Chapter 5: Pathology of the vestibular system

Richard R. Gacek

Knowledge of the pathophysiology of vestibular disorders is essential for a logical accurate evaluation and management of the vertiginous patient. The diagnosis of vestibular system disease, particularly of peripheral disorders, depends primarily on a carefully obtained history with some assistance from tests of hearing function and vestibular sensitivity (caloric, positional tests). Radiological tests (computerized tomography, magnetic resonance imaging) are helpful in the evaluation of neoplastic and inflammatory disorders which affect the labyrinth, eighth cranial nerve and central nervous system (posterior fossa). A reliable body of information necessary to derive an accurate diagnosis of such disease comes from the study of temporal bones from patients with vestibular disorders.

Vertigo or dysequilibrium is a result of an asymmetry in the peripheral or central portions of the vestibular system. The severity of the dysequilibrium depends on the magnitude and speed of onset of the asymmetry. Compensatory mechanisms usually correct for small asymmetries, thus rendering the patient almost asymptomatic. However, recurrent and progressive asymmetries produce troublesome vestibular symptoms. Since other sensory modalities also participate in spatial orientation, pathologies involves the visual, proprioceptive systems, cerebellum and reticular formation may also be responsible for dysequilibrium. However, the present discussion will be limited to pathologies involving the input from vestibular labyrinthine sense organs which project to the brainstem forming important motor reflex connections. The asymmetries in the vestibular pathway may be located in the sense organ, the first order vestibular neuron, the vestibular nuclei and their connections to the extraocular muscles, contralateral vestibular nuclei, and the vestibulocerebellar and the vestibulospinal tracts. It is appropriate to discuss these pathologies at the peripheral and central levels. A number of clinical reports have emphasized that the majority of clinical disorders producing vertigo are located peripherally, that is in the sense organ or the first order vestibular neuron. Central vestibular pathways are less frequently responsible for dysequilibrium.

Peripheral vestibular system

Significantly more information is available about the pathology affecting vestibular sense organs and their nerve supply than any other segment of the vestibular pathway. The vulnerability of the peripheral vestibular system to various intrinsic and extrinsic pathologies along with a more complete histopathological documentation of these disorders are responsible for our present level of knowledge. Pathology in the peripheral vestibular system produces clinical symptoms by significant alteration of the action potentials directed through the vestibular nerve into the brainstem. It may be useful therefore to subdivide further the peripheral pathologies into those that affect the sense organ and those that affect the first order neuron. A helpful approach for discussing these for diagnostic and therapeutic reasons, is from the viewpoint of the pathophysiological mechanism responsible for vestibular asymmetry.
End organ pathology

Mechanical stimulation

Several pathological situations may be responsible for recurrent or chronic dysequilibrium by mechanical stimulation of the vestibular sense organs in an unphysiological fashion. Essentially this mechanism produces an unphysiological change in the action potentials leading from a specific end organ by such mechanical stimulation. There are several well known clinical examples of this form of pathology.

Erosion of the bony labyrinth

Erosion of the bony labyrinth capsule by cholesteatoma may occur as a result of pressure from the enlarging sac and/or a chemical process of bone erosion probably mediated through collagenolytic enzymes (Abramson, 1969; Abramson and Gross, 1971). When fenestration of the bony labyrinth capsule has occurred, an opportunity for the transmission of pressure from the ear canal to the membranous labyrinth is present. True fistulization of the perilymphatic space and the middle ear space through such bony fistulai is extremely rare. Of course, the transmission of positive or negative pressure in the ear canal thereby displacing the cupula of the fenestrated bony canal will activate the vestibulo-ocular reflex accompanied by the symptoms of rotatory vertigo. The lateral, superior and posterior semicircular canals may be involved by this pathology in decreasing order of frequency (Ritter, 1970; Gacek, 1974). The bony wall of the cochlea may also be eroded or fistulized by cholesteatoma or chronic osteitis. Such erosion is usually in association with fistulization of the bony vestibular labyrinth and is manifested by a sensorineural hearing loss which may assume a descending or flat threshold pattern. The most frequent location of erosion of the cochlear wall is over the basal end (promontory) (Gacek, 1974). Since fistulization of the cochlear wall is not indicated by a specific diagnostic test, the condition is usually recognized during surgery for cholesteatoma; it should be suspected in all cases undergoing surgery for extensive disease.

It should be mentioned that along with the bony fistulization of the labyrinth capsule, varying degrees of a localized inflammatory process occur along the endosteal membrane and perilymphatic space adjacent to the fistula. Undoubtedly such inflammatory reactions are also responsible for dysequilibrium, in addition to the vertigo produced by activating the fistula mechanically. Therefore, this pathological circumstance has an inflammatory as well as a mechanical mechanism.

Since the cholesteatoma membrane is pathological tissue, surgical removal is a desirable goal. A general rule suggests that the cholesteatoma matrix can usually be removed safely from a small fistula (< 2 mm) without tearing the underlying endosteal membrane (Gacek, 1974). Safe removal of the cholesteatoma is usually not possible over a larger fistula because of the greater duration of the pathological erosion, with a greater degree of adherence by fibrous tissue to the membranous labyrinth. However, this is not an inviolate rule.

Hennebert's sign

A positive vestibulo-ocular response with clinical symptoms may also occur in the presence of a normal tympanic membrane and middle ear space when positive or negative
pressure is applied to the tympanic membrane. Dysequilibrium and ocular deviation in the absence of clinical middle ear disease is referred to as Hennebert's sign and can be explained on the basis of mechanical stimulation of vestibular sense organs by depression and withdrawal of the stapes footplate in the oval window (Nadol, 1977). The mechanical stimulation depends on distension of the membranous wall of vestibular sense organs especially the saccular wall, which may contact the undersurface of the stapes footplate. A pushing or pulling effect on the membranous walls by the footplate initiates the mechanical displacement. Contact with other vestibular sense organs (cristae ampullaris) may then allow transmission of pressure introduced through the ossicular chain producing vestibular stimulation and ocular deviation.

**Ossicular stimulation of the vestibular sense organs**

Mechanical stimulation of the vestibular sense organs may occur as a result of a stapedectomy procedure used to correct the hearing loss caused by otosclerosis. Because the utricular macula lies close to the oval window in the vestibule, it may be contacted by a prosthesis which extends excessively beyond the level of the window. Particularly in the case of the piston type prosthesis which must be inserted beyond the level of the window to prevent refixation by bony and fibrous tissue, an excessively long prosthesis may make contact with the utricular macula. Depression of the incus during surgery while the patient is under local anaesthesia can be used to determine the proper length of the prosthesis. The long prosthesis syndrome is usually manifested by ataxia exacerbated by the Valsalva manoeuvre, heavy lifting or bending over, and often takes the form of dysequilibrium or ataxia rather than rotatory vertigo. Unrelieved mechanical stimulation by a stapes prosthesis in this manner may ultimately result in a sensorineural hearing loss because of the traumatic labyrinthitis which is produced.

**Cupulolithiasis**

Cupulolithiasis is a well-known form of pathology responsible for paroxysmal positional vertigo (type III Aschan). The accumulated histopathological evidence indicates that the posterior semicircular canal is responsible for the vertigo and nystagmus produced in the head down position with the Hallpike manoeuvre (Gacek, 1985). This nystagmus is rotatory and directed toward the undermost ear (clockwise with left ear down, counter-clockwise with right ear down) which is visible with the unaided eye 1-3 seconds after the provocative position has been assumed. The duration of nystagmus is short (20-25 seconds), reappears briefly in reversed direction when the sitting position is resumed and fatigues on repeated provocation (Hallpike, 1949). The neural pathways from the posterior canal sense organ which input to the brainstem and extraocular muscles explain the direction of nystagmus provoked in this position by a gravity sensitive cupula and also that resulting from selective ablation of the innervation of the posterior canal crista.

Histopathological observations (Schuknecht, 1969; Schuknecht and Ruby, 1973) of the posterior canal crista in patients with benign paroxysmal positional vertigo revealed basophilic deposits embedded into the cupula of the posterior semicircular canal of the undermost ear in the provocative position. Presumably these deposits are derived from the otoconial blanket located over the utricular macula, the probable source for otoconia in the pars superior of the labyrinth. These otoconia are thought to be dislodged from the utricular macula as a result of
head trauma, acute and chronic inflammatory conditions, ageing, or surgical insult to the labyrinth. The otoconia gravitating into the most dependent portion of the labyrinth (that is posterior canal ampulla) are most likely to become embedded into the cupula of the posterior canal rendering it gravity-sensitive during the positional test. Clinical proof that the posterior canal crista is responsible for the symptomatology in this syndrome is available in the form of the complete relief afforded by selective denervation of the posterior canal in the undermost ear (Gacek, 1985). Experimental evidence that increasing the specific gravity of the cupula allows it to respond to gravity has been produced by using deuterium oxide to increase the specific gravity of the cupula (Money and Myles, 1974). In both the experimental animal and human subjects, this resulted in positional nystagmus of the peripheral type.

**Inflammation**

Inflammation of the labyrinth is termed labyrinthitis and may be classified as either bacterial or viral. Bacterial labyrinthitis may occur as an extension of infection from the middle ear space or the intracranial cavity. Acute or chronic bacterial otitis media may extend into the labyrinth either through a fistula of the bony labyrinth associated with cholesteatoma, or via the round window membrane or oval window. Suppurative labyrinthitis may also occur as an extension of bacterial meningitis along the fluid pathways that connect the subarachnoid space and the perilymphatic space of the cochlea; these are the cochlear aqueduct or the cribrose area in the base of the modiolus of the cochlea.

Bacterial labyrinthitis can be classified into four stages (Schuknecht, 1974a):

1. acute or toxic (serous)
2. acute suppurative
3. chronic suppurative
4. fibrosseous.

The acute toxic or serous form of labyrinthitis will occur as a result of chemical changes in the perilymphatic space caused by a toxic or suppurative process which impinges on a membrane barrier of the labyrinth, such as the round window membrane, or the membrane covering a bony fistula. During this stage, chemical changes in the perilymphatic space may occur without the invasion of bacterial organisms and the inflammatory cell component which accompanies bacterial invasion. Although vertigo with nystagmus may be present at this stage, the disturbance in vestibular physiology is reversible if the toxic (inflammatory) process adjoining the vestibular labyrinth is controlled medically or surgically.

The second stage of acute suppurative labyrinthitis develops when invasion of the perilymphatic space by bacterial organisms has occurred with an accompanying response from the host organism in the form of inflammatory cells and fibrocytes. At this stage, irreversible destruction of auditory and vestibular function has occurred and the goal of treatment is to control the extension of infection so that invasion of the subarachnoid space is prevented. Adequate treatment with chemotherapeutic agents may suffice to control acute suppurative disease, but surgical drainage may also be necessary.

The third stage in suppurative labyrinthitis is the chronic stage where involvement of the labyrinth by bacterial organisms with an inflammatory tissue response has occurred over
a long period of time usually as an extension of chronic inflammatory middle ear and mastoid disease. Complete irreversible loss of vestibular and auditory function invariably occurs and the primary goal is to eradicate the inflammatory process in order to prevent intracranial extension.

The final or healed stage of suppurative labyrinthitis is the fibrosseous response that is generated by the host organism as the inflammatory process has been successfully controlled. At, first, a dense fibrous tissue response occurs to obliterate the labyrinthine spaces with a resultant complete loss of auditory and vestibular function and then ultimately calcification and osteoneogenesis may occur to obliterate some or all of the labyrinthine spaces (labyrinthitis ossificans).

The most common bacterial organisms responsible for acute serous or suppurative labyrinthitis are pneumococci, streptococci, and *Haemophilus influenzae*, while the chronic form is caused by a mixture of Gram-negative bacilli (*Pseudomonas, Proteus, Escherichia coli*).

A more common form of labyrinthitis is that which is seen as a result of invasion by viral agents (Bordley, Brookhauser and Worthington, 1972). Viruses such as mumps, the influenza viruses, adenoviruses and other viral agents have been associated with an acute disturbance of auditory and vestibular function manifested as sustained vertigo and nystagmus lasting 3-5 days with a gradual lessening of the spontaneous nystagmus and vagal symptoms. As these symptoms abate and the patient recovers balance by use of the compensatory mechanisms, varying degrees of residual permanent loss of auditory and vestibular function may be seen. The viraemia reaches the fluid pathways of the labyrinth either directly from the bloodstream or by way of the subarachnoid space. The viral agents probably affect the structures located within the scala media and the sense organs of the vestibular labyrinth (Karmody, 1983). Hair cells of the organ of Corti as well as the strial vascularis and spiral ganglion may be affected by the viral infection. Cystic degeneration, hair cell loss, and round cell infiltrates are the characteristic findings in the end organs of both the auditory and vestibular labyrinth.

Of course, viral labyrinthitis is beyond the presently available therapeutic management programmes. However, steroids have been shown to be of some benefit to hearing recovery in those patients where the loss is not greater than 90 dB (Wilson, Byl and Laird, 1980). Recovery from vestibular symptoms after viral labyrinthitis is gradual and depends primarily on compensatory mechanisms involving the visual, proprioceptive and cerebellar pathways. Fortunately, viral labyrinthitis is usually unilateral and therefore function of the contralateral ear is sufficient to enable a patient to manage reasonably well.

**Degeneration**

Degeneration of the sensory cells of the vestibular sense organs is associated with vestibular symptoms and eventually may lead to a loss of vestibular sensitivity. Since the hair cell is the transducer by which the mechanical stimulation of the sense organ is transformed into an electrical impulse (action potential) in the vestibular nerve fibres, deterioration of these sensory cells is important in the normal function of the vestibular apparatus. Two well-known causes of vestibular sensory cell degeneration are ototoxic drugs, and the ageing process.
Ototoxicity

Most therapeutic agents, particularly the aminoglycosides, that are harmful to the labyrinth will cause degeneration of the vestibular sensory cells as well as severe toxic effects on the organ of Corti. Streptomycin (McGee and Olszewski, 1962; Wersall and Hawkins, 1962) and gentamicin (Lundquist and Wersall, 1967) are unique because of their ability to affect the vestibular hair cells before affecting those of the organ of Corti. Therefore, these drugs are potent vestibulotoxic agents. Since the hair cells are surrounded in a perilymph fluid environment, blood-borne chemicals will reach the sensory cells of the vestibular and auditory neuroepithelium by way of perilymph which is a derivative of blood. A large number of animal experiments supported by clinical trials in patients treated for vestibular disorders (Schuknecht, 1957) have demonstrated that streptomycin sulphate administered parenterally will cause degeneration of the hair cells of the cristae and the maculae of the labyrinth. This effect will be manifested clinically by ataxia after approximately 20-25 g of streptomycin and will usually result in a loss of vestibular function as measured by absence of the vestibulocular reflex at 30-40 g total dosage. If the streptomycin is discontinued at the point where the vestibulocular reflex is absent following a strong ice-water stimulus, no auditory deficit will occur. Therefore this method of destroying vestibular hair cells is useful in the management of patients with disabling Ménière's disease or in patients who have Ménière's disease in an only hearing ear. The temporal bones of patients treated with streptomycin sulphate have demonstrated almost complete loss of vestibular hair cells in the cristae with a partial loss in the maculae. The vestibulotoxic effect therefore appears to be more severe on the sense organs of the semicircular canals. Patients who have been treated with streptomycin sulphate and have bilateral vestibular hair cell ablation, compensate well, not only because of other equilibrium systems, but also because residual hair cell function in the maculae serve as an important vestibular input.

Ageing

The ageing process probably has a degenerative effect on the vestibular sense organs, although direct histopathological documentation of this effect has not been presented. The probability of this effect is based on clinical experience, animal experiments, and some brief reports of ageing effects in the human sense organs (Schuknecht, Igarashi and Gacek, 1965; Johnsson, 1971). Clinical experience based on older patients often reveals complaints of dysequilibrium either of a rotatory or positional nature that occur periodically, particularly with rapid changes in position. Nevertheless, tests of vestibular function, auditory function and radiological tests are usually normal for age in these patients. It seems reasonable to suspect pathology in either the peripheral or central nervous system. However, in many aged patients with dysequilibrium the absence of other central nervous system abnormalities points toward a peripheral aetiology. Animal studies have revealed changes (loss or deformed otoliths) in the otoconial blanket, and the accumulation of lipofuchsin pigment within the sense organs of the vestibular labyrinth. This pigment is known to accumulate with age. Degeneration of the vestibular neurons and sensory cells as well as the make-up of the otoconial blanket of the macular sense organs occur in the ageing ear. The syndrome of cupulolithiasis is known to occur in the aged patient probably as a result of loss of otoconia from the utricular macula leading to benign paroxysmal positional vertigo. In addition to the gravity-sensitive change in the cupula of the posterior canal sense organ, the loss of a significant portion of the otoconial blanket of the utricular macula prevents the utricle from exerting an inhibitory effect.
on the semicircular canal input, thereby allowing an increased neural input from the excited crista. These clinical and histopathological observations point to ageing degenerative processes affecting the vestibular system similar to that in the auditory sense organ with increasing age.

**Trauma**

Trauma to the temporal bone and the vestibular sense organs may occur in several forms. Usually the injury results from fracture through the bony labyrinthine capsule or disruption of the fibrous and bony barriers in the oval or round windows of the labyrinth. Before discussing these categories of direct and indirect trauma to the vestibular labyrinth, it should be noted that injury to the vestibular labyrinth with clinical symptoms may occur in the absence of any disruption of the bony vestibular labyrinth. Labyrinthine concussion as a result of head injury is a well-known clinical phenomenon resulting in dysequilibrium, vertigo and positional vertigo (Barany, 1921; Dix and Hallpike, 1952). The histopathology of this injury is not well documented because of the absence of temporal bone material procured at the time of such injury. However, experimental evidence indicates that injury to the otoconial blanket of the macular sense organs with disruption of otoconia is one effect that follows concussion (Schuknecht, 1962). A release of a significant number of otoconia which then become embedded into the posterior canal cupula may produce the condition known as cupulolithiasis. Furthermore, bleeding into the perilymphatic space is known to occur following head blows in the experimental animal (Schuknecht and Davison, 1956). The chemical change in the perilymphatic fluid resulting from blood causing a chemical labyrinthitis is also a possible explanation for dysequilibrium.

**Temporal bone fractures**

Temporal bone fractures are divided into longitudinal and transverse. Although the more common (80%) longitudinal fracture frequently involves the middle ear, ossicular chain, and facial nerve canal, it does not usually directly involve the vestibular labyrinth. However, transverse fracture of the petrous portion of the temporal bone as a result of severe injury to the base of the skull frequently produces a fracture line through the bony labyrinth and/or the internal auditory canal (Stenger, 1909). This occurs because it is the weakest point in the petrous segment of the temporal bone. The fracture through the vestibular labyrinth will produce the clinical signs of severe labyrinthine injury with vertigo and a sustained spontaneous nystagmus which gradually resolves over the period of several days to a week. The injury to the blood supply and the membranous structures of the labyrinth results in a degeneration of the vestibular sense organs and ultimately in fibrousseous obliteration of the vestibular labyrinth.

Vestibular symptoms gradually subside as the loss of vestibular and auditory function becomes complete. If residual vestibular function is present, it may be responsible for persistent dysequilibrium. Complete ablation in the form of labyrinthectomy or vestibular nerve section may be required to relieve symptoms. An unusual, but potentially significant long-term complication of temporal bone fracture which extends through the external auditory canal is cholesteatoma which develops from entrapped stratified squamous epithelium in the fracture line. Such cholesteatomata may reach considerable size eventually destroying both labyrinthine and facial nerve function.
**Surgical fistulization**

Surgical fistulization of the vestibular labyrinth usually involves the lateral semicircular canal prominence. Such fistulization is caused by inadequate awareness of landmarks in a temporal bone obscured not only by pathology, but also by a poorly developed air cell system. Should such injury occur, a serous and serofibrinous labyrinthitis with ultimate degeneration of the vestibular and auditory sense organs will follow if preventive measures are not taken (Altmann, 1946). These preventive measures may be a form of firm sealing of the surgical bony fistula using bone wax or tissue to prevent a persistent communication between the fluid spaces of the labyrinth and the middle ear.

**Direct penetrating injury**

Direct penetrating injury to the oval window may occur from a slender instrument introduced into the ear canal and through the tympanic membrane. Such accidental introduction of a penetrating instrument may sublux or fracture the stapes footplate producing an oval window to middle ear fistula. The perilymphatic fistula results in a serous and serofibrinous labyrinthitis with various degrees of dysequilibrium and vertigo. The dysequilibrium gradually subsides even if there is degeneration of the vestibular system. However, auditory function will eventually be lost if the fistula is not repaired as soon as possible after the injury (Arragg and Paparella, 1964).

**Perilymph to middle ear fistula**

A perilymph to middle ear fistula may occur through either the oval or round windows as a result of indirect injury to the window membranes. Such indirect injury occurs as a result of abrupt severe changes in middle ear or subarachnoid space (cerebrospinal fluid) pressure (Pullen, 1972; Goodhill, 1971). Injuries such as these are associated with severe barotrauma, extreme physical exertion or impact noise. Symptoms associated with perilymph fistula may include a variety of vestibular and auditory symptoms and findings. The fistula test is often negative and therefore not always helpful in identification. The persistence of vertigo and nystagmus with or without auditory deficit over a prolonged period of time (1-2 weeks) following an injury associated with sudden pressure changes should raise the suspicion of perilymph fistula. Repair of the fistula is essential to achieve reversal of the serous labyrinthitis before progression to fibrinous or degenerative labyrinthitis has occurred. However, clear identification of a membrane defect by adequate surgical exposure is a prerequisite to accurate diagnosis and successful repair with an appropriately placed tissue graft.

**Vascular injury**

Vascular injury to the vestibular and auditory labyrinth can be divided into those that result from occlusion of the blood supply to the labyrinth and those that occur as a result of excessive bleeding into the labyrinth.
Occlusion of vascular supply

Occlusion of arterial vessels to the vestibular labyrinth can produce degeneration of both the neural and sensory components of the vestibular labyrinth. The best known example of this is occlusion of the anterior vestibular artery (Lindsay and Hemenway, 1956). The clinical manifestations of this event are the acute onset of vertigo which is sustained over several days with spontaneous resolution. Loss of function of the sense organs supplied by the superior division of the vestibular nerve occurs while hearing remains unaffected if cochlear branches are not occluded.

The histopathology of this condition shows degeneration of the superior division of the vestibular nerve and its branches along with the sense organs supplied by the superior vestibular division. Although complete compensation of this partial vestibular deficit usually occurs, persistent vestibular symptoms in the form of paroxysmal positional vertigo may result if the otoconial loss from the utricular macula is large and becomes embedded into the cupula of the posterior canal.

Excessive bleeding into the labyrinth

Excessive bleeding into the vestibular labyrinth has been documented as a result of subarachnoid haemorrhage or spontaneous intralabyrinthine bleeding secondary to a major blood dyscrasia. Massive bleeding into the subarachnoid space along with increased subarachnoid pressure may force significant amounts of blood elements into the perilymphatic spaces of both the vestibular and the auditory labyrinth along the communicating channels between perilymph and cerebrospinal fluid (Perlman and Lindsay, 1939; Holden and Schuknecht, 1968). These channels are the cochlear aqueduct, the cribrose area of the cochlea and other channels that surround the vestibular nerve fibres as they penetrate the otic capsule. Massive bleeding into the perilymphatic space is responsible for sustained dysequilibrium and hearing loss probably as a result of a chemical alteration in the perilymphatic environment surrounding the vestibular and auditory nerve fibres.

Bleeding into the perilymphatic space may also occur as a result of spontaneous haemorrhage associated with a blood dyscrasia. A well known example of such haematological disorder is leukaemia, where extensive bleeding into the perilymphatic spaces of the vestibular and auditory labyrinth may cause sustained vertigo and nystagmus with loss of auditory function (Schuknecht, Igarashi and Chasin, 1965). The ultimate loss of labyrinth function resulted from the chemical labyrinthitis caused by the massive infusion of blood elements in the perilymphatic compartments.

Neoplasia

Neoplasia originating in the vestibular labyrinth has been reported in the form of neural tumors or schwannomata arising from the peripheral branches of the vestibular nerve or the cochlear nerve within the bony labyrinth. Intralabyrinthine neuromata (schwannomata) have been described by several authors (Wanamaker, 1972; Stewart, Liland and Schuknecht, 1975; DeLozier, Gacek and Dana, 1979). Unlike the intracanalicular form of neuroma, those of the intralabyrinthine vestibular type produce significant vestibular symptoms resembling those seen in Ménière's disease. Recurrent episodic vertigo and fluctuating sensorineural
hearing loss have been the usual clinical symptoms associated with this entity. The preoperative clinical diagnosis of a surgically proven intralabyrinthine neuroma has been Ménière's or atypical Ménière's disease.

The histopathological picture consists of a schwannoma arising from the myelinated labyrinthine segments of the vestibular and auditory nerves which then expands to occupy the perilymphatic compartment of the vestibule. The tumours which arise from the cochlear nerve proliferate into the scale tympani but are also associated with episodic vertigo and sensorineural hearing loss. The episodic vertigo may be the result of chemical changes produced by the tumour which then affect the vestibular nerve fibres. It is also possible that the episodic vertigo is a result of progressive endolymphatic hydrops caused by tumour obstruction of the drainage system (ductus reuniens). Endolymphatic hydrops has also been observed in the temporal bones containing an intralabyrinthine neuroma. Since the vestibular ganglion is remotely located in the internal auditory canal and therefore not affected by the enlarging tumour, the vestibular nerve to the brainstem remains capable of transmitting pathological input thereby accounting for the severity of vestibular symptoms with this form of neuroma.

Other forms of neoplasia which may involve the labyrinth include malignancies such as squamous cell carcinoma or adenocarcinoma which may destroy the bony otic capsule and eventually affect the vestibular labyrinth. However, the otic capsule is generally resistant to neoplastic invasion from an extrinsic source and is violated only late in the course of metastatic disease.

**Metabolic alteration**

This category includes vestibular pathologies which result in labyrinthine symptoms because of chemical or ionic changes in the fluid environment of the labyrinth, namely the perilymphatic and endolymphatic compartments. Normal function of the labyrinth depends on the maintenance of normal ionic and chemical composition of endolymph and perilymph. The vastly different ionic composition of endolymph and perilymph (endolymph - high in potassium, low in sodium; perilymph - low in potassium, high in sodium) permits a standing potential differential of approximately 120 mV to exist between endolymph and the compartment surrounding the hair cells and nerve fibres (perilymph). An alteration in this chemical composition will lead to dysfunction and dysequilibrium because of a change in the action potentials of the vestibular nerve. Such changes are more likely to occur in the perilymphatic fluid since it is the compartment most easily affected by various inflammatory or traumatic insults to the otic capsule or its natural fenestrae (oval and round windows). Furthermore, this is the fluid environment which is critical for normal hair cell and vestibular nerve function.

Common examples of an alteration in perilymph composition affecting vestibular physiology are:

(1) the serous labyrinthitis which occurs following oval window surgery (Hohmann, 1962)
(2) sensorineural hearing loss with vertigo associated with chronic inflammatory disease in the round window niche.

Following stapedectomy, dysequilibrium (especially positional) and sensorineural hearing loss are common for several days. Gradual resolution of symptoms with return of cochlear function parallels the readjustment in clinical changes produced by the surgery. A similar resolution of labyrinthine symptoms occurs when chronic inflammatory middle ear disease is surgically controlled. The term 'serous labyrinthitis' is used to describe such reversible forms of labyrinthine irritation.

A second example of labyrinthine physiology distributed by chemical alteration in the fluid compartments is that responsible for the clinical symptoms of Ménière's disease. It is now established that the pathological correlate of Ménière's disease is progressive endolymphatic hydrops as a result of endolymphatic sac dysfunction. This pathology has been demonstrated in human temporal bone material (Hallpike and Cairns, 1938; Lindsay, 1942; Schuknecht, Benitez and Beekhuis, 1962 as well as in the experimental animal (Kimura, 1967; Schuknecht, Northrop and Igarashi, 1968). The progressive endolymphatic hydrops may require various time intervals in different species to develop following sac dysfunction (destruction). Eventually progressive distension of the endolymph compartment leads to disruption of the membranous walls of either the pars inferior or the pars superior of the labyrinth. Theoretical (Lawrence and McCabe, 1959; Dohlman, 1965), as well as experimental evidence (Silverstein, 1970), indicates that these events permit release of high potassium endolymph which drastically alters the ionic composition of perilymph by raising the potassium level. High potassium levels in the perilymph diminish the standing action potentials in the vestibular nerve resulting in a sudden asymmetry of input to the vestibular nuclei. Clinically these changes are manifested by dysequilibrium and nystagmus. After the membrane breaks heal, ion composition in perilymph gradually returns to a normal level. Nerve action potentials also recover to a normal pattern resulting in symmetry of input to the brainstem. The resolution of vestibular symptoms follows.

The sensorineural hearing loss which occurs in Ménière's disease can be accounted for by a similar pathophysiological mechanism. Early in the development of endolymphatic hydrops when hearing loss is the earliest presenting symptom, a low frequency sensory pattern of loss is seen. The accumulation of endolymph in scala media with the gradient being greatest at the apical turn and less at the basal turn is consistent with the ascending threshold elevation pattern. Furthermore, changes in endolymphatic volume are consistent with the fluctuations in threshold sensitivity which are characteristic of Ménière's disease. Long durations of endolymphatic hydrops with episodic vertigo are commonly associated with increased sensorineural hearing loss frequently with speech discrimination loss. Although light microscopic evaluation of the organ of Corti fails to reveal corresponding sensory lesions to account for the sensory and neural deficits, degeneration of apical spiral ganglion cells has been observed in Ménière's disease (Lindsay, Kohut and Sciarra, 1962). It seems possible that ultrastructural degenerative changes in auditory nerve terminals within the organ of Corti may also help to explain some of the permanent neural auditory deficits (speech discrimination loss) seen in later stages of the disease. Such nerve terminal injury could result from repeated potassium intoxication following membrane ruptures of pars inferior.
In a similar way, morphological changes in terminal portions of vestibular neurons may occur following repeated insults from potassium contamination of the surrounding perilymph. Degeneration of vestibular ganglion cells has not been observed in temporal bones from patients with Ménière's disease. However, it is well known that vestibular ganglion cells do not degenerate readily following injury to their axonal processes while cochlear ganglion cells are very susceptible to such injury. Therefore, the decreased vestibular sensitivity often seen later in the course of Ménière's disease may be explained by the ultrastructural morphological changes in peripheral terminal portions of vestibular neurons.

Neural (first order vestibular neuron) pathology

Inflammation

The vestibular ganglion located in the internal auditory canal may be affected by various viral agents resulting in the condition called vestibular neuritis (neuronitis). Vestibular neuritis is manifested clinically by a sudden onset of sustained vertigo and dysequilibrium accompanied by a spontaneous nystagmus lasting from 3 to 7 days followed by gradual resolution. These vestibular signs and symptoms usually occur in the absence of involvement of the auditory system, thus supporting the supposition that the selective involvement of the vestibular system is extralabyrinthine, that is at the vestibular nerve level. Clinical supporting evidence that viral agents are responsible for this condition is based on epidemiological evidence of an increased incidence of this vestibular syndrome during an epidemic of viral infections and clinical evidence than an upper respiratory viral disorder frequently precedes the vestibular syndrome (Stahle, 1966; Coats, 1969).

Vestibular neuritis may take one of two clinical forms - acute or chronic. The acute form is manifested by a single prolonged vestibular disorder which does not recur after resolution. The chronic form includes those patients who have recurrent vestibular attacks without hearing loss following the initial episode (Dix and Hallpike, 1952). These recurring attacks of episodic vertigo may be of varying duration. Although the vestibular attacks usually last one or more days, they may occasionally resemble the original episode. Nevertheless, the episodes are longer in duration than the attacks which are observed in Ménière's disease. The clinical diagnosis is based upon a history of a preceding viral episode, the length of the attacks, the exclusion of auditory symptoms and a reduced vestibular sensitivity in one ear in the presence of normal hearing. Although vestibular neuritis is usually unilateral, bilateral vestibular neuritis may occur in a small number of cases.

The histopathological observations in this disorder demonstrate degeneration of the vestibular ganglion and its processes in the presence of a normal auditory end organ and nerve. In addition to the reduced number of vestibular ganglion cells and nerve fibres, a round cell infiltrate is frequently observed surrounding the vestibular nerve fibres in the internal auditory canal. Treatment of vestibular neuritis may be necessary only for the chronic form. A progressive degeneration of the vestibular nerve in the chronic form will usually permit episodes of diminishing severity which may be managed non-surgically. However, occasionally severity of symptoms and the magnitude of disability may justify selective vestibular ablation in a particular patient.
Degeneration

Degeneration of the vestibular nerve may be caused by non-inflammatory agents. Demyelination and degeneration of vestibular neurons has been observed in carcinomatous encephalopathy (Schuknecht, 1974b) and diabetes mellitus (Naufal and Schuknecht, 1972). The degeneration of the first order vestibular neuron is responsible for varying severities and forms of dysequilibrium ranging from episodic vertigo to ataxia. A persistent or recurring dysequilibrium frequently having a duration of days or weeks is usually seen with these forms of degenerative neuropathy. The degenerative process may also involve the auditory nerve or may involve primarily the vestibular nerve. Histopathological documentation exists in the form of degeneration of the vestibular nerve and its ganglion in the presence of normal sense organs. Decreased vestibular sensitivity determined by the caloric test is the clinical correlate of this degenerative process. Demyelination of the vestibular nerve has not been documented in demyelinating disorders such as multiple sclerosis and amyotrophic lateral sclerosis where dysequilibrium and ataxia are common clinical features. It is presumed that the vestibular system and other equilibrium modalities are affected centrally in these neurological disorders. Degeneration of the vestibular nerve may also occur as a result of the ageing process on neural and vascular structures of the labyrinth. Patients with degenerative ageing processes affecting the vestibular nerve usually also have sensorineural hearing loss as a result of degeneration of the auditory nerve.

Trauma

Although transverse fractures of the temporal bone usually involve the vestibular labyrinth and the internal auditory canal when vestibular symptoms are present, occasionally the fracture line will skirt the vestibular labyrinth and sense organs and extend into the bony channels through which the vestibular nerve branches reach the sense organs. Fractures which injure vestibular nerve fibres in this way produce a self-limiting form of vertigo, because of the adjustment to partial vestibular ablation that is made by the host. Auditory function will be preserved provided that the fracture has spared the cochlea. No treatment is required for such an injury which is identified clinically by demonstration of a decrease in vestibular function, but the presence of normal auditory function.

Compression

Compression of the seventh and eighth cranial nerves may occur in the internal auditory canal from vascular, neoplastic and osseous disorders.

Vascular

Although it is possible that a large vessel such as the anterior inferior cerebellar artery or a tortuous basilar artery may significantly compress the seventh or eighth nerves in or near the internal auditory canal, this condition probably exists less frequently than it has been clinically reported. A loop of the anterior inferior cerebellar artery resting against the facial and vestibular nerves within the internal auditory canal is a common finding in normal temporal bone specimens, yet dysfunction of these nerves was not a clinical finding in the patients from whom the temporal bones were acquired. Nevertheless, a number of clinical reports (Janetta, 1980) have indicated that a loop of vessel resting on the vestibular or seventh
nerves in the internal auditory canal is responsible for various vestibular and facial nerve symptoms. Relief of these symptoms is purported to follow when the vessel has been dissected away from the nerve structures and cushioned with an intervening sponge implant. Pressure against the nerves in the internal auditory canal by a pulsating vessel which may become more tortuous with age is a possible mechanism by which vestibular symptoms may occur at the neuronal level. Since neural-vascular arrangement is often not associated with clinical symptoms, convincing documentation that such vascular compression is responsible for the clinical disorder must be made carefully with an unbiased approach.

Neoplasm

The seventh and eighth nerves may be compressed in the internal auditory canal or cerebellopontine angle as a result of extrinsic compression by a neoplasm from an adjacent part of the temporal bone. Benign expanding tumours arising from the petrous apex (Gacek, 1975; DeLozier, Parkins and Gacek, 1979) (epidermoid, mucocele, abscess, cholesterol granuloma, neurofibroma, chondroma, menigioma), or the jugular foramen (Gacek, 1983) (neurofibroma, paraganglioma, menigioma, chondroma) may compress the nerves in the internal auditory canal. The auditory deficit produced is a retrocochlear pattern of sensorineural hearing loss. The pathological correlate is degeneration of cochlear neurons with an intact organ of Corti. Vestibular symptoms vary from intermittent dysequilibrium, to episodic vertigo to positional vertigo. Although the cells of the vestibular ganglion do not degenerate as readily as those of the cochlea, atrophy will eventually occur (years) after compression of their axons.

Osseous compression

Compression of the nerves in the internal auditory canal may be produced by disorders of bone metabolism. Sclerosteosis is a rare inherited bone disorder where periosteal bone growth continues and obliterates the bony channels of the temporal bone which carry neural and vascular structures (Nager and Hamersma, 1986). Vestibular and auditory symptoms of eighth nerve compression are similar to those described from neoplastic compression. Decompression of venous drainage channels has been successful in prolonging life in these patients.

It is conceivable that other disorders of bone metabolism (fibrous dysplasia, osteopetrosis) may also be responsible for seventh and eighth nerve symptoms as a result of compression in the internal auditory canal.

A more common association of dysequilibrium and a disorder of the otic capsule is seen in otosclerosis. Vestibular symptoms are frequently present in patients with otosclerosis. The exact pathophysiological mechanism responsible for vestibular symptoms ranging from episodic vertigo to dysequilibrium in this condition which is primarily manifested by a conductive auditory deficit is not known. However, compression of vestibular nerve fibres by the otosclerotic focus as they pass through the otic capsule is a plausible explanation.
Neoplasia

The vestibular nerve may be affected by either benign or malignant neoplasms. The most common benign tumour to involve the nerves contained within the internal auditory canal is the eighth nerve neuroma (schwannoma) which usually arises from the myelinated segment of the vestibular division. Since the schwann cell (myelinated) portion of the eighth nerve is located lateral (distal) to the glial-schwann cell junction, these tumours arise within the internal auditory canal and extend into the cerebellopontine angle when they have filled the canal. Most vestibular neuromata (60-70%) arise from the superior division of the nerve which makes up a majority of the vestibular nerve population. Rarely the neuroma may arise from the cochlear division of the eighth nerve.

These schwann cell tumours are divided into two histological types: Antoni A and B. The Antoni A variety is formed of tightly packed flattened schwann cells the nuclei of which are frequently stacked in layers (pallisading) and with dense cytoplasm forming the substance of the tumour. Surgically these tumours are firm, relatively avascular and well encapsulated. The Antoni B form is made up of plump cells with foamy cytoplasm, loosely arranged with areas undergoing fatty and cystic degeneration. Surgically these tumours appear soft, cystic, somewhat vascular with a thin capsule.

It is not surprising that the vestibular sensitivity test (ENG) is the most frequently abnormal study in the diagnosis of eighth nerve neuroma (Erickson, Sorenson and McGavran, 1965). This is often the case even though vestibular symptoms (vertigo, ataxia, positional vertigo) are usually mild or absent. The relatively mild vestibular symptoms are probably explained by the slow destruction of vestibular neuronal units, thus allowing for compensation by the host. This relationship is emphasized by the observation of a small occult vestibular neuroma in the temporal bones from patients without balance symptoms.

The vestibular neuroma usually presents clinically as a result of effects produced on adjacent nerve structures in the bony internal auditory canal. Of the two nerves in the internal auditory canal, the cochlear nerve is more susceptible to compression. Therefore, the most common clinical deficit is hearing loss and tinnitus (Erickson, Sorenson and McGavran, 1965). The typical hearing deficit produced by nerve compression (retrocochlear lesion) with subsequent degeneration of cochlear neurons is a severe loss in speech (word) discrimination out of proportion to the pure threshold elevation. An additional common pattern is a high frequency pure tone loss which is related to compression of the neurons innervating the basal turn of the cochlea since they are located near the periphery of the cochlear nerve trunk in the internal auditory canal. However, many variations in the audiometric picture of hearing loss may be demonstrated as a result of cochlear nerve compression from the vestibular neuroma. Therefore, additional pathophysiological mechanisms of sensorineural hearing loss may be responsible. Ischaemia of various segments of the end organ secondary to vascular compression in the internal auditory canal by tumour and changes in the perilymph surrounding cochlear nerve fibres and hair cells are two additional abnormalities which may account for sensorineural hearing deficits. Although slow compression of the facial nerve in the internal auditory canal by the tumour results in flattening of the nerve trunk with an ostensible loss of axons, motor paralysis of facial muscles is not a common clinical finding even with large eighth nerve tumours. This paradox is best explained by the fact that surviving motor axon terminal sprout to re-innervate adjacent denervated facial muscle fibres.
over time and provide adequate motor function. Although the neuroma is the most common benign neoplasm to involve the seventh and eighth nerves in the internal auditory canal, other tumours which may also simulate this picture are meningioma, epidermoid, haemangioma, arachnoid cyst, lipoma, granuloma.

Malignant neoplasms may metastasize to the temporal bone in two ways: by haematogenously to the marrow space of the petrous apex, and to the internal auditory canal by way of the subarachnoid space. Neoplastic replacements of the marrow in the petrous apex cause deficits of the fifth and sixth cranial nerves early in development and affect the seventh and eighth nerves in the internal auditory canal when they attain large size. However, when malignant tumours spread to the subarachnoid space of the internal auditory canal, facial nerve paralysis and eighth nerve symptoms are frequent and prominent.

The clinical picture produced by involvement of the nerves in the internal auditory canal by malignant neoplasm differs greatly from the clinical presentation of a slow growing benign tumour. Vestibular symptoms are prominent and sustained because of the rapid onset of a significant asymmetry produced when neoplasm destroys significant numbers of vestibular neurons. Sensorineural hearing loss, usually of the typical retrocochlear pattern, accompanies the vestibular deficit. Infiltration and destruction of the facial nerve motor axonal coupling by the malignant tumour cells is manifested by paralysis of the facial musculature. The most common primary malignancies that metastasize to the internal auditory canal are carcinoma of the breast, lung, kidney and prostate gland (Schuknecht, Allam and Murakami, 1968). Carcinoma of the middle ear or nearby nasopharynx may extend into the labyrinth resulting in sensorineural hearing loss and vertigo from a serofibrinous labyrinthitis. Such extension from the middle ear space across the bony labyrinth capsule does not occur readily because of the resistant nature of otic capsule bone. This barrier may be crossed by tumour cells either through the oval or round windows or through a fenestration of the otic capsule.

Central vestibular system

Since a small percentage (less than 10%) of patients presenting with vertigo represent central nervous system pathology (Barber, 1984), the recognition of these disorders is dependent on a strong index of suspicion. The major portion of central vestibular pathways are located in the brainstem and cerebellum so that most central vestibular pathology is located in the posterior cranial fossa (infratentorial). As indicated in the discussion of the peripheral vestibular disorders, pathology affecting the central nervous system may also be of inflammatory, neoplastic, vascular, congenital and degenerative types.

Central vestibular disorders of neoplastic, degenerative or vascular causes usually demonstrate multiple neurological deficits in addition to vestibular symptoms and signs. These additional defects should be documented by neurological consultation. Intrinsic lesions of the posterior fossa (vascular, neoplastic) involve significant portions of the brainstem and frequently affect the nearby nuclei such as the abducens nucleus, the facial nucleus, nucleus ambiguus and the trigeminal nucleus and tracts producing neurological signs which permit a relatively obvious diagnosis. However, early neoplasms of the cerebellum, particularly the cerebellar vermis may initially produce only positional vertigo and nystagmus of the non-fatiguing (type I or type II) type (Gregorius, Crandall and Baloh, 1976). Hearing and vestibular (ENG) tests are usually normal at this early stage. Extrinsic lesions (cerebellar
tumours and cysts, the Arnold Chiari malformation) may compress the brainstem and interrupt vestibulo-ocular pathways within the brainstem or near the surface of the fourth ventricle. Interruption of these pathways may be manifested by unique signs such as downbeat nystagmus, upbeat nystagmus, positional nystagmus, or perverted induced nystagmus. An understanding of the involvement of these pathways is helpful to the diagnosis of central vestibular disorders.

**Positional nystagmus**

Positional nystagmus of central origin is usually of the non-fatiguing variety (types I and III), but occasionally the fatiguing variety (type III) may be associated with central pathology (Harrison and Ozsahinoglu, 1975; Watson et al, 1981). However, usually types I and II are central in origin whereas type III is peripheral in origin. Positional nystagmus is frequently seen in cerebellar lesions particularly when the vestibulocerebellum (flocculonodular lobe) is involved primarily or secondarily by neoplasm. This clinical sign is probably caused by a loss of the inhibitory effect of the cerebellum on the vestibular nuclei where vestibulo-ocular neurons are located.

**Downbeat spontaneous nystagmus**

This form of spontaneous nystagmus may reflect lesions which interrupt the excitatory pathways to the inferior rectus muscle (Baloh and Spooner, 1981). This excitatory pathway which relays the input from the posterior semicircular canal originates from the medial vestibular nucleus in the caudal brainstem, crosses the midline to send its fibre projection in the contralateral medial longitudinal fasciculus and terminates in the trochlear nucleus and the inferior rectus subnucleus of the oculomotor complex. Brainstem lesions, such as vascular infarcts, demyelinating disorders and the Arnold Chiari malformation, have been identified as causes for spontaneous downbeat nystagmus. The mechanism of the downbeat nystagmus is based on an interruption of the excitatory pathway to the inferior rectus muscle. The unopposed contraction of the superior rectus which receives its excitatory input from the anterior semicircular canal by way of the brachium conjunctivum is responsible for the upward drift of the globe while the fast phase in a downward direction represents the compensatory movement. Downbeat spontaneous nystagmus may also be associated with lesions of the cerebellar flocculus as a result of loss of the inhibitory input to the superior rectus at the level of the superior vestibular nucleus.

**Upbeat spontaneous nystagmus**

Upbeat spontaneous nystagmus may result from lesions of the posterior fossa which affect the brachium conjunctivum and other nearby fibre pathways (Nakada and Remler, 1981). This vestibulo-ocular reflex finding is produced by interruption of fibre pathways which carry excitatory input to the superior rectus muscle from the anterior semicircular canal through the brachium conjunctivum by way of the superior vestibular nucleus. Ablation of this input leads to unopposed action of the inferior rectus muscle resulting in a downward drift of the eyes with an upward compensatory fast phase.
**Perversion of nystagmus**

Perversion of nystagmus may be produced by lesions that compress the vestibulo-ocular pathways near the floor of the fourth ventricle in the caudal brainstem. The vestibulo-ocular neurons serving the medial and lateral rectus muscles, as well as interneurons in the abducens nucleus which project to the contralateral medial rectus are located superficially at this level of the brainstem. When the horizontal vestibulo-ocular pathways are interrupted at this point in the posterior brainstem, the intact excitatory vestibulo-ocular pathways in the brachium conjunctivum and the rostral medial longitudinal fasciculus produce vertical and rotatory eye displacement. Therefore vertical and rotatory nystagmus may be observed instead of horizontal nystagmus when the lateral canal is calorically stimulated.

**Internuclear opthalmoplegia**

This distinctive oculomotor deficit is produced when a focal lesion (demyelinating) of the medial longitudinal fasciculus interrupts the projection of the abducens interneurons which excite the contralateral medial rectus subnucleus. This interruption of the abducens interneuron results in a dissociated eye displacement on lateral gaze. It is a frequently observed clinical sign in multiple sclerosis.

**Conclusion**

The preceding anatomicophysiological discussion of the pathology of vertigo is not intended to represent a comprehensive list of pathologies which affect the vestibular system. This presentation provides a description of the various mechanisms by which the normal physiology of the vestibular system may be disrupted producing dysequilibrium or vertigo. An understanding of the mechanism by which asymmetry in the vestibular system is produced not only facilitates diagnosis but allows for logical management. The examples discussed represent the more common disorders encountered in otoneurological practice. It is appreciated that a significant number of unknown pathologies are seen daily in clinical practice. Further information will be necessary in order to clarify the pathophysiology of these disorders. Such documentation may be represented by observations provided by newer clinical technologies (magnetic resonance imaging), and experimental study in the laboratory animal of vestibulopathophysiology using physiological and morphological (ultrastructural or histochemical) techniques. The emphasis in these experimental studies may be directed toward alterations in the make-up and function of the cupula, otoconia, or the ciliary structures of the hair cells in the vestibular receptors. Temporal bone post-mortem material is still a valuable source because of the insight that it provides to disorders that affect the human vestibular system. The acquisition of temporal bone material should be encouraged for study by both light and electron microscopic techniques.