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**Assessment of diagnostic approaches to idiopathic sudden sensorineural hearing loss and their influence on treatment and outcome.**

Ramesh Nosrati-Zarenoe<sup>1</sup>, Magnus Hansson<sup>2</sup> and Elisabeth Hultcrantz<sup>1</sup>

1. Dept. of Clinical and Experimental medicine, Div. of Otorhinolaryngology, Linköping University, Linköping, Sweden

2. Dept of Clinical Chemistry, Karolinska University Hospital, Huddinge, Sweden

***Running title:*** Assessment of diagnostic protocol in ISSNHL

## ***Abstract***

**Objectives:** To investigate different diagnostic test-batteries for sudden sensorineural hearing loss (SSNHL) and evaluate their value in management of idiopathic SSNHL.

**Methods:** The first 400 patients submitted to the Swedish national database for SSNHL were analyzed. Information was collected at the first visit about the patient's past medical history, potential precipitating events traumata, family medical history, hearing loss, current disease, diagnostic protocol and treatment using questionnaires as well as two audiograms for each patient, one at the first visit to the ENT-clinic and one three months later.

**Results:** 65% of these 400 patients underwent hematological tests and 40% had an MRI/CT. 22/160 MRI investigated had pathological findings: five acoustic neuromas, one subdural hematoma, one pons infarction, five vascular abnormalities and ten patients had accidental findings not connected to the hearing tracts. 300 of these 400 patients were evaluated as idiopathic sudden sensorineural hearing loss (ISSNHL); 24% of them had one or more pathological tests. No significant correlation was found between either the MRI findings or the laboratory findings with regard to either treatment or hearing recovery in patients with ISSNHL.

**Conclusion:** Results from a database for SSNHL demonstrate no correlation between laboratory findings, treatment and outcome in 400 patients. The patients with pathological tests were not treated differently from those with normal tests or no tests taken. The value of laboratory findings and MRI might increase if the results are categorized to more specific diagnoses.

**Key Words:** Sudden deafness, Sudden sensorineural hearing loss, acoustic neuroma, Borrelia infection.

## ***Introduction***

Sudden Sensorineural Hearing Loss (SSNHL) is a rapid loss of hearing usually in one ear.

Over the years, incidence seems to have increased. In Japan during the last thirty years, the frequency of those seeking help has increased from 3.9 to 27.5 per 100.000 persons per year [1]. Of these, it is said that one third recover spontaneously without any treatment [2]. There are different hypotheses regarding the etiology of SSNHL such as infections, vascular catastrophes, autoimmune disease or abnormal cellular stress responses and intracochlear membrane rupture [3]. Because there may be several causes of the symptom SSNHL, the diagnostic test-batteries used are often based on more than one of these hypotheses.

In 2002, two of the current authors, in agreement with the vast majority of the ENT clinics throughout Sweden, established a national database for SSNHL to provide access to a sufficiently large number of patients to allow study of the management of SSNHL. This database is now of sufficient size that it is possible:

- 1) to evaluate whether, and in what manner, different blood tests and other diagnostic tools are used,
- 2) to estimate their influence on treatment policy beyond excluding patients with a known specific diagnosis, and
- 3) to analyze whether the two foregoing factors result in different hearing outcomes for the patients.

The optimal situation would be that every patient receives a specific diagnosis which can be associated with a suitable, specific, effective treatment. The concept, Idiopathic SSNHL, would then be replaced with a multitude of different diagnoses affecting hearing. If instead a specific, so far idiopathic, disorder is hidden in the concept, perhaps other approaches to diagnosis will have to be developed. Thus far, diagnosis is based on the patient's audiogram,

medical history and physical examination, while identification of a specific cause for the sudden hearing loss is rather unusual.

The purpose of the present investigation is to explore the different diagnostic test-batteries for SSNHL used at present in Sweden and to evaluate whether and in what manner, positive diagnostic findings influence the choice of treatment and whether the treatment given influences the outcome of ISSNHL.

## ***Material and Methods***

### **Material**

90% of the ENT-clinics in Sweden, spread over entire country, had agreed to participate in gathering the data for the SSNHL database; only data for patients with an initial diagnosis of SSNHL were to be reported. Sudden Sensorineural Hearing Loss was defined as a mean hearing loss equal or greater than 30 dB at three contiguous frequencies occurring within 24 hours [5].

Construction of the database was approved by the local ethics committee at Linköping University in March 2002, and data from the first 400 patients submitted were to be used in the analysis.

### **Diagnostic protocol**

The diagnostic protocol included a questionnaire and two audiograms [6].

At the first visit, after informed consent, a questionnaire was filled in for each patient by an otorhinolaryngologist. Three months later, after a final check for completeness by an otorhinolaryngologist at the same clinic, the questionnaire together with the two audiograms, was submitted for inclusion in the database. The questionnaire covered the patient's past medical history, potential precipitating events preceding the SSNHL, traumas, family history of different diseases especially hearing loss, the current disease, the diagnostic protocol including laboratory and radiological tests and further audiological examinations and a record of all treatment provided to the patient as a result of the reported symptoms. The time course of the hearing loss's onset and associated symptoms, such as tinnitus and vertigo were documented. The questionnaire always included the results of an ENT examination. Two pure tone audiograms were requested—one taken at the first visit to the ENT clinic due to the

symptoms of SSNHL and another after the three months. A copy of previous audiograms was asked for in cases where patients were known to have a prior diagnosed hearing loss before the onset of SSNHL.

Information on radiological investigations (MRI or CT), laboratory work-ups and the use of brainstem response audiometry (BRA) or a vestibular work-up were requested. This information request was phrased in general terms so as not to influence the doctors' own diagnostic practices or their decision-making process.

The ENT-clinics participating in the database had different policies regarding hematological examinations ranging from no laboratory tests to the administration of tests covering different hypotheses concerning SSNHL such as infections, vascular catastrophes, autoimmune cause or and membrane breaks. In case of reports of pathological test results the complete lab-sheet for that patient was required.

The questions about treatment included the use of corticosteroids, antiviral therapy, rheological treatment or "other" drugs, and prescription of rest or surgery of suspect fistula.

### **Categorization of laboratory tests**

Before analysis, pathological results of laboratory tests were categorized by one or more pathological values:

1. "Arteriosclerosis associated variables": LDL-cholesterol/ HDL-cholesterol ratio  $>3$ , Total cholesterol  $>5$  mmol/L and C- reactive protein (CRP)  $>3$  mg/L in patients with or without earlier known cardiovascular disease.
2. "Inflammation/infection": CRP  $>10$  mg/L, Erythrocyte sedimentation rate  $>20$  mm, Leukocyte count  $>10 \times 10^9$  ml/L, Hemoglobin count (Hb)  $<120$  g/L, Thrombocyte count  $>150 \times 10^9$  ml/L and Borrelia tests "positive" (IgG antibodies and IgM antibodies) in patients with or without ongoing clinical infection.

3. “Autoimmune variables”: HSP-70, Cardiolipin, Antiphospholipid, Anti-Neutrophilic Cytoplasmic Antibodies (ANCA) and Antinuclear antibodies (ANA) “positive”.

### **Assessment of hearing loss and hearing recovery**

The hearing loss was characterized by comparison of the audiogram taken at the first visit after onset of SSNHL to an audiogram taken not more than two years before the acute hearing loss. If no previous audiogram was available, hearing was compared to the non-affected ear in its present state.

Four frequency regions were created to describe the hearing loss [6]:

#### *Low frequency region:*

1. Pure-tone average (PTA) of low frequencies (125, 250, 500 Hz) > PTA of mid frequencies (1000, 1500, 2000 Hz) and high frequencies (3000, 4000, 6000 Hz) by at least 10 dB.
2. Hearing loss in the low and mid frequencies – PTA of low frequencies > PTA of mid frequencies with a difference less than 10 dB.

#### *Mid frequency region:*

1. PTA of mid frequencies > PTA of low- and high frequencies by at least 10 dB.
2. Hearing loss in the low and mid frequencies – PTA of mid frequencies > PTA of low frequencies with a difference less than 10 dB.

#### *High frequency region:*

1. PTA of high frequencies > PTA of low- and mid frequencies by at least 10 dB.
2. Hearing loss in the mid and high frequencies – PTA of high frequencies > PTA of mid frequencies with a difference less than 10 dB.

*Flat loss:*

The differences between the PTA for all three frequency regions were less than 10 dB.

The audiogram taken at the first visit and the audiogram obtained three months after the onset of SSNHL were compared with respect to the PTA characterizing the loss to determine the degree of hearing recovery and remaining hearing loss (table I).

**Table I.** Definition of improvement and remaining hearing loss after recovery.

Hearing improvement		Remaining hearing loss after recovery	
Large improvement	>30 dB	No remaining hearing loss	Difference between initial audiogram and audiogram at the follow-up < 10 dB
Moderate improvement	10 – 30 dB	Partial recovery	The difference $\geq 10$ dB and the improvement $\geq 10$ dB
No improvement	$\pm 10$ dB	No regress	The difference $\geq 10$ dB and the improvement < 10 dB

## Statistics

As is the case with most clinical research, many of the data elements in the current study do not fulfill minimal criteria for parametric statistical analysis and many of the measurements are bounded even if otherwise continuous. The method used for all analyses regarding hearing recovery was ordinal/ordered logistic regression using Minitab software (version 15 for Windows). This method performs a logistic regression on an ordinal response variable (categorical variables that have three or more possible levels with a natural ordering) with the help of both continuous and categorical predictors

Age between patients with pathological laboratory tests and those with normal laboratory tests, interval between onset of hearing loss and first visit at the ENT-clinics, pure-tone

average between different frequency regions were done using a Student's t-test with the level of significance set at  $p < 0.05$ .

## ***Results***

There were two areas of interest in the management of each case presenting SSNHL: 1. the course of diagnosis for all 400 SSNHL patients, and 2. the course and outcome of treatment for those 300 SSNHL patients that, after the diagnosis process, can be classified as having ISSNHL.

The first 400 patients were reported to the database from 42 clinics evenly distributed over the country (including from five university clinics). This was about 50% of the country's ENT clinics. Of these 400 patients, 300 were evaluated by the authors as suffering from ISSNHL. Remaining 100 patients either received other end-diagnoses or did not fulfill our criteria for ISSNHL: 58 had a hearing loss at the first visit of less than 30 dB and 26 had a progression of their hearing loss over more than 24 hrs. Sixteen patients received another specific diagnosis for their hearing loss within the three months after presenting at the clinic: Eight developed signs of fluctuating hydrops or Ménière's disease, as diagnosed by fluctuations of their audiograms among other symptoms. One patient had SSNHL as an ototoxic side effect of treatment with Ciprofloxacin. Seven were diagnosed after MRI and are presented separately in table II. Five of them had acoustic neuroma, one suffered from subdural hematoma and one from a brain infarction in pons.

## **Questionnaire**

The three hundred of the total of 400 patients in the database that fulfilled our criteria for ISSNHL were further analyzed. This group consisted of 154 men and 146 women ranging in age from 8 to 87 years with a mean of  $57.4 \pm 16.2$  years. Hearing loss occurred in the right ear for 159 patients and in the left ear for 141 patients. None of the patients was bilaterally affected. Further descriptive data, see table III. The mean time from onset of the hearing loss

**Table II.** Patients where MRI resulted in a specific diagnosis as cause of SSNHL, audiometric configuration, initial treatment and hearing improvement (n=7).

Patient	Diagnosis	Audiometric configurations	Treatment	Hearing improvement
1	Acoustic neuroma	Low frequency loss	Corticosteroids	Audiogram missing
2	Acoustic neuroma	Low frequency loss	No treatment	No improvement
3	Acoustic neuroma	Mid frequency loss	Corticosteroids	Large improvement
4	Acoustic neuroma	Mid frequency loss	No treatment	Moderate improvement
5	Acoustic neuroma	“Flat loss”	Prescribed to	Large improvement
6	Subdural hematoma	Audiogram missing	No treatment	Audiogram missing
7	Pons infarction	Mid frequency loss	Corticosteroids + Antibiotics + Antiviral therapy	No improvement

to the first visit at the ENT-clinics was 13 days for those who came directly to the ENT-clinics, and 23 days for the patients referred from general practitioners ( $p < 0.05$ ).

All variables in the questionnaire were analyzed using ordinal/ordered logistic regression looking for interactions with hearing recovery and remaining hearing loss as dependent variables. Age at initial contact and/or presence of vertigo at the onset of the hearing loss were significantly related to a lower chance of hearing improvement and greater chance for remaining hearing loss independent of treatment or no therapy. See table IV.

“Heredity for hearing loss” was significantly correlated to lower chance for hearing improvement (table IV).

**Table III.** Profiles of patients with SSNHL (n=300)

Variables		
Gender	Female	146
	Male	154
Age	Mean $\pm$ SD (years)	57.4 $\pm$ 16
	Range (years)	8 - 87
Affected ear	Left	141
	Right	159
Prevalence of associated symptoms	Tinnitus	149
	Vertigo	
	With nystagmus	0
	Without nystagmus	12
	No info. about nystagmus	1
	Tinnitus and vertigo	
	With nystagmus	16
	Without nystagmus	49
	No info. about nystagmus	10
	No information about tinnitus or vertigo	1
No associated symptoms	62	
Interval between onset of hearing loss and first visit at the ENT-clinics (n=300)	Median (days)	5
	Inter-quartile range (days)	1 – 16
Referred from GPs (n=154)	Median (days)	6
	Inter-quartile range (days)	3 – 21
Visited the ENT-clinic themselves (n=146)	Median (days)	3
	Inter-quartile range (days)	1 – 10

### Radiological examination

158 (40%) of the 400 patients had an MRI or CT. Of these, 22 had pathological findings: five had acoustic neuroma, one had subdural hematoma, one had pons infarction (table II) and five had different vascular abnormalities which might have had a possible connection to SSNHL, all of them with a low-frequency hearing loss (see table V). The remaining 10 patients of the 22 had accidental findings not connected to the hearing tracts. No significant correlation was

found between pathological MRI-findings and either hearing recovery or persisting hearing loss for the 300 patients with ISSNHL.

**Table IV.** Outcome measures after ISSNHL with respect to hearing improvement and remaining hearing loss using Ordinal logistic regression (n=300).

Variable	Hearing improvement			Remaining hearing loss		
	Odds ratio	95% CI	<i>p</i>	Odds ratio	95% CI	<i>p</i>
Increase of age	1.03	1.01 – 1.05	0.000	0.98	0.96 – 0.99	0.001
Vertigo at onset	1.77	1.06 – 2.95	0.03	0.40	0.24 – 0.67	0.000
Heredity for hearing loss (parents or siblings with hearing loss or having had ISSNHL)	2.08	1.10 – 3.94	0.02	ns	ns	ns
Prescribed to rest or be on sick leave initially	0.46	0.27 – 0.79	0.005	ns	ns	ns

CI= Confidential Interval

**Table V.** Patients with low frequency loss and vascular changes as possible cause of ISSNHL shown by MRI (n=5). Treatment and outcome.

Patient	Diagnosis	Audiometric configurations	Treatment	Hearing recovery
1	ISSNHL	Low frequency loss	Corticosteroids + Antiviral therapy	No improvement
2	ISSNHL	Low frequency loss	Corticosteroids	No improvement
3	ISSNHL	Low frequency loss	Corticosteroids	Moderate improvement
4	ISSNHL	Low frequency loss	Prescribed rest	Moderate improvement
5	Myeloma	Low frequency loss	Cytostaticum	Moderate improvement

## Hematological examination

258 (65%) of the total 400 patients had hematological tests taken. The blood screening varied from simple routine tests to a complete analysis covering most hypotheses (infections, vascular catastrophes, autoimmune disease or membrane rupture) concerning SSNHL such as C-reactive protein (CRP), Hemoglobin (Hb), HSP70, Anti-Neutrophilic Cytoplasmic Antibodies (ANCA) tests and Borrelia tests. Blood samples for Borrelia analyses were often taken—in 81% of the patients evaluated as having ISSNHL (see table VI).

**Table VI.** Prevalence of Laboratory screening and Borrelia analyses (IgM and/ or IgE) in 400 patients with SSNHL.

	Laboratory screening	Borrelia included	Borrelia positive (one test)
Total	258 / 400 (65%)	198 / 258 (77%)	18 / 198 (9%)
Evaluated as ISSNHL	196 / 300 (65%)	159 / 196 (53%)	17 / 159 (11%)

Of the 300 patients classified as having ISSNHL, 196 had one or more laboratory tests taken; 24% (47) of these had one or more pathological findings. One of them received a specific diagnosis (Myeloma) also verified by MRI. The group categorized as having pathological “arteriosclerosis associated variables” (n=13) was significantly older than those with normal laboratory tests (n=148),  $65 \pm 11$  years resp.  $56 \pm 17$  years,  $p=0.016$ .

The 27 patients with “inflammation markers” were of the same age as the ones with normal laboratory tests. Of these, 15/27 had positive Borrelia findings.

Seven patients were regarded to have pathological “autoimmune variables”. No age difference was seen between those with pathological “autoimmune variables” and those with normal laboratory tests.

The ordinal/ordered logistic regression analysis showed no association between any of the laboratory tests and either hearing improvement or remaining hearing loss when evaluating the tests separately or after categorization in comparison with those who had normal laboratory findings.

## **Therapy**

182 (61%) of 300 patients with ISSNHL were treated medically. Of these, 166 patients were given corticosteroids either as single treatment or in combination with antiviral therapy, antibiotics or blood thinning therapy (acetylsalicylic acid). The corticosteroid primarily used was prednisolone (84%). The dosage, duration of treatment and tapering schedule varied from 80 mg to 25 mg per day for five days to four weeks [6]. Three patients were only given antiviral therapy, six others only antibiotics, two were only given acetylsalicylic acid, and five received other different drugs. “Large improvement” of hearing was in total seen in 36%, “Moderate improvement” in 36% and “No improvement” in 28% (see table I).

26% (77 of 300 patients) were prescribed “rest” or “stay home on sick leave” for up to four weeks—22 of them as the only treatment. Patients who had been prescribed rest or been on sick leave during the first period of the disease had higher chance for hearing improvement (OR 0.46, 95% CI 0.27 – 0.79,  $p=0.005$ ) regardless of other treatment (table IV).

96 patients did not receive any treatment at all. 26% of them had a large improvement of hearing, 34% moderate improvement and 40% no improvement. These patients came significantly later (median days 8, inter-quartile range 4 – 44) to the ENT-clinics after the onset of SSNHL than those treated medically (median days 4, inter-quartile range 1 – 10),  $p=0.001$ . On the other hand, for patients who came on corresponding days to the ENT-clinic there was no difference in hearing outcome between the ones who were medically treated or not [6]. The medical treatment had no significant correlation with either hearing improvement or remaining hearing loss.

## **Audiometry**

Audiograms from 293/300 patients with ISSNHL were analyzed; seven were excluded because of lack of final audiograms. 40% had their hearing loss in the low frequency region of  $53 \pm 18.5$  dB, 28% in the mid frequency region of  $66.1 \pm 22.7$  dB, 23% in the high frequency region of  $60.7 \pm 23.6$  dB and 9% had a “flat loss” of  $79 \pm 19$  dB. See table VII.

Patients with hearing loss in mid frequency region had significantly higher odds for hearing improvement compared to those in the groups with a hearing loss in the low frequency region (OR 2.43, 95% CI 1.38 – 4.27,  $p=0.002$ ), the high frequency region (OR 3.83, 95% CI 1.99 – 7.37,  $p=0.000$ ) and “flat loss” (OR 2.75, 95% CI 1.16 – 6.50,  $p= 0.021$ ). The odds for a residual hearing loss was lower for patients with hearing loss in the mid frequency region compared to those with a hearing loss in the low frequency region (OR 0.45, 95% CI 0.26 – 0.78,  $p=0.005$ ), the high frequency region (OR 0.31, 95% CI 0.16 – 0.58,  $p=0.000$ ) and “flat loss” (OR 0.43, 95% CI 0.18 – 1.01,  $p= 0.05$ ).

**Table VII.** PTA in dB of the affected frequency regions shown in the initial audiogram (N=293).

	Low frequency region (n=116)	Mid frequency region (n=83)	High frequency region (n=68)	Flat loss (n=26)
Range	30 – 108 dB	30 – 108 dB	30 – 110 dB	46 – 105 dB
Mean ± SD	53 ± 18.5 dB	66.1 ± 22.7 dB	60.7 ± 23.6 dB	79 ± 19 dB

**\*\*\*  $P < 0.001$**

**\*\*  $P < 0.01$**

**\*  $P < 0.05$**

## ***Discussion***

Idiopathic diseases are “idiopathic” only as long as we do not know the causative agent. An acute hearing loss can be a symptom caused by a multitude of known diseases within the vascular system or by different traumas and tumors within the hearing tracts [7, 8]. In most cases of SSNHL, it will not be possible to arrive at a specific diagnosis. However, the assessment will still be done according to these possible mechanisms in order to find the approximately 10% for which one can arrive at an identifiable, and hopefully treatable diagnosis [9].

The present evaluation of 400 patients in the Swedish database does not give evidence that ISSNHL belongs to any of the categories of diseases listed above. Even so, 65 % of them have still been medicated—seemingly in vain.

## **Questionnaire**

Prognostic factors for ISSNHL have been studied by many authors. The findings from this database demonstrate that presence of vertigo and higher age at onset are related to a reduced probability for recovery, which also is in accordance with earlier studies [5, 10]. Presence of tinnitus has been considered a positive prognostic factor for hearing recovery by Cvorović et al 2008 [10], but in the present study no such connection was found. However, “heredity for hearing loss” or a close relative who has had ISSNHL was a predictor for poor hearing improvement. This might suggest that in these cases, ISSNHL are the first sign of a hereditary progressive hearing loss.

## **Radiological examination**

The finding of 3.2% acoustic neuromas in this material of 400 patients is a low number compared to other studies on SSNHL [8] and could be due to the fact that only 38% of the

patients had had an MRI or CT. Perhaps there are still hidden acoustic neuromas in the remaining 62%?

Apparently even a reversible hearing loss can be caused by an acoustic neuroma. In our material, the hearing loss for the patients with acoustic neuroma was experienced in all frequency regions (table II) and hearing improvements were seen irrespective of treatment received. It is interesting that the one patient with neuroma that had a “flat loss” experienced a large hearing improvement although only rest had been prescribed. Otherwise, it might be expected that an acoustic neuroma would react to corticosteroids and thereby give improved hearing when the tumor diminishes or ceases pressing on the blood vessels feeding the cochlea as discussed in earlier works [11]. Since hearing improvement occurred for almost all of these patients with tumors before their final diagnosis was set, we suggest that a radiological examination of all patients with ISSNHL be done so as not to miss a treatable acoustic neuroma.

In the present material, different vascular abnormalities were also found by MRI in just as many patients as those with acoustic neuroma. All five of them had a low-frequency hearing loss which theoretically can be hypothesized to be due to an occlusion of a blood vessel feeding that part of the cochlea—something which cannot presently be radiologically visualized. However, none of these patients had been given any specific treatment associated with their vascular abnormality except for the one with myeloma and occlusion of one of the AICAs (table V). The MRI examination is most often done several weeks after the first visit at the ENT-clinic which makes it difficult for the physician to take the findings into consideration while deciding the acute treatment of the hearing loss. If some patients have their SSNHL due to vascular accidents, the CT or MRI must be done as part of the initial examination to be of value for the patients—just as is the case with treatment of stroke and heart infarction.

## **Laboratory examinations**

When a test battery is used for blood laboratory examination, the results are not always easy to evaluate: pathological tests may not necessarily be specific for the patient's hearing disorder and even so, you often need at least two tests with weeks in between to see rising titres of, for example, *Borrelia* antibodies to be sure that a possible infection is ongoing and not already passé.

Serological *Borrelia* analyses were those most frequently performed, with 11% yielding pathological findings. This is in accordance with earlier studies in which both serum and CSF analysis had been performed [12]. A third of the patients with increased *Borrelia* titers were initially treated with antibiotics, but, in our analysis, hearing outcome was not related to the treatment given. This is in agreement with earlier studies with respect to ISSNHL [13], and similar to results from the use of antibiotics for treatment of patients with facial palsy and high *Borrelia* titers. If the infection is ongoing, it should always be treated with antibiotics since neuroborreliosis is a severe chronic disease—even if the antibiotics do not specifically cure the hearing loss. High titers in a presenting patient would at least justify a second test is taken in order to substantiate an ongoing infection independently of whether the initial hearing loss has improved or not. However, very few follow-up tests had been taken in the present material.

We categorized the patients with pathological results of laboratory tests into “arteriosclerotic causes”, “inflammatory/infectious causes” or “autoimmune causes” to see whether one group or the other had different outcomes or had received different treatment. No difference could be discerned in medical treatment policy applied to patients in the different categories: the only alternative was corticosteroids or “nothing” and there was no difference in the outcomes regardless of the option chosen. However, in the atherosclerosis group where a rheological treatment might theoretically have been appropriate, potential differences may be hidden by

the fact that only a small fraction of the patients had their total cholesterol and LDL/HDL ratio evaluated. The association between increased CRP levels and atherosclerosis is obscured by other acute inflammatory reactions and also by the lack of standardized time intervals between the onset of SSNHL and the blood sampling. These circumstances may indicate that CRP is not the ideal marker for atherosclerosis in this setting. From the data obtained, no significant association was found between therapy and atherosclerosis, markers of inflammatory activity or signs of autoimmunity.

## **Treatment**

Only 61% of the patients with ISSNHL had received some type of drug therapy with the aim of influencing the outcome. 91% of them were treated with corticosteroids even if the underlying etiology was unknown. The outcome, that the ones who had received corticosteroids had the same odds for recovery as those who did not get any drugs, is in accordance with the conclusions in the latest Cochrane report from 2006 [14]. The studies included in this report where positive effects for corticosteroids were proposed all had too few patients for such conclusions. The same can be said about the original study by Wilson from 1980 [5] where only 67 patients were evaluated in subgroups. One weakness of the present study is that, for natural reasons, the treated patients are not matched with not treated patients. A randomized placebo controlled study with high power is necessary to evaluate whether or not there is an effect of corticosteroids. Such a randomized placebo controlled study is currently in progress in Sweden.

In our data, corticosteroids did not influence outcome in any patients with positive autoimmune signs although an effect on those might have been expected [15]. The reason can be that too few patients had had those tests taken.

On the other hand, the 26% of patients who had been prescribed to rest had better odds for recovery. Earlier, bed rest and sick leave were the standard treatment for ISSNHL patients,

but this is now very uncommon and no research seems to have been done concerning that specific treatment modality. Probably all who are afflicted by ISSNHL would gain from rest, especially those who in their questionnaire reported recent stress before the onset of the disease.

## **Audiometry**

The site of damage to the cochlea might be hypothesized based on the shape of the audiogram: A moderate hearing loss in any of the frequency bands can be regarded as a possible dysfunction of the outer hair cells while a hearing loss of more than 40 dB would be seen to indicate dysfunction/damage also including the inner hair cells. A flat loss might be a hypothesized result from an interference with the vascular stria or spiral ligament giving a hearing loss due to an acute ionic balance disturbance. A low frequency loss may be regarded as a sign of hydrops. In Germany, these hypotheses for ISSNHL have been the basis for consensus therapy since 2004 [16].

One hypothesis about variation in recovery is that different types of hair cells are involved: If only the outer hair cells are damaged, a central adaptation might be possible so the remaining undamaged outer hair cells can reorganize the cortical pattern and in that way restore hearing [17]. If however, the inner hair cells are involved it is more difficult to visualize a reorganization as their number in the cochlea is so limited and they are strictly tonotopically arranged both in the cochlea and all along the central pathways. The weakness of this theoretical approach regarding the site of damage and the possibility of recovery is that it does not fit well with the clinical observation that patients with all types of audiograms seem to have a chance for spontaneous recovery in varying degrees. In addition, the hearing improvement can come about as quickly as the onset of the hearing loss. A more slowly developing recovery over a couple of months would better fit the theory regarding reorganization [17].

The results that patients with an hearing loss in the mid frequency region had the best recovery rate has been reported earlier in several studies [2, 5, 18] and can be explained on the basis of a vascular theory for ISSNHL: In the cases when two arteries are supplying the cochlea, which occurs in about 50% of the cases [19] and where the main internal auditory artery is occluded distally to the branching of the anterior vestibular artery, one would theoretically expect a hearing loss in the lower and mid frequency region of the cochlea which has a chance of recovery through collaterals from the second main artery [20]. The same reasoning can be applied to the five patients in the present investigation with vascular aberrations that were seen on MRI, all of whom had low frequency hearing loss and experienced none or moderate improvement. They may have had the same occlusion of the main auditory artery, but with no collateral supply from a second artery [20].

## ***Summary and Conclusion***

Analysis of 400 patients with sudden sensorineural hearing loss in a national database demonstrates that MRI is an underused resource to get specific diagnoses for the condition both with respect to acoustic neuromas and vascular abnormalities. Regardless of diagnostic protocol, treatment is mainly limited to corticosteroids or no medical treatment with no difference in outcome. Hearing loss in the mid frequency region has the best odds for recovery regardless of the treatment chosen. Patients who are prescribed rest, recover better than without rest. A randomized placebo controlled study with high power is necessary to evaluate whether or not there is an effect of corticosteroids and further research concerning vascular impact in the idiopathic cases is recommended.

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***Corresponding author:***

Elisabeth Hultcrantz MD, PhD  
Professor of Oto-Rhino-Laryngology  
Div of Oto-Rhino-Laryngology, Dept. of Clinical and Experimental Medicine  
Linköping University, University hospital  
SE 58185 Linköping  
Sweden  
Tel: +46-13-224029  
Fax: +46-13-222558  
E-mail: Elisabeth.Hultcrantz@liu.se