

## Sudden hearing loss

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**Abstract.** *Sudden hearing loss.* This update on the latest studies and management policies for patients suffering from sudden sensorineural hearing loss (SSHL) represents a cooperative effort of Belgian ENT surgeons from various corners of the country. SSHL has an incidence ranging from 5 to 20 cases per 100,000 persons per year, and is a relative medical emergency, as only 30% to 65% of the patients recover spontaneously.<sup>1-3</sup> Nowadays, treatment varies a great deal between countries and hospitals. The various etiologies and therapeutic modalities are reviewed, and evidence levels are indicated. Finally, diagnostic and therapeutic organigrams are proposed along with a Belgian therapeutic cocktail in view of conducting a large Belgian study on the management of SSHL.

### Introduction

Sudden sensorineural hearing loss (SSHL) is defined as a sensorineural hearing loss that settles within less than 3 days, and that is at least 30 dB over three consecutive frequencies ranging between 0.125 to 8 kHz in comparison to the contralateral side.<sup>3</sup> The incidence of SSHL ranges between 5 and 20 cases per 100,000 persons per year. SSHL represents about 1% of all sensorineural hearing losses.<sup>1,3</sup>

### Etiology of SSHL<sup>3-5</sup>

The cause of the sudden hearing loss is mostly unknown. Based on presumptive evidence, a few hypotheses have been put forward:

- The “viral hypothesis” (in 30% to 40% of the cases, an upper

respiratory tract infection precedes, within a month, the hearing loss).

- The “vascular hypothesis” (micro-emboli, micro-thrombosis, slowing of the cochlear blood flow following increase of blood viscosity by a “sludge” effect -intravascular red blood cell aggregation in case of stasis, spasm, systemic hypotension and intralabyrinthic hemorrhage).
- The “immunological hypothesis” (antibodies directed against epitopes present in the inner ear).
- The “pressure origin” (hydrops is sometimes exclusively confined to the cochlea).

Sometimes, the cause of SSHL can be identified, and a specific treatment initiated.

The etiology of SSHL can be classified into categories: (1) viral and infectious, (2) autoimmune,

(3) traumatic, (4) vascular, (5) neurological, (6) tumoral, (7) ototoxic and (8) pressure related. There are multiple conditions within each of these categories that have been associated with sudden hearing loss.

The following is a partial list of reported causes of SSHL:

*Infectious:* meningococcal meningitis, herpes viruses (simplex, varicella zoster), cytomegalovirus, mumps, HIV, mycoplasma, toxoplasmosis, syphilis, measles (rubeola), rubella, Lyme disease.

*Autoimmune:* lupus erythematosus, polyarteritis nodosa, Cogan's syndrome, Wegener granulomatosis, relapsing polychondritis, Behçet syndrome, Kawasaki disease, temporal arteritis (Horton disease).

*Traumatic:* perilymphatic fistula, temporal bone fracture, barotrauma, blast injury ...

**Vascular:** vertebrobasilar vascular attack, stroke, sickle cell disease, decompression, sickness from SCUBA diving ...

**Neurological:** multiple sclerosis, migraine ...

**Tumoral:** vestibular schwannoma (acoustic neuroma), leukemia, myeloma, metastasis to internal auditory canal, meningeal carcinomatosis ...

**Ototoxic causes:** amikacin, vancomycin, erythromycin, cisplatin ...

**Pressure attack:** hydrops, Ménière's disease ...

### History and physical examination

SSHL is a relative medical emergency, and diagnostic workup and management should be started without delay. The primary objective is to rule out treatable causes. It is important to find out the detailed circumstances of the hearing loss and the time course of its onset. The presence of associated symptoms, such as tinnitus, vertigo or dizziness, aural fullness, and otalgia should also be specifically asked about, along with details of previous or concurrent viral infections, previous otologic surgery or the use of ototoxic drugs. Any history of trauma, diving, flying and intense noise exposure should be noted. Past medical history of other diseases associated with SSHL should also be obtained such as diabetes, autoimmune disorders, malignancies, neurological conditions, and hypercoagulation state. Otoscopic findings should be normal. The Ramsay-Hunt zone should be inspected for the presence of vesicles which appear in case of a varicella zoster reactivation. An audiogram (pure tone, speech and

tympanometry including stapedial reflex testing) should be performed for all patients with SSHL. In case of vertigo, an electro-nystagmography (ENG) or a videonystagmography (VNG) must also be performed. A brain-stem evoked response audiometry (BERA) should be proposed though not too early, in order to avoid noise injury. If BERA responses cannot be evoked due to profound hearing loss, or if the BERA is pathological, a magnetic resonance imaging (MRI) scan is recommended at least one month after onset in order to look for the presence of tumors in the cerebello-pontine angle or multiple sclerosis. In the presence of associated symptoms such as vertigo, an MRI examination should be performed systematically. Certain authors, in fact, recommend an MRI examination in all cases because a vestibular schwannoma (acoustic neuroma) is found in about 2% of SSHL and has even been described with partial hearing recovery.<sup>6</sup>

Blood tests should be based on the history and the suspected diagnosis. An extensive set of tests should not be performed systematically in view of costs and lack of specificity. Following laboratory tests can be useful: hemoglobin (Hb), hematocrit (Htc), red blood cell count (RBC), white blood cell count (WBC), platelets, C-reactive protein (CRP), serological test for Lyme disease (*Borrelia burgdorferi*) and syphilis (*Treponema pallidum* hemagglutination assay, TPHA). Specific and efficient drugs for the two latter diseases exist, and outcome improves with earlier onset of therapy. Herpes serology is not of great interest as the test is not sensitive enough, quite expensive and

its results usually arrive too late in terms of treatment. Practically, the diagnosis of herpes is mainly clinical (vesicles in Ramsay-Hunt zone).

Finally, in case of bilateral or recurrent episodes of sudden hearing loss, immunological tests looking in particular for anti-cochlear antibodies should be requested.

### Disease progress and prognosis

In a prospective study by Mattox and Simmons, 65% of the patients with SSHL recovered spontaneously and independent of medical management.<sup>2</sup>

### Factors affecting prognosis are:

- Amount of hearing loss: most authors concur in saying that the greater the loss, the worse the prognosis.<sup>1,5</sup>

- Delay of therapy onset: most authors again agree that the shorter the delay, the greater the chances of recovery. Pajor *et al.*<sup>7</sup> quantitatively expressed the chance of recovery as function of the delay of therapy onset: 66% for a delay shorter than 7 days, 25% for a delay between 8 and 14 days, and 16% for a delay between 15 and 30 days. Mosnier *et al.*<sup>1</sup> report similar results for total and partial recovery rates: < 7 days: 70%; 7-30 days: 50% and for more than 30 days: 10%. Thus, treatment should ideally start before 7 days, and hearing improvement can occur within 30 days of hearing loss onset. However, because most of the spontaneous recoveries occur within the first few days, it is difficult to establish with certainty that early therapy is the real cause of improved recovery with faster

therapy onset. For Tran Ba Huy,<sup>8</sup> treatment delay between 1 to 6 days does not appear to influence the final degree of hearing loss.

– Microvascular lesions: Hirano *et al.*<sup>9</sup> demonstrated that patients with diabetes, hypercholesterolemia and high blood pressure have a poor prognosis.

– Age: according to Hirano *et al.*,<sup>9</sup> prognosis worsens above the age of 60. This author suggested that the age effect is related to the higher amount of patients with microvascular lesions above the age of 60. Mosnier *et al.*,<sup>1</sup> however, did not find that age affected prognosis because he placed a prognostic threshold at 40 years of age (too young to see a difference between the two groups of patients).

– Frequency profile of the hearing loss: according to Mosnier *et al.*,<sup>1</sup> ascending or horizontal curves have a better prognosis than descending or V-shaped curves. Fetterman *et al.*<sup>10</sup> do not find any differences with respect to the shape of the audiometric curve. Tran Ba Huy<sup>8</sup> also found that ascending audiometric curves have better prognosis. Audiometric curves that slope down at high frequencies have less favorable prognosis, especially when the hearing loss is pronounced.

– Presence of vertigo: Pajor *et al.*<sup>7</sup> found a recovery rate of 51% for sudden hearing losses without vertigo, whilst only 33% for SSHL with associated vertigo. According to the findings of Nakashima,<sup>11</sup> the association of vertigo and predominantly high frequency hearing loss has the worst prognosis. However, Fetterman *et al.*<sup>10</sup> and Mosnier *et al.*<sup>1</sup> didn't observe this relation.

– Tinnitus: no significant correlation.<sup>1</sup> Certain authors suggested

that the presence of tinnitus facilitates recovery, but statistical analyses are not significant.<sup>1</sup>

– Prognosis is worse when SSHL affects an ear that had already been damaged due to chronic excessive noise exposure.<sup>5</sup>

– Otoacoustic emissions: The presence of otoacoustic emissions is associated with a good prognosis. In some patients with SSHL, otoacoustic emissions can be registered when the hearing loss is up to 35-40 dB HL. According to Nakashima *et al.*,<sup>11</sup> this observation suggests that in some cases of SSHL, external hair cells function normally.

### Current treatment modalities

When the cause of SSHL is known, management can be focused. The majority of SSHL cases, however, have no identifiable cause. In this paper, we will limit our discussion to the management of patients with idiopathic SSHL.

SSSL management is a subject of controversy: high spontaneous recovery rate and low incidence hinder the validation of empirical treatment modalities. Various treatments have been proposed. A review of the literature confirms that only few of those have proven efficacy. The following review is based on recent peer-reviewed articles evaluated by the authors, and rated between Ia and III according to Belgian evidence levels (BEL).

#### *Anti-inflammatory and immunosuppressive drugs*

In the eighties, double-blind studies were performed concerning the treatment of SSHL with oral steroids.<sup>12,13</sup> Treatment consisted of

oral steroid therapy (dexamethasone) tapered over 10-12 days.<sup>12</sup> A significant effect on hearing recovery in patients with a hearing loss between 40 and 90 dB HL was found.<sup>12</sup> The overall recovery rate for patients treated with dexamethasone during twelve days was 89%, compared to 44% recovery without steroids.<sup>13</sup> However, recovery was defined as a hearing improvement of more than 50% of the initial loss at three frequencies relevant to speech understanding.<sup>13</sup> In 1996, Hughes *et al.*<sup>3</sup> recommended treatment with prednisone 1 mg/kg/day for at least 10 days and up to one month (BEL III).

In a recent double blind prospective study, Cinamon *et al.*<sup>14</sup> suggested that prednisolone 1 mg/kg/day had no therapeutic advantage over a placebo (BEL Ib). However, Alexiou *et al.*<sup>15</sup> performed a retrospective study in 2001 concerning the use of 500-1000 mg of prednisolone for three days, and found that glucocorticoids should be recommended for the treatment of SSHL, particularly for patients with hearing loss in the lower and middle frequencies (BEL Ib).

#### *Vasodilators / rheologic agents*

Many vasodilators have been used for treating SSHL.

Procaine, just as other local anesthetics, causes arteriolar vasodilation. Procaine hydrochloride in the form of intravenous infusions is advocated for the treatment of SSHL by several authors (vasoactive therapy ...)<sup>16</sup> However, a double-blind clinical study has concluded that procaine therapy is not superior to a placebo (BEL II).<sup>16</sup>

A recent retrospective study showed that the use of low

molecular-weight heparin could improve hearing in SSHL. Considering the side-effects of this treatment, it should be used with caution (BEL III).<sup>17</sup>

In a preliminary report, Gersdorff *et al.*<sup>18</sup> concluded that 12 g of piracetam administered as an intravenous infusion over 15 minutes significantly increased the chance of complete recovery for patients with SSHL (BEL III).

### *Hemodilution*

A hematocrit drop leads to a reduction of blood viscosity and a reduction of venous return resistance, and hence to an increased cardiac output. At micro-circulatory level, a drop in hematocrit values results in a higher perfusion rate and higher oxygen delivery. Optimum oxygen delivery is reached at a hematocrit value of 30%. Therapeutic hematocrit reduction has to be performed in a hospital environment because severe hypotension can occur, even several hours after administration of the drugs (BEL II).<sup>19</sup>

### *Antiviral agents*

Animal models of viral labyrinthitis were developed by Stokroos *et al.*,<sup>20</sup> and treatment with a combination of prednisolone and acyclovir resulted in higher recovery of hearing compared to either drug alone.

Combining acyclovir with prednisolone, however, has no established beneficial effect in humans with SSHL, as reported by Westerlaken *et al.*<sup>21</sup> and Tucci *et al.*<sup>22</sup> A critical factor for success with acyclovir is the delay of treatment onset: the mean delay of treatment onset in two studies on SSHL was 4 days, whereas antiviral therapy must be started within 3 days after onset of the disease.

Thus, as discussed by Kuhweide *et al.*,<sup>23</sup> if started early, the combination of acyclovir and prednisolone might yet prove to be effective for SSHL, and is certainly reasonable if clinical signs of varicella zoster virus (Herpes zoster oticus, Ramsay-Hunt) are present (BEL III).

### *Diuretics*

The use of diuretics may be indicated when endolymphatic hydrops is suspected, even in the absence of vertigo. For these patients, Claes *et al.*<sup>24</sup> suggest the use of hydrochlorothiazide (25–50 mg/day) or acetazolamide (500 mg/day), or a combination of hydrochlorothiazide 25 mg with triamterene 50 mg in association with a salt free diet during 3 months. They also strongly recommend adding betahistine 16 mg  $\times$  3/day. Patients are also recommended to avoid coffee, alcohol, smoking and stress, which are known triggers for vertigo attacks in Ménière's disease (BEL III).

### *Hyperbaric oxygen therapy (HBO)*

Breathing 100% oxygen at supra-atmospheric pressures increases the amount of oxygen in the arterial circulation, and favors oxygen supply to tissues, even when vascularisation is compromised. During HBO, an important pO<sub>2</sub> rise in the endolymph and perilymph has been measured. During an HBO session, which lasts 90 minutes and which is administered with a frequency of one per day, a patient is placed in a pressure chamber and breathes 100% oxygen at 2.5 atmospheres, through a mask or oxygen hood. A control audiometry must be performed after 10 sessions. When

the patient's hearing does not improve, treatment is not prolonged. When hearing improves, HBO is prolonged for 5 days or even longer until thresholds stabilize. The atmospheric pressure increase during a HBO session can be problematic for patients with Eustachian tube dysfunction. Tympanometry can be performed prior to a HBO session to check Eustachian tube function. When middle ear and environmental pressure cannot be equalized, tympanostomy tubes must be placed. HBO appears to be effective up to three months following the onset of the hearing loss. In general, HBO is prescribed in cases where drug therapy has not resulted in significant improvement of hearing thresholds (BEL III).<sup>25</sup> In cases of (suspected) decompression sickness, HBO treatment is the first treatment of choice; in these cases, commencing HBO treatment as soon as possible is mandatory. Special treatment schedules are used for emergency treatment of diving pathology, the description of which is beyond the scope of this review.

### *Other agents and procedures*

Some studies have shown that carbogen, a combination of 95% oxygen and 5% carbon dioxide, increases the partial pressure of oxygen in perilymph. However, recent studies have failed to prove any benefit from carbogen therapy (BEL Ib).<sup>26</sup>

Fibrinogen and LDL apheresis has recently been found to be effective in the treatment of patients with SSHL. Indeed, a multicenter study reports that a single fibrinogen/LDL apheresis lasting for 2 hours could be used as an alternative to infusion treatment and prednisolone for

10 days. Patients with plasma fibrinogen higher than  $8.68 \mu\text{mol/l}$  would appear to have a higher degree of improvement, especially if serum LDL concentrations are also raised. Apheresis for SSHL is common practice in Germany (BEL Ia).<sup>27</sup>

Recently, studies have proven the efficiency of some vitamins and oligoelements.

A prospective double blind study found that the combination of 167 mg of oral magnesium and steroids improves hearing in patients with SSHL more than steroids alone (BEL Ib).<sup>28</sup>

The use of the antioxidant vitamin E for reducing cochlear damage has been proposed. Animal studies suggest that ototoxic drugs, noise exposure, and inflammation in the cochlea cause damage through release of free oxygen radicals. In animal models on ototoxicity, vitamin E has been shown to prevent cell damage. In clinical studies, the combination of steroids, carbogen, magnesium and vitamin E (twice a day 600 IU) yielded better results than without vitamin E (BEL II).<sup>29</sup>

### **Suggested therapeutic management**

No single treatment has proven absolute efficacy for SSHL, and a variable amount of recovery has been reported depending on the treatment protocol and study. Thus, from a medico-legal point of view, it is careful to treat a patient with idiopathic SSHL. The main difficulty lies in the poorly understood pathophysiologic processes of the disease. However, hypotheses on the possible etiologies exist, and we would like to propose a therapeutic approach that covers the main causes, that is

feasible, and that avoids side-effects and economic burden (work absence, treatment and hospitalization costs ...).

We recommend outpatient treatment because no study proves that hospitalizing a patient improves recovery rate.

The following "Belgian" therapeutic cocktail has not been studied previously but all components are proven effective, and substance interaction is unlikely. The various components of this cocktail were selected with the objective of covering as many etiologies as possible. We would like to submit a proposal for a large national double-blind prospective study on the effects of this "Belgian cocktail" versus for example steroids.

The authors of this review agree that every patient should be treated as soon as possible. Furthermore, we propose two determinants in deciding on the treatment modality for SSHL: delay of therapy onset and frequency profile of the hearing loss (curve type):

- for the ascending curves (highest loss at low frequencies), we propose treatment with triamterene combined with an oral steroid. If the hearing loss is due to hydrops, recovery may be expected within a week. If full recovery is not achieved at the end of a week, the Belgian cocktail should be administered, and hearing should be measured every week.
- for the other audiometric curve types, the treatment modality should depend upon the delay since the onset of the hearing loss. If the delay is less than one month, the drugs listed below could be used:

- steroids: prednisolone 1 mg/kg
- piracetam:  $3 \times 3 \text{ 1200 mg/day}$  (10.8 g/day)
- vitamin E:  $2 \times 600 \text{ IU/day}$
- magnesium: 167 mg/day
- + Audiometry once a week.

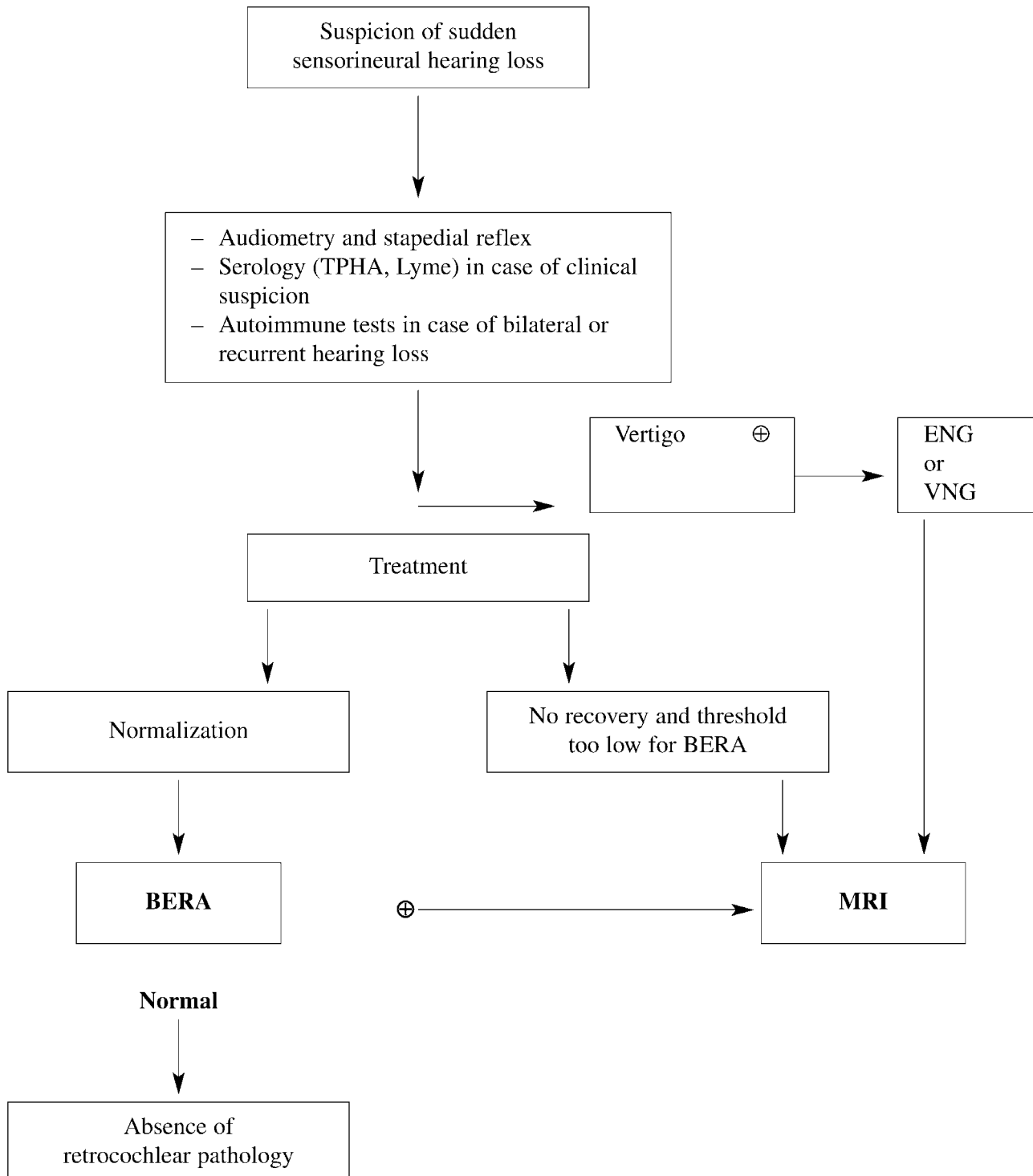
If the onset of hearing loss is less than 3 days, we recommend to add acyclovir ( $5 \times 800 \text{ mg/day}$  for 7 days), particularly if clinical sign of herpes reactivation such as auricular vesicles and facial weakness, and perhaps also pain and rotatory vertigo are present. When hearing thresholds do not improve after one week of treatment, continuation of the "Belgian cocktail" is recommended.

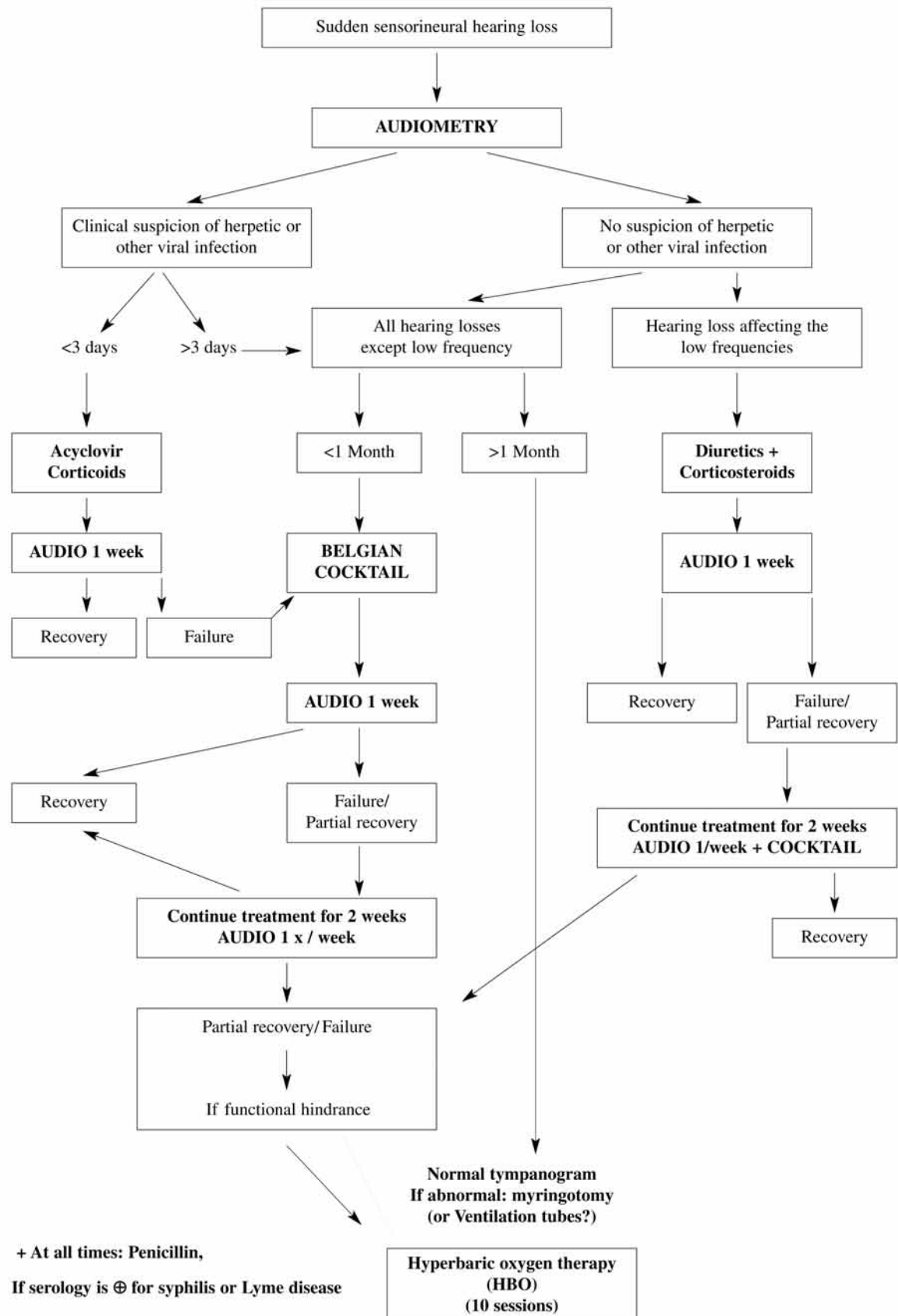
If the onset of hearing loss is more than one month ago, or if the first treatment regimen has failed, HBO should be proposed. In general, medical treatment is administered first, but as soon as a month has passed, HBO is mandatory. However, no benefit can be gained from HBO more than 3 months after onset of SSHL. Upon completion of 10 HBO sessions, the patient's hearing should be checked and in case of treatment failure, HBO therapy stopped. In case of improvement, more HBO sessions are prescribed, five at a time, until stabilization of the thresholds.

If barotrauma is the cause of SSHL, we propose HBO as first choice treatment. A myringotomy with ventilation tube is necessary because pressure changes during the HBO session might further damage the inner ear when the round window is ruptured due to the barotrauma.

The "Belgian SSHL-cocktail", thus, consists of different tablets, some of which are prescribed as a generic preparation:

## DIAGNOSIS



**TREATMENT**

R/ vitamine E acetate 50%:  
800 mg capsules (60)

1 capsule 3 times daily

R/ magnesium aspartate dihydrate: 725 mg capsules (60)

1 capsule 3 times daily

R/ piracetam 1200 (any company)

R/ medrol 32

### Patient information

We do not recommend hospitalisation but we do advise patients not to expose themselves to a noisy environment. We explain that although we will try to find the diagnosis, often no cause can be found. Infection or a central cause are to be excluded first. We also point out that a weekly evaluation of hearing is necessary to decide on the next treatment. Contra-indications to therapeutic management are looked for, specifically with regard to corticoids. The other components have virtually no contra-indications (cf. compendium). When HBO is necessary, possible contra-indications for this treatment are discussed with the hyperbaric physician (most of these are relative contra-indications). Finally, we give a prognosis based on the various criteria discussed above.

### Final take-home notes

In summary, sudden hearing loss without detectable cause is a relative medical emergency (3 days in case of Herpes zoster and one week for the other cases). Audiometry should be performed to confirm the diagnosis. Treatment should be started without delay and treatment modality should depend on the delay of treatment onset, frequency profile of the hearing loss, and clinical signs of infection with Herpes

viruses, Lyme disease (*Borrelia burgdorferi*) or *Treponema pallidum*. Finally, retrocochlear pathology has to be excluded by performing BERA and/or MRI.

### Conclusion

The diagnosis of sudden hearing loss is easily obtained by audiometry. It is important to determine the exact onset date of the hearing loss. On the other hand, a wide range of causes exists, and the exact etiology often remains unknown despite extensive investigations. Several hypotheses exist, which is our rationale for a cocktail of drugs covering the main causes of sudden deafness according to disease duration. We hope to set up a double-blind study to determine whether this cocktail could benefit patients in the long-run.

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**CME questions**

1. Sudden sensorineural hearing loss (SSHL):
  - A – presents as a conductive hearing loss
  - B – presents as a perceptive hearing loss
  - C – its etiology is often immunological
  - D – is always viral in origin
  - E – never recovers spontaneously
2. Sudden sensorineural hearing loss:
  - A – represents 1% of the sensorineural hearing losses
  - B – only affects the elderly
  - C – an RSV viral episode is always preceding
  - D – can reveal an acoustic neuroma
  - E – is always accompanied by tinnitus
3. During anamnesis and clinical examination of a patient with SSHL, one finds:
  - A – occasionally the cause
  - B – often a family history of hearing loss
  - C – a slightly red tympanic membrane
  - D – a history of glue ear during childhood
  - E – intake of antibiotics in the weeks preceding the hearing loss
4. Prognosis appears less favorable in the following situations:
  - A – hearing loss affecting the high frequencies
  - B – with a delay greater than a month
  - C – presence of vertigo
  - D – age over 60
  - E – presence of microvasculature pathologies (diabetes, hypertension, hypercholesterolemia, ...)
5. The “Belgian cocktail” must be suggested in the following cases:
  - A – suspicion of Herpetic infection
  - B – only if the delay is <3 weeks
  - C – only if the delay is >3 weeks
  - D – in case of HBO failure
  - E – in case of hearing loss affecting the low frequencies
6. Etiological assessment of sudden hearing loss:
  - A – systematic blood test
  - B – blood test if there is a suspicion of syphilis
  - C – blood test if there is a suspicion of Lyme disease
  - D – blood test if there is a suspicion of Herpes
  - E – blood test if there in case of recurrent hearing loss

7. In clinical studies, the following treatments have shown to improve sudden sensorineural hearing loss with ascending curves:
- A – corticosteroids
  - B – heparin
  - C – hemodilution
  - D – HBO
  - E – diuretics
8. In case of hearing loss with an ascending curve:
- A – hydrops can be suspected
  - B – start the treatment by associating corticosteroids with a diuretic
  - C – do not hesitate to start immediately with HBO
  - D – a higher chance of an acoustic neuroma and an MRI must be requested
  - E – recovery must be rapid, and if the patient does not show any signs of improvement after a week, then do not hesitate to administer the Belgian cocktail
9. Which of the following statements are true?
- A – Do not hesitate to give acyclovir in case of viral infection irrespective of the delay
  - B – Do not hesitate to give acyclovir in case of viral infection as long as the delay does not exceed 3 days
  - C – Suggest the Belgian cocktail in case of treatment failure one week after acyclovir (in case of viral infection)
  - D – In case of descending hearing loss, suggest HBO immediately
  - E – In all cases, suggest HBO as soon as the delay is 3 weeks
10. Which of the following statements are false?
- A – Only ask for an MRI in cases with vertigo and abnormal ENG
  - B – Request an MRI in cases with a hearing loss around 60 dB
  - C – Hydrops excludes the presence of a retrocochlear pathology
  - D – Recovery of hearing excludes retrocochlear pathology
  - E – There are no contraindications to HBO

<b>Answers:</b> 1B; 2AD; 3A; 4ABCDE; 5B; 6BCE; 7AE; 8ABE; 9BCE; 10ABCDE
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