Neonatal Pharmacology
MIDW 125

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Objectives

1) Discuss the limitations in the availability of information in neonatal therapeutics
2) Describe the general pharmacokinetic differences between neonates (term and preterm), older children and adults
3) Describe how physiologic growth affects the pharmacokinetics in neonates
4) List medications used in the treatment of medical conditions encountered in the neonatal intensive care unit (apnea of prematurity, neonatal abstinence syndrome, patent ductus arteriosus, persistent pulmonary hypertension, respiratory distress syndrome, sepsis)
5) Discuss possible adverse effects of these medications
6) Identify medications that must be used with extreme caution in neonates
7) List medications that should be avoided in neonates
8) Be able to calculate a neonatal drug dose
9) Identify useful references for neonatal drug dosing and therapeutics
Background
Chloramphenicol & Gray Baby Syndrome

• Premature neonates received chloramphenicol prophylaxis (100 mg/kg/day PO)
  – Death 6/15 prophylaxis vs. 2/15 no prophylaxis
  – “gray baby syndrome”: vomiting, gray skin, cyanosis, hypotension, hypothermia, cardiovascular collapse

• Mechanism:
  – Chloramphenicol toxicity
  – Neonates:
    • ↓UDP glucuronyl transferase
    • ↓Glomerular filtration
Barriers to Neonatal Research

1) Ethical Issues

2) Technical Issues
   – Recruitment of adequate numbers at a given stage of growth and development
   – Blood volumes

3) Funding

https://pediatrictrials.org/
Neonatal Pharmacokinetics
Absorption
Oral

• Extent of absorption
  – Gastric acid production increases after birth
  – Bile salt pool changes

• Rate of absorption
  – Slower gastric emptying in lower birthweight and younger neonates
  – Breastmilk increases gastric emptying
Absorption Other Routes

- **Transdermal**
  - Preterm neonates have thinner stratum corneum
  - Stratum corneum more hydrated and vascularized
  - Larger body surface area

- **Intramuscular**
  - Higher density skeletal muscle capillaries
  - Inefficient muscle contractions

- **Rectal**
  - Higher bioavailability due to immature enzymes
  - Rectal pulsatile contractions higher leading to expulsion of solids

- **Intrapulmonary**
  - Unclear
Distribution

• Body Composition
  – Body water, muscle, fat
  – Blood brain barrier “leaky”

• Protein Binding
Body Composition

Preterm neonate
- TBW 85%
- ECF 60%
- ICF 25%

Term neonate
- TBW 80%
- ECF 45%
- ICF 35%

Infant 1 year
- TBW 60%
- ECF 25%
- ICF 35%

Adult man
- TBW 60%
- ECF 20%
- ICF 40%

ECF, extracellular fluid; ICF, intracellular fluid; TBW, total body water

Anaesth Int Care Med 2010;12:79-84
Body Composition

![Chart showing body composition]

Proportion of body composition (%)

- Muscle
- Fat

- Preterm
- Term
- Adult

Anaesth Int Care Med 2010;12:79-84
Protein Binding

• Lower concentration of plasma proteins
  – Lower albumin
  – Lower α1-acid glycoprotein

• Results in more “free drug” for drugs that bind extensively to plasma proteins

• Drugs can displace bilirubin from albumin → risk of kernicterus
Metabolism

**Phase 1 Reactions**

- Decreased in neonates

- **CYP1A2** *caffeine, theophylline*
  - Adult levels by 3-6 mos

- **CYP2D6** *codeine*
  - Adult levels by 10 yrs

- **CYP2C9** *phenytoin*
  - 30% adult activity at 1 yr
  - Exceeds adult activity in older child

- **CYP3A4/7** *midazolam*
  - Exceeds adult activity at 1 yr
Metabolism

Phase 2 Reactions

- **Glucuronidation**
  - Neonate 10% adult activity
  - Adult activity by 2mos-3yrs

- **Sulfation**
  - Neonates 66% adult activity

- **Acetylation**
  - Neonates poor activity
  - Adult activity by 15 mos-4yrs

- **Methylation**
  - Neonate 150% adult activity
Case Example – Metabolism

Drug Metabolism Reviews 1983;14:295-335
Renal Elimination

• Glomerular filtration rate
  – Increases in first 2 wks of life

• Tubular secretion
  – Slowly increases after birth

• Tubular reabsorption
  – Adult levels by 6 mos
# Creatinine Clearance

<table>
<thead>
<tr>
<th>Age</th>
<th>SCr (mmol/L)</th>
<th>GFR (ml/min/1.73m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premature neonate</td>
<td>27-88</td>
<td>11-15</td>
</tr>
<tr>
<td>Neonate</td>
<td>27-88</td>
<td>17-60</td>
</tr>
<tr>
<td>Infant</td>
<td>18-35</td>
<td>39-114</td>
</tr>
<tr>
<td>Child</td>
<td>27-62</td>
<td>89-165</td>
</tr>
<tr>
<td>Adolescent</td>
<td>44-88</td>
<td>89-165</td>
</tr>
</tbody>
</table>

Johns Hopkins: The Harriet Lane Handbook, 19th ed
Case Example – Elimination

- Gentamicin – eliminated almost entirely unchanged in the urine

<table>
<thead>
<tr>
<th>Age</th>
<th>Half-life (hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult</td>
<td>2 – 4</td>
</tr>
<tr>
<td>Neonate</td>
<td>1.5 – 9</td>
</tr>
<tr>
<td>Preterm neonate</td>
<td>11 – 13</td>
</tr>
</tbody>
</table>
## Bottom Line for Drug Dosing

<table>
<thead>
<tr>
<th>Pharmacokinetic Parameter</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Absorption</strong></td>
<td></td>
</tr>
<tr>
<td>PO, PR, IM, inhalation</td>
<td>Unclear effect on drug dosing</td>
</tr>
<tr>
<td>Transdermal route</td>
<td>Increased absorption, use caution</td>
</tr>
<tr>
<td><strong>Distribution</strong></td>
<td></td>
</tr>
<tr>
<td>Water-soluble drugs</td>
<td>Larger single dose per kg</td>
</tr>
<tr>
<td>Highly protein bound drugs</td>
<td>Smaller single dose per kg</td>
</tr>
<tr>
<td><strong>Metabolism</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Less frequent dosing and/or lower total daily</td>
</tr>
<tr>
<td></td>
<td>dose per kg</td>
</tr>
<tr>
<td><strong>Elimination</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Less frequent dosing and/or lower total daily</td>
</tr>
<tr>
<td></td>
<td>dose per kg</td>
</tr>
</tbody>
</table>
Neonatal Pharmacodynamics

• Development can alter response to a drug
  – Efficacy
  – Toxicity

• Less well understood than pharmacokinetics
Neonatal Pharmacodynamics

**MORPHINE**
- Preterm neonates may have less analgesia
- Neonates more sensitive to respiratory depression

**MIDAZOLAM**
- Neonates may be more sensitive

**VALPROIC ACID**
- Risk of liver toxicity higher in infants
Apnea of Prematurity

• Prolonged respiratory pause of ≥15-20 sec, or one associated with bradycardia or color change

• The respiratory pause may be:
  – Central (no respiratory effort)
  – Obstructive (usually due to upper airway obstruction)
  – Mixed

• Most common in neonates ≤ 34 weeks GA
Apnea of Prematurity

• Methylxanthines – stimulate central respiratory drive
  – Theophylline no longer used
  – Caffeine is the drug of choice
<table>
<thead>
<tr>
<th>Dosing</th>
<th>Adverse Effects</th>
<th>Other</th>
</tr>
</thead>
</table>
| **Loading Dose:** 20 mg/kg IV/PO | **CNS:** insomnia, irritability  
**CVS:** tachycardia  
**GI:** vomiting, diarrhea, reduced feeding  
*Long-term effects unclear, but does not appear to affect behaviour and brain development* | Avoid in arrhythmias  
Do not use caffeine benzoate (associated with kernicterus) |
| **Maintenance Dose:** 5-10 mg/kg IV/PO q24 hrs  
(Start at 5 mg/kg and increase in increments of 2.5 mg/kg) |                                                        |                                            |

http://www.mdconsult.com.ezproxy.library.ubc.ca/books/  
J Pediatr Child Health 2011;47:167-72  
C&W Neonatal Drug Dosage Guidelines
Let’s Calculate

**Case**: 2 day old neonate, born at 27 weeks GA
Apnea, bradycardia, desaturation x 12 hours
Weight 1200 grams

- What dose of caffeine would you give?
  - Loading Dose?
  - Maintenance Dose?
Neonatal Abstinence Syndrome

• Approximately 11% of infants reported to be exposed to alcohol and/or illicit drugs before delivery

• Major maternal substances of abuse that affect newborns are opioids, cocaine, amphetamines, alcohol and tobacco
Neonatal Abstinence Syndrome

• **CNS:**
  – Jittery, tremulous
  – Sleep disturbance
  – Irritability
  – Excessive crying
  – Hypertonicity, hyperactive reflexes
  – Seizures

• **Respiratory:**
  – Apnea
  – Tachypnea
  – Yawning

• **Autonomic:**
  – Sweating
  – Temperature instability
  – Mottling
  – Hypertension

• **Gastrointestinal:**
  – Ineffective feeding
  – Hyperphagia
  – Excessive sucking
  – Diarrhea
Neonatal Abstinence Syndrome

- Opioids – prevent withdrawal syndrome in neonates who have been exposed to opioids in utero
  - Maternal use of heroin, oxycodone, methadone
  - Morphine in the drug of choice for the neonate

- Try to avoid giving naloxone (opioid antagonist) to neonate
## Neonatal Abstinence Syndrome

### Morphine

#### Dosing

| Starting Dose: | 0.03 mg/kg PO q3hr |
|               | 0.015 mg/kg PO q3hr PRN |

**Dose Adjustment:**
Increase dose by 20-50% until symptoms are controlled

**Weaning:**
Decrease dose by 10% q2days
D/C once dose 0.02 mg

#### Adverse Effects

- **CNS:** oversedation
- **CVS:** hypotension
- **GI:** vomiting, constipation
- **GU:** urinary retention

#### Other

**Monitoring:**
Signs and symptoms of withdrawal

*Onset of withdrawal may be slower and duration maybe longer for maternal use of methadone*

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C&W Neonatal Drug Dosage Guidelines
Patent Ductus Arteriosus

• Ductus arteriosus patent at birth
  – Functional closure (smooth muscle constriction) occurs in the first few hours and induces hypoxia necessary for anatomic closure
  – Anatomic closure occurs later (days to weeks)

• Persistent PDA if not closed at 72 hrs of life
  – Neonates > 32 wks GA: 20%
  – Neonates < 28 wks GA: 60%
Patent Ductus Arteriosus

• Treatment of PDA dependent on gestational age, clinical status

• NSAIDs – inhibit prostaglandins
  – Drug of choice is indomethacin or ibuprofen
  – Surgical closure if drug treatment fails or contraindicated
# Patent Ductus Arteriosus

## Indomethacin, Ibuprofen

## Dosing

<table>
<thead>
<tr>
<th>Indomethacin:</th>
<th>Adverse Effects</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PNA 0-7 Days:</strong></td>
<td><strong>CNS:</strong> intracranial hemorrhage</td>
<td>If ductus arteriosus doesn’t close 48H after last dose or if it re-opens, a 2nd course may be given</td>
</tr>
<tr>
<td>0.2 mg/kg IV at Hour 0</td>
<td><strong>GI:</strong> reduced intestinal blood flow, bleeding, NEC</td>
<td>neonate is kept NPO for up to 48 hrs after treatment</td>
</tr>
<tr>
<td>0.1 mg/kg IV at Hour 12</td>
<td><strong>Heme:</strong> bleeding</td>
<td>If anuria or marked oliguria (&lt; 0.6 mL/kg/hr) occurs after the first or second dose, the next dose should not be administered until urine output has returned to normal</td>
</tr>
<tr>
<td>0.1 mg/kg IV at Hour 36</td>
<td><strong>Renal:</strong> reduced urine output, elevated SCr</td>
<td></td>
</tr>
<tr>
<td><strong>PNA &gt; 7 days:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.2 mg/kg IV at Hour 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.2 mg/kg IV at Hour 12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.2 mg/kg IV at Hour 36</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ibuprofen lysine:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 mg/kg at hour 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 mg/kg/dose at hour 24 and 48</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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C&W Neonatal Drug Dosage Guidelines
Let’s Calculate

**Case**: 6 day old neonate, born at 26 weeks GA
Has worsening respiratory distress, bounding pulses, and a murmur. ECHO reveals PDA.
Weight 900 grams

- What dose of indomethacin would you give at 0, 12, and 36 hours?
Respiratory Distress Syndrome

• Most common respiratory disorder in preterm infants

• Also known as hyaline membrane disease

• Clinical diagnosis is made in preterm infants with respiratory difficulty that includes tachypnea, retractions, grunting respirations, nasal flaring and need for ↑ FiO2
Respiratory Distress Syndrome

• Antenatal glucocorticoids – accelerate fetal lung maturity and reduce incidence/severity of RDS
  – Betamethasone IM

• Lung surfactant – avoids or reduces lung injury
  – Prophylactic:
    • ≤ 26 weeks
    • 27-34 weeks, if intubate at birth
  – Rescue:
    • ≤ 34 weeks and respiratory distress requiring intubation
Respiratory Distress Syndrome

**bLES**

<table>
<thead>
<tr>
<th>Dosing</th>
<th>Adverse Effects</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>bLES (bovine lipid extract surfactant)</strong></td>
<td><strong>Resp:</strong> Pulmonary hemorrhage, apnea</td>
<td>Chest x-ray after administration</td>
</tr>
<tr>
<td>5 mL/kg via ETT</td>
<td>ETT blockage</td>
<td></td>
</tr>
<tr>
<td>May repeat x 1 dose after 8 hrs if ventilated and high O2 requirement</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

C&W Neonatal Drug Dosage Guidelines
Sepsis

• Acute bacterial infection, characterized by nonspecific signs

• Early-onset sepsis risk factors:
  – Premature +/- prolonged rupture of membranes
  – Maternal GBS
  – Maternal fever
  – Prematurity
  – Chorioamnionitis

• Late-onset sepsis risk factors
  – Endotracheal intubation
  – Lines, catheters
  – Broad-spectrum antibiotics
Sepsis

• Early-onset sepsis
  – Ampicillin + Gentamicin

• Late-onset sepsis
  – Cloxacillin or Vancomycin + Gentamicin
## Sepsis

<table>
<thead>
<tr>
<th>Dosing</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;1200 g</td>
<td>1200-2000 g</td>
</tr>
<tr>
<td><strong>Ampicillin IV</strong></td>
<td></td>
</tr>
<tr>
<td>50 mg/kg Q12h</td>
<td>50 mg/kg Q12h (0-7 d) or Q8h (&gt;7d)</td>
</tr>
<tr>
<td></td>
<td>50 mg/kg Q8h (0-7 d) or Q6h (&gt;7d)</td>
</tr>
<tr>
<td><strong>Cloxacillin IV</strong></td>
<td></td>
</tr>
<tr>
<td>25 mg/kg Q12h</td>
<td>25 mg/kg Q12h (0-7 d) or Q8h (&gt;7d)</td>
</tr>
<tr>
<td></td>
<td>25 mg/kg Q8h (0-7 d) or Q6h (&gt;7d)</td>
</tr>
</tbody>
</table>

**Derm:** rash, phlebitis

C&W Neonatal Drug Dosage Guidelines
# Sepsis

<table>
<thead>
<tr>
<th>Dosing</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td><strong>&lt;28 wks</strong></td>
</tr>
<tr>
<td>Gentamicin IV</td>
<td>2.5 mg/kg Q24h</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Renal:</strong> Renal impairment</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Check levels</em></td>
</tr>
</tbody>
</table>

C&W Neonatal Drug Dosage Guidelines
# Sepsis

<table>
<thead>
<tr>
<th>Dosing</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td><strong>&lt;27 wks</strong></td>
</tr>
<tr>
<td><strong>Vancomycin</strong></td>
<td>15 mg/kg Q24h</td>
</tr>
<tr>
<td>IV</td>
<td></td>
</tr>
</tbody>
</table>

**Renal:** Renal impairment  
**Other:** red man syndrome (flushing, redness, hypotension)  
*Check levels*  

C&W Neonatal Drug Dosage Guidelines
Let’s Calculate

**Case**: 5 day old neonate, born at 27 weeks GA
Has worsening respiratory distress, hypotension, and a fever. The team suspects sepsis.

Weight 1000 grams

- What doses of ampicillin and gentamicin would you give?
Pain and Sedation

• By late gestation, the fetus has developed the anatomic, neurophysiological, and hormonal components to perceive pain

• Preterm infants may demonstrate exaggerated pain response

• Neonates in the NICU exposed to multiple painful or noxious stimuli
## Pain and Sedation

<table>
<thead>
<tr>
<th>Dosing</th>
<th>Adverse Effects</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acetaminophen</strong></td>
<td><strong>Liver:</strong> Hepatotoxicity</td>
<td>Opioid sparing</td>
</tr>
<tr>
<td>10-15 mg/kg PO Q4-6h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max 60 mg/kg/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Morphine</strong></td>
<td><strong>Resp:</strong> Respiratory</td>
<td>Use lower starting doses for</td>
</tr>
<tr>
<td>100 mcg/kg IV bolus,</td>
<td>depression, apnea</td>
<td>premature neonates</td>
</tr>
<tr>
<td>then 10-20 mcg/kg/hr IV</td>
<td><strong>CVS:</strong> Hypotension</td>
<td>Post-op pain may require higher</td>
</tr>
<tr>
<td>IV infusion</td>
<td><strong>GI:</strong> Ileus, constipation</td>
<td>doses</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Midazolam</strong></td>
<td><strong>Resp:</strong> Respiratory</td>
<td>Use lower starting doses for</td>
</tr>
<tr>
<td>200 mcg/kg IV bolus,</td>
<td>depression</td>
<td>premature neonates</td>
</tr>
<tr>
<td>then 30-70 mcg/kg/hr IV</td>
<td><strong>CVS:</strong> Hypotension</td>
<td></td>
</tr>
<tr>
<td>IV infusion</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Safe Prescribing in Neonates

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Date on the prescription</strong></td>
<td>* Ensures proper documentation/timeliness</td>
</tr>
<tr>
<td><strong>2. Ensure weight and allergy status on prescription</strong></td>
<td>* Enables second check</td>
</tr>
<tr>
<td><strong>3. Use generic drug names</strong></td>
<td>* Sound alike/look alike brand names (eg. LOSEC, LASIX)</td>
</tr>
<tr>
<td><strong>4. Order medications in milligrams (not mL or tablet).</strong></td>
<td>* Different strengths/formulations</td>
</tr>
<tr>
<td><strong>5. Specify intended dose (mg/kg/day or mg/kg/dose)</strong></td>
<td>* Be aware of max doses</td>
</tr>
</tbody>
</table>
## Safe Prescribing in Neonates

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
</table>
| **6. Watch your zeros!** | * 5 mg vs 5.0 mg  
* 0.1 mg vs 1 mg |
| **7. Indicate route of administration** | * PO, PR, topical etc. |
| **8. Indicate frequency of administration – including PRN’s** | * Prevent overdosing |
| **9. Include indication for medication** | * Allows for second check |
| **10. Print name and contact information; College ID, Phone number, signature** | * So that we can track you down! |
“High Alert” Drugs

• Drugs that bear a heightened risk of causing significant patient harm when used in error

• Safeguards should be taken to reduce the risk of errors
  – Limited access
  – Auxiliary labels
  – Standardized ordering, storage, preparation, administration
  – Independent double checks

“High Alert” Drugs

<table>
<thead>
<tr>
<th>Class</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenergic agonists</td>
<td>Dopamine, Epinephrine</td>
</tr>
<tr>
<td>Inotropes</td>
<td>Digoxin, Milrinone</td>
</tr>
<tr>
<td>Antithrombotic agents</td>
<td>Heparin</td>
</tr>
<tr>
<td>Hypoglycemics</td>
<td>Insulin</td>
</tr>
<tr>
<td>Hypertonic solutions</td>
<td>Dextrose 20%</td>
</tr>
<tr>
<td>Concentrated electrolytes</td>
<td>Magnesium sulfate, Potassium chloride, Potassium phosphate, Sodium chloride &gt; 0.9%</td>
</tr>
<tr>
<td>Sedation agents</td>
<td>Midazolam</td>
</tr>
<tr>
<td>Opioids</td>
<td>Morphine</td>
</tr>
<tr>
<td>Neuromuscular blockers</td>
<td>Pancuronium, Succinylcholine</td>
</tr>
</tbody>
</table>

Let’s Calculate

**Case:** 8 day old neonate, born at 39 weeks GA
Congenital heart disease, receiving diuretic (furosemide) which has resulted in hypokalemia.
K = 2.7 mmol/L (normal 3.5-5.5 mmol/L)
Weight 3000 grams

- The physician orders 15 mmol KCl IV to give over 30 minutes.
- Let’s check it out!
<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosages &amp; Intervals of Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potassium Chloride</td>
<td><strong>Maintenance Requirements:</strong></td>
</tr>
<tr>
<td></td>
<td>PO: 2-3 mmol(mEq)/kg/day. For oral use either the injectable dosage form or the oral liquid may be administered in divided doses bid-tid diluted in feeds.</td>
</tr>
<tr>
<td></td>
<td>IV Continuous infusion: 2-3 mmol (mEq)/kg/day diluted in 24H maintenance IV Fluid</td>
</tr>
<tr>
<td></td>
<td><strong>Hypokalemia (K⁺ &lt; 2.8 mmol/L):</strong></td>
</tr>
<tr>
<td></td>
<td>IV Intermittent Infusion: 0.5-1 mmol/kg/dose</td>
</tr>
<tr>
<td></td>
<td><strong>All doses must be diluted in dextrose or saline IV solutions prior to administration.</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Maximum Potassium Concentrations for Intravenous Administration:</strong></td>
</tr>
<tr>
<td></td>
<td>Peripheral Line: 0.1 mmol/ml</td>
</tr>
<tr>
<td></td>
<td>Central Line: 0.2 mmol/ml</td>
</tr>
<tr>
<td></td>
<td><strong>Rate of Administration:</strong></td>
</tr>
<tr>
<td></td>
<td>0.2 mmol/kg/hr to a maximum of 0.5 mmol/kg/hr (rates &gt; 0.3 mmol/kg/hr should be used only in infant's with severe potassium depletion.)</td>
</tr>
</tbody>
</table>
Let’s Calculate

Case:

- Weight 3000 grams (=3 kg)
- The physician orders 15 mEq KCl IV to give over 30 minutes.

- $15 \text{ mmol} \div 3 \text{ kg} = 5 \text{ mmol/kg}$

5 to 10 fold overdose!!!
Let’s Calculate

Case:
• Weight 3000 grams (=3 kg)

• Dose = 0.5 mmol/kg x 3 kg = 1.5 mmol
• Rate = 0.2 – 0.5 mmol/kg/hr
  – Give over 1 – 2.5 hrs
# Medications to Avoid in Neonates

<table>
<thead>
<tr>
<th>Medication</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sulfa drugs</strong>&lt;br&gt;Eg. sulfamethoxazole/trimethoprim (Septra)</td>
<td>Displaces bilirubin from albumin → Kernicterus</td>
</tr>
<tr>
<td><strong>Ceftriaxone</strong></td>
<td>Displaces bilirubin from albumin → Kernicterus</td>
</tr>
<tr>
<td></td>
<td>Biliary sludge</td>
</tr>
<tr>
<td></td>
<td>Interaction with calcium (eg. TPN)</td>
</tr>
<tr>
<td><strong>Nitrofurantion</strong></td>
<td>Hemolytic anemia</td>
</tr>
<tr>
<td><strong>Erythromycin</strong>&lt;br&gt;(except topical)</td>
<td>Pyloric stenosis</td>
</tr>
</tbody>
</table>
# Medications to Avoid in Neonates

<table>
<thead>
<tr>
<th>Preservatives/excipients</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzyl alcohol</td>
<td>Neonatal gasping syndrome (metabolic acidosis, neurologic deterioration, gasping respirations)</td>
</tr>
<tr>
<td>Propylene glycol</td>
<td>Hemolysis, central nervous system depression, hyperosmolality, and lactic acidosis</td>
</tr>
<tr>
<td>Ethanol</td>
<td>Central nervous system depression, respiratory depression</td>
</tr>
</tbody>
</table>
Medications to Avoid in Neonates

Over-the-counter cough and cold medicines with certain active ingredients are being relabelled to say: “Do not give to children under 6.”

<table>
<thead>
<tr>
<th>Therapeutic Category (Purpose)</th>
<th>Active Ingredients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antihistamines (for helping with symptoms such as nasal congestion, sneezing/running nose)</td>
<td>brompheniramine maleate, chlorpheniramine maleate, dexbrompheniramine maleate, clemastine hydrogen fumurate, diphenhydramine hydrochloride, diphenypyraline hydrochloride, doxylamine succinate, pheniramine maleate, phenyltoloxamine citrate, promethazine hydrochloride, pyrilamine maleate, and triprolidine hydrochloride</td>
</tr>
<tr>
<td>Antitussives (used to treat cough)</td>
<td>dextromethorphan, dextromethorphan hydrobromide, and diphenhydramine hydrochloride</td>
</tr>
<tr>
<td>Expectorants (used to loosen mucus)</td>
<td>guaifenesin (glyceryl guaiacolate)</td>
</tr>
<tr>
<td>Decongestants (used to treat congestion)</td>
<td>ephedrine hydrochloride/sulfate, phenylephrine hydrochloride/sulphate, and pseudoephedrine hydrochloride/sulphate</td>
</tr>
</tbody>
</table>

Useful References

- [http://www.neonatology.org/neo.clinical.html](http://www.neonatology.org/neo.clinical.html)
- [http://www.neonatology.org/neo.computers.html](http://www.neonatology.org/neo.computers.html)
- NeoFax. Thompson Reuters 2012.