Prof. Dr. med. Anne Leuppi-Taegtmeyer, PhD, MRCP(UK)
anne.leuppi-taegtmeyer@usb.ch

Peri-operative drugs and breastfeeding

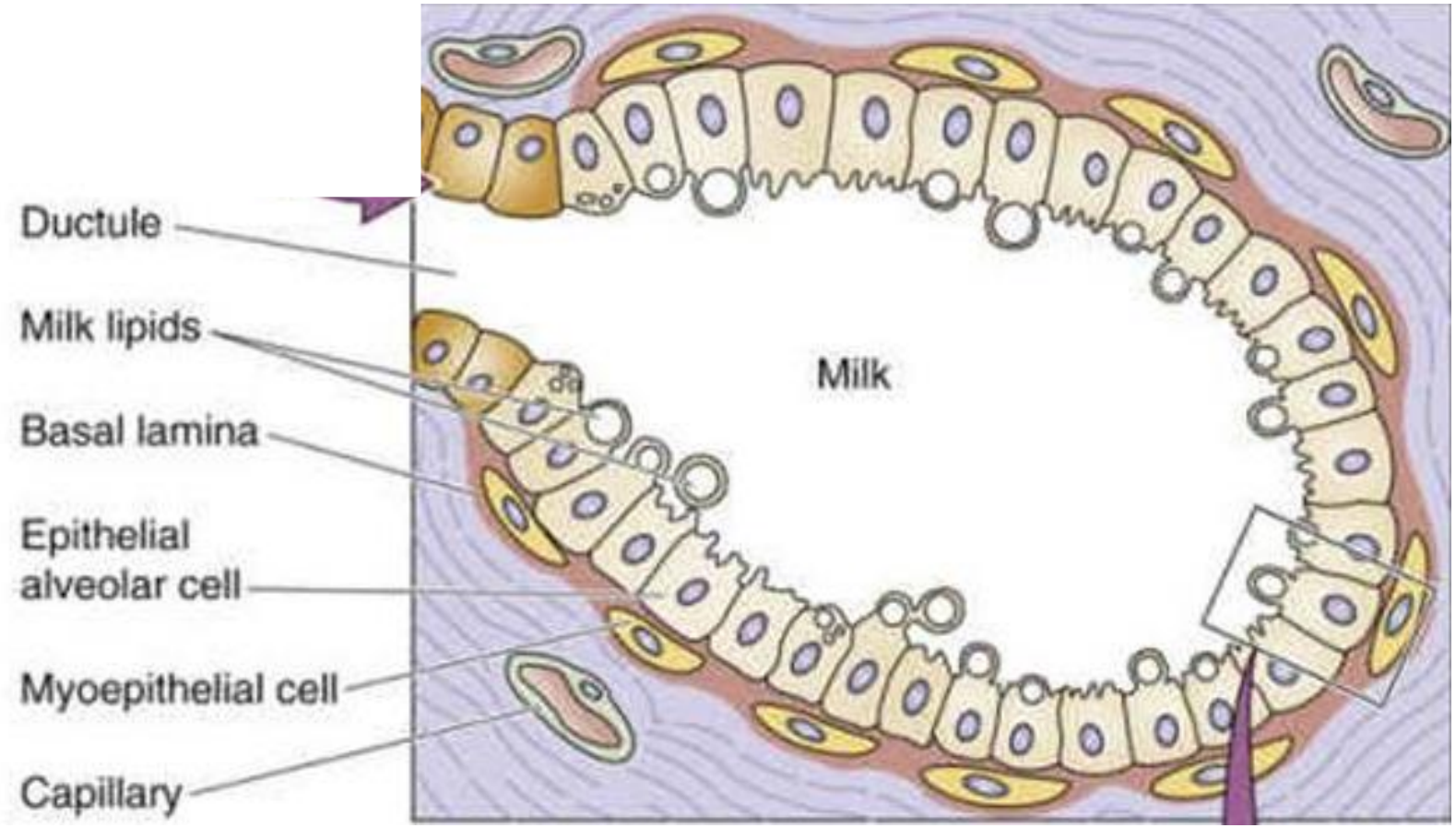
SAOA 07.05.2022

Outline

1. Lactation and drugs
2. Commonly used peri-operative drugs
3. Recommendations
4. Resources
5. Pharmacovigilance

1. Lactation and drugs

Breast milk



https://doctorlib.info/physiology/medical/319.html

Transferability of drugs into breast milk

- Drug characteristics:
  - Small (MW < 500 D)
  - Low protein binding
  - Fat soluble, basic molecules – «trapping» (milk pH 6.35 – 7.35)
- Measures of transferability and exposure:

  Maternal milk-plasma quotient
  - > 1 = accumulation in milk
  - Range 0 – 4

  Relative infant dose (%) *=% of maternal dose ingested (per kg body weight)*

  < 10% = considered safe

Breastfeeding and pharmacology

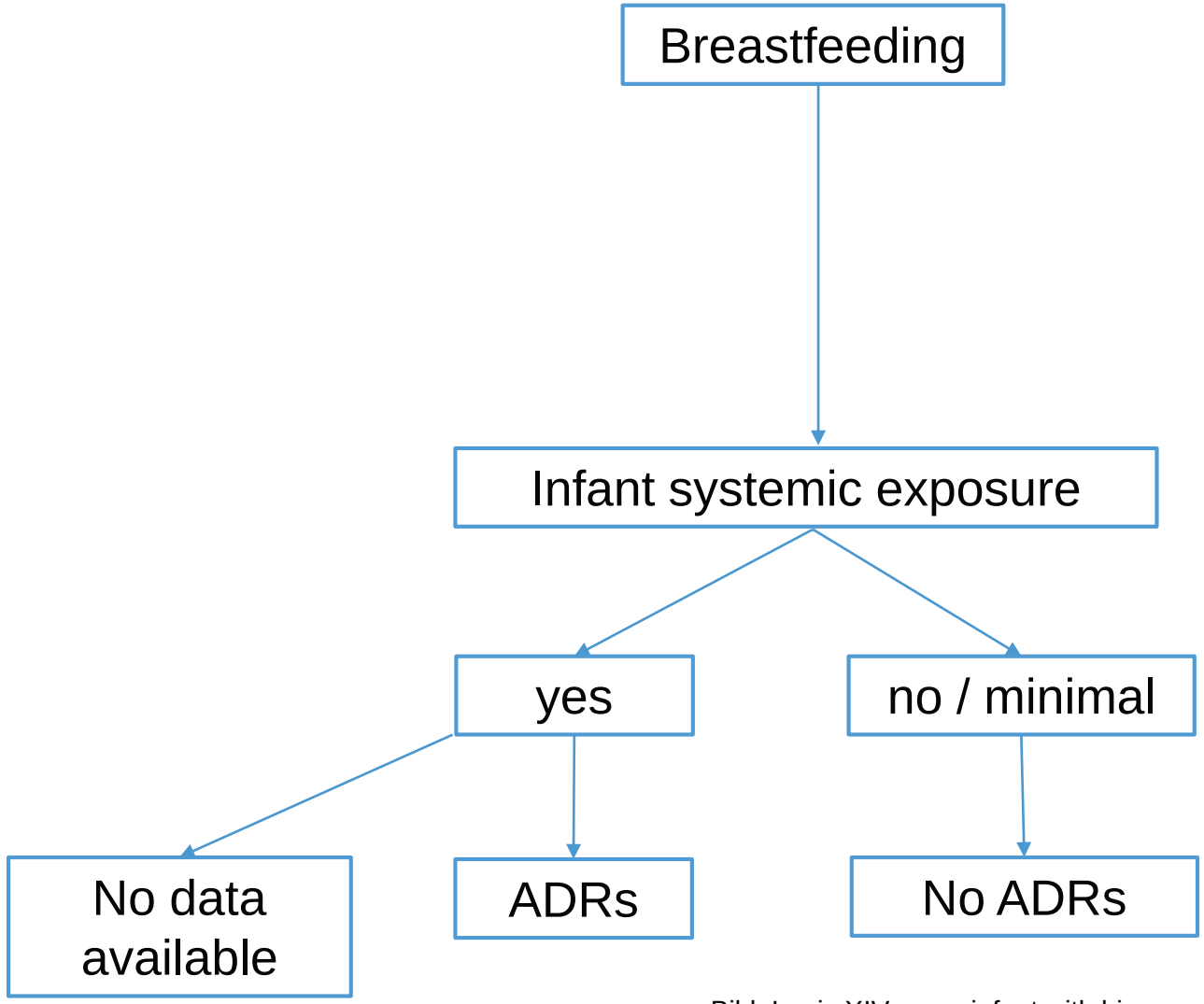


Bild: Louis XIV as an infant with his nurse Longuet de la Giraudière, Charles Beaubrun

Breastfeeding and pharmacology

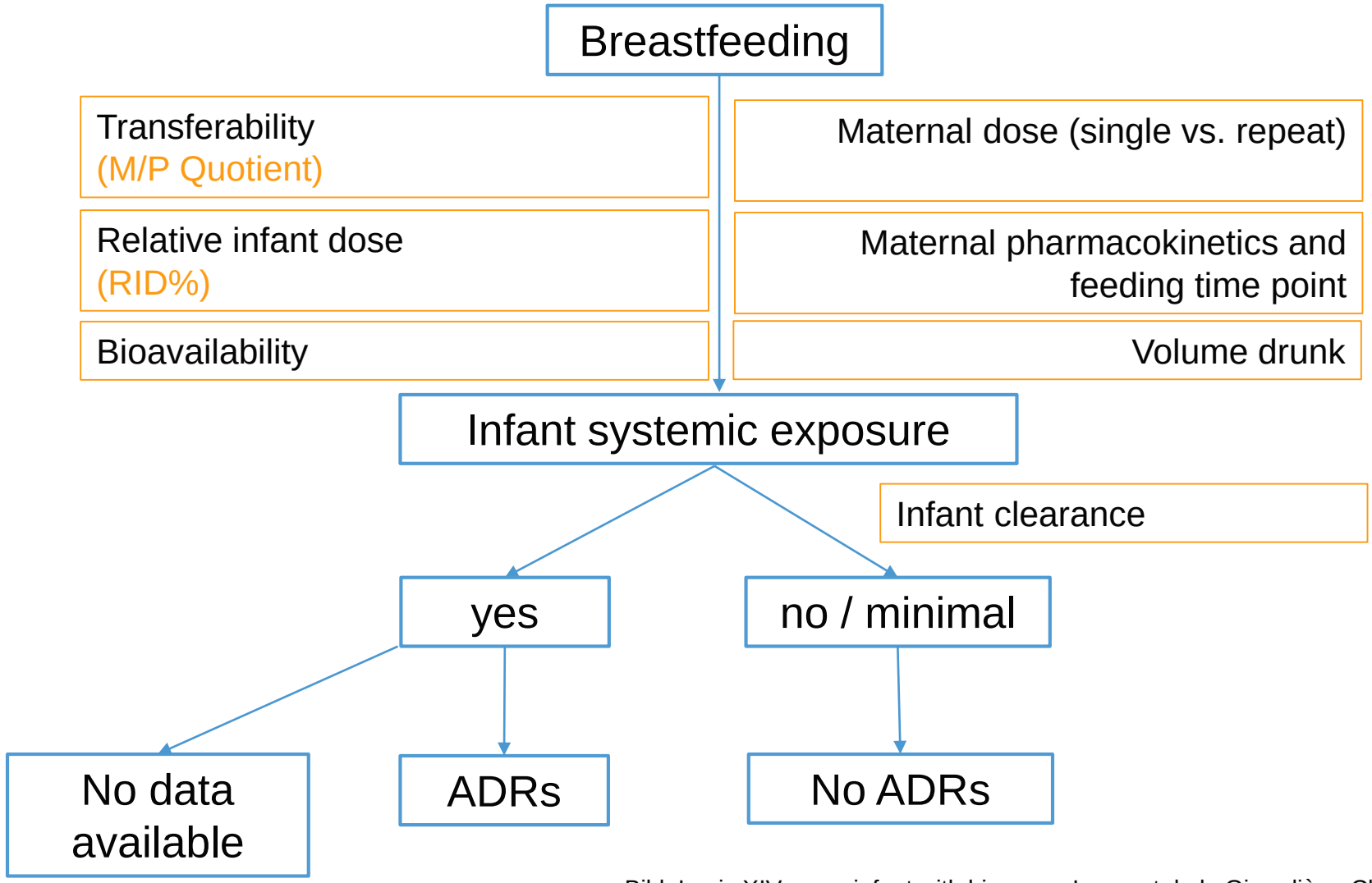
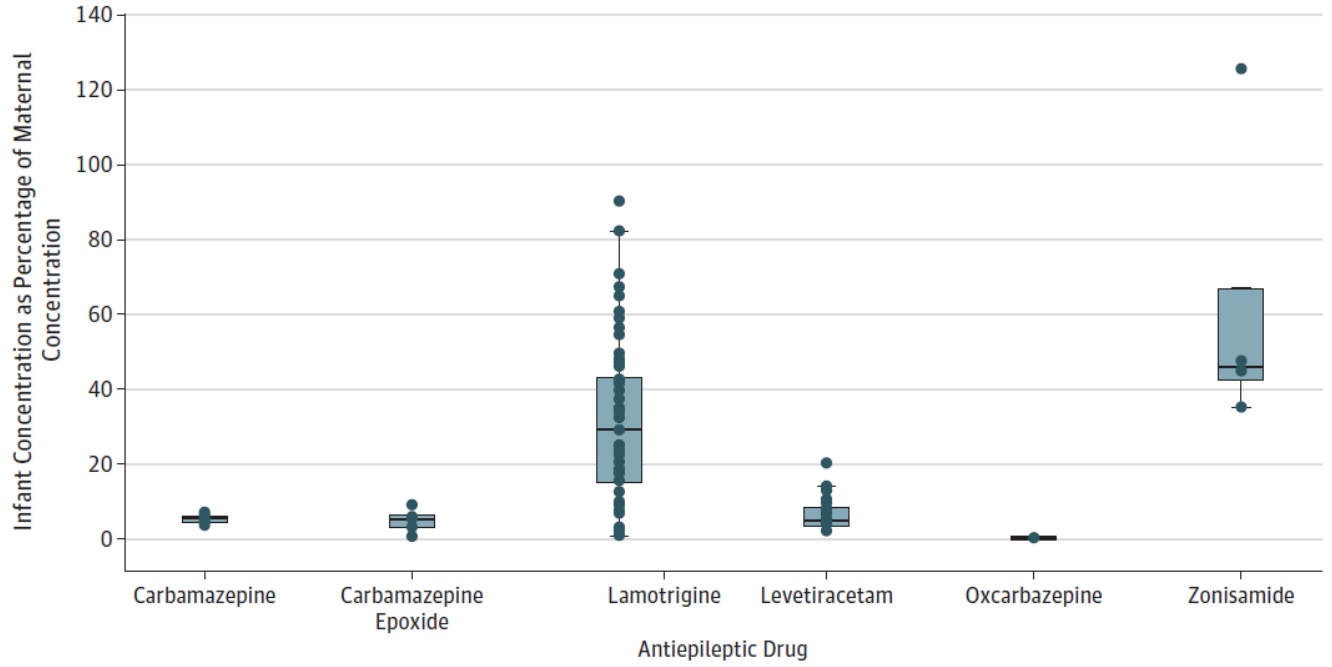


Bild: Louis XIV as an infant with his nurse Longuet de la Giraudière, Charles Beaubrun

Infant systemic AED exposure compared to M/P

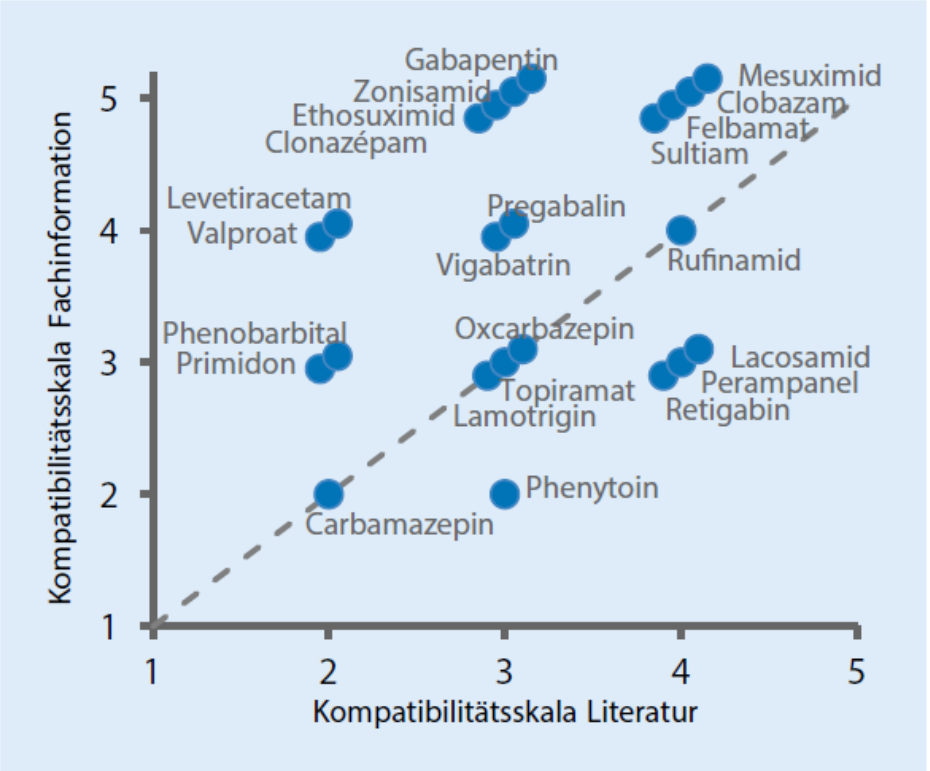
Figure 1. Box Plots



M/P	0 – 2	0 – 3	0.2 – 1	1 – 3	< 1	0.4 - 1

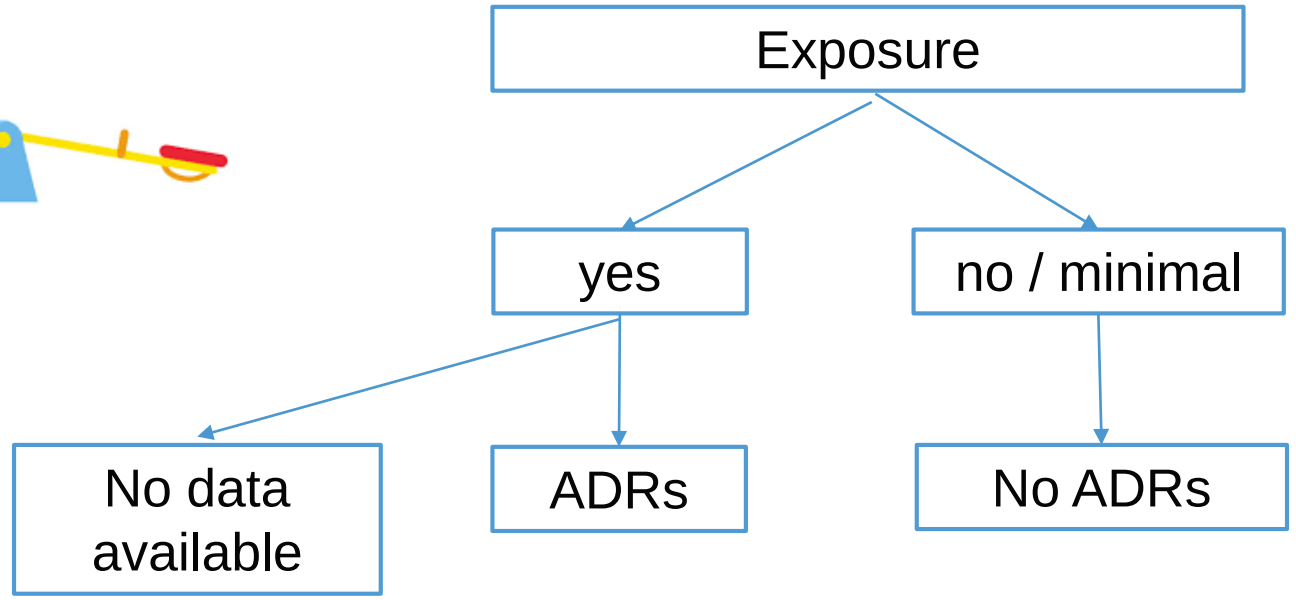
Birnbaum AK, et al JAMA Neurol. 2020 Apr 1;77(4):441-450.

Product label vs. literature AED and breastfeeding compatibility



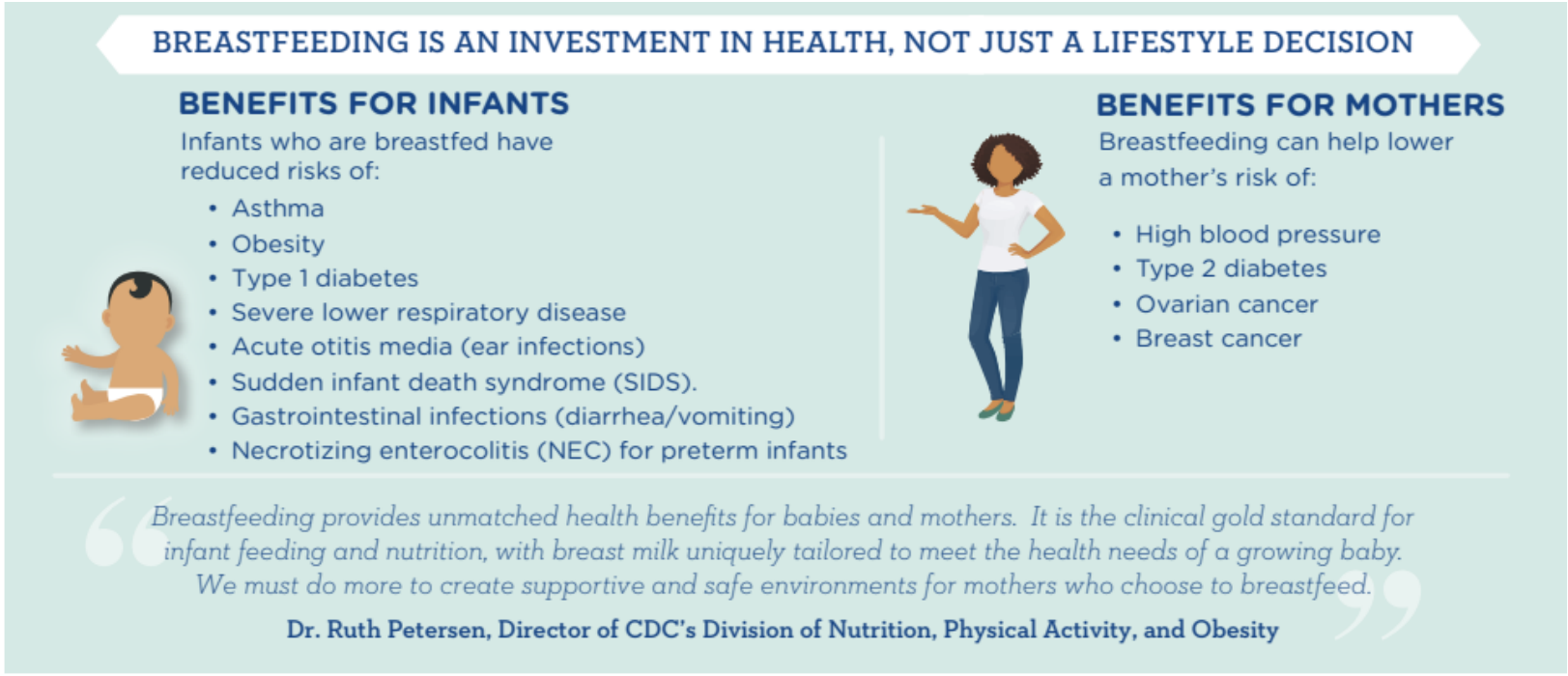
Crettenand M, et al. Nervenarzt. 2018 Aug;89(8):913-921.

How to proceed: pharmacologists` pragmatic approach



Caution advised Breastfeeding unsafe Breastfeeding safe

The importance of breastfeeding



- Human milk is best nutrition for infants.
- Contact with healthcare potential risk factor for early weaning
- Rapid decrease in milk production with missed feedings possible

2. Commonly used peri-operative drugs

Intravenous anesthetic agents

Drug	M/P Quotient	RID	Recommendation
Propofol	< 1	0.025%	Compatible
Etomidate	1.2	n/a	Compatible
Ketamine	n/a – likely low	n/a	Prefer alternative

Volatile anesthetic agents

- Sevofluarne, isoflurane, desflurane, nitrous oxide, halothane
- Rapid clearance (short half-lifes)
- Compatible

Paralytic and reversal agents

- Depolarising and non-depolarising neuromuscular blocking agents: compatible
- Reversal agents (neostigmine, glycopyrrolate): compatible

Local anesthetics

- Lidocaine, bupivacaine and ropivacaine: compatible

Opioid analgesics (narcotics)

Drug	M/P Quotient	RID	Bioavail.	Recommendation
Fentanyl	n/a	0.033%	n/a	SIngle i.v. or epidural doses compatible
Remifentanil	n/a	n/a	n/a	Compatible
Hydromorphone	2.57	0.67%	32%	Prefer alternative
Morphine	1.1 – 3.6	0.8 - 12%	26%	Prefer alternative
Oxycodone	n/a	3%	87%	Do not use – CYP2D6
Codeine	n/a	n/a	90%	Do not use – CYP2D6
Tramadol	n/a	n/a	70%	Do not use – long-acting active metabolite
Pethidine	2.3	n/a	n/a	Do not use – long-acting active metabolite

Benzodiazepines

Drug	M/P Quotient	RID	Bioavail.	Recommendation
Midazolam	0.15	n/a	27%	Single dose
Lorazepam	0.15 - 0.26	n/a	90%	Single dose
Diazepam	0.1 – 0.58	n/a	99%	Single dose – long half-life

Nonsteroidal anti-inflammatory drugs

- NSAIDs, coxibs and Paracetamol all compatible **except**
  - Aspirin in analgesic doses – Reye`s syndrome risk
  - infants with PDA

Antiemetics

Drug	M/P Quotient	RID	Bioavail.	Recommendation
Metoclopramide	n/a	n/a	70%	Compatible - secretagogue
Domperidone	n/a	n/a	15%	Compatible - secretagogue
Ondansetron	n/a	n/a	70%	Compatible
Dexamethason	n/a	n/a	85%	Compatible (? suppresses lactation)

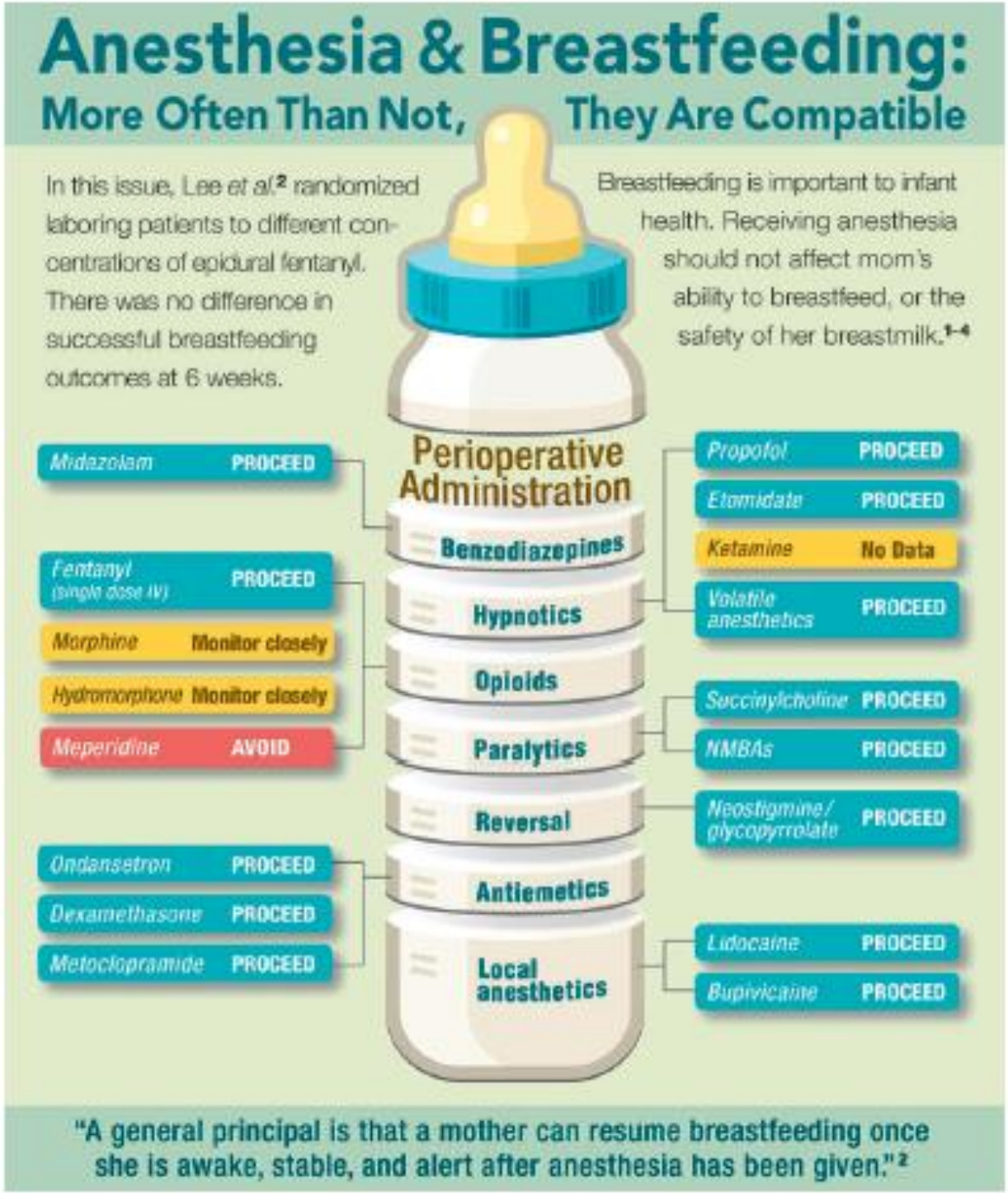
3. Recommendations

Shift during past decade

«Pump and dump» for 24 h post anesthesia

Feed once awake enough post anesthesia

Infographic
Anesthesiology 2017



ASA Statement 2019

American Society of Anesthesiologists™

Statement on Resuming Breastfeeding after Anesthesia

Committee of Origin: Obstetric Anesthesia

(Approved by the ASA House of Delegates on October 23, 2019)

The American Society of Anesthesiologists (ASA) offers this statement to provide anesthesiologists with evidence based information so they may appropriately counsel nursing mothers undergoing surgery who are concerned about adverse neonatal effects from medication exposure via breastmilk. The committee reviewed existing guidelines and reviews on the concentration of anesthetic drugs in breast milk to produce the overview and recommendations included in this statement.[1-6]

ASA Statement 2019

1. All anesthetic and analgesic drugs transfer to breastmilk; however, only small amounts are present and in very low concentrations considered clinically insignificant.
2. Narcotics and/or their metabolites may transfer in slightly higher levels into breastmilk; therefore, steps should be taken to lower narcotic requirements by adding other analgesics when appropriate and avoiding drugs that are more likely to transfer (i.e., have a higher RID).
3. Because pain interferes with successful breastfeeding, women should not avoid pain medicines after surgery. Despite an excellent safety record, breastfeeding women who require narcotic pain medicines should always watch the baby closely for signs of sedation: difficult to wake and/or slowed breathing.

ASA Statement 2019

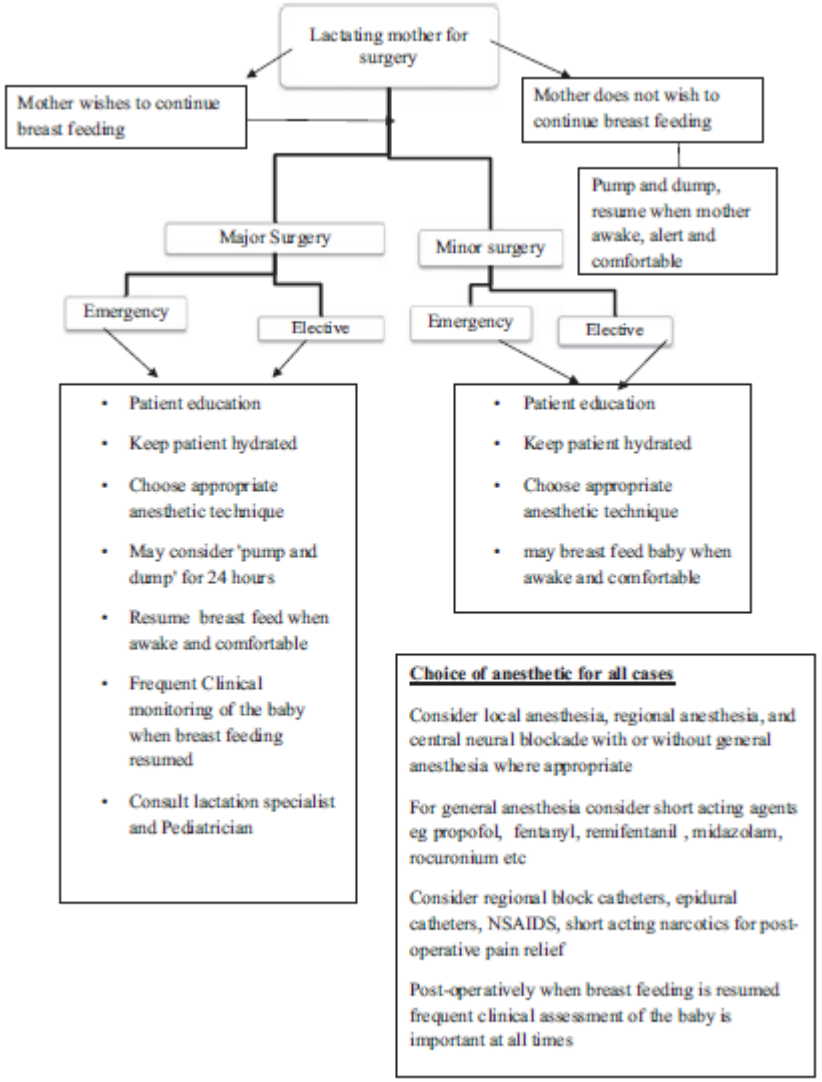
4. When possible, spinal or epidural anesthesia consisting of local anesthetic and a long- acting narcotic, should be used for cesarean delivery to reduce overall post-operative pain medication requirements.
5. Patients should resume breastfeeding as soon as possible after surgery because anesthetic drugs appear in such low levels in breastmilk. It is not recommended that patients “pump and dump.”

Further recommendations

- Consider local anesthesia, regional anesthesia, and central neural blockade with or without general anesthesia where appropriate
- For general anesthesia consider short acting agents eg propofol, fentanyl, remifentanil , midazolam, rocuronium
- Consider regional block catheters, epidural catheters, NSAIDS, short acting opioids for postoperative pain relief
- Frequent clinical assessment of the baby
- No iodine contrast agents
- Multidisciplinary and interprofessional approach

Dalal PG, Bosak J, Berlin C. Safety of the breast-feeding infant after maternal anesthesia. Paediatr Anaesth. 2014 Apr;24(4):359-71. doi: 10.1111/pan.12331. Epub 2013 Dec 24. PMID: 24372776

Management pathways



Dalal PG, Bosak J, Berlin C. Safety of the breast-feeding infant after maternal anesthesia. Paediatr Anaesth. 2014

Sloan Kettering Postoperative Lactation Program

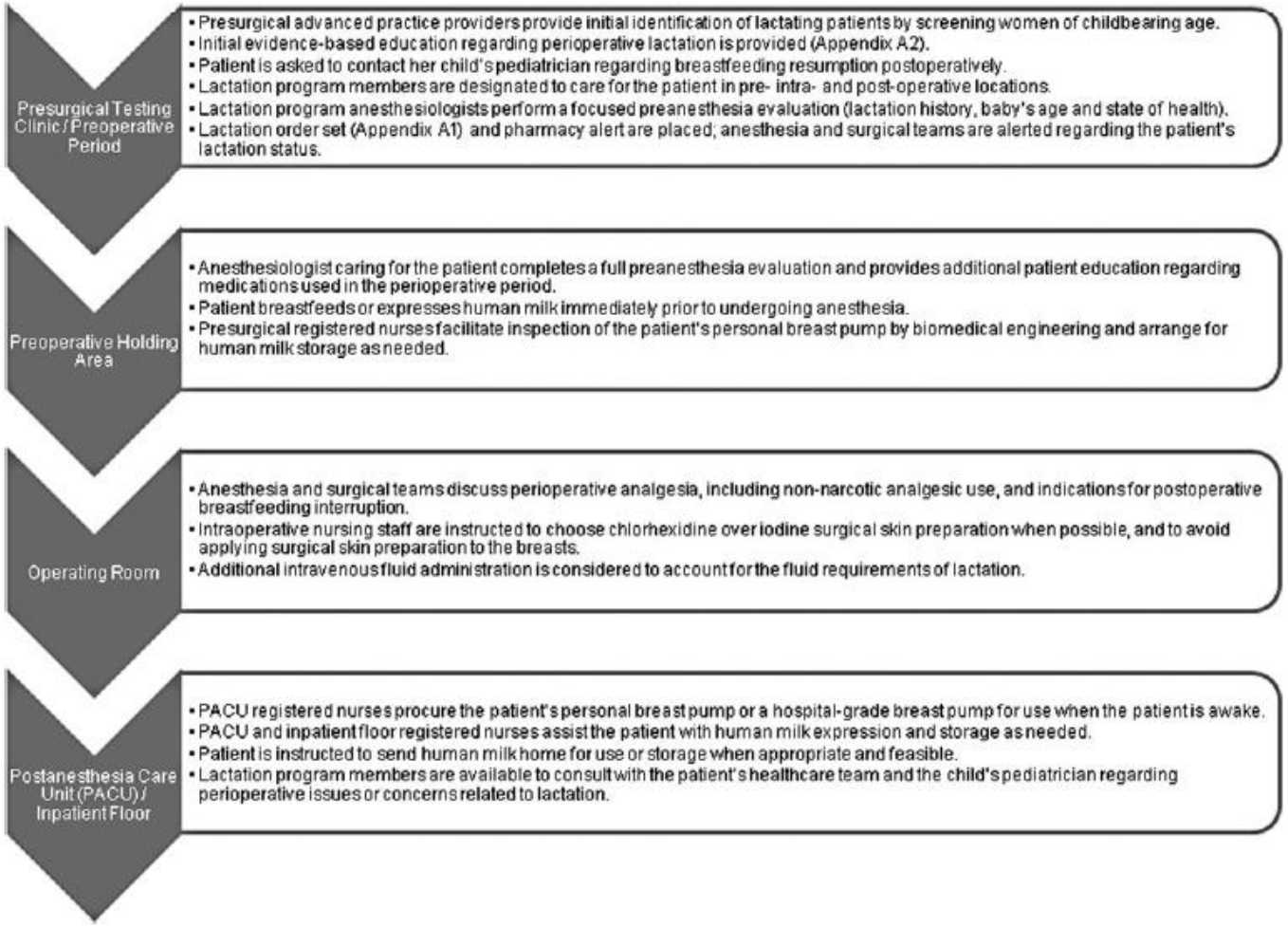
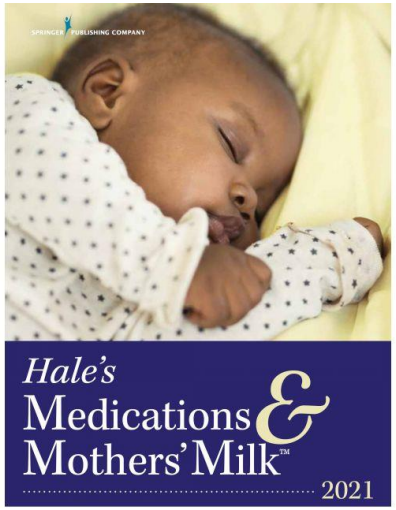


FIG. 1. Workflow for care of the lactating patient in the perioperative period.

4. Resources

Resources

- Drugs and lactation database: LactMed
- embryotox.de
- Medsafe NZ
- Swiss Teratogen Information Service (STIS)
- Swiss Academy of Perinatal Pharmacology (SAPP)



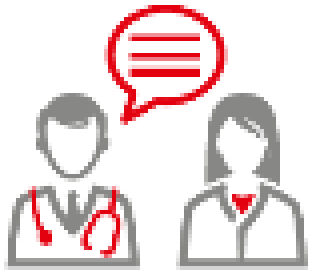
Brigg`s Drugs in Pregnancy and Lactation, 12th Edition 2021

5. Pharmacovigilance

Pharmacovigilance reporting duty

HMG Art. 59 und AMV Art. 63/66/Anhang 3; 1.1.2019:

Personen, die Arzneimittel berufssmässig anwenden oder abgeben oder als Medizinalperson dazu berechtigt sind haben eine **Meldepflicht, unerwünschte Arzneimittelwirkungen bei der Behörde zu melden.**



Swissmedic Meldeformular

Elektronisches Vigilance-Meldeportal ElViS

https://www.swissmedicinfo.ch/

Summary

1. Lactation and drugs
2. Commonly used peri-operative drugs
3. Recommendations
4. Resources
5. Pharmacovigilance

References

Jonathan P. Wanderer, James P. Rathmell; Anesthesia & Breastfeeding: More Often Than Not, They Are Compatible. *Anesthesiology* 2017; 127:A15

Amy I. Lee, Robert J. McCarthy, Paloma Toledo, Mary Jane Jones, Nancy White, Cynthia A. Wong; Epidural Labor Analgesia—Fentanyl Dose and Breastfeeding Success: A Randomized Clinical Trial. *Anesthesiology* 2017; 127:614–624

Dalal PG, Bosak J, Berlin C. Safety of the breast-feeding infant after maternal anesthesia. Paediatr Anaesth. 2014 Apr;24(4):359-71. doi: 10.1111/pan.12331. Epub 2013 Dec 24. PMID: 24372776.

Simon JA, Carabetta M, Rieth EF, Barnett KM. Perioperative Care of the Breastfeeding Patient. AORN J. 2018 Apr;107(4):465-474. doi: 10.1002/aorn.12101. PMID: 29595905.

Rieth EF, Barnett KM, Simon JA. Implementation and Organization of a Perioperative Lactation Program: A Descriptive Study. Breastfeed Med. 2018 Mar;13(2):97-105. doi: 10.1089/bfm.2017.0193. Epub 2017 Dec 22. PMID: 29271670; PMCID: PMC5863089.

Cobb B, Liu R, Valentine E, Onuoha O. Breastfeeding after Anesthesia: A Review for Anesthesia Providers Regarding the Transfer of Medications into Breast Milk. Transl Perioper Pain Med. 2015;1(2):1-7. PMID: 26413558; PMCID: PMC4582419.

Mitchell J, Jones W, Winkley E, Kinsella SM. Guideline on anaesthesia and sedation in breastfeeding women 2020: Guideline from the Association of Anaesthetists. Anaesthesia. 2020 Nov;75(11):1482-1493. doi: 10.1111/anae.15179. Epub 2020 Aug 1. PMID: 32737881.

Statement on Resuming Breastfeeding after Anesthesia. https://www.asahq.org/standards-and-guidelines/statement-on-resuming-breastfeeding-after-anesthesia

Montgomery A, Hale TW; Academy Of Breastfeeding Medicine. ABM clinical protocol #15: analgesia and anesthesia for the breastfeeding mother, revised 2012. Breastfeed Med. 2012 Dec;7(6):547-53. doi: 10.1089/bfm.2012.9977. PMID: 23215911.

https://www.medsafe.govt.nz/profs/puarticles/lactation.htm

https://www.ncbi.nlm.nih.gov/books/NBK501922/