



Uhthoff's Phenomenon

Prof. Christian Lueck

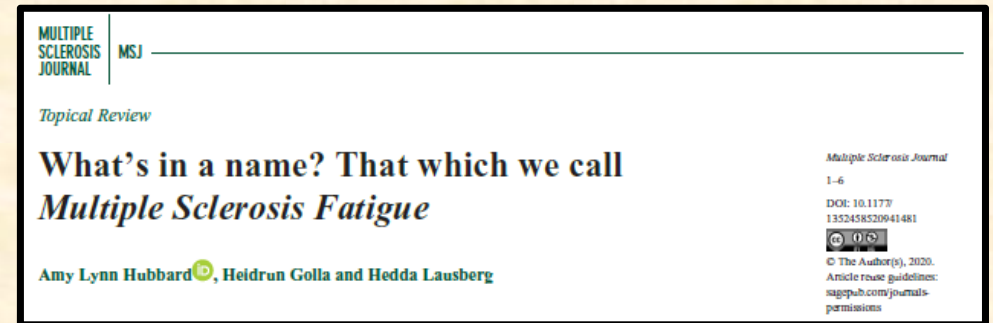
Department of Neurology

Canberra Hospital

Australian National University Medical School

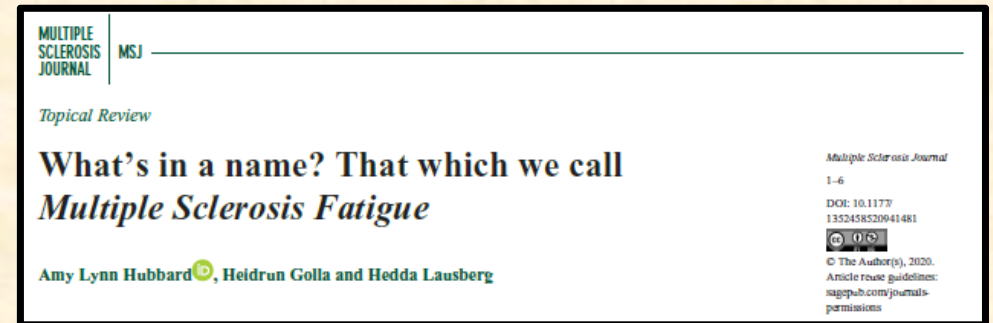
MS Fatigue

- problems with definition:
 - ‘fatigue’ not necessarily correct term
 - (‘tiredness which occurs after engaging in some type of activity’)
- 5 different phenomena of ‘daily-onset MS tiredness’ suggested:
 - transitory ‘state’ of limited predictability
 - not just lassitude; may be motor, sensory, and/or cognitive impairment
 - impairment often unrelated to previous activity (but within-patient consistency)
 - triggered by heat, improved by cooling
 - often reflected in gait



MS Fatigue

- problems with definition:
 - ‘fatigue’ not necessarily correct term
 - (‘tiredness which occurs after engaging in some type of activity’)
- 5 different phenomena of ‘daily-onset MS tiredness’ suggested:
 - transitory ‘state’ of limited predictability
 - not just lassitude; may be motor, sensory, and/or cognitive impairment
 - impairment often unrelated to previous activity (but within-patient consistency)
 - triggered by heat, improved by cooling
 - often reflected in gait

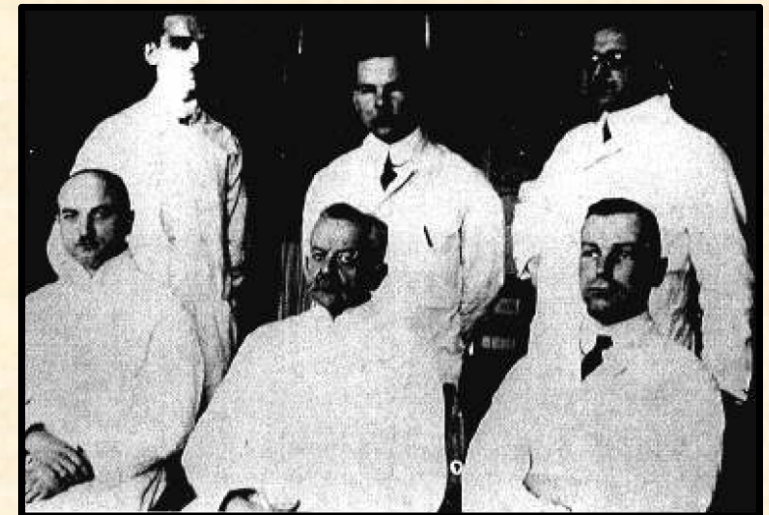


Wilhelm Uhthoff (1853-1927)

- Professor of Ophthalmology, Universities of Marburg and Breslau
- specialised in visual disorders due to abnormalities of nervous system:
 - i.e. a neuro-ophthalmologist
- 1890 - described temporary vision loss associated with exercise in optic neuritis:
 - Uhthoff W. Untersuchungen über die bei den multiplen Herdsklerose vorkommenden Augenstörungen. *Arch Psychiatr Nervenkranken* 1890;**21**:55-116, 303-410



Wikipedia



Selhorst & Saul, *J Neuro-Ophthalmol* 1995;15:63-69

Uhthoff's Phenomenon: History

- 1890, Wilhelm Uhthoff:
 - worsening of vision on exercise in 4 patients
 - (one patient also mentioned deterioration of vision when standing in front of hot stove)
- after WW1, induced pyrexia became fashionable therapy for MS:
 - many authors reported benefit
 - some patients deteriorated (or even died)
- diagnostic 'hot bath test':
 - 10-15 minutes in 41.1-43.3°C
 - clinical deterioration in >80%; 60% developed new signs
 - discontinued in about 1983

The Hot Bath Test in the Diagnosis of Multiple Sclerosis

Amir S. Malhotra, MD, Hershel Goren, MD

• The sensitivity and specificity of the hot bath test in the diagnosis of multiple sclerosis (MS) were studied. New neurological signs developed in 60% of the patients with MS. Such changes were not observed in control subjects.

(JAMA 1981;246:1113-1114)

Table 1.—Body Temperature Producing Change in Neurological Examination

Increase in Body Temperature, °C

SHORT COMMUNICATION

Acta Neurol Scand., 1985;72:65-67

Key words: Hot bath test; multiple sclerosis; oligoclonal bands; visual evoked responses.

The hot bath test in multiple sclerosis: comparison with visual evoked responses and oligoclonal bands*

Loren A. Rolak and Tetsuo Ashizawa
Department of Neurology, Baylor College of Medicine, and The Veteran's Administration Medical Center, Houston, Texas, USA

ABSTRACT – We studied 50 patients with definite, probable, and possible multiple sclerosis (MS), prospectively (20 patients) and retrospectively (30 patients), to determine the value of the hot bath test for diagnosing MS and to compare it to visual evoked responses and oligoclonal bands. The hot bath test was abnormal in 8 of the 23 patients with definite MS (35%), and 4 of the 27 patients with probable or possible MS (15%). Only one patient with an abnormal hot bath test did not also have other evidence of definite multiple sclerosis. Our results suggest that the hot bath test seldom adds diagnostic information, especially when tests for evoked responses and oligoclonal bands are available.

Accepted for publication December 4, 1984

Uhthoff's Phenomenon: Description

- definition:
 - 'temporary (< 24 hours) stereotyped worsening of neurological function among multiple sclerosis patients in response to increase in body temperature.'
 - effects usually reversible
 - also occurs in other types of optic neuritis (e.g. NMO)
 - not the same as a true relapse
- common:
 - 52% patients with optic neuritis experience Uhthoff's phenomenon:
 - only 16% experience complete recovery; sign of poor remyelination?
 - 60% - 80% patients with MS exhibit Uhthoff's phenomenon (mostly non-visual):
 - sensory disturbance, weakness, double vision
 - reading, writing, memory, information-processing

Short Report

MULTIPLE SCLEROSIS JOURNAL | MSJ

The time course and phenotype of Uhthoff phenomenon following optic neuritis

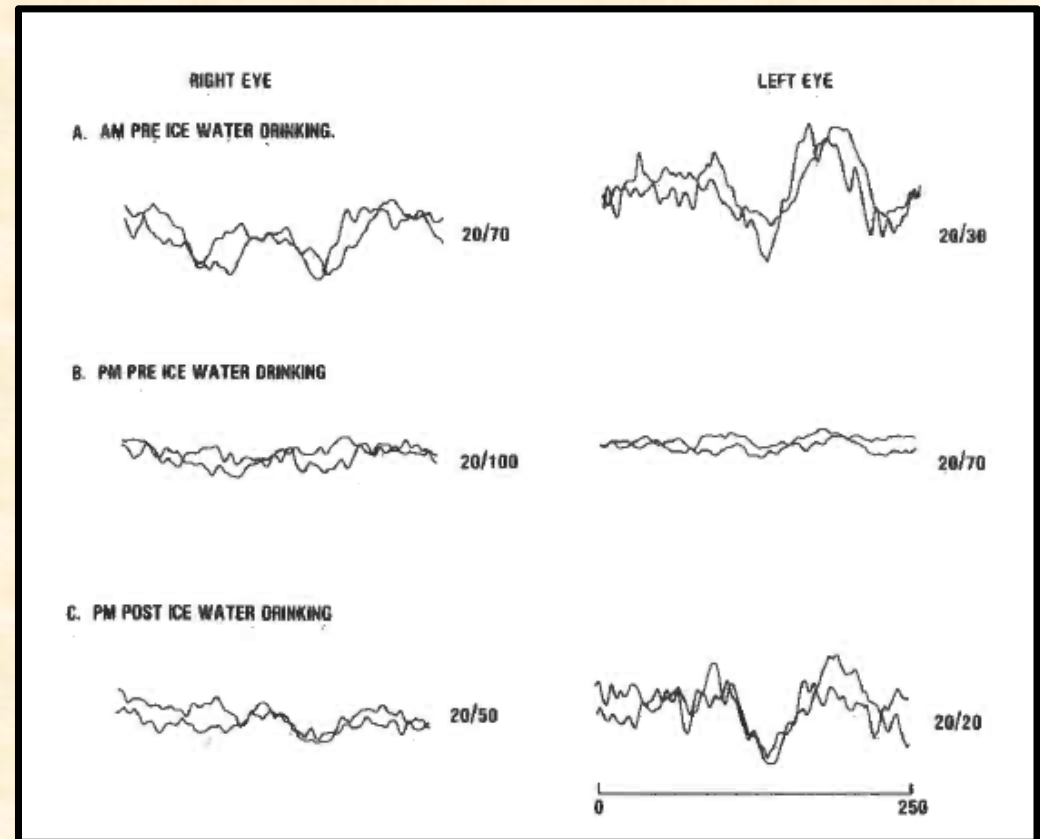
Clare L Fraser¹, Indran Davagnanam², Mark Radon³ and Gordon T Plant^{1,4}

Multiple Sclerosis Journal
18(7) 1042-1044
© The Author(s) 2012
Reprints and permissions:
sagepub.co.uk/journalsPermissions.nav
DOI: 10.1177/1352458511431074
msj.sagepub.com

SAGE

Uhthoff's Phenomenon: Description

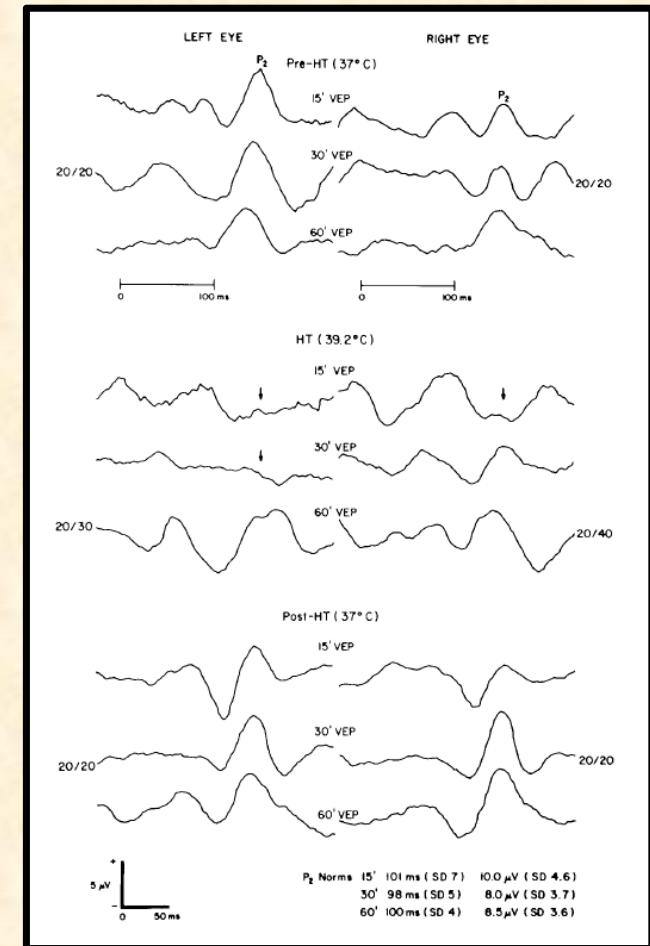
- phenomenon provoked by:
 - hot shower, sauna, sunbathing, use of hair dryer, exercise, circadian change in body temperature:
 - pilot with vision deteriorating from 20/30 in morning to 20/50 in afternoon (with corresponding changes on VER)
 - also: emotional events, menstruation, smoking, altered lighting, digesting a (hot) meal, fever
 - onset of worsening can be quite rapid:
 - rare reports of drowning in hot bath or death from sunbathing



Scherokman et al., *Ann Neurol* 1985;17:418-419

Uhthoff's Phenomenon: Pathophysiology

- likely to be due to altered neural conduction
- warming and cooling cause transient block and restoration of conduction, respectively:
 - electrophysiology
 - VER/visual acuity/flicker fusion
- effect can be seen at temperature rises as little as 0.2° - 0.5° C
- mechanism:
 - shortening of action potential on background of reduced safety factor
 - reduced WBC nitric oxide (? related to increased noradrenaline):
 - would explain persistent reduction in fatigue with prolonged cooling – sustained benefit from wearing cooling garment 45-60 minutes 2-3 x/day
 - other suggestions: heat shock proteins, circulatory changes, effects of serum calcium/other humoral substances



Saul et al., *J Neuro-Ophthalmol* 1995;15:70-78

Uhthoff's Phenomenon: Clinical Implications

- distinguish from relapse
- strategies for symptomatic improvement:
 - avoidance of exacerbating circumstances
 - active cooling:
 - cold drinks, freezer gel ice packs, cool shower, cooling vests
 - increase action potential duration:
 - potassium channel blockade (4-aminopyridine)
 - delaying sodium channel inactivation (scorpion venom/pyrethroids)
 - N.B. 4-AP often effective, but mechanism of action not clear



<https://seppelec.com/en/refrescos.php>
<https://www.amazon.com/Reusable-Cold-Packs-Injuries-Compress/dp/B07QDPFPW9>
<https://www.everydayhealth.com/multiple-sclerosis/treatment/cooling-products-multiple-sclerosis/>
<https://prescriptiongiant.com/product/fampridine-generic-dalfampridine/>

References

- Fraser CL et al. The time course and phenotype of Uhthoff's phenomenon following optic neuritis. *Mult Scler* 2012;**18**:1042-4
- Frohman TC et al. Uhthoff's phenomena in MS – clinical features and pathophysiology. *Nat Rev Neurol* 2013;**9**:535-40
- Hubbard AL et al. What's in a name? That which we call *Multiple Sclerosis Fatigue*. *Mult Scler* 2020 (ePub ahead of print)
- Malhotra AS, Goren H. The hot bath test in the diagnosis of multiple sclerosis. *JAMA* 1981;**246**:1113-4
- Opara JA et al. Uhthoff's phenomenon 125 years later – what do we know today? *J Med Life* 2016;**9**:101-5
- Panginikkod S et al. Uhthoff phenomenon. *Stat Pearls*. NCBI Bookshelf: NBK470244
- Rae-Grant AD. Unusual symptoms and syndromes in multiple sclerosis. *Continuum* 2013;19:992-1006
- Rolak LA, Ashizawa T. The hot bath test in multiple sclerosis: comparison with visual evoked responses and oligoclonal bands. *Acta Neurol Scand* 1985;**72**:65-7
- Saul RF et al. Visual evoked potentials during hyperthermia. *J Neuro-ophthalmol* 1995;**15**:70-8
- Selhorst JB, Saul RF. Uhthoff and his symptom. *J Neuro-ophthalmol* 1995;**15**:63-9
- Smith K et al. The pathophysiology of multiple sclerosis. In: Compston A et al. (Eds.) *McAlpine's Multiple Sclerosis*, Churchill Livingstone Elsevier. 2006