Children are not little adults

Anna Burgess & Lucy Wheeler
Paediatric Pharmacists
Noah's Ark Children's Hospital for Wales
Cardiff and Vale UHB

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Learning Outcomes

- By the end of the session, you should be able to:
  - Describe changes in the way infants and children handle drugs from birth to adulthood
  - Identify risk issues within paediatric pharmaceutical care and how to address them
  - Recognise problem excipients in medicines for children and how these can be overcome
  - Discuss issues surrounding medicines reconciliation on a paediatric ward

Fun Quiz – Stand by your answers!

1. What percentage of a new born baby (born at term) is water?
   A. 60%
   B. 70%
   C. 80%

Fun Quiz!

2. Compared to adults, how likely are medication errors to occur in children?
   A. More likely
   B. As likely
   C. Less likely

Fun Quiz!

3. Which of the following excipients in oral formulations would concern you in medicines for children?
   A. Sorbitol
   B. Propylene glycol
   C. Ethanol

Fun Quiz!

4. When taking a medication history from a paediatric patient, which is the best source of information?
   A. Patient/carer
   B. GP record
   C. Patient's own medication

Introduction

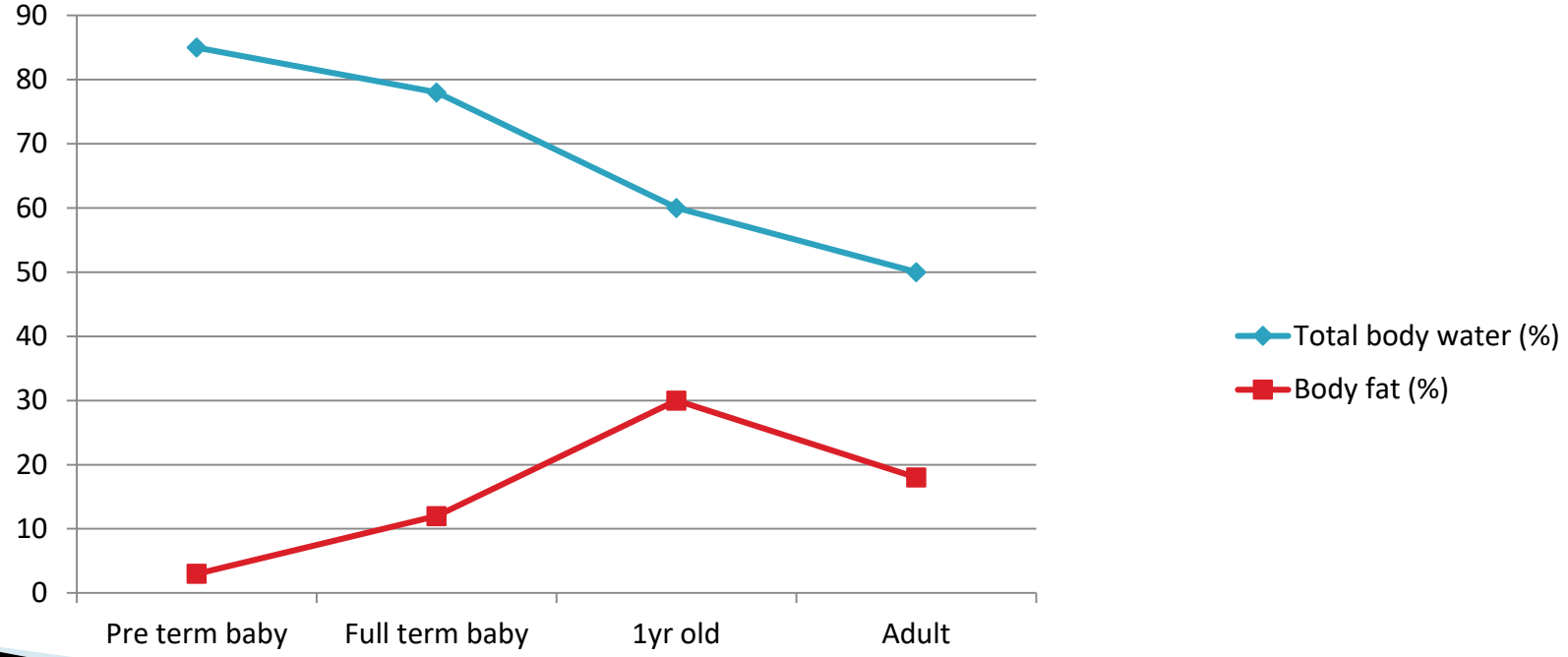
- Children are not just ‘small adults’ especially when drug handling is concerned; they are not ‘just children’ either
- Range of patients – premature babies, born as early as 24 weeks gestation, to 18-year-old adolescents
- They suffer from cardiac, respiratory, renal, and other system diseases, in the same way as adults.

Drug handling in Children: Absorption

- Orally → Gastric pH is high and gastric emptying is slow
  - Some drugs are erratically absorbed (increased or decreased)
    - Phenoxymethylpenicillin avoided in neonates
    - Ranitidine given TDS up to 6 months, then BD
- Intramuscular
  - Muscle mass is low & blood flow is reduced
  - Absorption unpredictable, avoid if possible

Distribution:

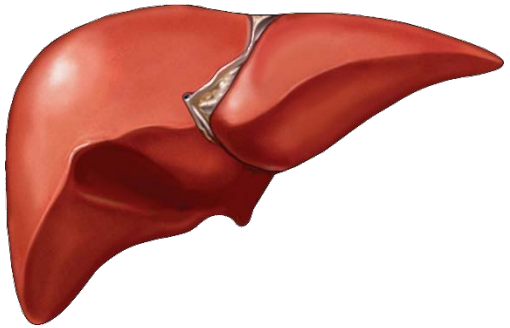
Water and Fat by age



Metabolism

- Reduced capacity in preterm babies and infants
  - As liver enzymes are induced, metabolism increases
  - Phenobarbital has half life of 70-200 hours in neonate then 20-50 hours at 2 weeks. Once daily → Twice daily

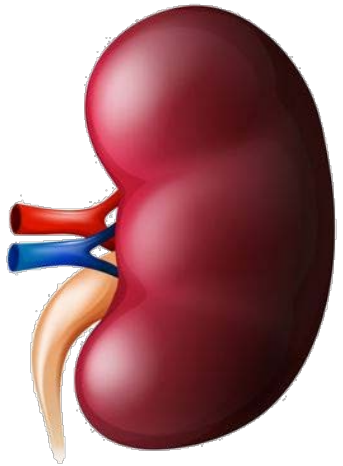
- ↑ metabolism in 1- 9 year olds
  - Relatively large size of liver
  - Theophylline clearance increased
  - Larger doses needed
    - Child 1 month- 12 years: 1mg/kg/hour
    - Child 12-18 yrs and adult: 0.5-0.7mg/kg/hour



Excretion

- Renal function reduced in neonates
- Drug frequencies may change after 7 days

- Benzylpencillin
  - Under 7 days: 25mg/kg every 12 hours
  - Over 7 days: 25mg/kg every 8 hours
- Gentamicin
  - Under 7 days: 5mg/kg every 36 hours
  - Over 7 days: 5mg/kg every 24 hours



But remember…

- Small people have small doses
- Always question doses >1mL in neonates
- Is the dose lower than an ‘adult’ dose?
- Question anything requiring multiple tablets/ampoules per dose
- Factor of 10 errors are common
- Mistaking milligrams and micrograms can happen – take extra care

Risks within paediatric pharmaceutical care

- Medication errors are more common in children
  - 3x more likely when the patient is a child
- Age range 0-18 years
  - pre-term neonates, term neonates, infants, children and adolescents
- Patients at extremes of age are more vulnerable than others
- Formulations
  - Liquid preparations
    - Different strengths available
    - Excipients
  - Ability to swallow tablets and capsules

Why are medication errors more common in children?

- Doses calculated individually based on age, weight and clinical condition → increased opportunity for, and higher risk of dosing errors
- Having to use formulations designed for adults
- Higher use of unlicensed and 'off-label' medicines
- Potentially complicated calculations
- Complexity of labelling
- Lack of familiarity

Types of errors

- Incorrect dose selection from reference source
  - Age group
  - Indication
  - mg/kg/dose vs mg/kg/day vs age banded doses
  - mg/kg vs mg/m^2
- Weight in kilograms vs pounds
- Miscalculation
- Renal or hepatic problems
- Allergies

Aciclovir

Check this dose

- Lisa is 6yr and weighs 20kg

PATIENT'S NAME Lisa Simpson HEALTH RECORD NUMBER K025678

MORNING (around 0800); MIDDAY (between 1200 & 1400); EVENING (around 1800): BEDTIME (around 2200)

ENTER DOSE AGAINST TIME REQUIRED. USE ONE ROUTE ONLY FOR EACH ENTRY

REGULAR MEDICINES — MONTH Jun - Jul — YEAR 2017

DATE 30 1

DATE → 30/6/17 | ROUTE → IV | SPECIFY TIME IF REQUIRED ↓ | DOSE ↓ | SIGN DOSE CHANGE ↓

MEDICINE (Approved Name): Piperacillin and tazobactam

SPECIAL INSTRUCTIONS

PRESCRIBER'S SIGNATURE: J Hibbert bleep No. 4567

PHARMACIST SUPPLY

Morning	0600	1.8mg
Midday	1200	1.8mg
Evening	1800	1.8mg
Bedtime	0000	1.8mg

DATE → | ROUTE → | SPECIFY TIME IF REQUIRED ↓ | DOSE ↓ | SIGN DOSE CHANGE ↓ | MEDICINE (Approved Name) | SPECIAL INST

Morning

y intravenous infusion

For Neonate
90mg/kg every 8 hours.

For Child 1 month–11 years
90mg/kg every 6–8 hours (ma

For Child 12–17 years
4.5g every 8 hours; increas
severe infections.

Home › Drugs › PIPERACILLIN WITH TAZOBACTAM

PIPERACILLIN WITH TAZOBACTAM

Indications and dose

Hospital-acquired pneumonia,
Septicaemia,
Complicated infections involving the urinary-tract,
Complicated infections involving the skin,
Complicated infections involving the soft-tissues

By intravenous infusion

For Neonate
90mg/kg every 8 hours.

For Child 1 month–11 years
90mg/kg every 6–8 hours (max. per dose 4.5g every 6 hours).

For Child 12–17 years
4.5g every 8 hours; increased if necessary to 4.5g every 6 hours, increased frequency may be used for severe infections.

Types of errors

- Confusion between units
  - mg, microgram, nanogram, picogram
- 10 fold, 100 fold, 1000 fold over or under-doses
- Infusion rates
  - microgram/kg/hour vs microgram/kg/minute
- Confusion between dose in mL or mg
- Abbreviations e.g. units not U
- Decimal points and leading zeros
  - Diazepam .5mg
  - Diazepam 5.0mg

What can I do to help mitigate the risks?

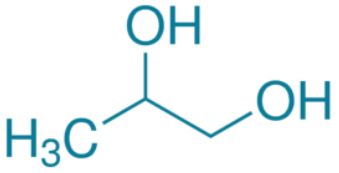
- Accurate drug histories and medicines reconciliation
- Double check calculations
- If you are dispensing or checking large quantities of a medicine for a child, stop and check the dose
  - Remember the captopril error!
- Check if the preparation you are dispensing or checking is suitable for use in **this** child on this occasion

Excipients in medicines for children

- Widespread unlicensed and ‘off-label’ use of adult medicines
- Need to chose a formulation carefully
  - Unable to metabolise or eliminate an excipient in the same way as an adult
- Problem excipients:

Excipient	Main safety concern
Propylene glycol	CNS effects, particularly in <4yr
Ethanol	Intoxication
Sorbitol	Osmotic diarrhoea and GI discomfort
Glucose or Sugar	Obesity and tooth decay
Artificial sweeteners	Unsuitable for use in patients with phenylketonuria
Colourants	Sensitivity and hyperactive behaviour

Propylene glycol (PG)



- PG is a solvent used in a variety of oral liquid, topical, and injectable medicines
- PG is particularly toxic in patients unable to metabolise and eliminate it
- CNS depression is its main toxic action
- Also hepatic or renal impairment, seizures, intravascular haemolysis, arrhythmia, lactic acidosis, respiratory depression and hyperosmolality
- European proposed safety limits for PG

	Neonates up to 28 days	1 month – 4 yr	5 – 17 yr
Safety limits (max daily dose)	1mg/kg	50mg/kg	500mg/kg

Example

- Amiloride 5mg/5mL oral solution sugar free (Rosemont) contains 0.1mL PG per 5mL → 2.07% w/v
- The lowest neonatal dose is 100 microgram/kg BD
  - A 3.5kg neonate would receive 700 microgram per day = 0.7mL
- 0.7mL oral solution contains 14.49mg PG

- Neonatal safety limit = 1mg/kg PG → 3.5mg
- This preparation is not suitable for use in a neonate

Ethanol

- Widely used as a solvent in oral formulations
- Risk of acute intoxication with accidental overdose and chronic toxicity with long-term use
- Children, especially those <6yr, are more vulnerable to the effects:
  - drowsiness, behavioural changes, impaired ability to concentrate at school

	< 6 yr	6 – 12 yr	> 12 yr
US FDA Safety limits	≤ 0.5%	5%	10%
Proposed European ethanol thresholds	BAC level ≤ 1mg/100mL (6mg/kg)	BAC level ≤ 12.5mg/100mL (75mg/kg)	-

Example

- Phenobarbital Elixir BP (15mg/5mL) contains 38% v/v ethanol → 30.4% w/v
- Usual maintenance dose: 1 month – 11 year = 2.5-4mg/kg OD-BD
  - 3yr old weighing 14kg on lowest dose would take 35mg OD = 11.7mL
- 11.7mL elixir contains 3.55g ethanol

- European safety limit (6mg/kg) = 84mg ethanol
- This preparation is not suitable for use in this child
- An unlicensed alcohol-free phenobarbital 50mg/5mL suspension is available

Sorbitol and artificial sweeteners

- Sorbitol is a sugar alcohol
- Used as a sweetener, vehicle and stabilising agent
- Common adverse effects: osmotic diarrhoea and GI discomfort
- Oral dose >140mg/kg/day may result in GI symptoms

- Artificial sweeteners include saccharin and aspartame
- Aspartame is a source of phenylalanine – avoid in children with PKU
- Cross reactions with sulphonamides

Colouring agents

- Used to:
  - improve acceptability to patients
  - aid identification
  - prevent counterfeiting
  - increase stability of light-sensitive drugs
- Artificial colours are banned in foods for infants and children
  - does not apply to medicines
- Associated with adverse effects including
  - hypersensitivity
  - gastrointestinal intolerance
  - dermatological reactions
  - carcinogenicity

Medicines Reconciliation: Role Play

- 4 groups
  - Pharmacy technician
  - Patient
  - Parent/carer
  - Observer (s)

Patient 1: James

- 8 yrs old
- 48kg
- PC: unwell, tired, vomiting
- PMH: Congenital adrenal hyperplasia

Patient 1: James

- GP record
  - Hydrocortisone 10mg tablets: Take HALF a tablet TWICE a day
- Patient's own medication:
  - Hydrocortisone 10mg tablets: Take HALF a tablet TWICE a day
  - Fludrocortisone 250microgram/5mL solution: Take 6mL DAILY

Patient 1: James

- Hydrocortisone 10mg tablets: Take HALF a tablet TWICE a day (morning and evening)
- Hydrocortisone 1mg/1mL solution: Take 5mL at lunchtime (at school)
- Fludrocortisone 250microgram/5mL solution: Take 6mL (300 microgram) DAILY

Patient 1: James

Learning

- Always use at least 2 sources to confirm medication history
- Parents/carers often best source
- Handwritten ‘specials’ may not show up on GP record
- Consider impact of medication at school

Patient 2: Fatima

- 12 yrs old
- 40kg
- PC: Increased work of breathing
- Diagnosis: Exacerbation of asthma
- PMH: Asthma

Patient 2: Fatima

- GP record
  - Salbutamol MDI : Inhale as directed
  - Aerochamber yellow: as directed
  - Clenil modulite 100: 2 puffs twice daily

- Patient's own medication
  - Nil

Patient 2: Fatima

- Salbutamol MDI – as needed
- Clenil 100 inhaler: 2 puffs twice daily (when at Mum's house; not used at Dad's)
- Aerochamber : no longer used
  - Also inappropriate as patient is 12yrs old

Patient 2: Fatima
Learning

- Check with patient if old enough
- Consider compliance especially with inhalers
- Consider shared living arrangements
- GP issues may not be up to date

Patient 3: Oliver

- 2 yrs 9 months old
- 15.2kg
- PC: seizures
- PMH: Epilepsy (known to neuro team)

Patient 3: Oliver

- GP record
  - Sodium valproate 200mg/5mL solution: 140 mg (3.5mL) am & 160mg (4mL) pm
  - Levetiracetam 100mg/mL solution: 3 mL (300mg) twice a day

- Patient's own medication
  - Sodium valproate 200mg/5mL solution: (3.5mL) am & (4mL) pm
  - Levetiracetam 100mg/mL solution: no directions

Patient 3: Oliver

- Drug chart
  - Sodium valproate 200mg/5mL solution: 200mg (5mL) twice a day
  - Levetiracetam 100mg/mL solution: 100mg twice a day

Patient 3: Oliver Learning

- Epilepsy medication can change often
  - Sometimes via telephone
- Clinic letters may be more up to date than GP records
- Always check with parents/carers

Patient 4: Alya

- 4 years old
- 23kg
- Admitted with: ?Chest infection
- PMH: Global developmental delay, spasms

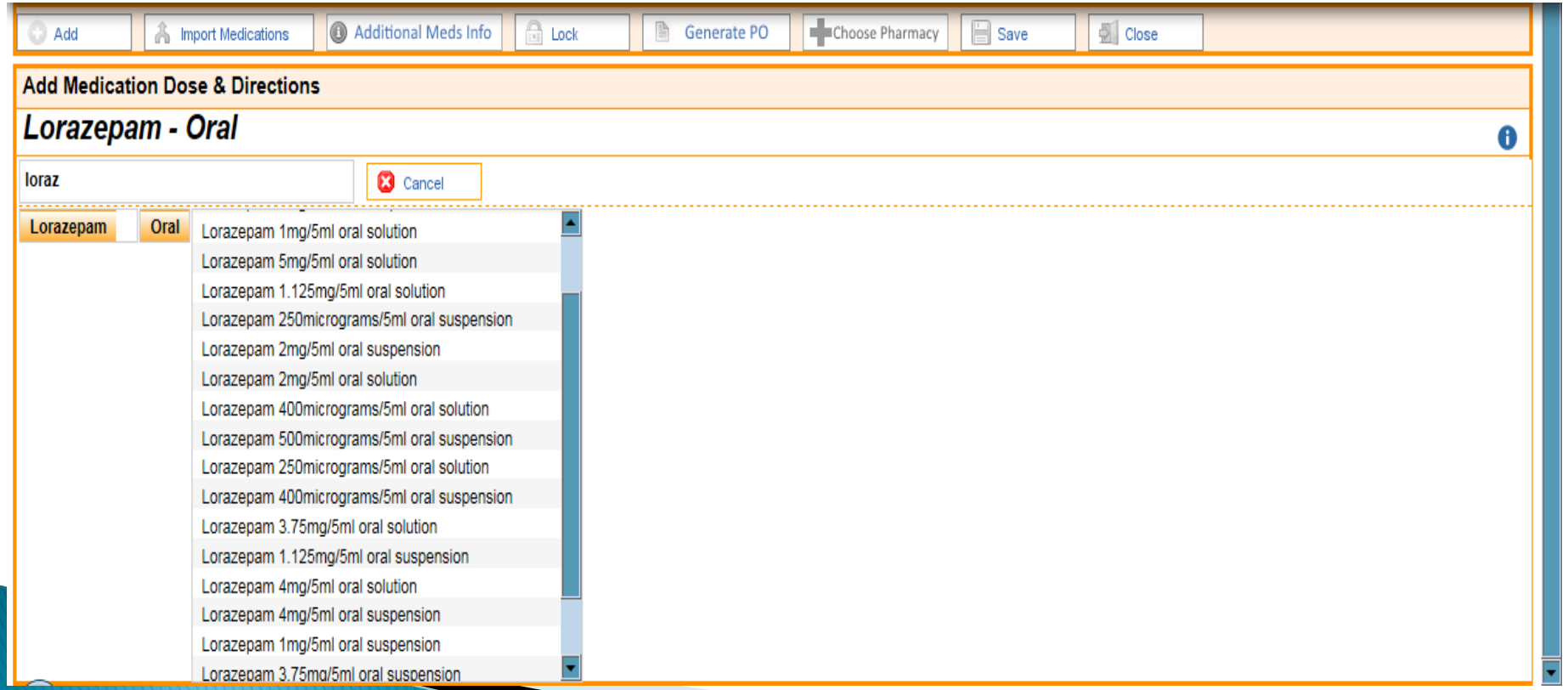
Patient 4: Alya

- GP Record:
  - Not available
- Discharge letter from 15th June 2017:
  - Lorazepam 1mg/1mL solution: 2mL three times a day
- Own medication:
  - Lorazepam 1mg/5mL solution: 2mL three times a day

Patient 4: Alya

- Lorazepam 1mg/1mL: 2mg (= 2mL) three times daily
- Different strength issued by GP and dispensed by community pharmacy
  - This is common
  - Dose should have been altered
  - 1mg/1mL solution: 2mg dose = 2mL
  - 1mg/5mL solution: 2mg dose = 10mL

Patient 4: Alya



Patient 4: Alya

Learning

- Some liquids have MANY different strengths
  - Lorazepam at least 18
- If unlicensed, specials companies can make any strength
- Always check dose with parents (sometimes will only know dose in mL). Also GP, clinic letters, previous admissions
  - At least 2 sources, but 3 or more if any doubt

Useful resources for paediatrics

- BNF for Children https://bnfc.nice.org.uk/
- Medicines for Children leaflets http://www.medicinesforchildren.org.uk/
- Evelina London Paediatric Formulary
- Neonatal and Paediatric Pharmacists Group (NPPG) – here to help technicians too! http://www.nppg.org.uk/
- Neonatal Formulary
- Martindale
- Summary of Product Characteristics (SPC) if licensed product

NPPG

Any questions?