We are IntechOpen, the world’s leading publisher of Open Access books
Built by scientists, for scientists

4,300
Open access books available

116,000
International authors and editors

130M
Downloads

154
Countries delivered to

TOP 1%
Our authors are among the most cited scientists

12.2%
Contributors from top 500 universities

WEB OF SCIENCE™
Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com
Chapter 8

Hearing and Vestibular Testing in Menière’s Disease

Madalina Gabriela Georgescu

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/66382

Abstract

Audiological and vestibular testing plays an important role in diagnosis of Menière’s disease, as disease per se and as staging diagnosis. A battery of tests are recommended in order to have a better evaluation of the disease. Audiological testing includes pure tone audiometry, with highlights of bone conduction especially in acute episodes of Menière’s disease, speech audiometry and glycerol test when hearing loss is documented, ABR and electrocochleography. Besides these investigations, vestibular investigations are also recommended in order to evaluate the degree of vestibular lesion present from the beginning of Menière’s disease—electro- and videonystagmography, head impulse test, vestibular evoked myogenic potentials and computerized dynamic posturography.

Keywords: pure tone audiometry, glycerol test, auditory brainstem response, vestibular evoked myogenic potentials

1. Introduction

The aim of this chapter is to clearly identify the usefulness of audiological investigations, both for hearing and for vestibular function, in positive diagnosis of Menière’s disease and in staging the lesion. This is important for counselling the patients regarding the disease long-term evolution and also for appropriate management of the disease.

Inner ear spaces of the anterior and posterior labyrinth communicate in between and endolymphatic hydrops present in the Menière’s disease usually affects both auditory and vestibular sensorial structures located in the two parts of the inner ear.

In this chapter, hearing and vestibular testing will be presented, as tests are recommended for positive and differential diagnosis of the Menière’s disease. Regarding Menière’s disease diagnostic, audiological and vestibular testing plays an important role in diagnosis of the disease per se and for staging diagnosis. Besides medical importance, accurate diagnosis is also...
important for counselling the patients regarding the disease long-term evolution and also for appropriate management of the disease.

2. Audiological evaluation

Audiological testing includes pure tone audiometry, with highlights of bone conduction especially in acute episodes of this disease, glycerol test when hearing loss is documented, auditory brainstem response (ABR) and electrocochleography.

2.1. Pure tone audiometry

Pure tone audiometry is a subjective method of hearing evaluation. Patient must signalize the faintest sound he/she hears. Pure tone with specific frequencies is used (125, 250, 500, 1000, 2000, 4000, and 8000 Hz), based on the human normal hearing frequency range (20–20,000 Hz).

Sounds are presented both in air and bone conduction in order to have an accurate image of the hearing.

The result of the test is shown in a graph, a Cartesian system with frequency tested (in Hz) on horizontal axis and intensity (in dB HL) on the vertical one. Frequency varies between 125 and 8000 Hz and intensity between −10 and 120 dB (the latest represents the painful sensation, not an audible one = uncomfortable level). Based on patient’s response, the least audible intensity (threshold) on each tested frequency is plotted.

Threshold notation is standardized internationally (ISO system) and colors as well: red for the right ear and blue for the left ear (Figure 1):

- Air conduction: “circle” for the right ear and “X” for the left ear
- Nose-opened brackets for bone conduction: “<” and “>” in unmasked condition and “[“ and “]” in masked condition

Normative for hearing thresholds (THR) were established based on nonotological history teenagers’ responses decades ago and normal hearing stands for hearing thresholds between −10 and +20 dB on all frequencies, without differences between air and bone conduction (Figure 2).

Pure tone audiometry is the method of choice for hearing evaluation also in Menière’s disease patients in [1, 2]. When hearing loss (HL) is permanent, Menière’s disease patients experience

---

Figure 1. Standardized notation for hearing thresholds.
sensorineural hearing loss (average of hearing THR on 0.5, 1, and 2 kHz greater than 20 dB), with pathological thresholds on low frequencies (Figure 3).

Figure 2. Pure tone audiometry—normal hearing in both ears.

Figure 3. Low frequency sensorineural hearing loss in left ear.

cochlear sensorineural hearing loss (SNHL) is accompanied by recruitment, a phenomenon of increased loudness perception—above an increase threshold, higher intensity sounds are as loud to the hearing impaired person as for a normal hearing one and thus disturbing.
Some authors describe in Menière’s disease patients a particular type of recruitment—hyper- or overrecruitment: loudness in the affected ear overtakes the normal ear at high intensities in [3–5].

When differences between air conduction thresholds in both ears exceed 40dB for supra-aural earphones or 55 dB when insert earphones are used, air conduction masking is mandatory for that specific frequency where this difference exists. For bone conduction, masking is mandatory whenever more than 10dB difference between bone and air conduction thresholds is present on that specific frequency. Bone conduction masking is essential in differentiating conductive and sensorineural hearing loss.

It is not unusual to have a conductive component of the hearing loss in Menière’s disease acute phase—disturbances in endolymph metabolism lead to pressure variations at the round and oval window with secondary increases of impedances. High impedances diminish air transmission of the sounds, with consecutive cochlear conductive hearing loss (Figure 4). In these cases, middle ear test (tympanometry and acoustically evoked stapedius reflex) shows no impairment of the middle ear as cause of the conductive component of the hearing loss.

2.2. Speech audiometry

Besides pure tone audiometry, speech audiometry complements auditory evaluation. It is a more complex test, since evaluates the entire auditory pathway as hearing is a cortical process. Speech audiometry is also a subjective audiological test where the tested person has to repeat the heard stimuli—numbers, monosyllabic, disyllabic words, or sentences.

The result of the test is a Cartesian graphic with percentage of correct repeated stimuli on the vertical axis for each intensity tested and with intensity of the stimulus on the horizontal axis. For each intensity, a phonemic-balanced list of 10 stimuli (numbers, monosyllabic, disyllabic words, or sentences) is presented. These percentages draw a curve which crosses the 50% line at some specific intensity. This crossing represents the threshold of speech audiometry. For normal hearing, conductive or cochlear sensorial sensorineural hearing loss, this threshold must correlate with pure tone average ±7 dB (Figure 5).

![Figure 4. Conductive (a) or mixed (b) hearing loss due to cochlear conductive hearing loss.](image-url)
If in cochlear sensorineural hearing loss of other etiology there is a good correlation (±7 dB) between pure tone and speech audiometry THR, in prolonged Menière’s disease, some differences may appear.

Another parameter used in interpretation of the speech audiometry is the maxim of intelligibility/discrimination. It represents the highest percentage of correct repeated stimuli the patient obtains. For normal hearing or conductive hearing loss persons, 100% intelligibility is reached.

Sensorineural hearing loss induced distortions in audition which can limit the maximum of discrimination. Speech audiometry can draw attention on the estimated site of hearing loss, cochlear, or retrocochlear: in cochlear lesions, once the maximum score of discrimination is reached, it remains constant as higher intensities are tested. In retrocochlear sensorineural hearing loss an odd phenomenon occurs—as intensity increases, the patient understands less word (roll-over phenomenon).

2.3. Glycerol test

In patients with Menière’s disease and permanent sensorineural HL, if low frequencies THR are greater than 40 dB, glycerol test is recommended. Since endolymphatic hydrops is the pathophysiological mechanism of the Menière’s disease, oral administration of a hypertonic solution will extract liquids from tissues, including from the endolymphatic space. Thus, the endolymphatic pressure is diminished and hearing and vestibular sensorial epithelium recovers from increased pressure. The clinical effect of this restoration is improvement of both auditory and vestibular system function 2 h and 30 min after the ingestion, when both pure tone audiometry and speech audiometry are repeated.

Hearing improvement can be documented by pure tone audiometry and speech audiometry. An improvement of the THR on at least 10dB on three consecutive frequencies in pure tone audiometry and/or a more than 12% improvement of speech audiometry THR is considered
a positive glycerol test (Figure 6). Some authors consider this as an indication for diuretic treatment, since the endolymphatic system has the capacity to modify its pressure after oral administration of a hyperosmolar solution.

2.4. Brainstem evoked response audiometry (BERA)/auditory brainstem response (ABR)

ABR—is an objective electrophysiological audiological method that allows recording of the electrical activity evoked by neural activity in the auditory pathways, from the cochlea to the brainstem (lateral lemniscus) in Refs. [6, 7]. Surface electrodes are used in this far-field technique. Most commonly used acoustic stimulus is the click—a brief (0.1 ms) rectangular stimulus. Click-evoked ABR reflects hearing sensitivity in the frequency range of 1–4 kHz with a high correlation with pure tone audiometry threshold in this frequency domain, especially at 4 kHz where the stimulus’ energy is maximum.

ABR is the first evoked potentials, with seven characteristic waves in the first 10 ms after click stimulation at high intensities: 70–90 dB normal hearing level (nHL). These waves were first described by Jewett, as response of different auditory pathway structures after acoustic stimulation:

- wave I: proximal auditory nerve
- wave II: distal auditory nerve
- wave III: cochlear nuclei
- wave IV: superior olivar complex
- wave V: lateral lemniscus

![Figure 6. Positive glycerol test.](image-url)
wave VI: medial geniculate body (thalamus)—probable
wave VII: medial geniculate body (thalamus)—probable

First five are mostly used in interpretation of the BERA recordings. In Menière’s disease patients, BERA is mandatory in order to rule out a retrocochlear etiology of the sensorineural hearing loss. Latencies, interpeak intervals and interaural differences of the latencies and interpeak intervals are the parameters used for this differential diagnosis (Figure 7).

In general, ABR exhibits a sensitivity of over 90% and a specificity of approximately 70–90%. Findings suggestive of retrocochlear pathology may include any one or more of the following:

- Absolute latency interaural difference wave V (IT5)—prolonged as compared with normative data.
- I–V interpeak interval interaural difference (IPI1-5)—prolonged as compared with normative data; greater than 0.2 ms in unilateral or symmetrical hearing loss, or greater than 0.3 ms in patients with asymmetrical or with noise-induced hearing loss. Interaural IPI difference criterion requires no correction for audiogram differences.
- Absolute latency of wave V—prolonged as compared with normative data.
- Absolute latencies and interpeak intervals latencies I–III, I–V, III–V—prolonged as compared with normative data.
- Absence of the later waves.
- Absent auditory brainstem response in the involved ear even though hearing is normal or mildly impaired.
- ABR traces not replicable.
- Abnormally low V:I amplitude ratio (less than 1.0)—less sensitivity than latency measurements.

Figure 7. Parameters used in ABR interpretation.
2.5. Electrocochleography

Electrocochleography (ECochG) is an objective audiological test that measures the electrical potentials derived from the cochlear hair cells and the auditory nerve in [8–10]. These potentials are produced between an electrode on the cochlear promontory and an earlobe electrode, within a time frame of 5 ms after stimulation with alternative repetitive very short acoustic signals (click). Averaging of a large number of potentials (1000 sweeps) is needed in order to record the ECochG characteristic wave. Click is the most common stimuli used in ECochG due to its effect of very good synchronization of a large number of cochlear nerve fibers, mandatory for eliciting a measurable action potential. Click has an abrupt onset, very short duration and broad frequency spectra, thus stimulating a very large number of hair cells in the basal turn of the cochlea, where the speed of the travelling wave is the fastest.

Magnitude and quality of the response depends on the electrode type—trans tympanic electrode fixed directly on the promontory gives the best recordings, but it is an invasive audiological investigation. Alternatively, with good clinical results are used extratympanic electrodes, place in the external auditory canal, as close as possible to the eardrum or on the eardrum itself.

Synchronization of the auditory nerve fibers after above-mentioned stimulation gives birth to global action potential. Its origin lies into the inner ear hair cells and cochlear nerve.

Global action potential consists of presynaptic and postsynaptic potentials (Figure 8).

The first one includes cochlear microphonic (CM) that originates in the outer cochlear hair cells and summating potential (SP) arising from the inner cochlear hair cells. Postsynaptic potentials, known as global action potential of the cochlear nerve, is generated by all cochlear nerve fibers, fired in synchrony by the acoustic stimulus.

In endolymphatic hydrops, due to the increased pressure in scala media, basilar membrane vibrates asymmetrical. These changes of the traveling wave lead to several dysfunctions: distorted cochlear microphonics, enlargement of the summating potential and broadening of the

Figure 8. Global action potential.
action potential. Magnitude of the AP compared with SP (SP/AP ratio) is increased in endolymphatic hydrops (>30%). The SP/AP amplitude ratio has 50–60% sensitivity in Ménière’s disease diagnosis and 95% specificity in Refs. [11, 12] (Figure 9).

Recently, an area ratio (Figure 10) seems to be a more sensitive parameter for detecting endolymphatic hydrops [13]. An increase of more than 2 of SP/AP area together with the increase of SP/AP amplitude ratio increases sensitivity and specificity in Menière’s disease diagnosis to 92 and 83.9%, respectively [14]. Some EP machines enabled automatically measurement of the area ratio.

3. Vestibular evaluation

Vestibular investigations are also recommended in Menière’s disease patients not only as a recommended battery test for positive diagnosis, but also in order to evaluate the degree of vestibular lesion which is present from the beginning of the Menière’s disease.

Both vestibulo-ocular reflex (VOR) and vestibulospinal reflex (VSR) should be evaluated. Besides bed-side evaluation, objective vestibular tests are performed for a quantitative measure of these two vestibular reflexes useful in understanding the vestibular deficits as the disease proceeds.
3.1. Vestibulo-ocular reflex

3.1.1. Electronystagmography (ENG)/videonystagmography (VNG)

Electro- or videonystagmography allows quantification of the nystagmus, as specific sign of vestibulo-ocular reflex dysfunction. Nystagmus, as a conjugate movement of eyes with a slow and a fast phase provoked by vestibular asymmetry, reflects variations of the corneo-retinian potential during eyes movement (Figure 11). The slow phase is the effect of vestibular stimulation and its amplitude is proportional to the intensity of vestibular stimulation. The fast phase is central in origin and reflects only the reflex movement of the eyes to return to their normal position in the orbit. The fast phase direction gives the nystagmus direction.

The corneo-retinian potential can be measured by surface electrodes fixed around the eyes, horizontal and vertical or registered with infrared camera (Figure 12) in Refs. [15–17]. Conventionally, for horizontal electrodes, the upward fast phase is considered right beating nystagmus, while the downward fast phase is considered left beating nystagmus. For vertical electrodes, the upward fast phase is considered superior beating nystagmus, while the downward fast phase is considered inferior beating nystagmus.

Quantification of the nystagmus is based on several parameters:

- Direction of the nystagmus—linear, vertical, rotatory; right-, left-, superior- or inferior-beating nystagmus.
- Velocity of the slow phase, vestibular in origin (Figure 12).

Figure 11. Nystagmus recording = variations of the corneo-retinian potential.

Figure 12. Calculation of nystagmus slow phase velocity.
Several tests are included in the electro-/videonystagmography (ENG/VNG): spontaneous nystagmus, positional, and positioning nystagmus, as well as provoked nystagmus (post or perrotatory nystagmus and caloric nystagmus). The provoked test is recommended only if patient is not in an acute vertigo phase.

Rotatory and caloric testing evaluates semicircular canal function in response to rotation or irrigation with warm and cold water/air of the external ear canal. Bithermal irrigation causes convective movement of endolymph in the ipsilateral horizontal semicircular canal, caloric test being the only available test that gives information regarding each horizontal semicircular canal. The movement of the endolymph provoked by variation of temperature and, secondarily, endolymph density results in deflection of the cupula of the irrigated semicircular canal. Motion of the cupula leads to vestibular hair cell excitation or inhibition with consecutive change of the discharge rate in the superior vestibular nerve fibers. The difference between the excitatory and inhibitory discharge rates of the two superior vestibular nerves reaches the vestibular nuclei. From here compensatory eye movements are elicited (slow phase of nystagmus), followed by rapid corrective saccades (fast phase of nystagmus).

In Menière’s disease patients, results in ENG/VNG differ depending on the phase (acute, subacute, or chronic) and the duration of the disease.

At the beginning of an acute phase, due to the minor ruptures in the Reissner’s membrane and an increase of potassium concentration in the endolymph, the vestibular sensorial epithelium in the affected ear is stimulated and the spontaneous nystagmus beats toward the Menière’s ear (Figure 13). Soon after, due to constantly increasing of the potassium concentration, the vestibular hair cells are intoxicated and their function decrease. In this stage, spontaneous nystagmus changes its direction toward the healthy ear.

In the next days after the acute spell of the Menière’s disease results in rotatory and caloric test varies—either hypofunction in the affected ear (Figure 14), or symmetric functionality of the inner ears. The absence of a fixed vestibular lesion is the case in most of patients. In prolonged Menière’s disease (long-term/chronic effect) usually patients’ express caloric hypofunction of the affected ear (1/2–2/3 of patients) as VOR reflects the decreased input from the damaged

![Figure 13. Spontaneous nystagmus: A—initial phase of the spell (towards the affected ear); B—end of the spell (towards the non-affected ear).](http://dx.doi.org/10.5772/66382)
ear. Caloric stimulation can be done sequential with warm and cold water, respectively, for each ear, or simultaneously. Bilateral cold water (30°C) irrigation shows rapidly the affected ear—the ear toward the nystagmus appears.

In rotatory chair test, results are usually normal. Directional preponderance is rarely seen, usually in long-duration Menière’s disease, when vestibular lesion is stable at some extent (Figure 15). But immediately after an acute attack, VOR gain is increased in rotation toward the affected ear [18].

In between the acute spells, Menière’s disease patients can experience positional vertigo, usually due to benign paroxysmal positional vertigo (BPPV). Disturbances in endolymph metabolism affect the function of the stria vascularis with secondary negative effects on the otolithic membrane. Still, BPPV is more frequently associated with vestibular migraine than Menière’s disease.

3.1.2. Video head impulse test

The video head impulse test (HIT) evaluates as well semicircular canal function. Integrity of the VOR allows the tested subject to maintain sight fixed during high-acceleration high-velocity...

Figure 14. Left ear caloric hyporeflexia-hypofunction index > 30%.

Figure 15. Symmetrical VOR response in rotatory test.
head rotations in space (gain values close to 1.0, as the ratio between eye and head velocity). Rotation is performed in each plane with an excitatory effect on each of the six semicircular canals.

A positive HIT stands for complete lesion of the fibers connected with the tested semicircular canal. In comparison with caloric testing, video HIT is abnormal in much more small numbers of Menière’s disease patients, maybe because vestibular lesion is not complete.

3.2. Vestibulospinal reflex (VSR)

Equilibrium is a complex process, essential in human well-being and daily activities. It allows standing on different supports as well as walking and other movements without falling or disequilibrium.

Body and head position in space, related to gravity and environment landmarks (of verticality for example), is based on normal and correlated information’s form sensorimotor, visual and vestibular systems. The most important, for sure until adult life, is the sensorimotor system—proprioceptors from feet and neck contribute mostly in equilibrium as we move in space.

As long as the child grows, visual information becomes more important in equilibrium, especially when visual surroundings are difficult.

A vestibular system develops in function in the first year of life and contributes progressively more to equilibrium. Its contribution increases in the case of a lesion in either of the other two systems [15–17]. Besides this, a severe unilateral vestibular deficit or bilateral vestibular lesion has a huge impact on equilibrium, at least for several weeks until a unilateral vestibular deficit is compensated by the other ear.

In Menière’s disease, pathophysiology of the disease explains the fluctuating vestibular function of the affected ear. So, we do not have a stable deficit, at least not a complete one, or from the very beginning of the disease. For this reason, vestibular investigations have different results, from patient to patient, as we discussed in the ENG section.

3.2.1. Computerized dynamic posturography

Computerized dynamic posturography (CDP) contributes with specific parameters in monitoring patients with Menière’s disease—for appropriate diagnostic and management. CDP is based on a force plate system capable of measuring the antero-posterior balance of the center of gravity of the tested subject and automatically compare this balance with normal values for patient’s group of age.

Sensory organization test (SOT) is the most common test of CDP. It allows a selective use of each of the three systems involved in equilibrium during six different conditions of testing (Figure 16) in [19] and thus a global and selective evaluation of equilibrium, based on the system used for maintaining the standing position during testing in [20].

As long as projection of the center of gravity (COG) during testing is inside the base support area and no external support is used for stabilize, patient is able to maintain his/her equilibrium and normal result will be displayed at the end of the test (Figure 17). When patient
cannot voluntary control its balance within the parameters described, he will obtain a pathological score of equilibrium, displayed at glance with colors convention and also with numeric values (Figure 18).

In Menière’s disease patients, CDP usually display normal results, since in between the spells patient has no equilibrium problems and the acute vestibular deficit of the affected ear was

Figure 16. CDP/SOT testing conditions (www.nervecenter.natus.com).

Figure 17. CDP—normal result.
compensated already. Immediately after the acute phase, vestibular scores can be abnormal, mainly in vestibular condition.

3.2.2. Vestibular evoked myogenic potentials

Vestibular evoked myogenic potentials (VEMPs) are relatively new objective test designed to measure otolithic function in [21]. In response to loud sound stimulation (95–97dB nHL), saccular vestibular sensorial epithelium generates activity in the inferior vestibular nerve and further in the vestibulospinal and vestibule-ocular pathway.

Action potential transmitted through the vestibulospinal pathway generates muscular responses in the effectors of the vestibulospinal (cervical muscles — cervical vestibular evoked myogenic potential: cVEMP) or vestibule-ocular reflex (extraocular muscles — ocular vestibular evoked myogenic potential: oVEMP).
cVEMP represents an inhibitory biphasic response in the ipsilateral sternocleidomastoid muscle after loud sound stimulation of the sacculae, which can be recorded by surface electrodes. A positive-negative P13-N23 potential is recorded with normal latencies of 13 and 23 ms, respectively (Figure 19). The greatest sensitivity of sacculocolic reflex is for 200–1000 Hz stimuli in Refs. [22, 23], a frequency range highly correlated with saccular function and resonance properties as well (which are correlated with saccular size).

Late N34-P44 potentials are not saccular in origins. The amplitude of the response varies with contraction level of the muscle (Figure 20).

A clinical value of cVEMP is based on comparison of cVEMP amplitude in response to each saccular stimulation. For this reason, contraction level should be measure as well and rectified traces are evaluated. A difference of more than 30% between cVEMP amplitudes is considered abnormal, in result either to saccular hypofunction or hyperfunction depending on the pathology.

In Menière’s disease, endolymphatic hydrops involves the sacculae from the very initial stages of the disease with secondary variations in sacculae’s mechanical properties. Since cervical VEMP depends on the physical characteristics of the sacculae, cVEMP is included in the vestibular battery test for Menière’s disease diagnosis. In more than 50% of Menière’s disease patients, click-evoked cVEMP is abnormal or absent in Refs. [24, 25].

It also has been studied frequency tuning of cVEMP in endolymphatic hydrops and it appears that VEMP is recorded at higher frequencies and across broader frequency ranges than in normal inner ears due to changes in saccular resonance characteristics [26].

These two changes (blunting and frequency shift of cVEMP) are greater as the Menière’s disease has a longer evolution and greater severity in [27]. Additionally, over 20% of Menière’s disease patients have abnormal cVEMP results in the non-affected ear in Ref. [28], recommending VEMP as a predictor test for bilateral Menière’s disease.
Another study revealed a correlation between cVEMP threshold variations in between affected and nonaffected ear and the severity of Menière’s disease in Ref. [29].

In a small series of Menière’s disease patients, VEMP increased in amplitude, even three times at the end of positive glycerol test (Figure 21) as an argument of presence of the endolymphatic hydrops in the sacculae in Ref. [30].

3.2.2.2. Ocular VEMP

Ocular VEMP (oVEMP) is a newer variant of VEMP which measures saccular function in response to very loud sound stimulation (about 120–130 dB SPL) or utricular function in response to vibrations applied to the cochlea. Electrodes placed below the orbit record excitatory response in the contralateral inferior oblique muscle when in a flexed state by looking upward in Ref. [31].

The first negative (excitatory) component of the oVEMP at a latency of about 10 ms is called n10. This n10 component most likely indicates the myogenic potentials of inferior oblique muscle.

Additionally, in patients with early Menière’s disease tested at attack, the contralateral oVEMP n10 is enhanced compared to measures in the same patients at quiescence. We speculate that this enhancement by Menière’s disease attack could be due to mechanical changes in the labyrinth that enhance the sensitive response of utricular receptors to bone conduction vibrator stimulation. It seems that alterations in frequency tuning discussed in cVEMP are also present in sound-evoked oVEMP in Menière’s disease patients in Ref. [32].

Author details

Madalina Gabriela Georgescu

Address all correspondence to: madalina.georgescu@gecad.com

“Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania
References


