Ether (anaesthetic)

Introduction
Ether (diethyl ether) is an inhalational general anaesthetic agent listed in the 2004 WHO Model Formulary for induction and maintenance of general anaesthesia in adults and children.\(^1\) It is a potent anaesthetic that made modern surgery possible. A second and related product listed in the Formulary is the halogenated anaesthetic halothane. This is more stable and safer to use than ether, and offers more precise control over the anaesthetic state.\(^2\)

Product and Dosage\(^1,3,4,5\)
Ether for anaesthetic use is usually supplied in air-tight, amber-coloured, glass bottles. It is highly flammable, and there is a risk of explosion when mixed with oxygen or nitrous oxide (these risks not associated with halothane). Ether degenerates on exposure to light, heat and air and this is retarded by the addition of stabilisers. It should not be stored in polyvinyl chloride (PVC) bottles as it softens the PVC through which it can permeate.\(^6\)

Ether anaesthesia is administered in various ways, ranging from ‘open ether’ methods using a simple Schimmelbusch type mask, through simple draw-over vaporisers, to more expensive temperature and flow-compensated vaporisers such as the Epstein-Macintosh-Oxford (EMO) or Portable Anaesthesia Complete (PAC) type vaporisers.\(^7\)

For induction of anaesthesia the concentration in the inspired gas is up to 15%; for maintenance of light anaesthesia, the concentration in air is 3-5% (with or without muscle relaxants); for deep anaesthesia the concentration is up to 10%. Reduced inspired concentrations may suffice in elderly patients.

Unwanted effects
- Ether irritates the respiratory mucosa – salivary and bronchial secretion are stimulated and laryngospasm may occur. These effects are concentration-dependent. Induction therefore may be slow and difficult.
- Recovery from prolonged anaesthesia is slow and the incidence of postoperative nausea and vomiting is high.
- Ether can cause potentially fatal convulsions. This is most likely in febrile children with sepsis given atropine and when the ambient temperature is high.
- Ether causes vasodilation that may lead to a substantial fall in blood pressure and reduce renal blood flow. However, renal failure has not been reported.
- Ether can prolong prothrombin time and increase capillary bleeding.
- It can raise the intracranial pressure, especially in a spontaneously breathing patient.
- Unlike halothane, ether is not regarded as hepatotoxic. However, occasional cases of fatty liver and other degenerative hepatic changes have been reported.
• Because ether is both inflammable and explosive it is potentially dangerous to the patient and the operation theatre personnel alike. Sources of ignition include surgical diathermy, static electricity and sparks from defective switches or equipment.

Dependence on ether and ether vapour has been reported. It is subject to international control under the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances (1988).

**Contraindications**
The relative contraindications to the use of ether include:
• Operating theatres where diathermy is in use or where the atmosphere cannot be made free from possible sources of ignition.
• Fever, especially in children.
• Raised intracranial pressure.
• Severe systemic disease affecting the heart, lungs, kidneys or liver.

**Ether should be used with particular precaution:**
• In patients with diabetes, as ether can further increase blood sugar concentrations.
• In women who are pregnant, as ether crosses the placenta and can depress neonatal respiration.
• At high altitudes, because above 2000 m its boiling point is lowered.

**Evidence of value**
The advantages of ether are that:
• It is relatively cheap, and costs less than halothane (and the other volatile inhalational anaesthetics currently in use).
• In the concentrations normally used, it stimulates respiration and circulation and thereby encourages its own absorption. Therefore, in a fit patient it may be used with air as the carrier gas, whereas oxygen is required for halothane (and most other volatile agents).
• It has good muscle relaxant property so that even major surgery may be undertaken without the use, or with minimum use, of a neuromuscular blocker.
  • It has a relatively wide therapeutic index and is the safest for use in relatively inexperienced hands.

Some of the disadvantages of ether can be minimised with attention to technique and detail. Induction can be made less troublesome with prior use of halothane, or an intravenous agent like thiopental and intubation under succinylcholine blockade. Although flammable, explosions rarely occur with ether because of the caution normally exercised in its use.

**Recommendation**
Ether is an effective inhalational general anaesthetic, but its many disadvantages make it less suitable than halothane in most settings. However, ether should continue to be listed in the WHO Model List of Essential Medicines because of its low cost and relative safety in inexperienced hands. It has a particular place in patients in whom halothane is contraindicated. We recommend that the WHO Model Formulary mentions that halothane (or possibly one of the newer fluorinated agents like isoflurane...
or sevoflurane) should be used in preference to ether where cost, training, equipment and patient susceptibilities permit.

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(October 2004)

References


Search Strategy

A survey of medical literature was carried out to identify clinical trials, systematic reviews or meta-analyses, practice guidelines and adverse drug reaction reports relevant to the clinical use of ether as an anaesthetic. A remarkable paucity of recent literature was noted.

Electronic databases, websites and journals searched between 11/07/2004 to 15/07/2004

Medline accessed through Pubmed

Search on Jul 11, 2004 with keywords ether AND anaesthesia

With Search period: Last 10 y and Limits: Articles with abstracts / Clinical trial / Keyword in title/abstract, returned 7 citations – only 2 were relevant.

With Search period: Last 10 y and Limits: Articles with Review Articles / Clinical trial / Keyword in title/abstract, returned 85 citations – only 3 were relevant.

Anesthesia & Analgesia
http://www.anesthesia-analgesia.org

Advanced search with ether as the keyword (in title / abstract) returned 56 hits (Sep, 1965 to present) – 18 relevant to clinical use of ether. Most relevant hits were dated more than 25 years back and no abstracts for these are available.

Anaesthesia and Intensive Care
http://www.aaic.net.au/

Online search of years 1996 - 2004, for all types of articles, with ether as the search term, retrieved 3 citations – none relevant.

Anesthesiology
www.anesthesiology.org/

Online search with ether as the search term, without any qualifications, returned 269 citations. A refined search with ether in the abstract returned 15 citations – none relevant.

European Journal of Anesthesia
http://www.eja-online.org/

No citation retrieved with ether as the keyword

Journal of Clinical Anesthesia
Website could not be accessed

ingenta website
www.ingenta.com/journals/
Search of online articles with anesthetic ether as the search term returned 41 hits. Four hits were relevant but dealt with historical or mechanistic aspects of ether.

Journal of Cardiothoracic & Vascular Anesthesia
http://www.jcardioanesthesia.com/

Journal of Paediatric Anaesthesia
Search of the Blackwell Science website (http://www.blackwell-synergy.com/) with ether as the search term returned 23 hits – 5 were relevant.

Acta Anaesthesiologica Scandinavica
Search of the Blackwell Science website (http://www.blackwell-synergy.com/) with ether as the search term returned 24 hits – 5 were relevant.

World Anaesthesia
Search of World Anaesthesia webpage through http://search.ox.ac.uk/web/medsci/clinmedic/anaes/ returned 16 hits – some showing relevance of ether in the developing world.

BMJ Clinical Evidence website http://www.clinicalevidence.com/
Search with the search term ether anaesthesia returned 4 hits – none relevant.

International Anesthesiology Clinics http://www.anesthesiACLinics.com
Online search with ether as the search term returned 13 hits - 5 were relevant but 3 of these were of a historical nature.

Current Opinion in Anesthesiology www.currentopinion.com
Online search with ether as the search term returned 10 hits – none relevant.

In addition, the following sources were searched from 1970 to present.

- British Medical Journal
- British Journal of Pharmacology
- British Journal of Clinical Pharmacology
- Molecular Pharmacology
- The New England Journal of Medicine

Finally, various textbooks and references on anaesthesia were consulted. Most current editions do not discuss ether at all, except in a historical context. Martindale and Dollery's Therapeutic Drugs were also consulted, and thankfully retain their monographs /entries on anaesthetic ether.