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Nitrous Oxide and Oxygen Mixture (Entonox®), and Acute Procedural Pain

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Abstract

We describe the introduction of a nitrous oxide and oxygen mixture (Entonox) policy into paediatric practice by the Acute Pain Team, its aim being to improve the management of acute paediatric procedural pain. We report the implementation of this policy and an audit of the first 108 administrations.

Key words: Nitrous oxide – Entonox – Analgesia – Audit – Self-administration

Introduction

Nitrous oxide was the first inhalational agent discovered to have anaesthetic properties. Known as 'laughing gas', it was used extensively in the latter part of the nineteenth century, but was soon superseded by ether as an anaesthetic agent.

Nitrous oxide is a weak anaesthetic agent, which has sedative, analgesic and anxiolytic properties. Because it is a weak anaesthetic agent, when it is mixed with 50% oxygen, it rarely produces loss of consciousness. However, nitrous oxide possesses profound analgesic effects. An inhaled concentration of 25% nitrous oxide and oxygen has been compared favourably with a standard dose of morphine for the relief of postoperative pain after upper abdominal surgery in adults[1].

Entonox, the gaseous mixture of 50% nitrous oxide in oxygen, was introduced commercially in 1965, and is still extensively used as an analgesic agent by the ambulance service, the dental profession and, of course, during labour. Apart from its common intermittent administration to the fetus via the placenta during the birth process, nitrous oxide has to date found a limited place in paediatric practice.

With the upsurge of interest in acute paediatric pain over the last 10 years and the establishment of paediatric acute pain teams, there has been a re-examination of the potential role of this agent with its unusual route of administration and unique pharmacokinetics in paediatric practice.

Other published reviews describing the use of Entonox in paediatric practice have concentrated on the need for the presence of dedicated anaesthetic personnel to administer the gas, particularly when using continuous flow apparatus. Such apparatus is necessary in smaller children because of their inability to operate the demand valve of the self-administration apparatus. Techniques using varying concentrations of nitrous oxide have emphasised the need for the additional application of monitoring devices[2].

In this article we describe the introduction into our hospital of a nurse-led, nurse-initiated, nurse-administered nitrous oxide policy, and describe an audit of the first 108 administrations.

Pharmacology

Entonox is the trade name for a compressed gas mixture containing 50% oxygen and 50% nitrous oxide. The gas is contained in blue cylinders with blue and white quartered shoulders, at a pressure of 13 700 kPa.

At temperatures below –7°C, liquefaction and separation of the individual components in the cylinder can occur. This may lead to the delivery of an uneven mixture: too much oxygen at the beginning and then an excess of nitrous oxide at the end of the cylinder life. It is therefore possible that a hypoxic mixture, i.e. a gaseous mixture containing less than 21% oxygen, could eventually be delivered from such a cylinder.

If an Entonox cylinder has been exposed to low temperatures, the cylinder should be stored horizontally at a temperature > 5°C for 24 hours and the cylinder inverted several times in order to allow remixing.

Nitrous oxide is a weak anaesthetic but a strong analgesic. The explanation for this analgesic effect is obscure, but may involve action at opioid receptors, since analgesia is partially antagonised by naloxone[1,3]. However, a concentration of 50%, in the absence of other CNS depressants, rarely produces loss of consciousness.

Inhalation produces the rapid onset (within 2–3 breaths) of analgesia because of the low blood:gas solubility coefficient. Onset time is proportional to the depth of respiration. Because nitrous oxide is not metabolised, and completely eliminated by exhalation, the offset of its action is also rapid. Consequently, it is non-cumulative. Inhalation of Entonox can produce nausea and vomiting, drowsiness, dysphoria, amnesia and mild cardiovascular depression.

Prolonged administration, i.e. for more than 8 hours, can affect vitamin B_{12} synthesis by inhibiting methionine synthetase, and can also interfere with folic acid metabolism and the synthesis of DNA and proteins. Megaloblastic anaemia may result. Bone marrow aplasia can occur following prolonged administration.

During nitrous oxide administration, the gas diffuses into air-containing spaces in the body. Because it is 34 times more soluble than nitrogen, it diffuses into cavities more rapidly than nitrogen diffuses out. This causes an increase in the volume of the space and therefore an increase in any pressure effect of that gas-filled cavity. Consequently, its administration is particularly hazardous in the presence of pneumothorax, pulmonary bullae, bowel distension, or during middle ear surgery[4].

Apparatus

Entonox is usually self-administered. The cylinder is connected to either a mouth piece or a mask (Figure 1) via a length of high-pressure hose and a demand valve (Figure 2).

The demand valve opens when a small negative pressure (–2 cm to –4 cm H_2O) has been generated by the patient's respiratory effort. In order to create this negative pressure the mask needs to be applied tightly to the face. If a mouthpiece is used, inhalation must only occur through the mouth and not through the nose. Nitrous oxide is exhaled via the expiratory port of the demand valve. Thus gas flow is intermittent. The resistance to inspiration provided by the valve limits the use of the apparatus to children of approximately five years of age and over (20 kg and above). It is possible to administer nitrous oxide to smaller children via an anaesthetic 'T'-piece circuit through which gas flow is continuous. However, this does not constitute self-administration, and requires the presence of an anaesthetist.

It is a safety feature of self-administration that, should the patient become drowsy, the mask will then fall away from the face, so terminating the inhalation of Entonox.

Introduction of Nurse-led Administration of Entonox into Paediatric Wards – Derbyshire Children's Hospital

Having assessed the potential for the use of Entonox in our practice, the Acute Pain Service drafted a policy document in 1998, which was subsequently ratified by the hospital Drugs and Therapeutics Committee (Appendix 1).

This document described the indications and contra-indications to Entonox (Table 1), instructions for its administration, prescription via the standing order process and also a section giving advice on practical matters.

Our expectations were that nurses would make the clinical decision that Entonox was indicated, prescribe the drug and initiate the procedure without any medical involvement unless problems occurred.

Mindful of the fact that nurse administration was desired, we were particularly careful to stress that no other sedative drugs should be administered concurrently with Entonox. This was in order to avoid over-sedation and its attendant hazards, which nurses practising alone might not be equipped to manage.

Implementation of the Policy

Education and Training

As an acute pain team, it is our strongly held belief that education is the key to the safe implementation of any policy. Experience has

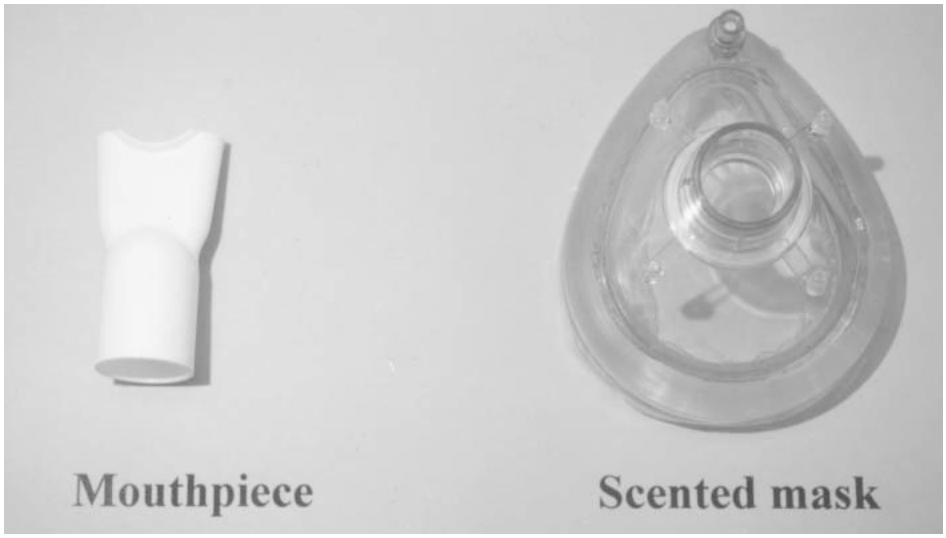

Figure 1. Devices used to administer nitrous oxide

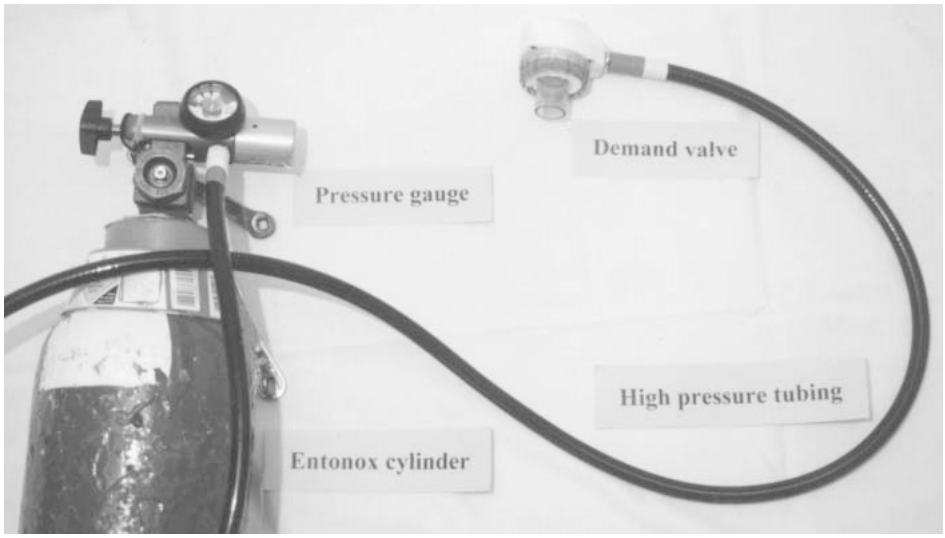

Figure 2. Entonox apparatus

Table 1. Indications and contra-indications to Entonox therapy

Indications	Contraindications
Removal of pins or K wires	Existing pneumo-thorax
Change of plaster	Acute head injury
Change of dressing	Bullous emphysema
Removal of drains	Prolonged continuous usage (> 48 hours) can cause leucopenia
Removal of packs	Administration of sedatives
Splinting fractures	
Application of traction	

taught us that it is fundamental to set aside protected time for nurse education in pain policies. We believe this to be a wise investment of resources as it results in nurses acquiring the knowledge necessary to implement new skills confidently, but above all, safely.

A 90-minute training programme was devised, which consisted of a short talk on the pharmacology of Entonox, a demonstration of the apparatus and the viewing of a short video depicting its use in practice. This was followed by a detailed discussion of the policy document with particular reference to indications and contra-indications. A competency package was then issued to each nurse.

Following this seminar, nurses were encouraged to identify suitable patients, contact the pain team and observe Entonox administration. Subsequently, the nurse administered Entonox under the supervision of the acute pain nurse specialist. If this was performed competently and knowledge was satisfactory according to set criteria, a certificate of competency was issued.

It has been possible to cascade this practical instructive process so that senior nurses and liaison sisters, once competent, have then in turn acted as instructors supervising administrations by other nurses (Figure 3). This has facilitated the dissemination of the practice to all areas of the hospital. Our emphasis is always on strict adherence to the policy and the availability of the emergency duty on-call anaesthetist, who is a member of the pain team, to trouble-shoot, should any problems arise.

Educational updates are planned after an 18-month period. To date, 16 nurses have been trained in this way.

Progress

Initially, the practice was implemented slowly, because it took a considerable time to purchase our own apparatus. Until this was available, it was necessary to borrow the cylinders from other areas of the hospital, making staff less likely to utilise the technique. In addition, some nurses expressed doubts about its efficacy. This had been anticipated, but as the number of successful administrations increased, enthusiasm for its use rose as the advantages began to be appreciated.

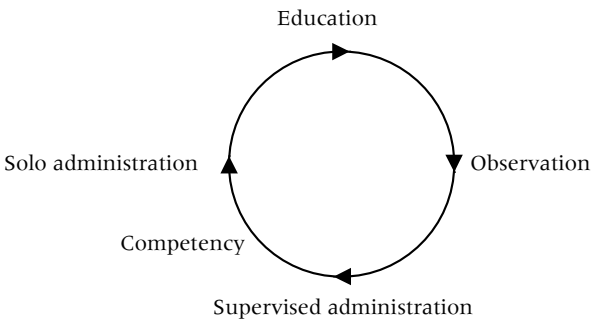

Figure 3. The educational training circle

Audit

Because this policy was nurse-led, an audit of each administration seemed desirable. Information was gathered concerning the implementation of the policy, any problems with administration, quality of analgesia (classed by the operator after consultation with the parent and child as excellent, good or poor), incidence of side-effects, and acceptability (Appendix 2). The policy was introduced in late 1998. Data collection began in 1999. We report the results of 108 administrations to 91 patients. This probably represents a minor level of under-reporting related to incomplete or absent forms.

Results

Ninety one children received 108 administrations of Entonox for a variety of procedures. The mean age was 8 years (range 4–15 years). One child with special needs refused to try the apparatus. Weight was not recorded as weight-related dosage adjustments to inhalation therapy are unnecessary. The mask was chosen on 80 occasions (73%) and the mouthpiece on 28 occasions (27%) (Table 2).

The variety of procedures where Entonox was used for analgesia is shown in Figure 4. The commonest indications were change of abscess dressing and application of traction for fractured femur. These two indications accounted for more than 70% of episodes, and many of these children received multiple administrations.

The age range of children undergoing the various procedures is shown in Table 3. A small number of children aged 4 years were sufficiently co-operative to use the apparatus.

Table 2. Demographic data	
Number of administrations	108
Age (range)	8 years (4–15 years)
Refusals	1
Mask	80 (73%)
Mouthpiece	28 (27%)

Analgesia was excellent or good in 93% of children. In only 7% was a poor effect reported (Figure 5). Of these 7%, many were very anxious children. The subsequent use of Entonox in most of these children was achieved successfully.

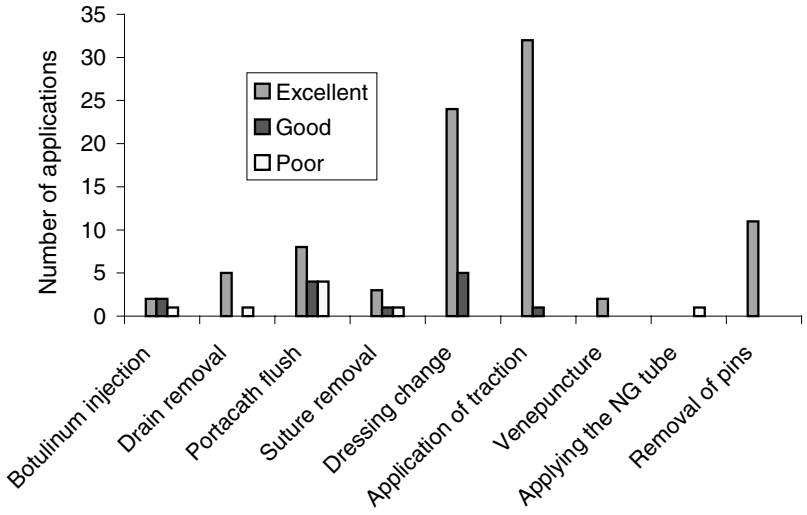

Figure 4. The quality of analgesia during various procedures

Table 3. Range of procedures when children received Entonox

Procedure	*n*	Age range (years)
Botulinum injections	5	7–15
Drain removal	6	9–15
Portacath flush	16	4–11
Suture removal	5	12–14
Change of dressing	29	6–14
Adjustment of traction/orthopaedic	44	5–15
Venepuncture	2	4
Insertion of NG tube	1	11
Total	108	4–15

Only one child complained of feeling nauseated during nitrous oxide therapy. No child vomited. Three children complained of dizziness, one of headache and one of buzzing in the ears during inhalation.

All these side-effects resolved rapidly on termination of therapy. Some of the spontaneous comments noted on the audit form by nurses, parents and children are shown in Table 4. These signify that the cerebral effects of nitrous oxide are pleasant for children and induce a sense of disinhibition and euphoria. There were no negative comments. To date, there has been no necessity to contact the emergency duty anaesthetist for assistance with Entonox administration.

Table 4. Comments made by children and nurses using Entonox

Children	Nurses
'It made me tell the nurses I love them'	'Parents would certainly advocate its use again'
'It made me feel fizzy'	'This is wonderful stuff'
'I didn't need my Mum as I had the gas to help me'	'Each time this child uses nitrous oxide the results get better'
'I was very giggly'	'Relies on it every time she comes to the ward'
	'Difficult to know when to stop using it, he quite likes it'
	'Asks for leg doing as he knows he is having nitrous oxide and isn't worried about procedure'
	'She kept asking to have her traction dressings re-done because she liked the gas'

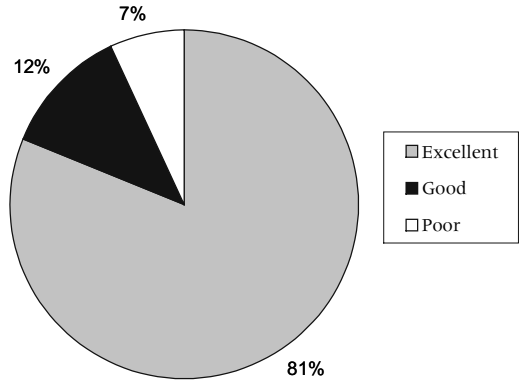

Figure 5. The overall quality of analgesia

Many of the administrations were outside the original policy indications. This indicated that nursing staff were identifying new, appropriate applications for Entonox therapy.

Discussion

We conclude from the results of our audit that the introduction of Entonox into acute procedural pain management has been a success, with 93% of administrations providing good or excellent analgesia. This is in line with the results of other workers who have reported similar success rates for the reduction of fractures[5,6] and the tolerance of gastrointestinal endoscopy[7] in children.

The incidences of side-effects, such as nausea, vomiting and drowsiness, were reassuringly low. The low incidences of sedation supports the stricture in our policy that no sedatives should be administered concurrently with Entonox. One recent study has shown that concurrent administration of midazolam with Entonox may result in an unacceptable level of sedation and even produce general anaesthesia[8]. Other workers have shown that, when midazolam and nitrous oxide were administered to two groups of children (one group with tonsillar-hypertrophy and the other a group of controls), episodes of partial upper airway obstruction occurred in both groups, though more frequently in the tonsillar-hypertrophy group (50%) compared with the controls (16%)[9]. This again supports the contention that combinations of sedatives and analgesics can produce potentially serious side-effects.

All our children were able to undertake normal activities within 10 minutes of discontinuation of nitrous oxide therapy. This is confirmation of its short duration of action and negligible residual effect. The low incidence of nausea and vomiting supports our view that a specific period of starvation prior to nitrous oxide administration is not necessary. Nevertheless, this is an area where more guidance may be advisable in the future.

The acceptability of the inhalational method of administration has been impressive as evidenced by the verbal comments of some of the children. There is no doubt that the majority experience pleasant cerebral effects, so much so that we are mildly concerned about the potential for addiction and for mother substitution with repeat administrations.

A more concrete advantage of Entonox therapy has been the anecdotal reporting of a reduction in the use of oral morphine as a sedative and analgesic, especially in the out-patient department, where its unpredictable absorption and long duration of action make it particularly unsuitable.

A small reduction in the number of children who would have required general anaesthesia in order to facilitate removal of orthopaedic wires and pins has also been a positive advantage of this therapy.

We intend to document these two advantages more closely during the next audit.

Conclusion

We have found Entonox to have wide application for the relief of acute procedural pain in paediatric practice. Its uses range from facilitating the removal of surgical drains to the tolerance of venepuncture in the needle phobic. Moreover, indications for its use are widening. Nurses are enthusiastic and are identifying new clinical situations where they feel this therapy has a place, and pressing for these indications to be included in our policy.

Entonox has led to an improvement in the quality of care for children undergoing painful procedures. Our audit shows that a nurse-led, nurse-administered policy has been introduced safely with low incidences of side-effects. Further audit will concentrate on widening the indications for the use of Entonox, documenting its substitution for other sedatives and analgesics, and enumerating the number of children where Entonox therapy enables general anaesthesia to be avoided. Entonox for procedural pain deserves wider attention in paediatric practice.

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Appendix 1

SOUTHERN DERBYSHIRE ACUTE HOSPITALS NHS TRUST

ACUTE PAIN SERVICES

ENTONOX – SELF-ADMINISTRATION

Introduction

Entonox, or 'gas and air', as it is commonly known, is a gaseous mixture of 50% nitrous oxide and 50% oxygen. It is presented in a blue cylinder with blue and white shoulders. The cylinder is connected to a demand valve via a piece of black high-pressure hose. The demand valve leads to a mouthpiece or facemask. This apparatus enables the gas to be self-administered. The demand valve only opens when sufficient negative pressure has been generated by the patient's inspiratory effort. Gas then flows into the patient's lungs.

Nitrous oxide is a powerful analgesic. Its pain-relieving properties are similar to those of a dose of morphine. However, the onset of action is fast – within 2–3 breaths – and lasts as long as the gas is breathed. When the mask or mouthpiece is removed, the drug is rapidly breathed out via the lungs and its action ceases after a couple of minutes, with no after effects.

This fast onset and offset make it a very suitable agent for providing analgesia for procedures which are painful but of short duration.

Suitable indications	Suitable contraindications
Removal of pins or K wires	Existing pneumothorax
Change of plaster of Paris	Acute head injuries
Change of dressings	Prolonged continuous usage (> 48 hours – can cause leucopenia)
Removal of drains	Concurrent administration of sedatives
Removal of packs	
Immobilisation of fractures	

This is not a comprehensive list. Other indications may be added in the future, subject to approval.

Age Range

Children should be old enough to understand how to operate the demand valve and the instructions given by the nurses. This probably means children of 5 years and above, although this may be variable.

GENERAL NOTES ON AVAILABILITY AND PROCUREMENT

- Ideally the doctor should prescribe Entonox on the PRN portion of the treatment card. However, nurses may also prescribe Entonox via the standing order process.

Sample Prescription

AS REQUIRED PRESCRIPTIONS		
DRUG (approved) name: ENTONOX: 50% NITROUS OXIDE, 50% OXYGEN		Dose:
Route: INHALATION	Indication/Max. frequency: CHANGE OF DRESSING AS PROTOCOL	Pharm:
Start Date:	Signature:	Stop date:

- One cylinder will be available in the Outpatients Department, Children's Emergency Department and another on Sunflower Ward to be shared between all ward areas at the Children's Hospital.
- The cylinder is opened and closed by turning the rotating knob situated at the top of the apparatus. Turn the knob clockwise to close the cylinder and anticlockwise to open the cylinder.
- When the cylinder is empty, ring the porters and ask them to change it. They will be expected to inform pharmacy.
- Turn off the cylinder using the rotating knob.

Training

A short training programme will be set up by the acute pain team. It will take the following format:

- The Pharmacology of Entonox (Dr Vater).
- A practical demonstration of the apparatus (the acute pain nurse).
- A short training video.

Certificates of competency will be issued following observation and subsequent supervised administration of Entonox.

Notes on Usage

- Explain the sequence of events to the child.
- Familiarise him/her with the mouthpiece/mask and demand valve.
- Make sure that the mask or mouthpiece is a good fit. You will hear the noise of the demand valve opening when the apparatus is used correctly. The child *must* only mouth-breathe when using the mouthpiece.
- Warn the child that he/she may possibly feel a little light-headed and/or drowsy after using

the apparatus for a few minutes. If this occurs the child should remove the mask or mouthpiece and inform the nurse. The feeling will pass off quickly.

- Ask the child to take deep breaths in and out and encourage the parent or carer, if present, to assist the child with his/her co-operation. However, only the child should hold the mask or mouthpiece.
- Wait for a minute or so before commencing the procedure.
- The child's breathing needs to be supervised throughout to ensure that they are receiving the Entonox.
- Observe for nausea, which is occasionally troublesome.
- There is no need to record routine physiological observations. Effectiveness of pain relief should be assessed and recorded on the acute pain chart.
- Entonox *cannot* render the child unconscious, therefore it is inherently safe.
- Contact the acute pain nurse (Debra Hessell: Bleep 1283 DCGH), the ED1 anaesthetist or the anaesthetist in theatre if you are experiencing any problems (in that order).
- Discontinue administration of Entonox when the procedure is over.
- Wash the mouthpiece/facemask in medical detergent.
- There is no need to limit the child's mobility once a 5–10 minute rest period has passed following removal of the mask/mouthpiece. The vast majority of the gas will have been excreted by this time. The child should be ready to resume normal activities within 30 minutes.
- Complete audit form.

Appendix 2

PAEDIATRIC ENTONOX

EVALUATION FORM

We are interested in discovering the exact efficacy of nitrous oxide therapy.

Please complete this brief form for each patient. Information will be used for audit purposes.

ADDRESSOGRAPH LABEL

Ward/Department:

Date:

Procedure:						
Mask/mouthpiece:						
Co-operation with apparatus:	Poor		Good		Excellent	

SIDE-EFFECTS

Nausea:	
Dizziness:	
Amnesia:	
Other (*state what*):	

Drowsiness	
Dreams (bad)	
Hyperventilation	
Noises	

QUALITY OF ANALGESIA

Poor		**Good**		**Excellent**	

COMMENTS FROM CHILD/PARENT/NURSE (GOOD, BAD, FUNNY)

Would you use nitrous oxide for this child again? If no, state why.

By using nitrous oxide for this child, did it prevent them having:

GA		Oral morphine		Sedation	

Any other comments (please indicate if the child is a special needs patient, etc):