Guidelines

Guideline on anaesthesia and sedation in breastfeeding women 2020

Guideline from the Association of Anaesthetists

J. Mitchell,1 W. Jones, 2 E. Winkley3 and S. M. Kinsella4

1 Consultant, Department of Anaesthesia, University Hospital Ayr, Ayr, UK
2 Specialist Pharmacist, Breastfeeding and Medication, Portsmouth, UK
3 Consultant, Department of Anaesthesia, Northumbria NHS Foundation Trust, UK
4 Consultant, Department of Anaesthesia, St Michael’s Hospital, Bristol, UK

Summary
Breastfeeding has many health benefits for the mother and infant. Women who are breastfeeding may require anaesthesia or sedation. Concerns regarding the passage of drugs into breast milk may lead to inconsistent advice from professionals. This can sometimes result in the interruption of feeding for 24 hours or longer after anaesthesia, or expressing and discarding (‘pumping and dumping’) breast milk; this may contribute to early cessation of breastfeeding. However, there are data regarding the transfer of most anaesthetic drugs into breast milk. We advise that breastfeeding is acceptable to continue after anaesthesia and should be supported as soon as the woman is alert and able to feed, without the need to discard breast milk. We provide evidence-based information on the pharmacokinetics of drugs commonly used during anaesthesia so that professionals can undertake a risk-benefit discussion with the woman. We advise the development of local policies that aid logistical planning and guide staff to facilitate breastfeeding during the woman’s hospital stay.

Correspondence to: S. M. Kinsella
Email: mikekinsella@anaesthetists.org
Accepted: 11 June 2020
Keywords: anaesthesia; adverse effects; anaesthesia; general; anaesthesia; regional; breast feeding; pre-operative assessment; surgery

This is a consensus document produced by members of a Working Party established by the Association of Anaesthetists of Great Britain and Ireland. It has been seen and approved by the Board of Directors of the Association of Anaesthetists. It has been endorsed by the Royal College of Midwives and the Royal College of Obstetricians and Gynaecologists, and supported by the Obstetric Anaesthetists’ Association and the Royal College of Anaesthetists.

Twitter: @jmitchelldoc; @ElaineW14626897; @BfWendy; @mikekinsella10

Recommendations

1 Women should be encouraged to breastfeed as normal following surgery.
2 There is no need to express and discard breast milk after anaesthesia.
3 Anaesthetic and non-opioid analgesic drugs are transferred to breast milk in only very small amounts. For almost all drugs used peri-operatively, there is no evidence of effects on the breastfed infant.
4 Drugs such as opioids and benzodiazepines should be used with caution, especially after multiple doses and in babies up to 6 weeks old (corrected for gestational age). In this situation, the infant should be observed for signs of abnormal drowsiness and respiratory
depression, especially if the woman is also showing signs of sedation.

5 Codeine should not be used by breastfeeding women following concerns of excessive sedation in some infants, related to differences in metabolism.

6 Any women with an infant < 2 years should routinely be asked if they are breastfeeding during their pre-operative assessment.

7 Opioid-sparing techniques are preferable for the breastfeeding woman. Local and regional anaesthesia have benefits in this regard, and also have the least interference with the woman’s ability to care for her infant.

8 Where possible, day surgery is preferable to avoid disrupting normal routines. A woman having day surgery should have a responsible adult stay with her for the first 24 h. She should be cautious with co-sleeping, or sleeping while feeding the infant in a chair, as she may not be as responsive as normal.

9 Breastfeeding support should be accessible for lactating women undergoing surgical and medical procedures.

10 Patient information leaflets and additional resources should be available containing information on the compatibility of anaesthetic agents and analgesics during breastfeeding, and guidance on breastfeeding support in the peri-operative period.

What other guideline statements are available on this topic?

Online resources include lactation specific databases such as the UK Drugs in Lactation Advisory Service (UKDILAS) [1], Drugs and Lactation Database (LactMed) [2], and Hale [3]. There are several publications that give guidance on the compatibility of breastfeeding following anaesthesia [4–7].

Why were these guidelines developed?

Accessing information on the risks of drugs during breastfeeding can be challenging, as many of the more commonly used resources, such as the British National Formulary, err on the side of caution in line with the manufacturers’ recommendations and licences. Anaesthetists are unlikely to access specialist information sources. This guideline also provides information for other health professional groups who will look after women who are breastfeeding.

How and why does this statement differ from existing guidelines?

This guideline contains pharmacokinetic data on medications used during anaesthesia to ensure anaesthetists have the required knowledge to support women who are lactating, in order to minimise interruptions to breastfeeding after surgery. This is in accordance with recommendations from the National Institute for Health and Care Excellence (NICE) [8], which also provides advice on peri-operative care for breastfeeding women.

Introduction

Breast milk is recommended as the best source of nutrition for infants and young children [8–12]. It has been demonstrated to offer significant short- and long-term health benefits for both infant and mother. These include the protection of infants from childhood diseases, and long-term health benefits such as a reduction in the risk of obesity. Maternal health benefits include a reduction in the risk of breast and ovarian cancer, and a lower risk of hip fracture due to osteoporosis later in life [13].

The World Health Organization (WHO) recommends exclusive breastfeeding up to 6 months of age, and continued breastfeeding along with complementary foods up to 2 years or beyond [10]. Maternity units across the UK are encouraged to engage with the United Nations Children’s Fund (UNICEF) Baby Friendly Initiative [14], an evidence-based programme to support women to start and continue breastfeeding. This includes initiating breastfeeding after anaesthetic interventions, including general anaesthesia in an obstetric setting. However, limited formal support is in place for women receiving anaesthesia beyond the perinatal period.

While the incidence of breastfeeding beyond 6 weeks is still relatively low in the UK compared with other European countries [9], active measures are in place to encourage and support ongoing breastfeeding. Recent information from Scotland found that 18% of infants were still being breastfed at 13–15 months [15]. Therefore, it is important that appropriate consideration is given to women with infants up to 2 years of age, who require surgical or medical procedures, as they may still be breastfeeding.

The advice that is currently given to breastfeeding women who require an anaesthetic is variable and inconsistent, sometimes resulting in the interruption of feeding for 24 h or longer, or expressing and discarding breast milk due to concerns regarding the possible adverse effects of drugs passing into the breast milk [16]. This may contribute to early cessation of breastfeeding [17]. The Breastfeeding Network ‘Drugs in breastmilk’ Service [18] is contacted frequently with concerns relating to the inconsistent and often incorrect advice given regarding cessation of breastfeeding after anaesthesia.
Obstetric surgery is undertaken frequently, with little debate about the passage of anaesthetic agents across the placenta and potential effects on the neonate [19]. Immediately after delivery, the intercellular gaps in the milk glands are wide open to facilitate the passage of immunoglobulins to line the baby’s gut, and during this period drugs are also freely able to pass into breast milk. However, women having a caesarean section are encouraged to breastfeed as soon as they are alert and able to hold the baby in recovery. There is considerable overlap between the drugs used in anaesthesia after the peripartum period and those used during caesarean section, yet the intercellular gaps close soon after birth so passage of drugs into breast milk is much lower. It is therefore illogical to advise expressing and discarding in the former situation. The risk-benefit balance should take into consideration possible consequences that include: breast engorgement/ blocked ducts or mastitis, which potentially require antibiotics; refusal of the infant to feed from a bottle; and reactions to cow’s milk protein.

**Review of the evidence**

We conducted a literature search using PubMed, using the search terms: anaesthesia; breastfeeding; breastmilk; surgery. We consulted relevant sources of information including: lactation specific databases (UK Drugs in Lactation Advisory Service (UKDILAS) [1], Drugs and Lactation Database [2], Hale [3], Jones [20], Martindale [21] and the WHO [22]); current guidelines; and breastfeeding expert journals and websites. A list of drugs used perioperatively was compiled, including reference to the Association of Anaesthetists National Essential Anaesthesia Drugs List (NEADL) [23]. As many of these sources are freely available, individual references are not provided for each item, but further information is provided later.

**Pre-operative factors – assessment, consent and peri-operative planning**

Breastfeeding is rarely considered before surgery, yet causes considerable anxiety and concern in women who are facing surgery, (personal communication, Breastfeeding Network ‘Drugs in breastmilk’ Service). A woman may not mention that she is breastfeeding at the time of pre-operative assessment as she may not have considered this to be significant, or may be concerned that she will be subjected to critical comments, especially if she is continuing to feed an older child.

The following should be considered (Box 1):

- Does the woman wish to continue to breastfeed? In general, this should be assumed and supported regardless of the age of the infant. The clinician’s role is not to discuss the woman’s choice of infant feeding, beyond encouraging her to continue breast feeding should she so wish.
- What is the impact on ongoing lactation if interrupted by expressing and discarding, including the risk to the woman of blocked ducts/mastitis, or the risks of exposure to artificial formula in an allergic infant? These factors should be set against any hesitations that the woman may have about adverse effects from drug transfer into breast milk.
- Is the infant able to feed from another container such as a bottle or cup, or eating solid foods alongside breastfeeding? This may facilitate care of the infant at home. Not all babies who are exclusively breastfed will take expressed milk from a bottle; this may lead to dehydration if breastfeeding is interrupted.
- In pre-term infants, the risk of necrotising enterocolitis needs to be considered if breast milk is replaced, even temporarily, by formula milk.

Anaesthetic options should aim to ensure the delivery of anaesthesia and postoperative analgesia that will minimise any impact on breastfeeding in the postoperative period. It is important to consider factors that are important

---

**Box 1 Pre-operative considerations**

Discuss with the woman:

- Her wishes to continue to breastfeed.
- The most suitable type of anaesthesia that is the least disruptive to breastfeeding. Early return of consciousness after general anaesthesia is desirable. Assure her that effective analgesic and anti-emetic strategies will be used.
- The transfer of drugs to breast milk, both intra-operative and postoperative, and any risks of this vs. the benefits of continuing breastfeeding.

Document a plan to recommence breastfeeding as soon as possible after surgery, in line with locally developed guidelines.

Discuss expressing and storing of breast milk if the child is unable to stay with the woman on the ward, or if surgery is prolonged. This should be carried out with input from an expert in infant feeding, or other specially trained member of staff.
to the woman as part of shared decision-making. Women should be advised that expressing and discarding (‘pumping and dumping’) of breast milk after anaesthesia is not necessary. However, some women may wish to ensure that their infant is not exposed to any medication at all. Prior expression and storage of milk may be possible. If a woman chooses to express and discard after drug exposure, evidence-based material should be provided on the elimination time of the drugs so that she can resume normal breastfeeding as soon as possible (see next section).

Fasting times should be minimised to avoid dehydration in accordance with national guidance. An effective anti-emetic strategy should be used, which may include prophylactic treatment.

Regional anaesthesia has the advantage of the least interference with the woman’s ability to care for her infant. Local anaesthetic supplementation should be encouraged to reduce the need for systemic analgesics.

Opioids are more likely to be required if general anaesthesia is used. Opioid effects may vary from person to person due to greater or lesser metabolism (pharmacokinetic differences), or from a different sensitivity to the same blood level (pharmacodynamic differences). They are also likely to increase with repeated doses. When using strong opioids during breastfeeding, a woman should observe her infant for a change in behaviour; if sedation and drowsiness develop in the infant, she should withhold breastfeeding and seek medical advice. The order of sensitivity from adverse drug effects of opioids, due to immature hepatic and renal function, decreases from pre-term > neonates > young infants; extra caution should be taken in infants less than 6 weeks of age (corrected for gestation). It is also advisable to seek signs of excessive maternal effects as an indicator of potential infant effects. Dihydrocodeine or morphine are the preferred agents (see below).

Postoperative analgesic strategies will vary depending on the intra-operative management (e.g. less early pain if regional anaesthesia or nerve blocks used). However individual needs for analgesia will also vary. Multimodal analgesia with non-opioid drugs should be encouraged, as paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs; including cyclo-oxygenase-2 inhibitors) are compatible with breastfeeding. Breastfeeding women should have appropriate opioid analgesia, but the lowest effective dose should be used for the shortest period of time [24, 25].

Day surgery is preferable for breastfeeding women [26]; however, additional considerations and support need to be in place if the woman requires an overnight stay.

Transfer to breast milk of drugs used peri-operatively

Lactmed is a useful source for information on individual drugs [2]. Box 2 gives summary information on drug transfer. Detailed pharmacokinetic data are provided in Appendix 1. Appendix 2 gives pharmacokinetic principles involved in drug transfer to breast milk.

Intravenous anaesthetic agents

Most intravenous anaesthetic agents have poor bioavailability and short half-lives [1, 2, 3, 18, 19], so are compatible with use during surgery on a lactating woman. Small amounts remain in body fat stores for 24–48 h, but this does not preclude resumption of normal breastfeeding. A breastfeeding woman may need to take precautions if she

<table>
<thead>
<tr>
<th>Box 2 Transfer to breast milk of drugs used peri-operatively</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drugs used during anaesthesia and after surgery pass in low levels into milk and women can breastfeed as normal after:</td>
</tr>
<tr>
<td>- Anaesthetics: propofol, thiopental, etomidate, ketamine, sevoflurane, isoflurane, desflurane, nitrous oxide and halothane</td>
</tr>
<tr>
<td>- Sedatives: midazolam, single dose diazepam</td>
</tr>
<tr>
<td>- Analgesics: paracetamol, ibuprofen, diclofenac, naproxen, celecoxib, ketorolac, parecoxib, morphine dihydrocodeine, pethidine, remifentanil, fentanyl and alfentanil</td>
</tr>
<tr>
<td>- Local anaesthetics</td>
</tr>
<tr>
<td>- Neuromuscular blockers: suxamethonium, rocuronium, vecuronium, atracurium, neostigmine and sugammadex</td>
</tr>
<tr>
<td>- Anti-emetics: ondansetron, granisetron, cyclizine, prochlorperazine, dexamethasone, metoclopramide and domperidone</td>
</tr>
<tr>
<td>Use with caution while breastfeeding:</td>
</tr>
<tr>
<td>- Tramadol – observe child for unusual drowsiness</td>
</tr>
<tr>
<td>- Oxycodone – greater risk of drowsiness in doses &gt; 40 mg.day$^{-1}$</td>
</tr>
<tr>
<td>Analgesics that are contra-indicated while breastfeeding:</td>
</tr>
<tr>
<td>- Codeine – observe child for unusual drowsiness</td>
</tr>
<tr>
<td>- Aspirin (analgesic doses)</td>
</tr>
</tbody>
</table>
normally co-sleeps with her infant, as her natural responsiveness may be inhibited [27].

Propofol: minimal amounts (0.025%) of propofol are transferred to breast milk. This is not a concern even when propofol is used by infusion for maintenance of anaesthesia. Breastfeeding may be resumed as soon as the woman has recovered sufficiently from general anaesthesia [27].

Thiopental: amounts in milk are very small; no waiting period is required before resuming breastfeeding [28].

Etomidate: rapidly redistributed from the central nervous system. Amounts of etomidate in milk are very small and decrease rapidly. No waiting period is required before resuming breastfeeding.

Ketamine: no data are available on the transfer of ketamine into human milk, but levels are likely to be low. Other induction agents should be used if possible. Ketamine should only be used with careful monitoring during breastfeeding. The woman should be advised to observe the infant for signs of drowsiness and poor feeding, and, if observed, to contact a medical professional. Rapid redistribution from plasma makes adverse effects in the infant unlikely [3].

Volatile agents (sevoflurane, isoflurane, desflurane, nitrous oxide and halothane)
These agents are largely cleared after anaesthesia by exhalation, with some metabolism. Due to their short half-life and rapid clearance, use during anaesthesia will not preclude subsequent breastfeeding.

Sedative agents
Benzodiazepines are used for conscious sedation during procedures, and occasionally as premedication. Lorazepam, midazolam and temazepam are shorter-acting benzodiazepines than diazepam [2].

Midazolam: extensive first-pass metabolism results in low systemic bioavailability after oral doses, so blood levels in the infant after breastfeeding can be expected to be low [20]. Breastfeeding can be resumed after a single dose of midazolam as soon as the woman has recovered from the procedure.

Diazepam: this has an active metabolite, desmethyl-diazepam, which has a prolonged half-life. It is known to be transferred in breast milk in significant levels. Use of diazepam may be considered as a one-off dose before a procedure [2].

Dexmedetomidine: metabolised to inactive metabolites in the liver. Excretion into breast milk is unknown, so should be used with caution. The half-life is 2 h [3].

Analgesic agents
Analgesia should be individualised. If opioid analgesia is required, the lowest effective dose should be used for the shortest time possible.

Paracetamol: although studies show a wide variation in the concentration of paracetamol in breast milk, the amount of paracetamol that an infant would ingest via breast milk is significantly less than the paediatric therapeutic dose.

NSAIDs
Ibuprofen: has been used extensively for postpartum pain and during lactation, and is considered safe to use during breastfeeding.

Diclofenac: small amounts are detected in breast milk. It has been used extensively during lactation and is considered safe to use during breastfeeding.

Naproxen: although it has a longer half-life than diclofenac, naproxen is widely used after caesarean section; breastfeeding may continue as normal.

Celecoxib: the relative dose that infants are exposed to via milk is very low, and breastfeeding may continue.

Dexmedetomidine: metabolised to inactive metabolites in the liver. Excretion into breast milk is unknown, so should be used with caution. The half-life is 2 h [3].
metabolisers will have little analgesic effect from codeine, whereas ultrarapid metabolisers will have very marked
effects and side-effects. There are large ethnic differences in
the frequencies of variant alleles: the proportion of poor
metabolisers is 5–10% of the European Caucasian
population, but lower in Asians; the proportion of ultrarapid
metabolisers is up to 28% in Middle Eastern and Northern
African populations, up to 10% in Caucasian populations,
and up to 1% in Asians [31].

Women who are ultrarapid metabolisers produce
much higher concentrations of morphine in breast milk,
which in extreme cases may lead to severe neonatal
depression and death in the infant [32]. Furthermore,
codeine is secreted in breast milk due to high lipophilicity
and weak protein binding, with the potential for
metabolism by the infant.

In the UK, the Medicines and Healthcare Products
Regulatory Agency (MHRA) suggest that in the majority of
women, codeine taken in moderation and for a short duration
is suitable for the breastfed infant or child [33]. However, due
to the inability to predict which infants may be sensitive, other
bodies such as the US Food and Drug Administration (FDA)
and the European Medicines Agency advise that
breastfeeding women should not take codeine [34, 35].

Because there are other alternative weak opioid analgesics,
we recommend that breastfeeding women should not take
codeine unless the regulatory advice is modified.

If a dose of codeine has been taken by a breastfeeding
woman, then discarding breast milk for 15 h should allow
full clearance from maternal plasma and insignificant
transfer to breast milk thereafter.

Dihydrocodeine: the analgesic effect of
dihydrocodeine appears to be mainly due to the parent
compound. The oral bioavailability of dihydrocodeine is
20% due to substantial first-pass metabolism. The half-life
is quoted as 3.5–5h [21]. It is metabolised in the liver by
CYP2D6 to dihydromorphone, which has potent analgesic
activity. However, the CYP2D6 pathway only represents a
minor route of metabolism, with other metabolic pathways
being involved. The metabolism of dihydrocodeine is not
affected by individual metabolic capacity as the analgesic
effect is produced by the parent drug, in contrast to
codeine which is a prodrug. Dihydrocodeine may be the
preferred weak opioid for postoperative use in the
breastfeeding woman, due to its cleaner metabolism
compared with codeine and wide experience of use after
caesarean section [36], although the NHS Specialist
Pharmacy Service recommend observing the woman for
signs of significant opioid adverse effects [24].

Tramadol: tramadol and its active metabolite O-
desmethyltramadol are excreted into breast milk. There
have been case reports of respiratory depression and death
associated with the use of this medication. The FDA issued a
statement in April 2017 warning against taking tramadol
while breastfeeding [34]. The UKDILAS has reviewed this
statement, and recommended that “despite the FDA
warning, tramadol can continue to be used (with caution)
during breastfeeding”; however, the infant should be
observed for increased sleepiness, signs of respiratory
depression, sedation and decreased alertness [24].

Maternal excess effects may also feature [37]. It is advisable
to restrict the use of tramadol in breastfeeding women to in-
patient use, and limit the total dose.

Oxycodone: breastfed infants may receive > 10% of a
therapeutic dose. It may pose a greater risk of causing infant
sedation than other drugs, and this risk is dose-related.
The metabolism is similar to codeine: poor CYP2D6
metabolisers may have decreased clearance of oxycodone,
and ultrarapid metabolisers higher concentrations of the
more potent metabolite oxymorphone, leading to sedation.

Multiple case reports and studies have reported sedation,
respiratory depression and difficulty feeding in infants
exposed to oxycodone via breast milk, especially at doses
> 30 mg.day\(^{-1}\) [2, 38]. As with any opioids, caution should
be used when giving oxycodone as a single dose intra-
operatively, and the infant monitored for sedation after
breastfeeding. Maternal excess effects may also feature.
Repeated dosing of oxycodone should be avoided when
breastfeeding.

Hydromorphone: a potent narcotic analgesic. There
are limited data. Use of intra-nasal hydromorphone
produced low levels in breast milk [39]. However, there is a
report that a 6-day-old baby exposed to 4 mg every 4 h
exhibited respiratory depression and needed to be treated
with naloxone, after which it recovered [40]. This drug
should be used with caution in breastfeeding women.

Pethidine: this has a long-acting metabolite,
nornercuridine. However, after a single dose, breastfeeding
may continue as soon as the woman is awake and alert.

Remifentanil: there are no published data on
maternally administered remifentanil use and its effect on
the breast-fed infant. Remifentanil patient-controlled
analgesia is used for labour analgesia in preference to other
opioids, due to a short context sensitive half-life of < 10 min
and minimal neonatal sedation [41, 42]; it can therefore be
considered acceptable in lactating women. Low
bioavailability via the oral route.

Fentanyl: alfentanil: after a single dose of fentanyl
intravenously, minimal amounts are detected in breast milk.
Low bioavailability via the oral route. Breastfeeding is considered acceptable following single doses of fentanyl to the woman. This is also extrapolated to alfentanil [5].

**Other analgesics**

Clonidine may reduce prolactin secretion and therefore could conceivably reduce milk production in the early postpartum period. It is minimally secreted into milk. There are no reports of neonatal toxicity during breastfeeding.

**Local anaesthetics**

These amino amide compounds are lipid soluble. They may be secreted in small amounts in breast milk. As local anaesthetics are commonly used during labour analgesia or obstetric anaesthesia, there has been extensive investigation on possible neonatal effects secondary to direct placental transfer, with no evidence of harm. Local anaesthetics can be used in lactating women with no need to interrupt breastfeeding.

**Neuromuscular blocking drugs**

Non-depolarising neuromuscular blocking drugs are quaternary ammonium compounds with poor lipid solubility and poor oral bioavailability. They are ionised at physiological pH and will not be present in milk in significant amounts [6].

- Suxamethonium: unlikely to be present in breast milk in significant amounts as it is ionised at physiological pH; poor oral absorption with rapid elimination from maternal circulation. Breastfeeding may be resumed once the woman has recovered from neuromuscular block [21].

**Neuromuscular blocker reversal drugs**

Neostigmine: a quaternary ammonium compound with a half-life of 15–30 min. The amount transferred to breast milk is probably too small to be harmful [21].

- Sugammadex: no information is available on the clinical use of sugammadex during breastfeeding. Animal studies have shown excretion of sugammadex in breast milk. Because sugammadex is a large, highly polar molecule, the amount in milk is likely to be very low and oral absorption by the infant is unlikely [43]. Sugammadex is acceptable to use during breastfeeding. After administration of sugammadex, patients taking oral hormonal contraceptives must be advised to follow ‘missed pill rules’.

**Anti-emetics**

- Ondansetron: there are no studies on transfer into breast milk, although there are data from animal studies. It has been reported as being compatible with use in lactating women, although the license suggests that it should be avoided in breastfeeding. It has a licence for use in children from 6 months of age; the exposure of the infant through breast milk will be lower than when it is directly administered.

  - Granisetron: no data are available on its transfer into human milk; levels are likely to be low.

  - Cyclizine: there are no reports of levels entering breast milk or data on which to base conclusions. Unlikely to produce adverse effects if used short term.

  - Prochlorperazine: oral bioavailability is low due to high first-pass metabolism. It is compatible with use during breastfeeding.

  - Dexamethasone: no data are available on the transfer of dexamethasone into human milk. Other corticosteroids have been used extensively during breastfeeding with no evidence of any effects.

  - Metoclopramide: also used as a galactagogue, so may increase milk supply. It may be used in lactating women.

  - Domperidone: when taken orally, levels in milk are low due to first-pass hepatic and intestinal metabolism. Used as a galactagogue, so may increase milk supply; ensure the woman has access to a breast pump if there is any delay in feeding her infant.

**Cardiovascular drugs**

- Atropine: a tertiary amine, rapidly absorbed from the gastrointestinal tract and found in trace concentrations in breast milk; may have antimuscarinic effects in the infant. Lactation may be inhibited. Compatible with breastfeeding.

  - Glycopyrronium: a quaternary ammonium compound which does not readily cross the central nervous system membrane barriers. Poor bioavailability, probably preferred antimuscarinic. Compatible with breastfeeding.

  - Ephedrine: on an acute basis it is not likely to harm a breastfeeding infant.

  - Phenylephrine: due to poor oral bioavailability of 38%, it is not likely to produce clinical effects in a breastfed infant.

**Antibiotics**

Short courses of antibiotics are commonly used perioperatively. There is no evidence of harmful effects in breastfeeding women. For detailed information please consult Lactmed [2] or sources in Appendix 3.

**Supportive care**

The UNICEF Baby Friendly Initiative [14] encourages support for women to continue breastfeeding. Points
related to supportive care for women are shown in Box 3. Women who are having an operation will have the normal peri-operative anxieties and concerns, as well as disruption of their normal breastfeeding routines.

It is important, therefore, that the hospital provides a suitable environment for breastfeeding; this is likely to include a single room where family members can accompany her, attention to minimising the time that she is in the theatre suite, and timing the surgery so that she can feed the infant just before leaving the ward for surgery. A specific hospital guideline will make it easier to accommodate all these factors.

Staff who are trained in breastfeeding support should be available to help if required, including help with expressing milk if there is a prolonged separation. A breast pump should be available, if required, to reduce the risk of developing mastitis.

Women should be given advice on who to contact with queries once they leave the hospital. Day case surgery guidelines have previously advised that a patient is accompanied for 24 h by a responsible adult, but this requirement is currently being questioned [44]. However, this policy should still be encouraged for breastfeeding women.

Breastfeeding women should be cautious if co-sleeping, or sleeping while feeding the infant in a chair, because she may not be as responsive as normal.

Women should be advised on a strategy for tailing off analgesic medication that includes stopping opioid medication first, then NSAIDs, and finally paracetamol.

Appendix 3 gives links to further information for professionals and patients, and Appendix S1 in the online Supporting Information shows a sample patient information leaflet.

In summary, the pharmacological aspects of anaesthesia and sedation require little alteration in breastfeeding women. However, supportive care for the woman in the peri-operative period, and accurate advice, will ensure minimal disruption to this important part of childcare.

Acknowledgements
We would like to thank K. Allegaert for his helpful comments. These guidelines were sent for consultation to the Medicines and Healthcare Products Regulatory Agency and UNICEF, besides the endorsing supporting organisations. WJ is the author of Breastfeeding and Medication [20], and owner of the website www.breastfeeding-and-medication.co.uk. No other competing interests declared.

References
## Appendix 1
Pharmacokinetic information for anaesthetic and other drugs [2, 3, 20, 21]

<table>
<thead>
<tr>
<th></th>
<th>Plasma protein binding</th>
<th>Milk:plasma ratio (aim &lt; 1)</th>
<th>Half-life</th>
<th>Relative infant dose (aim &lt; 10%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous anaesthetics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propofol</td>
<td>99%</td>
<td>0.3–0.4</td>
<td>1–3 days</td>
<td>4.4</td>
</tr>
<tr>
<td>Thiopental</td>
<td>60–96%</td>
<td>0.3–0.4</td>
<td>3–8 h</td>
<td>1.77–5.94</td>
</tr>
<tr>
<td>Etomidate</td>
<td>76</td>
<td>0.3–0.4</td>
<td>3–8 h</td>
<td>1.77–5.94</td>
</tr>
<tr>
<td>Ketamine</td>
<td>47%</td>
<td>0.3–0.4</td>
<td>3–8 h</td>
<td>1.77–5.94</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Midazolam</td>
<td>97%</td>
<td>0.15</td>
<td>3 h</td>
<td>0.63</td>
</tr>
<tr>
<td>Diazepam</td>
<td>99%</td>
<td>0.2–2.7</td>
<td>43 h</td>
<td>0.88%–7.14%</td>
</tr>
<tr>
<td>Analgesics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paracetamol</td>
<td>10–25%</td>
<td>0.91–1.42</td>
<td>2 h</td>
<td>6.41%–24.23%</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>&gt;99%</td>
<td>0.84–1.59</td>
<td>1.85–2 h</td>
<td>0.1–0.7</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>99.70%</td>
<td>0.84–1.59</td>
<td>1.1 h</td>
<td>0.3–0.7</td>
</tr>
<tr>
<td>Naproxen</td>
<td>99.70%</td>
<td>0.84–1.59</td>
<td>12–15 h</td>
<td>0.3–0.7</td>
</tr>
<tr>
<td>Celecoxib</td>
<td>97%</td>
<td>0.84–1.59</td>
<td>11 h</td>
<td>0.3–0.7</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>80–85%</td>
<td>0.84–1.59</td>
<td>2–4 h</td>
<td>1.9–5</td>
</tr>
<tr>
<td>Alfentanil</td>
<td>92%</td>
<td>0.84–1.59</td>
<td>2–4 h</td>
<td>0.26–0.4%</td>
</tr>
<tr>
<td>Morphine</td>
<td>92%</td>
<td>0.84–1.59</td>
<td>3–8 h</td>
<td>0.26–0.4%</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>45%</td>
<td>0.84–1.59</td>
<td>3–8 h</td>
<td>0.26–0.4%</td>
</tr>
<tr>
<td>Tramadol</td>
<td>80–85%</td>
<td>0.84–1.59</td>
<td>1–2 h</td>
<td>0.26–0.4%</td>
</tr>
<tr>
<td>Dihydrocodeine</td>
<td>8–19%</td>
<td>2.4</td>
<td>7 h</td>
<td>2.86</td>
</tr>
<tr>
<td>Codeine</td>
<td>7%</td>
<td>1.35–2.5</td>
<td>2.9 h</td>
<td>0.6–8.1%</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>8–19%</td>
<td>2.56</td>
<td>2.6 h oral and i.v.</td>
<td>0.67</td>
</tr>
<tr>
<td>Anti-emetics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ondansetron</td>
<td>70–75%</td>
<td>2.5</td>
<td>3–4 h</td>
<td>0.67</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>70–75%</td>
<td>2.5</td>
<td>3–6 h</td>
<td>0.67</td>
</tr>
<tr>
<td>Domperidone</td>
<td>70–75%</td>
<td>2.5</td>
<td>3–4 h</td>
<td>0.67</td>
</tr>
</tbody>
</table>

i.v. intravenous
Appendix 2
Pharmacokinetic terms and implications

The information below is based on information from Breastfeeding and Medication [20] but should not be further reproduced without further permission from the author.

Oral bioavailability
The oral bioavailability of a drug is the percentage of the drug absorbed into the system having passed through the gut, liver or lungs. First-pass metabolism will reduce the availability. Most drugs given by injection only (i.e. there is no oral formulation available) have poor bioavailability, for example, insulin, heparin.

First-pass metabolism
Drugs which are inactivated by first-pass metabolism are preferred for use during lactation.

Active metabolites
The half-life of active metabolites needs to be taken into consideration where necessary.

Plasma protein binding
When drugs enter the maternal bloodstream following absorption, they either become bound to plasma proteins or remain free. Only the free part of the drug is able to penetrate the biological membranes. The more drug that is bound, the less is free to diffuse. Some drugs compete for binding sites normally occupied by bilirubin in the first week after birth.

Milk: plasma ratio
This measurement refers to the concentration of the protein-free fractions in milk and plasma. Any ratio > 1 implies that the drug may be unsuitable to be prescribed for a lactating woman. This ratio is not available in standard texts such as the BNF, but may be found in specialist texts.

Molecular weight
The larger the molecule, the harder it is for it to pass into breast milk.

Drug half-life
The longer the half-life of a drug, the greater the risk of accumulation in the woman and in the infant. The half-life of a drug is defined as the time taken for the serum concentration to decrease by 50%. It is determined by the rate of absorption, metabolism and excretion. Five half-lives have to elapse before steady state is reached. After this period, timing feeds to avoid peak levels has a minimal effect. Similarly, after five half-lives without further medication, almost all (98%) of the drug has been eliminated from the body. Neonates do not metabolise medication as fast as adults, due to immaturity of the liver.

Therapeutic range
If the level of the drug that reaches the infant comes into the therapeutic range, it would have the expected effect of that drug on the infant. If the level exceeds the maximum therapeutic concentration, side-effects would be noted in the infant. However, as in the vast majority of cases the amount of drug passing through breast milk is below the therapeutic level for that drug, no effect will be seen.

Relative infant dose
The relative infant dose is being increasingly recognised as a valuable guide to the safety of a drug taken by a breastfeeding woman. A drug with proportion < 10% is considered to be the preferred option.

Relative infant dose = \( \frac{\text{dose in the infant (mg)}}{\text{dose in the woman (mg/kg/day)}} \)

Doses can be obtained from e.g. Hale [3].

Theoretical dose calculation
Dose calculation of drug ingested by an infant can be calculated if the milk: plasma ratio is known, in conjunction with the volume of milk ingested.

\[
\text{Dose} = C \times \frac{(M/P)}{V} \\
C = \text{total dose of drug ingested by infant (mg)} \\
(M/P) = \text{milk/plasma concentration ration} \\
V = \text{volume of milk ingested by the infant (l)}
\]

This assumes that all the ingested drug is absorbed; however, many drugs have low oral bioavailability, which is a protective factor.

Summary of points to determine when a drug is likely to be compatible with use during breastfeeding
- relative infant dose < 10%
- Milk: plasma ratio < 1
- plasma protein binding > 90%
- molecular weight of the drug > 200
- poor oral bioavailability
- short half-life of active metabolites
- drug is licensed for paediatric use
Appendix 3
Resources for professionals and patients

- **UK Drugs in Lactation Advisory Service (UKDILAS)** provides evidence-based information to all UK healthcare professionals on the use of drugs during the breastfeeding period [24]. The service is provided via the UK Medicines Information Network by the Trent and West Midlands Regional Medicines Information Centres.
  
  https://www.sps.nhs.uk/category/usage/safety-in-lactation-usage
  https://www.sps.nhs.uk/articles/ukdilas/

- **Drugs and Lactation Database (LactMed)** is a database sponsored by the USA National Library of Medicine which contains information on maternal and infant levels of drugs, possible effects on breastfed infants and any effect on lactation [2].
  

- **The Breastfeeding Network** provides evidence-based information regarding breastfeeding and medication, and is a useful resource for patients and staff. The information is provided by qualified pharmacists who are also trained breastfeeding supporters.
  
  https://www.breastfeedingnetwork.org.uk/drugs-fact-sheets

- Available texts include:
  
  Hale TW. *Medications and Mothers Milk*. New York: Springer Press, 2017. (Also available as online access by subscription www.halesmeds.com)[2].
  

Supporting Information
Additional supporting information may be found online via the journal website.

Appendix S1. Patient information leaflet.
Safer, for everyone

Every anaesthetist aims to keep their patients safe. We aim to safeguard every anaesthetist - by educating, supporting and inspiring them throughout their career.

We represent the life-changing, life-saving profession of anaesthesia - by supporting, informing and inspiring a worldwide community of over 11,000 members.

Our work and members span the globe, yet our voice is local and personal. We stay in close contact with our members, look after their day-to-day wellbeing, and act as their champion.

Our world-class conferences, journal and online resources educate and inform, and our respected guidelines continually improve standards of patient safety.

We preserve and learn from the history of anaesthesia. We use that to inform the present, and facilitate vital research and innovation into its future.

As an independent organisation, we speak up freely and openly for the interests of anaesthetists and their patients. We influence policy, raise public awareness and are at the forefront of safer anaesthesia across the world.