Pharmacokinetics and transport of drugs into breastmilk

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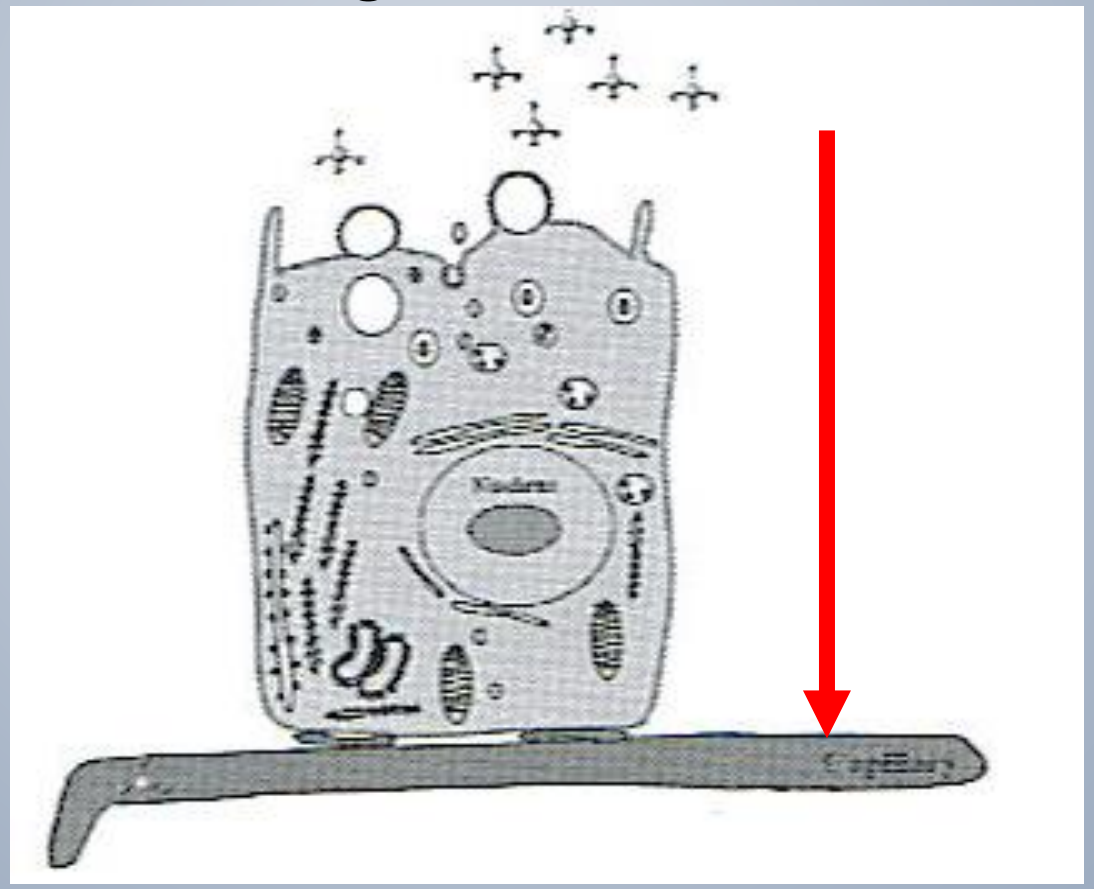
Understanding of pharmacokinetics

- How do we evaluate the risk of the drug passing through breastmilk?
- How do we manage breastfeeding?
- How do we support the mother

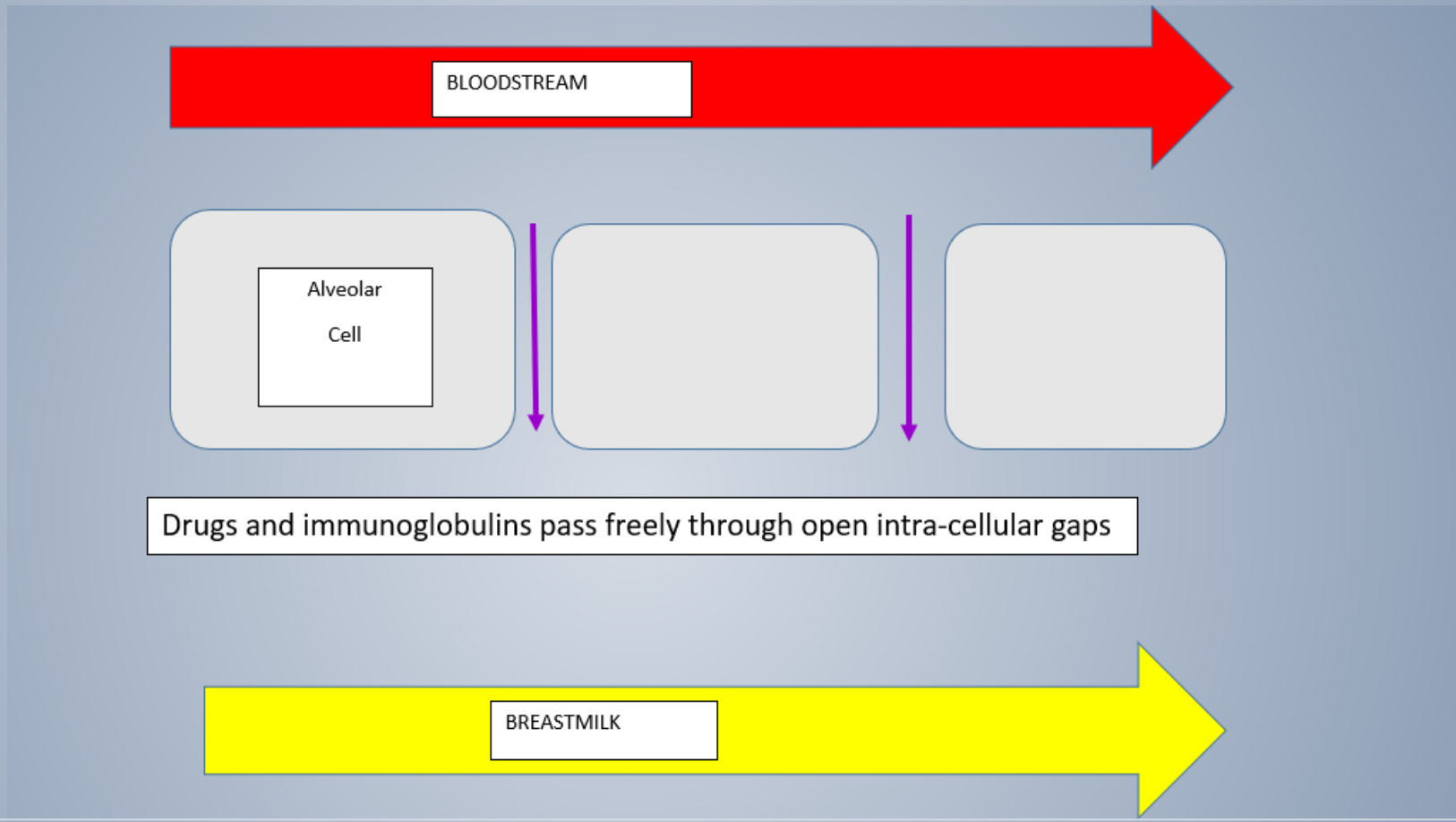
Drug passing to baby vs risk of not breastfeeding

How do drugs get into breastmilk

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

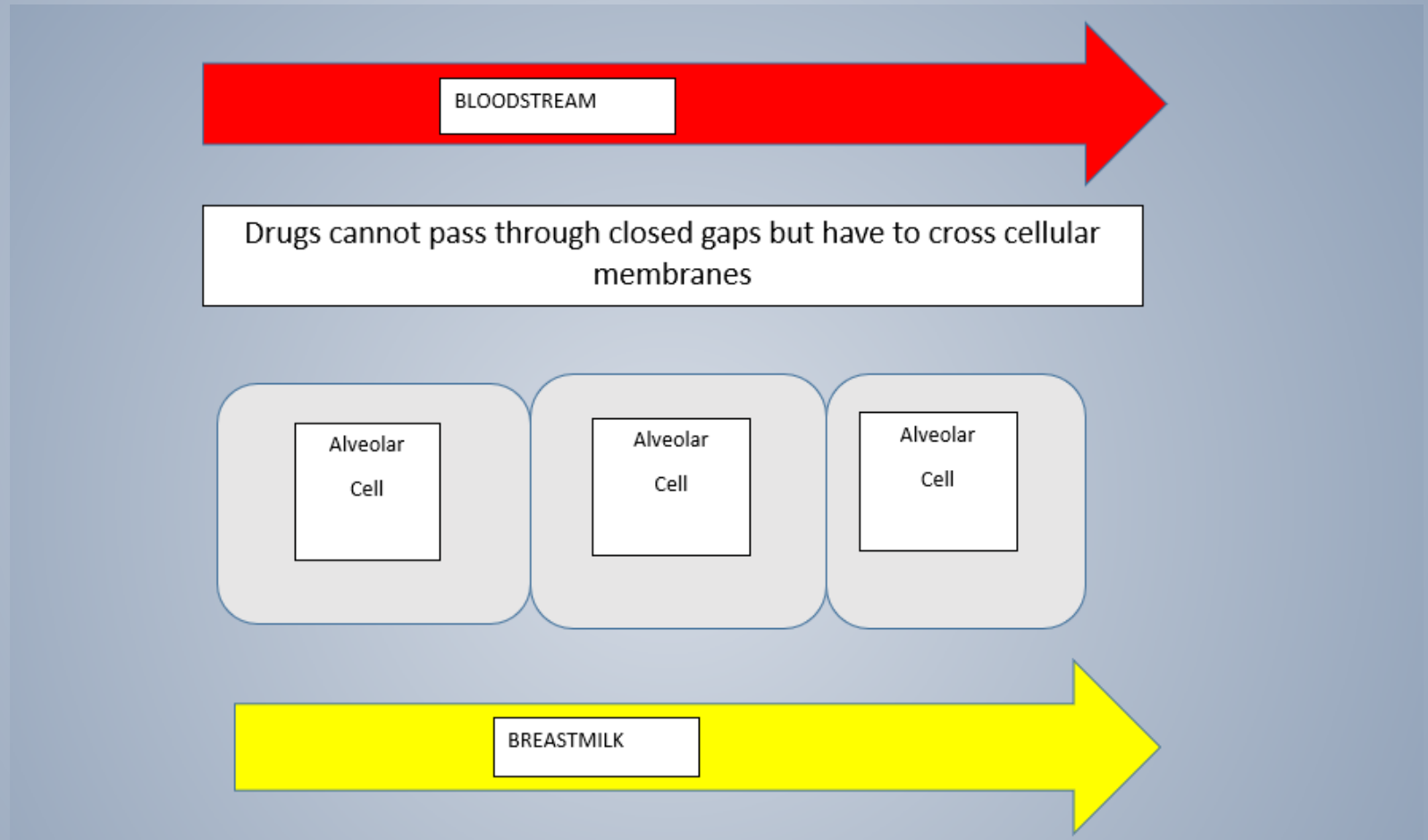


Transfer of drugs in the first few days after birth



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.

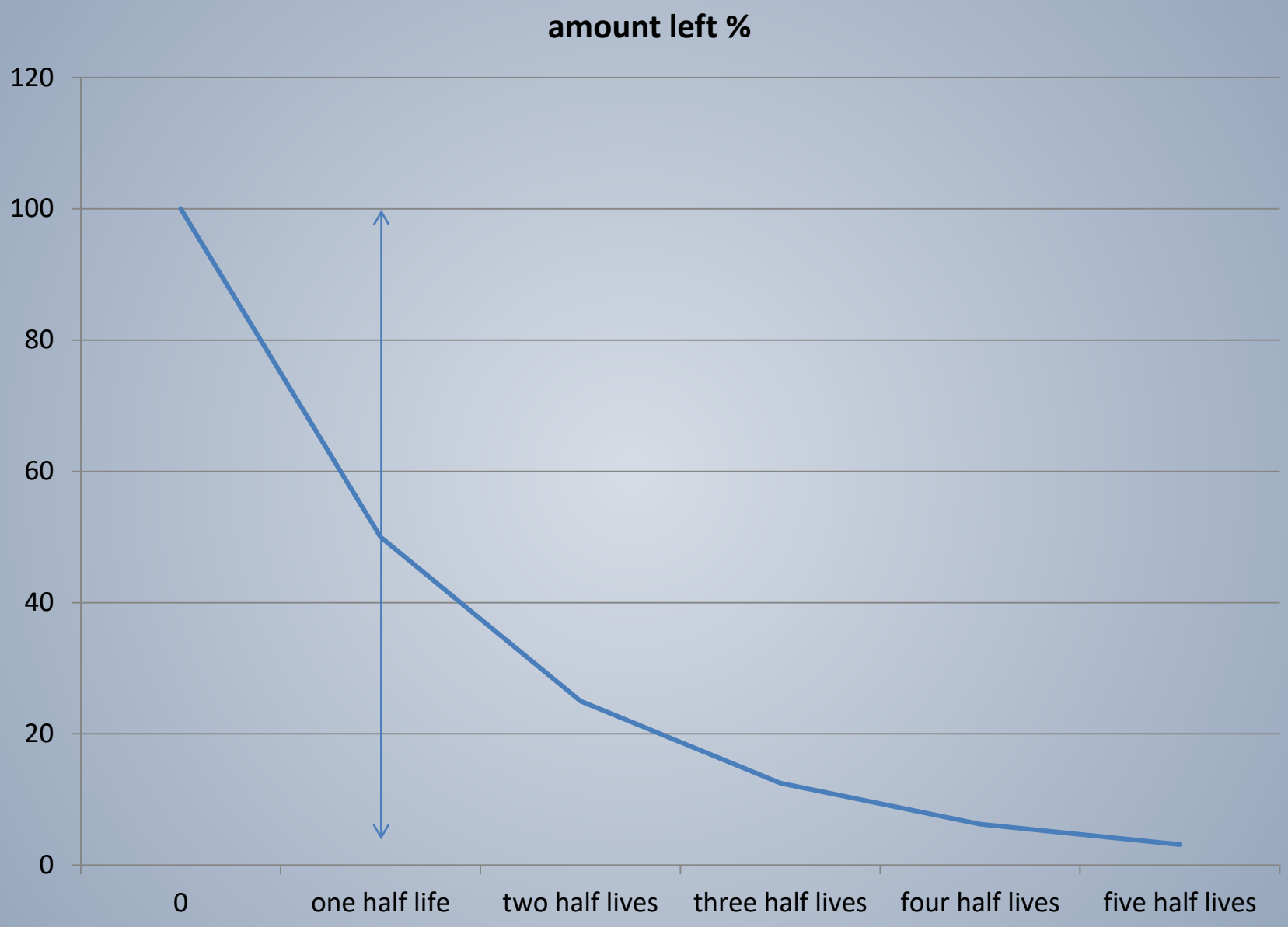
Transfer after the first few days after birth



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

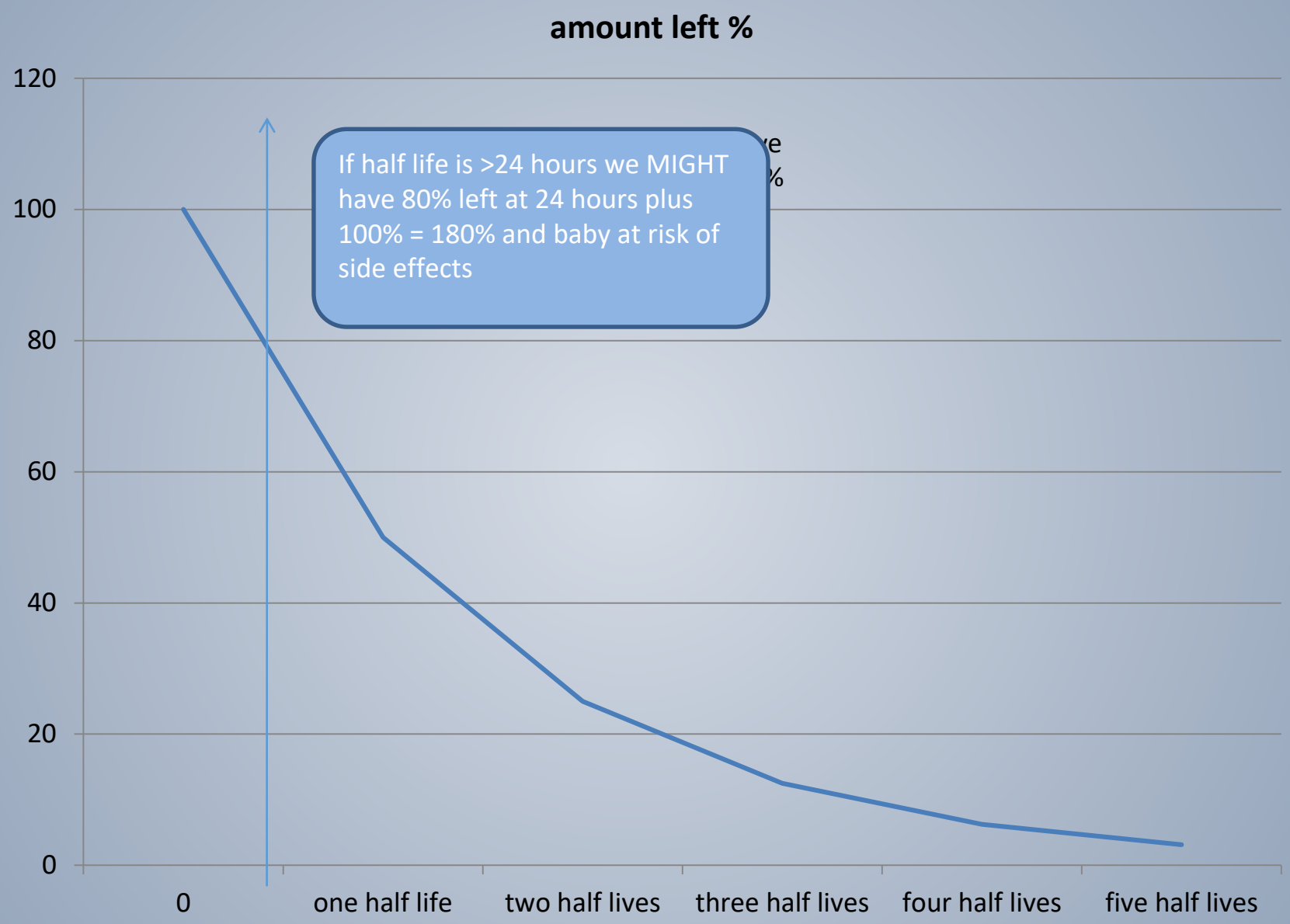
Half life of a drug

- The half life of a drug is the time taken for half of it to be metabolised.
- After one half life 50% of the original drug is in the body
- After two half lives 25% and so on
- After 5 half lives the drug is assumed to have left the body and therefore milk
- We prefer drugs with half lives < 24 hours for breastfeeding
- E.g Paracetamol 2 hours, amoxicillin 1.7 hours


amount left %
120
100
80
60
40
20
0
0
one half life
two half lives
three half lives
four half lives
five half lives

If half live is longer than 24 hours

- If after one half life we still have 80% of the drug left, and we take another dose the body has 180%
- After two half lives there is 40% of the first dose, 80% of the second dose and 100% of the third dose = 220%
- After three half lives 20% of the first dose, 40% of the second dose, 80% of the third dose and another 100% = 240% so the drug is accumulating in breastmilk and may produce adverse effects in the baby
- E.g. Fluconazole half life in a baby < 6 weeks 88 hours, with older babies 30 hours


amount left %
120
100
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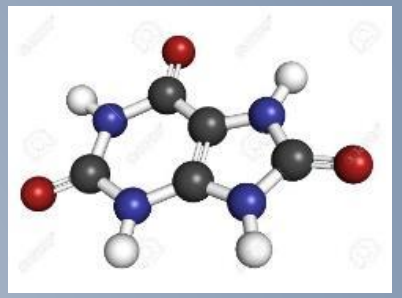
40
20
0
If half life is >24 hours we MIGHT have 80% left at 24 hours plus 100% = 180% and baby at risk of side effects
0
one half life
two half lives
three half lives
four half lives
five half lives

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

Therapeutic range

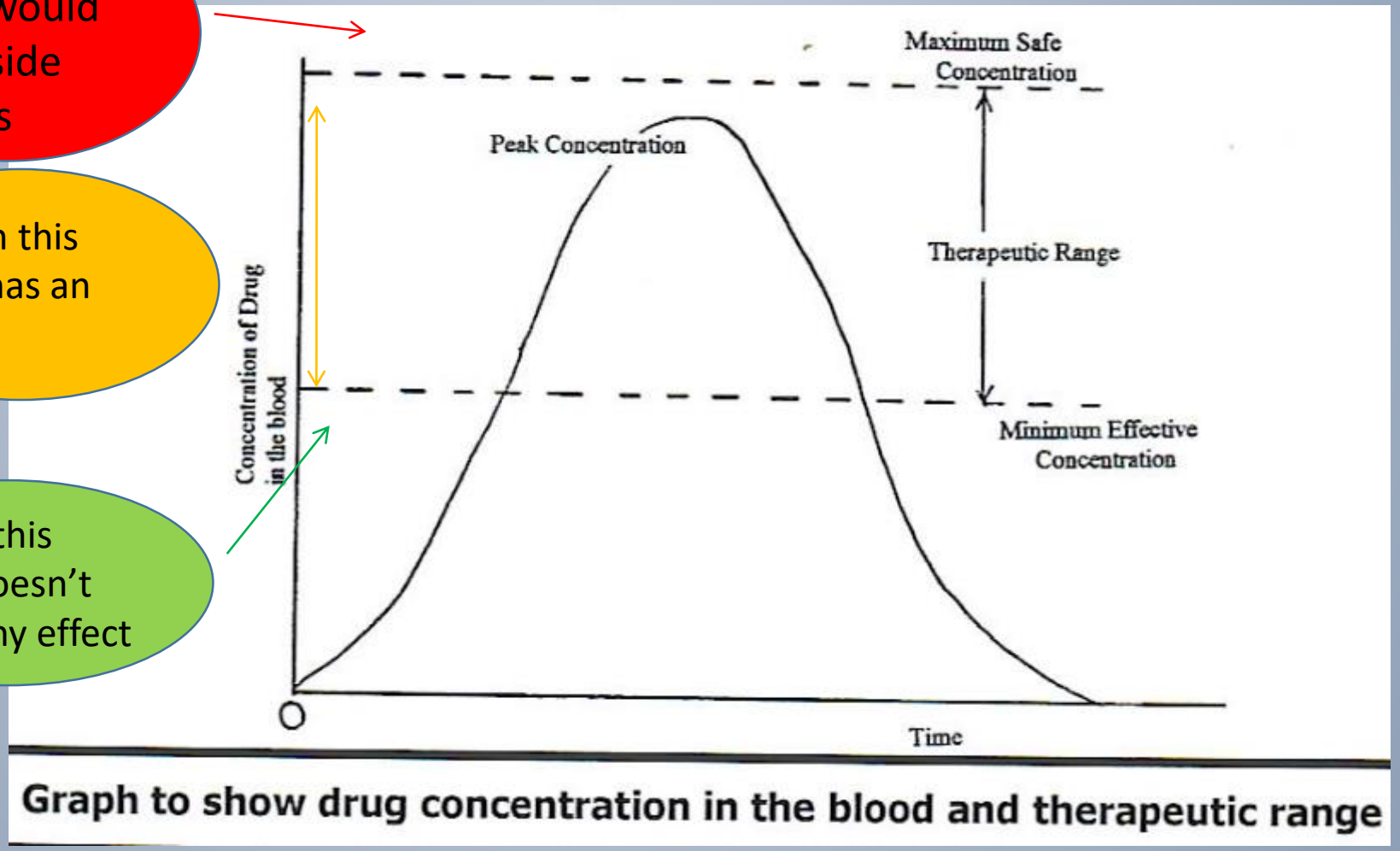
- The therapeutic range varies between drugs
- Some drugs have very narrow ranges and need drug monitoring e.g. digoxin, lithium, warfarin
- Others have very wide ranges so that the doses are less critical e.g. paracetamol
- Drugs which can be given to children are safe in breastfeeding as they reach sub therapeutic levels
- Drugs which exceed therapeutic levels can lead to side effects and toxicity e.g fluconazole can cause vomiting and stomach cramps in babies from the levels passing through milk

Therapeutic Range

Above this level would have side effects

Within this level has an effect

Below this level doesn't have any effect



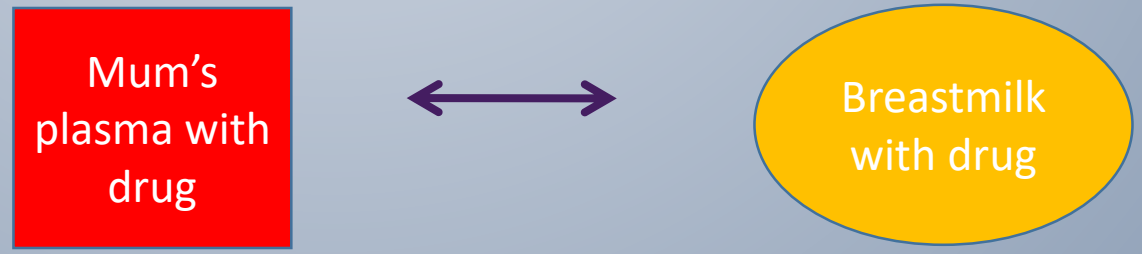
Graph to show drug concentration in the blood and therapeutic range

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 s breastfeeding mother is highly protein bound >90%
- Data is only available in specialized texts

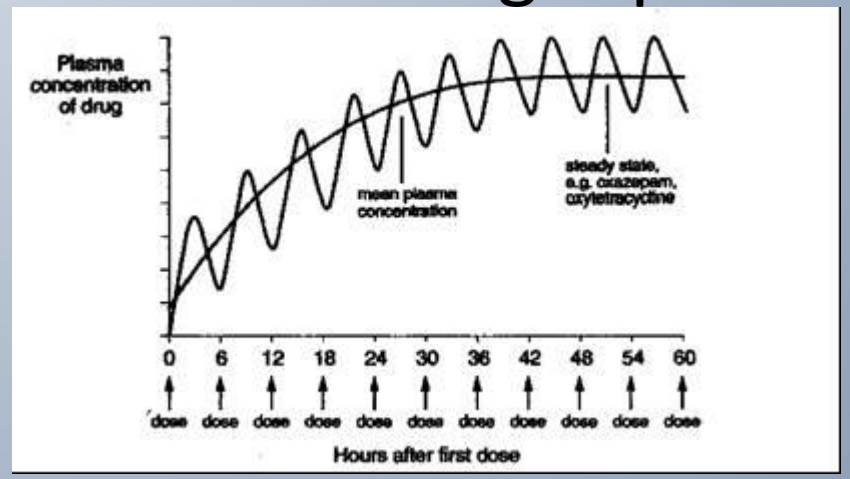
Milk Plasma Ratio

- 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 breastilk, it is not stuck in milk



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



Pumping and dumping of breastmilk

- To pump milk may be necessary to maintain supply if mum cant breastfeed temporarily. However there are several things we need to consider before suggesting it is discarded. (Dumping sounds like it is valueless and as professionals we may not understand how disheartening it is to throw away milk which we value as the best nutrition for the baby)
- Can we talk about pump and save if we need time to check whether a drug is compatible with breastfeeding?
- Don’t use it as a throw away comment as if milk supply is atap which can be turned off

Pumping

- Does mum have a breast pump?
- Does she have clear instructions on how often to pump and when she can return to breastfeeding?
- It takes determination to maintain a supply so even temporary discarding may damage ongoing supply
- If mum does not pump frequently enough she may risk engorgement or mastitis
- Not all babies will accept bottles of milk

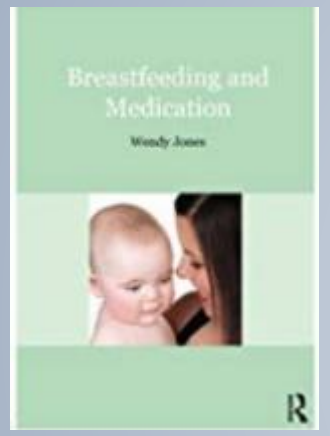
Let’s change the conversation

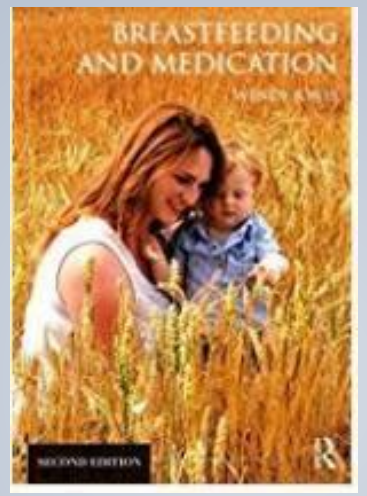
- Provide mothers (and their partners) with evidence based information
- Let’s use shared decision making and trust
- Let’s promote and support breastfeeding wherever possible?
- Let’s support mum so that she can continue to breastfeed as normal

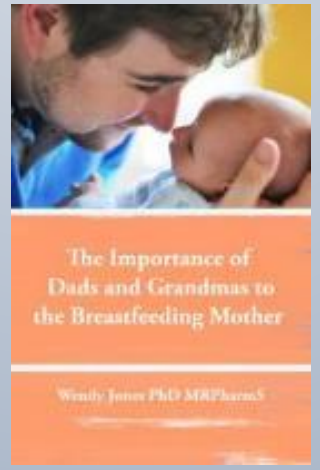
Summary

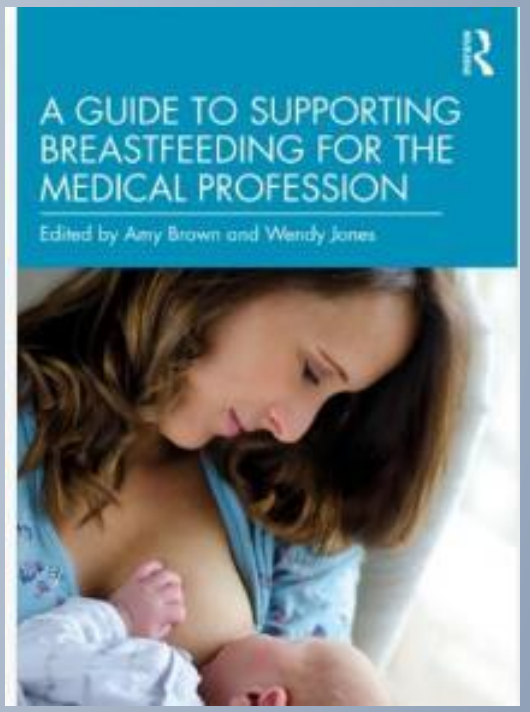
- We can use pharmacokinetics to assess safety of a medication
- We can access specialist reference sources to check the data
- We can support mums with expressing if it is necessary and develop a care plan for breastfeeding continution

My published books









Healthcare professionals need training on breastfeeding, the safety of drugs in breastmilk and sensitivity to the needs of mothers around infant feeding.

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