17 years) suggest a role of this solvent at the level of the central nervous system. So our hypothesis might provide a novel PD neurotoxicant. In future studies, n-hexane might be developed to produce animal models of PD. The development of animal models is essential for better understanding pathogenesis and progression of PD and testing therapeutic agents for the treatment of PD patients.

References


Hypothesis: Chronic fatigue syndrome is caused by dysregulation of hydrogen sulfide metabolism

Chronic fatigue syndrome (CFS), which is also known as myalgic encephalomyelitis (ME), is a debilitating, multi-system disease whose etiology is unclear, and for which there are as yet no reliable treatments. Here the hypothesis is advanced that the multi-system disturbances in CFS/ME are caused by disturbances in the homeostasis of endogenous hydrogen sulfide (H$_2$S) and result in mitochondrial dysfunction.

Research on H$_2$S – the gas that causes the characteristic smell of rotten eggs – dates to the 1700’s and has shown a remarkable range of effects in both animals and humans. At high concentrations, H$_2$S has a variety of biological toxicities including being instantaneously deadly; at low concentrations some evidence suggests that H$_2$S has beneficial effects and can act as an endogenous biological mediator – the third such gaseous mediator discovered (after nitric oxide and carbon monoxide). The brain, pancreas and the gastrointestinal tract produce H$_2$S. Endogenous H$_2$S plays a role in regulating blood pressure, body temperature, vascular smooth muscle, cardiac function, cerebral ischemia, and in modulating the hypothalamus/pituitary/adrenal axis. It even has been called a “master metabolic regulator”.

Recent research has demonstrated that at low, non-toxic doses, exogenous H$_2$S produces a reversible state of hibernation-like deanimation in mice, causing a decrease in core body temperature, an apnea-like sleep state, reduced heart and respiration rates, and a severe metabolic drop [1]. These characteristics are not unlike the symptoms and extreme “de-animation” experienced by CFS/ME patients. Moreover, H$_2$S affects biological networks that are disrupted by CFS including neurologic, endocrine and immunologic systems. Therefore, a plausible etiology of CFS is an increase in the activity of endogenous H$_2$S, thereby inhibiting mitochondrial oxygen utilization.

H$_2$S and Mitochondria

In this view, fatigue and the other CFS/ME symptoms could be due to diminished physiological and cellular energy due to reduction in the capacity of mitochondria to utilize oxygen and synthesize ATP. Specifically, H$_2$S binds to the mitochondrial enzyme cytochrome c oxidase, which is part of Complex IV of the electron transport chain, and attenuates oxidative phosphorylation and ATP production.

Consistent with this finding, recent research on low level H$_2$S toxicity points to increased formation of free radicals and depolarization of the mitochondrial membrane, a condition that would decrease ATP synthesis [2]. If poisoning renders mitochondria inefficient, one would expect cells to shift to anaerobic mechanisms, a shift that has been reported for CFS patients. Also consistent with this hypothesis is the fact that mitochondria are organelles descended from ancient eukaryotic sulfur-utilizing microbes. Thus, it is not surprising that they show a very high affinity for sulfide.

Of course, H$_2$S or sulfide may not directly affect mitochondria by binding to them. Genomic changes could mediate some of the effects of H$_2$S. Some studies have found evidence for the involvement of the cytochrome c oxidase gene in CFS/ME. Also, investigators have found CFS abnormalities in genes related to fatty acid metabolism, apoptosis, mitochondrial membrane function, and protein production in mitochondria. Given a predisposing genetic background, H$_2$S may lead to genomic instability or cumulative mutations in the mitochondrial DNA [3].

Alternatively, the effects of H$_2$S could be initially mediated by changes in the redox potential of cells or changes in their sulfur metabolism, especially in glutathione. Another possible mechanism is a direct effect of H$_2$S on the immune system. Recent research indicates that exogenous hydrogen sulfide induces functional inhibition and cell death of cytotoxic lymphocyte subsets of CD8 (+) T cells and NK cells.

Finally, H$_2$S plays a pivotal role in both aerobic and non-aerobic organisms as a signaling molecule. Bacteria in the gut both produce and resemble Rosenthal fibres. Neuropathol Appl Neurobiol 2003:250:556–60.


Wang Qing-Shan
Xie Ke-Qin

Institute of Toxicology, Shandong University, 44 West Wenhua Road, Jinan 250012, PR China

Tel.: +86 531 88382132; fax: +86 531 88382553

E-mail addresses: keqinx@sdu.edu.cn, wangqs1222@mail.sdu.edu.cn (X. Ke-Qin)
for body homeostasis, and causes CFS. Understanding the role of 
H2S in the body, and, in particular, in mitochondrial function, 
may provide a unifying lens through which to view the diverse 
manifestations of this complex disease.

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Marian Dix Lemle 
3135 Ellicott Street, NW 
Washington, DC 20008, 
United States 
Tel.: +1 202 537 0344; fax: +1 202 775 0045 
E-mail address: mdlemle@yahoo.com

doi:10.1016/j.mehy.2008.08.003

A novel approach in preventing the occurrence of diabetic foot infections – The finger socks

Fig. 1. The finger socks.

Diabetic foot infections with eventual dramatic consequences continue to be a challenge for practitioners. Given the high cost of the treatment of these usually polymicrobial and resistant infection [1], preventing measure are to be taken primarily into consideration.

The skin as the first line in defense system is to be preserved intact. Many microorganisms enter to deep tissues of the foot via cracks and splits resulting from either the neuropathic foot or other traumatic factors. The fore-foot, mainly the toes, is the origin of many foot infections. The interdigital space of the foot, as it is overlaid by a thinner skin, is subjected to skin cracks more than any other areas of the foot. Another threatening factor to skin breaks is the adjacent toe itself. A callus formation, a toe deformity or an overgrown nail causes continuous trauma to the nearby toe consequently impairing the skin integrity.

Many measures are taken to decrease the incidence of diabetic foot infections. “The finger socks” (Fig. 1) may play a novel role in adding to this decrease rate. This recently manufactured and still not worldwide known interesting design, the finger socks, by covering each toe independently could be promising to prevent the web spaces from providing a nidus for microbial invasion as well as to prevent the above mentioned adjacent threat and subsequent cracks to the interdigital space consequently lowering the rate of deep tissue infections.

References


Mesut Mutluoglu 
Department of Underwater and Hyperbaric Medicine, 
Gulhane Military Medical Academy Haydarpasa Teaching Hospital, 
34668 Uskudar, Istanbul, 
Turkey

doi:10.1016/j.mehy.2008.08.004


Mesut Mutluoglu 
Department of Underwater and Hyperbaric Medicine, 
Gulhane Military Medical Academy Haydarpasa Teaching Hospital, 
34668 Uskudar, Istanbul, 
Turkey

doi:10.1016/j.mehy.2008.08.004


Gunalp Uzun 
Department of Underwater and Hyperbaric Medicine, 
Gulhane Military Medical Academy Haydarpasa Teaching Hospital, 
34668 Uskudar, Istanbul, 
Turkey 
Tel.: +90 216 542 2787; fax: +90 216 348 7880 
E-mail address: gunalpuzun@yahoo.com (G. Uzun)

Senol Yildiz 
Department of Underwater and Hyperbaric Medicine, 
Gulhane Military Medical Academy Haydarpasa Teaching Hospital, 
34668 Uskudar, Istanbul, 
Turkey

doi:10.1016/j.mehy.2008.08.004