Disclosure

- The program chair and presenters for this continuing education activity have reported no relevant financial relationships.
Pediatric Clinical Pearls:
Statins in Pediatric Heart Transplantation

Emily Benefield, PharmD, BCPS, BCPPS
Advanced Clinical Pharmacist-Pediatric Solid Organ Transplant
Primary Children’s Hospital
Salt Lake City, UT
Learning Objective

- Evaluate the potential benefits and risks of using HMG co-A reductase inhibitors (statins) following pediatric heart transplantation.
What do the guidelines say?

- “In adults, the use of statins beginning 1 to 2 weeks after heart transplant is recommended regardless of cholesterol levels.”
  - Class I, Level of evidence A
- “Routine use of statins in recommended for all pediatric patients with evidence of hyperlipidemia, CAV, or after retransplantation.”
  - Class IIa, Level of evidence C
- “Routine use of statins is recommended for adolescents and selected younger children with an increased risk of rejection and CAV.”
  - Class IIb, Level of evidence C
- “Statin therapy has been shown to reduce CAV and improve long-term outcomes regardless of lipid levels and should be considered for all heart transplant recipients (adult and pediatric).
  - Class I, Level of evidence A

CAV = Cardiac Allograft Vasculopathy

# Initial Pediatric Evidence for Statin Use

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>Immunosuppression</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mahle WT, et al.</td>
<td>Pravastatin (n=90) vs no statin (n=39)</td>
<td>Steroid sparing</td>
<td>Trend toward ↓ incidence of CAV (≥50% stenosis) (p=0.07) in univariate analysis</td>
</tr>
<tr>
<td>Lukito CC, et al.</td>
<td>Atorvastatin initiation ≤ 9 weeks of transplant (n=33) vs. no statin/late start (n=32)</td>
<td>CSA predominate Induction with daclizumab and OKT3</td>
<td>↓ incidence of CAV (≥25% stenosis) (p&lt;0.005) ↓ episodes of rejection treated in the first year post-transplant (p=0.0005)</td>
</tr>
</tbody>
</table>

CAV = Cardiac Allograft Vasculopathy, CSA = Cyclosporine, OKT3 = Muromomab

Retrospective Review of Pediatric Statin Use

- Registry data
- Statin in first year post-transplant (n=317) vs. no statin prior to event (n=647) in children 5-18 years of age
- Baseline characteristics:
  - Tacrolimus based immunosuppressive regimens most common
  - Statin group:
    - Induction therapy more common
    - Maintenance steroids more common
    - More patients with panel reactive antibody > 10%
- Results:
  - ↑ incidence of rejection following the first year post-transplant
  - No difference in overall survival or CAV

Key Takeaways

- Statins remain standard of care for all heart transplant patients at high risk for CAV despite new evidence that may have selected for patients at higher risk of rejection.
Dexamethasone versus Prednisolone in Pediatric Asthma: Less is More!

Chelsey Jensen, PharmD, BCPS
Pediatric Clinical Pharmacist: Medication Therapy Management
Children’s Hospitals and Clinics of Minnesota
Minneapolis, MN
Do You Utilize Dexamethasone for Management of Acute Asthma Exacerbations in Your Practice?

A  YES
B  NO
# Quick Guideline Review: Asthma Exacerbation Management

<table>
<thead>
<tr>
<th>Home</th>
<th>NAEPP 2007</th>
<th>GINA 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initiate OCS treatment under certain circumstances (AAP)</td>
<td>Add OCS for patients with severe exacerbation or not responding to treatment over 48 hrs (AAP)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Primary Care/ED/Hospital</th>
<th>NAEPP 2007</th>
<th>GINA 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>SABA + OCS + oxygen +/- ipatropium +/- IV magnesium</td>
<td>SABA + early initiation of OCS + controlled oxygen +/- ipatropium +/- IV magnesium</td>
<td></td>
</tr>
</tbody>
</table>

**Bottom line:** “systemic corticosteroids speed resolution of exacerbations and prevent relapse, and should be utilized in all but the mildest exacerbations”

OCS, oral corticosteroids; SABA, short acting beta agonist; AAP, asthma action plan
## What Agent What Dose: Guidelines

<table>
<thead>
<tr>
<th>Drug</th>
<th>NAEPP 2007</th>
<th>GINA 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednisolone/prednisone</td>
<td>Adult: 40-60 mg in a single or divided doses for 5-10 days</td>
<td>Adult: 1 mg/kg, max 50 mg/day x 5-7 days</td>
</tr>
<tr>
<td></td>
<td>Child: 1-2 mg/kg/day, max 60 mg in 2 divided doses for 3-10 days</td>
<td>Child 6-11 years: 1-2 mg/kg/day , max 40 mg/day x 3-5 days</td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>N/A</td>
<td>200 mg in divided doses</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>N/A</td>
<td>Oral dexamethasone for 2 days can also be used</td>
</tr>
</tbody>
</table>

“Other systemic corticosteroids such as hydrocortisone and dexamethasone given in equipotent daily doses are likely to be as effective as prednisolone”
# Let’s Compare

<table>
<thead>
<tr>
<th>Medication</th>
<th>Route</th>
<th>Potency</th>
<th>Onset</th>
<th>Duration</th>
<th>Taste</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednisolone</td>
<td>PO</td>
<td>4</td>
<td>1-2 hrs</td>
<td>1-2 days</td>
<td>Poor, bitter</td>
<td>Most</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>PO</td>
<td>25 to 30</td>
<td>1 hr</td>
<td>2.5-3 days</td>
<td>Excellent *compounded</td>
<td>Least</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>IM</td>
<td>25 to 30</td>
<td>&lt;1 hr</td>
<td>3-6 days</td>
<td>N/A</td>
<td>Middle</td>
</tr>
</tbody>
</table>
Compliance

- Caregivers report compliance to OCS regimen only 64% of the time

- Impact of non-compliance
  - 14 day ED relapse rate with OCS compliance 6.3%
  - 14 day ED relapse rate with OCS non-compliance 17.4%

- As many as 70% of the parents of children receiving either oral prednisone or IM dexamethasone said they would prefer the IM injection
Adverse Effects

- Nausea/Vomiting
  - General
    - Dex <1%
    - Pred 5-10%
  - Clinical studies
    - Pred: 5.7%
    - Dex: 0%
## Meat and Potatoes: Single Oral Dose

<table>
<thead>
<tr>
<th>Author</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altamini et al 2006, Canada</td>
<td>134 children 2-16 yo ED patients</td>
</tr>
<tr>
<td></td>
<td>PO Dex 0.6 mg/kg x 1 vs Pred 2 mg/kg/day x 5 days</td>
</tr>
<tr>
<td></td>
<td>No statistical difference (clinical difference?)</td>
</tr>
<tr>
<td></td>
<td>5-day relapse rates of 6.6% with Dex versus 1.8% with Pred</td>
</tr>
<tr>
<td>Cronin et al 2016, Dublin</td>
<td>226 children 2-16 yo ED patients</td>
</tr>
<tr>
<td></td>
<td>PO Dex 0.3 mg/kg x 1 vs. Pred 1 mg/kg/day x 3 days</td>
</tr>
<tr>
<td></td>
<td>No significant difference</td>
</tr>
<tr>
<td></td>
<td>13.1% Dex group required further OCS within 14 days vs. 4.2% Pred</td>
</tr>
</tbody>
</table>
## Meat and Potatoes: Multiple Oral Doses

<table>
<thead>
<tr>
<th>Author</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qureshi et al 2001, US</td>
<td>628 children 2-18 yo ED patients</td>
</tr>
<tr>
<td></td>
<td>PO Dex 0.6 mg/kg x 2 vs. Pred 2 mg/kg/day x 5 days</td>
</tr>
<tr>
<td></td>
<td>No significant difference</td>
</tr>
<tr>
<td></td>
<td>10-day relapse rates of 7.4% with Dex versus 6.9% with Pred</td>
</tr>
<tr>
<td>Greenberg et al 2008, US</td>
<td>89 children 2-18 yo ED patients</td>
</tr>
<tr>
<td></td>
<td>PO Dex 0.6 mg/kg x 2 vs. Pred 2 mg/kg/day x 5 days</td>
</tr>
<tr>
<td></td>
<td>No significant difference</td>
</tr>
<tr>
<td></td>
<td>10-day relapse rates of 15.7% with Dex versus 8% with Pred</td>
</tr>
</tbody>
</table>
# Meat and Potatoes: Hospitalization

<table>
<thead>
<tr>
<th>Author</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parikh et al 2015, multicenter</td>
<td>40,257 children 4-17 yo HOSPITALIZED patients, 2.9% received Dex</td>
</tr>
<tr>
<td></td>
<td>No Dex dosing or route information</td>
</tr>
<tr>
<td></td>
<td>LOS shorter in Dex group</td>
</tr>
<tr>
<td></td>
<td>No difference in all cause re-admission</td>
</tr>
<tr>
<td></td>
<td>Lower cost</td>
</tr>
</tbody>
</table>
Pediatric Study Conclusions

- No difference in rate of hospitalization during initial ED visit
- No statistical difference in relapse rate between groups at any time point up to 30 days
- Patients who received Dex were less likely to experience vomiting in either the ED or at home
- Compliance rate when measured was >96%

“Practitioners should consider single or 2-dose regimen of dexamethasone as a viable alternative to a 5 day course of prednisone/prednisolone”
Key Takeaways

- Dexamethasone and prednisolone are equally efficacious.
- Dexamethasone is better tolerated than prednisolone and simplicity is preferred by families.
- Suggest dexamethasone 0.6 mg/kg (max 16 mg) X1 and repeat in 48 hours for pediatric patients with acute asthma.
Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulators: Changing the Future of Cystic Fibrosis Treatment & Management

Claire Elson, PharmD, BCPPS
Clinical Pharmacy Specialist
Children’s Mercy Hospital
Kansas City, MO
Learning Objective

- Recall relevant drug information regarding CFTR modulators and the pharmacist role with these novel therapies.
Cystic Fibrosis (CF) Basics

- Epidemiology
  - 30,000 individuals in the US
  - 1,000 new diagnosis annually

- Pathophysiology
  - Autosomal recessive mutation in gene encoding the cystic fibrosis transmembrane conductance regulator (CFTR) protein
  - Mutations classified based on functional mechanism into classes I to VI
Manifestations

SINOPULMONARY DISEASE
• Obstructive pulmonary disease
• Nasal polyps
• Infection (sinus, pneumonia, etc.)

HEPATOBILIARY DISEASE
• Biliary: obstruction
• Hepatic: cirrhosis

PANCREATIC DISEASE
• Exocrine: insufficiency
• Endocrine: growth, diabetes

GASTROINTESTINAL
• Obstruction
• Malnutrition & malabsorption

INFERTILITY
• Males: absence of vas deferens
• Females: mucoid obstruction

www.fairview.org
CF Therapeutic Areas

**Historical**

- Lung disease
  - Anti-obstructive
  - Anti-infective
  - Anti-inflammatory
- Pancreatic insufficiency & Gastrointestinal Disease

**Future**

- Drug Pipeline
  - CFTR Modulation
    - Ivacaftor (Kalydeco®)
    - Lumacaftor + Ivacaftor (Orkambi®)
    - Ataluren
    - VX-861 + Ivacaftor
    - Riociguat
    - QBW251
    - N91115
    - QR-010

Acure4lilchris.blogspot.com
www.cff.org/research/DrugDevelopmentPipeline/
Ivacaftor/Lumacaftor (Orkambi®)

- FDA approved for CF patients > 6 years old with homozygous F508del mutation
- Dosing & Formulations
  - 6-11 years old: 100 mg lumacaftor/125 mg ivacaftor
  - > 12 years old: 200 mg lumacaftor/125 mg ivacaftor
- Directions: Two (2) tablets by mouth twice daily
- Outcomes (> 12 years old)
  - FEV1, BMI and Exacerbation Rate
  - Non-significant improvement CFQ-R respiratory domain
- AWP: $23907.70/28 day supply
Pharmacist Role

- Medication Counseling
  - Administration
  - Drug interactions
- Medication adherence
- Medication access
  - Outpatient
  - Inpatient
- Clinical trials and research
Key Takeaways

- **Key Takeaway #1**
  - CF pharmacotherapy is changing to more targeted therapies with the introduction and expansion of CFTR modulators.

- **Key Takeaway #2**
  - As more combinations of CFTR modulators are developed, it is essential to critically evaluate overall healthcare impact in CF.

- **Key Takeaway #3**
  - Pharmacists play a critical role in monitoring these therapies, especially medication adherence and drug interactions.
In which of the following pediatric heart transplant patient populations is statin therapy recommended?

A. Those at increased risk of cardiac allograft vasculopathy
B. Pediatric patients > 8 years-of-age
C. Children receiving proliferation signal inhibitors
D. Patients at high risk for post-transplant lymphoproliferative disorder
Dexamethasone has been shown to be equally effective to prednisolone for children with acute asthma exacerbation

A TRUE
B FALSE
Which CFTR disease causing mutation does NOT have an FDA approved CFTR modulator?

- A  G551D
- B  Homozygous F508del
- C  Heterozygous F508del
- D  R117H
Getting Higher and Higher: Levetiracetam Loading Doses in Status Epilepticus

Stephanie Weightman, PharmD, BCPS, BCPPS
Clinical Pharmacist – Emergency Department
Children’s Health – Children’s Medical Center Dallas
Examine new recommendations of larger loading doses of levetiracetam in acute management of pediatric status epilepticus
What’s the actual mechanism of action?

- Binds to synaptic vesicle protein SV2A
  - Saturable and stereoselective

- Inhibition of voltage-dependent N-type calcium channels

- Facilitation of GABA-ergic inhibitory transmission

- Reduction of delayed rectifier potassium current

Where is levetiracetam’s place in acute management of status epilepticus (SE)?

- Levetiracetam use varies by patient age
- Prevention of SE-induced brain edema and neuronal loss
- ↑ antioxidant cysteine/glutamate exchanger
- A pharmacist’s dream!

Itoh K et al. *Brain Res.* 2015;1608:225-34.
Increasing Levetiracetam Doses in Acute Management

- Single dose 29.4 ± 13.5 mg/kg within 30 minutes of seizure
  - 74 patients (mean age 5.59 ± 5.6 years)
  - Serial seizures (79%), single seizure (12%), SE (8%)
  - 89% seizure-free at 1 hour
    - >80% SE patients

- Loading dose 50 mg/kg (range 25 – 70 mg/kg) + maintenance 25 mg/kg BID
  - 32 patients (2 months – 18 years)
  - 16 patients with SE
    - 46.87% SE patients responded favorably; clinical and EEG improvement at 30 minutes

High-dose Levetiracetam for Acute Seizure Exacerbation

- 9 patients (mean age 2.0 ± 1.2 years)
- Mean dose 228 ± 48 mg/kg/day
- Levetiracetam-naïve
  - 30 mg/kg/dose
  - Day 1: every 8 hours
  - Day 2: every 6 hours
  - Day 3: every 4 hours
- 8/9 patients resolution in acute repetitive seizures
- Tolerated without agitation, behavioral changes, or somnolence

Evidence Based Guidelines

Neurocritical Care Society 2012

- SE in critically ill patients
- Levetiracetam 20 – 60 mg/kg (1000 – 3000 mg)
  - Emergent, Urgent, Refractory (Class IIb, level C)

American Epilepsy Society 2016

- Convulsive SE
- Levetiracetam 60 mg/kg; max 4500mg/dose
  - Second therapy phase (Level U)

ESETT Study

Key Takeaways

- **Key Takeaway #1**
  - Newer data increasingly supports the use of high dose levetiracetam loading doses (60 mg/kg/dose) in acute status epilepticus.

- **Key Takeaway #2**
  - ESETT study may help elucidate levetiracetam’s preferred place in acute status epilepticus management.
Delirium in the NICU: Not Just a PICU Problem

Bob John, Pharm.D.; BCPS; BCPPS
NICU Clinical Pharmacy Specialist
The Children’s Hospital at Saint Francis
December 5, 2016
Objectives

- Describe identification tools and treatment plans for delirium that have been used in neonates
My NICU Currently Evaluates Neonates for Delirium

A. TRUE
B. FALSE
Delirium in Pediatrics

- Delirium
  - An acute and fluctuating change in awareness and cognition
  - Occurs in the setting of serious medical condition
- Pediatric Intensive Care Unit (PICU) delirium recognized in more than 20% of patients

Case Reports of Delirium in Neonates
<table>
<thead>
<tr>
<th>Case</th>
<th>Symptoms</th>
<th>Medications</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant boy • Congenital heart defects • ECMO</td>
<td>• Altered sleep wake-cycle • Increased agitation</td>
<td>• Fentanyl • Morphine • Lorazepam</td>
<td>• Olanzapine 1.25 mg orally as needed for agitation</td>
</tr>
</tbody>
</table>

ECMO=extracorporeal membrane oxygenation

<table>
<thead>
<tr>
<th>Case</th>
<th>Symptoms</th>
<th>Medications</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant girl</td>
<td>• Increasing respiratory support</td>
<td>• Morphine 20 mcg/kg/hr</td>
<td>• Quetiapine 0.5 mg/kg every 8 hours</td>
</tr>
<tr>
<td>(CGA*=17 weeks)</td>
<td>• Increased agitation</td>
<td>• Midazolam 70 mcg/kg/hr</td>
<td>• Increased to every 6 hours after 5 days</td>
</tr>
<tr>
<td></td>
<td>• Frequently inconsolable</td>
<td>• Dexmedetomidine 0.8 mcg/kg/hr</td>
<td>• Tapered off over 2 weeks</td>
</tr>
<tr>
<td></td>
<td>• Altered sleep wake-cycle</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CGA= Corrected Gestational Age, mcg= microgram, kg=kilogram, hr=hour
*Corrected age is calculated by subtracting the number of weeks born before 40 weeks of gestation from the chronological age

<table>
<thead>
<tr>
<th>Case</th>
<th>Symptoms</th>
<th>Medications</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infant girl</strong></td>
<td>• Increasing respiratory support</td>
<td>• Fentanyl 1 mcg/kg/hr</td>
<td>• Quetiapine 0.5 mg/kg every 8 hours for 2 months before transferred out</td>
</tr>
<tr>
<td>(CGA*=11 weeks)</td>
<td>• Increased agitation</td>
<td>• Dexmedetomidine 0.3 mcg/kg/hr, increased to 0.6 mcg/kg/hr</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Frequently inconsolable</td>
<td>• No benzodiazepines in the previous 7 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• CAPD=16</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CGA= Corrected Gestational Age, mcg= microgram, kg=kilogram, hr=hour, CAPD=Cornell Assessment of Pediatric Delirium

*Corrected age is calculated by subtracting the number of weeks born before 40 weeks of gestation from the chronological age
<table>
<thead>
<tr>
<th>Case</th>
<th>Symptoms</th>
<th>Medications</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| **Infant boy** (CGA*= 4 weeks)  | • Increased agitation  
• Frequently inconsolable  
• CAPD scores 12-14 | • Morphine 100 mcg/kg as needed   
• Midazolam 50 mcg/kg/hr | • Quetiapine 0.5 mg/kg every 8 hours for 5 weeks then transferred to rehabilitation center |

CGA= Corrected Gestational Age, mcg= microgram, kg=kilogram, hr=hour, CAPD=Cornell Assessment of Pediatric Delirium

*Corrected age is calculated by subtracting the number of weeks born before 40 weeks of gestation from the chronological age

<table>
<thead>
<tr>
<th>Case</th>
<th>Symptoms</th>
<th>Medications</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| Infant girl (CGA* unknown) | • Altered sleep-wake-cycle  
• Increased agitation  
• Unstable vital signs | • Morphine 40 mg (5 mg/kg) every 6 hours  
• Lorazepam 4 mg (0.5 mg/kg) every 6 hours  
• Methadone 5 mg (0.6 mg/kg) every 6 hours  
• Furosemide 400 mcg/kg/hr | • Risperidone 0.125 mg at bedtime via NG  
• Dose increased to 0.3 mg  
• Dose tapered off over 6 weeks |

CGA= Corrected Gestational Age, mcg= microgram, kg=kilogram, hr=hour, CAPD=Cornell Assessment of Pediatric Delirium, NG = nasogastric tube  
*Corrected age is calculated by subtracting the number of weeks born before 40 weeks of gestation from the chronological age

Monitoring for Delirium

- Vital signs
  - Heart rate, blood pressure, respiratory rate

- Behavior
  - Altered wake-sleep cycle, inconsolable

- Medications
  - Opioids – morphine, methadone, fentanyl
  - Benzodiazepines – lorazepam, midazolam

- Assess and document every 8-12 hours
  - At least once per shift

Monitoring for Delirium

- Cornell Assessment Pediatric Delirium tool (CAP-D)
  - 0 to 18 years of age
- Pediatric Confusion Assessment Method for ICU (pCAM-ICU)
  - 5 years of age and older

Treatment Options
Pharmacologic

- Atypical Antipsychotics
  - **Quetiapine** 0.5 mg/kg orally every 8 hours
    - One case report increased to every 6 hours
  - **Risperidone** 0.125 mg orally daily at bedtime
    - One case report increased to 0.3 mg once daily
  - **Olanzapine** 1.25 mg orally at bedtime as needed for agitation

- Baseline and repeat EKG
- Taper dose up only if needed and down

Key Takeaways

- **Key Takeaway #1**
  - Delirium is a concern in neonates in both the NICU and PICU

- **Key Takeaway #2**
  - CAP-D is the only scoring system that has been validated in neonates

- **Key Takeaway #3**
  - Atypical antipsychotics have been used to treat delirium in neonates
## Appendix 1

### Summary of Case Reports

<table>
<thead>
<tr>
<th>Case</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| **Infant girl** (CGA=17 weeks) | • Quetiapine 0.5 mg/kg every 8 hours  
• Increased to every 6 hours after 5 days  
• Tapered off over 2 weeks |
| **Infant girl** (CGA=11 weeks) | • Quetiapine 0.5 mg/kg every 8 hours for 2 months |
| **Infant boy** (CGA= 4 weeks)   | • Quetiapine 0.5 mg/kg every 8 hours for 5 weeks |
| **Infant girl** (CGA unknown)    | • Risperidone 0.125 mg at bedtime via NG  
• Dose increased to 0.3 mg  
• Dose tapered off over 6 weeks |
| **Infant boy**         | • Olanzapine 1.25 mg orally as needed for agitation |

*Corrected age is calculated by subtracting the number of weeks born before 40 weeks of gestation from the chronological age.*
Not This Again: Vancomycin PK Primer

Kyana D. Stewart, MS, PharmD, BCPS
Clinical Specialist Pharmacist, Pediatric Infectious Diseases
Antimicrobial Stewardship Program Co – chair
Children’s Health System, Children’s Medical Center
Dallas, Texas
Learning Objective

- Describe key pharmacokinetic parameters that may impact vancomycin efficacy in complex pediatric patients
Vancomycin Quick Review

- **Mechanism of action**
  - Binds to peptidoglycan in gram + bacterial cell wall inhibiting synthesis

- **Killing profile**
  - Slowly cidal against MRSA
  - Static against enterococci

- **Site penetration**
  - CNS < 10%
  - Lung 15 – 20%
  - Sternal bone 50 – 60%
  - Heart valve ~ 12%
  - Adipose tissue ~ 15%
  - Muscle 10%
  - Bone 10 – 15%

- **PK/PD Parameter for efficacy**
  - AUC:MIC > 400
I promise vancomycin PK relationships are only understood by a true Jedi
Peaks and Troughs

Trough only
Alter frequency to meet target

Trough targets and AUC target mismatch

Pharmacodynamic Parameter for Efficacy

Lodise T, Drusano G, Zasowski E, et al. CID 2014
Dosing Strategies to Optimize PK/PD Endpoint

**Increased frequency of administration**
- Every 8 – 12 hour frequency not fit for pediatric patients to reach target attainment
  \[ C_{\text{min}} = 15 – 20 \text{ mg/L} \]

**Increased total daily dosing**
- 20 mg/kg/dosing minimum needed to achieve adult serum targets in pediatric patients
- Oops...vanc induced nephrotoxicity 😞

**Surrogate or Actual Target?**
- Trough target & AUC:MIC mismatch
- Vancomycin as a narrow therapeutic index drug?

Dosing Strategies to Optimize PK/PD Endpoint

Increased frequency & continuous infusions

- Optimize frequency based on age and developmental PK/PD changes
  - Infants and children
  - Rapid metabolic changes
  - Rapid fluid shifts

Utilization of loading doses for earlier target attainment

- 30 mg/kg/dose suggested in 2009 guidelines
- Mixed data in pediatrics
  - Weight and age stratified loading dose regimen proposed (16 – 30 mg/kg/dose)
- Renal impairment must be considered

Methods of AUC Extrapolation

- Linear Trapezoidal Rule
  - Break into pieces and add them up!
  - Will require multiple serum concentrations
  - \[ \text{AUC} = \sum \frac{C_1 + C_2}{2} \times (t_2 - t_1) + \ldots \]

- Vancomycin AUC Bedside Method
  - Obtain MIC from clinical laboratory
  - Estimate CrCl using the modified Schwartz
  - Calculate vancomycin clearance
    - \[ \text{CL} \text{ (L/h)} = 0.248 \times \text{Wt}^{0.75} \times (0.48/\text{SCR})^{0.361} \times \frac{\text{Ln} \text{ (age)/7.8}}{0.995} \]
  - \[ \text{AUC (mg hr/L)} = \text{Daily vancomycin dose (mg/day) / Calculated CL} \]
Key Takeaways

- **Key Takeaway #1**
  - Vancomycin frequency of administration should be empirically increased as age decreases outside of the neonatal period to attain acceptable serum targets.

- **Key Takeaway #2**
  - A tiered approach that utilized AUC based extrapolations may be a better reflection of adequate serum exposure as compared to serum trough measurements.

- **Key Takeaway #3**
  - Consideration of loading doses for earlier target attainment may be advantageous in pediatric patients.
In patients $\geq 1$ year of age, levetiracetam loading doses should never exceed 30 mg/kg/dose (maximum 1000 mg/dose).

A  TRUE

B  FALSE
Symptoms of delirium in a neonate can be identified by utilizing which of the following scales?

A. Delirium Rating Scale–Revised -98 (DRS-R98)
B. Pediatric Confusion Assessment Method for ICU (pCAM-ICU)
C. Sophia Observation Withdrawal Symptoms-Pediatric Delirium Scale (SOS-PD)
D. Cornell Assessment Pediatric–Delirium (CAP-D)
The pharmacodynamic parameter for efficacy of vancomycin is reflected by which of the following?

- A Serum trough level
- B AUC > 400 mg/L*hr
- C AUC/serum trough level
- D AUC/MIC > 400 mg/L*hr