

# Hold the gas? Inhaled nitric oxide of no benefit to most premature babies

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A new Johns Hopkins Children's Center study challenges the widespread practice of treating premature babies with nitric oxide gas to prevent lung problems, neurological damage and death. The research, based on analysis of 22 major studies of the effect of nitric oxide in babies born before 34 weeks of age, found no evidence of benefit in most infants.

Overall, the Hopkins review found that babies who received nitric oxide in the neonatal [intensive care unit](#) didn't fare any better than those who didn't. The babies who received the treatment were no less likely to die, develop chronic lung disease of prematurity, suffer cerebral palsy or have neurological or cognitive impairments, the researchers found.

The findings, to appear in the February issue of the journal *Pediatrics*, point against the routine use of inhaled nitric oxide in all [premature babies](#) and call for careful, case-by-case evaluation of each baby's degree of brain and lung maturation to determine if nitric oxide would help, hurt or do nothing for a patient, the researchers say.

“What we call for is careful evaluation by a team of clinicians of each patient's risk-benefit profile, factoring in birth weight, degree of prematurity and degree of lung and brain maturation,” says lead investigator Pamela Donohue, Sc.D. Because the investigators noticed a small, yet sufficiently intriguing difference in risk in some babies, the researchers stopped short of advocating complete abandonment of the treatment.

Babies who did not receive nitric oxide had no greater risk of dying than those who got the treatment. Untreated babies were also no more likely to develop chronic lung disease of prematurity than those treated with nitric oxide. However, when the researchers analyzed the data differently and looked at whether a baby had a greater risk of either dying or developing lung disease, a small difference emerged. The combined risk of death and lung disease was 7 percent higher among babies who didn't get the treatment.

“We can't say whether this small difference signals a true clinical benefit, but we have to at least allow for the possibility that it might portend better outcomes for at least some babies,” says senior investigator Marilee Allen, M.D., a neonatologist at Hopkins Children's.

The efficacy of nitric oxide has been well documented in near-term babies, or those born after 34 weeks, but the new Hopkins Children's findings show that nitric oxide gas has no therapeutic value in most premature babies born at 34 weeks or earlier.

None of the 14 trials that analyzed the risk of death found differences in death rates between preemies who received nitric oxide and those who didn't. Nine studies compared long-term death rates among children after one year and up to five years after birth. Again, none found a difference in death rates. The dose of nitric oxide had no bearing on how well a baby fared and neither did the baby's weight at the time of birth, the researchers found. One study found a higher death rate among babies born weighing 1,000 grams or more and treated with inhaled nitric oxide.

None of the 12 trails that analyzed the risk for developing chronic lung disease found differences among babies regardless of whether they received nitric oxide after birth or not. Four studies, however, revealed a 25-percent lower risk for lung disease among babies treated with a dose of 10 parts per million (gas-to-air ratio), a difference that vanished with

lower and higher doses.

The analysis showed no differences in the risk of brain damage, neurological deficits, cerebral palsy or developmental impairment between babies who received nitric oxide and those who did not. One of four studies using head ultrasounds to detect brain injury found 4-percent lower risk in babies treated with nitric oxide. The other three studies did not. None of six trials evaluating cognitive development found differences between treated and untreated babies. Seven studies of cerebral palsy risk found no differences, nor did six studies of neurological and developmental impairment of children who received [nitric oxide](#) as babies and those who did not.

The research was conducted in collaboration with the Johns Hopkins Evidence-based Practice Center (EPC), one of 13 federal centers designed to generate, assemble, and synthesize knowledge and evidence necessary for the effective and efficient application of medical and public health practices.

**More information:** [pediatrics.aappublications.org/](https://pediatrics.aappublications.org/)

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