Nitrous oxide - no laughing matter

by Andrea Robertson

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Nitrous oxide (often called 'laughing gas'), in combination with oxygen (50% of each gas), has been in use for two centuries as a simple anaesthetic agent, and in obstetric care since the 1930s. It is the most popular form of anaesthesia in UK labour wards, where it is available in 99% of consultant units (Chamberlain et al, 1993), as well as in birth centres and for home births.

In the UK, the most common proprietory brand is called Entonox which is supplied by the British Oxygen company (BOC) although there is another product suppled by Linde Gas (trade name Equanox). Although the standard mixture of 50% of each gas is supplied through fixed, wall-mounted machines In the majority of modern and purpose built maternity units in the UK, some facilities exist that enables a flexible mixture of gases to be selected, from a mix of 30 per cent nitrous oxide and 70 per cent oxygen to 70 per cent nitrous oxide and 30 per cent oxygen. Portable machines, more often used in birth centres or for home births use the standard 50/50 per cent combination of gases.

Nitrous oxide is often referred to by midwives, especially when talking to women about it, as 'gas and air'. This is an erroneous description as it fails to recognise the concentration of both the oxygen or to actually describe the element of gas that is the Nitrogen. By using this description the substance would appear to be regarded as a simple, relatively non-invasive and innocuous alternative to heavier drugs with their associated known side-effects for the mother and baby. Many pregnant women regard nitrous oxide (or simply "the gas") as a safe alternative to pethidine and have come to rely on it to ease pain in the harder parts of labour. For some, using nitrous oxide is regarded as the same as having no drugs in labour, because of its promotion as safe and its long history of use.

The use of nitrous oxide in maternity care is virtually unknown in the USA and most of Europe. Nitrous oxide is used in the USA and most western countries as an anaesthetic in dentistry and also in accident and emergency departments when a readily available anaesthetic is needed for minor procedures.

How are safe levels of exposure determined?

Given the concern for the health and safety aspects of exposure to anaesthetic gases for health workers, an occupational exposure standard (OES) for each gas has been established. "An OES represents airborne concentrations averaged over a specified time period which, according to available scientific knowledge, will not damage the health of workers exposed to those levels by inhalation day after day" (Meldrum 1999). The process for establishing an OES involves research reviews, independent evaluation and careful analysis of available data.

The Health and Safety Commission has an independent committee of experts in occupational health known as the Working Group on the Assessment of Toxic Chemicals (WATCH). Their task is to evaluate the review of the toxicological and occupational exposure data on anaesthetic gases compiled by the Health and Safety Executive (HSE). When such an assessment was applied to Nitrous oxide, factors were identified that led to the conclusion that there was a safety time limit that should be applied to its exposure . "'WATCH' concluded that the toxicological mechanism was the inhibition of enzyme vitamin B12 methionine synthetase leading to impairment of folate metabolism and DNA synthesis. They also concluded that the critical No-observed Adverse Effect Level(NOAEL) for developmental toxicity in rats was 500ppm. Applying a factor of five to this NOAEL to allow for the uncertainty in extrapolating from animals to humans, and taking into account the exposure concentrations at which effects on DNA synthesis had been seen in humans, WATCH recommended an Occupational Exposure Standard (OES) of 100ppm(as an eight-hour time weighed average) for nitrous oxide.

The Committee on Toxicology (COT) was also consulted by the Health and Safety Commission and agreed with the findings of WATCH. The COT also considered the results of studies in humans occupationally exposed to nitrous oxide for prolonged periods of time. Their conclusion was that while the available human studies had limitations, the data tended to reinforce the concerns which arise because of the effects seen in animals (Meldrum 1999).

The Health and Safety Commission's Advisory Committee on Toxic Substances (ACTS) has also investigated the effects of anaesthetic gases on employees. They concluded "that there may be a risk to health from repeated exposure to persistently high levels of anaesthetic agents, but levels could be identified at which there is no risk to health". Consequently ACTS recommended that Occupational Exposure Standards were necessary to protect the health of those regularly exposed (Health Services Advisory Committee 1995).

As a result of these investigations, the OES for nitrous oxide in the UK came into effect in January 1996. This advises that exposure should be limited to 100 parts per million (ppm) in an eight hour time weighed analysis (TWA) in any 24 hour period. The basis for the establishment of the limit was considered to "be the inactivation of vitamin B12 and developmental toxicity of the fetus, effects which may be inter-related"(Health and Safety Executive 2001).

Other countries have established different levels; for example, the USA sets a limit of 50ppm (Occupational Safety and Health Administration US Department of Labor), whereas in Australia the limit is 25ppm

(Australian Government National Occupational Health and Safety Commission, 1995).

In April 2005, the definition of occupational exposure standard/level was replaced with the definition of workplace exposure limit (WEL). The WEL identifies the average level of the maximum concentration of an airborne substance within the reference time period, and applies this to the potential exposure inhalation time for employees working within this environment.

Potential health implications

It is concerning that, considering the widespread use of nitrous oxide and subsequent exposure for health care workers in the maternity services, that research on these effect has been so limited. This is particularly so when compared with studies and information undertaken for other health care workers, for example; in anaesthetics and dentistry

Nitrous oxide has been shown to inactivate the part of vitamin B12 that synthesises folate, methionine and thiamin, all of which are involved in normal cell division and DNA production. There is concern that this effect may be the underlying cause of increased level of morbidity in health workers exposed to nitrous oxide

Such morbidity includes higher rates of miscarriage, myeloneuropathy and infertility for female workers (Rowland et al 1992, Ahlborg et al 1996)). Rowland et al (1992) found an "association between occupational exposure to high levels of unscavenged nitrous oxide and reduced fertility in female dental assistants", and a longer mean time to conception among women who worked with unscavenged nitrous oxide for five or more hours per week.

The study of Swedish midwives undertaken by Ahlborg et al (1996) demonstrated that shift work (two-shift or three-shift rotas or only nights) and frequent, high occupational exposure to nitrous oxide may have a negative effect on the ability of women to become pregnant. They report that "the Swedish eight hour time weighed average exposure is mostly very low for midwives owing to the rather infrequent, and short (usually about 30 minutes and rarely more than two hours for each delivery). Greater than 30 deliveries where nitrous oxide was used may well correspond to equal or greater than five hours of nitrous oxide exposure per week", a level they considered to be high enough to affect fertility.

While Ahlborg et al (1996) suggest no correlation between the occupational exposure of midwives to nitrous oxide and spontaneous miscarriage, they note that the exposure levels in most cases for Swedish midwives is very low due to typical usage patterns.

For the pregnant midwife, working in a labour ward, there are additional concerns. Referring back to the revised WEL, where the reference point for exposure is over a defined period of time, this could have implications for midwives who are working long shifts, or who have consecutive shifts in a 24 hours period (a late to an early shift) or where they are in a hazardous environment from the viewpoint of ventilation, attending a home birth.

Bodin (1999) found an association between exposure of pregnant midwives to nitrous oxide and an association with reduced birth weight and an increase in the odds of their baby being small for gestational age. Others (Crawford 1986, Aldridge 1986) suggested that there are few risks, however their work reported on very short exposures to anaesthetics of pregnant women undergoing short operations, such as cervical cerclage, rather than on- going occupational exposure during pregnancy.

Schumann (1990) recommends that given the known hazards of this gas, women in their first trimester of pregnancy, women using IVF, those with known neurological complaints and personnel with severely compromised immune systems should all avoid exposure. She points out that "the lipid solubility of the gas, the trace accumulations over time and the relatively slow elimination from the body, makes the burden of short term repeated exposure greater than for a single exposure".

MacArthur et al (1991) reported a relationship between the nitrous oxide inhalation analgesia and fatigue in postnatal women. They suggested that there is pharmacological evidence that nitrous oxide interferes with vitamin B12 metabolism and the fatigue experienced by these women postnatally exhibited a delayed onset and eventual resolution as would be expected. They noted that the toxicological effect with regard to pregnancy is based upon studies done in rats but suggests that the possibility that the intermittent exposure to inhalation analgesia in labour could produce such a delayed and prolonged effect in women, needs to be answered. One aspect of this finding would be how much nitrous oxide women in labour and their attendants are being exposed to particularly where labour suites do not have adequate ventilation and/or scavenging, .

There may also be exposure implications for the men who attend a woman during labour. Research in the 1960s (Watson 1962, Blair et al 1969, Brodsky 1984) showed that there was a link between low levels of vitamin B12 and sperm with morphologic abnormalities, suggesting reduced fertility in men. This will be a greater problem for male midwives, anaesthetists and doctors who work in maternity units especially in areas where waste gases are not effectively scavenged. In addition, the wellbeing of the expectant father should not be overlooked.

Assessing the risks

The limited research evidence of the effects of nitrous oxide exposure when its use is so widespread and the recent WATCH recommendation makes it now a possibility that an employer who allowed their employees to be exposed to levels above the OES for nitrous oxide would be liable to prosecution under the Health and Safety at Work Act 1974 (Quilliam 2000). Under the Control of Substances Hazardous to Health Regulations (2002), which first came into effect in 1988, a risk assessment for exposure to anaesthetic gases including nitrous oxide has to be carried out. This is to enable identification of the hazardous substances present within the workplace and to consider the risks these substances present to health. A risk assessment is required for all employees and should include any specific risks to women of childbearing age who could become pregnant and any risks to new and expectant mothers.

Within the COSHH regulations employers are required to ensure their employees are provided with suitable information, instructions and training about:

- The nature of substances they work with or are exposed to,
- the risks created by exposure to those substances, and
- the precautions they should take.

Employees should also receive sufficient information and instructions on:

- Control measures, their purpose and how to use them,
- results of any exposure monitoring and health surveillance (without giving people's names), and
- emergency procedures.

It is extremely important to ensure that employees understand the risks from exposure to hazardous substances. In addition, control measures will not be fully effective if employees do not know how to use them properly or the importance of reporting faults. (Health and Safety Executive 2003)

Nitrous oxide and oxygen mixes are supplied through equipment with a demand valve that is opened when the user inhales via a mask or mouthpiece. This system is designed to prevent a constant stream of nitrous oxide entering the ambient air. This type of dispenser can be fitted with a scavenger device to reduce the amount of nitrous oxide escaping into the surrounding air and portable devices, suitable for domiciliary applications are also available.

Both those working with nitrous oxide and those responsible for providing a safe working environments should be aware of the implications of and safety measures required for any substance they use or are in contact with. This would involve knowledge of the type of ventilation and filtration that operates in the maternity unit and to ensure that it is performing adequately. Staff should be appropriately trained in the effective use of scavenger units and any other control measures that have been installed. COSHH regulations also require that scavenging equipment and ventilation units must be serviced at least every 14 months.

Effective ventilation and/or scavenging systems should reduce waste gases in the ambient air of treatment rooms to acceptable levels. The hospital building note for the ventilation of labour rooms requires six to seven changes of air per hour, whereas theatre recovery rooms are required to have 15 changes of air per hour (Health Services Advisory Committee 1995).

Working practices, type of mask, scavenging equipment and room ventilation have previously been shown to influence the nitrous oxide exposure of midwives (Ahlborg 1996). Several studies have shown that midwives have been regularly exposed to levels of nitrous oxide that are often much higher than permitted when their working environments have not been properly ventilated (Munley et al 1986, Newton 1992, Mills et al 1996, Newton et al 1999, Henderson et al 2003).

Pascoe (2003) highlights that "it is possible that the OES (for nitrous oxide) could be exceeded in many healthcare settings if control systems are not adequate. Employers should assess the risk and equipment, and procedures should be put in place to address it. Nitrous oxide levels should be monitored regularly and

periodic auditing of procedures should be undertaken." These risk assessments should be undertaken wherever midwifery care is being provided, to include antenatal wards and home births as the same regulations apply in all settings.

Midwives' working environments

Nitrous oxide is heavier than air and does not disperse uniformly but collects in clouds or 'hot spots', usually at floor level, especially in still air (Piziali et al, 1976). Movement in the room may stir up this layer and these gases can also flow through doorways into surrounding areas - high levels of nitrous oxide have been measured even in those areas of the labour ward where nitrous oxide was not in use (Mills et al, 1996). This nitrous oxide-laden air could then spread throughout other areas in the vicinity of the labour ward, increasing exposure risk for midwives who are not directly involved with labouring women, unless the area is effectively ventilated.

Midwives often work for extended periods in labour wards, sometimes for months at a time, or permanently, in the case of senior staff. In addition, during any given shift, midwifery practice standards require midwives to remain with labouring women as much as possible. Periodically, a midwife may also be required to care for other women during a shift, as a second midwife, or to leave the labour ward and attend women labouring in the community either during that shift or later if on call. In this way, midwives may be exposed to many hours of nitrous oxide laden air, in rooms with the doors closed to ensure privacy for the labouring woman. During labour, midwives, doctors and partners can all find themselves exposed to a cloud of nitrous oxide both around the labouring woman, unless the maternity unit has an effective ventilation and/or scavenging system in place (Newton et al, 1999).

How is exposure measured?

It is clear that regular testing is necessary to ensure that midwives are not being exposed to unsafe levels of nitrous oxide, especially when there are any changes in working practices. As long ago as 1990 (Schumann 1990) attention had been drawn to the particular hazards for personnel including obstetric nurses and midwives of their exposure to nitrous oxide and suggested that health personnel participate in control of their own exposure.

To determine individual exposure levels, most researchers have used personal exposure diffusers, which passively absorb nitrous oxide from the surrounding air. These are worn in a pocket, as close to the mouth as possible, and then analysed to produce an eight-hour TWA exposure of the wearer to nitrous oxide (or other gas). This type of monitoring will reflect the personal exposure to nitrous oxide rather than the level in the ambient air. This is important, because as Mills et al (1996) noted, "the actual ambient exposure recorded did not correlate strongly with the exact times that Entonox was in use". The possibility that the rooms may have been contaminated by nitrous oxide use prior to the shift in question, the variation in proximity of the midwife to the expiratory outlets of the demand valve and the variable amounts of ventilation in each room are suggested as reasons for the low correlations.

Henderson et al (2002) recommend that a combination of a personal diffuser (to measure ambient exposure)

and regular measurement of exhaled breath (to check levels of nitrous oxide in tidal air from the lungs) is necessary to ensure that midwives are not being exposed to unacceptably high levels of nitrous oxide in their workplaces. Henderson et al (2003) demonstrated that individual midwives had differing uptake patterns for nitrous oxide. Their survey revealed that midwives in general had high levels of exposure to nitrous oxide and they have highlighted the need for greater engineering controls in order to ensure that midwives' daily exposure to nitrous oxide is below the occupational standard.

Although Henderson et al (2003), Newton et al (1999) and Mills et al (1996) reported inadequate ventilation and no access to scavenging systems for nitrous oxide in their studies (and some more modern maternity units may now have suitable equipment installed) these studies demonstrate the need for universal control of occupational exposure to nitrous oxide. No midwife anywhere should be exposed to levels above the exposure standard for the country that she/he is working in.

It is also clear that further research is needed into the biological mechanisms used by the body to eliminate nitrous oxide, and into ways of effectively measuring individual exposure levels.

What do the manufacturers advise?

The BOC Medical Reference Guide (2001), in a section dealing with the effects of exposure to nitrous oxide, mentions the inhibition of vitamin B12 and further states that if exposure to nitrous oxide is greater than six hours (therapeutic dose), it can also interfere with folate metabolism and DNA synthesis, impairing bone marrow function. Linde Gas LLC USA (1998) also comment on this in their safety data sheet .

Of particular importance is the advice about the transport of nitrous oxide. When transporting gases, staff should be appropriately trained in safe transport of medical gases and follow the manufacturers instructions set out in their safety data sheets. This is especially important if the gas is to be used for a home birth. It would also be wise to check that the car insurance includes the carriage of medical gases

How midwives can reduce risk

Midwives working with nitrous oxide should explore their level of exposure to nitrous oxide and ask managers to investigate the measures in place to reduce the risks to health. Steps midwives can take are described in Box 1

BOX 1
Steps midwives can take to reduce risk of over exposure to nitrous oxide.

- Educating themselves about health and safety regulations, in particular COSHH. Information is available at www.hse.gov.uk. There is also a useful chapter in the book Legal Aspects of Midwifery by Bridgit Dimond (2002).

- Seeking details about testing that has been done within their unit and checking that the results show levels of nitrous oxide are within the prescribed OES.

- Requesting that the levels of nitrous oxide in units and surrounding areas be tested to ensure that exposure is within the prescribed OES. The testing should take into account worst case scenarios by accounting for clients using nitrous oxide for a prolonged period of time as some women may use it for longer than others.

- Checking the ventilation systems used in the unit and common areas. Checking that scavenger units are installed in the labour rooms. This equipment should be tested for effectiveness every 14 months and staff trained in its use.

- Obtaining and wearing a personal exposure meter, attached in the collar area or top pocket of your uniform. Wearing a personal exposure meter will reflect the personal exposure level rather than the concentration in the environment/ambient air.

- If planning to get pregnant, midwives should advise their manager, and ask to see the COSHH assessment (and/or operational policy for the use of nitrous oxide) for the unit to determine if it is safe to continue working there. It might be advisable to work in other areas for a while before getting pregnant, to avoid risks to fertility and to be sure that levels of vitamin B12 and folate are normal before conceiving.

- Educating themselves about the regulations specific to new and expectant mothers. Information is available at www.hse.gov.uk/pubns/indg373.pdf

- Checking blood levels of vitamin B12 at regular intervals to be sure they are not dangerously low.

- For the sake of everyone's health in the maternity unit, midwives may want to look at other ways of helping women through labour without the use of nitrous oxide.

- Midwives involved with home births may be wise to restrict the use of nitrous oxide in the home, unless their equipment includes a portable scavenger unit. While there may be minimal risk to the woman from exposure to nitrous oxide for a relatively short time, a midwife who also works in a hospital setting may already have a level of personal exposure to nitrous oxide.

The labouring woman and her baby

There is scant information about the effects of nitrous oxide on the health of the labouring woman and her baby. It has been assumed that her much more limited exposure to this gas makes it safe for her and her unborn child.

However, since it has been shown that maternity units and labour rooms in particular often have high ambient levels of nitrous oxide present, it is clear that labouring women may also be exposed to nitrous oxide for long periods, especially if the labour is long and drawn out. In a busy unit, where labour rooms are in almost constant use, the level of nitrous oxide in the ambient air could be quite high. How this may affect labouring women has not been studied. Heath et al (1994) suggested that in order to reduce the degree of pollution in the delivery suite, the use of nitrous oxide and oxygen should be restricted to the late first stage and second stage of labour. However, any use should be only in areas where effective ventilation and/or scavenging equipment, as recommended by the manufacturers, is in place so that compliance with the occupational exposure limit can be assured.

At this time, no research has been done to determine the effects of exposure to nitrous oxide during labour and birth on newborn babies. Again, a lack of evidence does not necessarily indicate that there are no effects. Jacobsen et al (1988) in Sweden investigated the reasons for teenage addiction to amphetamines; they found a strong correlation between the exposure of an unborn baby to nitrous oxide during labour and a five-fold increased risk of that child developing an addiction to amphetamines in later life. The degree of risk was associated with the length of exposure to the gas during birth. Although some may view this research as contentious, it raises important questions that need answering and in the meantime, a cautious approach to the impact of nitrous oxide on women and babies would seem prudent.

Conclusion

The safe use of nitrous oxide is an important issue for midwives, labouring women and unborn babies. The potential health effects of over exposure to this gas are well known and have been outlined by both the manufacturers and the various Government Committees that have reviewed its use. Midwives frequently have different working conditions from anaesthetists and other allied health workers whose workplaces have active ventilation and where the equipment used for dispensing anaesthetic gases has the required scavenger units in place.

Until safe workplaces can be provided to all midwives, and the regular testing procedures are in place to check individual exposure levels and ambient working environments, it seems prudent for midwives (and labouring women) to avoid over-exposure to nitrous oxide. One approach to this would be to reduce its use in labour, limiting its use to short periods in the transitional phase of labour and finding alternative, less invasive ways of easing labour pain. Although at first sight such suggestions might seem controversial, when considering the information presented in this paper and the perhaps the neglected skills of midwifery with regard to pain relief, these would seem both sensible, and overdue. As Quillam (2000) states: "it is shocking that most midwives working with nitrous oxide will have no awareness of its possible risk to

themselves and that most NHS Trusts will have done nothing to address the issue". Perhaps now is the time then.

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