The Concept of a Rupture Risk Envelope for the Cochleo-Saccular Membranes

Daniel J. Pender

1 Department of Otolaryngology, Columbia University, New York City, NY, United States.

Abstract

Introduction Alterations in endolymphatic pressure have long been suspected of being associated with the development of endolymphatic hydrops and rupture of the membranous labyrinth. More recently, there has been a focus on how membrane mechanics might contribute to membrane rupture. This is suspected to involve the viscoelastoplastic properties of these membranes.

Objective To construct a rupture risk envelope for the cochleo-saccular membranes based on viscoelastoplasticity to provide insight into lesion behavior in Meniere disease.

Methods Reported deformation data from a collagen model of the cochleo-saccular membranes was utilized. Yield stress was defined as 80% of ultimate failure stress. The yield points at various strain rates were used to construct a rupture risk envelope for the membranes.

Results The rupture risk envelope was found to be downward sloping in configuration. At the highest strain rate of 385% per minute, the membrane yield was associated with greater stress (7.0 kPa) and lesser strain (30%); while at the lowest strain rate of 19.2% per minute, there was substantially less membrane yield stress (4.3 kPa) but it was associated with greater strain (44%).

Conclusion The concept of a rupture risk envelope based on viscoelastoplasticity provides insight into hydropic lesion behavior in Meniere disease. This concept helps to explain how variations in membrane distensibility might occur as suspected in the double hit theory of lesion generation in Meniere disease. Slowly developing lesions would appear have a lower rupture risk while rapidly developing lesions would appear to have a greater risk of early membrane rupture.

Keywords ► Meniere disease ► vestibular science ► Reissner membrane

Introduction Meniere disease was first described in 1861, and is a clinical entity characterized by hearing loss, tinnitus and vertigo.1 The associated pathology known as endolymphatic hydrops was first described in 1938.2 The pathophysiology is suspected to entail rupture of the labyrinth membranes, especially the thin and delicate cochleo-saccular membranes of the pars inferior portion. These cochleo-saccular membranes consist of a single basement membrane, less than 5 microns thick, covered on both sides by a single layer of epithelial cells. Rupture of these membranes causes the release of
potassium-rich endolymph into the surrounding perilymph with a neurotoxic effect. The etiology remains enigmatic but may involve heredity, auto-immunity, and inflammation.

The reason why some membranes in Meniere disease only distend while others rupture remains enigmatic. A double-hit mechanism that involves a change in membrane distensibility is theorized to play a role in this process. However, the biomechanics of how this might come about remained speculative. Recent investigations suggest that hydropic lesion behavior may be determined by the viscoelastoplastic properties of cochleo-saccular membranes, especially the sensitivity to strain rate. The aim of this study is the construction of a rupture risk envelope for the cochleosaccular membranes, based on viscoelastoplasticity, to provide insight into the lesion behavior in Meniere disease.

**Methods**

A model membrane consisting of precipitated collagen was used to emulate the cochlea-saccular membranes. The reported deformation data from this collagen model of the cochlea-saccular membranes was utilized in this analysis. The onset of rupture risk was defined as the yield point of a collagen model membrane when subjected to in vitro tensile testing. The yield point is defined as the point where the load deformation curve starts to flatten, indicating incipient membrane failure. This yield point stress was defined as 80% of the reported failure stress on the load deformation curve, as shown in the load-deformation grid to graphically construct the rupture risk envelope.

**Results**

Table 1 presents the calculated yield point data for a collagen model of the cochlea-saccular membranes. These values are derived from reported strain rate and linear modulus data from a mesh membrane of precipitated collagen. This shows that at the highest reported strain rate of 385% per minute, the linear modulus is high (25kPa per unit of strain), and an early yield point at 30% strain is reached at elevated stress (7.0 kPa). In contrast, at the lowest reported strain rate of 19.2% per minute, the stress mounts more slowly as strain proceeds to 44% and the membrane yields at a lower stress (4.3 kPa). Thus, higher strain rate is associated with higher membrane stress and earlier onset of incipient membrane failure.

The rupture risk envelope defined by the locus of yield points is shown in Fig. 2. This rupture risk envelope exhibits a downward sloping pattern as the strain rate decreases. The dotted lines also show the projected behavior of the risk envelope at strain rates above and below those reported.

**Discussion**

Summary of Results: The concept of a rupture risk envelope arises from the locus of membrane yield points at different strain rates. The yield point is essentially the dividing line between terminal zone of linear membrane distention and the onset of exaggerated membrane distention that portends rupture. The rupture risk envelope graphically encapsulates

<table>
<thead>
<tr>
<th>Strain rate %/minute</th>
<th>Linear modulus kPa/%</th>
<th>Yield stress kPa</th>
</tr>
</thead>
<tbody>
<tr>
<td>19.2</td>
<td>15.7</td>
<td>4.3</td>
</tr>
<tr>
<td>38.5</td>
<td>16.6</td>
<td>4.8</td>
</tr>
<tr>
<td>192.0</td>
<td>20.9</td>
<td>6.1</td>
</tr>
<tr>
<td>385.0</td>
<td>25.0</td>
<td>7.0</td>
</tr>
</tbody>
</table>

Fig. 1 Model’s load-deformation curve, with yield point indicated as 80% of failure stress. Source: Roeder et al.

Fig. 2 The rupture risk envelope, as the locus of membrane yield points at various strain rates.
the variation in distensibility of the membrane at different strain rates.

**Analysis of Results:** All membranes will distend when stressed and will rupture if sufficiently strained. Strain rate is known to be a dynamic factor that appears to play a significant role in the timing of rupture risk. Higher strain rates are associated with less distention and earlier failure, while lower rates afford greater distention before failure.

Membrane strain behavior appears to be determined by two main factors: the character of the applied force and the nature of the material resistance. The character of the applied force refers to the manner in which the specimen is stressed. When force is applied to a membrane specimen in vitro by a mechanical tensometer, as shown schematically in Fig. 3 and used with permission, the strain rate can be controlled with precision. The stress and strain induced in the specimen can also be measured directly and simultaneously with great accuracy by means of calibrated sensors. However, when force is to be applied in vivo, (by mechanical indentation or by hydraulic injection pressure), strain rate, stress and strain cannot be measured directly. Instead, these parameters must be estimated via a calculation that depends on the size, shape, and wall thickness of the membranous chamber. These considerations suggest that in vitro tensometric testing is the preferred reference standard for determining the load-deformation characteristics of this biological tissue.

The nature of material resistance refers to the factors that control membrane reaction to applied force. These factors include collagen’s architecture, fiber density, and molecular behavior. Collagen architecture refers to the geometric organization of the collagen fibrils. This can vary greatly, from highly aligned collagen bundles that offer a stiffer resistance to stretching (e.g., human tendon) to loose mesh-like collagen fibers that offer a more lax resistance (e.g., skin basement membrane). And these responses are not fixed but can be modulated by the rate at which the tissue is stretched, as noted below.

Collagen fiber density has a demonstrable effect on elastic modulus. Collagen concentration appears to have a linear relation to both elastic modulus and rupture stress. This implies that an increased collagen fiber density will strengthen a membrane while a loss of fiber density will weaken it.

Collagen’s molecular behavior is dependent on temperature and strain rate. These features are interactive, in that one can aggravate or mitigate the other. Thus both temperature and strain rate need to be controlled in specimen testing. If the specimen temperature is too low, it causes collagen to fracture in a brittle, glass-like manner. At an intermediate temperature, known as the glass transition temperature, \( T_g \), collagen will exhibit what is described as a leathery viscoelastic behavior, with some limited distention, before fraying and shredding, which leads to full rupture. At higher temperatures, it will exhibit a more rubbery and stringy distention before finally rupturing. In mammals, tissue collagens generally have a glass transition temperature \( T_g \) of 35°C, which is close to body temperature, suggesting that collagen in vivo will exhibit a leathery viscoelastic behavior. Thus, in vitro tensometer testing should be performed with the specimen in a bath of physiologic fluid set at body temperature, to control the effect of temperature on tissue behavior.

The effect of temperature on collagen’s behavior described above can be mimicked by strain rate effects. High strain rates favor brittle, glasslike rupture, with less distention akin to low temperature effects; intermediate strain rates favor a leathery response, with moderate distention and shredding; and low strain rates tend to produce a more pronounced distention with a stringy type of failure. It should be noted that strain rate sensitivity is not a linear function. Below a certain threshold, strain rate has no apparent effect on load-deformation characteristics. Only above this threshold does it come into play. Accordingly, optimal tissue testing should encompass a range of strain rates to determine the strain rate threshold and the effect of higher strain rates on the tissue in question. It should also be noted that as strain rate increases, the toe region of the typical sigmoid viscoelastoplastic response curve progressively diminishes and virtually disappears. This implies that at high strain rates, the stress buffer provided by the very distensible toe region is lost. This loss of the toe region accounts for the rigid and brittle behavior of the polymer at high strain rate.

Comparison of Results with Published Data: The concept of a membrane rupture risk envelope reported herein is consistent with the results of creep testing. In polymer creep testing, variable amounts of strain are imposed almost instantaneously at time = 0. With low degrees of imposed strain and associated low stress levels, a polymer may be able to distend considerably before rupture. When high degrees of strain are imposed instantaneously with associated high stress, the material tend to rupture acutely. Such data permit construction of a creep rupture envelope for polymers.

Commentary on Methodology and Limitations: This study assumes that raised endolymphatic pressure is the driving force behind displacement of the cochlea-saccular membranes. Some studies have failed to document an elevated
endolymphatic pressure acting on the membranous laby-
rinth in experimental hydrops in Guinea pigs. Others have
noted that experimental infusions into the endolymph have
raised pressure in both endolymph and perilymph, but
without a measureable differential between them. Such
findings may be a reflection of the fact that these membranes
are especially pliant at low initial pressure, as indicated by
the ‘toe’ region of the viscoelastoplastic load deformation
curve in Fig. 1. This figure indicates that substantial
membrane deformation can occur at pressures that are
near zero.

Furthermore, this study focuses exclusively on the
cochlea-saccular membranes. The model collagen mem-
brane described herein is devoid of epithelial cells. Ep-
ithelial cells have been shown to increase the mechanical
resistance of an artificial skin, consisting of collagen
covered with layers of epithelial cells. This is thought to
reflect the presence of a cytoskeleton network of actin and
microtubules within the several cellular layers. However
the Reissner membrane has only a single layer of epithelial
cells on each surface, and the extent to which it alters the
mechanical behavior of the collagen basement membrane
is uncertain. It is, however, known that the intercellular
adhesions give way before the Reissner collagen mem-
brane itself fails, suggesting that the basement membrane
is carrying most of the load.

It has been shown that these membranes are substanc-
tially weaker than the pars superior membranes and
can, therefore, be more susceptible to pressure-induced
displacement. This is in accord with a biomechanical
analysis that quantified the heightened stress proclivities
in the cochlea-saccular membranes compared with those
in the thicker pars superior membranes. It is also consist-
tent with the findings that in Meniere disease the hydropic
lesions always occur initially in the cochlea-
saccular membranes.

Additionally, while certain genes are suspected to play a
structural role in Meniere disease, this study is focused
exclusively on the rupture risk behavior of the collagen
membrane model itself. Potential contributions to the de-
velopment of Meniere disease by genetic factors such as the
OTOG gene are beyond the scope of this study.

Finally, this study focuses on the early phase of the
hydropic process in the cochlea and saccule membranes,
and the initial potential for rupture therein, based on bio-
mechanics. What happens to these membranes in later
stages of the disease, when damage is more extensive and
has spread to the pars superior, is beyond the scope of the
current study.

Conclusions
The concept of a rupture risk envelope is presented for a
model of the cochleo-saccular membranes. This concept
helps to explain how variations in membrane distensibility
might occur, as suspected in the double-hit theory of
lesion generation in Meniere disease. This suggests that
membrane lesion behavior in Meniere disease is not a
simple static entity but instead represents a spectrum of
responses that depend on certain dynamic factors. These
include not only the rate and degree of force applied to the
membrane, but also the membrane’s viscoelastoplastic
behavior. Membrane viscoelastoplasticity hinges on the
membrane’s collagen architecture, fiber density, and mol-
ecular behavior, which, in turn, control its strain rate
characteristics and propensity for failure. The concept of
a rupture risk envelope encompasses all of these various
response elements to provide insight into acute membrane
failure, chronic membrane distention, and various inter-
vening combinations.

Presented At
International Otopathology Society.
Harvard Medical School.
Boston, Massachusetts, June 11, 2019.

Funding Sources
None.

Conflict of Interests
The author has no conflict of interests to declare.

References
16 Shinozaki N, Kimura RS. Scanning electron microscopic observations on the distended Reissner’s and saccular membranes in the guinea pig. Acta Otolaryngol 1980;90(5-6):370–384