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Meniere's Disease in Flight Crew

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An Outline and the Nature of Meniere's Disease

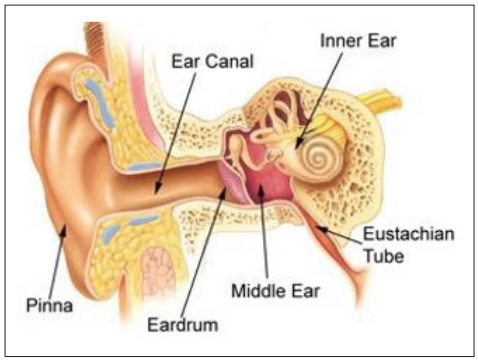

Figure 1: Ear Anatomy

Sudden changes in balance are often debilitating for many patients in the general population but even more for sufferers in a safety-critical role, such as machinery operators, drivers, aviation industry workers, air traffic controllers, pilots, or others. 98 % of the presentation of vertigo in general practice is Benign Paroxysmal Positional Vertigo (BPPV), Acute Vestibular Neuritis and Meniere's disease (MD) [1-3].

MD is a multifactorial, progressive, chronic, usually unilateral, inner ear (figure-1) disorder characterised by a triad of symptoms: vertigo, hearing loss and tinnitus [4-7]. There are 12 in 1000 people worldwide, or 17-46 cases per 100,000, suffering from MD, which makes up about 1% of the global population [8,9]. There is a slight increase in the female-to-male ratio of 1.3-1, and MD usually affects middle-aged individuals, primarily of white northern European descent [10]. A recurring episode of vertigo lasts from 20 minutes to several hours, a maximum of 24 hours, and is accompanied by nausea and vomiting. Although no cause for MD has been identified, there is evidence that environmental, weather change, emotional and physical stress, severe obesity, and urban life in the industrial area increase the risk of MD [7]. Also, genetic influence is predominantly autosomal dominant, and if there are several family members with Sensorineural Hearing Loss (SNHL), migraine, or recurrent vertigo, they should proceed with MD investigations [7].

Before starting any investigations in aircrew, it is important to first differentiate any acute vertigo from in-flight spatial disorientation, which is part of an anticipated physiological reaction to a specific aviation environment, and also consider all possibilities of other neurological, middle and inner ear conditions, cardiovascular, blood and other systemic diseases [11].

Defining the diagnosis of MD is essential due to its association with other co-morbidities (arthritis, gastroesophageal reflux disease, irritable bowel syndrome, migraines) and exclusion of other MD mimicking disorders (figure-2) [7].

Meniere's Disease Symptoms

1. Fluctuating vertigo takes the form of rotatory spinning or rocking form lasting from 20 minutes to 24 hours, associated with nausea and vomiting [5-7].
2. Fluctuating hearing loss usually starts at lower frequencies and can be mixed conductive and mostly SNHL initially, which usually develops into permanent SNHL hearing loss in the following decade [5,7].
3. Tinnitus is ringing, hissing, whistling, buzzing or other audible sensations with different intensities and can be present without other symptoms [5].
4. Ipsilateral aural fulness and head pressure sensations are usually associated with episodes of hearing loss [5-7].

Central nervous system
Acoustic neuroma
Multiple sclerosis
Vascular loop compression of eighth nerve
Basilar/vertebral artery insufficiency
Arnold-Chiari malformation
Cerebellar tumors
Transient ischemic attacks
Peripheral vestibular system
Benign positional vertigo
Syphilitic endolymphatic hydrops
Post-concussive hydrops
Post-infectious hydrops (history of sudden sensorineural hearing loss, chronic otitis media, or labyrinthitis)
Autoimmune inner ear disease
Perilymphatic fistula
Otosclerosis
Migraine induced vertigo
Other
Diabetes
Thyroid disease
Cogan's syndrome
Anemia

UpToDate

Figure 2: Differential diagnosis for MD [5].

Diagnosis

The Classification Committee of the Bárány Society, The Japan Society for Equilibrium Research, the European Academy of Otology and Neurotology (EAONO), the Equilibrium Committee of the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) and the Korean Balance Society, met in 2014 and developed the following international consensus on diagnostic criteria of MD [7].

Definitive MD

1. Two or more spontaneous episodes of vertigo, each lasting 20 minutes to 12 hours.
2. Audiometrically documented low to medium-frequency sensorineural hearing loss in one ear, defining the affected ear on at least one occasion before, during or after one of the episodes of vertigo.
3. Fluctuating aural symptoms (hearing, tinnitus or fullness) in the affected ear.
4. Not better accounted for by another vestibular diagnosis [7].

Probable MD

1. Two or more episodes of vertigo or dizziness, each lasting 20 minutes to 24 hours.
2. Fluctuating aural symptoms (hearing, tinnitus or fullness) in the affected ear.
3. Not better accounted for by another vestibular diagnosis [7].

Postulated Theories of MD Pathogenesis

1. The abnormal flow of endolymph, its resorption, or calcium deposits blocking the flow is one of the theories supporting Endolymphatic Hydrops (EH) (figure-3) [12]. Expansion of endolymphatic fluid results in rupture of the vestibular membrane, causing the mix of peri and endolymphatic matters and explaining unexpected, sudden loss of balance and hearing. Healing of the vestibular membrane leads to repair of the peri and endolymph and is followed by restoration of balance and hearing. Not every EH will give symptomatic MD, but every MD will have EH [7].
2. Hypoplasia of the vestibular aqueduct [13].
3. Developing autoantibodies against endolymphatic sac [14,15].
4. Genetics, Autosomal dominant inheritance in 8-9% of European population [7,16].
5. Vascular pathology associated with migraine is common [7,16].

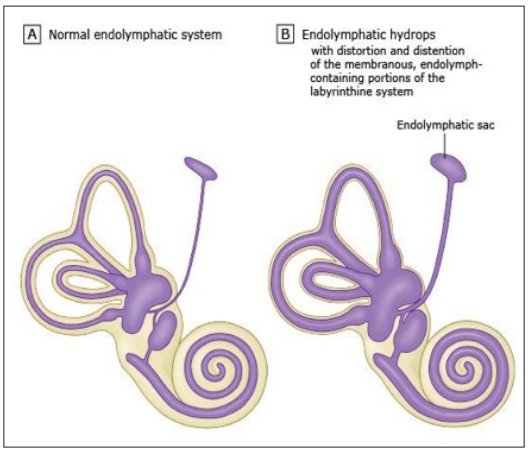

Figure 3: Normal Endolymphatic System and EH [5].

Testing

Although there are no specific diagnostic tests and a definitive diagnosis of EH can only be made postmortem, there are many tests available to assist a physician in definng the diagnosis of MD and excluding other pathology [5,7].

1. Audiometry – fluctuating SNHL, lower to mid-frequency.
2. Vestibular testing: electronystagmography (ENG), the Caloric (figure-4), rotary chair testing, and computerised dynamic posturography.

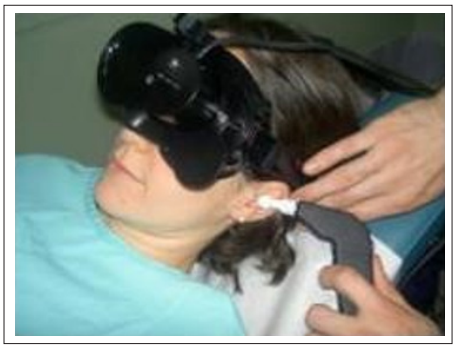

Figure 4: Caloric Testing [17].

1. Imaging: MRI/CT
2. Apart from excluding other causes, 3 Tesla MRI with intratympanic gadolinium application can confirm visualisation of EH in 93 % of symptomatic ears and 65% in asymptomatic contralateral ears and is more objective and accurate if used later when MD symptoms are more established [18,19].
3. Blood tests : CBC, TFT, BSL,ESR CRP,ANA, CBC,RFT, Allergy tests ,VDRL,FTA-ABS.
4. Other tests: antibodies against inner ear antigens, endolymphatic hydrops tests - including glycerine, urea, or sorbitol "stress" tests.
5. Newer diagnostic tests:

- The video head impulse test (vHIT) - records the eye movement response to head impulses.
- The Vestibular Evoked Myogenic Potential (VEMP) - records the reaction of the muscle activity to a repetitive sound stimulus in the ear.
- The Ocular Vestibular Evoked Myogenic Potential (oVEMP) galvanic vestibular stimulation is recorded from ocular musculature.
- The Cervical Vestibular Evoked Myogenic Potential (cVEMP), the same stimulation is recorded from cervical musculature (figure-5).

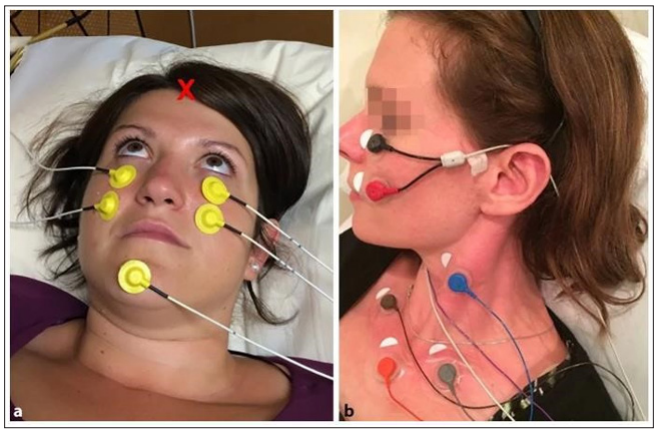

Figure 5: Placement of Electrodes an oVEMP and cVEMP [20]

The Available Treatments
Although no definitive cure for MD has been established, the current conservative management of MD puts a positive perspective on the outcome for most MD sufferers and aims at improving the patient's quality of life [5].

Diet and Lifestyle
Current recommendations for MD treatment are to be initiated with an emphasis on diet and lifestyle. Although solid evidence is lacking in some randomised control studies that limiting salt, caffeine and alcohol intake to one daily, nicotine, stress, monosodium glutamate [MSG] and allergies can reduce the onset of MD [21,22]. On the contrary, other evidence suggests that salt restriction to 2-3 g daily, reducing caffeine and alcohol intake to one daily, can reduce the onset of MD and should be part of the initial treatment and be applied for life [23-25].

Vestibular Rehabilitation
Even though vestibular rehabilitation has no impact on the treatment of acute vertigo due to MD and will not reduce the frequency of attacks, exercises are still recommended to improve the balance between the episode of acute vertigo and, in some cases only in postoperative treatment for acute vertigo seen after vestibular neurectomy or labyrinthectomy [21,23,24].

Pharmacotherapy-First Line
Pharmacotherapy of MD is usually recommended along with lifestyle changes and as a part of initial management. Betahistine and diuretics may reduce EH [25]. Better tolerance to Betahistine put their usage in front of diuretics and aims to lower the severity and intensity of MD attacks. Unlike with use in diabetics, there is no need to monitor the metabolic effects of Betahistine (blood pressure, kidney function, and electrolytes). Recommended usage of the typical maintenance dose is 8 to 16 mg orally three times per day, up to six months before it is tapered down [26,23]. Betahistine is still recommended as the first choice, although there was limited evidence in one study that Betahistine can reduce the frequency of vertigo attacks due to MD [27]. The second pharmacotherapy of concomitant use is recommended with diuretics [23]. Usually recommended diuretics are hydrochlorothiazidetriamterene 25 mg/37.5 mg orally once daily, furosemide 20 mg orally once daily, or acetazolamide 250 to 500 mg orally twice daily.

Vestibular suppressants like benzodiazepine and antiemetics are added in acute vertigo episodes. Given the potential for drowsiness and sedation, the lowest possible dose should be used of clonazepam, diazepam, promethazine, and ondansetron [5]. Benzodiazepines recommended are - clonazepam 0.25 mg to 0.5 mg orally two to three times daily as needed or diazepam 1 to 5 mg orally twice daily as needed.

Antiemetics recommended are promethazine 12.5 to 25 mg orally every six to eight hours as needed or ondansetron 4 mg orally two to three times daily as needed.

Pharmacotherapy-Second Line
Glucocorticoid therapy, systemic or intratympanic , is the next step in treatment for refractory, persistent symptoms [5,24,28-30]. Intratympanic dexamethasone injections have proven to improve vertigo in MD patients, although less effective than intratympanic gentamycin [31].

Additional Treatments
In case of failure of all treatments mentioned above by MD that causes an impairing effect on the person's life with uncontrollable severe vertigo and apparent hearing loss, additional procedures are recommended, depending on the hearing level in the affected ear.

Patients with Preserved Hearing in the Affected Ear
If resistant to previous therapy, a non-destructive surgical procedure in which the endolymphatic sac and duct are open to improving drainage of endolymph. The majority of this procedure improved vertigo, hearing and tinnitus, although proven non-efficacious in some earlier studies [32-34]. If not successful, endolymphatic sac procedures (including decompression or shunting) or sacculotomy should be followed with intratympanic gentamycin. Furthermore, if intratympanic gentamycin application is not efficacious, the last and most drastic measures in treating severe and disabling MD symptoms when all treatments prove unsuccessful are Labyrinthectomy and vestibular neurectomy. Labyrinthectomy, surgically destruction of the entire labyrinth structure, is nearly a 100 % successful treatment of vertigo but also destroys the hearing apparatus causing permanent hearing loss [35].

Vestibular neurectomy – surgical lysis of the vestibular nerve, also has a very high success rate with reliving vertigo in up to 95 % of patients, preserving sensorineural hearing loss, but its major downside is the need for craniotomy and its a risk [35].

Patients with Complete Hearing Loss in the Affected Ear
Intratympanic injections of gentamycin have been proven as an adequate substitute in the majority of refractory vertigo due to MD that was unsuccessful treatment with systemic or intratympanic steroid [5,36-38].

Additionally, before establishing suitable treatment for MD, care need to be taken to also assess occupational disability due to MD and classify MD as:
" Mild – Intermittent or continuous dizziness/unsteadiness that precludes working in a hazardous Moderate – Intermittent or continuous dizziness that results in a sedentary occupation Severe disability – Symptoms so severe as to exclude gainful employment "[39].

The Effect of the Aviation Environment on the MD
- Pure oxygen affects the middle ear and sinuses [40]. Inhaling pure oxygen by military pilots during flights and hypobaric chamber training can cause middle ear trauma and possibly MD [41,42].
- Adjustment to pressure changes , significantly lower pressure changes and humidity, can exacerbate MD [7,40,43].
- High and abnormal G has input into the vestibular apparatus [40]. During the flight, the inner ear is exposed to different G forces, affecting function and labyrinth structure and can cause EH and MD [6,44].
- The eustachian tube dysfunction potentially can cause secondary MD since disturbed inner ear pressure can be exacerbated with the Valsalva manoeuvre [6,24,45].
- Pilots are more at risk of MD and developing EH since the increased risk of respiratory infection, otitis media, labyrinthitis and acoustic trauma, tympanic membrane perforation, and vertigo [6,7,45] (figure-6).
- Middle ear barotrauma is common among aircrew, and passengers (20-50%), followed by inner ear barotrauma and is a risk factor for EH and MD (figure-6)[6,46].
- A study on exposure to air pollution and specific meteorological factors on MD identified higher incidence of MD, particularly in the presence of O3 and CO [47].

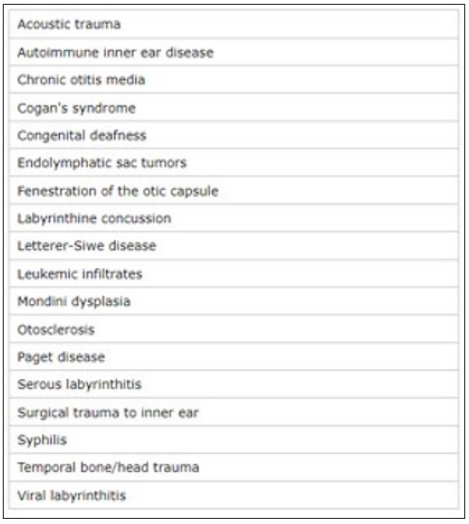

Figure 6: Causes of EH [5].

The Effect of the MD and its Treatment on the Pilot's Ability to Fly

How MD affects the pilot's ability to fly is expressed in acute overt or insidious onset of their possible incapacitations.

1. **Overt Incapacitation**
- acute disorientation and loss of situational awareness due to acute vertigo
- poor communication due to loss of hearing
- failed performance since the association of nausea and vomiting in an acute episode
- distraction due to acute ear pain

2. **Subtle Incapacitation**
- distraction and reduced concentration due to symptoms of MD
- distraction due to social, family, employment pressure
- depression, anxiety

Since many MD symptoms are subjective and subject to self-reporting if concealed by a pilot, MD has the potential for subtle incapacitation in its mild form. Pilots' concerns about MD's implications on employment, family and social consequences can pose a distraction. Tinnitus, for example, as a single symptom, strongly correlates with depression and anxiety among sufferers [48]. Consequently, tinnitus, in combination with vertigo and hearing loss, can have an even more harmful and profound effect on pilots' performance.

Treatment of the MD contains many medications that exhibit potential serious adverse effects that would present a risk for incapacitation for the pilot and are not recommended during flying except for thiazide diuretics that are used in managing hypertension in pilots.

Betahistine can cause drowsiness; Steroids can cause changes in mood, blurred vision, nervousness, diabetes, HTN, difficulty sleeping, and glaucoma; Benzodiazepine and antiemetics have the potential for drowsiness and sedation; Endolymphatic sac procedures, sacculotomy, and intratympanic gentamycin risk causing hearing loss, and in addition to hearing loss, intratympanic gentamycin can cause tinnitus; Finally, Labyrinthectomy, surgically destruction of the labyrinth, causes a 100 % hearing loss, with vestibular neurectomy that carries a risk of craniotomy and its consequences.

Guidance Material from Various Authorities about MD

ICAO - International Civil Aviation Organization

In its Medical Manual, ICAO comments about Meniere disease in a very general manner and gives broad recommendations that applicants with MD should be assessed accordingly, and MD has taken into account [49].

UK CAA-Civil Aviation Authority

UK CAA Medial standards are easy to follow since they provide un-ambiguous and exact requirements that MD, treated or untreated, is not acceptable for Class 1 or 2 medical certification, initial or recertification [50].

UAE GCAA – General Civil Aviation Authority

The equal recommendation comes from the UAE's GCAA CAR MED Medical regulation. They are following UK CAA and treating MD as entirely unacceptable in any form for pilot certification [51].

NZ CAA - Civil Aviation Authority

In its regulations, New Zealand CAA considered MD a concern to flight safety and confirmed the diagnosis of MD as a condition of aeromedical significance. However, NZ CAA does not reject an applicant from the start of diagnosis of MD. This aviation authority requires further information to be provided by ENT specialists in formal reports, including audiometry and other tests as recommended by a specialist, giving the impression that recertification of pilots with MD in NZ is possible [52].

Australian CASA – Civil Aviation Safety Authority

Australian Aviation Authority classifies the MD as unfavourable but does not reject the condition. They focused more on vertigo as a symptom that mandated pilot's grounding and DAME reporting, requiring further investigation and opinion with a minimum grounding period of six months, usually longer than in other aviation jurisdictions. However, CASA is unclear whether vertigo will be considered for certification due to MD [40].

EASA – European Union Aviation Safety Agency

EASA is not specifying MD but only vestibular disturbance as a condition incompatible with flying. They consider certification of flight crew after complete recovery and full ENT investigations without specifying the grounding period [53].

The USA FAA – Federal Aviation Administration

FAA, in its recommendations for the cases of MD, requires an applicant to submit all pertinent medical records documentation, including a neurologic report and specific details about the dose of the medications used and its side effects [54].

The USA AOPA – Aircraft Owners and Pilot's Association

The FAA will consider MD medical certifications for pilots after thorough ENT, and other documentation of diagnosing, testing and treatment of MD is done. FAA decisions will be made case-by-case basis after a substantial grounding period of twelve months [55].

Summary and Recommendations on Fitness to Fly with MD

Vertigo, hearing loss and tinnitus, the main symptoms of MD, can negatively affect flight safety and are conditions that can be incompatible with flying. When this triad represents MD, the safety risk is amplified, and the pilot's fitness is even more questionable and requires more examinations and testing. However, no specific diagnostic test exists for MD. Despite the lack of clear cause, specific tests, or specific treatment and cure for MD, there are

still numerous investigations and procedures in its management available to make the sufferers of MD have a reasonable quality of lifestyle. Nonetheless, whether these measures are sufficient to make a pilot with MD fit to return to work remains unanswered.

Many aggravating influences exist in the aviation environment, such as pure oxygen, pressure changes, G-force, and frequent respiratory and ear infections in pilots, which make pilots more susceptible to MD. The complexity of MD adds a further burden on the recertification of the pilot since the effect of MD on the pilot's ability to fly presents the risk of sudden or subtle incapacitation. Also, the treatment of MD has many potential side effects that can affect the pilot's performance and pose a risk to flight safety.

Every aviation authority reviewed in this paper, including ICAO, identifies MD as a condition of aeromedical significance. However, there are variations in the aeromedical disposition of pilots with MD between different jurisdictions. Unlike the UK CAA and the UAE GCAA, which unconditionally deny any certification of MD cases, other aviation bodies are mostly equivocal in their requirements for MD pilot certification. CASA and EASA are similar in their approach to vertigo management and consider MD unfavourable without clear rejection of MD applicants. In addition to a specific investigation, NZ CAA requires a detailed case review before making a decision.

Finally, the most favourable authority appears to be the FAA, which gives the potential pilot applicant a chance to be certified after a detailed and thorough specialist investigation and a substantial 12month grounding period. However, a clear pathway for certifying MD pilots has not yet been established.

Diagnosing MD in flight crew must start with grounding until the specialist's complete examination, investigation, and observation is made and reviewed by AME. Ruling out all other possible causes and associated diseases is a must. Certification exceptions and flying waivers are granted rarely in exceptional circumstances and are plausible to only a few aviation authorities. This flexibility and possibility of certification in pilots demands further exploration.

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