Inhaled Nitrite Therapy May Help Babies Suffering in a Low-Oxygen State

Bethesda, Maryland — Scientists from the National Institutes of Health (NIH) Clinical Center and the Loma Linda University School of Medicine have found that use of an inhaled nitrite spray may help babies diagnosed with persistent pulmonary hypertension of the newborn (PPHN). Premature newborns and those with pneumonia or heart problems often develop PPHN. This often-fatal disease causes high blood pressure in an infant's lungs and places the baby in a low-oxygen state. The collaborative study findings are reported in Nature Medicine (September 12, 2004 online version; October, 2004, print version).

Nitrite, a simple salt in the blood that dilates the blood vessels in the lungs, reacts with de-oxygenated hemoglobin (the respiratory protein of the blood) and is converted to nitric oxide when the human body is in a low-oxygen state. Nitric oxide or NO is a short-lived gas produced by cells lining the blood vessels and has an important role in regulating blood flow. The NIH-Loma Linda research team theorized that the naturally-occurring conversion of nitrite to nitric oxide might help babies with high blood pressure in the lungs. The researchers thought the nitrite conversion mechanism might act to lower the lung blood pressure and thus raise oxygen levels.

The NIH-Loma Linda research team studied the effect of nitrite inhalation in an animal model of PPHN. They compared the administration of NO to the administration of plain nitrite.

"Nitrite inhalation rapidly reduced pulmonary pressures by 65 percent" said Christian Hunter, PhD, a fellow in the NIH Clinical Research Training Program for Medical and Dental Students and fourth-year Loma Linda medical student and lead author of the study. "The nitrite had a much longer effect than the nitric oxide. In one case, we administered the inhaled nitrite for 20 minutes and the high blood pressure levels were reversed for an hour."

Mixing nitrite with plain saline, filling a plastic inhaler and then administering it holds great potential for becoming a much simpler and more economical way to treat newborns, according to principal investigator Mark Gladwin, MD, Critical Care Medicine Department, NIH Clinical Center.

"The current clinical standard for treating these infants is to administer nitric oxide gas every day through a complex delivery system which requires high-level monitoring not available in small community hospitals or developing countries," he said. "This approach costs thousands of dollars a day and the delivery systems themselves run tens of thousands of dollars. Our findings demonstrate this has potential to be done in an easier and more cost-effective manner."

"This research shows that a common agent found in nature can have profound health benefits worldwide," said Dr. John I. Gallin, NIH Clinical Center director. "It emphasizes the importance of persistent, ongoing clinical research to life and health. This is the type of work that will continue and expand when the Clinical Center opens the Mark O. Hatfield Clinical Research Center later this year."

Nitrite is also available for human use as an antidote for cyanide poisoning and is used in meat curing.

Further research is necessary to determine the safety and efficacy of inhaled nitrite for human use. Plans are underway to begin clinical trials by early 2005. Scientists from the National Heart, Lung and Blood Institute, NIH; the National Institute of Diabetes, Digestive and Kidney Diseases, NIH; and the Center for Perinatal Biology and Division of Neonatology, Loma Linda University School of Medicine also participated in this study.