

# Neonatal prescribing

Dr Lynda Brook

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Association for  
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# Neonatal prescribing

- Why are neonates different?
- Common symptoms and problems
  - Pain
  - Nutrition
  - Seizures
  - Other symptoms
- Summary and conclusions

# Why are neonates different?



- Size
- Immature metabolism
- Routes for drug administration
- Developmental expression of pain and other symptoms

# Size

- Neonates, particularly sick and preterm neonates have
  - Increased body surface area to weight ratio
  - Less ability to generate heat in brown fat or through shivering
  - And consequently greater difficulty maintaining body temperature
- Organs such as liver and brain are relatively larger
- More body water and less body lipid

# Neonatal drug disposition

- Limited gastric acid production
- Delayed gastric emptying
- Slower gastrointestinal but faster (unpredictable) intramuscular absorption
- Immature hepatic function
  - Limited capacity for gluconeogenesis
  - Risk of hypoglycaemia
  - Reduced capacity for hepatic conjugation
- Limited protein binding
- Reduced renal clearance



# Hepatic metabolism

- Phase 1 primary oxidation
- Phase 2 conjugation
  - Drug molecules are joined (conjugated) with molecules made in the liver to facilitate excretion in the bile or urine
- Maturation of different enzymes at different rates
  - Significant activity by 2 months of age
  - Adult levels by 1 year of age
- Neonates require decreased dose for drugs primarily excreted via hepatic metabolism
  - Ideally first dose based on body weight
  - Subsequent doses based on response

# Renal excretion

- Kidney development completed at 34 weeks
- Water soluble drugs and other toxins are filtered and actively secreted by the kidney
- Glomerular filtration rate (GFR)
  - Reduced in term neonates
  - Even more reduced in preterm neonates
  - Increases in preterm and term neonates in first 2 weeks of life
- Mature renal function
  - GFR by 2 years of age
  - Tubular secretion by 1 year
- Neonates require increased dosing interval for drugs primarily excreted via the kidney

# Metabolism of important drugs in palliative care

Drug	Non renal elimination	Comments
Morphine	90%	Half-life increased in severe hepatic impairment Active metabolites accumulate in renal failure
Midazolam	100%	Prolonged half-life in hepatic and/or renal impairment
Phenobarbital	70%	Long half life Induces hepatic glucuronidation
Hyoscine hydrobromide	45%	
Cyclizine	[75%]	Inactive metabolites excreted in urine
Haloperidol	100%	
Paracetamol	100%	



# Routes for drug administration

- Enteral route
  - Limited if gastrointestinal malformation
  - Impaired absorption
- Buccal route
  - Useful alternative to enteral route
  - Increasing experience
- Intravenous route
  - Use pre-existing venous access especially when withdrawing life sustaining treatments
  - Peripheral venous access short term and unreliable for care at home
  - Central venous access requires surgery and expertise
- Subcutaneous route
  - Can be used effectively
  - Limitations in small babies with limited subcutaneous tissue
  - Practical problems with siting subcutaneous line in very small babies

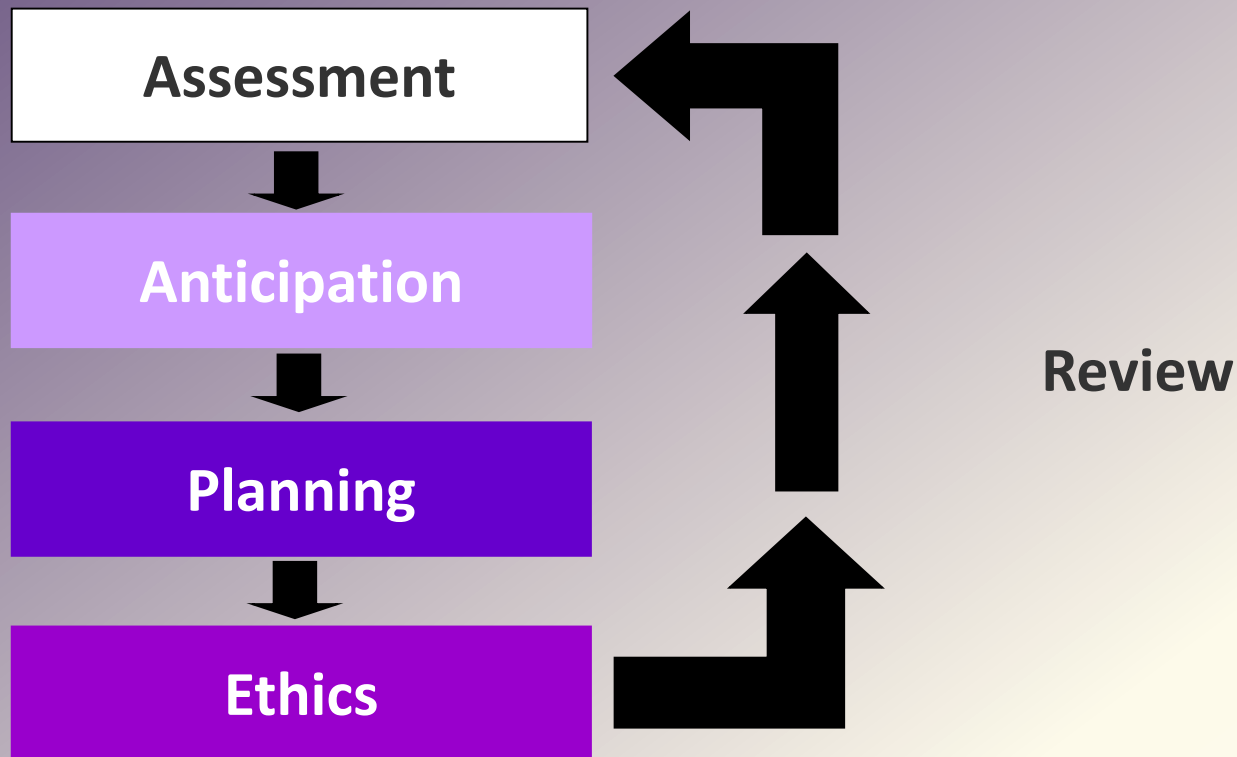
# Common symptoms and problems

- Series of symptom prevalence in palliative care have included few, if any, neonates
- Widespread recommendations for practical, consensus and evidence based guidance on symptom management
- Alder Hey
  - Pain
  - Seizures
  - Loss or lack of enteral route
  - Irritability
  - Dyspnoea
  - Apnoea
- Mancini, Uthaya, Wood et al 2011
  - Pain
  - Seizures
  - Secretions
  - Fluids and Nutrition
  - Ventilation and Oxygen

# Development and expression of pain and other symptoms

- Neonates are more sensitive to pain than children or adults
- Expression of pain is limited to facial expression, crying and physiological variables
- Scales for measurement of pain in neonates utilise physiological variables which may not be appropriate in chronic pain or end of life care at home
- No scales or measures for systematic evaluation of other symptoms in neonates

# Effective symptom management



# General principles



- Normal neonatal comfort measures
  - Warmth
  - Security
  - Skin-skin contact if possible
  - Nesting
- Care for the mother
- Consider other family members particularly siblings

# Pain assessment

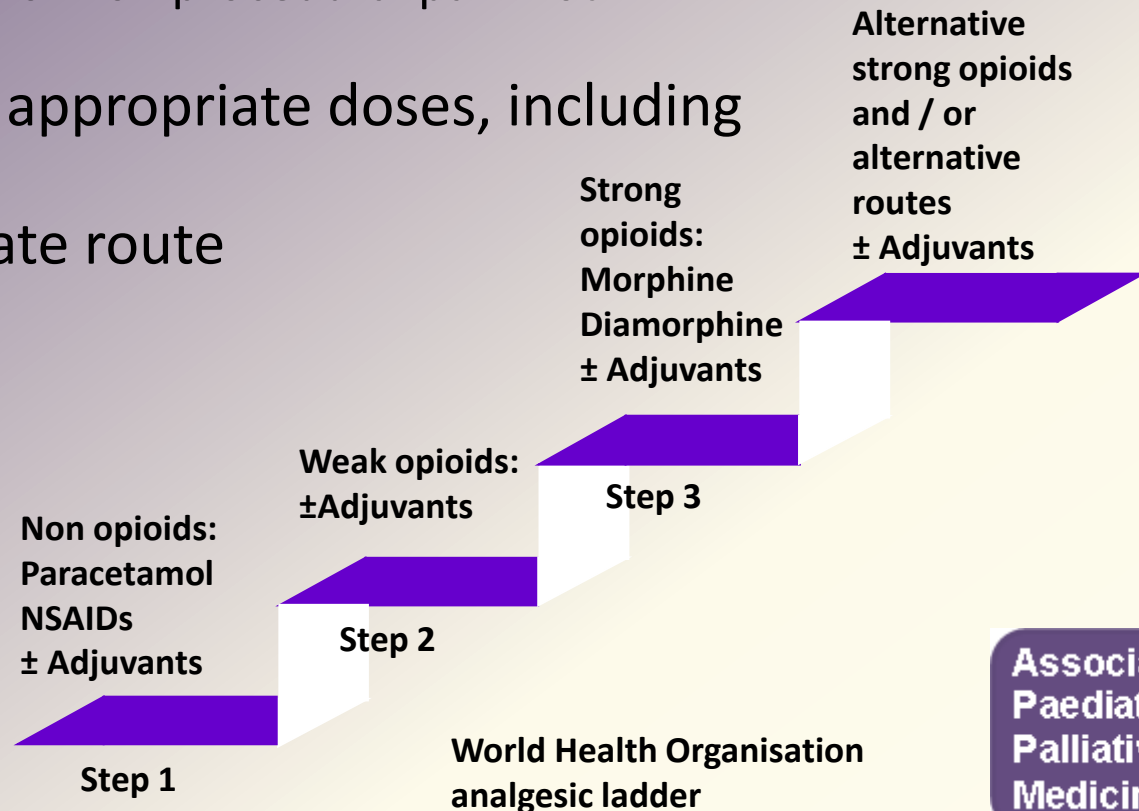
- Always consider pain as a possibility
  - Procedural pain
  - Disease related pain
- Appropriate pain scales
  - Majority post-operative pain scales
  - Majority designed for research rather than clinical use
  - Many validated in groups including neonates and some preterm neonates
- Lower birth weight infants are less likely to receive analgesic medications



# Pain management

(evidence quality moderate)

- Use WHO analgesic ladder
- Consider also sucrose
  - Appropriate for acute procedural pain
  - Use in chronic or non procedural pain not evaluated
- Age/ gestation appropriate doses, including loading doses
- Most appropriate route
- Remember to re-evaluate



# Neonatal seizures

- Atypical compared with older children or adults
  - Focal twitching
  - Apnoea
  - Generalised tonic spasm
  - Rhythmic cycling movements of arms and or legs
- Differentiate from “jitteriness”



# Seizures (evidence quality low)

- Goal is to ensure baby (and family) are not distressed by seizures
- Complete freedom from seizures may not be achievable or realistic
- All abnormal movements are not necessarily seizures
- Identify reversible underlying cause
  - Treat where appropriate
  - Hypoglycaemia
  - Disturbance in calcium and magnesium levels
- Maintenance treatment
  - Phenobarbital enterally
  - Can also be given by continuous intravenous or subcutaneous infusion
- Breakthrough seizures
  - Buccal midazolam
  - Continuous intravenous or subcutaneous infusion of midazolam (or clonazepam)

# Loss of enteral route

- Common problem in neonatal palliative care
- Ethical and practical considerations
- In those infants able to take and tolerate milk feeds, provision should be determined by
  - Condition of the baby
  - Cues the infant demonstrates
- Oral nutrition only withheld if
  - It will cause pain and discomfort
  - Death is imminent
- Baby is dying from condition which has resulted in loss of enteral route: not dying from or dehydration **starvation**

# Loss of enteral route

(evidence quality low)

- Reduce volume of enteral feeds if vomiting is a problem
- Ensure medication for symptom management
  - Consider alternative routes
- Balance benefits and burdens of artificial nutrition and hydration
- GMC guidance on withholding fluids and nutrition at end of life
- Oral feeds, breast feeds or dummy to suck on for comfort
- Primary goal is comfort, not the provision of nutrition

# Irritability

- Non specific cerebral irritability
- Often associated with hypoxic brain injury
- Exclude treatable factors
  - Warmth
  - Security
  - Positioning
  - Hunger/ suckling
  - Avoiding excess stimuli – noise, light
- Consider and treat pain
- Exclude other treatable underlying causes
- Consider sedation
  - Chloral hydrate
  - Midazolam
  - Phenobarbitone

# Dyspnoea

- Sensation of breathlessness
  - Not the same as hypoxia or cyanosis
  - Increased work of breathing
  - Difficulty feeding
- Management
  - Positioning to ensure airway
    - Consider prone
  - Reduce respiratory effort – nasogastric feeds
  - Strong opiates in half analgesic doses significantly reduce sensation of breathlessness in adults
  - Benzodiazepines may reduce anxiety associated with breathlessness in adults and children

# Apnoea

- Periods of irregular breathing or stopping breathing
- Whose problem is it?
  - Unlikely to be distressing for baby
  - May be part of normal dying process
- Management plan determines appropriate monitoring

# Excess respiratory tract secretions

(level of evidence very low)

- Secretions may accumulate and cause distress for the baby and family
- Positioning may allow secretions to drain without more specific intervention
- Gentle suctioning
- Consider medications to decrease respiratory and salivary secretions
  - Hyoscine hydrobromide
  - Glycopyrronium

# Summary and conclusions

- More deaths occur in the first month of life than at any other time
- Providing the most appropriate care for babies with life threatening illness involves both ethical and practical considerations
- All babies receiving palliative care must have consideration given to relief of pain and discomfort.
- Symptom management in the neonate needs to take into account differences in body composition and drug metabolism
- Effective symptom management can usually be achieved using the principles of palliative care developed for other age groups