Analgesia and Breastfeeding

Wendy Jones PhD MRPharmS MBE
www.breastfeeding-and-medication.co.uk

Understanding of pharmacokinetics

- Using pharmacokinetics we can evaluate the risk of the drug passing through breastmilk
- Do we need to “manage” breastfeeding and would it help?
- How do we support the mother to feed as she has chosen?
- Breastmilk is about so much more than milk

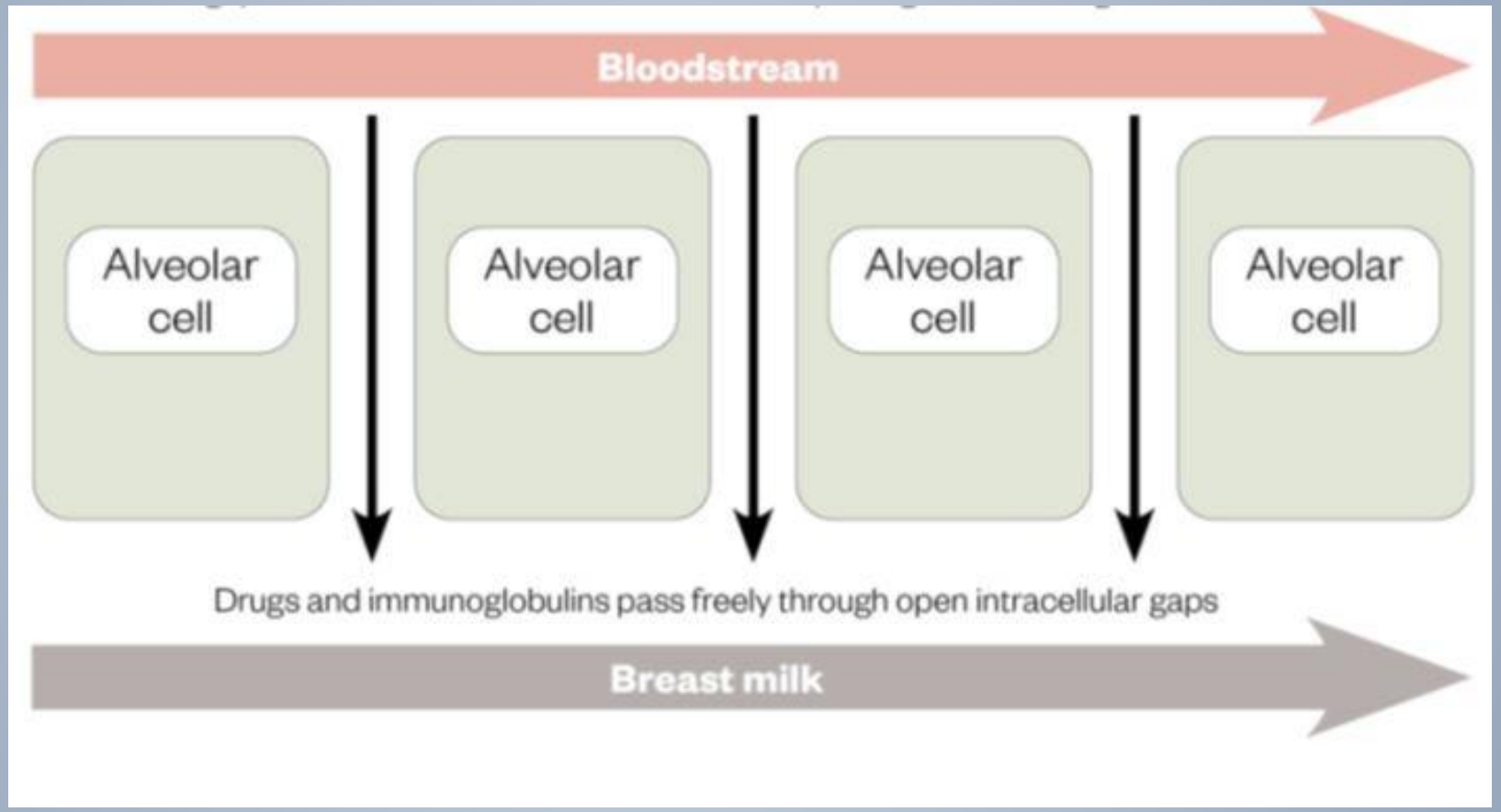
  Drug passing to baby vs risk of not breastfeeding

https://www.youtube.com/watch?v=tS4wkZ2UNUs&t=17s

Which drugs to choose where possible

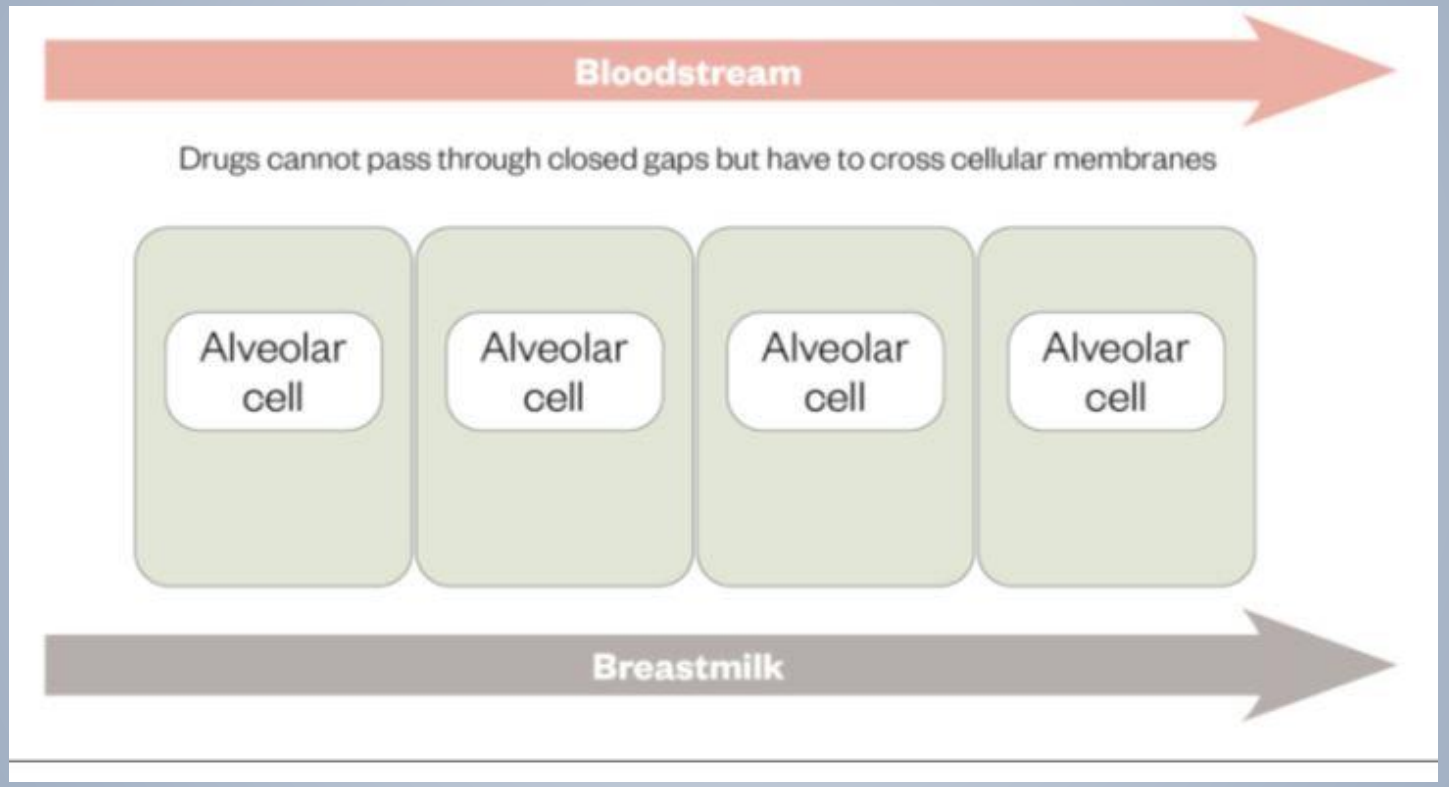
- Anything licensed for children
- Drugs we have data on
- Pharmacokinetic data:
  - Poor bio availability
  - Extensive plasma protein binding > 98%
  - Short half life
  - Low milk plasma ratio <1
  - Relative infant dose <10% (only available in specialist texts)

Transfer of drugs in the first few days after birth



The gaps between the cells are wide open to allow the passage of immunoglobulins which are large molecules. This allows free passage of all medication BUT this is when we give most drugs to breastfeeding women with least concern.

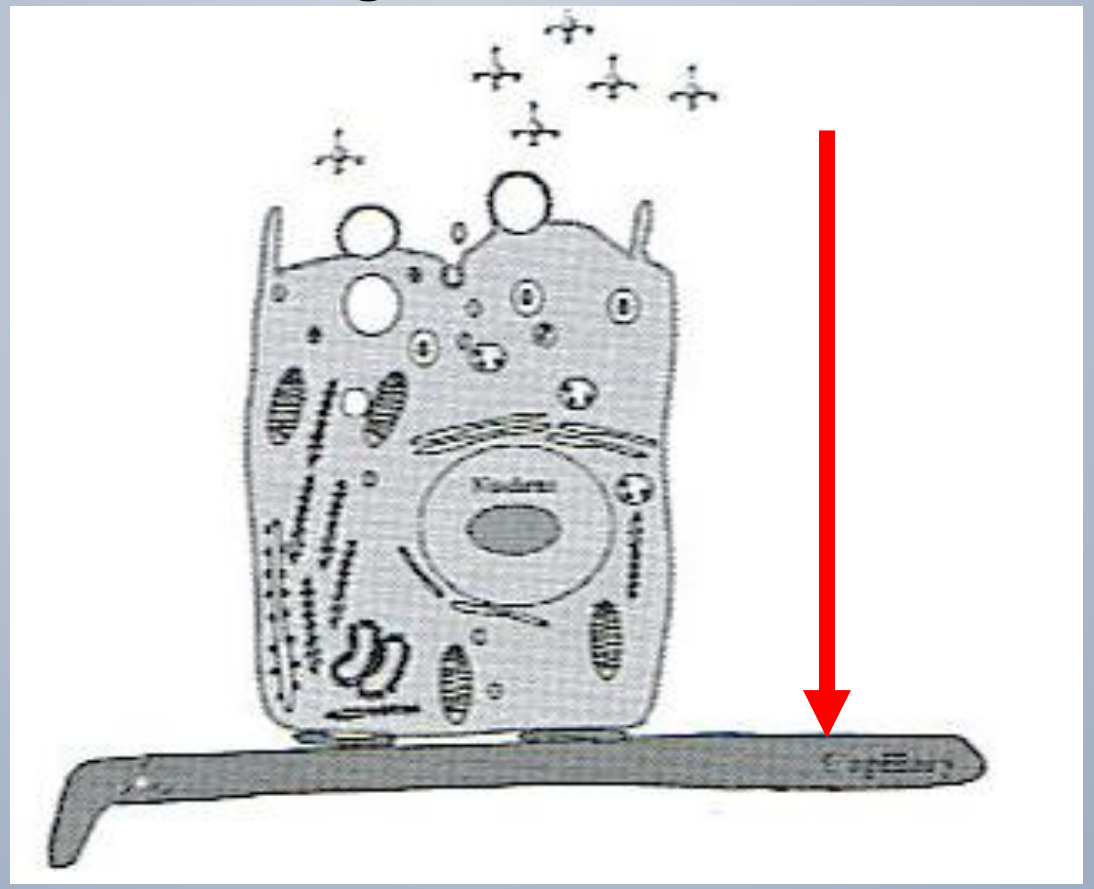
Transfer after the first few days after birth



After the first few days the gaps between the cells close and prevent the passage of large molecules further. Drugs now have to pass across the cell membranes

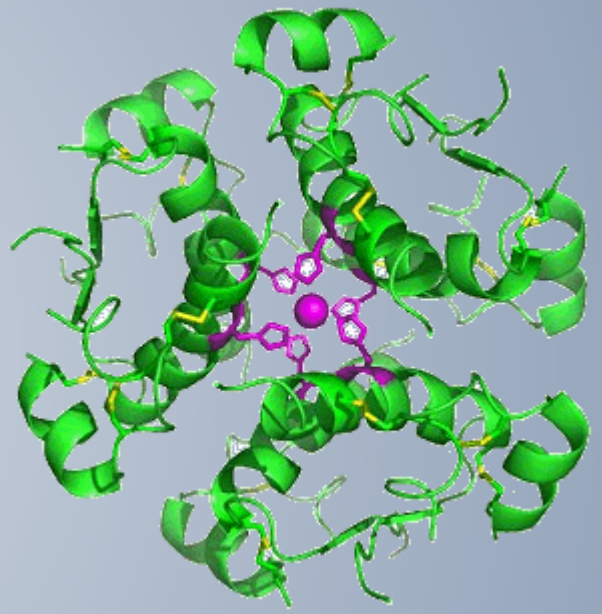
How do drugs get into breastmilk

"Simple" diffusion - 99% drugs pass this way and have to cross the cell membranes to get into milk



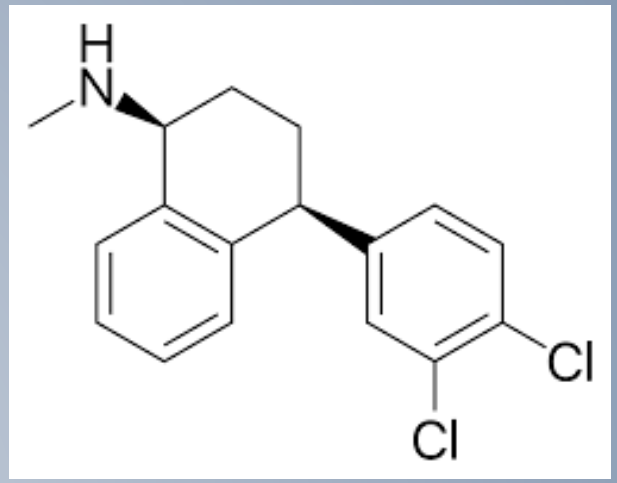
Oral bioavailability

- Drugs with poor oral bioavailability are large molecules which cannot pass through cell membranes
- They are usually drugs given ONLY by injection/infusion
- If a drug can’t get be absorbed from the gut however much is in milk, baby can’t absorb it e.g. gentamycin, teicoplanin, meropenem

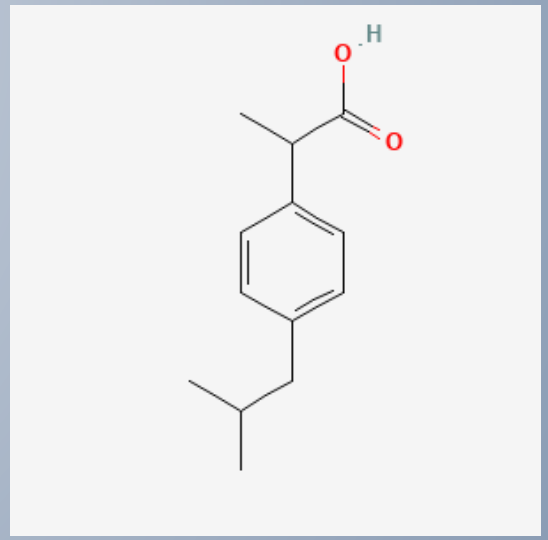


Plasma Protein Binding

- Drugs which are highly bound to proteins in the maternal plasma are unable to transfer into breastmilk in high levels
- Ideal drug for breastfeeding mother is highly protein bound >90%
- Data is only available in specialized texts



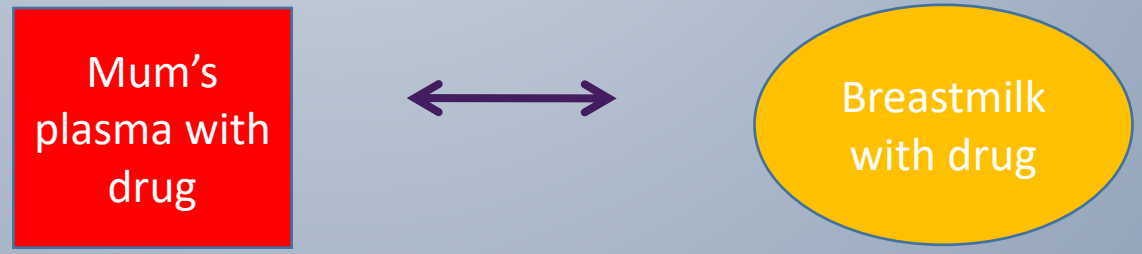
Sertraline 98%



Ibuprofen >99%

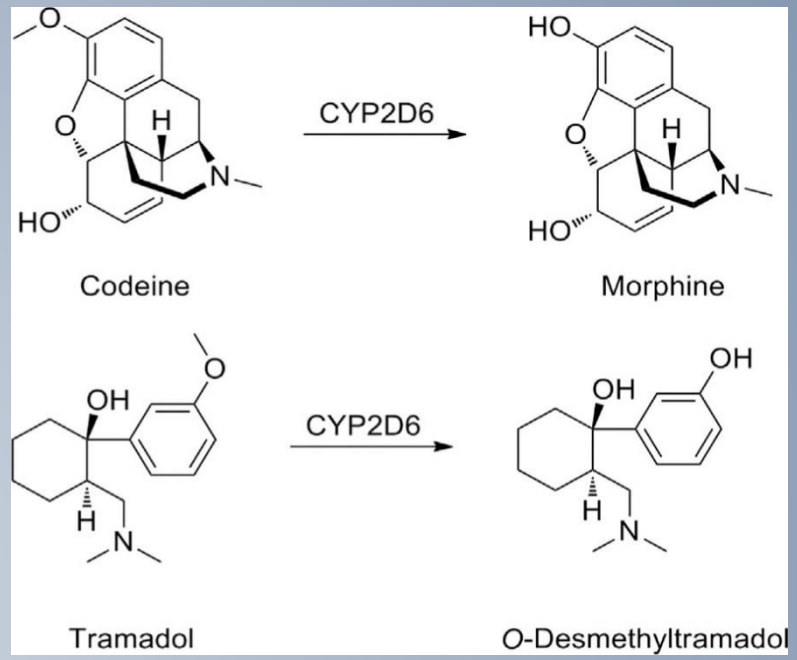
Milk Plasma Ratio

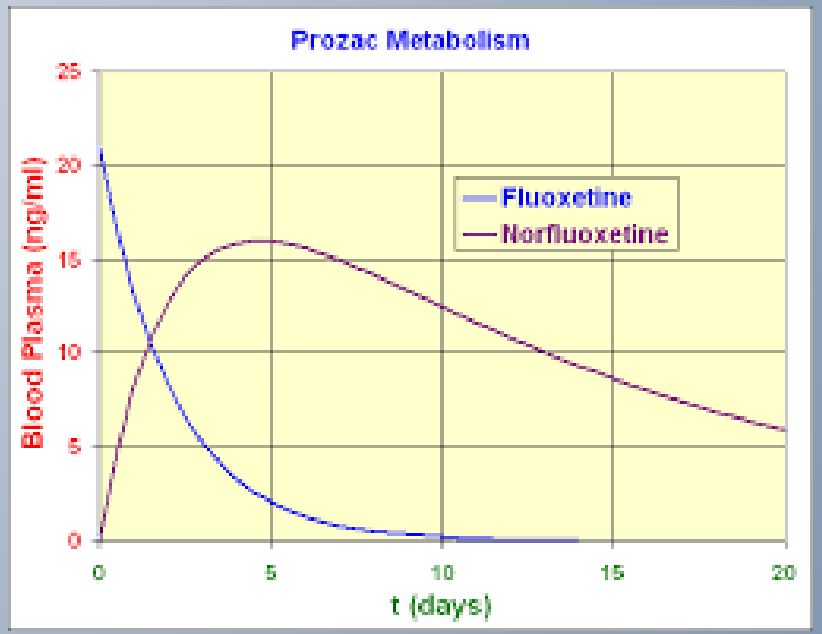
- the higher the M/P ratio, the more drug is found in breastmilk
- The M/P is the ratio of the amount of drug in the maternal plasma and the amount of drug in milk
- For breastfeeding mothers we choose drugs with MP ratio <1
- M/P ratios above 1 suggest that the drug concentrates in breastmilk e.g iodine up to 26, cannabis 8, alcohol 1
- As the level in the mother's blood falls the drug is pulled back from breastmilk, it is not stuck in milk



Active metabolites

- Some metabolites may have longer half-lives than the original drug and so can extend levels in milk making them less suitable for lactating mothers
- E.g. Fluoxetine half-life 2-3 days . Norfluoxetine 360 hours (15 days)
- Codeine and Tramadol CYP2D6 influence





Relative Infant dose

- Widely being recognised as gold standard
- RID < 10% compatible
- First introduced by Bennet 1996
- Widely used by Hale

Relative Infant Dose

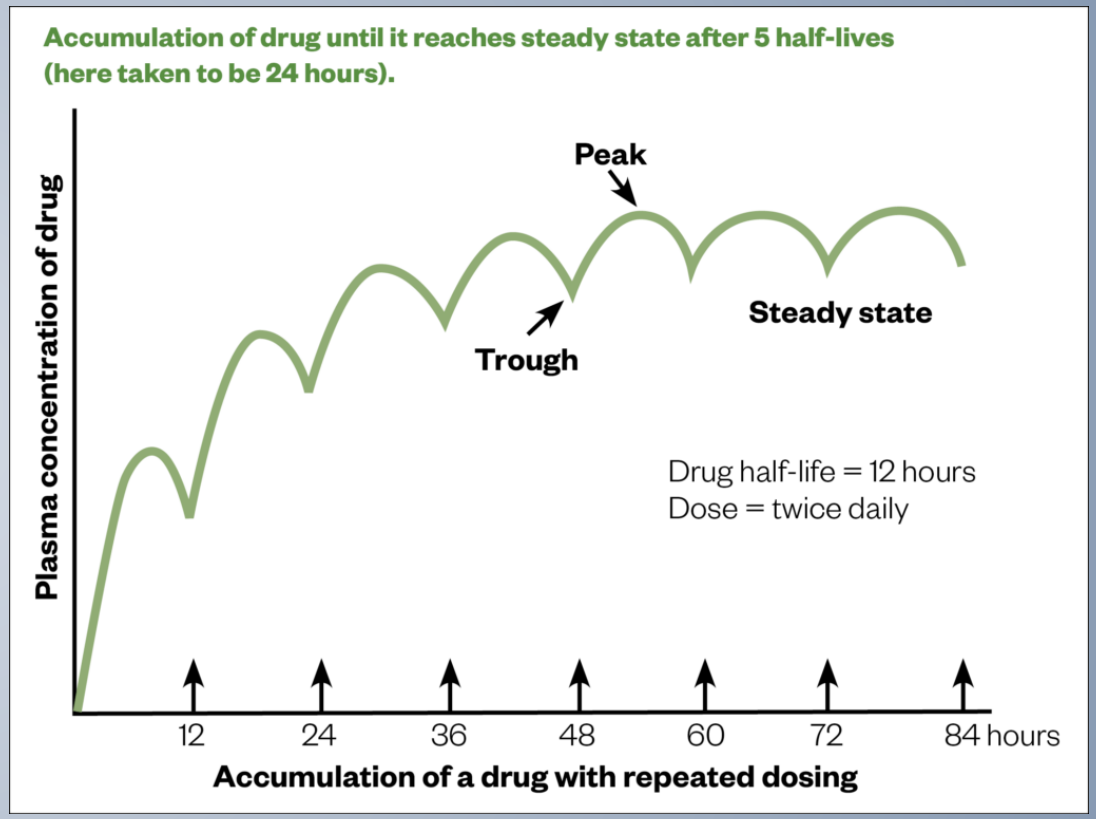
$$\text{RID} = \frac{\text{Dose.infant}\left(\frac{mg/kg}{day}\right)}{\text{Dose.mother}\left(\frac{mg/kg}{day}\right)}$$

Dose.infant = dose in infant/ day

Dose.mother = dose in mother/ day

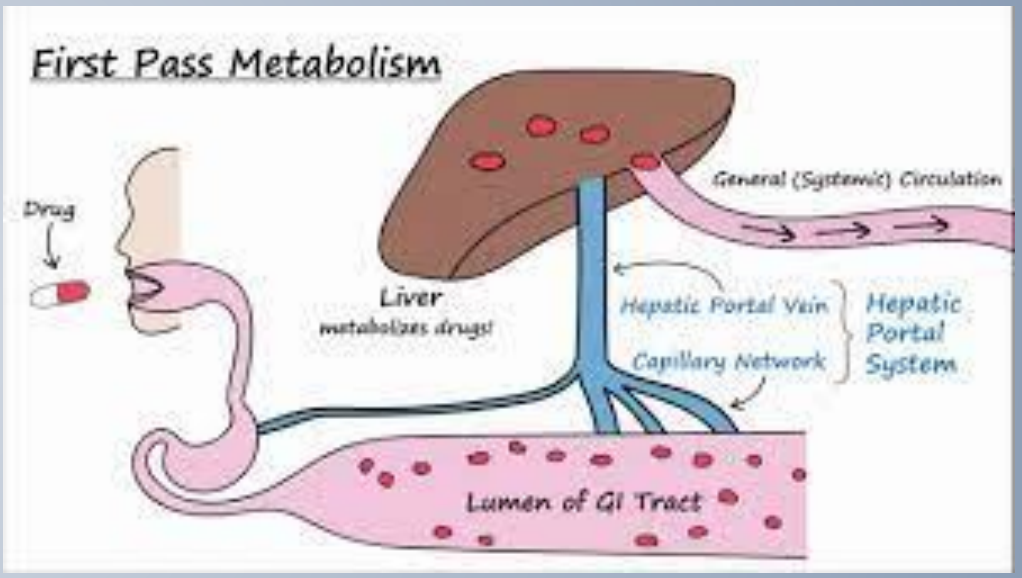
Timing of drugs and feeds

- The time to maximum level in breastmilk is often quoted
- Mums try desperately to time feeds with drug levels at their lowest
- BUT … once any drug has been taken for 3 days (or 5 half lives) reaches steady state so timing is pointless



First pass metabolism

- The drug is absorbed from the GI tract and passes via the portal vein into the liver where it may be metabolized.
- This means that less drug is available to pass into the blood stream E.g. morphine



First do no harm?

- No breastfeeding mother should be left in pain or asked to choose between breastfeeding and medication
- Need to use evidence based information rather than just the BNF which is still currently based largely on the SPC of manufacturers although it is changing
- Telling a mother to interrupt breastfeeding may put her at risk of mastitis and may cause difficulties for the baby who hasn't ever taken milk from a bottle
- Breastfeeding isnt just about food

Non steroidal anti-inflammatory drugs

- Ibuprofen: Protein binding >99%, RID <0.66%
- Diclofenac: Protein binding 99.7%, RID 0.05%
- Naproxen: Protein binding 99.7%, RID 3.3%
- Celecoxib: Protein binding 97%, RID <0.7%
- In a research study For adult ED patients with acute extremity pain, there were no clinically important differences in pain reduction at 2 hours with ibuprofen and paracetamol or 3 different opioid and paracetamol combination analgesics. **(https://jamanetwork.com/journals/jama/article-abstract/2661581?redirect=true)**
- Don't under rate paracetamol plus NSAID – add in opioid if necessary but remember to co-prescribe laxative!

Codeine

- MHRA recommendation should not be used during breastfeeding
- Metabolism can vary – may be ineffective, effective, produce adverse events in mother and baby
- If mother regularly has taken it in the past it is unlikely to accumulate in her milk because of her metabolism
- Be careful in opioid naïve patients
- Tell family to observe baby for drowsiness and failure to wake for feeds
- Use at lowest dose for shortest period possible
- Half life 3 hours

https://breastfeeding-and-medication.co.uk/thoughts/breastfeeding-and-codeine

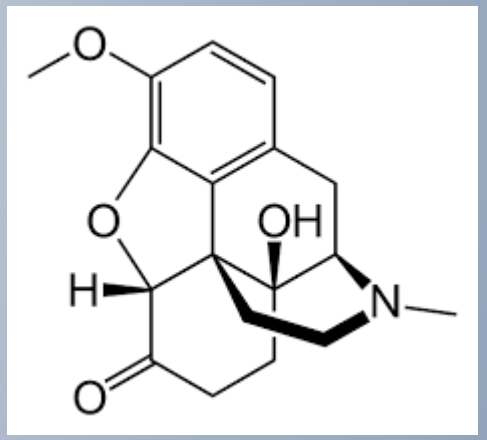
Dihydrocodeine

- Preferred opioid in breastfeeding for TTO (Morphine better post-op)
- Use at lowest dose for shortest period possible
- Can be bought over the counter as Paramol™
- Use in combination with paracetamol and NSAID if necessary
- The oral bio availability is 20% due to substantial first pass metabolism.
- The half life is quoted as 3.5-5h .
- It is metabolised in the liver by CYP2D6 to dihydromorphine, which has potent analgesic activity

https://breastfeeding-and-medication.co.uk/fact-sheet/dihydrocodeine-and-breastfeeding

Oxycodone

- More likely to cause drowsiness in the baby than other opioids as shown in research study below
- Use at lowest dose for shortest period possible
- Be careful in opioid naïve patients
- Half life 2-4 hours
- RID < 4.55% (significantly below 10%)
- Watch for drowsiness (occurs in 20%)



Lam J, Kelly L, Ciszkowski C, et al. Central nervous system depression of neonates breastfed by mothers receiving oxycodone for postpartum analgesia. J Pediatr. 2012 Jan;160(1):33-37.

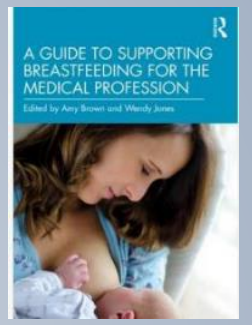
Morphine

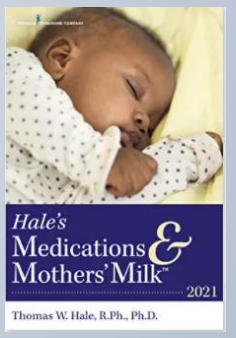
- Subject to extensive first pass metabolism
- Used widely post caesarean section
- Morphine is considered to be the benchmark for the treatment of severe pain in breastfeeding mothers. (https://www.sps.nhs.uk/articles/safety-in-lactation-opioid-analgesics/)
- Little published data on oral morphine, most on IV, IM
- Absolute bioavailability for morphine was estimated to be 23.9% after oral solution, 22.4% after MST-Continus

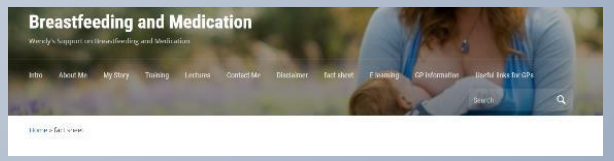
https://www.bps.ac.uk/publishing/our-journals/british-journal-of-clinical-pharmacology/volume-27/issue-4/the-bioavailability-and-pharmacokinetics-of-morphi#:~:text=Absolute%20bioavailability%20for%20morphine%20was,and%206%20h%20(buccal).

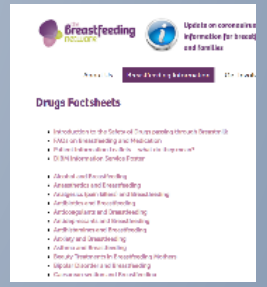
Resources

- LactMed - https://www.ncbi.nlm.nih.gov/books/NBK501922/
- UKDILAS - https://www.sps.nhs.uk/articles/ukdilas/
- Hale – Medications and Mothers Milk - https://www.halesmeds.com/
- BfN Factsheets www.breastfeedingnetwork.org.uk/drugs-factsheets/
- Breastfeeding and Medication https://breastfeeding-and-medication.co.uk/fact-sheet/list-of-factsheets-available-on-breastfeeding-and-medication









Healthcare professionals need to use evidence based sources to check the safety of drugs in breastmilk and be sensitive to the needs of mothers around infant feeding.

Contact details
wendy@breastfeeding-and-medication.co.uk

www.facebook.com/breastfeedingandmedication