AMERICAN COLLEGE of NURSE-MIDWIVES
With women, for a lifetime®

POSITION STATEMENT

Nitrous Oxide for Labor Analgesia

The American College of Nurse-Midwives (ACNM) maintains the following:

- Women should have access to a variety of measures to assist them in coping with the challenges of labor. Among these should be nitrous oxide (N_2O) analgesia, which is commonly used in many other countries.
- Research has supported the reasonable efficacy, safety, and unique and beneficial qualities of N_2O as an analgesic for labor and its use as a widely accepted component of quality maternity care.
- Certified nurse-midwives and certified midwives should be trained to administer and oversee safe use of N_2O analgesia during labor.
- Women should be educated about the use of N_2O as an option for pain relief in labor.
- Research and evaluation of the use of N_2O analgesia should continue in all obstetric/anesthesia departments to facilitate the inclusion of N_2O as an option for women in labor throughout the United States.

Background

The experience of labor pain differs among women, and the response to pain is highly individual.[1] Women should have access to a variety of approaches to promote comfort and reduce pain throughout labor, but women in the United States have fewer options than those in many other advanced countries.[2]

A blend of inhaled N_2O 50% and oxygen 50% is used for analgesia in labor in many countries with high standards for safe and effective health care, including Australia, Canada, Finland, Sweden, and the United Kingdom.[3,4] However, in recent years this option has not been readily available in the United States.[3] In the United States, epidural administration of local anesthetic agents and systemic (intravenous or intramuscular) administration of opioids (narcotics) are the two most frequently employed pharmacologic methods for labor analgesia.[5]

Nitrous oxide is a less potent analgesic than epidural or other neuraxial anesthesia but may be more effective than systemic opioids,[4] with the exception of intravenously administered, short-acting, very potent, synthetic opioids such as remifentanil.[6] Nitrous oxide works by increasing the release of endogenous opioid polypeptide compounds (endorphins), corticotropins, and dopamine that are produced in the mother's brain.[7] The analgesic efficacy of inhaling a relatively low concentration of N_2O is limited; a few women reported little or no benefit at all.

However, it is effective enough for the majority of women who try it, and most who have used it said they were satisfied.[8]

Nitrous oxide has the following unique attributes:

1. Despite widespread and extensive use of N_2O for labor analgesia in many countries since the early 1900s,[8] no studies or published observations have identified significant adverse effects on the neonate. The need for neonatal resuscitation is not increased, and newborn alertness and responsiveness during the important early period of maternal-infant bonding and early effective breastfeeding are unaffected.[4] It is safe for a woman to use N_2O throughout the entire second stage of labor.[4,8]

2. Nitrous oxide analgesia can be administered quickly, easily, and safely and has a very rapid onset of action.

3. Nitrous oxide analgesia can be discontinued as quickly and easily as it is started. The effects begin to dissipate immediately after the woman stops breathing N_2O and are completely gone within five minutes.

4. Nitrous oxide analgesia has no adverse effects on the progress of labor; the spontaneous vaginal birth rate is unaffected. Administration of N_2O is not associated with increased risk of maternal or fetal complications and does not require more intensive or invasive monitoring.

5. After a brief period of explanation and supervision, N_2O is self-administered through a mask that the woman holds to her own face. Self-administration allows the woman to determine when and how much N_2O she uses.

6. If a woman doesn't like or tires of using N_2O, she can stop using it and begin using another method without residual effects.

Concerns Related to N_2O Analgesia for labor in the United States

A long-standing concern about the use of N_2O analgesia in labor pertains to the reproductive risk to female health workers, including midwives and labor nurses, who work closely with patients who use it.[7] A more recent concern is related to abnormal apoptotic cell "suicide" in brain cells of newborn rodents exposed to very high and long periods of (especially relative to the period of rapid, rodent brain development) exposure to N_2O and a wide class of other neuro-active drugs, including virtually all general anesthetics.[9] The time of susceptibility is the period of neuro-synaptogenesis, which includes the first week of life in rats and the last three months of gestation and first three years of post-natal life in immature humans. These two concerns affect completely different pathogenic pathways. Because of the seriousness of these concerns, some of the most important findings and conclusions from the Sanders et al. review are summarized below.[9]

> Inactivation of methionine synthase causes few cases of illness but underlies the concern about occupational risk from repeated exposures to N_2O. Most of the few

health problems that have been attributed to N_2O, including occupational health risks, are due to inactivation of an enzyme that is necessary for normal cell function and cannot be produced in the absence of vitamin B12. Decreased methionine synthase can result in genetic and protein aberrations that result in very few cases of disease but may result in reproductive failure due to repetitious (usually employment-based) exposures to N_2O. Persons with hereditary vitamin B12 deficiency disorder, pernicious anemia, Crohn's disease, ileal disease, or chronic malnutrition due to alcoholism are at increased risk. In addition, pregnant women who adhere to a strict completely vegan diet are at risk as are many elderly persons, up to 20% of whom are deficient in vitamin B.

The only other groups at high risk for acute pathology from exposure to N_2O are long-term recreational N_2O drug abusers and surgical patients who receive high doses of N_2O *anesthesia*—not analgesia—for 6 hours or more. Exposure to anesthetic concentrations continuously for more than 3-6-hours may cause biochemical changes, but clinical effects have not been shown in healthy people without reduced vitamin B12/folate stores when exposed for less than 12 continuous hours. Given the frequent use of high concentrations of N_2O during surgery and the scarcity of disease caused by methionine synthase deficiency, this is not a significant problem. In any case, the problem can be solved by treating high-risk individuals with vitamins.

Occupational risks are related to subfecundability and increased incidence of spontaneous abortions, presumably caused by inactivation of methionine synthase due to exposure to N_2O. Dose—the concentration inhaled and the duration of exposure—is always important. Cumulative body burden, which is increased by repetitive exposures and reduced by *restitution*, is also a consideration. Cellular-level damage can begin during a midwife's or labor nurse's shift in a poorly ventilated hospital where N_2O is used without scavenging. Scavenging equipment uses suction to eliminate contaminated exhalations of patients using N_2O from the immediate environment, eg, the labor or operating room. However, the damage-producing process, stops or pauses, occur when the midwife leaves the hospital's contaminated environment. While away from the hospital, the body begins to repair any cellular-level damage. Our survival depends on the ability of our body to heal. Healing the damage that has not yet reached a point of actual pathology is restitution. However, if a midwife returns to work in a N_2O polluted environment before restitution is complete, the damage-producing process can accumulate, and restitution will be incomplete. Over time, the damage may produce noticeable effects in the form of subfecundability or an increased incidence of spontaneous abortions.

Subfecundability in the form of maternal absorption of malformed conceptions has been found in animal studies of the reproductive effects of exposure to N_2O. However, these studies used very prolonged exposures to very high doses of N_2O, limiting applicability to the clinical setting. The results of 1 study indicated that dental assistants working in settings that did not use scavenging of exhaled N_2O took longer on average to conceive. The researchers estimated that the ambient air in which they worked was contaminated by greater than 1,000 parts per million (ppm) of N_2O.[9] Nitrous oxide-

induced fertility problems occur in rats at 1,000 ppm but not at 500 ppm or less, and rats are known to be particularly sensitive to damage from N_2O.

Current standards in the United States for management of waste anesthetic gases call for limiting occupational exposure to N_2O to not more than an 8-hour time-weighted average (TWA) concentration of 25 ppm. In the United Kingdom, Finland, Germany, and Sweden, 100 ppm is the upper limit. The standard of 25 ppm in the United States was set arbitrarily during the 1970s without benefit of actual data. Nevertheless, the American Society of Anesthesiologists (ASA), the National Institute of Occupational Safety and Health (NIOSH) and the US Occupational Safety and Health Administration (OSHA) all believe that this standard has been effective in protecting American health workers. Concerns about reproductive toxicity from occupational exposure to N_2O at levels less than the 25 ppm standard are not supported by the available data, and these data do not include findings from prospective studies.

Apoptotic loss of neurons in the brains of newborn rodents exposed to N_2O creates concern about exposure of fetuses and young children. Additionally, apoptotic neuronal death or, as shown in some studies, seemingly severe but *reversible* neuronal damage in the brains of newborn rodents, mainly rats, occur after exposure to very high concentrations of N_2O. In some studies, hyperbaric chambers were used to force more N_2O into the rats' blood than would be possible at normal atmospheric pressures. Results from studies using 5-day old rhesus monkeys suggest that the rat studies "may be of less clinical importance than initially feared." The greatest concerns related to these findings have come from pediatricians and anesthesiologists worried about the large numbers of newborns and other very young children who require long surgeries, often to repair congenital heart and other major structural defects. Although there are other anesthetics, use of N_2O facilitates more rapid induction and emergence from anesthesia in children and adults. Sanders et al. found no evidence of apoptosis in neonatal rat brains from exposure to N_2O concentrations less than 75%.

While N_2O is not without side effects and will not be agreeable to or effective for every woman in labor, it is an inexpensive, simple, reasonably safe, and effective analgesic. It is important that midwives know about N_2O analgesia and be able to offer it to women during labor.

REFERENCES

1. Lowe, NK. The nature of labor pain. *Am J Obstet Gynecol*. 2002;186(5):S16–S24.
2. Marmor TR, Krol DM. Labor pain management in the United States: Understanding patterns and the issue of choice. *Am J Obstet Gynecol*. 2002;186:S173-S180.
3. Rooks JP. Nitrous oxide for pain in labor – why not in the United States? *Birth*. 2007;34:3-5.
4. Rosen MA. Nitrous oxide for relief of labor pain: A systematic review. *Am J Obstet Gynecol*. 2002;186:S110-S126

5. Declercq ER, Sakala C, Corry MP, et al. *Listening to Mothers LL: Report of the Second National U.S. Survey of Women's Childbearing Experiences*. New York, NY: Childbirth Connection; 2006.
6. Volmanen P, Akural E, Raudaskoski T, et al. Comparison of remifentanil and nitrous oxide in labour analgesia. *Acta Anaesthesiol Scand*. 2005;49(4):453-458.
7. Hawkins, LF, Chestnut DH, Gibbs CP. Obstetric anesthesia. In: Gabbe SG, Niebyl JR, Simpson JL, eds. *Obstetrics: Normal and Problem Pregnancies*. 4th ed. New York, NY: Churchill Livingstone; 2002.
8. Rooks J. Use of nitrous oxide in midwifery practice—complementary, synergistic, and needed in the United States. *J Midwifery Womens Health*. 2007;52(3):186-189
9. Sanders RD, Weimann J, Maze M. Biologic effects of nitrous oxide: a mechanistic and toxicologic review. *Anesthesiol*. 2008;109(4):707-722.

Source: Division of Standards and Practice
Approved: ACNM Board of Directors December, 2009
Reviewed: August 2011