1. ANAESTHETICS

1.1 General anaesthetics and oxygen

For proposed ‘yellows’: Are these medicines for children?

Do these medicines meet a public health?

??? Halothane

Are they registered for use in (all age categories of) children?

UK

**Induction of anaesthesia**
By inhalation through specifically calibrated vaporiser
Child 12–18 years
increased gradually according to response to 2% (up to 4% in child over 16 years) in oxygen or nitrous oxide-oxygen

**Maintenance of anaesthesia**
By inhalation through specifically calibrated vaporiser
Child 1 month–18 years
0.5–2%

**CD - BNFC 2006**

1) For induction of anesthesia, a concentration of 0.5% to 2.5% in nitrous oxide/oxygen has been used in children (1 to 12 years of age) (Naito et al, 1991b; Johannesson et al, 1987b; McAteer et al, 1986b; Sigurdsson & Lindahl, 1983a). For maintenance, usual concentrations have been 0.8% to 2.5% in nitrous oxide/oxygen (Naito et al, 1991b; Johannesson et al, 1987b; McAteer et al, 1986b).

2) The minimum alveolar concentration (MAC) of halothane decreases with increasing age (Prod Info Fluothane(R), 1998a; AMA Department of Drugs, 1994c; Dale & Brown, 1987d). MAC values in infants and children 3 years of age are 1.08% and 0.9%, respectively (Prod Info Fluothane(R), 1998a).

3) Premedication with a combination rectal solution of diazepam 0.5 milligram/kilogram, morphine 0.15 milligram/kilogram, and scopolamine 0.01 milligram/kilogram (30 to 40 minutes prior to induction) may be useful in reducing airway reactions to halothane anesthesia in children (Johannesson et al, 1987b).

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http://www.thomsonhc.com/hcs/librarian/ND_PR/Main/SBK/5/PFPUI/7wY1SX1UAf0IJ /ND_PG/PRIH/CS/EA0A04/ND_T/HCS/ND_P/Main/DUPLICATIONSHIELDSYNC/53 57A7/ND_B/HCS/PFActionId/hcs.common.RetrieveDocumentCommon/DocId/1449/Co ntentSetId/31/sectionId/pediatricDosageSection/SearchTerm/halothane%20/SearchOpti on/BeginWith#ip3 acessão em 11/06/2007
Are there any unanswered/unexpected clinical issues with respect to effectives or safety?
Yes

Additional comments if any:

Cautions
Avoid for dental procedures in those under 18 years unless treated in hospital (high risk of arrhythmia); avoid in porphyria;
Hepatic impairment
Avoid if history of unexplained pyrexia or jaundice following previous exposure to halothane

CD - BNFC 2006

Halothane is a volatile liquid anaesthetic. Its advantages are that it is potent, induction is smooth, the vapour is non-irritant, and seldom induces coughing or breath-holding. Despite these advantages, however, halothane is much less widely used than previously owing to its association with severe hepatotoxicity.

Halothane causes cardiorespiratory depression. Respiratory depression results in elevation of arterial carbon dioxide tension and perhaps ventricular arrhythmias. Halothane also depresses the cardiac muscle fibres and may cause bradycardia. The result is diminished cardiac output and fall of arterial pressure. Adrenaline (epinephrine) infiltrations should be avoided in children anaesthetised with halothane as ventricular arrhythmias may result.

Halothane produces moderate muscle relaxation, but this may be inadequate for major abdominal surgery and specific muscle relaxants are then used.

CSM advice (halothane hepatotoxicity)

In a publication on findings confirming that severe hepatotoxicity can follow halothane anaesthesia the CSM has reported that this occurs more frequently after repeated exposures to halothane and has a high mortality. The risk of severe hepatotoxicity appears to be increased by repeated exposures within a short time interval, but even after a long interval (sometimes of several years) susceptible patients have been reported to develop jaundice. Since there is no reliable way of identifying susceptible patients the CSM recommends the following precautions prior to use of halothane:

1. a careful anaesthetic history should be taken to determine previous exposure and previous reactions to halothane;
2. repeated exposure to halothane within a period of at least 3 months should be avoided unless there are overriding clinical circumstances;
3. a history of unexplained jaundice or pyrexia in a patient following exposure to halothane is an absolute contra-indication to its future use in that patient.

CD - BNFC 2006
**Do these medicines meet a public health?**

- **Ketamine** Yes

**Are they registered for use in (all age categories of) children?** Yes

<table>
<thead>
<tr>
<th>Route</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>I.M.</td>
<td>3-7mg/kg</td>
</tr>
<tr>
<td>I.V.</td>
<td>Range: 0.5-2mg/kg, use smaller doses (0.5-1mg/kg) for sedation for minor procedures; usual induction dosage: 1-2mg/kg</td>
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<tr>
<td></td>
<td>Continuous I.V. infusion: Sedation 5-20mcg/kg/minute; start at lower dosage listed and titrate to effect</td>
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<td>Maintenance: supplemental doses of 1/3 to 1/2 of initial dose.</td>
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**Induction and maintenance of anaesthesia (short procedures)**

By intravenous injection over at least 60 seconds

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonate</td>
<td>1–2 mg/kg produces 5–10 minutes of surgical anaesthesia, adjusted according to response</td>
</tr>
<tr>
<td>Child 1 month–12 years</td>
<td>1–2 mg/kg produces 5–10 minutes of surgical anaesthesia, adjusted according to response</td>
</tr>
<tr>
<td>Child 12–18 years</td>
<td>1–4.5 mg/kg (usually 2 mg/kg) produces 5–10 minutes of surgical anaesthesia, adjusted according to response</td>
</tr>
<tr>
<td>Neonate</td>
<td>4 mg/kg usually produces 15 minutes of surgical anaesthesia, adjusted according to response</td>
</tr>
<tr>
<td>Child 1 month–18 years</td>
<td>4–13 mg/kg (4 mg/kg sufficient for some diagnostic procedures), adjusted according to response; 10 mg/kg usually produces 12–25 minutes of surgical anaesthesia</td>
</tr>
</tbody>
</table>

**Induction and maintenance of anaesthesia (longer procedures)**

By continuous intravenous infusion
Neonate
initially 0.5–2 mg/kg followed by a continuous intravenous infusion of
500 micrograms/kg/hour adjusted according to response; up to 2 mg/kg/hour may be
used to produce deep anaesthesia

Child 1–18 years
initially 0.5–2 mg/kg followed by a continuous intravenous infusion of 0.6–
2.7 mg/kg/hour adjusted according to response

CD BNFC-2006

Are there any unanswered/ unexpected clinical issues with respect to effectives or
safety? Yes.

In children anesthetized with halothane, ketamine had a dose-dependent effect on IOP
(intraocular pressure), with 6 mg/kg of the drug causing a small increase in IOP at 5 to
10 minutes and 3 mg/kg not altering the IOP. The higher dose of ketamine also was
associated with an increased incidence of postoperative complications.
Nagdeve NG, Yaddanapudi S, Pandav SS. The effect of different doses of ketamine on
intraocular pressure in anesthetized children. Journal of pediatric ophthalmology and

Ketamine is used rarely now. It has good analgesic properties at sub-anaesthetic
dosage. It has particular value in children requiring repeated anaesthesia; however,
recovery is relatively slow. There is a high incidence of extraneous muscle movements;
also cardiovascular stimulation, tachycardia, and raised arterial pressure may occur.
The main disadvantage of ketamine is the high incidence of hallucinations,
nightmares, and other transient psychotic effects; these can be reduced when drugs
such as diazepam are also used. Ketamine is contra-indicated in children with
hypertension and is best avoided in those prone to hallucinations or nightmares. It also
has abuse potential and may lead to dependance.

CD BNFC-2006

Additional comments if any:

Revisão sistemática Cochrane: no one
Ensaios controlados: 163
Heinz P, Geelhoed GC, Wee C, Pascoe EM. Is atropine needed with ketamine sedation?
A prospective, randomised, double blind study. Emergency medicine journal 23(3):206-
Publication type: Journal Article; Multicenter Study; Randomized Controlled Trial

Akbas M, Titiz TA, Ertugrul F, Akbas H, Melikoglu M. Comparison of the effect of
ketamine added to bupivacaine and ropivacaine, on stress hormone levels and the
Roback MG, Wathen JE, MacKenzie T, Bajaj L A randomized, controlled trial of i.v. versus i.m. ketamine for sedation of pediatric patients receiving emergency department orthopedic procedures.48(5):605-12, 2006.


For 'greens': Is there any reason not to endorse these as essential medicines for children?

**Nitrous oxide**

Do these medicines meet a public health? **Yes**

Are they registered for use in (all age categories of) children? **Yes**

**Maintenance of light anaesthesia**
By inhalation using suitable anaesthetic apparatus
Child 1 month–18 years
as a mixture with 25–30% oxygen

**Analgesia**
By inhalation using suitable anaesthetic apparatus
Child up to 18 years (but see notes above)
as a mixture with 30–50% oxygen, according to the patient’s needs

CD- BNF 2006

Continuous inhalation of nitrous oxide 30% with oxygen 70% was reported effective as analgesic in children presenting to the emergency room with mild lacerations (Gamis et al, 1989). In this study, pain perception was diminished with the use of the nitrous oxide mixture in children more than 8 years of age; although a trend toward a decrease in pain perception was observed in younger patients (2 to 7 years), this was not significant. Adverse effects were not observed during administration. The use of higher concentrations of nitrous oxide (40% to 50%) may produce greater analgesia and need to be evaluated in pediatric outpatients.


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http://www.thomsonhc.com/hcs/librarian/ND_PR/Main/SBK/6/PFPUI/CALDee1U1Bj1B/ND_PG/PRIH/CS/2510F1/ND_T/HCS/ND_P/Main/DUPLICATIONSHEILDSYNC/44D712/ND_B/HCS/PFACTIONId/hcs.common.RetrieveDocumentCommon/DocId/0769/ContentSetId/31/sectionId/pediatricDosageSection/SearchTerm/nitrous%20oxide%20/SearchOption/BeginWith#ip3 acesso em 05/06/2007.

Are they any unanswered/unexpected clinical issues with respect to effectiveness or safety? **No.**

Are there special requirements or training needed for safe/effective use? **Yes.**
Additional comments if any:

Nitrous oxide must be given with oxygen, otherwise hypoxia will occur.
Martindale 33 ed., P.1265

The use of high doses of opioids such as fentanyl with nitrous oxide may result in a drop in heart rate and cardiac output. Combined use of nitrous oxide and methotrexate may increase the side-effects of methotrexate therapy
Martindale 33 ed., P.1265

Nitrous oxide is used for maintenance of anaesthesia and, in sub-anaesthetic concentrations, for analgesia. For anaesthesia it is commonly used in a concentration of 50 to 70% in oxygen as part of a balanced technique in association with other inhalational or intravenous agents. Nitrous oxide is unsatisfactory as a sole anaesthetic owing to lack of potency, but is useful as part of a combination of drugs since it allows a significant reduction in dosage.

A mixture of nitrous oxide and oxygen containing 50% of each gas (Entonox®, Equanox®) is used to produce analgesia without loss of consciousness. Self-administration using a demand valve may be used in children who are able to self-regulate their intake (usually over 5 years of age) for painful dressing changes, as an aid to postoperative physiotherapy, for wound debridement and in emergency ambulances.

Nitrous oxide may have a deleterious effect if used in children with an air-containing closed space since nitrous oxide diffuses into such a space with a resulting increase in pressure. This effect may be dangerous in the presence of a pneumothorax which may enlarge to compromise respiration.

Special care is needed to avoid hypoxia if an anaesthetic machine is being used; machines should incorporate an anti-hypoxia device. Exposure of children to nitrous oxide for prolonged periods, either by continuous or by intermittent administration, may result in megaloblastic anaemia owing to interference with the action of vitamin B₁₂. For the same reason, exposure of theatre staff to nitrous oxide should be minimised. Depression of white cell formation may also occur.
CD BNF2006

Action proposed for the Committee to take: To approve
For 'greens': Is there any reason not to endorse these as essential medicines for children?

**Oxygen**

Do these medicines meet a public health? **Yes**

Are they registered for use in (all age categories of) children? **Yes**

It is used as a diluent in gaseous anaesthetics. Martindale 33 ed., P.1200
See check list nitrous oxide.

Are they any unanswered/unexpected clinical issues with respect to effectiveness or safety? **No**.

Are there special requirements or training needed for safe/effective use? **Yes**.

Additional comments if any:

Any fire or spark is highly dangerous in the presence of increased oxygen concentrations especially when oxygen is used under pressure.

Metal cylinders containing oxygen should be fitted with a reducing valve by which the rate of flow can be controlled. It is important that the reducing valve should be free from all traces of oil or grease, as otherwise a violent explosion may occur. Combustible material soaked in liquid oxygen is potentially explosive and the low temperature of liquid oxygen may cause unsuitable equipment to become brittle and crack. Liquid oxygen should not be allowed to come into contact with the skin as it produces severe 'cold burns'.

Oxygen intended for aviation or mountain rescue must have a sufficiently low moisture content to avoid blocking of valves by ice on freezing.

High concentrations of oxygen should be avoided in patients whose respiration is dependent upon hypoxic drive, otherwise carbon dioxide retention and respiratory depression may ensue.

Martindale 33 ed., P.1200

Action proposed for the Committee to take: To approve
For 'greens': Is there any reason not to endorse these as essential medicines for children?

Thiopental

1.1 General anaesthetics and oxygen

Do these medicines meet a public health? Yes

Are they registered for use (all age categories of) children? Yes

Are they any unanswered/unexpected clinical issues with respect to effectiveness or safety? No.

Are there special requirements or training needed for safe/effective use?

Intravenous injections are normally given as a 2.5% solution; the BNFC recommends that intravenous infusions are given as a 0.25% solution.

MARTINDALE - The Complete Drug Reference

Administration

For intravenous injection, dilute to a concentration of 25 mg/mL with Water for Injections, and give over at least 10–15 seconds; for intravenous infusion dilute to a concentration of 2.5 mg/mL with Sodium Chloride 0.9%

CD- BNFC - 2006

Additional comments if any:

For the induction of anaesthesia in children, UK licensed product information recommends that thiopental sodium is given by slow intravenous injection (over 10 to 15 seconds) in a dose of 2 to 7 mg/kg; the dose may be repeated after 1 minute.

MARTINDALE - The Complete Drug Reference

Induction anesthesia: I.V.:
Neonates: 3-4 mg/kg
Infants: 5 -8 mg/kg
**Induction of anaesthesia**

By slow intravenous injection

<table>
<thead>
<tr>
<th>Age Category</th>
<th>Dosage</th>
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<tbody>
<tr>
<td><strong>Neonate</strong></td>
<td>4 mg/kg repeated after 1 minute if necessary</td>
</tr>
<tr>
<td><strong>Child 1 month–18 years</strong></td>
<td>4 mg/kg (max. 150 mg) repeated after 1 minute if necessary</td>
</tr>
</tbody>
</table>

CD- BNFC-2006

Barbiturate anaesthetics are contra-indicated when there is dyspnoea or respiratory obstruction such as in acute severe asthma or when maintenance of an airway cannot be guaranteed.

Barbiturate anaesthetics should be used with caution in shock and dehydration, hypovolaemia, severe anaemia, hyperkalaemia, toxaemia, myasthenia gravis, myxoedema and other metabolic disorders, or in severe renal disease. Caution is also required in patients with cardiovascular disease, muscular dystrophies, adrenocortical insufficiency, or with increased intracranial pressure. Reduced doses are required in the elderly and in severe hepatic disease.

Barbiturates including **thiopental** sodium have been associated with acute attacks of porphyria and are considered unsafe in porphyric patients.

Martindale 33 ed., P.1269

**Cautions**

Cardiovascular disease; reconstituted solution is highly alkaline—extravasation causes tissue necrosis and severe pain; avoid intra-arterial injection.

**Hepatic impairment**

reduce induction dose in severe liver disease

**Contra-indications**

Porphyria; myotonic dystrophy

**Breast-feeding**

present in milk—manufacturer advises avoid


**Action proposed for the Committee to take:** To approve