Antibiotic Dosing in the Elderly

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Nebraska Medicine
Disclosure

• I have no relevant disclosure

• The presentation includes the off-label use of nitrofurantoin for the elderly
Objectives

• To evaluate the incidence of adverse events associated with antibiotic therapy in long-term care facilities (LTCF)

• To describe changes in pharmacokinetic and pharmacodynamic processes due to aging

• To discuss recently revised renal dosing recommendations for nitrofurantoin and oseltamivir

• To outline practical strategies for antibiotic dosing in LTCF
Goals of Antimicrobial Stewardship

Minimize Adverse Outcomes

Optimize Treatment of Infection

CDC. The Core Elements of Antibiotic Stewardship for Nursing Homes. Available at: http://www.cdc.gov/longtermcare/index.html
Incidence of Adverse Drug Events in LTCF

- Evaluation of adverse drug events (ADE) in two large academic LTCF totaling 1229 beds

- 815 ADE identified among >1200 residents (9.8 events per 100 resident-months)
  - >25% of events were serious
  - 42% deemed preventable
  - Mostly from monitoring (80%) and ordering (59%) errors

- 105 (13%) from antimicrobial use
  - Quinolones, clindamycin, and TMP-SMX most commonly implicated

### Risk Factors Associated with ADE

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Odd Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>On 6-8 medications*</td>
<td>1.4</td>
<td>0.9 – 2.0</td>
</tr>
<tr>
<td>On 9-11 medications*</td>
<td>1.7</td>
<td>1.1 – 2.6</td>
</tr>
<tr>
<td>On ≥12 medications*</td>
<td>2.1</td>
<td>1.3 – 3.5</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>3.1</td>
<td>1.7 – 5.6</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>2.4</td>
<td>1.7 – 3.5</td>
</tr>
<tr>
<td>Antimicrobials</td>
<td>1.9</td>
<td>1.3 – 2.8</td>
</tr>
</tbody>
</table>

* Compared to residents on 1-5 medications.
# Risk Factors for Adverse Drug Events in Massachusetts LTCFs

## Selected Patient Characteristics with ADE vs. Controls

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Case (n = 410)</th>
<th>Control (n = 410)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>83.3 (8.3)</td>
<td>84.3 (9.0)</td>
</tr>
<tr>
<td>New resident</td>
<td>70 (17.1)</td>
<td>25 (6.1)</td>
</tr>
<tr>
<td>0-4 Medications</td>
<td>69 (16.8)</td>
<td>147 (35.0)</td>
</tr>
<tr>
<td>≥5 Medications</td>
<td>341 (83.2)</td>
<td>263 (64.1)</td>
</tr>
<tr>
<td>Antimicrobials</td>
<td>142 (34.6)</td>
<td>57 (13.9)</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>194 (47.3)</td>
<td>149 (36.3)</td>
</tr>
<tr>
<td>Cardiovascular drugs</td>
<td>242 (59.0)</td>
<td>201 (49.0)</td>
</tr>
<tr>
<td>Gastrointestinal drugs</td>
<td>314 (76.6)</td>
<td>308 (75.1)</td>
</tr>
<tr>
<td>Non-opioid analgesics</td>
<td>273 (66.6)</td>
<td>258 (62.9)</td>
</tr>
</tbody>
</table>

Data presented as number (percentage)
Characteristics with bold font has p < 0.05

### Independent Risk Factors Associated with ADE

![Graph showing odds ratio for independent risk factors associated with ADE](image-url)

ADE less likely  
ADE more likely
Variability in Antibiotic Prescribing in LTCF

- Provincial-wide analysis of antibiotic use in Ontario LTCF
- 78% of ~67,000 residents received an antibiotic course during 2010
- Most commonly used antimicrobials

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>2nd or 3rd-Generation Fluoroquinolones</th>
<th>Penicillins</th>
<th>1st-Generation Cephalosporins</th>
<th>Sulfonamides</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. (%) of Treatment</td>
<td>18217 (35.4)</td>
<td>8776 (17.0)</td>
<td>5762 (11.2)</td>
<td>5166 (10.0)</td>
</tr>
</tbody>
</table>

- Duration of therapy was highly variable
  - >7 days was most common (44%)
  - Only 14% received <7 days of therapy
- Prescribers appeared to be driving force for duration of therapy
  - Similar characteristics between residents treated by short-, medium-, long-duration prescribers

Evidence of Inappropriate Antibiotic Use in Long-Term Care Facility

- Review of 100 random courses of antibiotic over 6 months in LTCF
- 1351 total days of therapy (DOT) prescribed; 42% were inappropriate
- >60% of courses at least partly unnecessary
- Even when antibiotic indicated, ~50% of DOT inappropriate
- 20 adverse outcomes
  - 5 *Clostridium difficile* infections
  - 5 with resistant pathogens
  - 10 experienced ADE

Reasons for Inappropriate Antimicrobial Prescribing in Urinary Tract Infections

• Evaluated antibiotic appropriateness for treatment of urinary tract infections
  o Does patient meet criteria for start antibiotic?
  o Is antibiotic regimen (agent, dose, frequency, duration) consistent with national guidelines?
  o Did patient develop *C difficile*?

• Urinalysis sent for 172 patients
  o Only 15% met criteria for treatment
  o Yet 56% started on antibiotics
  o Two out of five patients received antibiotic inappropriately

• 8 times more like to develop *C difficile* infection with inappropriate antibiotic

Take Home Points

- Adverse drug events are common in LTCF (~10 events per 100 resident-month)
  - Most are associated with errors in monitoring and ordering
  - Antimicrobials among most commonly implicated class of agent

- Antimicrobial prescribing is highly variable in LTCF
  - Choice of agent and duration driven by prescriber preference, not patient conditions
  - Fluoroquinolones most commonly prescribed agent
  - Duration of therapy >7 days most commonly used

- Up to 40-60% of residents receive antimicrobial inappropriately
  - ~40% did not fit criteria to initiate therapy
  - Half to two-thirds receive longer duration than needed
  - ~45% receiving inappropriate dose
Pharmacokinetics (PK): A brief review

• What the body does to the drug

• Absorption
  o How do drugs reach bloodstream
  o Occurs in small intestine for oral medications
  o Drugs pass through GI tract wall into capillary

• Distribution
  o Where do drugs go after reaching bloodstream
  o Determined by protein binding and volume of distribution
  o Volume of distribution in turns determined by drug characteristics, body composition

• Metabolism:
  o How does body modify chemical structure of drugs
  o Primarily in the liver by enzyme systems
  o Can occur in lungs, kidneys, GI tract
  o Make drug inactive and prepare for elimination

• Excretion:
  o How does the drugs get removed from the body
  o Primarily in urine and/or feces
  o Can be of both active or inactive drugs

Collectively, these four processes determine drug concentrations in the body
Pharmacodynamics (PD): A brief review

• What does the drug do to the body?

• Because antimicrobial is directed toward microbes
  ○ Desired effect: bacterial killing
  ○ Undesirable effect: any physiologic changes on the body (e.g., QTc prolongation)
PK: Drug Concentration vs. Time Graph

Cmax (peak)

Elimination ($t_{1/2}$) influences this portion of the curve

Cmin (trough)

AUC (area under the curve)

MIC

Drug Concentration

Time (hours)
PK-PD of Antimicrobial Agents: Time vs. Concentration Dependence

Table 1. Pharmacokinetic and pharmacodynamic parameters correlating with antibacterial efficacy in animal infection models.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time above the MIC</td>
<td>Penicillins, cephalosporins, carbapenems, aztreonam, macrolides, and clindamycin</td>
</tr>
<tr>
<td>24-hour AUC/MIC</td>
<td>Aminoglycosides, fluoroquinolones, azithromycin, tetracyclines, vancomycin, and quinupristin/dalfopristin</td>
</tr>
<tr>
<td>Peak/MIC</td>
<td>Aminoglycosides and fluoroquinolones</td>
</tr>
</tbody>
</table>

NOTE. AUC = Area under the concentration-vs.-time curve.
## PK Processes Affected by Age-Related Physiologic Changes

<table>
<thead>
<tr>
<th>PK Process</th>
<th>Age-Related Physiologic Changes</th>
<th>Potential Clinical Consequences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absorption</td>
<td>↓ gastric acid secretion</td>
<td>Increased risk of drug-induced esophageal lesions</td>
</tr>
<tr>
<td></td>
<td>↓ gastric emptying</td>
<td>Change is drug solubility</td>
</tr>
<tr>
<td></td>
<td>↓ splanchnic blood flow</td>
<td>Change in T&lt;sub&gt;max&lt;/sub&gt; and C&lt;sub&gt;max&lt;/sub&gt;</td>
</tr>
<tr>
<td></td>
<td>↓ gastrointestinal motility</td>
<td></td>
</tr>
<tr>
<td>Distribution</td>
<td>↓ muscle mass</td>
<td>Increased concentration of water-soluble drugs</td>
</tr>
<tr>
<td></td>
<td>↓ total body water</td>
<td>Increased half-life of lipid-soluble drugs</td>
</tr>
<tr>
<td></td>
<td>↑ total body fat</td>
<td>Increased free drug and associated toxicity</td>
</tr>
<tr>
<td></td>
<td>↓ protein binding site</td>
<td></td>
</tr>
<tr>
<td>Metabolism</td>
<td>↓ hepatic blood flow</td>
<td>Reduced drug metabolism</td>
</tr>
<tr>
<td></td>
<td>↓ liver mass</td>
<td>Increased half-life of hepatically metabolized drugs</td>
</tr>
<tr>
<td></td>
<td>↓ activity of metabolic enzymes</td>
<td></td>
</tr>
<tr>
<td>Elimination</td>
<td>↓ renal blood flow</td>
<td>Reduced elimination of water soluble drugs</td>
</tr>
<tr>
<td></td>
<td>↓ glomerular filtration capacity</td>
<td>Increased half-life of renally eliminated drugs</td>
</tr>
</tbody>
</table>

Age-Related Changes in Pharmacodynamics

- Less well characterized than age-related PK changes

- Aging may result in
  - Change in number of drug receptors
  - Change in receptor binding affinity
  - Change in receptor sensitivity (usually increased)

- Age-related PD changes may increase sensitivity to toxic effect of antimicrobials
  - May change drug effects on pathogens due to altered PK/drug concentrations
  - More prone to renal toxicity from aminoglycosides
  - More prone to neuropsychiatric effects of antivirals (acyclovir, oseltamivir)

Age-Related Distribution Changes Associated with Antimicrobial Agents

- Changes in drug distribution
  - Elderly with lower total body water
  - Water-soluble drugs have a “smaller tank” to dissolve in → higher drug concentration

- The case for gentamicin
  - Reference range for volume of distribution = 0.2 to 0.3 L/kg
  - Zaske, et al. found highly variable value in elderly (0.07 to 0.53 L/kg)
  - Triggs & Charles reviewed 8 studies
    - Similar distribution volume in studies with mean ages of 39, 61, and 80 yrs (~0.35 L/kg)

- Implication: careful monitoring and dose determination required in elderly

Estimated gentamicin volume of distribution in Elderly with normal and abnormal serum creatinine

Age-Related Changes in Renal Elimination Associated with Antibiotics

• An important area in antibiotic therapy
  o Most antibiotics are eliminated renally
  o ↓ renal blood flow → reduce drug delivery to glomeruli for elimination
  o ↓ number of functional glomeruli → reduce excretory capacity
  o Net results: ↑ drug concentration, ↑ half-life, ↑ likelihood of toxicity

• Zaske, et al found longer half-life with reduced creatinine clearance (CrCl)
  o CrCl 41 ml/min → t ½ = 5.8 hrs
  o CrCl 115 ml/min → t ½ = 2.52 hrs

Comparative PK of Gentamicin by Age

<table>
<thead>
<tr>
<th>Mean Age (Range)</th>
<th>Clearance (mL/min/kg)</th>
<th>Half-Life (hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>33 (4-67)</td>
<td>1.148</td>
<td>2.2</td>
</tr>
<tr>
<td>39 (17-55)</td>
<td>1.67</td>
<td>2.5</td>
</tr>
<tr>
<td>48 (19-86)</td>
<td>0.772</td>
<td>4.7</td>
</tr>
<tr>
<td>55 (19-87)</td>
<td>1.09</td>
<td>2.8</td>
</tr>
<tr>
<td>59 (37-82)</td>
<td>1.43</td>
<td>2.5</td>
</tr>
<tr>
<td>61 (not stated)</td>
<td>1.83</td>
<td>4.7</td>
</tr>
<tr>
<td>72 (55-86)</td>
<td>1.06</td>
<td>3.2</td>
</tr>
<tr>
<td>76 (65-95)</td>
<td>0.736</td>
<td>5.7</td>
</tr>
<tr>
<td>80 (70-96)</td>
<td>1.00</td>
<td>4.1</td>
</tr>
</tbody>
</table>


Examples of Antimicrobials Requiring Dose Adjustment for Renal Insufficiency

• **Penicillins**
  - Amoxicillin
  - Ampicillin
  - Amoxicillin/clavulanate
  - Ampicillin/sulbactam
  - Piperacillin/tazobactam

• **Cephalosporins**
  - Cephalexin
  - Cefuroxime
  - Cefixime
  - Cefpodoxime
  - Cefazolin
  - Ceftazidime
  - Cefepime

• **Carbapenems**
  - Ertapenem
  - Imipenem/cilastatin
  - Meropenem
  - Doripenem

• **Monobactam**
  - Aztreonam

• **Fluoroquinolones**
  - Ciprofloxacin
  - Levofloxacin

• **Macrolides**
  - Clarithromycin

• **Aminoglycosides**
  - Gentamicin
  - Tobramycin
  - Amikacin

• **Others**
  - Vancomycin IV
  - Daptomycin
  - TMP/SMX
  - Fluconazole
  - Oseltamivir
Examples of Antimicrobials Not Requiring Dose Adjustment for Renal Impairment

- Dicloxacillin, cloxacillin
- Nafcillin, oxacillin
- Ceftriaxone
- Azithromycin
- Moxifloxacin
- Doxycycline, minocycline
- Tigecycline
- Linezolid, tedizolid
- Clindamycin
- Metronidazole
- Vancomycin PO
- Micafungin, caspofungin, anidulafungin
- Voriconazole
How to Quantify Renal Function?

- Primarily refer to capacity of glomerular filtration
- Numerous marker available to quantify
  - Inulin
  - Iohexol
  - 99 mTc-DTPA
  - Cystatin C
  - Iothalamate
  - 125-I Iothalamate

### Sensitivity and Clinical Utility of Renal Function Tests

<table>
<thead>
<tr>
<th>Method</th>
<th>Accuracy</th>
<th>Clinical Utility</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inulin clearance</td>
<td>++++</td>
<td>+</td>
<td>$$$$$</td>
</tr>
<tr>
<td>Radiolabeled markers</td>
<td>+++</td>
<td>+</td>
<td>$$$</td>
</tr>
<tr>
<td>Non-isotopic contrast agents</td>
<td>+++</td>
<td>++</td>
<td>$$$</td>
</tr>
<tr>
<td>Creatinine Clearance</td>
<td>++</td>
<td>+++</td>
<td>$$</td>
</tr>
<tr>
<td>Serum Creatinine</td>
<td>+</td>
<td>+++</td>
<td>$</td>
</tr>
</tbody>
</table>

+, least acceptable; ++, adequate; +++, better; ++++, best
Should Serum Creatinine Alone be Used?

• Serum creatinine influenced by
  o Dietary intake (fish, red meat)
  o Muscle mass
  o Renal function

• Normal range: 0.5 to 1.5 mg/dL (44 to 133 μmol/L)

• Swedko, et al, found use of serum creatinine alone underestimated renal failure in elderly
  o Severe renal failure: 54% has SCr <1.7 mg/dL
  o Renal failure: 87% with SCr <1.7 mg/dL
  o Detection sensitivity: women < men

Table 2. Characteristics of Serum Creatinine as a Test for Renal Failure*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal Failure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity, %</td>
<td>12.6</td>
<td>7.3</td>
<td>22.9</td>
</tr>
<tr>
<td>Specificity, %</td>
<td>99.9</td>
<td>100.0</td>
<td>99.3</td>
</tr>
<tr>
<td>Negative likelihood ratio</td>
<td>0.87</td>
<td>0.92</td>
<td>0.77</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Severe Renal Failure</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity, %</td>
<td>45.5</td>
<td>29.7</td>
<td>77.8</td>
</tr>
<tr>
<td>Specificity, %</td>
<td>99.1</td>
<td>99.8</td>
<td>98.3</td>
</tr>
<tr>
<td>Negative likelihood ratio</td>
<td>0.55</td>
<td>0.70</td>
<td>0.23</td>
</tr>
</tbody>
</table>

* A serum creatinine level of 1.7 mg/dL (150 μmol/L) was used. Renal failure was defined as a Cockcroft and Gault formula glomerular filtration rate of 50 mL/min or less; severe renal failure, a Cockcroft and Gault formula glomerular filtration rate of 30 mL/min or less.
Creatinine Clearance Estimation by Cockcroft-Gault Equation

- Originally developed during 1970s
  - Based on 249 male veterans in Canada
  - Ranging in age between 19-92 years old; 50% in 50 to 69 age range
  - Mean weight was 72 kg

- Multiply x 0.85 for woman
- Take into account age, weight, gender, serum creatinine

- Common (and controversial) questions
  - What weight to use?
  - Should low SCr (e.g., 0.4 mg/dL) be rounded up?

\[
C_{er} = \frac{(140 - \text{age}) \times \text{wt kg}}{72 \times \text{Ser (mg/100 ml)}}
\]
Impact of Various Body Weights and Serum Creatinine Concentrations on the Bias and Accuracy of the Cockcroft-Gault Equation

Mary A. Winter, Pharm.D., Kelly N. Guhr, Pharm.D., and Gina M. Berg, Ph.D.

• Retrospective analysis of 3678 patients with stable renal function
• Compared creatinine clearance (CrCl) calculated based on
  • Cockcroft-Gault equation (CG)
  • 24-hour urine collection
• Determined accuracy of CrCl calculated by CG using
  • Ideal body weight vs. actual body weight
  • Rounding serum creatinine to 0.8 mg/dl or 1 mg/dl
• CG CrCl estimates more accurate if
  • Underweight → use actual body weight
  • Normal weight → use ideal body weight
  • Overweight or obese → use adjusted body weight
  • Use actual serum even if SCr <0.8 mg/dL
Take Home Points

• Pharmacokinetic/pharmacodynamics process are not always comparable between younger and elderly patients

• Metabolism and Renal elimination are frequently reduced in elderly
  o Reduction in renal elimination is of bigger concern with antimicrobial dosing

• Methods are available to quantify renal function
  o Cockcroft-Gault equation provide useful CrCl estimation for drug dose adjustment
  o Should also pay attention to clinical status (e.g., urine output)
Nitrofurantoin

• Indicated for treatment of cystitis

• Only antimicrobial listed on Beer’s Criteria for Potentially Inappropriate Medication

• 2012 recommendations
  o Avoid use for long term suppression or CrCl <60 mL/min
  o Concern for pulmonary and liver toxicities
  o Questionable efficacy with CrCl <60 mL/min due to inadequate urine concentration

• 2015 recommendations
  o Avoid use for long term suppression, CrCl <30 mL/min
  o Concern with pulmonary and liver toxicities especially with prolonged use

Basis for 2012 Nitrofurantoin Recommendations

- Review of 912 cases of ADR in Sweden over 10 years
- 447 (48%) with pulmonary toxicity
  - Acute pulmonary hypersensitivity in 398
  - Chronic interstitial pneumonitis in 49
- Death resulted in 11 patients
  - 6 from pulmonary toxicity
  - Treatment duration ≥8 years in 3 patients
  - Other fatal reactions include hematologic toxicities and one case of cirrhosis

**TABLE II  Fatal Cases of Nitrofurantoin Reactions**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Year of Death</th>
<th>Age (yr) and Sex</th>
<th>Adverse Reaction</th>
<th>Daily Dose (mg)</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1970</td>
<td>76,M</td>
<td>Agranulocytosis</td>
<td>150</td>
<td>3 mo</td>
</tr>
<tr>
<td>2</td>
<td>1972</td>
<td>69,F</td>
<td>Chronic pulmonary reaction</td>
<td>Unknown</td>
<td>Long periods 1959–1971</td>
</tr>
<tr>
<td>3</td>
<td>1972</td>
<td>69,F</td>
<td>Chronic pulmonary reaction, polyneuropathy</td>
<td>100</td>
<td>9 yr</td>
</tr>
<tr>
<td>4</td>
<td>1972</td>
<td>77,F</td>
<td>Chronic pulmonary reaction</td>
<td>100</td>
<td>8 yr</td>
</tr>
<tr>
<td>5</td>
<td>1972</td>
<td>85,M</td>
<td>Pancytopenia</td>
<td>150</td>
<td>1 wk</td>
</tr>
<tr>
<td>6</td>
<td>1973</td>
<td>74,M</td>
<td>Chronic pulmonary reaction</td>
<td>150</td>
<td>4 yr</td>
</tr>
<tr>
<td>7</td>
<td>1974</td>
<td>64,F</td>
<td>Hepatic cirrhosis</td>
<td>50</td>
<td>23 mo</td>
</tr>
<tr>
<td>8</td>
<td>1974</td>
<td>79,F</td>
<td>Agranulocytosis</td>
<td>200</td>
<td>5 days</td>
</tr>
<tr>
<td>9</td>
<td>1975</td>
<td>66,F</td>
<td>Acute pulmonary reaction</td>
<td>150</td>
<td>1 day</td>
</tr>
<tr>
<td>10</td>
<td>1976</td>
<td>71,F</td>
<td>Thrombocytopenia</td>
<td>200</td>
<td>6 days</td>
</tr>
<tr>
<td>11</td>
<td>1976</td>
<td>81,F</td>
<td>Acute pulmonary reaction</td>
<td>150</td>
<td>1 day</td>
</tr>
</tbody>
</table>

New Data on Nitrofurantoin (NTF) and Reduced Renal Functions

- Retrospective review of Kaiser database on safety and efficacy (2007-2013)
  - 13,421 received nitrofurantoin; compared to 32,100 received other antibiotics
- Lung injury
  - NTF vs. others: RR 0.90 (95% CI 0.81 – 1.01)
  - >14 days therapy vs. less: RR 1.50 (95% CI 1.03 – 2.19)
- Efficacy as function of CrCl (mL/min)
  - <30: 97.1%
  - 30-60: 97.3%
  - >60: 96.6%
  - P-value = 0.16

- Retrospective review of single hospital experience of NTF in renal insufficiency
  - 26 patients with CrCl <60 mL/min received nitrofurantoin
  - 18 (69%) were successfully treated
  - 8 (31%) failed therapy
    - 5 due to resistance
    - 2 patients had CrCl <30 mL/min

Oseltamivir

- Indicated for treatment and prevention of influenza A and B
- Converted to active drug, which is almost entirely renally eliminated
- Dosing recommendations changed based on new PK/PD modeling data

### New Oseltamivir Dosing
(Since 2014 – 2015 flu season)

<table>
<thead>
<tr>
<th>CrCl (mL/min)</th>
<th>Treatment</th>
<th>Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;60</td>
<td>75mg BID</td>
<td>75mg daily</td>
</tr>
<tr>
<td>&gt;30-60</td>
<td>30mg BID</td>
<td>30mg daily</td>
</tr>
<tr>
<td>&gt;10-30</td>
<td>30mg daily</td>
<td>30mg q48h</td>
</tr>
<tr>
<td>HD</td>
<td>30mg post-HD</td>
<td>30mg after q other HD</td>
</tr>
</tbody>
</table>

### Old Oseltamivir Dosing
(Before 2014 – 2015 flu season)

<table>
<thead>
<tr>
<th>CrCl (mL/min)</th>
<th>Treatment</th>
<th>Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;30</td>
<td>75mg BID</td>
<td>75mg daily</td>
</tr>
<tr>
<td>≤30</td>
<td>75mg daily</td>
<td>75mg q48h</td>
</tr>
</tbody>
</table>

PK/PD Modeling Data for Oseltamivir

Definitions
Normal: CrCl > 90 mL/min
Mild renal insufficiency (RI): CrCl 60-90 mL/min
Moderate RI: CrCl 30-60 mL/min
Severe RI: CrCl < 30 mL/min

Take Home Points

• Use of nitrofurantoin traditionally contraindicated with CrCl <60 mL/min
  o New Beer’s list lowered CrCl <30 mL/min
  o Limited data demonstrated similar efficacy with CrCl 30-60 mL/min vs >60 mL/min
  o Avoid chronic use (e.g., >14 days) to minimize pulmonary toxicities
  o Avoid use in <30 mL/min due to limited data on efficacy

• Oseltamivir dose should be reduced when CrCl <60 mL/min
  o New renal dosing guideline since 2014-2015 season
Computer Decision Support to Guide Drug Dosing in Renal Insufficiency

Other outcomes:
- Length of stay reduced by 0.2 day in intervention group ($p = 0.009$)
- No difference in overall and pharmacy costs
Practical Strategies for Antibiotic Dosing in Elderly

- Did patient fit criteria to start antibiotics (McGeer\textsuperscript{1} or Loeb\textsuperscript{2} criteria)?

- Is patient being prescribed a renally eliminated antibiotic?

- Calculate CrCl based on Cockcroft-Gault equation

- Refer to drug reference to determine if dose is appropriate

Questions?
Antibiotic Dosing in the Elderly

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