

Effects of Hyperbaric Oxygen Therapy on Nitric Oxide Generation in Humans

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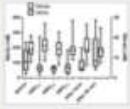

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Table 1

Nitric Oxide

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In Press, Uncorrected Proof — Note to users

Effects of hyperbaric oxygen on nitric oxide generation in humans

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Highlights

- Hyperbaric oxygen (HBO₂) reduces nasally and orally exhaled NO in humans.
- Nitrate and nitrite reduction to NO by oral bacteria is disrupted by hyperbaric oxygen.
- The decrease in orally exhaled NO by HBO₂ partly depends on reduced oral NO generation.
- The decrease in nasally exhaled NO by HBO₂ suggests reduced iNOS activity in the nasal airways.
- HBO₂ seems to affect NO generation both from NOS-dependent and nitrate/nitrite-dependent pathways.

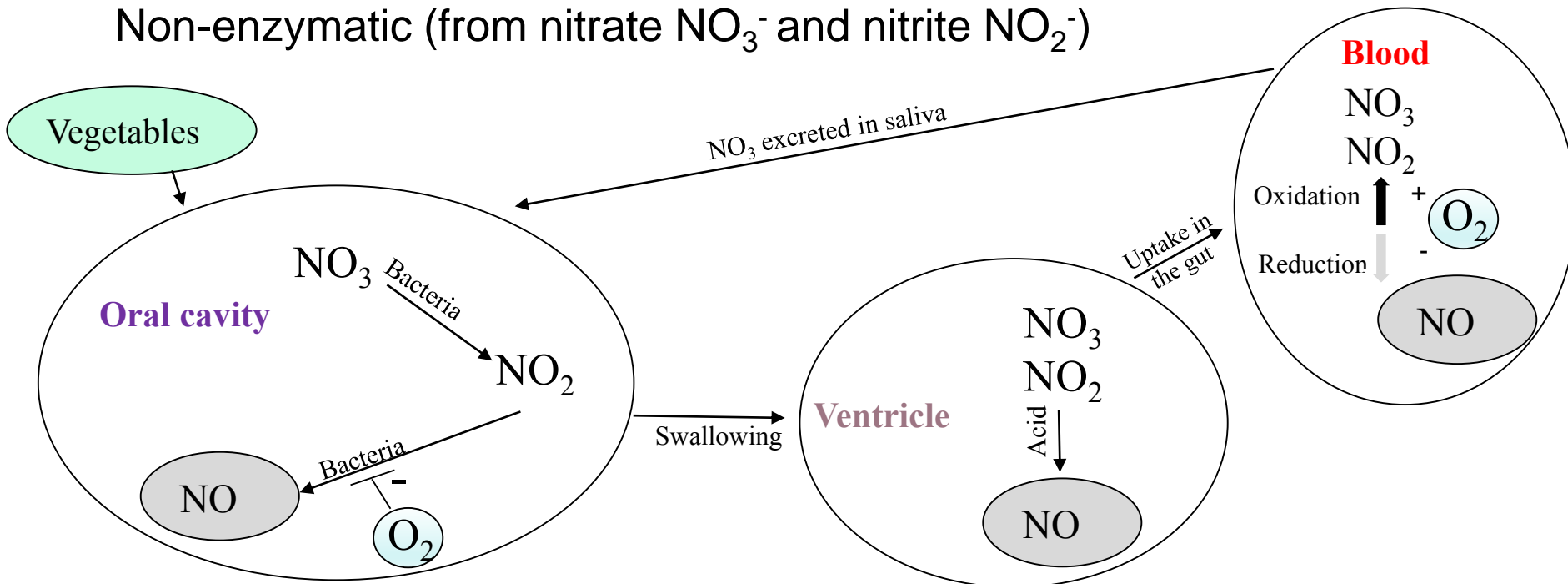
NO production

Enzymatic, isoenzymes

→ NOS 1 (endothelium), 2 (inflammatory and in nasal sinuses), 3 (neurons)

→ L-arginine + 3/2 NADPH + H⁺ + 2 O₂ → citrulline + NO + 3/2 NADP⁺

Non-enzymatic (from nitrate NO₃⁻ and nitrite NO₂⁻)



Effect of NO

- $\text{NO} \rightarrow \text{sGC} \rightarrow \text{cGMP}$
- Protein nitrosylation
- Direct DNA-effect

- Vasodilatation
- Inhibition of platelets
- Inhibition of mitochondrial respiration
- Regulation of nerve transmission
- Regulation of intestinal motility
- Protection of ventricular mucosa
- Potential pathological effects (hypertension, vascular damage)

HBO-chamber Sechrist



Experiment A ,
controlled
-exhaled NO
-blood
-saliva
-before/after

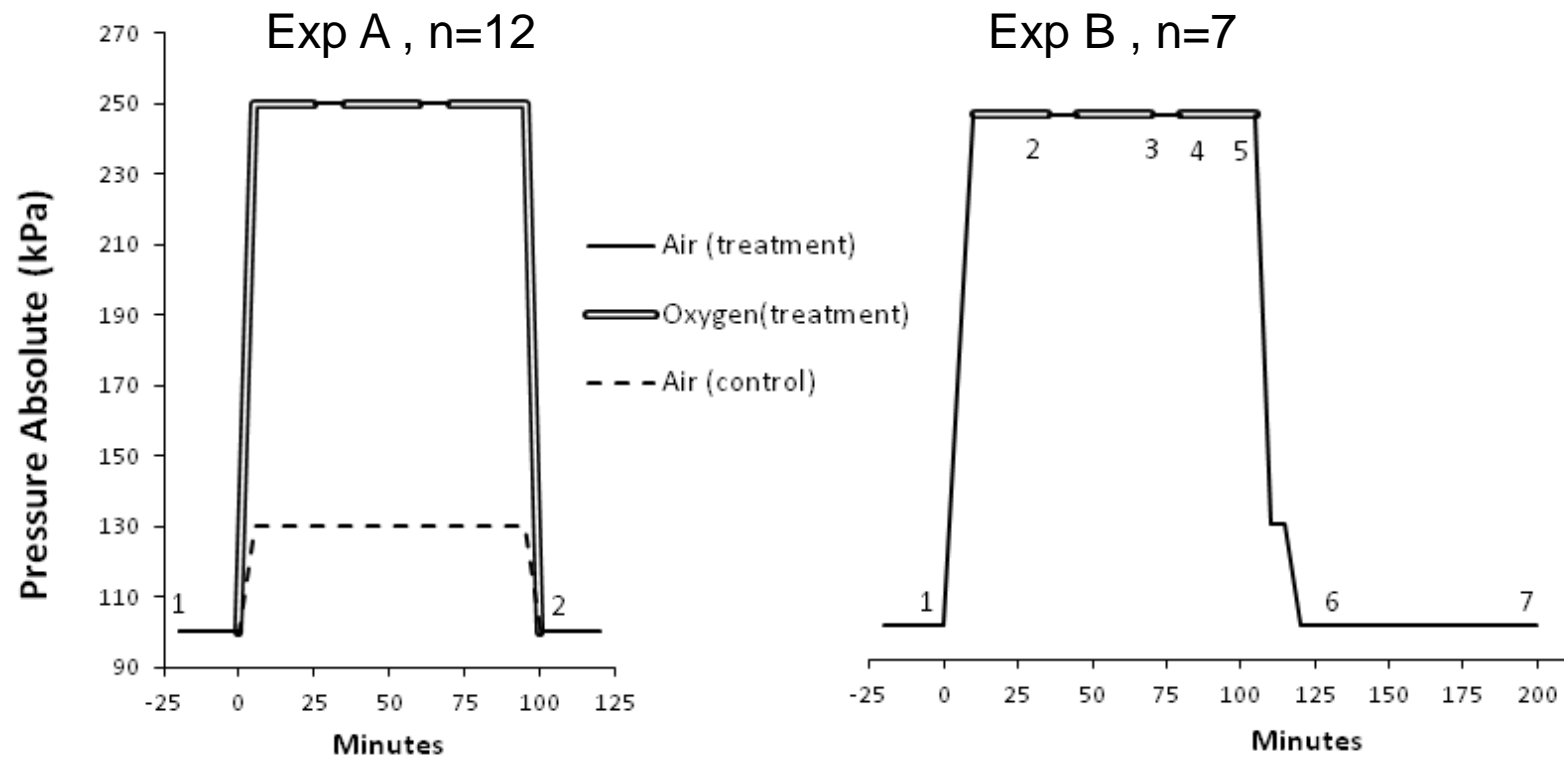


HBO Chamber HAUX Quadro 3200

Experiment B
-blood
-saliva
-before- during
and after HBO



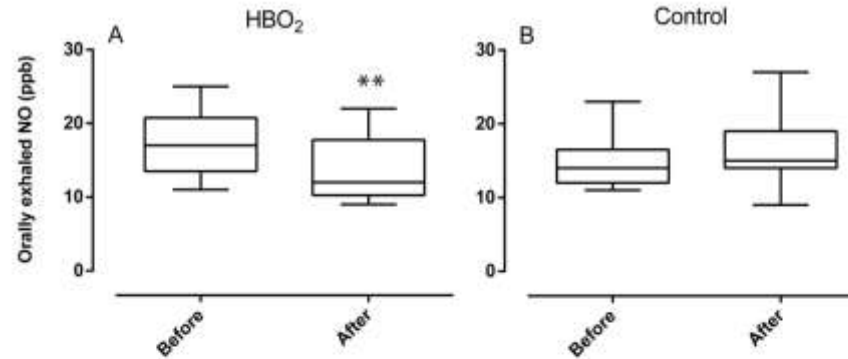
HBO protocols



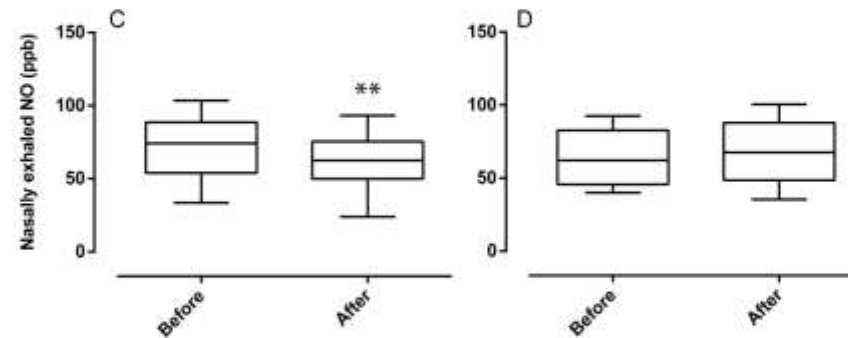
Numbers indicate sampling of blood (1, 2, 3, 5, 6, 7) and saliva (1, 4, 6).
Exhaled NO sampling in exp A only.

Results, exhaled NO

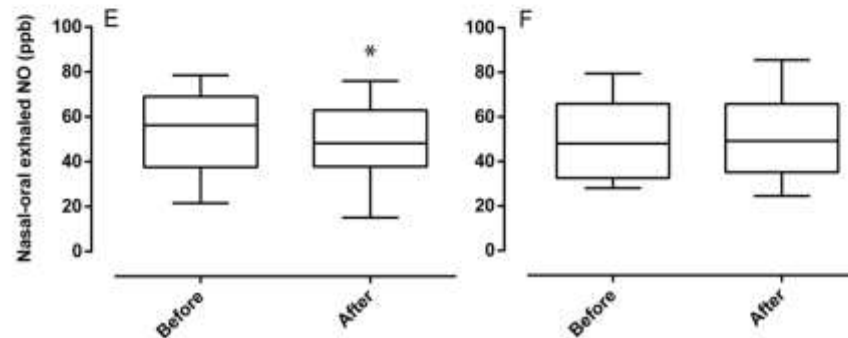
- Mouth



- Nose

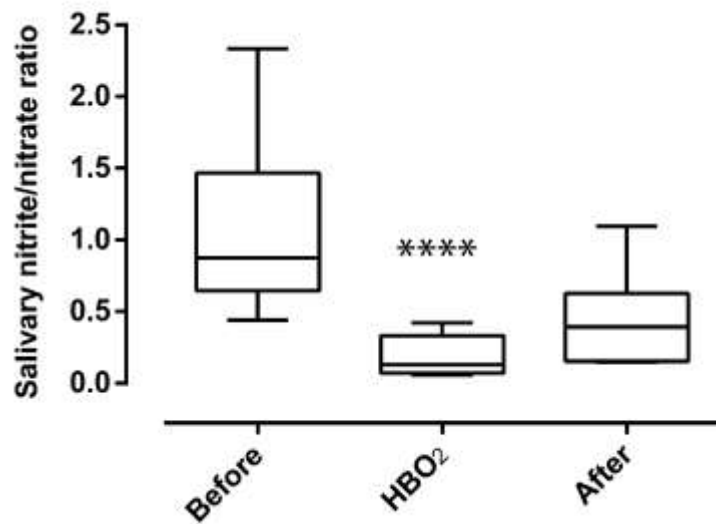


- Nose-mouth

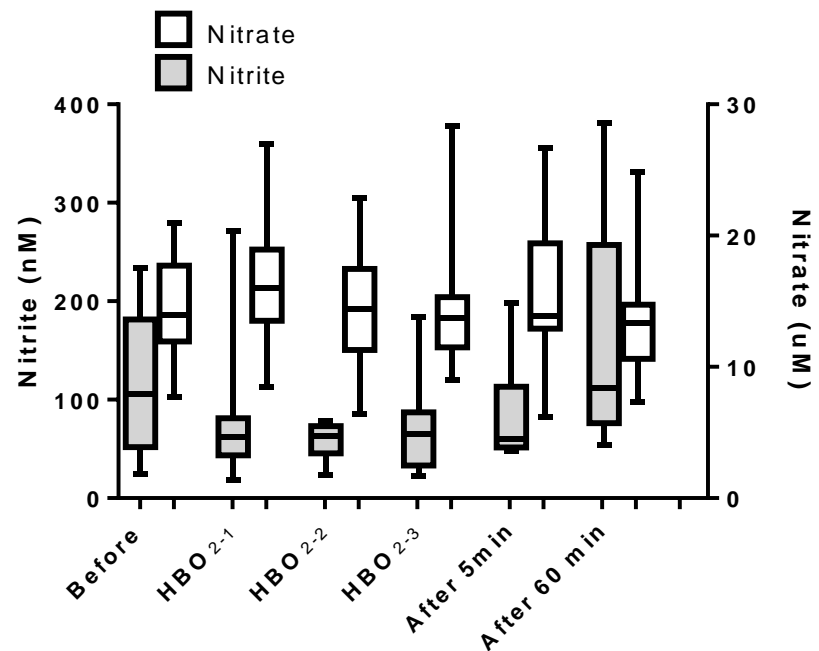


Nitrite and nitrate

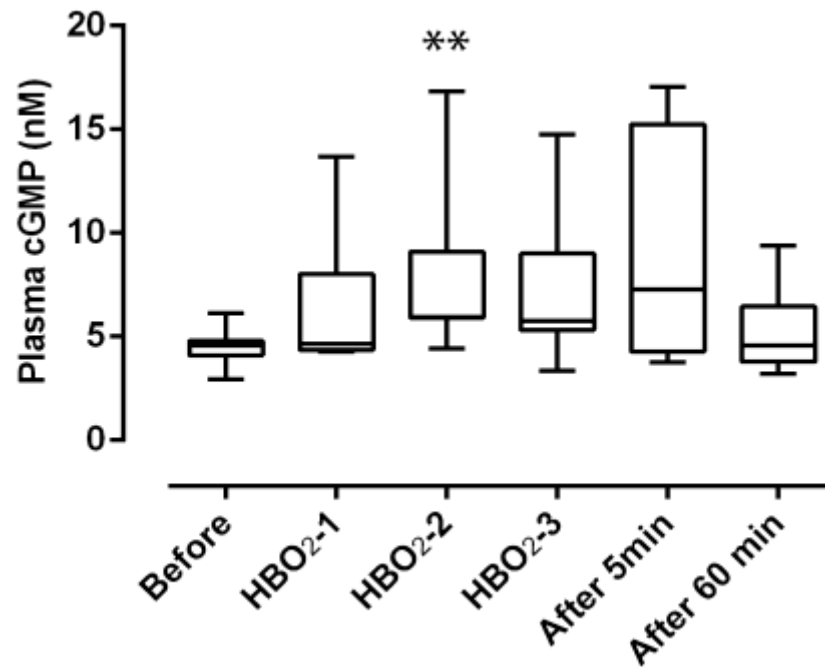
SALIVA



PLASMA



cGMP



cit/arg

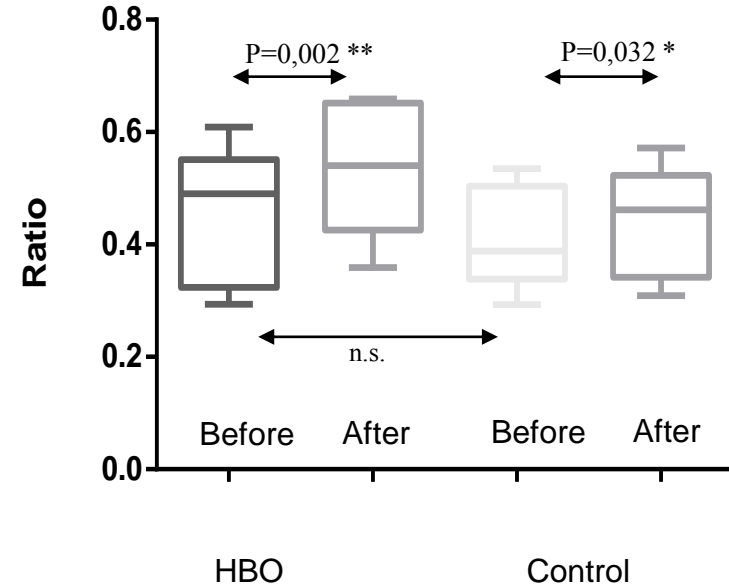
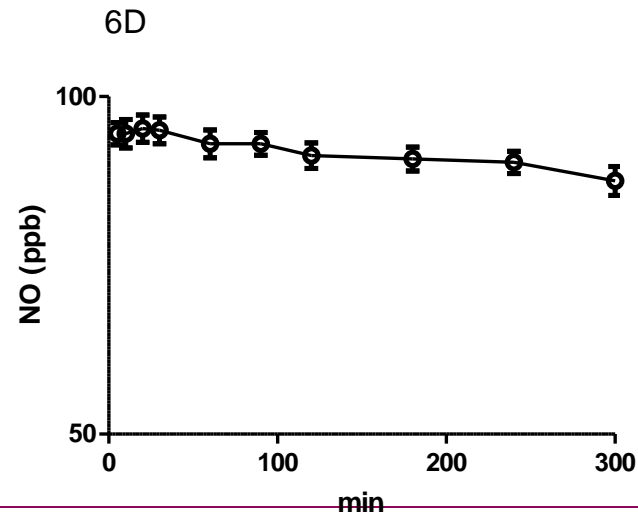
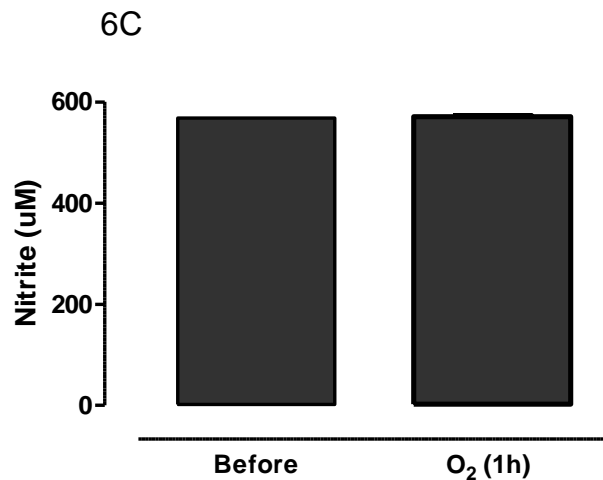
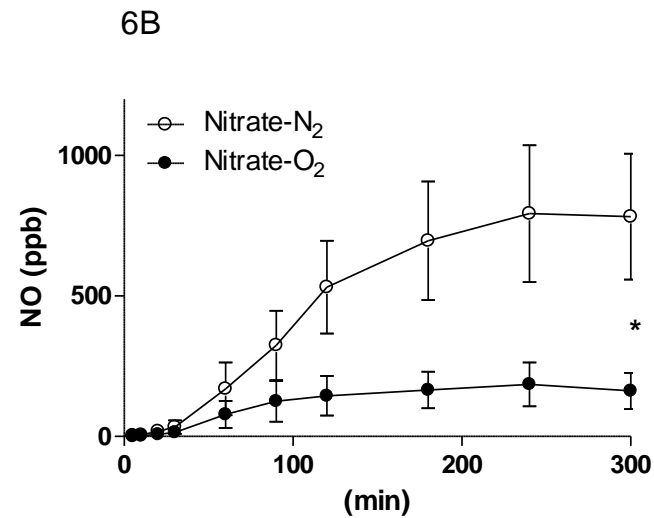
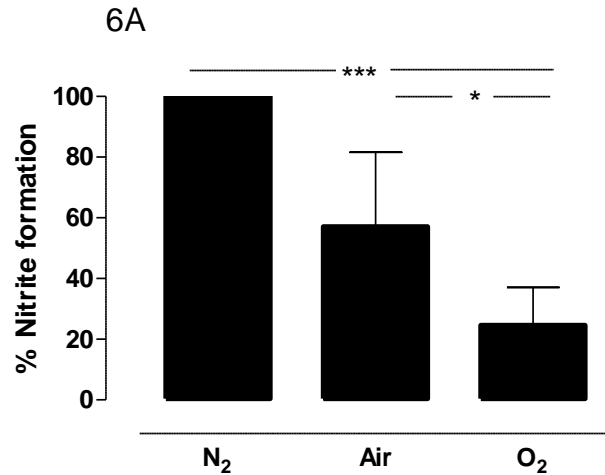


Figure not shown in
manuscript

In vitro experiment at 100 kPa

- Oral tongue scrape samples in a Muller-Hinton medium
- A known concentration on nitrate (NO_3)
 1. Bubbling with O_2 , air or N_2 in sample tubes for 2 minutes, incubated at 37°C → analysis of NO_2 and NO_3
 2. (1) → In a gas-tight bag, atmosphere of O_2 or N_2 , incubation, NO sampling at regular intervals for 300 minutes
 3. Control experiments for NO_2 oxidation and NO oxidation (O_2 -bubbling)

In vitro



Conclusions

Effects in healthy subjects and oral bacteria

- HBO decreased the orally and nasally exhaled NO
- HBO decreased nitrite/nitrate ratio in saliva, indicating an effect locally in the mouth not previously observed.
- Oxygen inhibited oral bacteria- nitrite- and NO-production, *in vitro*
- Exhaled NO decrements during HBO cannot solely be attributed to lung effects

Conclusions cont.

- HBO may inhibit iNOS (nasal NO decrease).
- HBO increased plasma cGMP and cit/arg ratio, indicating an increase in systemic NO-production. The observed plasma-nitrite decrease, however, makes these results difficult to interpret. Future studies including N¹⁵-marked NO₂ and NO₃ could clarify this further.
- A clinical study is warranted for direct tracheal, nasal and intestinal NO-, plasma nitrite/nitrate and cGMP-measurments during HBO.

Thank you!

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**Former Head of Hyperbaric Medicine, Dr Folke Lind
Prof. Claes Frostell**

Methods

- CHEMOLUMINISENSE



- ELECTROCHEMICAL:

