DIETARY SODIUM DOES NOT CAUSE MENIERE'S DISEASE

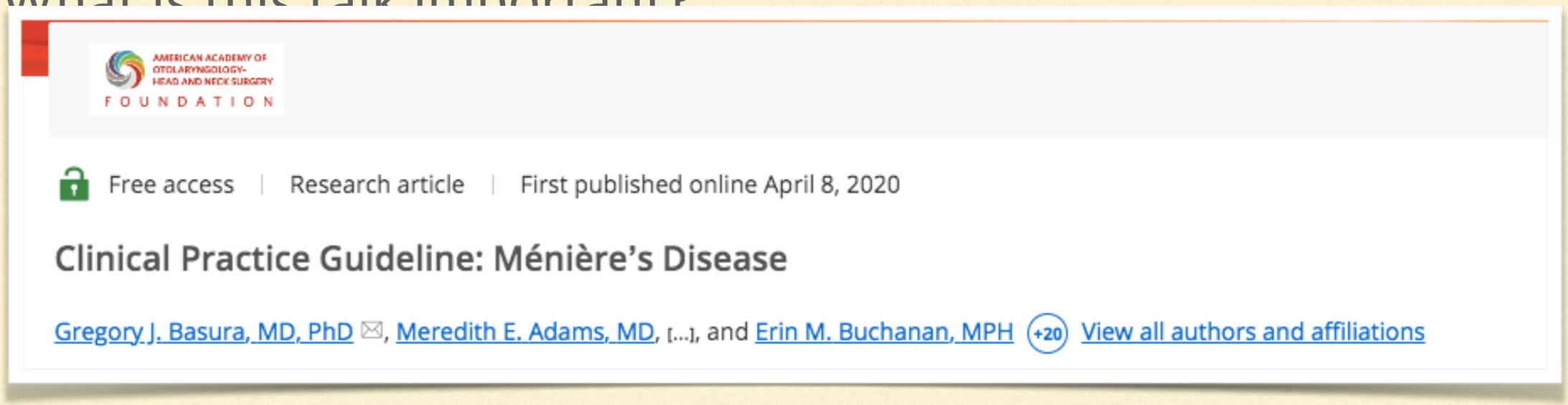
Michael Oldenburg MD

OUTLINE

- Background
- Pathology
- Pathophysiology
- Salt theory
- Animal evidence
- Human evidence
- Alternative theories

WHY?

- What is this talk important?



WHY?

- What is this talk important?

Is there a special diet I should follow to avoid an attack?	Diet may not affect everyone the same way. However, increased sodium consumption can increase fluid in the inner ear. Reading food labels can help you keep track and avoid excessive sodium consumption. Foods that are naturally low in sodium include fresh fruits and vegetables, whole food (not processed), and fresh beef, poultry, and fish. Also, increased caffeine consumption has been known in some to trigger an attack, but it does not affect everyone.
What lifestyle changes can I make to help prevent symptoms?	MD is a very complex disease and can be very difficult to treat. However, living a healthy lifestyle and developing coping mechanisms is a great practice to maintain good health. It may also help to control symptoms of MD. Examples of this are •Limit salt/sodium in your diet •Avoid excessive caffeine, alcohol, and nicotine •Eat well-balanced meals throughout the day •Drink plenty of water throughout the day, avoiding high-sugar beverages •Manage stress appropriately. ○ Get plenty of exercise ○ Get enough sleep ○ Join a support group ○ Journal ○ Practice breathing exercises •Identify and manage any allergies •Patients with increased bouts of vertigo should be assessed for sleep apnea.

WHY?

- What is this talk important?

Dietary Modifications

The primary dietary modifications recommended in clinical practice have been sodium restriction and caffeine reduction/elimination, with some also limiting alcohol use. An SR[209] found no clinically important results from RCTs comparing sodium restriction and no sodium restriction or caffeine restriction and no treatment/usual care. There were no RCTs or SRs to support that these dietary restrictions prevent MD attacks. As such, they categorized both as "unknown effectiveness." One identified RCT[210] found no evidence that dietary sodium restriction was effective in controlling symptoms of MD. However, the number of

WHY?

- What is this talk important?
  - If these recommendations are not supported by sound theory or evidence they can
  - Be harmful to patients
  - Inhibit the progress of discovering the true mechanism

EARLY DESCRIPTIONS

ARTICLE VIII.—*Case of Menière's Disease.* By BYROM BRAMWELL, M.B., Physician and Pathologist to the Newcastle-upon-Tyne Infirmary.

(*Read before the Northumberland and Durham Medical Society, 11th November* 1875.)

IN the year 1861, a French surgeon, Menière, described a series of cases characterized by the following symptoms: vomiting, deafness, noise in the ears, pallor, a reeling gait; and he showed by post-mortem demonstration, that the symptoms did not depend upon disease of the central nervous system, as was formerly supposed, but upon structural lesions in the internal ear.

In some cases the onset was so severe as to resemble apoplexy. He mentions the case of a girl who caught cold whilst menstruating, was seized with deafness, giddiness, and vomiting, and died in five days. After death the only lesion found was a kind of bloody exudation into the semicircular canals and vestibule.

EARLY DESCRIPTIONS

MÉNIÈRE'S FAMOUS AUTOPSY AND ITS INTERPRETATION

MILES ATKINSON, M.D., F.R.C.S. (Eng.)
NEW YORK

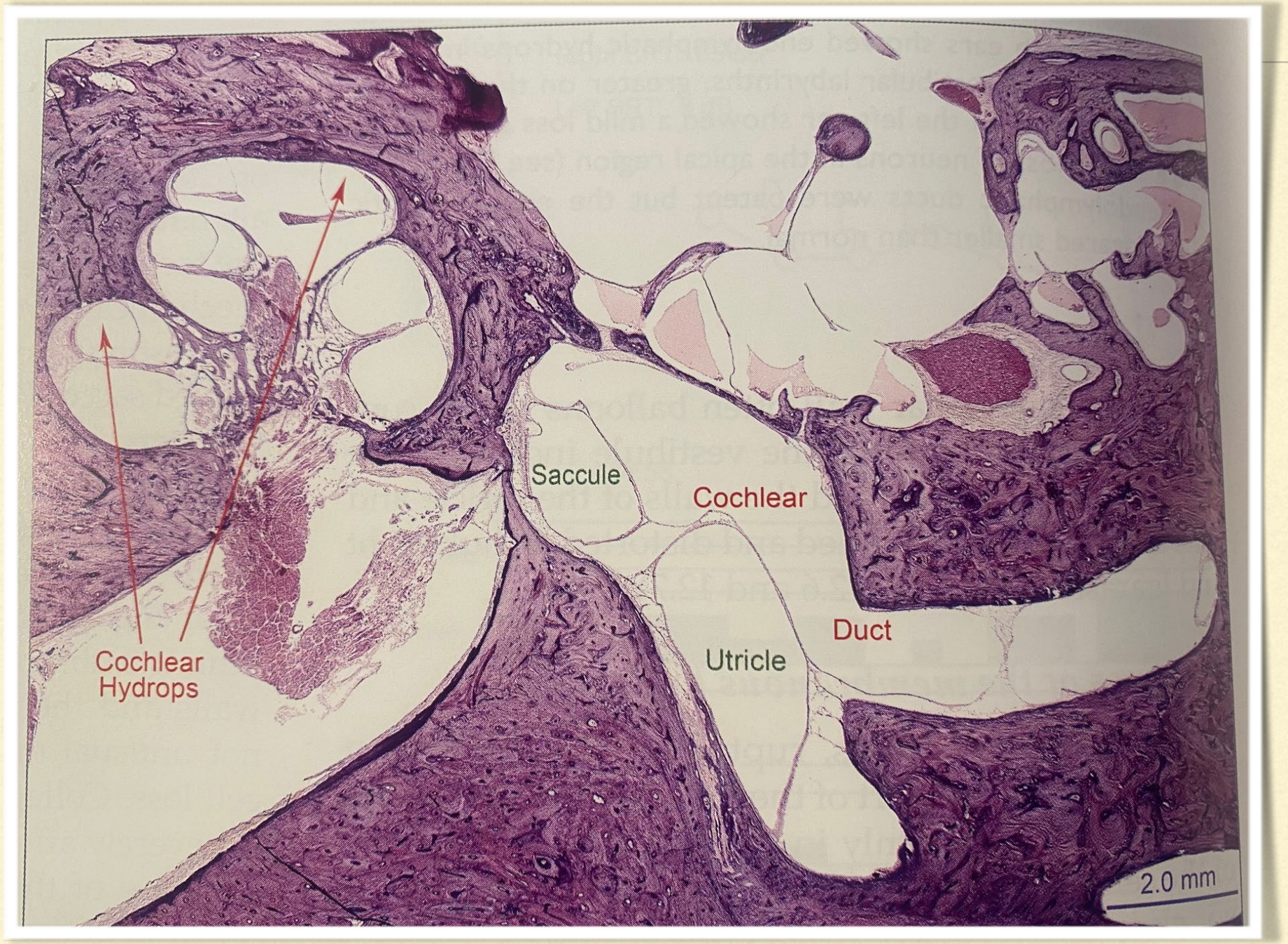
and widely taught. This teaching is based on a misinterpretation of Ménière's description of the autopsy in a single case which he published in his original paper, and the doctrine has led to great confusion of thought. It is in the hope of finally setting the record straight that this account of the famous but ill fated necropsy has been written.

It should be taught in the lecture rooms, it should be shouted from the medical housetops, that hemorrhage into the labyrinth is not the cause of Ménière's disease. When speakers utter the old heresy, as still, regrettably, they do, even those who should know better, they should be hunted from the rostrum; when a writer writes it, his editor should scratch it out with the reddest of red ink. Somehow or other this false doctrine must be finally expunged, for it impedes understanding.

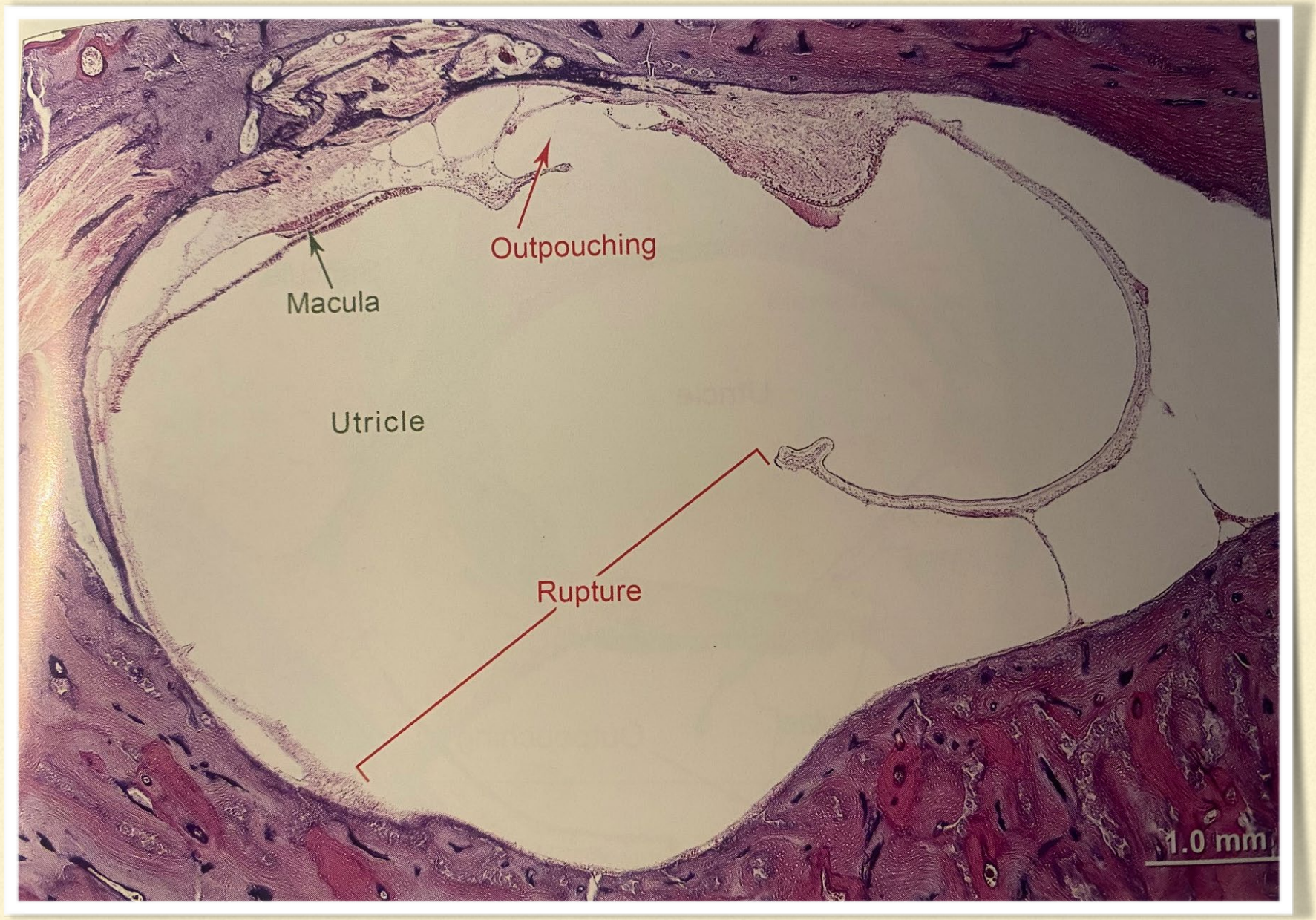
MODERN MENIERE'S

- Spontaneous episodic vertigo >20 minutes associated with fluctuating hearing loss, tinnitus, aural fullness

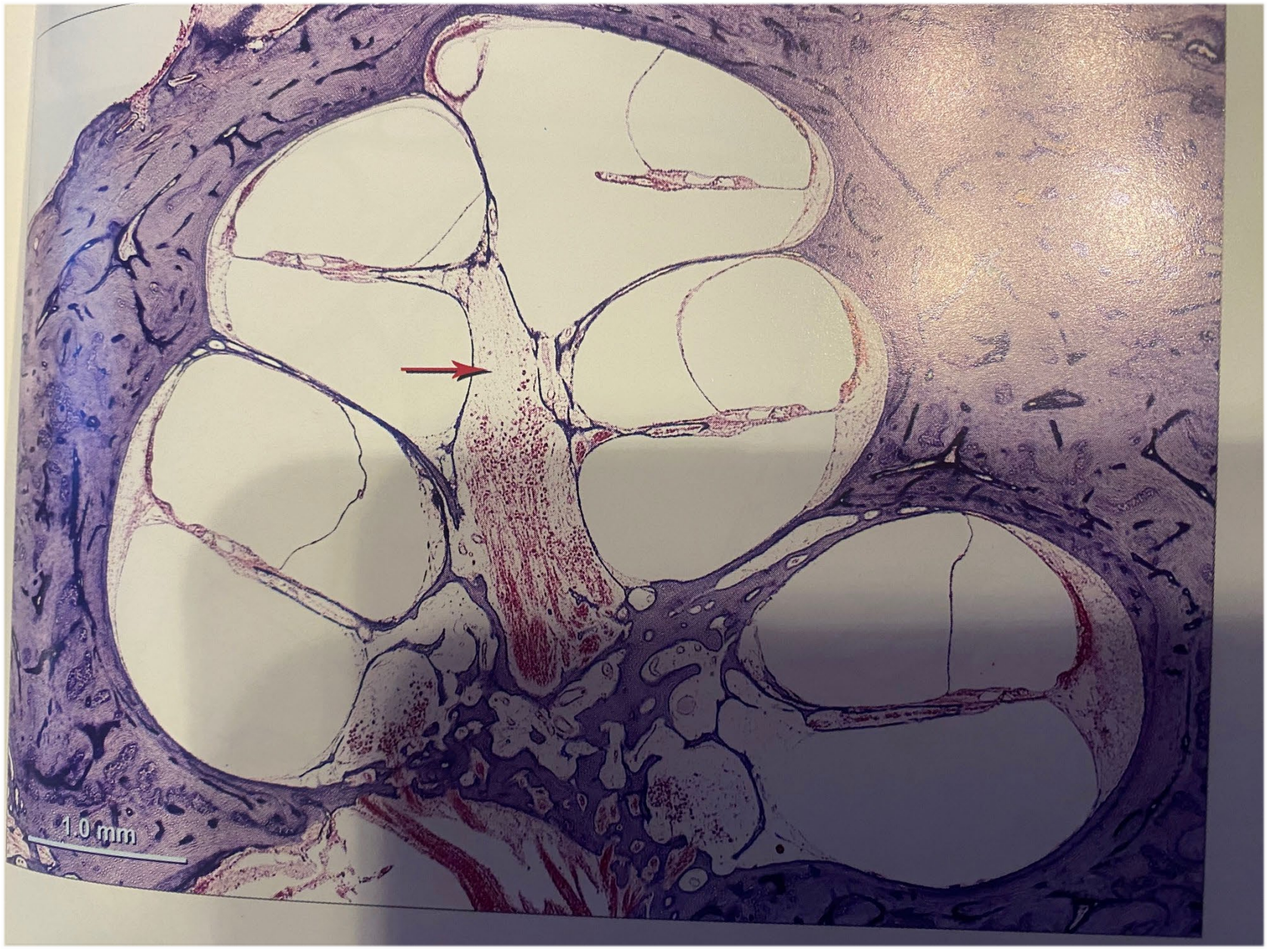
MODERN MENIERE'S



MODERN MENIERE'S



MODERN MENIERE'S



MODERN MENIERE'S

- To explain Meniere's disease any hypothesis must explain
  - Episodic nature of vertigo and hearing loss
  - Presence of wide variety of triggers
  - Association with migraines
  - The development of endolymphtic hydrops and membrane ruptures
  - The predilection for low frequency hearing loss

SALT AS A HYPOTHESIS FOR DRIVING PATHOLOGY

- **Observation/Hypothesis:**
- **Where did this theory start? 1930s**
- Because of the endolyphatic hydrops, it is assumed that there is abnormal sodium regulation in the endolymphatic space
- It is hypothesized that dietary sodium intake could induce symptoms in patients with Meniere's

SALT AS A HYPOTHESIS FOR DRIVING PATHOLOGY

- **Hypothesis**:
  - If the hypothesis is true you should observe:
    - Association between dietary sodium intake and Meniere's incidence
    - Meniere's patients should have higher dietary sodium intake than control group
    - A consistent decrease in Meniere's symptoms with reduction in sodium intake
    - The ability to re-produce the phenotype in animal models with increased sodium diet
    - Should also be able to explain the predilection for low frequency hearing loss

TESTING THE HYPOTHESIS

- Hypothesis:
  - The origin

II. CLINICAL EXPERIMENTS WITH REFERENCE TO THE INFLUENCE OF THE WATER METABOLISM ON THE EAR

S. H. Mygind
and
Dida Dederding

Copenhagen

> Acta Otolaryngol. 1966 Jun 27:Suppl 224:449+. doi: 10.3109/00016486709123623.

Glycerol test in Ménière's disease

I Klockhoff, U Lindblom

PMID: 5992698 DOI: 10.3109/00016486709123623

We have endeavored to demonstrate the influence of the water metabolism on the ear both by dehydration and by hyperhydration.

Already Politzer[1], by his well known pilocarpin treatment aimed at dehydration, pilocarpin giving rise to strong perspiration and salivation with an eventual subsequent improvement of audition. Hence P. Schubert[2], in 1892, drew attention to the fact that the improvement in hearing depended upon the patient's simultaneously being deprived of a sufficient quantity of liquid and becoming thirsty.

TESTING THE HYPOTHESIS

- Hypothesis:
  - The origin

Glycerol Infusion Versus Mannitol for Cerebral Edema: A Systematic Review and Meta-

Jia Wang [1]; Yan Ren [2]; Li-Juan Zhou [1]; Lian-Di Kan [1]; Hu
Hong-Mei Fang [1]

[1]Department of Pharmacy, Sir Run Run Shaw Hospital, School of I versity, Hangzhou, China; and [2]Department of Nephrology, Zhejian Hospital, Hangzhou, China

Neuronal uptake and metabolism of glycerol and the neuronal expression of mitochondrial glycerol–3–phosphate dehydrogenase

Nga Huynh Tran Nguyen [1], Anders Bråthe, Bjørnar Hassel

Affiliations + expand

PMID: 12716415 DOI: 10.1046/j.1471-4159.2003.01762.x

Differential effects of hypertonic mannitol and glycerol on rat brain metabolism and amino acids

Glycerol may have two roles in energy production. First, it may fuel ATP formation by entering glycolysis and oxidative metabolism. Second, glycerol-3-phosphate may serve in the glycerol-3-phosphate shuttle, which translocates reducing equivalents into mitochondria. In this shuttle cytosolic

TESTING THE HYPOTHESIS

- Whats Missing?

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TESTING THE HYPOTHESIS

- Whats Missing?
  - I could not find any studies looking at data to assess whether Menieres patients had higher sodium intake than the general population
  - Nor are there assessments of sodium intake around the time of symptoms

SALT AS A HYPOTHESIS FOR DRIVING PATHOLOGY

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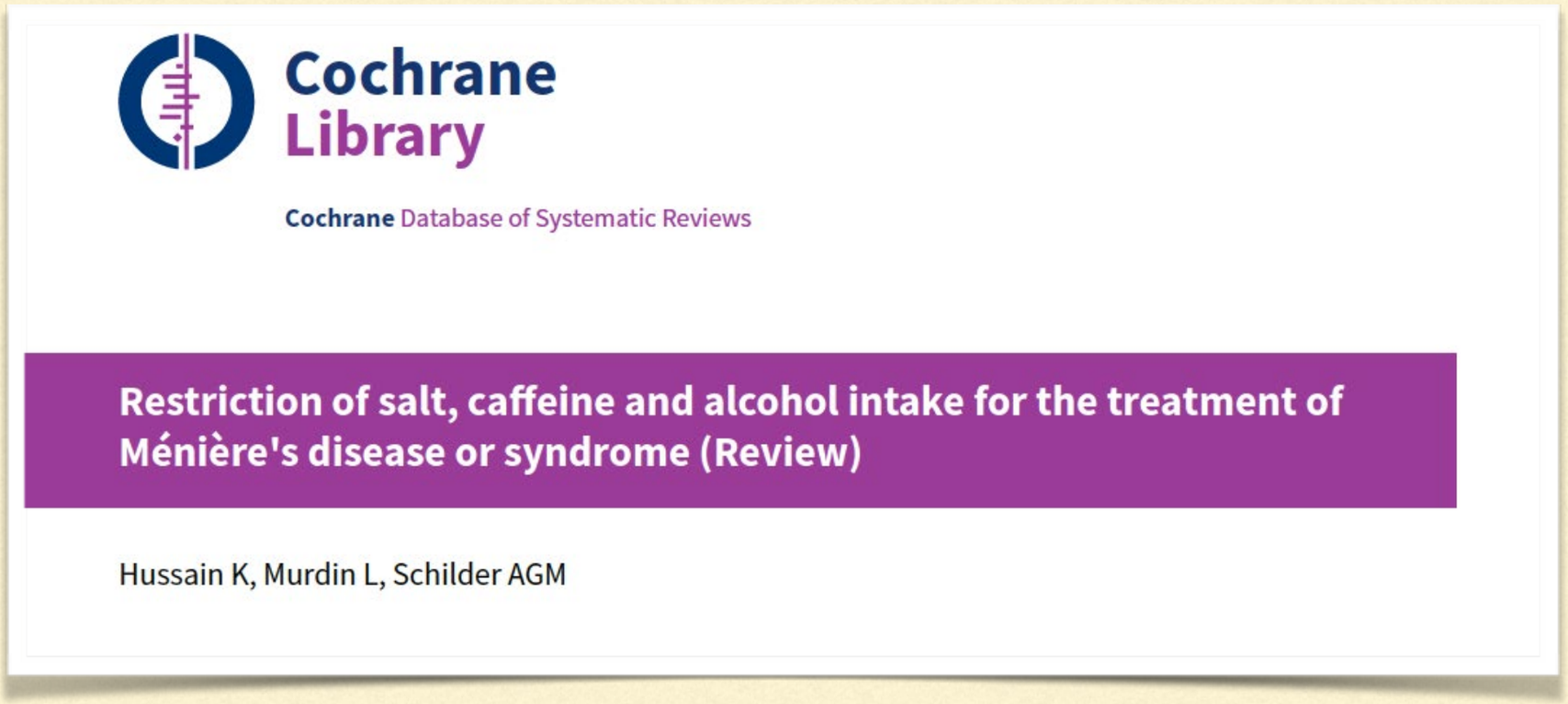
SALT AS A HYPOTHESIS FOR DRIVING PATHOLOGY

- Evidence
  - Interventions to lower sodium intake in menieres disease


Cochrane Library

Cochrane Database of Systematic Reviews

Restriction of salt, caffeine and alcohol intake for the treatment of Ménière's disease or syndrome (Review)

Hussain K, Murdin L, Schilder AGM

SALT AS A HYPOTHESIS FOR DRIVING PATHOLOGY

Hormonal changes following a low-salt diet in patients with Ménière's disease

Takenori Miyashita [a,*], Ryuhei Inamoto [a], Shinjiro Fukuda [a], Hiroshi Hoshikawa [a], Hirofumi Hitomi [b], Hideyasu Kiyomoto [c], Akira Nishiyama [b], Nozomu Mori [a,d]

[a] *Department of Otolaryngology, Kagawa University, Kagawa, Japan*
[b] *Department of Pharmacology, Kagawa University, Kagawa, Japan*
[c] *Division of Integrated Nephrology and Telemedicine, Tohoku Medical Megabank Organization, Tohoku University, Sendai, Japan*
[d] *Osaka Bay Central Hospital, Japan*

- 13 patients - non randomized
  - No control group
  - Measured urinary sodium levels initially and at 2 ye
  - Divided into groups with >3 g per day and <3 g per

Table 2
Vertiginous states.

	Group 1 ($n=7$)	Group 2 ($n=6$)	Total ($n=13$)
Class A	7 (100%)	4 (66%)	11 (84%)
Class C	0	1 (17%)	1 (8%)
Class D	0	1 (17%)	1 (8%)

Table 3
Changes in the hearing levels.

	Group 1 ($n=7$)	Group 2 ($n=6$)	Total ($n=13$)
Improved	1 (14%)	0	1 (8%)
Unchanged	6 (86%)	3 (50%)	9 (69%)
Deteriorated	0	3 (50%)	3 (23%)

SALT AS A HYPOTHESIS FOR DRIVING PATHOLOGY

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ANIMAL MODELS

- Ablation of the endolymphatic duct results in ELH but no episodic vertigo
  - Tried adding aldosterone to this model but still no spontaneous vertigo
- No animal model of only changing sodium in the diet
- To induce vertigo
  - Instilled LPS, aldosterone to induce ELH then injected epinephrine to the middle ear which induced vestibular dysfunction

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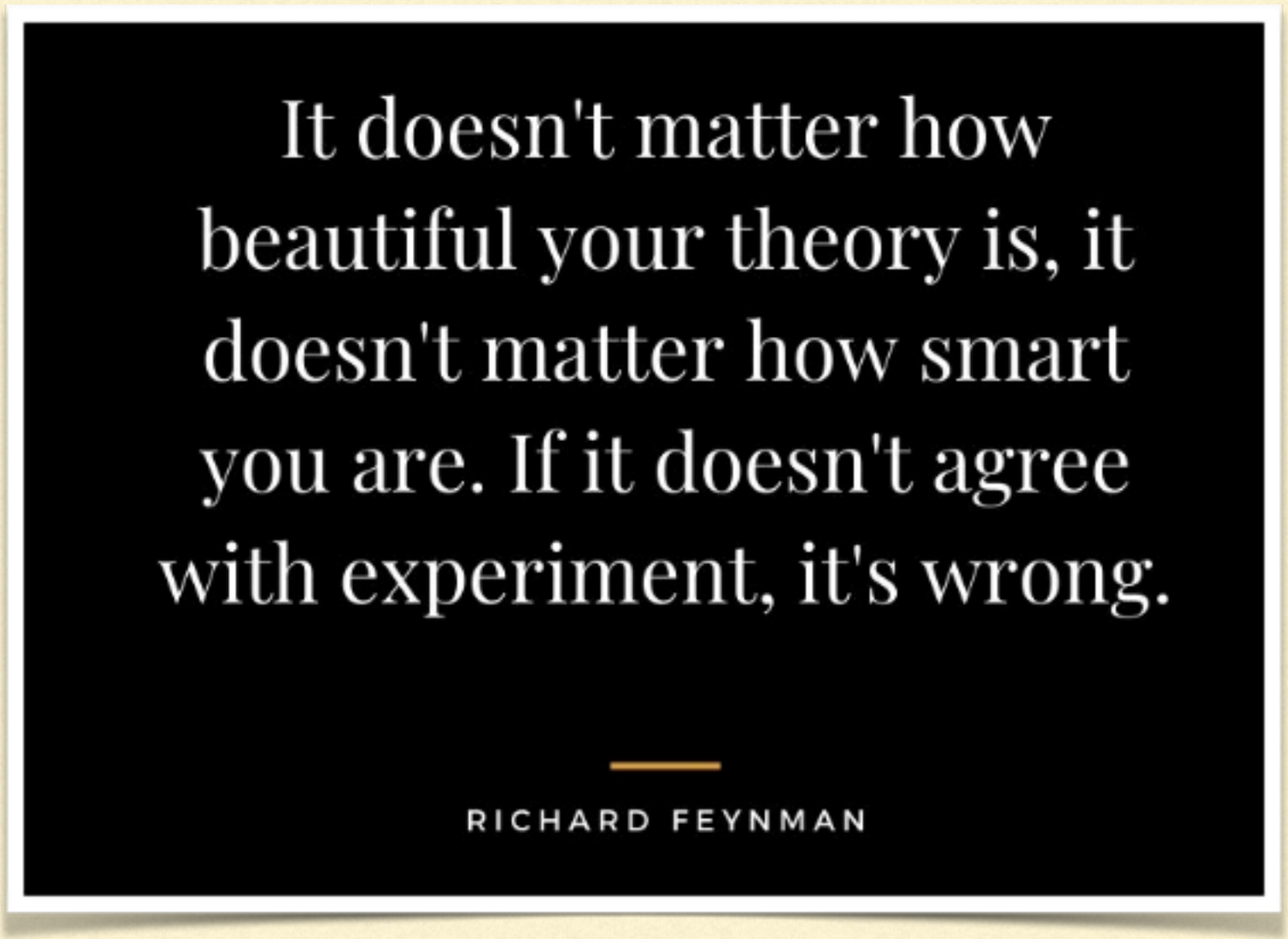
SALT AS A HYPOTHESIS FOR DRIVING PATHOLOGY



SO HOW DO WE FIGURE THIS OUT?

ALTERNATIVE HYPOTHESIS

What happens if there is dysfunction of the mitochondria in the inner ear?

POSSIBLE MECHANISMS

Am J Otolaryngol
3:353–360, 1982

Possible Functional Roles of Na^+,K^+-ATPase in the Inner Ear and Their Relevance to Ménière's Disease

MURIEL D. ROSS, PH.D.,* STEPHEN A. ERNST, PH.D.,* AND THOMAS P. KERR, B.A.†

POSSIBLE MECHANISMS

the guinea pig, Na^+,K^+-ATPase was concentrated in the stria vascularis (8 mol/kg dry

brane (0.4 mol). The concentrations of th
ATPase decreased in the apical direction. Th

and entry rate.[31,33–35,37,38] In related in vivo and in vitro studies it was found that ouabain greatly reduces both the energy utilization[39] and the respiratory rate[40] of the stria. The in vitro work in particular suggests that a substantial portion of oxidative metabolism in this part of the cochlea is linked to sodium pump turnover and consequent hydrolysis of ATP. This "pacemaker" effect of Na^+,K^+-ATPase on tissue respiration was described originally by Whittam and Willis,[41] who demonstrated it in slices of kidney cortex.

It had been shown much earlier, by Meyer zum Gottesberge et al.[42] that oxygen consumption normally declines in the apical direction of the cochlea, as does the endocochlear potential.[43,44] Thus, there appears to be a relationship between the levels of Na^+,K^+-ATPase, oxygen consumption, and the endocochlear potentials generated in the various cochlear turns.

5. Mitochondria-rich cells in the ES have a higher activity of Na^+, K^+-ATPase and a higher Na^+ permeability [11].

ATPase and a higher Na^+ permeability, strongly suggesting that molecules related to Na^+ transport may be densely located in mitochondria-rich cells. Mitochondria-rich cells in ES have characteristic qualities of Na^+ absorption

POSSIBLE MECHANISMS

THE METABOLISM OF BETAHISTINE IN THE RAT

L. A. STERNSON, A. J. TOBIA, G. M. WALSH, and A. W. STERNSON

Drug Metabolism and Disposition March 1974, 2 (2) 123-128;

Studies to determine the subcellular distribution of betahistine oxidase activity indicate that the preponderance of oxidative activity originated in the mitochondrial fraction, suggesting that the metabolic route involves the direct oxidation of betahistine to 2-pyridylacetaldehyde by MAO.

POSSIBLE MECHANISMS

Betahistine effects on cochlear blood flow: from the laboratory to the clinic

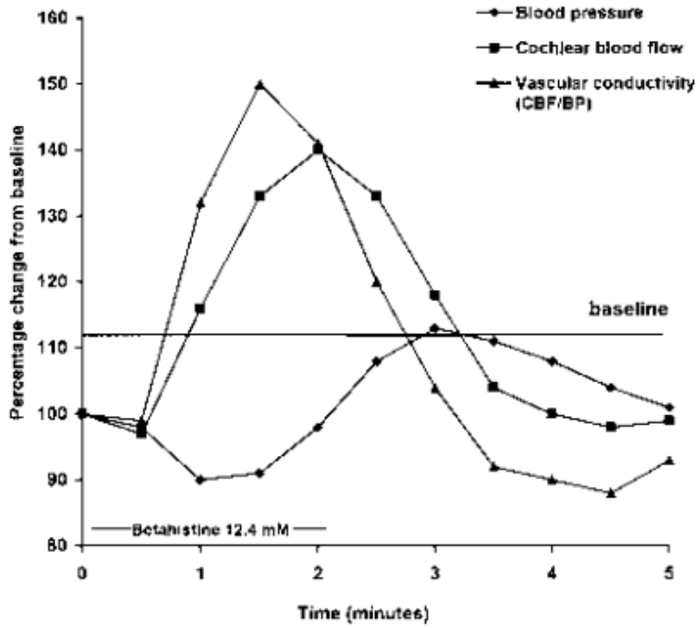


Fig. 1. The effect of intravenous betahistine on cochlear blood flow (CBF), blood pressure (BP) and cochlear vascular conductivity.

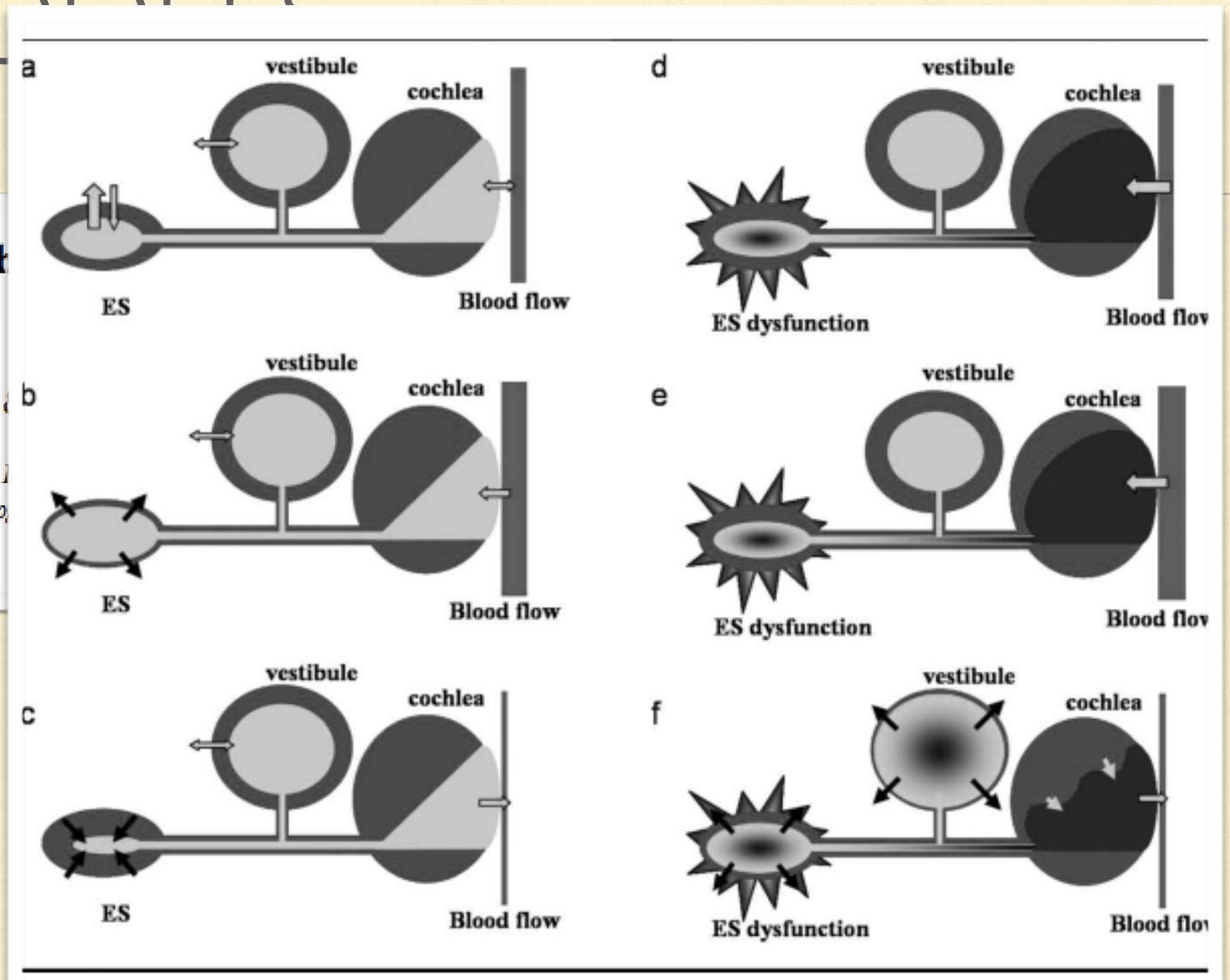
The development of laser Doppler flowmetry techniques has contributed greatly to the study of cochlear blood flow (CBF). In animal models, intravenous betahistine dihydrochloride clearly increased CBF in a dose-dependent manner. This effect was greater in the cochlear vasculature than in the systemic vascular bed. The effects of betahistine were blocked by the alpha 2-

ANIMAL MODELS

Effect of inner ear blood flow ch

MASAYA TAKUMIDA[1], NANA AKAGI[2]

[1]*Department of Otolaryngology, Hiroshima University*
Japan, Tokyo, Japan and [3]*Department of Otolaryngolo*



: 8. Schematic representation of inner ear blood flow (IBF) changes in the normal (a, b, c) and model animals (d, e, f). (a) Inne
omeostasis, strictly regulated in normal animals. (b) When the IBF was increased, the endolymphatic volume increased, regulate
pansion of endolymphatic sac (ES) lumen. (c) When the IBF was reduced, the endolymphatic volume decreased, regulated b
se of the ES lumen and subsequent secretion of stainable substance. (d) Model animal, showing endolymphatic hydrops (EH) an
ıction, but no signs of vertigo. (e) When the IBF was increased in the model animals, there were no obvious changes in the inne
hen the IBF was decreased in the model animals, the volume of endolymph in the cochlea was reduced, resulting in foldi
er's membrane. The vestibular part represents the increased EH, which may cause the rapid ionic imbalance resulting in the ma
ular dysfunction. The ES also shows an abnormal reaction, denoting expansion of the ES lumen.

ANIMAL MODELS

Review

Protective Effect of Mitochondria-Targeted Antioxidants against Inflammatory Response to Lipopolysaccharide Challenge: A Review

Ekaterina M. Fock and Rimma G. Parnova *

In a wide range of cell types, LPS application disturbs cellular energetics, which manifests itself in a decline in respiratory complex activity, decline in the mitochondrial membrane potential, reduction in mitochondrial respiration, and suppression of ATP production in a tissue-, time-, and dose-dependent manner [19,22,28,84–89]. A critical

POSSIBLE MECHANISMS

Mitochondrial function and brain Metabolic Score (BMS) in ischemic Stroke: Evaluation of "neuroprotectants" safety and efficacy

Avraham Mayevsky*, Hofit Kutai-Asis, Michael Tolmasov

drop in oxygen supply to the brain tissue. Due to the lack of oxygen, mitochondrial dysfunction is developed and the production of ATP - the energy source of all brain physiological activities will be inhibited. In a

in CBF (1) and microcirculatory hemoglobin oxygenation (2). Therefore, the O_2 delivery (3) to the brain decreased and is detected as an increase in the intramitochondrial NADH (4). The next step is the inhibition of the ion pumps such as the Na^+ K^+ ATPase due to the low levels of ATP in the cell (5). The accumulation of K^+ in the extracellular space (6) and the increase in in the intracellular calcium (7) will be recorded. The last event (8) is the decreased spontaneous electrical

POSSIBLE MECHANISMS

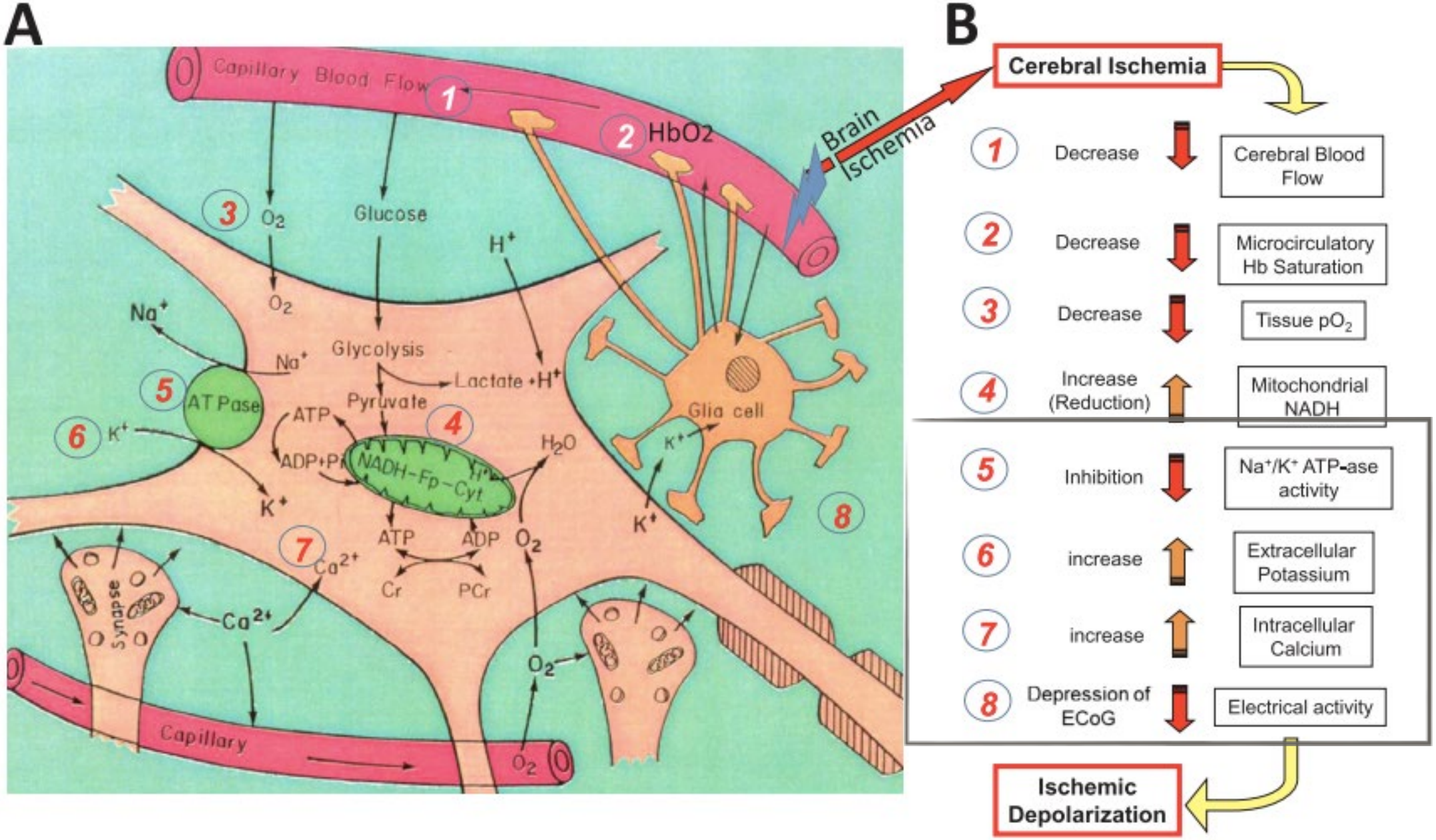


Fig. 1. A - Schematic presentation of the "basic building stones" of a typical cerebral cortex tissue. During an ischemic event, the sequence of the 8 early responses developed are presented in part A and B of the figure.

VASCULAR DYSFUNCTION

Vascular Findings in the Stria Vascularis of Patients With Unilateral or Bilateral Ménière's Disease: A Histopathologic Temporal Bone Study

*†Shin Kariya, *‡Sebahattin Cureoglu, §Hisaki Fukushima, *‡Shigenobu Nomiya, *‡Rie Nomiya, ‡Patricia A. Schachern, †Kazunori Nishizaki, and *||Michael M. Paparella

Conclusion: The stria vascularis may be ischemic bilaterally both in bilateral and unilateral Ménière's disease. Abnormal findings in the contralateral ears in unilateral Ménière's disease reported in previous studies might be related to poor vascularity of the stria vascularis. **Key Words:** Ménière's disease—Stria

VASCULAR DYSFUNCTION

Review

Experimental and Clinical Evidence of the Effectiveness of Riboflavin on Migraines

Gaku Yamanaka *, Shinji Suzuki, Natsumi Morishita, Mika Takeshita, Kanako Kanou, Tomoko Takamatsu, Shinichiro Morichi, Yu Ishida, Yusuke Watanabe, Soken Go, Shingo Oana and Hisashi Kawashima

Abstract: Riboflavin, a water-soluble member of the B-vitamin family, plays a vital role in producing energy in mitochondria and reducing inflammation and oxidative stress. Migraine pathogenesis includes neuroinflammation, oxidative stress, and mitochondrial dysfunction. Therefore, riboflavin

MITOCHONDRIAL DYSFUNCTION

Is Mitochondrial Dysfunction a Common Root of Noncommunicable Chronic Diseases?

Alexis Diaz-Vegas, Pablo Sanchez-Aguilera, [...], and Sergio Lavandero

CONCLUSIONS

- Current evidence does not support the hypothesis that dietary sodium plays a role in Meniere's disease
- Future guidelines should consider this in their recommendations
- Future research could consider looking at mitochondrial function in Meniere's disease

THANK YOU