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# Respiratory Abstracts

## METHEMOGLOBIN PRODUCTION IN NORMAL ADULTS INHALING INTERMITTENT HIGH CONCENTRATIONS OF NITRIC OXIDE

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**Background:** Background: In an era of increasing antibiotic resistance there is a need to explore non-specific antimicrobial agents. Nitric oxide (NO) is a gaseous molecule produced endogenously by the innate immune system and is important for clearance of bacteria from the lung. In vitro and in vivo animal studies have shown that this non-specific antimicrobial action of NO can be mimicked with exogenous NO gas (gNO) with minimal toxicity, mutagenic and other aversive sequelae to both animal and human tissues. It has recently been shown that multiple intermittent exposures of 160 ppm gNO for thirty minutes every four hours in rats significantly reduced the bacterial burden in a pneumonia model while adverse effects and complications were avoided. The purpose of this study was to specifically examine the methemoglobin levels of 160 ppm gNO in the healthy adult human.

**Methods:** Ten healthy adult volunteers participated and signed informed consent. Each subject was challenged with a single thirty minute exposure to 160 ppm gNO with a devic that was designed to deliver a consistent dosage with less than 2 ppm nitrogen dioxide regardless of the subject's inspiratory flow, tidal volume and respiratory rate. Inspired nitric oxide (NO), nitrogen dioxide (NO2) and oxygen (O2) concentrations were measured continuously with an electrochemical analyzer. Continuous monitoring of arterial methemoglobin saturation (SpMet), arterial blood oxygen saturation (SpO2) and heart rat was recorded with a noninvasive pulse oximeter. NO kinetics were then monitored for 3.5 hours post treatment. Five of the subjects additionally received five treatments every fou hours over a 20 hour time period.

**Results:** All subjects (n=10) tolerated the treatments without incident during and for two weeks following the study. The average increase in SpMet during any single treatment wa 1.3% (SEM=0.05) with the highest SpMet observed of 2.7 % for any treatment during the study. There was no accumulative SpMet noted after five treatment cycles over a 20 hour period. SpO2 remained above 94% during all phases of the study. The highest NO2 during treatments was 1.38 ppm with an average of 1.23 ppm (SD=0.13).

**Conclusion:** Results suggest that inhalation of 160 ppm for thirty minutes every four hou for five cycles is well tolerated in the healthy adult human. These results, coupled with other studies, justify further exploration of gNO as a potential non-specific antimicrobial agent.