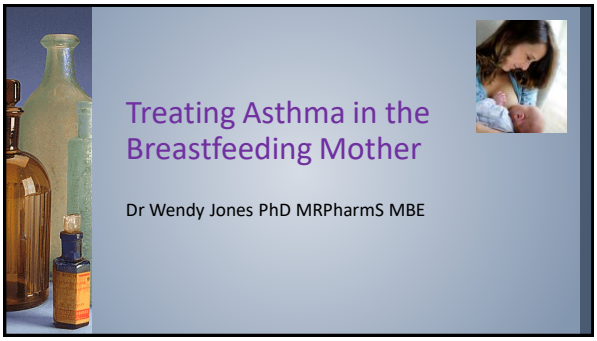
Treating Asthma in the Breastfeeding Mother
Dr Wendy Jones PhD MRPharmS MBE

1


Why is breastfeeding important?
› Breastfeeding has numerous health benefits for the mother and child. Exclusive breastfeeding for the first 6 months of an infant's life, with continued breastfeeding for up to 2 years or longer, is recognized as normal and the "gold" standard for infant feeding
World Health Organization Recommendations on Postnatal Care of the Mother and Newborn. Geneva, World Health Organization, 2013.

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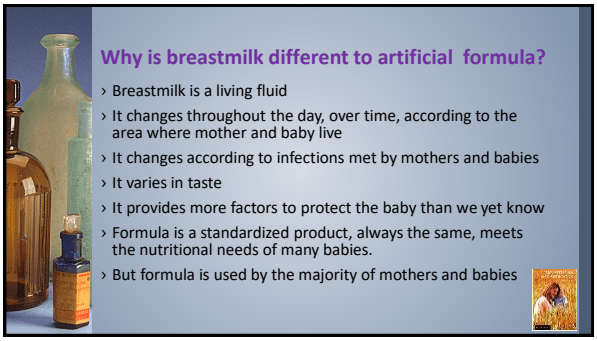
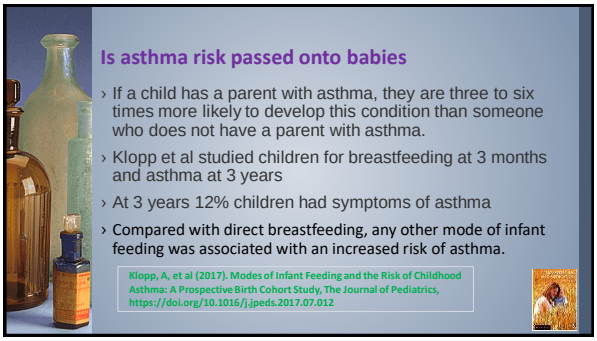

Why is breastmilk different to artificial formula?
› Breastmilk is a living fluid
› It changes throughout the day, over time, according to the area where mother and baby live
› It changes according to infections met by mothers and babies
› It varies in taste
› It provides more factors to protect the baby than we yet know
› Formula is a standardized product, always the same, meets the nutritional needs of many babies.
› But formula is used by the majority of mothers and babies

3


Is asthma risk passed onto babies
› If a child has a parent with asthma, they are three to six times more likely to develop this condition than someone who does not have a parent with asthma.
› Klopp et al studied children for breastfeeding at 3 months and asthma at 3 years
› At 3 years 12% children had symptoms of asthma
› Compared with direct breastfeeding, any other mode of infant feeding was associated with an increased risk of asthma.
Klopp, A, et al (2017). Modes of Infant Feeding and the Risk of Childhood Asthma: A Prospective Birth Cohort Study, The Journal of Pediatrics, https://doi.org/10.1016/j.jpeds.2017.07.012

4

Research published in August 2022

- Studied 2021 mother-child dyads with follow up for 4-6 years
- Women reported the duration of any and exclusive breastfeeding and child asthma outcomes
- Longer duration of exclusive breastfeeding had a protective association with child asthma

5

Impact of breastfeeding on asthma outcomes

- Babies that were breastfed for 2-4 months had only 64% likelihood of having as many asthma outcomes as those who were breastfed less than 2 months;
- those breastfed for 5-6 months had 61% likelihood,
- those breastfed for more than 6 months had a 52% likelihood."
- With exclusive breastfeeding protective associations were stronger in dyads with children born by vaginal vs caesarean delivery although interactions did not reach statistical significance

Wilson, K. et al. 2022. The association between duration of breastfeeding and childhood asthma outcomes. Annals of Allergy, Asthma and Immunology. DOI:https://doi.org/10.1016/j.anai.2022.04.034

6

Prescribing for breastfeeding women

- Most drugs prescribed during lactation are outside of the product licence
- Outside of licence does not imply contra-indicted, merely that the manufacturers have not been required to take responsibility when launching the drug nor to update later
- There are other specialist sources of information on safety

NICE Maternal and Child Nutrition PH11 2008 Rec. 18

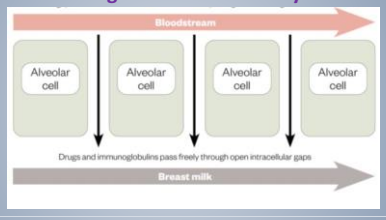
7

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)

8

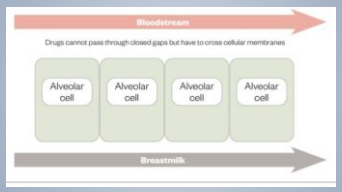
Transfer of drugs in the first few days after birth



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.

9

Transfer after the first few days after birth

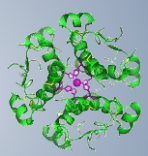


After the first few days the gaps between the cells close and prevent the passage of large molecules further. Drugs now have to pass across the cell membranes

10

Oral bioavailability

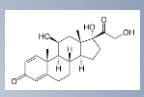
- Drugs with poor oral bioavailability are large molecules which cannot pass through cell membranes
- They are usually drugs given ONLY by injection/infusion
- If a drug can't get be absorbed from the gut however much is in milk, baby can't absorb it e.g. gentamycin, teicoplanin, meropenem



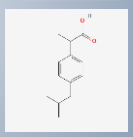
11

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



Prednisolone > 90%



Ibuprofen >99%

12

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,
- As the level in the mother's blood falls the drug is pulled back from breastmilk, it is not stuck in milk

Mum's plasma with drug ⟷ Breastmilk with drug

13

Relative Infant dose

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

Relative Infant Dose

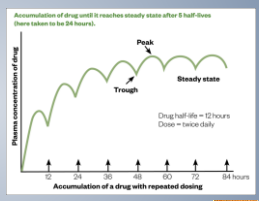
$$RID = \frac{\text{Dose.infant } \left(\frac{mg}{kg}/day\right)}{\text{Dose.mother } \left(\frac{mg}{kg}/day\right)}$$

Dose.infant = dose in infant/day
Dose.mother = dose in mother/day

14

Timing of drugs and feeds

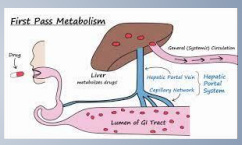
- The time to maximum level in breastmilk is often quoted
- Mums try desperately to time feeds with drug levels at their lowest
- BUT … once any drug has been taken for 3 days (or 5 half lives) reaches steady state so timing is pointless



15

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



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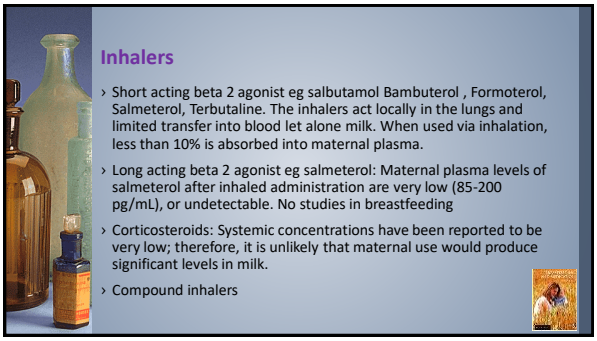
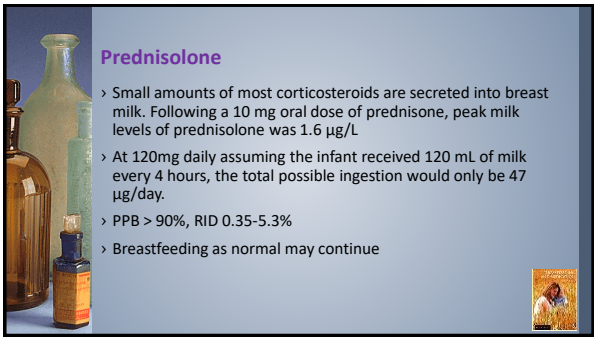
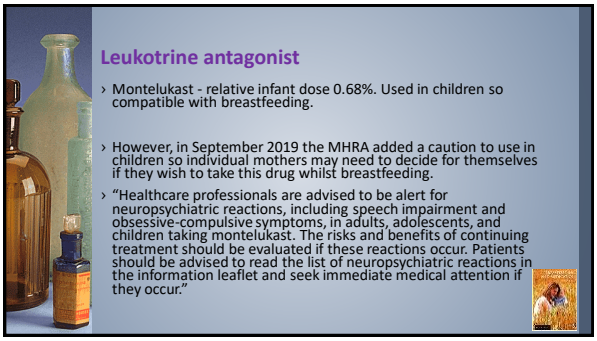

Inhalers
› Short acting beta 2 agonist eg salbutamol Bambuterol , Formoterol, Salmeterol, Terbutaline. The inhalers act locally in the lungs and limited transfer into blood let alone milk. When used via inhalation, less than 10% is absorbed into maternal plasma.
› Long acting beta 2 agonist eg salmeterol: Maternal plasma levels of salmeterol after inhaled administration are very low (85-200 pg/mL), or undetectable. No studies in breastfeeding
› Corticosteroids: Systemic concentrations have been reported to be very low; therefore, it is unlikely that maternal use would produce significant levels in milk.
› Compound inhalers

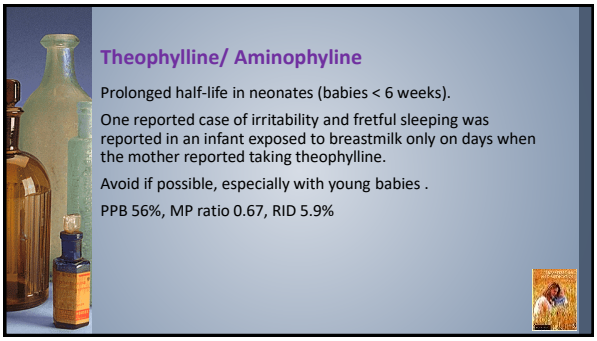
17


Prednisolone
› Small amounts of most corticosteroids are secreted into breast milk. Following a 10 mg oral dose of prednisone, peak milk levels of prednisolone was 1.6 µg/L
› At 120mg daily assuming the infant received 120 mL of milk every 4 hours, the total possible ingestion would only be 47 µg/day.
› PPB > 90%, RID 0.35-5.3%
› Breastfeeding as normal may continue

18


Leukotrine antagonist
› Montelukast - relative infant dose 0.68%. Used in children so compatible with breastfeeding.
› However, in September 2019 the MHRA added a caution to use in children so individual mothers may need to decide for themselves if they wish to take this drug whilst breastfeeding.
› "Healthcare professionals are advised to be alert for neuropsychiatric reactions, including speech impairment and obsessive-compulsive symptoms, in adults, adolescents, and children taking montelukast. The risks and benefits of continuing treatment should be evaluated if these reactions occur. Patients should be advised to read the list of neuropsychiatric reactions in the information leaflet and seek immediate medical attention if they occur."

19


Theophylline/ Aminophyline
Prolonged half-life in neonates (babies < 6 weeks).
One reported case of irritability and fretful sleeping was reported in an infant exposed to breastmilk only on days when the mother reported taking theophylline.
Avoid if possible, especially with young babies .
PPB 56%, MP ratio 0.67, RID 5.9%

20

Antibiotics

- The antibiotics:
- amoxycillin,
- Metronidazole
- Macrolides
- cephalosporins

are all compatible with normal breastfeeding

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

21

Risks of interrupting breastfeeding?

Breastmilk does not turn off like a tap

Risks of suddenly interrupting breastfeeding:

- Mastitis
- Baby refuses to feed from formula
- Baby intolerant of formula
- Milk supply drops
- How to restimulate supply

22

Conclusions

- Babies born to mothers who are asthmatic are at risk of developing asthma
- Exclusive breastfeeding lowers the risk of future asthma
- Drugs used treat symptoms of asthma are largely compatible with breastfeeding although may be outside of licence
- Breastfeeding matters to mothers and suspending breastfeeding even temporarily can cause harm

23

Resources

- My books ☺
- 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/
- www.breastfeeding-and-medications.co.uk
- www.breastfeedingnetwork.org.uk/drugs-factsheets/

24


Breastfeeding matters
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25