Pediatric Pearls: Tips and Tricks for the General Practitioner
Blake J. Larson, PharmD
Clinical Pediatric Pharmacist

Disclosure Statement:

- Blake J. Larson, Pharm.D.
- Potential conflicts of interest: None
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- Presentation of this slide indicates my agreement to abide by the non-commercialism guidelines provided on the CE Requirements

Why Pediatrics?
Learning Objectives

- Explain the differences in pharmacokinetics and pharmacodynamics in the pediatric population
- Discuss common disease states in pediatrics and related pharmacotherapy
- Identify the challenges that occur as patients transition from pediatric to adult medicine
Pre-test Questions

1. Hydrophilic drugs will have ______ distribution volumes and ______ plasma concentrations in neonates.
   a. Lower; lower
   b. Higher; lower
   c. Lower; higher
   d. Higher; higher

2. Updated perforated appendicitis guidelines in pediatrics recommend this dose of metronidazole (Flagyl):
   a. 10 mg/kg every 8 hours; max dose of 750 mg
   b. 30 mg/kg every 24 hours; max dose of 2000 mg
   c. 30 mg/kg every 24 hours; max dose of 1500 mg
   d. 15 mg/kg every 8 hours; max dose of 500 mg

3. Greater than _____ percent of children with chronic illnesses and special healthcare needs will survive past their 20th birthday.
   a. 60
   b. 70
   c. 80
   d. 90
**Introduction to Pediatrics**

- Not just “small adults”

- Pediatric population accounts for almost one-third of the US population

- >20 million ED visits occur among pediatric patients younger than 15, compared to 24 million visits among adults aged 45-75 in 2007

- AAP strongly recommends prescribers use pharmacist consultation, including the integration of clinical pharmacists in patient care rounds and activities that involve reviewing medication use procedures and orders.

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**Definitions**

- Neonates = birth to 28 days (may extend this for VLBW neonates)
  - Low birth weight (LBW) = 1500 - 2500 g
  - Very low birth weight (VLBW) = 1000 - 1500 g
  - Extremely low birth weight (ELBW) = <1000 g

- Premature is defined as being born before 37 weeks of gestational age
  - The earliest age at which the infant has at least a 50% chance of survival is generally believed to be 24 weeks

- Infants = 28 days to 12 months

- Children = 1 year to 12 years of age

- Adolescents = 13-17 years of age

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**Vital signs**

- Heart Rate
  - Birth to 3 months: 85 to 205 beats/min, decreases gradually to about 100 to 190 at age 2
  - Children: 80 to 140 beats/min
  - Children >10 years: closer to adults at 60 to 100 beats/min

- Respiratory Rate
  - 30 - 40/min in neonates and infants
  - 24 - 40/min in children up to 3 years of age
  - 22 - 34/min in children ages 3 to 5 years of age
  - 18 - 30/min in children ages 6 to 12 years of age
  - 12 - 16/min in children >12 years of age

- Blood Pressure
  - 60-84/31-53 for neonates
  - 80-98/46-56 for children ages 1 to 5 years of age
  - 91-106/53-63 for children ages 6 to 11 years of age
  - 99-122/79-97 for children ages 12 to 17 years of age
Introduction to Pediatrics

• Medication use in pediatrics
  - Off label use of medications occurs often
    - Up to 79% of inpatient prescriptions involve off label medication use in the United States
    - Use of primary literature is crucial in providing evidence based care to infants, children and adolescents
  - Increased risk of liability
  - Limited formulations
    - Children will reject medications on the basis of color, taste, texture, and temperature, rendering even the most potent of oral medications useless
    - Child Life Specialists
  - Orphan Drug Act
  - Rounding of doses
  - Monitor patient weights often!

Introduction to Pediatrics

• Neonates
  - Dosing recommendations may be given on the basis of weight as well as postnatal age or post-conceptional age
  - Will lose about 10% of their body weight in the first week of life
    - Use birth weight as dosing weight during this time
  - Temperatures are best measured rectally in neonates
  - Sustained temperatures over 38°C requires evaluation
  - There are no neonate specific reference ranges of lab values for commonly used tests such as blood chemistry, hematology, or liver function tests
    - SCr in the first 48 hours of life is not a reliable indicator of kidney function - reflects mother’s SCr
    - ELBW and VLBW neonates - very difficult to maintain normal electrolyte balance
      - Difficult to predict when renal function will become normal, if ever
      - Often more useful to follow trends in lab values rather than single values

Pediatric Pearl Topic #2

Pediatric Pharmacokinetics/Pharmacodynamics

Absorption

Metabolism

Distribution

Excretion
**PK/PD**

- **Gastric pH**
  - Neonates will have higher gastric pH
  - More relevant to chemical stability of the drug rather than ionization
    - Example: beta-lactams

![Image](image1.png)

**Figure 1.** Plasma concentration vs. time profiles for penicillin in neonates, infants, and children after oral administration of a single 11,000-unit/100 lb dose.

- **Gastric Emptying**
  - Increases dramatically during the first week of life
  - Extends rate at which medications are distributed along the primary absorptive site
  - Other factors can influence gastric emptying during the newborn period, including prematurity, GERD, respiratory disease, congenital heart disease, and caloric density of feeds
  - Frequency and amplitude of intestinal contractions are reduced in the newborn and young infant
  - Most children usually attain adult motility patterns by 6-8 months of life
  - Combined factor of gastric emptying and GI motility will increase the time to achieve maximal plasma concentrations in neonates, with further prolonged Tmax in premature neonates

**PK/PD**

- **Suppositories**
  - Suppositories that deliver their contents over hours will very likely be expelled before liberating the entire drug dose

- **Topicals**
  - Children have markedly larger surface area per unit of mass than adults
  - Greater degree of hydration to skin
  - Higher rates of perfusion
    - All of these contribute to enhanced drug permeability

- **Intramuscular**
  - Young infants have increased skeletal muscle capillary density compared to adults by about 50%, resulting in greater IM bioavailability
  - **IM volumes**
    - Newborns and small infants: 0.5 mL max volume
    - Small children: 1 mL max volume
    - School aged children and older: 2 mL max volume

![Image](image2.png)

**Image 2.** Example of suppository and topical preparations.
PK/PD

- Around 80% of a pre or full term neonate’s body weight is composed of water
- Gradually decreases throughout the first 4 months of life
- Even the fat in these younger patients consists of a higher proportion of water and a lower proportion of lipid compared to adults
- Hydrophilic drugs that restrict their distribution to body water show larger apparent distribution volumes and lower plasma concentrations in neonates and young infants
- Compared with infants, young children will have peak concentrations that are almost 33% greater and almost 50% greater in older children
- Neonates and young infants (<6 months) experience higher unbound fractions of drugs than do older children and adults
  - Reduction in circulating plasma proteins
  - Lower binding affinity for fetal albumin

PK/PD

- CYP3A4 levels increase steadily throughout infancy, maturing to adult levels by 1 year of age
  - Clearance of sildenafil rapidly increases within the first 10 days of life
- CYP2D6 achieves adult levels by 2 weeks of age
- Terminal half-life of phenytoin (CYP2C9) drops from avg of 20 hours at birth to 8 hours by 2 weeks of life
- Omeprazole (CYP2C19) shows higher rates of clearance in young infants and shorter half-lives during the first 5 years of life
- CYP1A2 enzymes are absent in fetal development at only 4-5% of adult levels in neonates. This increases to 55% of adult activity between 1-9 years of life
PK/PD

- Phase II Metabolism reactions
  - UGT1A1: Involved in metabolism of APAP, ibuprofen, and warfarin
    - Absent in fetal liver, followed by immediate acquisition shortly after birth, reaching adult levels between 3 and 6 months of life
  - UGT1A9: Involved in metabolism of APAP and ibuprofen
    - Reaches 44% of adult values by 6 months of life, increases to 64% at 2 years of age

- Although compensatory clearance pathways exist, the overall rate of clearance for drugs eliminated through the bile will be reduced in the newborn
  - 70% of ceftriaxone dose is recovered in the urine of neonate compared to 40% to 60% in children and adults
  - Ceftriaxone will displace bilirubin from albumin in the neonate and increase risk for kernicterus (contraindicated in premature neonates)
  - Reduced levels of alcohol dehydrogenase in neonates and infants
    - Avoid elixirs

- How do we measure renal function in children?
  - The Bedside Schwartz Equation!
    - eGFR = [0.413 x height (in cm)] / Scr (in mg/dL)
  - What about the original Schwartz equation?
    - Found to overestimate renal function by as much as 20-40%
    - Some institutions still use the original Schwartz equation
  - Do not use Cockcroft-Gault or Jeliffe in pediatrics
    - Can consider using for adolescents
  - Let’s test your math skills!
    - Calculate eGFR for a 2 year old patient
      - Ht: 89 cm
      - Scr: 0.3
PK/PD

Normal GFR in Children and Young Adults

<table>
<thead>
<tr>
<th>Age</th>
<th>Mean GFR +/- SD in mL/min/1.73m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 week</td>
<td>40.6 +/- 14.8</td>
</tr>
<tr>
<td>2-8 weeks</td>
<td>65.8 +/- 24.8</td>
</tr>
<tr>
<td>&gt;8 weeks</td>
<td>95.7 +/- 21.7</td>
</tr>
<tr>
<td>2-12 years</td>
<td>113.0 +/- 27.0</td>
</tr>
<tr>
<td>13-21 years (males)</td>
<td>140.0 +/- 30.0</td>
</tr>
<tr>
<td>13-21 years (females)</td>
<td>118.0 +/- 22.0</td>
</tr>
</tbody>
</table>

PK/PD

• Glomerular function in neonates

Figure 9. Postnatal acquisition of functional renal filtration capacity as a function of gestational age.

PK/PD

• Example: Dosing of fluconazole in neonates

  • Half-life of fluconazole in a premature infant is 88 hours compared to full term counterpart at 20-25 hours

  • Prophylaxis for invasive candidiasis

    • GA <30 weeks
      - PNA <7 days: IV: 3-6 mg/kg/dose twice weekly
      - PNA >7-42 days: IV: 3-6 mg/kg/dose every 72 hours
      - PNA >42 days: IV: 6 mg/kg/dose every 48 hours

    • GA 30-40 weeks
      - 6 mg/kg/dose every 48 hours
Med Safety and Toxicology

• Adverse drug events occur more frequently in pediatric patients than in adults
  • In 2001, the incidence of medication errors in pediatric patients was reported as 5.7 per 100 medication orders
  • Most (79%) of potential ADEs occurred at the stage of ordering, most of them dosing errors
    • IV anti-infectives, fluids and electrolytes, analgesics and sedatives
  • Limited buffering capacity in children
  • Caregivers may be asked to crush tablets, dilute them in water, and give an aliquot of this preparation
  • Always recommended doses be express in both milligrams and milliliters

Med Safety and Toxicology

• Culture of Safety
  • Transparency
  • Training and Education
    • Pediatrics should be a required therapeutics course in the curriculum of pharmacy schools
    • Some students are never exposed before graduation to the unique challenges and differences of pediatric pharmacology - leads to fear of treating children
  • Residency training
  • Medication reconciliation
  • Training modules
• Formulary management
• Technology
  • Computerized prescriber order entry (CPOE)
  • EMRs
  • Pharmacy systems
  • ADTs
  • Smart pumps
  • Barcode scanning
Med Safety and Toxicology

• Communication is key!

  • Studies have shown that without intervention, only 50% of caregivers give an accurate dose of liquid medicines to the children in their care
    • This can be increased to 95% using a 1-3 minute intervention
      • Can also improve adherence from 62% to 91%
  
  • Children can generally begin providing and receiving information during health care visits at age 3, with greater involvement starting at age 7
  
  • Consider factors that affect caregiver medication administration hesitance
    • Cultural beliefs, socioeconomic status, psychosocial differences among age groups (child vs. adolescent), multiple caregivers, drug formulations
  
  • Speaking to children vs. speaking to parents/caregivers

Med Safety and Toxicology

• Medication adherence
  
  • In general, younger children under 5 years of age have great medication adherence with treatment of chronic illnesses
  
  • Confusion between caregivers of who has given a medication can occur
    • Can result in under or overdosing
  
  • Assuming patients over 6 years of age can swallow pills
  
  • Palatability
    • Clindamycin, oral steroids
  
  • Inappropriate measurements
    • Using kitchen spoons for measuring doses
  
  • Discussions of medication adherence need to start while they are young!

Med Safety and Toxicology

• Childhood poisonings remain a common occurrence
  
  • Medication adherence

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Exposures/100k population</th>
<th>Number of Exposures</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>2813</td>
<td>112,159</td>
</tr>
<tr>
<td>1</td>
<td>8294</td>
<td>331,962</td>
</tr>
<tr>
<td>2</td>
<td>8245</td>
<td>332,730</td>
</tr>
<tr>
<td>3</td>
<td>3711</td>
<td>149,840</td>
</tr>
<tr>
<td>4</td>
<td>1863</td>
<td>75,254</td>
</tr>
<tr>
<td>5</td>
<td>1090</td>
<td>45,469</td>
</tr>
<tr>
<td>Child 6-12</td>
<td>464</td>
<td>135,145</td>
</tr>
<tr>
<td>Teen 13-19</td>
<td>511</td>
<td>153,137</td>
</tr>
</tbody>
</table>

A report from the American Association of Poison Control Centers Toxic Exposure Surveillance System.
Med Safety and Toxicology

- Toxicology - Common exposures
  - Iron: Antidote = deferoxamine
  - Salicylates: Antidote = sodium bicarbonate
  - Acetaminophen: Antidote = N-acetylcysteine (NAC)
  - Antihistamines: Use BZDs for seizures or delirium, NaBicarb for arrhythmias
  - Beta blockers/CCBs: Pressor support, glucagon, insulin
  - Opioids: naloxone, pressor support, seizure management
  - Sulfonylureas: IV dextrose, glucagon
  - Foreign body ingestion: button/disk batteries biggest concern

Med Safety and Toxicology

- Liquid tobacco (E-cigs)
  - Concentrate of nicotine as high as 36 mg/mL
    - Regular cigarette contains 13-30 mg nicotine
    - An estimated 40-60 mg of nicotine may be lethal in a child
  - Mild/moderate toxicity: GI upset, N/V, dizziness, HA, tachycardia
  - Severe toxicity: Seizures, confusion, bradycardia, hypotension, high doses can cause fatal respiratory depression
  - Treatment is primarily supportive and symptomatic
    - Vomiting is common: treat with ondansetron and IV fluids
    - BZDs for seizures or severe agitation
    - Atropine for bradycardia
    - Pressors for hypotension

Pediatric Pearl Topic #4

Pediatric Advanced Life Support (PALS)
PALS

- Vital signs
  - Heart Rate
    - Birth to 3 months: 85 to 205 beats/min, decreases gradually to about 100 to 190 at age 2
    - Children: 80 to 140 beats/min
    - Children >10 years: closer to adults at 60 to 100 beats/min
  - Respiratory Rate
    - 30 - 60/min in neonates and infants
    - 24 - 40/min in children up to 3 years of age
    - 22 - 34/min in children ages 3 to 5 years of age
    - 18 - 30/min in children ages 6 to 12 years of age
    - 12 - 16/min in children >12 years of age
  - Blood Pressure
    - 60-84/31-53 for neonates (Hypotension = SBP<60)
    - 80-98/34-56 for children ages 1 to 5 years of age (Hypotension = SBP<70)
    - 91-106/53-63 for children ages 6 to 11 years of age (Hypotension = SBP<70 + (age in years x 2))
    - 99-122/59-70 for children ages 12 to 17 years of age (Hypotension = SBP<90)

Overall, children have an incredible ability to heal
- Usually young, healthy bodies and organ function
- Most common life-threatening emergencies:
  - Respiratory failure (often ID related)
  - Seizures
  - Anaphylaxis
  - Supraventricular tachycardia (SVT)
  - Bradycardia
  - Cardiac arrest

PALS

Respiratory/Anaphylaxis Medications

<table>
<thead>
<tr>
<th>Medication (Neutralized)</th>
<th>5–10 kg</th>
<th>10–20 kg</th>
<th>Greater than 20 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenaline (0.9% w/v)</td>
<td>0.5 mL</td>
<td>0.5 mL</td>
<td>0.5 – 1 mL</td>
</tr>
<tr>
<td>Diazepam (0.1 mg/mL)</td>
<td>Report dose p.r.n.</td>
<td>Report dose p.r.n.</td>
<td>Report dose p.r.n.</td>
</tr>
<tr>
<td>Diphenhydramine (HCl)</td>
<td>NA</td>
<td>1 mL</td>
<td>3 mL</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>0.25 mg</td>
<td>0.5 mg</td>
<td>0.5 mg</td>
</tr>
<tr>
<td>Ketamine (10 mg/mL)</td>
<td>0.5 mL</td>
<td>0.5 mL</td>
<td>0.5 mL</td>
</tr>
<tr>
<td>Epinephrine 1 mg/mL</td>
<td>2.5 mL</td>
<td>5 mL</td>
<td>5 mL</td>
</tr>
<tr>
<td>Periostab use</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**PALS**

**Respiratory/Anaphylaxis Medications**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose (mg/kg)</th>
<th>Route</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epinephrine</td>
<td>1.2-2.4</td>
<td>IV</td>
<td>0.015</td>
<td>0.03</td>
</tr>
<tr>
<td>Magnesium Sulfate</td>
<td>25-50</td>
<td>IV</td>
<td>0.075</td>
<td>0.25</td>
</tr>
<tr>
<td>Sodium Bicarbonate</td>
<td>1-2</td>
<td>IV</td>
<td>0.3-0.5</td>
<td>1-2</td>
</tr>
</tbody>
</table>

**Cardiovascular Resuscitation**

- Fluids
  - Fluid bolus
    - 20 mL/kg of NS or LR, may give an additional 20-40 mL/kg depending on response and/or severity
  - 10 mL/kg for patients with cardiogenic shock
- Daily fluid requirements
  - Holliday-Segar method

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Hourly Fluid Requirements</th>
<th>Daily Fluid Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td>4 mL/kg</td>
<td>100 mL/kg</td>
</tr>
<tr>
<td>10-20</td>
<td>40 mL+2 mL/kg</td>
<td>1000 mL+50 mL/kg</td>
</tr>
<tr>
<td>&gt;20</td>
<td>60 mL+1 mL/kg</td>
<td>1500 mL+25 mL/kg</td>
</tr>
</tbody>
</table>

Let's test your math skills! Calculate hourly fluid requirement for a 4 year old weighing 15 kg.
Pediatric Pearl Topic #5

Pain and Sedation

• Often referred to as “the fifth vital sign”
• A couple decades ago, a common misconception was that neonates could not feel pain, and if they did, they would not remember the experience
  - Elements of peripheral and central nervous system necessary for pain transmission and perception developed by end of first trimester
  - Structures necessary for pain modulation through descending pain pathway complete by 30-32 weeks gestation
• Lower pain threshold and hypersensitivity in premature neonates
• Studies have shown that children have suboptimal pain treatment compared to adults
• Untreated pain is associated with significant behavioral and biochemical consequences
  - Delayed healing, complicated recovery time, significant stress for patient and family

Pain and Sedation

• Indicators for pain
  - Increased respiratory rate, increased heart rate, oxygen desat, grimacing, high-pitched crying
  - Neonatal Infant Pain Scale (NIPS) and the Face, Legs, Activity, Cry, Consolability (FLACC) scale use these indicators up to age 4
  - Wong-Baker FACES scale used in children older than 4 years
  - Numeric pain scale may be used in patients 10 years and older

Wong-Baker FACES™ Pain Rating Scale

0 - No Hurt
2 - Hurts a Little Bit
4 - Hurts a Little More
6 - Hurts Even More
8 - Hurts Worse Lot
10 - Hurts Most

4/24/17
Pain and Sedation

- Non-pharm
  - Child Life Specialists - distract with play, bubbles, video games, movies, breathing exercises
  - Music Therapy
  - Neonates
    - Swaddling, rocking, pacifier use
    - Reduced lighting
    - Decrease amount of times/day the infant is touched
    - Decrease the volume of the unit in general (alarms, paging system, etc)

- Non-opioid analgesics
  - Acetaminophen
    - PO: 15 mg/kg/dose every 4-6 hours; max dose 650 mg; NTE 75 mg/kg/day
    - Rectal: 20 mg/kg/dose; contraindicated in immunocompromised children
    - IV: 10-15 mg/kg/dose (use 10 mg/kg in infants - higher AUC than older children)
  - Ibuprofen
    - PO: 10 mg/kg/dose every 6-8 hours; NTE 40 mg/kg/day
    - IV: 10-15 mg/kg/dose every 6-8 hours; NTE 2.4 g/day
  - Naproxen
    - PO: 10 mg/kg/dose every 6-8 hours; NTE 40 mg/kg/day
    - IV: 250-500 mg every 12 hours; max 1000 mg/day
  - Ketorolac
    - IM: 1 mg/kg/dose; max 30 mg
    - IV: 0.5-1 mg/kg/dose every 6 hours, max 30 mg; NTE 5 days
  - Naproxen
    - PO: 5-7 mg/kg/dose every 8-12 hours
    - IV: 0.05-0.1 mg/kg every 2-4 hours; keep initial dose lower than 2 mg

- Opioids
  - Morphine
    - IV, elixirs, tablets, SR products
    - Continuous infusion in neonates may be less efficacious
    - Reduced ability to metabolize morphine to active metabolite morphine-6-glucuronide
    - Concern for hypotension
    - IV: 0.05-0.1 mg/kg every 2-4 hours; keep initial dose lower than 2 mg
  - Fentanyl
    - IV, elixirs, tablets, SR products
    - Continuous infusion in neonates may be less efficacious
    - Reduced ability to metabolize morphine to active metabolite morphine-6-glucuronide
    - Concern for hypotension
    - IV: 0.05-0.1 mg/kg every 2-4 hours; keep initial dose lower than 2 mg

- Management
  - Monitor vital signs, pain scores, sedation level
  - Adjust as needed

- Ceiling effect - limited use in patients with moderate-severe pain
Pain and Sedation

- **Opioids**
  - **Hydromorphone**
  - Preferred in patients with renal failure because of its decreased amount of metabolites
  - IV: 0.01 mg/kg every 3-6 hours for infants <6 months
  - 0.015 mg/kg for older children; max dose 0.5-0.6 mg/dose initially
  - **Methadone**
  - Often used in neonates for neonatal abstinence syndrome or in patients who have had long-term use of opioids - wean them off using oral methadone
  - Typically will add oral clonidine as part of weaning procedure
  - Clonidine and dexmedetomidine work by augmenting the descending pain pathway
  - About 35-52% of critically ill infants and children develop withdrawal because of receiving long term opioids in the ICU
- **Oral Hydrocodone and Oxycodone products**
  - Hydrocodone: 0.1 mg/kg/dose every 4 to 6 hours for children <6 months
  - Oxycodone/APAP: 0.1 mg/kg/dose every 4 to 6 hours for children >2 years
  - **Methadone**
  - Often used in neonates for neonatal abstinence syndrome or in patients who have had long-term use of opioids - wean them off using oral methadone
  - Typically will add oral clonidine as part of weaning procedure
  - Clonidine and dexmedetomidine work by augmenting the descending pain pathway
  - About 35-52% of critically ill infants and children develop withdrawal because of receiving long term opioids in the ICU
- **Ketamine**
  - Often used for procedural sedation in children or RSI
  - IV: 1-2 mg/kg/dose; may repeat with additional doses of 0.5-1 mg/kg every 5 to 15 minutes as needed
  - Be sure to counsel family on dissociate effect
- **Propofol**
  - Procedural sedation
  - IV: 1-2 mg/kg/dose; may repeat with additional doses of 0.5 mg/kg every 3-5 minutes as needed
  - “Ketofol”: 0.5 mg/kg of ketamine and 0.5 mg/kg of propofol
- **Intranasal medications in children**
  - Ketamine: 3-6 mg/kg/dose split between each nostril
  - Midazolam: 0.2-0.4 mg/kg/dose split between each nostril
  - Fentanyl: 1.5 mg/kg/dose split between each nostril
  - Dexmedetomidine: 2-3 mcg/kg/dose split between each nostril

**Rapid Sequence Intubation**

<table>
<thead>
<tr>
<th>Induction Medications</th>
<th></th>
<th>Induction Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diazepam</strong></td>
<td>0.1-0.3 mg/kg IV/IO</td>
<td><strong>Diazepam</strong></td>
</tr>
<tr>
<td><strong>Fentanyl</strong></td>
<td>1-3 mcg/kg IV/IO BM</td>
<td><strong>Fentanyl</strong></td>
</tr>
<tr>
<td><strong>Ketamine</strong></td>
<td>1-2 mg/kg IV/IO 4-5 mcg/kg/d</td>
<td><strong>Ketamine</strong></td>
</tr>
<tr>
<td><strong>Midazolam</strong></td>
<td>0.1-0.3 mg/kg IV/IO 1-2 mcg/kg/d</td>
<td><strong>Midazolam</strong></td>
</tr>
<tr>
<td><strong>Propofol</strong></td>
<td>1-2 mg/kg IV/IO</td>
<td><strong>Propofol</strong></td>
</tr>
<tr>
<td><strong>Neuromuscular Blockade Medications</strong></td>
<td></td>
<td><strong>Neuromuscular Blockade Medications</strong></td>
</tr>
<tr>
<td>Succinylcholine &amp; vecuronium</td>
<td>1-3 mg/kg IV/IO BM</td>
<td>Succinylcholine &amp; vecuronium</td>
</tr>
<tr>
<td>Rocuronium</td>
<td>1 mg/kg IV/IO</td>
<td>Rocuronium</td>
</tr>
</tbody>
</table>

Use with caution in asthmatics, IC, neurologic disease, hypotension, renal failure, preeclampsia, diabetes, crush injury victims.
Pediatric Pearl Topic #6

Seizures

• Most common neurologic disorder of childhood
  • Occur in about 4% to 10% of children
  • Common in children with cerebral palsy or developmental delay, metabolic disorders, tumors, head trauma, drug ingestion, CNS infections

• At least 20% of epilepsies linked to genetic component
  • Even febrile seizures have a genetic component, with 25-40% of patients with family history

• Aura may precede a seizure in some children

• After a seizure, period of fatigue, confusion, or irritability occurs, known as the postictal period

Seizures

• Neonatal seizures occur in 1.8 to 3.5 of every 1000 newborns
  • Generally cause little to no brain injury
  • S/sx: eye deviations, lip smacking, apneic episodes
  • Benign familial neonatal seizure: presents within the first 3 months of life and resolves spontaneously by age 6 months
  • “Fifth-day fits”: benign idiopathic neonatal convulsions that appear at day 5 of life and end by day 15 of life
  • IV phenobarbital and phenytoin first line agents
  • Benzodiazepines may be used to immediate control of status epilepticus

• Some epileptic syndromes (Lennox-Gastaut) require several anticonvulsants
  • May still experience seizures
Seizures

- Ketogenic Diet
  - Popular therapy for patients with refractory seizures
  - Typically used in patient with symptomatic generalized epilepsy
  - Low protein and carbohydrate intake with high fat meals, thus inducing ketosis
  - Shown to reduce seizure frequencies by 50-70% in some studies
    - Specific mechanism is unknown
    - Requires strict control and adherence
    - Hospitalized during initiation of diet
    - Should not be initiated on valproic acid - risk of hepatotoxicity
    - Great opportunity for intervention by pharmacists
      - Dextrose should not be administered IV or in oral formulations
      - Requires thorough review of patient medication list and education to caretakers

- First generation anticonvulsants: carbamazepine, phenobarbital, phenytoin, valproic acid
  - Complex pharmacokinetics, require monitoring, drug interactions

- Second generation anticonvulsants: felbamate, gabapentin, lamotrigine, topiramate, oxcarbazepine, levetiracetam, zonisamide
  - More favorable drug profile, do not require monitoring

- Newer drugs: pregabalin, lacosamide, clobazam

- Tapering off medications should be done slowly, one medication at a time

---

Seizures

- Status Epilepticus

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Administration</th>
<th>Maximum dose</th>
<th>Maximum plasma level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diazepam</td>
<td>&gt;1 mg</td>
<td>IV or PO</td>
<td>0.5 mg/kg</td>
<td>5 mg/l</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>20 mg</td>
<td>IV</td>
<td>10 mg/kg</td>
<td>6 mg/l</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>0.05-0.1 mg/kg</td>
<td>IV</td>
<td>0.05-0.1 mg/kg</td>
<td>0.05-0.1 mg/l</td>
</tr>
<tr>
<td>Melatonin</td>
<td>0.1 mg/kg</td>
<td>IV</td>
<td>0.1 mg/kg</td>
<td>10 mg/l</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>20 mg/kg</td>
<td>IV</td>
<td>20 mg/kg</td>
<td>10 mg/l</td>
</tr>
<tr>
<td>Valproic acid</td>
<td>20-40 mg/kg</td>
<td>IV</td>
<td>60 mg/kg</td>
<td>40 mg/l</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>50-100 mg/kg</td>
<td>IV</td>
<td>300 mg/kg</td>
<td>200 mg/l</td>
</tr>
</tbody>
</table>
Infectious Diseases

• Appendicitis and Antibiotic Use
  • Appendicitis is the most common condition in children requiring emergency abdominal surgery
    • Diagnosed in 1% to 8% of children evaluated for abdominal pain
    • Older children and adolescents develop appendicitis more often than younger children
    • Younger children can be difficult to diagnose as the presentation may be nonspecific
  • S/sx: Anorexia, periumbilical pain (early), migration of pain to right lower quadrant (w/in 24 hours), vomiting, fever (24-48 hours after onset of symptoms)
  • Early appendicitis (non-perforated) treat with x1 dose of prophylactic ceftriaxone and metronidazole
  • Advanced appendicitis (perforated):
    • IV Ceftriaxone: 50 mg/kg every 24 hours; max dose 2000 mg
    • IV Metronidazole: 30 mg/kg every 24 hours; max dose 1500 mg
    • Continue therapy until afebrile, well controlled on oral analgesics, tolerating a regular diet, and WBC within normal limits
Infectious Diseases

• Neonatal Sepsis
  • Early onset sepsis (EOS): within first 7 days of life
  • Pathogens acquired perinatally from mother (group B strep, E coli)
  • S/sx are nonspecific: fever, hypotension, oxygen desats, apnea, increased respiratory rate, poor weight gain
  • Confirmed EOS is rare, occurring in 0.1% of neonates, however the use of empiric antibiotics for presumed EOS is high because:
    - Imprecision and unreliability of sepsis diagnostic tools
    - Overlapping symptomatology of sepsis and other common neonatal diseases
    - Fast onset of clinical deterioration and higher rate of mortality in neonates who develop sepsis compared to those who do not
  • Recommended all neonates with s/sx of sepsis undergo a diagnostic lumbar puncture
  • Treatment: Ampicillin and Gentamicin
    - Dosing dependent on postnatal age and weight
    - Treat x 7-10 days for presumed sepsis; longer if culture positive
    - Some centers substitute cefotaxime as empiric EOS therapy
    - Controversial

• Neonatal late onset sepsis (LOS)
  • Presents after the first 7 days of life
  • Pathogens also acquired from mother, but may also include postnatal exposure to other caregivers and from other nosocomial sources, including health care workers
  • Empiric therapy still ampicillin and gentamicin for neonates admitted from the community
  • Replace ampicillin with vancomycin if hospitalized since birth
  • Treat for 7-10 days

Example: Gentamicin dosing in neonates

<table>
<thead>
<tr>
<th>Age-directed dosing (Bradley, 2014) IV, IV</th>
<th>Weight-directed dosing (AAP, 2015) IV, IV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gestational age &gt;30 weeks:</strong></td>
<td>Body weight &lt; 1 kg</td>
</tr>
<tr>
<td>PWMA ≤ 24 days: 5 mg/kg/dose every 48 hours</td>
<td>PWMA ≤ 24 days: 5 mg/kg/dose every 48 hours</td>
</tr>
<tr>
<td>PWMA ≥ 25 days: 5 mg/kg/dose every 36 hours</td>
<td>PWMA ≥ 25 days: 5 mg/kg/dose every 36 hours</td>
</tr>
<tr>
<td><strong>Gestational age 28 to 34 weeks:</strong></td>
<td>Body weight 1 to 2 kg</td>
</tr>
<tr>
<td>PWMA ≤ 10 days: 4.5 mg/kg/dose every 24 hours</td>
<td>PWMA ≤ 10 days: 4.5 mg/kg/dose every 24 hours</td>
</tr>
<tr>
<td>PWMA ≥ 11 days: 5 mg/kg/dose every 36 hours</td>
<td>PWMA ≥ 11 days: 5 mg/kg/dose every 36 hours</td>
</tr>
<tr>
<td><strong>Gestational age &gt;35 weeks:</strong></td>
<td>Body weight &gt; 2 kg</td>
</tr>
<tr>
<td>PWMA ≤ 17 days: 4 mg/kg/dose every 24 hours</td>
<td>PWMA ≤ 17 days: 4 mg/kg/dose every 24 hours</td>
</tr>
<tr>
<td>PWMA ≥ 18 days: 5 mg/kg/dose every 24 hours</td>
<td>PWMA ≥ 18 days: 5 mg/kg/dose every 24 hours</td>
</tr>
</tbody>
</table>
Infectious Diseases

- Acute Otitis Media (AOM)
  - Most common diagnosis leading to antibiotic prescription in children
  - At least 90% of children will have at least one episode by 2-3 years of age
  - Most common pathogens include S. pneumoniae, H. influenzae, and M. catarrhalis
  - S/sx: fever, rhinorrhea, irritability, otalgia, tugging or rubbing the ear, middle ear effusion and inflammation
  - Mild cases of AOM are self-limiting
  - Initial observation allows delay in antibiotic therapy for up to 48-72 hours
  - Warranted in children 2 years and older with uncertain diagnosis and those 6 months to 2 years with uncertain diagnosis and non-severe infection
  - Resolve spontaneously in most children without the need for antibiotic therapy

- Acute Otitis Media (AOM)
  - Antibiotic therapy initiated in children with severe disease (bulging tympanic membrane, severe otalgia, temp of 39 C or greater)
  - Also initiated in children under 6 months of age
  - High dose amoxicillin first-line therapy (response rate >80%)
    - 80-90 mg/kg/day divided every 12 hours; max single dose 2000 mg
  - Amoxicillin/clavulanate or cefdinir can be considered if patient does not respond to high dose amoxicillin
    - Other candidates include children with antibiotic exposure within 30 days and children in whom H. influenzae or M. catarrhalis is suspected
    - Amoxicillin/clavulanate: 90 mg/kg/day amoxicillin divided every 12 hours; max single dose 270 mg. Use only the 600 mg/5 mL suspension
      - 600 mg/5 mL suspension has lower dose of clavulanate compared to the 250 mg/5 mL, and 400 mg/5 mL suspension
    - Cefdinir: 14 mg/kg/day in 1 to 2 divided doses
  - Duration of therapy
    - 10 days for children younger than 2 years or with severe disease
    - 5-7 days for children with mild-moderate disease (usually 6 years or older)

Pediatric Pearl Topic #8

Transitioning from Pediatric to Adult Medicine
Peds to Adults

Simpler Transition vs. More Complex Transition
- Single health condition vs. Multiple health conditions
- Low risk of future health problems vs. High risk of future health problems
- No dependence on medical equipment vs. Reliance on life-sustaining medical equipment
- Rare acute illness, medically stable vs. Frequent acute episodes, medically unstable
- Few medications vs. Multiple medications, medication problems
- No cognitive impairments vs. Profound mental retardation
- No physical impairments vs. Severe physical impairments
- Mentally healthy vs. Mentally ill
- No behavioral concerns vs. Serious behavioral concerns


Peds to Adults

- Children and youth with special health care needs (CYSHCN)
  - Asthma
  - ADHD
  - Diabetes mellitus
  - Sickle cell disease
  - Cerebral Palsy
  - Cystic fibrosis
  - Chronic kidney disease
  - Inflammatory bowel disease
  - Congenital heart disease
  - Childhood cancer survivors
  - Solid-organ transplant recipients
  - Spina bifida
  - Down syndrome
  - HIV/AIDS
  - Genetic and neuromuscular disorders

Peds to Adults

- Why is transition so important?
  - Failure to recognize and plan transition may result in patients dropping out of care
  - Poor transition processes are recognized to have significant effect on morbidity and mortality in young adults with chronic health needs
  - About 11.2 million children (15% of all children in the US) ages 0-17 years have special health care needs
    - About 500,000 of them turn 18 and enter adulthood in the US yearly
  - Survival rates have increased for children with chronic illnesses
    - >90% of CYSHCN will survive beyond their 20th birthday
### Peds to Adults

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Survival Info.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Childhood Cancers</td>
<td>• 46% of survivors are 20-40 y.o.</td>
</tr>
<tr>
<td></td>
<td>• 18% of survivors are &gt; 40 y.o.</td>
</tr>
<tr>
<td>Cystic Fibrosis</td>
<td>• Median survival 37 y.o.</td>
</tr>
<tr>
<td></td>
<td>• 50% are &gt; 18 y.o.</td>
</tr>
<tr>
<td>Congenital Heart Disease</td>
<td>• 85% reach adulthood</td>
</tr>
<tr>
<td></td>
<td>• Over 1,000,000 living with CHD</td>
</tr>
<tr>
<td>Down Syndrome</td>
<td>55-year life expectancy</td>
</tr>
<tr>
<td>Hemophilia</td>
<td>60-year life expectancy</td>
</tr>
<tr>
<td>Sickle Cell Disease</td>
<td>66-year life expectancy</td>
</tr>
<tr>
<td>Spina Bifida</td>
<td>&gt; 80% reach adulthood</td>
</tr>
</tbody>
</table>

**Challenges**

- **Patient challenges:**
  - Graduate HS, move away, new job
  - New relationships, personal choices and challenges
  - Focus on independence
- **Family challenges:**
  - Close ties with pediatric caregivers
  - Privacy becomes an issue
  - Lack of confidence in patient’s ability to provide self-care and lack of confidence in the adult medical team
- **Pediatric care team challenges:**
  - Bond with patient and family
  - Limited contact with adult providers and services
  - Lack of trust in adult healthcare system/providers
  - Lack of training on how or when to start transition

- **Institutional and System Challenges**
  - Aging out of treatment
  - Insurance coverage and funding changes with age
  - Services funded by Medicaid decrease after 21
  - Change in eligibility requirements (SSI, Medicaid)
  - Discontinued from parent’s health insurance
  - Inhibiting personal health insurance challenges
  - Poor reimbursement for transition services
- **Adult care team challenges:**
  - Concern about not having training in congenital and childhood chronic illnesses to prepare them to manage them (medical competency)
  - Too little (or too much) family involvement
  - Psychosocial needs of the patient
  - Limited contact with pediatric services and providers

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Peds to Adults

• What can we do?

 Begin discussions early!
  • Usually transition discussions should be held by the time the patient turn 12-13 years of age
  • Training on medication compliance and knowledge should start much earlier (as early as 3 years old depending on patient condition)

 By age 15 years, patient’s care team should initiate a jointly developed transition plan with involvement from both patient and caregivers

 By age 17 years, review and update the transition plan and prepare for adult care - begin implementation once the patient turns 18

 Transition plan should include clinic policies of both the pediatric and adult care facilities, registry procedures, personal/family/care team preparations and planning, and transfer of care logistics (insurance, location, etc)
  • “Get acquainted” visit with adult team one year before transfer

Peds to Adults

Table: Transition Readiness Assessment Questions 1.1

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>Don’t Know</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you have a care plan?</td>
<td>Yes</td>
<td>No</td>
<td>Don’t Know</td>
</tr>
<tr>
<td>Do you have a care plan?</td>
<td>Yes</td>
<td>No</td>
<td>Don’t Know</td>
</tr>
<tr>
<td>Do you know what medications you are taking?</td>
<td>Yes</td>
<td>No</td>
<td>Don’t Know</td>
</tr>
<tr>
<td>Do you take your medications correctly?</td>
<td>Yes</td>
<td>No</td>
<td>Don’t Know</td>
</tr>
<tr>
<td>Do you use a medical device?</td>
<td>Yes</td>
<td>No</td>
<td>Don’t Know</td>
</tr>
</tbody>
</table>

Stringing Together Our Pediatric Pearls

Intro to Peds

- Peds to Adults
- PK/PD
- Infectious Diseases
- Med Safety and Toxicology
- Pain/Sedation
- PALS
- Seizures
Let’s Test Your Knowledge!

1. Hydrophilic drugs will have ______ distribution volumes and ______ plasma concentrations in neonates.
   a. Lower; lower
   b. Higher; lower
   c. Lower; higher
   d. Higher; higher

2. Updated perforated appendicitis guidelines in pediatrics recommend this dose of metronidazole (Flagyl):
   a. 10 mg/kg every 8 hours; max dose of 750 mg
   b. 30 mg/kg every 24 hours; max dose of 2000 mg
   c. 30 mg/kg every 24 hours; max dose of 1500 mg
   d. 15 mg/kg every 8 hours; max dose of 500 mg

3. Greater than _____ percent of children with chronic illnesses and special healthcare needs will survive past their 20th birthday.
   a. 60
   b. 70
   c. 80
   d. 90

References

- Huang NN, High RH. Correlative of serum levels following the administration of oral and parenteral preparations of penicillin to infants and children of various age groups. Journal of Pediatrics. 1953; 42:657-658