



Paediatrics

Original Lecture by Judith Cope

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Learning Outcomes

1. Understand how paediatric patients are different to adults in terms of medicines use
2. Consider medication issues encountered in paediatric patients
3. Understand child development
4. Consider paediatric specific factors in prescribing
5. Apply paediatric knowledge in pharmacy practice

Dr Abraham Jacobi, more than 100 years ago, said...

“Paediatrics does **not** deal with miniature men and women, with reduced doses and the same class of disease in smaller bodies, but... has its own independent range and horizon.”

*Halpern SA. American pediatrics: the social dynamic of professionalism, 1880-1980.
Berkley: University of California Press, 1988:52*

QUESTION

In terms of medicines and health, how are children different to adults?

Think of 3 reasons and write them down

Children Are Different

- Vulnerable
- Behaviourally
- Psychologically
- **Ability to communicate**
- Level of learning
- **Growth and development**
- Sexual maturation
- **Pharmacokinetics**
- Pharmacodynamics
- Therapeutic windows
- Unique disease states

Stages of child development

Premature

<37 weeks gestation

Neonate

birth → 1 month

Infant

1 month → 1 year

Child

1 year → 12 years

Adolescent

12 years → 18 years

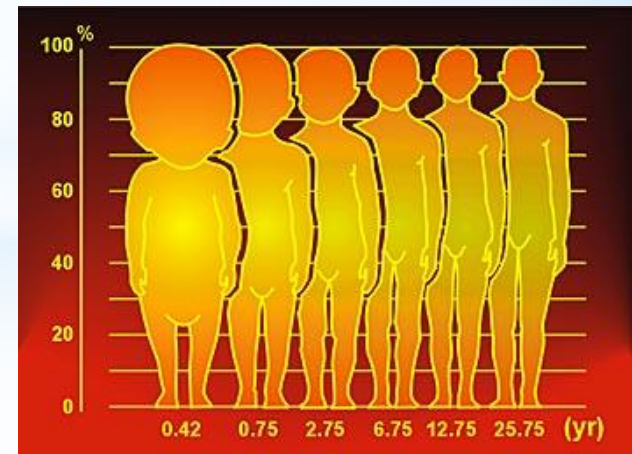


Child Development

Age-related changes in:

- body weight and composition
- differential increases in organ size
- change in organ perfusion (esp. muscle)
- absorption, distribution, metabolism and excretion

Most significant changes occur during neonatal and infant periods



Paediatric values

Age	Weight (kg)	Surface Area (m ²)	% of adult dose
Term	3.5	0.23	12.5
3 mths	6	0.31	15
6 mths	7.5	0.38	20
1 yr	10	0.47	25
3 yrs	14	0.61	33
5 yrs	18	0.72	40
7 yrs	22	0.86	50
10 yrs	32	1.1	60
12 yrs	40	1.3	75-100
14 yrs	50	1.5	80-100

Paediatric Pharmacopoeia 13th Ed. Royal Children's Hospital Pharmacy, Melbourne

Observations

Age	Pulse	Resp rate	BP (systolic)
Infant	110-160	30-40	70-90
Toddler	100-150	25-35	80-95
Preschooler	95-140	25-30	80-100
School-age	80-120	20-25	90-110
Adolescent	60-100	15-20	100-120

Paediatric Pharmacokinetics

- What age is a child?
 - Premature neonate, infant, child, adolescent
 - Maturation at different rates in children of the same age
- Consider the effects of disease
 - e.g. liver failure, renal failure, burns, cystic fibrosis

PK DIFFERENCES

ABSORPTION

- Volume of acid concentration of gastric fluid increases with age
 - Reaches adult values around ~ 2 years of age
 - Decreased acidity may enhance absorption of acid- labile medicines like penicillins and decrease absorption of medicines like itraconazole
- Slower gastric emptying and peristalsis
- Reduced gut flora
- Spitting out and vomiting (in the earlier stages)
- Disease state - GORD! (gastric pH is relatively high)

Oral absorption - So?

- Avoid oral use in neonates until full feeds established
- Consider if disease state will affect absorption
- Expect slower absorption in neonates & young infants up to 4-6 months
 - longer time to achieve therapeutic levels
- Give parents advice about whether to repeat dose if spat out or vomited

Intramuscular absorption

- Muscle mass low, reduced and variable blood flow, reduced muscle activity
 - Neonates, particularly if premature or paralysed (decreased contractions)
 - Shock (decreased blood flow)
- Variable, unpredictable and sometimes incomplete absorption from IM sites
- Potential for muscle damage with large volumes
- Painful!

Intramuscular absorption - So?

- Be kind! - don't use IM route if avoidable
 - Single injections or to avoid missing doses if IV temporarily unavailable.
 - Vaccines are usually IM injections
- Minimise volume
 - Maximum 0.5-1mL per site
- Have injection at room temperature
- Use smallest possible needle
- Consider clinical condition
- Use parents, distraction, tricky holding positions, special bandaids!

Percutaneous absorption

- Large surface area relative to body weight
- Well hydrated, thin, permeable skin
 - Increased cutaneous perfusion
 - Increased epidermal hydration
- Drug toxicity possible in infants:
 - E.g. Potent topical steroids

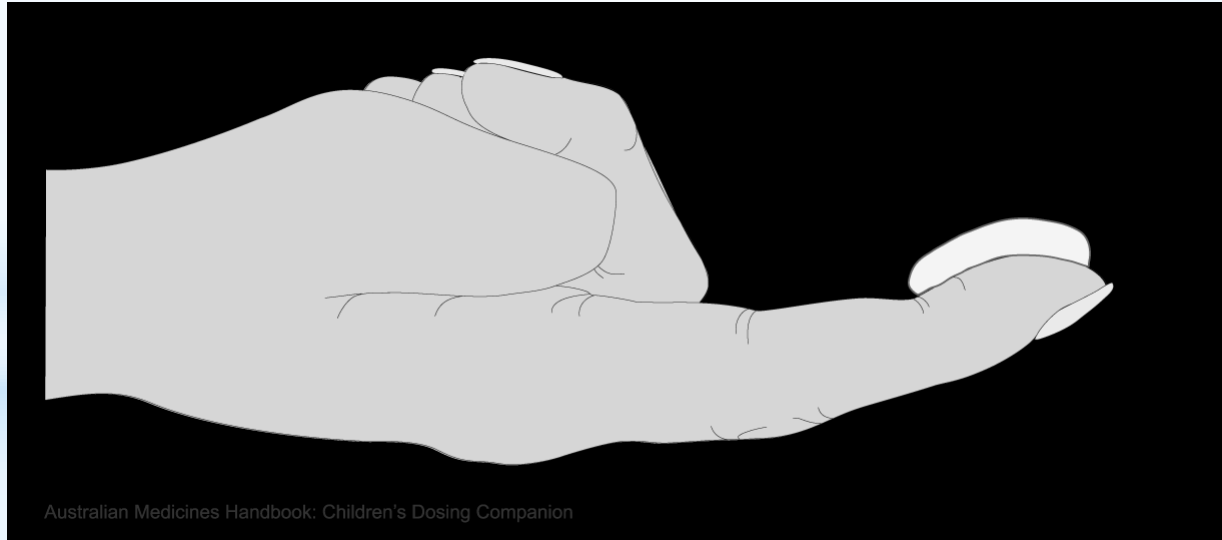
Percutaneous absorption - So?

- Don't use topical drugs unless you are happy for them to have systemic effects
- Caution where large areas of skin are damaged or inflamed (e.g significant burns, psoriasis or eczema)
- Remember excipients can cause toxicity too

Possible future route of administration of drugs!

Fingertip units

- *The fingertip unit is a simple way to measure how much cream or ointment to apply.
- *One fingertip unit is the amount of cream or ointment, squeezed out of a tube, from the tip of an adult's index finger to the first crease in the finger.



Fingertip units

- * One fingertip unit is enough to cover an area of skin twice the size of a flat adult hand with the fingers together.

Age of patient	Number of adult fingertip units to apply each dose				
	Face and neck	Entire arm and hand	Entire leg and foot	Front of chest and abdomen	Back and buttocks
3-12 months	1	1	1½	1	1½
1-3 years	1½	1½	2	2	3
3-6 years	1½	2	3	3	3½
6-10 years	2	2½	4½	3½	5
>10 years	2½	4	8	7	7

PK DIFFERENCES

DISTRIBUTION

- Total body fluid reduces with age (about ~ 92% in premature newborn and 50 - 60% in 12 years to adults)
 - Larger apparent volume of distribution for water soluble drugs
 - Higher doses often needed for water soluble drugs (e.g penicillin and aminoglycosides)
- Total body fat increases with age
- Reduced plasma protein binding in infants

PK DIFFERENCES

METABOLISM

- Enzymatic activity generally increases with age
 - E.g. CYP2D6 which is responsible for co-demethylation of codeine to morphine is decreased in infants, resulting in lack of efficacy and poor pain control
- Hepatic function may be greater in children than adults
 - Liver is larger compared to relative body size
 - Some epileptic medications require higher dose (mg/kg)

Metabolism - specific drugs

- Phenytoin elimination half-life
 - Preterm infants approx 75 hours at birth
 - Term infants - 24-48 hours
 - 14 days postnatal age - 8 hours
- Carbamazepine:
 - CYP3A4 higher in children and gradually changes to adult levels in adolescence.
- Paracetamol
 - Sulfation is major metabolic pathway in neonatal and early infancy - changes to glucuronidation over several months

Metabolism - So?

- Dose less frequently in infants (usually)
- Some drugs may need MORE frequent dosing and/or higher doses in older infants and children
- Use paediatric specific dose
- Monitor for effectiveness/toxicity
- Be aware of different metabolites - may be active eg theophylline to caffeine in infants

PK DIFFERENCES

EXCRETION

- Glomerular function reaches adult levels at 3-6 months of age
- Renal tubular secretion increases more slowly
- By 8-12 months renal function close to adult values
- Some diseases associated with rapid clearance of some drugs
 - eg aminoglycosides in children with CF
- Adaptive changes in renal blood flow

Excretion - So?

- Dramatically reduced doses or extending the interval is required in neonates for renally cleared drugs
- Consider patient specific factors (eg disease state)
- Adjust dose according to response

What are Potential Problems with Medicines Use in Paediatrics

- Unclear diagnosis
- Limited access to approved medications -
Including lack of suitable formulations
- Inability or diminished ability to tolerate,
recognise or communicate effects
- Administration difficulties
- Compliance difficulties
- Low blood volume - need for small blood samples

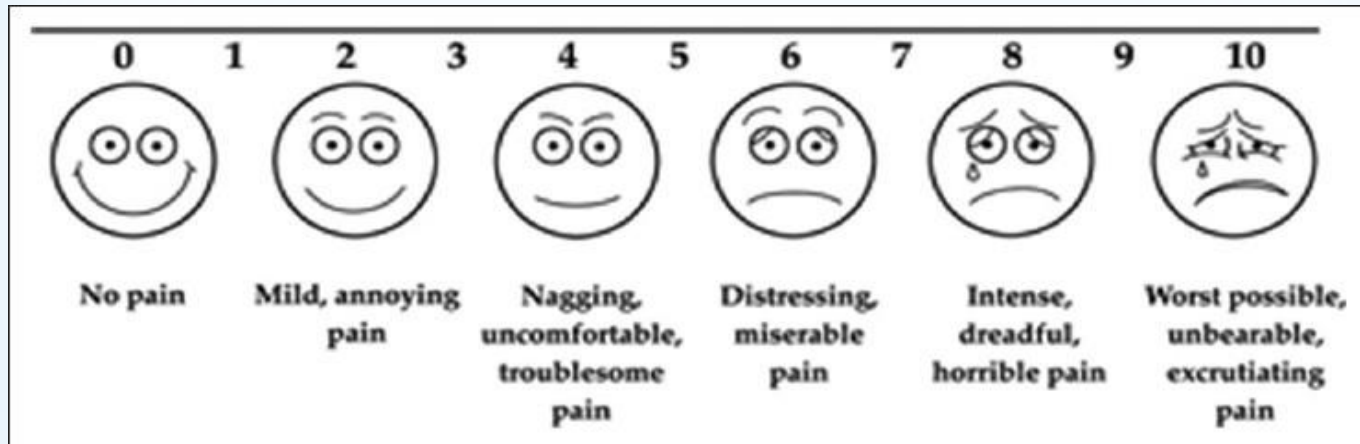
Barriers to communication

Anxiety:

- Fear of strangers inhibits cognitive cooperation and speech
- Fear of pain inhibits physical cooperation
- Fear of unfamiliar may make child less willing to report their condition

Children are less likely than adults to question those in authority

Pain Assessment in Children



WONG BAKER FACE SCALE

Pain Assessment in Children

The FLACC Pain Scale

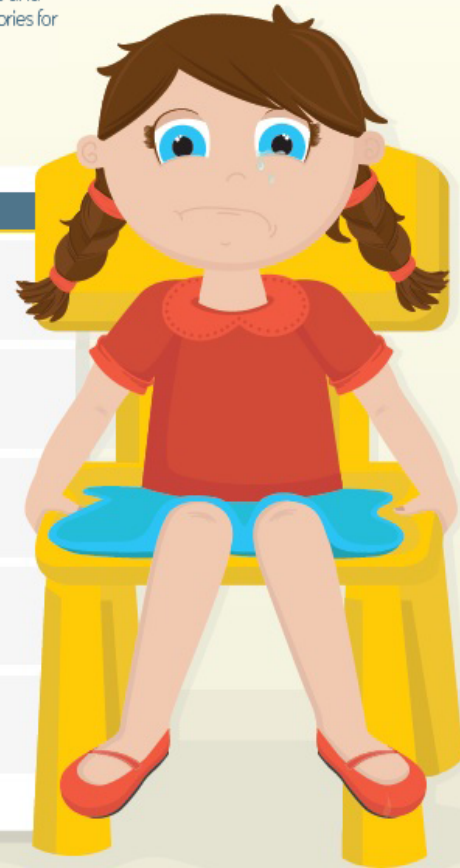
Sometimes it is difficult to assess pain in children who are non-verbal. The FLACC Pain Scale is a system that can help parents and professionals assess pain levels in children who have limited or no expressive communication. The diagram shows the categories for scoring. Zero, one or two points are given to each of the five categories: Face, Legs, Activity, Cry and Consolability.

Interpreting the Behaviour Score
Each category is scored on the 0-2 scale, which results in a total score of 0-10

0	relaxed and comfortable	4-6	moderate pain
1-3	mild discomfort	7-10	severe discomfort of pain or both

Categories ▼	Score Zero ▼	Score One ▼	Score Two ▼
Face F	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant quivering chin, clenched jaw
Legs L	Normal position or relaxed	Uneasy, restless, tense	Kicking or legs drawn up
Activity A	Lying quietly, normal position moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
Cry C	No crying (awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability C	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distractable	Difficult to console or comfort

If a child is showing these behaviours, it doesn't necessarily mean that they are in pain, as some of the behaviours measured by the FLACC scale can happen for other reasons. However, parents are advised to follow up high scores with a professional.



Adverse drug reactions (ADR)

Nature and severity of ADRs differs to adults

MEDICINE	ADR
lamotrigine	10 fold increase in incidence of skin reactions in children v's adults
Steroids	growth suppression
Aspirin	Reye's syndrome in <12yo
Tetracyclines	contraindicated in children <8 as can discolour teeth and cause enamel dysplasia which increases the risk of dental caries. They are also deposited in bone, causing deformities and inhibiting bone growth

Medication Safety in Children

Children are at increased risk of errors:

- Calculation errors
- Ten-fold dosing errors
- Preparation/ administration errors
- Lack of information

Errors in Children - the Evidence

- Similar overall medication error rate to adult patients (5.7 per 100 orders)

BUT

- Errors with potential to cause harm were **THREE times more likely** to occur
- Neonatal ICU particularly susceptible
 - Fortescue EB et al. *Pediatrics* 2003;111:722-729
- Intravenous fluids most commonly cited product involved
- Incorrect dosing most commonly reported error
 - Crowley E et al. *Curr Ther Res.* 2001;26:627-640

Examples of Actual Harm

- Trimethoprim/Sulphamethoxazole - 5 x overdose (Nausea & vomiting)
- Vancomycin - given over 30 mins (red man syndrome)
- Metoclopramide - child given adult dose (dystonic reaction)
- Codeine - 3 x overdose (drowsiness)

Pharmacist's Role

What can you do as a pharmacist to prevent or minimise medication errors?

Write down two ideas

Prescribing for children

- Factors to consider:
 - ☐ Age of child
 - ☐ Choice of drug
 - ☐ Choice of dose
 - ☐ Choice of formulation
 - ☐ Duration of therapy
 - ☐ Choice of administration technique
 - ☐ Choice of interval & timing
 - e.g. avoid schooltime, sleeping times

To reduce the potential for medication errors:

- Write orders clearly and concisely
- Write medication orders using **generic drug** names only.
- Be careful with **mg/kg/DAY** vs mg/kg/DOSE.
- Include the intended dose per kilogram on each order.
- Write the patient's **weight and age** on each order sheet.
- Never place a decimal and a zero after a whole number (4.0 mg should be 4 mg) and always place a zero in front of a decimal point (.2mg should be 0.2 mg). The decimal point has been missed and tenfold overdoses have been given.
- Always order medications as **mg, not mL** as different concentrations may exist of a given medication. There are a few exceptions such as co-trimoxazole (Septra®).
- It is best to write out “once daily” or “q24h.”
- **Do not abbreviate** drug names (levo, 6MP, MSO4, MgSO4, HCTZ).
- **Do not abbreviate microgram to µg**, use mcg, or even safer, write out microgram or use milligrams if possible (0.25 mg instead of 250 micrograms)

Resources for prescribing

- Paediatric Pharmacopoeia
- BNF for children
- AMH: Children's Dosing Companion



Formulation choice

DOSING CHOICE: mg/ kg

- Liquids often not available
 - Children often can not swallow tabs/caps
 - Extemporaneous formulations
 - Wrapped powders
 - Injections orally - pH/taste
 - orally and rectally
 - open capsules/crush tablets and disperse in water
 - Mixtures/Suspensions
- ?bioavailability of such formulations

Paediatric Considerations: Administration

Oral -

- Smell, appearance and after taste - disguised or masked with small quantities of food
- Should NOT be mixed with large quantities of food- Why?
- AVOID mixing or administering in baby's feeding bottle
- Unpleasant taste can be disguised by flavoring it or by giving a favorite food or drink immediately afterwards
- Liquid formulation is preferred for children under 5 years (LT tx use caps/tabs)
- Always provide oral syringe for accurate measurement (for liquid formulation)
- What to do if dose spat out or vomited

Enteral

Feeding Tubes

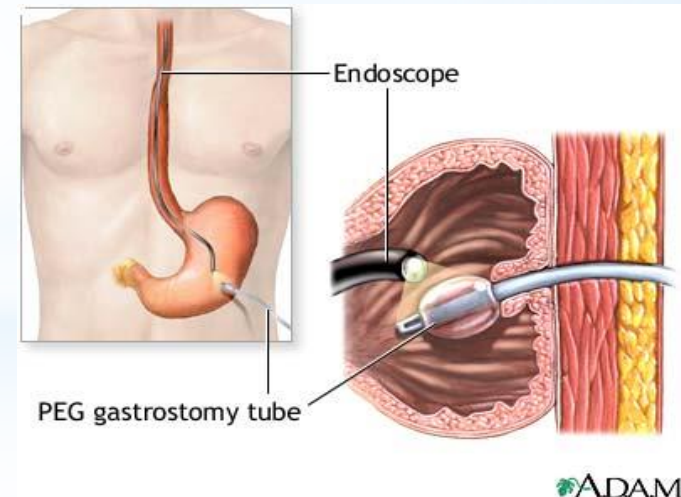
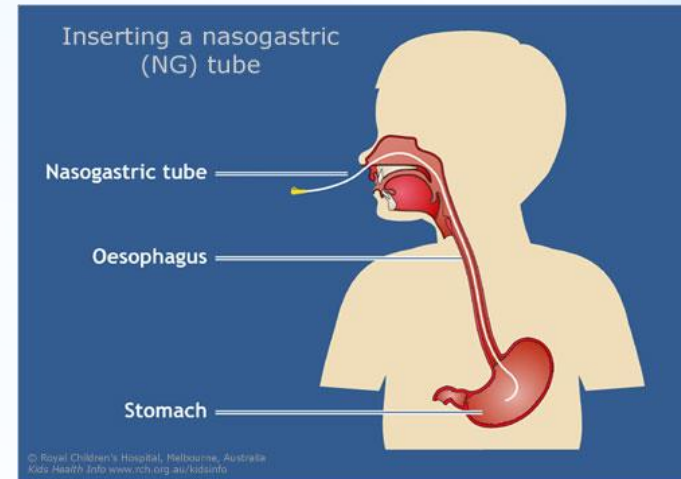
- Naso-gastric tube
- Transpyloric tube

Gastrostomy

- G-tube



- Mickey button



Enteral

Formulation choice

- Must be a liquid
- Size of suspension particles vs size of tube
- Binding or adsorption to plastic tubing
- Interaction with feeds (consistency)
- Nasogastric tube to a neonate: a sterile water must be used to accompany the medicine or to wash it down

References

- Martindale
- E-MIX <http://infotech.co.nz/manual/Formulation/oral.htm>
- Handbook of drug administration via enteral feeding tubes (White and Bradman)

Topical

Eye drops, ear drops

- Struggle!
- Volume
- Guides to parents

Creams, ointments

- Accidental ingestion or into eyes
- Systemic absorption
- Skin sensitivity

Inhalers

- Inspiration force
- Mask and spacer



Parenteral

Intramuscular

- Avoid!
- Local anaesthetic cream

Intravenous

- IV fluids – high risk
- Small veins
- Compatibilities - pH

References

- Children's Hospitals' own guides
- BNF / Martindale may have information
- Trissel's stability of compounded solutions

Paediatric Considerations: Compliance

Age of child

Beliefs of parents – religious, cultural, personal

- Perceived efficacy, side-effects
- Risk and severity of side-effects

Ease of administration

- inability to swallow the medicine
- Unattractive formulation (e.g. taste, smell, texture)
- Complexity of regimen e.g. cilicaine suspension

Paediatric Considerations: Compliance

Decreased understanding

- Purpose of medicine not clear
- Ambiguous instructions for administration

Environmental/ logistical factors

- At school, day care
- Storage (fridge?)
- Eye drops – need someone to administer

Compliance - Tips

Infants

- Minimum volume, oral syringe
- Avoid mixing with a feed

Toddlers

- Make nice tasting - mix with pureed fruit, strawberry "Quik", jam, honey, yoghurt
- Drink "chaser" afterwards
- Negotiate (where, when, who with, what with)
- Bribery only if needed

Compliance - Tips

Older children and adolescent

- Involve in counselling process - explain reasoning
- Take responsibilities like an adult
- Technology
- Minimise number of doses at school

Medication counselling

- Explain what the medicine is for, side effects, dose, duration, when to refer etc
- Advice on management of SE's
- Involve the child in the counselling process (encouraged to take responsibility)
- Be prepared to compromise
- Empower parents/carers to work out solutions for their family - information!
- Printed information (company/professional) - paediatric specific where possible

How to give medications to children

<https://www.rch.org.au/uploadedFiles/Main/Content/pharmacy/how-to-give-medications-to-children.pdf>

Improving concordance/compliance

- Improve choice and ease of application – empowers the patient:
 - Allowing children with asthma a choice in their inhaler device
 - Administering steroids once-daily at a time of their choosing
 - Prescribing of inhalers which fit a single spacer device
 - Allowing children with eczema to pick their favourite emollient
- **“Match the medicine to the patient”**

Pharmacist's responsibility..

- “To ensure that a child is able to receive the correct dose of their medicine in a way that is understandable, reproducible and acceptable to the child and carer.”
 - *Child Health – Working with the National Service Framework for Children, Young People and Maternity Services. 2006*

Key Messages (1)

What are the key messages?

- “Infants and Children are not just small adults”
- Keep in mind the pharmacokinetic differences and adjust as they grow older
- Use clinically proven paediatric doses where possible
- Do not exceed adult dose

Key Messages (2)

- Think about the “how” not only the “what”
 - Consider paediatric specific factors for prescribing, administration and to improve compliance e.g. formulation type, dose regimen

***Any management involves a whole family,
not just a patient***

CASE STUDY 1

You have just received a script for a 4 year old patient for SERETIDE 250/50 ACCUHALER 2 puffs BD

The parent tells you that the child has been on FLIXOTIDE 50mcg 2 puffs BD before and SALBULTAMOL prn.

- Is this appropriate ?
- What other questions would you ask the patient/parent?
- What other advice could you give the patient?

CASE STUDY 2

Doctor has prescribed trimethoprim 50mg BD for 3 days in a 2 year old patient (12 kg) for a UTI

- Is this an appropriate dose?
- What formulation can you use?
- How would you counsel the patient?
- What instructions would you give the patient/family?
- If It was for prophylaxis, what would the dose be?

CASE STUDY 3

Doctor wants to send a patient home with 5 day course of amoxicillin. Patient is 8 years old and weighs 20kg.

- What dose would you give the patient ?
- Which formulation would you give the patient?
- What instructions would you give the patient or the family?
- How would you explain what an anaphylactic reaction is?

CASE STUDY 4

Patient has been diagnosed with otitis media. The doctor has prescribed Cefaclor to treat the infection.

- Which group of antibiotics does cefaclor belong to?
- If the patient is allergic to penicillin, would it be safe to take cefaclor?

Patient is 4 years old and weight 15 kg.

- What would be an appropriate dose for this patient?
- What are some of the side effects the patient could experience?

Thank you!

Questions?

