovirus, parainfluenza, and herpes simplex viruses.

Cytomegalovirus

Cytomegalovirus (CMV) is the most common congenital infection in the United States and is thought to be the most common infectious cause of congenital deafness. Approximately 1% of all live births demonstrate CMV infection, which translates to 30-40,000 infected newborns annually. It is estimated that 6,000-8,000 of these infants will demonstrate CMV related disabilities at some point in their lifetime. Specifically, about 4,000 cases of sensorineural hearing loss are attributed to CMV infection annually. Fetal or neonatal CMV infection may occur via transplacental transmission, passage through an infected birth canal, or ingestion of infected breast milk. Intrauterine fetal infection most often occurs after primary infection in a previously seronegative mother. These women have a 40% transmission rate of infection to the fetus.
Additionally, fetal infection has been demonstrated in "immune" or seropositive mothers with a transmission rate between .15 and 1.0%.

The majority of congenital CMV infections are asymptomatic (90%). The remaining 10% will demonstrate some symptoms of infection during the neonatal period. Of this symptomatic 10%, 90% will demonstrate the typical cytomegalic inclusion disease (CID) of the newborn. Low birthweight, jaundice, hepatosplenomegaly, petechiae or purpura, microcephaly, and psychomotor retardation characterize CID. As many as 65% of these children will manifest sensorineural hearing loss (SNHL) which is most often bilateral and severe to profound. Infants with asymptomatic CMV at birth develop varying degrees of SNHL in 10-15% of cases. Risk factors for late development of SNHL include periventricular calcifications or significantly elevated maternal antibody titers throughout pregnancy.

The diagnosis of congenital CMV can be made by isolating the virus from urine culture obtained in the first few weeks of life. Alternatively, umbilical cord blood or infant serum can be tested for anti-CMV IgM antibodies. Antepartum diagnosis may be possible by viral isolation from amniotic fluid culture.

Currently there is not an established regimen to either prevent maternal primary infection or treat congenital infection. Trials with acyclovir in symptomatic children have shown a decrease in viral shedding in the urine but have demonstrated no beneficial effect in terms of clinical improvement. Gancyclovir and foscarnet are newer drugs shown to have anti-CMV effects but there are no studies for their use in congenital infection to date. Attempts to develop a CMV vaccine are underway. Trials with live-attenuated virus have shown both humoral and cellular immunity induction. Concerns over the potential for latent infection with live virus as well as failure to produce long-term immunity has precluded widespread use of this vaccine. An alternative vaccine utilizing viral envelope glycoproteins as antigens has shown positive results in preliminary studies.

Histopathologic studies of the temporal bones of infected infants revealed characteristic CMV inclusions in cells of the stria vascularis and epithelial cells of the endolabyrinth in the utricle, saccule and semicircular canals. This indicates fetal viremia which leads to infection of the endolympathic spaces as the pathogenic mechanism in intrauterine infection. Studies in mice have demonstrated meningogenic labyrinthitis with CMV infection spreading through the cochlear aqueduct and along CN VIII to involve the perilymphatic spaces.

Rubella

The introduction of the first rubella vaccine in 1969 has led to a dramatic decrease in the incidence of congenital rubella infection. The last rubella epidemic in the U.S. occurred in 1964 and 1965 and led to the birth of over 12,000 children with congenital rubella syndrome and hearing loss. In 1969 there were 58 cases per 100,000 persons, this has since dropped to less than .5 cases per 100,000 persons in 1983. Fetal infection with rubella, unlike CMV, has only been demonstrated with primary maternal infection. First trimester infections have the highest risk for transplacental fetal transmission and up to 90% of infected neonates will demonstrate symptoms of congenital rubella syndrome. Second or third trimester infection has shown a 50% transmission rate and only 25-50% of these infants will be symptomatic.

The three classic findings in congenital rubella syndrome are cataracts, heart malformations (PDA or PAS), and sensorineural hearing loss. Additional signs or symptoms may include retinopathy, thrombocytopenia, jaundice, psychomotor retardation, microcephaly, hepatosplenomegaly, pneumonitis, encephalitis, and long bone radiolucencies. Hearing loss is found in 50% or more of symptomatic infants and of those with silent infection at birth, 10-20% will subsequently be
found to have hearing impairment. The hearing loss is sensorineural and varies in severity. Audiogram often demonstrates a "cookie-bite" pattern with severe to profound loss in the midfrequencies that rises to moderate loss in the low and high frequencies. The vestibular system is less frequently and less severely affected by rubella infection. Some children have been found to have reduced or absent caloric responses on ENG but the majority have no vestibular deficits.

Infected infants shed rubella virus in their urine and definitive diagnosis can be made by culture and isolation of the virus. Alternatively, specific IgM antibody or a rise in IgG titers can aid diagnosis. There is no treatment for congenital rubella infection and management of affected children focuses on accurate audiologic diagnosis and follow up with auditory rehabilitation as indicated. Prevention of maternal infection with widespread vaccination programs is essential. Antepartum screening of maternal rubella immunity is routine and non-immune pregnant women are counseled of the potential for infection and to avoid contact with potential viral shedders. Fetal infection after vaccination can occur and although the risk of hearing loss in these infants is quite small vaccination during pregnancy is contraindicated.

Histopathologic studies of the temporal bones in congenital rubella syndrome have found cochleosaccular changes of the Scheibe type. Additional findings include partial collapse of Reissners membrane, abnormalities of the tectorial membrane, and atrophy or partial destruction of the stria vascularis. The organ of Corti, spiral ganglion, utricle, and semicircular canals appear to remain unaffected by rubella infection.

Mumps

Mumps infection is associated with the triad of parotitis, orchitis, and meningoencephalitis. Children and young adults are the most commonly infected age groups. As many as 20% of infections are asymptomatic, another 40-50% manifest as only an upper respiratory infection and 30-40% of patients present with either unilateral or bilateral parotitis. Meningitis, if present, is asymptomatic in 50-60% of cases and encephalitis is exceedingly rare (.002%). Deafness in association with mumps occurs in .05% of cases and will typically present as the parotitis is resolving. The hearing loss is characteristically sudden onset, severe to profound, and most often permanent. Eighty percent of cases involve unilateral impairment and the loss is greatest in the high frequencies. Associated tinnitus and aural fullness are not uncommon and occasionally patients will also have dysequilibrium or frank vertigo.

Diagnosis of mumps can be made by viral isolation from CSF, saliva, or urine or by demonstration of a fourfold or greater rise in specific antibodies in the acute phase compared to convalescent phase. There is no treatment for mumps or its associated hearing loss and focus should be on widespread vaccination programs to prevent primary infection. The vaccine in use today employs a live-attenuated virus. Although the vaccine can cause clinical illness, it has a proven record of safety and CNS complications, including SNHL, occur in only 1 per 1,000,000 vaccinations.

Both experimental studies in animals and histopathologic examination of human temporal bones have revealed two distinct pathophysiologic mechanisms for mumps labyrinthitis. The first is hematogenic spread with a viremia leading to infection of the stria vascularis. Degeneration of the organ of Corti, tectorial membrane, and cochlear neurons are found and are likely associated with changes in chemical composition or volume of the endolymph. Pathologic changes are more severe in the basal turn of the cochlea. The second mechanism is meningogenic spread through the cochlear aqueduct or CN VIII and into the perilymph. The findings of degeneration of modiolar neural elements as well as the demonstration of fibrosis and ossification of the perilymphatic spaces in patients that survive the acute illness indicate this route of invasion.
Measles

The rubeola virus is the causative agent in measles, a systemic illness characterized by rash, conjunctivitis, and mucosal Koplik spots. The current incidence of measles induced hearing loss is less than 1 per 1,000 cases. Prior to the development of the measles vaccine it was estimated to be responsible for 3-10% of cases of acquired deafness. Measles encephalitis occurs in .1% of cases, has an overall mortality rate of 15%, and 25% of survivors have permanent SNHL or other CNS sequelae.

The hearing loss in measles is most often seen in conjunction with the rash. It is sudden in onset and varies in severity from mild or moderate (55%) to profound (45%). The impairment may be unilateral or bilateral, sometimes with asymmetric involvement, is worse the in high frequencies, and is permanent. Up to 70% of patients also have vestibular losses demonstrable by reduced or absent caloric responses.

Diagnosis is aided by viral isolation from throat or urine culture, detection of viral antigen in pharyngeal epithelial cells, presence of IgM antibody, or a rise in IgG titers. Widespread vaccination with live-attenuated rubeola virus has lead to a 98% decrease in the incidence of measles since the 1960's. There is no specific treatment for measles and auditory rehabilitation with hearing aids or cochlear implantation may be of benefit in affected patients.

Temporal bone studies in hamsters have demonstrated viral antigen in the neuroepithelial cells of the cochlear and vestibular organs, the neurons of CN VIII, and the spiral and vestibular ganglia. Giant cells typical of measles infection were found in the organ of Corti and spiral ganglion cells. Evaluation of human temporal bones reveal similar findings. Cochlear degeneration and atrophy of the strial vascularis is maximal in the basal turn. The tectorial membrane is thickened or distorted. Membranous collapse and macular degeneration is seen in the utricle and saccule. The extensive degeneration of cochlear neuroepithelial structures likely explains the typical lack of recovery following measles induced hearing loss.

Varicella-Zoster

Primary infection with varicella-zoster causes chicken pox with its characteristic pustular rash. Hearing loss has occasionally been associated with chicken pox but it is typically a conductive loss secondary to an otitis media with effusion. Zoster is caused by reactivation of latent virus within affected ganglia with resultant pustular eruption along a dermatome. Herpes zoster oticus or Ramsay Hunt syndrome refers to viral reactivation from the geniculate ganglion of the facial nerve with the development of vesicles over the sensory distribution of the nerve.

Clinical presentation includes painful vesicles involving the external auditory canal and pinna, otalgia, and facial weakness or paralysis. Between 25-37% of patients will have auditory or vestibular complaints that may include decreased hearing, hyperacusis, tinnitus, dysequilibrium or vertigo. An audiogram proven SNHL occurs in 6% of cases. This loss is typically maximal in the high frequencies and associated ABR testing can show either a cochlear or retrocochlear abnormality. Caloric testing may reveal decreased or absent response in the affected ear.

Diagnosis is primarily based on clinical presentation although viral culture of vesicular fluid or viral antibody titers may be used to confirm the diagnosis. The natural course of the illness is spontaneous recovery of auditory and vestibular function over several weeks. The severity of the hearing loss and presence of vestibular symptoms have been inversely related to spontaneous recovery. Antiviral therapy with acyclovir has been shown to speed the resolution of skin lesions and decrease pain. Addition of corticosteroid may help to reduce facial nerve and/or labyrinthine
inflammation. Their effect on outcome has not yet been definitively established. Treatment should also include appropriate analgesic therapy.

The pathogenic mechanism of herpes zoster oticus is reactivation of latent virus within the geniculate ganglion with resultant spread of inflammation along CN VII to also involve CN VIII. Temporal bone studies at various times after infection have supported this mechanism. In the subacute stage, active neuritis involves the entire facial nerve, maximally at the geniculate ganglion. Inflammatory cells have also been found along the vestibulocochlear nerve and within the macula of the utricle and saccule. Destruction of the organ of Corti was near complete in the basal turn and to some extent involved the middle turn as well. Chronic changes include degeneration of neural structures and sensory end-organs as well as labyrinthine fibrosis and ossification.

Herpes Simplex

Herpes simplex virus (HSV) may be related to labyrinthine infection by two distinct mechanisms. HSV-1 has been hypothesized as a cause of idiopathic sudden sensorineural hearing loss (ISSNHL). Similar to the proposed theory of HSV-1 reactivation in the geniculate ganglion as a cause of Bell's palsy, it has been proposed that reactivation of HSV-1 in the spiral ganglion leads to SSNHL. HSV-2 is known to cause neonatal herpes simplex encephalitis. Extension of the meningoencephalitis along CN VIII to the labyrinth is a potential cause of acquired SNHL.

Experimental studies in animals have shown that both HSV-1 and HSV-2 have the potential to infect the labyrinth. Neuroepithelial cells of the cochlea, utricle, saccule, and semicircular canals are all affected by these viruses. Additionally, neurons in both the spiral and vestibular ganglia, as well as cochlear supporting cells, are affected. Although circumstantial evidence and serologic studies implicate HSV in auditory or vestibular loss in humans, definitive proof is not yet available.

Human Immunodeficiency Virus

Auditory and vestibular complaints are rare in AIDS patients although sudden hearing loss, tinnitus and vertigo have all been cited in the literature. The etiology of hearing loss in HIV is unclear. Potential mechanisms include primary labyrinthine infection with the HIV virus, secondary infection by opportunistic pathogens, neoplasm involving the inner ear, or ototoxicity of anti-HIV medications. Hearing loss has been shown to occur in 21-64% of AIDS patients. The most common finding is a mild SNHL although increasing loss may be seen in the low and high frequencies. ABR testing reveals both cochlear (prolonged wave I latency) and retrocochlear (prolonged wave V latency and wave III-V interpeak latency) abnormalities. It is thought that at least part of the hearing loss in these patients is attributable to central auditory dysfunction.

Temporal bone examination in AIDS patients has elicited variable findings. One study, reported in 1995, isolated CMV, adenovirus type 6, and HSV-1 from the inner ears of four AIDS patients. The sensory and neural components of these ears did not appear to be affected and there was no evidence of viral induced inflammation. Another study of the vestibular end-organs found hair cell inclusion bodies, viral-like particles, and malformation of hair bundles. A direct neuroepithelial infection with HIV was presumed based upon these findings. Other studies have found Pneumocystis and Cryptococcus within the temporal bone suggesting opportunistic otitis interna.

Protozoal Infections—Toxoplasmosis
Infections of the Labyrinth  May 2000

Infection with Toxoplasma gondii occurs via ingestion of protozoal cysts in undercooked meats or food products contaminated with cat feces. Acquired infection is most often asymptomatic or may produce a nonspecific illness with myalgias, fatigue, and lymphadenopathy. Congenital infection, on the other hand, may lead to severe malformations in the fetus. Congenital toxoplasmosis is typified by the triad of chorioretinitis, hydrocephalus, and intracranial calcifications. Additional features of the disease may include microcephaly, cataracts, microphthalmia, jaundice and hepatosplenomegaly. The estimated incidence of congenital toxoplasmosis in the U.S. is near 3,000 cases annually. The highest risk of transmission to the fetus occurs with primary maternal infection in the third trimester with a 60% transmission rate. The highest risk for severe manifestations of infection in the fetus occurs with early maternal infection, between 10-24 weeks gestation. About 75% of infected neonates will be asymptomatic at birth, 15% will have ocular problems, and 10% will demonstrate severe manifestations. As many as 85% of asymptomatic infants at birth will later present with decreasing visual acuity or intellectual function, hearing loss or precocious puberty.

Diagnosis of maternal infection can be made by documenting IgG seroconversion or a rise in IgG titers. Pregnant women with evidence of infection may then elect to have screening tests done to determine fetal infection. Current options for fetal screening include mouse inoculation or PCR analysis of amniotic fluid or IgM assays or quantitative maternal/fetal IgG analysis of umbilical cord blood samples. The reasoning for these seemingly invasive screening tests is that prenatal treatment has been shown to reduce both transmission and severity of illness in the fetus. Studies in France have shown a 70% reduction in fetal transmission among women with primary infection during weeks 16-25 who were given combination therapy with pyrimethamine and sulfonamide. Neonates with documented congenital infection should be given this regimen for the first year of life with the addition of folate acid supplements. Studies of treated infants have shown a reduction in the occurrence of chorioretinitis and hearing loss.

Fungal infections

Fungal labyrinthitis is exceedingly rare outside the context of host immunocompromise. The number of reported cases is increasing with concomitant increase in the prevalence of HIV infection and the use of immunosuppressive doses of steroids or chemotherapy. High risk populations include severe diabetics, patients undergoing chemotherapy, organ transplant recipients, and AIDS patients.

Reports in the literature have cited inner ear infection with Mucor, Cryptococcus, Candida, Aspergillus, and Blastomyces. In a study by Meyerhoff, et al in 1979 evidence of meningogenic, tympanogenic, and hematogenic spread of fungal infection to the labyrinth was found. Specifically, patients with Mucor, Candida, and Cryptococcus meningoencephalitis were found to have fungal invasion and inflammatory changes along the IAC and cochlear aqueduct which extended to involve both the cochlear and vestibular labyrinths. A patient with Mucor of the middle ear cleft was found to have gross fungal penetration through both the round and oval windows. Hematogenous spread to the labyrinth was seen in a patient with disseminated Candida septicemia in which fungus was identified in the perilymph and endolymph but could not be identified in either the IAC or the middle ear space. Pathologic findings in these temporal bones included destruction or atrophy of the organ of Corti, stria vascularis and spiral ganglion cells.

Treatment of this infection involves systemic antifungal therapy and optimization of host immune defenses if possible. Hearing loss induced by fungal labyrinthitis is often severe and permanent. Evaluation for amplification may be warranted.

Clinical presentation
Patients with an internal otitis may present with only auditory dysfunction--acute cochlear labyrinthitis, only vestibular dysfunction--acute vestibular labyrinthitis, or both--acute cochleovestibular labyrinthitis. Acute cochlear labyrinthitis, also known as idiopathic sudden sensorineural hearing loss (ISSNHL), is defined as a minimum of 30 dB deficit in three contiguous frequencies over a period of less that 3 days in a previously healthy individual. Three common pathogenic theories exist to explain ISSNHL, these are viral infection, vascular phenomenon, and intralabyrinthine membrane rupture. The majority of evidence in the literature, although some is admittedly circumstantial, supports a viral induced mechanism. Ninety percent of ISSNHL is unilateral, it is widely variable in severity, and is not uncommonly accompanied by aural fullness and tinnitus. Patients report a sudden onset, painless loss of hearing. Thirty to fifty percent of patients report a preceding or concurrent URI. Vestibular symptoms or dysequilibrium may be present.

The differential diagnosis of ISSNHL in addition to infectious etiologies, includes autoimmune labyrinthitis, head/temporal bone trauma, neoplasm, ototoxicity, and vascular accidents. Evaluation of these patients begins with complete physical exam with special emphasis on otologic and neurologic examination. Laboratory tests are directed toward ruling out specific causes of hearing loss and include CBC, ESR, blood glucose and FTA-ABS. Audiologic testing is instrumental in the evaluation of these patients and ENG testing is undertaken if indicated. Imaging studies such as CT scan or MRI can be useful to look for bony abnormalities, neoplasm, or central demyelination.

Many attempts at pharmacological treatment of ISSNHL have been made, including use of vasodilators, anticoagulants, plasma expanders, steroids, and carbogen. The majority of these therapeutic regimens have not been proven to be beneficial through clinical trials. The exception to this is oral steroid therapy. A doubly blinded study conducted by Wilson in 1980 involved 67 patients with ISSNHL. The treatment group received an oral steroid 12 day taper of dexamethasone or methylprednisolone, while the control group received placebo. The overall rate of partial or complete hearing recovery in the treatment group was 61% compared to 32% in the control group. Patients who benefited most from steroid therapy were those who demonstrated a moderate hearing loss (40-90 dB PTA in the midfrequency range) on initial audiogram. 78% of this group had improved hearing on subsequent testing. The relative odds favoring recovery in the steroid treated group was 4.39 to 1. Despite all of the supporting evidence for a viral etiology in ISSNHL, antiviral therapy has received relatively little attention thus far. Interferon has shown beneficial effect (64% recovery) in one study and trials are currently underway to compare outcome in patients treated with steroid alone vs. steroid plus antiviral therapy.

Overall, it is estimated that between 30-70% of patients will have partial or complete recovery of hearing. The prognosis for recovery seems to be related to patient age, time from onset to presentation, type of audiogram, and presence of vestibular symptoms. Patients younger than 40 have a higher chance for recovery. Patients seen within 10 days of onset and started on steroid therapy in that time have better outcomes. A mild hearing loss at presentation is associated with recovery in nearly 100% of cases. Those patients with moderate hearing loss will spontaneously recover function in 38% of cases, this can be increased to 78% with steroid therapy. Profound hearing loss carries the worst prognosis with less than 20% of cases having any recovery regardless of treatment. The presence of vertigo is associated with more extensive labyrinthine pathology and is a poor prognostic factor. Hearing thresholds at 6 weeks post-illness are often what the patient will have permanently. At this time, hearing aid fitting or cochlear implant may be considered for those patients with severe/profound losses.
Acute vestibular labyrinthitis, otherwise known as vestibular neuritis, is defined as a sudden unilateral vestibular weakness in the absence of concomitant auditory or CNS dysfunction in a previously healthy person. Diagnostic criteria for this entity, as set forth by Coates include: "1) an acute, unilateral, peripheral vestibular disorder without associated hearing loss, 2) occurrence predominantly in middle age, 3) a single episode of severe prolonged vertigo, 4) decreased caloric response in the involved ear, and 5) complete subsidence of the symptoms within 6 months." These criteria are somewhat restricted as it is clear from reports in the literature that there are both single and multiple attack forms of the illness, as well as cases of either concomitant or sequential bilateral involvement. Patients will report acute onset of vertigo of varying severity, not uncommonly associated with nausea and vomiting. Symptoms may progressively worsen over the first 24 hours and during this time the patient may complain of severe imbalance, falling and inability to focus the eyes. Symptoms gradually dissipate over several weeks to months.

Differential diagnosis of vestibular neuritis includes Meniere's disease, vestibular schwannoma, labyrinthine fistula, cerebellar infarction, multiple sclerosis, and dysequilibrium of aging. Evaluation of these patients begins with physical exam which will often reveal an obviously ill person who is pale, clammy, and sweating. They remain very still throughout the interview/exam as any movement precipitates the vertigo. Examination is often unremarkable other than gait unsteadiness and nystagmus. Audiologic testing is indicated to evaluate for associated cochlear loss. ENG may reveal nothing more than spontaneous nystagmus in the acute phase but later will likely demonstrate a reduced or absent response on the involved side. If the history is suggestive of a CPA mass or cerebellar infarct imaging with CT scan or MRI is warranted.

Treatment is supportive and includes hydration, antiemetics, and vestibular suppressants. Some authors cite that this disease is often benign and most patients recover with 2 months, implying a return to normal function. Others discuss patients recovery over 2-6 months but speak in terms of compensatory mechanisms adjusting to the permanent peripheral vestibular loss. Histopathologic studies which have demonstrated severe nerve fiber loss and cellular loss within the crista of the semicircular canals lend support to permanent loss of vestibular function and subsequent compensation by other mechanisms.

Bibliography


