Chapter 1

Introduction
History

In 1861, Prosper Menière (Figure 1) described the classical triadic symptomatology of hearing loss, vertigo and tinnitus, which he attributed for the first time to a labyrinthine disorder. Since Hallpike and Cairns and also Yamakawa in 1938 discovered hydrops of the endolymphatic system in the temporal bones of patients with Menière’s disease, endolymphatic hydrops has been generally accepted as the basic histopathological substrate of Menière’s disease. Hydrops may arise as a result of the destabilization of natural regulation through overproduction of and/or reduced absorption of endolymph.

Reduced absorption of endolymph

The endolymphatic sac (Figure 2) is considered to be responsible for the absorption of endolymph, endolymphatic pressure regulation and the degradation of waste products. Hydrops will be produced by disorders of this absorptive system.

The classical guinea pig model for Menière’s disease, in which endolymphatic hydrops was achieved by destruction of the endolymphatic sac and obliteration of the
endolymphatic duct⁴, is a nonphysiological profound model with shortcomings in relation to Menière's disease as seen in patients, in which endolymphatic sac tissue is still present.

**Overproduction of endolymph**

The specific chemical composition of endolymph and the generation of the transepithelial positive potential are considered to be regulated by a membrane-bound sodium-potassium activated adenosine triphosphatase (Na/K-ATPase) in the marginal cells of the stria vascularis and the dark cells of the vestibular labyrinth.

In the guinea pig high amounts of Na/K-ATPase were detected in several inner ear structures, and recent experiments have demonstrated a relationship between circulating adrenal steroids and Na/K-ATPase activity in the inner ear⁵⁶. The strial Na/K-ATPase activation by aldosterone may result in an increased secretion of potassium ions in the endolymphatic compartment and an overproduction of endolymph. This may contribute to the development of an endolymphatic hydrops, as seen in Menière’s disease.
Two-phase endolymphatic hydrops

We developed a more subtle animal model; the two-phase endolymphatic hydrops. This model is based on a combination of chronic endolymphatic sac dysfunction, induced by slight destruction of the most distal part of the endolymphatic sac, and acute stress-hormonal induced endolymph production by stimulation of the Na/K-ATPase in the stria vascularis with aldosterone.

This new experimental guinea pig model may show more resemblance to the pathophysiological process in Menière’s disease. A more realistic experimental model will attribute to new insights in the diagnosis and treatment of different stages of Menière’s disease.

Objectives of this study

In this thesis, the morphological and electrophysiological consequences of the two-phase endolymphatic hydrops model on the cochlear function in guinea pigs is evaluated. Light microscopy, scanning electron microscopy and transmission electron microscopy demonstrated morphological changes, while electrophysiology evaluated the significance of these morphologic changes, and was mentioned to demonstrate the dynamic influences of the compromising factors in our model.

Chapter 2 describes the light microscopic observations of the first phase of our two-phase endolymphatic hydrops model by damaging the distal portion of the endolymphatic sac.

Chapter 3 describes the light microscopic observations of the two-phase endolymphatic hydrops model in which the consequences of additional application of aldosterone, following endolymphatic sac dissection, were evaluated for their presence of hydrops, and their effects on cochlear and endolymphatic sac structures.

Chapter 4 describes the structures of the organ of Corti in the guinea pig which were studied with a sophisticated field emission scanning electron microscope to collect reference data, and which demonstrates interesting delicate structures.

Chapter 5 describes a further analysis of delicate structures such as the glycocalyx, which were found at low voltages with the sophisticated scanning microscope. After scanning microscopical observations, the specimens were embedded for additional transmission electron microscopical evaluation.

Chapter 6 describes the scanning observations of the sensory cell damage due to the two-phase endolymphatic hydrops, which showed interesting gradients of damage.

Chapter 7 describes a transmission electron microscopic evaluation of the ultrastructural changes of the cochlear structures in the two-phase endolymphatic hydrops.
Chapter 8 describes a transmission electron microscopic evaluation of the ultrastructural changes of the remaining parts of the endolymphatic sac in the two-phase endolymphatic hydrops.

Chapter 9 describes longitudinal recording of the compound action potential in our two-phase endolymphatic hydrops model by permanently implanted round window electrodes.

Chapter 10 summarizes the results of this study and conclusions are presented.

References


