ADULT PHARMACOKINETIC DOSING COMPETENCY

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OBJECTIVES

- Upon completion of this lecture, participants will be able to:
  - Describe the policy and procedure for pharmacokinetic dosing of vancomycin and aminoglycosides for adults patients at IMH
  - Identify target patient populations where additional monitoring is warranted
  - Outline documentation required for patients followed by the pharmacy pharmacokinetic consult service
  - Be prepared for completion of required case studies

NEW IMH PHARMACOKINETIC POLICY

- The ***Adult Pharmacokinetic Dosing Protocol*** will be initiated when the physician orders “Vancomycin Protocol”, “Vancomycin-Pharmacy to Dose”, or an equivalent order.
- Applies to aminoglycosides when ordered in the same manner.
- Will initiate the ordering and monitoring of vancomycin and aminoglycoside therapy.
- Pre-admission emergency department patients and surgical prophylaxis will not be included in this protocol.

PROCESSING NEW ORDERS

- Pharmacist will review and verify the order and initiate an appropriate initial dosing regimen
  - Loading doses will be reviewed and provided promptly
  - Orders for maintenance doses and monitoring will be provided prior to the next dose due
- Any order stating “pharmacy to dose” or “consult pharmacy” will be interpreted as full dosing privileges as stated within the protocol.
- Providers have the option of opting out of the pharmacy to dose protocol by not ordering it as so, discontinuing the order or notifying the pharmacist who will then discontinue the order.

PATIENT ASSESSMENT

- Pharmacist will review the appropriateness of the indication and dose the antibiotic based on the below information:
  - Clinical Indication
  - Age
  - Sex
  - Height/Weight
  - Renal function
  - Estimated PK parameters
- Routine monitoring will include the evaluation of clinical status, interpretation of relevant labs, drug concentrations, changes in renal function or fluid status, microbiology results, concurrent antimicrobial therapy and length of therapy.
- PK services will be provided until therapy is completed, discontinued or the patient is discharged.

PHARMACIST ORDERING

- **Doses**
  - Upon selecting a dosing regimen, the pharmacist will enter applicable orders.
  - All orders in response to “Pharmacy to Dose” will be entered or discontinued “per protocol-no cosign required.”
- **Serum Drug Concentrations**
  - The pharmacist will order serum drug concentrations for the drug as necessary “per protocol-no cosign required.”
- **Labs**
  - The pharmacist will ensure that relevant labs (CBC, SCr) are ordered. Any labs ordered will be entered as “per protocol-no cosign required.”

DOCUMENTATION

- Pharmacist will provide a **"Pharmacokinetic Note"** in the patient's chart via PowerChart with:
  - Upon initiation of therapy
  - Each resulted concentration and/or dose change
- The **"Pharmacokinetic Note- drug name"** must include the following:
  - General Information: drug, dosing style, indication, day of therapy, goal concentration
  - Laboratory Data: drug concentration, WBC, SCr, fever assessment)
  - Assessment
  - Recommendation: dosing and monitoring plan as well as signature and contact information

PHARMACIST PK CONSULT NOTES

Vancomycin - Pharmacist Pharmacokinetic Note

Patient: **MRN:** **FIN:**
Age: **Sex:** **DOB:**
Associated Diagnoses:
Author:

General:
Patient is receiving vancomycin for treatment of _____.
Today is day _____ of therapy.
Goal vancomycin trough is _____ mcg/mL.
Current Dose:

Labs:
(Pull in "Last 24 Hour" labs and additional labs from last 24 hrs)

Vitals:
(Pull in Vital Signs from last 24 hrs)

Vancomycin Concentration: *(Date & Time)*

Assessment:
(Based on appropriateness of concentration in regards to timing and previous doses assess whether goal concentration is achieved. If concentration was not appropriate discuss why.)

Recommendation:
(Considering patient's renal function, volume status, any special patient characteristics and reported concentrations, communicate recommendation for vancomycin dosing. Provide recommendation dosing and repeat vancomycin concentrations indicating date and time.)

Signature:
(Include name and contact number)

Patient: _____ **MRN: 20265** **FIN: 73440408**
Age: **63 years** Sex: **Male** DOB: **02/21/52**
Associated Diagnoses: **None**
Author: **Mihalevich, Robin L RPh**

General:
Patient is receiving _____ for _____ of _____. Today is day ___ of therapy. Goal vancomycin trough is ___mcg/mL.

Labs:
Last 24 Hours

Basic Metabolic Panel:	Hematology:
Sodium Lvl DH: ------	Hgb DH: 10.9 gm/dL (01/13/16)
Potassium Lvl DH: ------	Hgb A1c DH: ------
Phosphorus Lvl DH: ------	WBC DH: 5.4 10^3 (01/13/16)
Magnesium Lvl DH: 2.5 mg/dL (01/13/16)	Platelets: 237 10^3 (01/13/16)
BUN DH: ------	INR DH: ------
Creatinine DH: 1.43 mg/dL (01/13/16)	
Creatinine Clearance: ------	

Additional - Last 24 Hours

Blood Glucose, Capillary POC: 91 mg/dL (01/13/16)	Estimated Creatinine Clearance: 58.12 (01/13/16)	GFR African American: 64 (01/13/16)
GFR NonAfrican American: 53 (01/13/16)	Glucose Lvl: 84 mg/dL (01/12/16)	Glucose POC: 106 mg/dL (01/13/16)
Hct: 37.0 % (01/13/16)	MCH: 25.8 pg (01/13/16)	MCHC: 29.5 gm/dL (01/13/16)
MCV: 87.7 fL (01/13/16)	MPV: 9.7 fL (01/13/16)	RBC: 4.22 10^6 (01/13/16)
RDW: 20.5 % (01/13/16)	TSH: 0.903 mcIU/mL (01/12/16)	Vanco Tr: 16.20 ug/mL (01/12/16)

Vitals:

Vital Signs (last 24 hrs)	Last Charted
Temp Oral	36.5 DegC (JAN 13 07:00)
Heart Rate Peripheral	81 bpm (JAN 13 09:17)
Resp Rate	H 33br/min (JAN 13 07:00)
SBP	103 mmHg (JAN 13 07:00)
DBP	74 mmHg (JAN 13 07:00)
SpO2	97 % (JAN 13 09:17)
Weight	158 kg (JAN 13 08:41)

VANC Concentration:

Assessment:
Based on:

Recommendation:
Considering patient's renal function, volume status, and these reported concentrations, (plan change).

Recommend repeat vancomycin (repeat concentrations) concentration (time frame).

Discussed plan with provider_____, for questions contact

VANCOMYCIN

VANCOMYCIN PHARMACODYNAMICS OVERVIEW

- Concentration-independent bactericidal activity
- High inter-patient variability necessitates monitoring of serum concentrations
- Ideal pharmacodynamic target: $AUC_{0\text{-}24hrs}$:MIC ≥ 400

Study	Patients	Target	Result
Moise et al.	*S. aureus* PNA	AUC/MIC > 345	Clinical cure
		AUC/MIC > 866	Microbiological cure
Holmes et al.	MRSA bacteremia	AUC/MIC > 373	Clinical efficacy (reduced 30 day mortality)

*Karam CM et al. *Pharmacotherapy* 1999;19:257-66
*Moise-Broder PA et al. *Am J Health-Syst Pharm* 2000;57:S4-9
*Holmes NE et al. *Antimicrob Agents Chemother* 2013;57:1654-63

IMH VANCOMYCING DOSING RECOMMENDATIONS

- Choose appropriate **Vancomycin** goal trough concentration

Indication	Goal Trough Concentration (mcg/mL)
Skin and soft tissue infection, urinary tract infection	10-15
Bacteremia, endocarditis, meningitis, MRSA pneumonia, osteomyelitis, septic arthritis, pacemaker pocket infection, sternal wound infection, VAD infection, febrile neutropenia	15-20
Consider for meningitis	> 20

**All doses based on actual body weight and rounded to nearest 250mg*
**Maximum single dose is 2gm*

VANCOMYCIN LOADING DOSE

- Allows more rapid achievement of therapeutic concentrations, but not needed in all patients.
- Consider for: severe infections (goal trough of 15-20)

Target Trough Concentration	Recommended Loading Dose
15-20 mcg/mL	20 mg/kg

- Always use actual body weight
- Not affected by renal function
- Maximum dose= 2gm for most patients
  - **Special population: Obesity-** can give up to 3gm load in morbidly obese patients

VANCOMYCIN MAINTENANCE DOSE

- Select reasonable maintenance dose
  - 15mg/kg based on actual body weight
  - **Maximum dose of 2gm**

Empiric Vancomycin Maintenance Dose and Frequency						
Drug	Goal Trough Concentration	Maintenance Dose (Round to nearest 250 mg Maximum dose 2000mg)	Dosing Interval Based on Estimated CrCl (mL/min)			
			> 70	50 – 69	35 – 49	< 35 or Dialysis
Vancomycin	10 – 15 mcg/mL	15 mg/kg	q12h	q24h	q24h	Based on Concentration
	15 – 20 mcg/mL	15 mg/kg	q8h	q12h	q24h	Based on Concentration

VANCOMYCIN DOSING INTERVAL

- Based on $T_{1/2}$
  - Most important calculation:

$$T_{1/2}\ (\text{hrs.}) = \frac{0.693}{K_e\ (\text{hrs}^{-1})}$$

- Use closest interval that is longer than $T_{1/2}$
  - Ex: If $T_{1/2}$= 10 hours, choose q12h interval

- Intervals used at IMH
  - q8h
  - q12h
  - q24h
  - q36h
  - q48h

Interval should NEVER be shorter than $T_{1/2}$

OBESITY IN VANCOMYCIN DOSING

- Adipose tissue is ~30% water
  - Hydrophilic drugs (vanco) will distribute into adipose tissue
  - Increased Vd
- Obese patients have increased blood flow, increased cardiac output
  - Increased Vd and K_e
- **Dosing considerations:** Use actual body weight
  - Max single dose of 2g for maintenance doses
  - For **morbidly** obese patients:
    - May have to use more frequent intervals if subtherapeutic troughs
    - Frequent initial monitoring to ensure adequate concentrations

*Grace E. *J Antimicrob Chemother* 2012;67:1305-10
*Janson B et al. *Curr Opin Infect Dis* 2012;25:634-649

VANCOMYCIN TROUGH CONCENTRATIONS

- AUC:MIC not a clinically practical monitoring parameter
  - Requires multiple serum concentrations after a dose

- Trough concentration correlates with AUC:MIC
  - < 10 mg/L → resistance development
  - 15-20 mg/L → standard target for severe or complicated infections
    - Not based on clinical outcomes data
    - Trough concentration ≥15 mg/L correlates with AUC:MIC ≥ 400 for organism with MIC of 1
    - Higher doses increase exposure to certain tissues (i.e. lungs, CNS)

*Karam CM et al. *Pharmacotherapy* 1999;19:257-66
*Moise PA et al. *Antimicrob Agents Chemother* 2007;51:2582-6

WHEN TO MONITOR TROUGH CONCENTRATIONS

Is therapy continuing beyond 72 hours?	If no, or unsure, no need to monitor trough in most patients
New regimen/dose change	•Trough at steady state (prior to 4th dose acceptable in most patients) •Dosing interval≥48hrs prior to 3rd dose •No earlier than 30 min prior to dose
Acutely changing/ unstable renal function	Check trough immediately
Therapeutic trough (with stable renal function)	Troughs every 5-7 days

- Try to avoid troughs prior to 3rd dose
  - Can lead to inappropriate dose changes
- Once stable on regimen, monitor trough every 3-5 days
- Unstable renal function consider every 3 days
- Keep remaining duration of therapy in mind
  - Concentrations unnecessary close to end of therapy

HOW TO INTERPRET CONCENTRATIONS

- Verify concentration was drawn appropriately
- Trough ≥ to 30 mcg/mL, hold all further doses and order a random concentration
  - *Time random concentration based on clinical scenario- a good rule of thumb is to wait at least one dosing interval of current regimen, usually next day with am labs is fine*
- Trough > target, but < 30 mcg/mL:
  - If interval shorter than half-life → Lengthen interval
  - If interval is longer than half-life → Lower dose
  - *Remember, dosing is proportionate if you want a 50% lower concentration, you need to give 50% less drug*
- Trough < target, increase dose:
  - *Remember, dosing is proportionate if you want a 50% higher concentration, you need to give 50% more drug*

More frequent administrations often lead to accumulation!

VANCOMYCIN RANDOM CONCENTRATIONS

- **Random Concentrations**
  - May be necessary in the following situations: acute renal failure or steadily rising SCr, dosing the antibiotic by concentration, if patient is experiencing significant fluid status changes, and critically ill patients.
  - Generally ordered and drawn with AM labs. However situations may warrant specifically timed concentrations (e.g. 12 or 24 hours after a dose is administered).
  - If dosing by concentration, redose when concentration is $\leq$ 12-20 mcg/mL
  - Typical doses for redosing are 15-20mg/kg using total body weight (TBW)

OTHER LAB MONITORING

- **Serum Creatinine (SCr)**
  - Monitored at the initiation of therapy, and routinely during treatment. Typically, daily SCr is monitored for patients receiving treatment for confirmed infection until steady state is achieved and weekly thereafter.
  - In dialysis patients only monitor SCr with concentrations. Daily SCr is unnecessary since these patients have little to no renal function

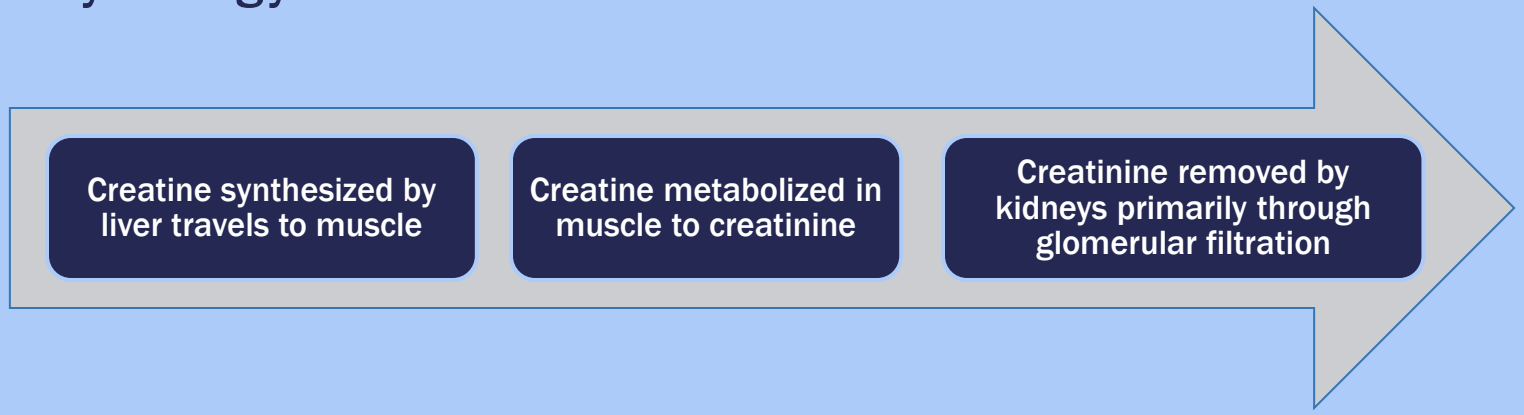
SPECIAL POPULATIONS

SPECIAL POPULATIONS

- **SCr does not reflect vancomycin clearance**
  - Amputees
  - Low muscle mass: cerebral palsy, muscular dystrophy, paraplegics, elderly/immobile, etc.
  - VAD patients/severe CHF
  - Critically ill/septic shock
  - DM
  - Cirrhosis
  - Acutely changing renal function
  - Cystic fibrosis
- **Altered Vd**
  - Burn patients
  - Critically ill/septic shock
  - Fluid overload
  - Severe CHF
  - Cirrhosis
  - ESRD

LOW SERUM CREATININE

- Physiology of creatinine



- Multiple reasons for low SCr leading to overestimation of clearance
  - **Low muscle mass** (elderly, paraplegia, cerebral palsy, muscular dystrophy, amputation, etc.)
  - **Liver dysfunction**
  - **ESRD** (tubular secretion of creatinine increases as GFR decreases)

LOW SERUM CREATININE DOSING CONSIDERATIONS

- Important to evaluate other markers of renal function
  - **Urine output, BUN**
- Keep in mind "normal" intervals based on age
  - Ex: 40 YO → q12h
    70 YO → q24h
- If any signs of renal dysfunction, consider dosing by concentration initially
  - SCr results that are "normal" in an average patient often indicate renal dysfunction in this population

ELDERLY

- Typically have low baseline SCr due to immobility

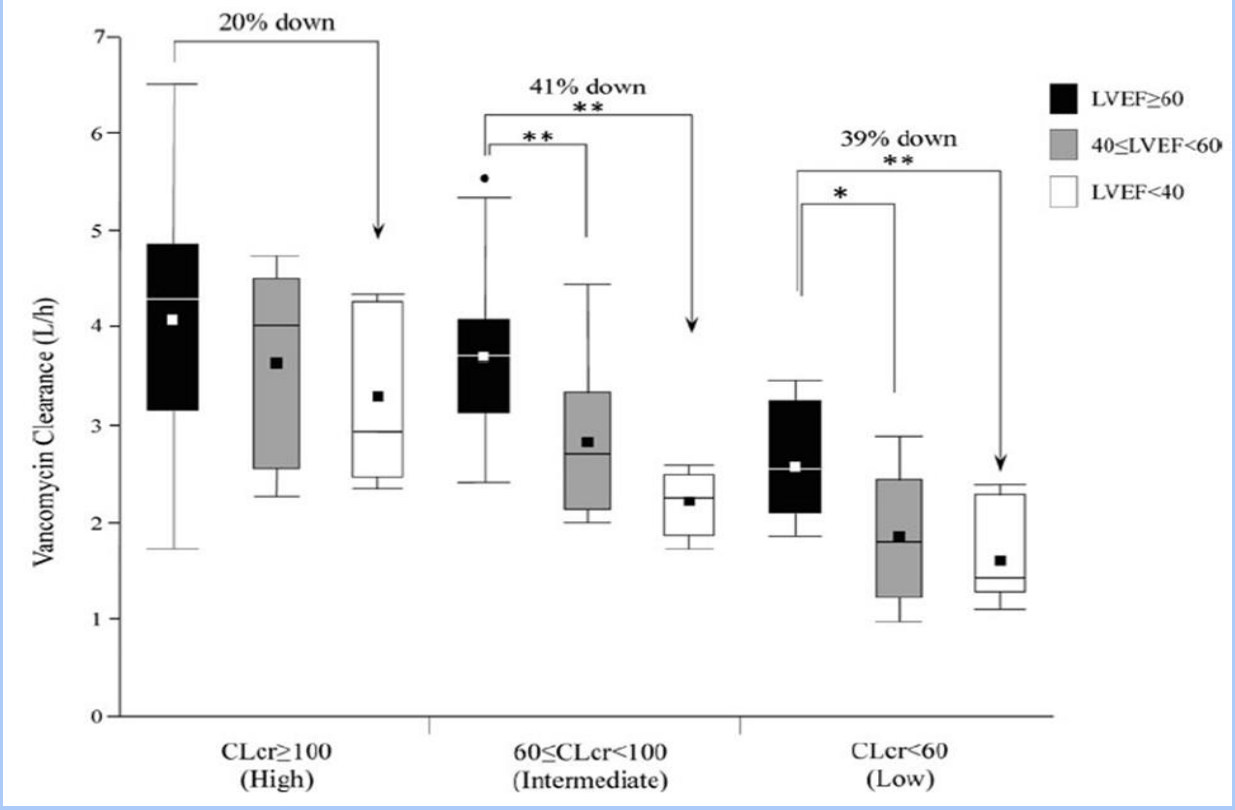
Design	PK analysis (n=269
Patients	Elderly patients (mean age 81 years)
Methods	Evaluated several methods of estimating renal function and compared to 24 hr. measured CrCl (MDRD, CKD-EPI, CG, CG w/SCr rounded to 1)
Results	▪ Cockroft-Gault equation most accurate predictor ▪ **Rounding SCr to 1 LESS accurate than not rounding**

- **Dosing considerations:**
  - Do not round SCr
  - Avoid very aggressive regimens (i.e. q8h intervals)

*Dowling TC et al. *Pharmacotherapy* 2013; 33:912-21

CHF

PK Analysis: Vancomycin Clearance in 101 CHF Patients



- Vancomycin clearance decreases linearly with cardiac output
- Calculated CrCl using Cockroft-Gault overestimates actual clearance in patients with low LVEF

*Shimamoto Y et al. *Eur J Clin Pharmacol* 2013;69:449-57

CRITICALLY ILL

- Significant alterations in the following:
  - Vd: Typically increased due to fluid resuscitation
  - Ke: Can be increased or decreased – highly variable vs. normal population
    - Augmented renal clearance: High cardiac output + low systemic vascular resistance
    - High rate of AKI
- SCr lags behind actual changes in renal function
  - Monitoring Urine Output is imperative
- **Dosing considerations:** Low threshold to dose by concentration initially due to high variability, high risk for poor outcomes if targets not reached

*Felton TW et al. *Diagn Microbiol Infect Dis* 2014; doi: 10.1016/j.diagmicrobio.2014.04.007
*Llopis-Salvia P et al. *J Clin Pharm Ther* 2006;31:447-54

BURN PATIENTS

- Increased clearance
  - Hypermetabolic state >48 hrs. after thermal injury
    - Increased tubular secretion and GFR
- Increased Vd due to fluid resuscitation and insensible losses
- **Dosing considerations:**
  - May need more aggressive regimens initially, but account for limited duration of hypermetabolic state

*Dolton M et al. *Burns* 2010;36:469-76
*Ellingsen M et al. *Burns* 2010;37:406-14

MENINGITIS

- Vancomycin CSF: serum concentration ratio
  - Inflamed meninges: 0.36-0.48
  - Uninflamed meninges: 0-0.18
- Clinical implications of CSF penetration
  - High trough concentration targets needed (~20 mg/L)
  - Vd increased when meninges inflamed
  - Vd decreases with decreasing inflammation
- **Dosing considerations:**
  - High trough targets initially but monitor for accumulation as inflammation dies down.

*Cooper GL et al. Vancomycin: a comprehensive review of 30 years clinical experience. San Diego: Park Row Publishers, 1986:23-38
*Albanese J et al. *Antimicrob Agents Chemother* 2000;44:1356-8

INTERMITTENT HEMODIALYSIS

- 3-4 hr. session using high-flux machine typically removes ~25-30% vancomycin serum concentration
- **Note:** 3-6 hr. redistribution phase after HD
  - Serum concentration falsely low during this period
- Load with standard loading dose: 20mg/kg (TBW)
- Order random concentration prior to each HD session
  - Example:
    - Intermittent HD Pt. with MRSA bacteremia. Pre-HD random concentration = 22 mg/L. Do you re-dose?
      - 22 x 0.7 = 15.4 mg/L
      - Post-HD concentration will be in re-dose range
      - For goal trough 15-20, we can generally re-dose when pre-HD concentration is 20-25 mg/mL

*Vandecasteele SJ et al. *Semin Dial* 2011;24:50-5

PERITONEAL DIALYSIS

- Clears vancomycin inefficiently
- Initial loading dose: 20mg/kg (TBW) x 1
- Repeat dose should be administered once concentrations are < 20mcg/mL
  - Generally drawn qHS prior to cycle
- Intra-peritoneal vancomycin is not recommended in patients with IV access

AMINOGLYCOSIDES

AMINOGLYCOSIDES

- Mechanism of Action
  - Inhibits bacterial protein synthesis by binding and interfering with the 30s subunit on the ribosome
- Bactericidal agents
- Concentration-dependent killing
- Post-antibiotic effect
- Spectrum
  - Gram negative bacteria
    - Including *Pseudomonas aeruginosa*
  - Gram positive activity
    - None appreciable when used alone
    - Used in combination with β-lactams for synergy

PK DRUG PROPERTIES

- Distribution
  - Hydrophilic agents
    - Goes where the fluid goes
  - Good penetration into bronchial and pleural tissues, pericardial tissue, interstitial fluid, urogenital and kidney tissues, burn eschar
  - Limited penetration into CSF, bone, tears, epithelial membrane, and adipose tissue
  - Volume of distribution
    - 0.25-0.3 L/kg X DW (kg)
    - 0.3 L/kg x DW (in ICU/ventilated patients)
    - 0.5 L/kg x DW (in burn patients)
    - (0.3 L/kg x DW) + Liters of extra fluid (in fluid overloaded patients)

AMINOGLYCOSIDES EXTENDED INTERVAL

- Extended interval dosing will be initiated for all patients when the physician writes for "Tobramycin/Gentamicin/Amikacin-Pharmacy to Dose"
- **Exclusion Criteria:**
  - Chronic renal insufficiency (CrCl < 20-30 mL/min
  - Acute renal failure (increase in SCr 30% above baseline)
  - Treatment of Gram (+) infections/synergy (endocarditis, meningitis, MSSA cellulitis)
  - ESRD on any form of renal replacement therapy
  - Pregnancy
  - Severe CHF patients/Cardiogenic shock
  - Liver failure with ascites
  - Burns covering > 20% of the total BSA
  - Surgical prophylaxis

AMINOGLYCOSIDES EXTENDED INTERVAL

- Determine Dosing Weight
  - Non-Obese Patients:
    - Use total body weight (TBW). Non-obese is defined as a TBW < 120% over ideal body weight (IBW)

      IBW (males) = 50 + (2.3 x height in inches > 60 inches)

      IBW (females) = 45 + (2.3 x height in inches > 60 inches)

  - Obese Patients:
    - Use adjusted body weight (ABW) in obese patients. Obese is defined as a TBW > 120% of IBW

      ABW (kg) = IBW + 0.4 (TBW - IBW)

AMINOGLYCOSIDES EXTENDED INTERVAL

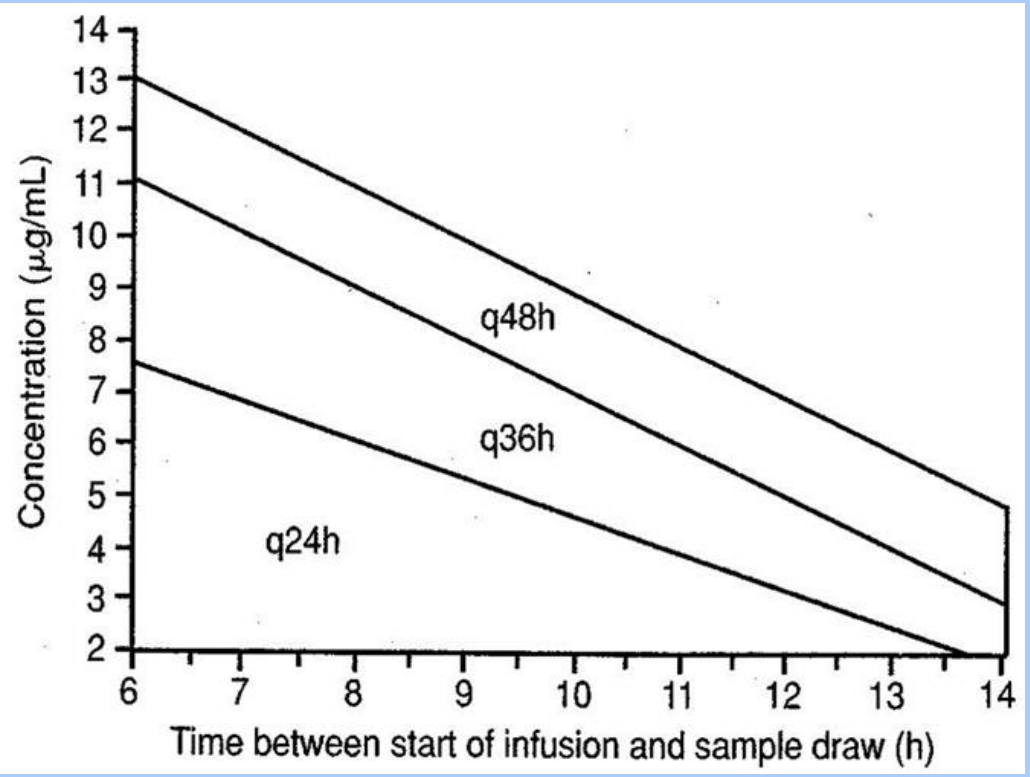
- Determine Dose
  - Gentamicin/Tobramycin:
    - 7mg/kg x DW (10mg/kg for cystic fibrosis)
  - Amikacin:
    - 15mg/kg x DW
- Determine Dosing Interval

CrCl (mL/mi)	Dosing Interval
>60	Q24h
40-59	Q36h OR use conventional dosing
20-39	Q48h OR use conventional dosing
<20	Not eligible, use conventional dosing

AMINOGLYCOSIDES EXTENDED INTERVAL - MONITORING

- **Random Concentrations**
  - Obtain **8-12 hours** after the start of the FIRST dose
  - Plot random concentration on the **Hartford Nomogram**
    - For amikacin, divide concentration by two and then plot on nomogram)
  - If concentration falls within an interval area = respective interval
  - If concentration falls on a line = extend to a longer dosing interval
  - If concentration falls above the 48 hour line = switch to traditional dosing

HARTFORD NOMOGRAM



Gentamicin/Tobramycin (7mg/kg/dose): plot on graph
Amikacin (15mg/kg/dose): divide concentration in half, then plot on graph
Plotting doses lower or higher than the above may over or underestimate clearance.

AMINOGLYCOSIDES EXTENDED INTERVAL - MONITORING

- **Trough Concentrations**
  - Once dosing interval has been determined, repeat concentrations will be monitored in the form of TROUGHS
  - Concentrations should be obtained no earlier than 30 minutes prior to the next dose
  - Goal Trough Concentrations
    - Gentamicin/Tobramycin <1 mcg/mL
    - Amikacin <4 mcg/mL
  - Extend dosing interval if trough is above goal or see Appendix A in protocol for PK based adjustments
  - Once stable on a dosing regimen, monitor trough every 5 to 7 days
  - If renal function is unstable consider checking trough every 3 days
- **Peak Concentrations**
  - NOT routinely done

AMINOGLYCOSIDES TRADITIONAL DOSING

- Traditional dosing protocol will be used for those patients who are excluded from the extended interval dosing protocol.
- Determine Dosing Weight and CrCl
- Determine Desired Concentration Based on Indication

Indication/ Site of Infection	Desired Concentrations (mcg/mL)			
	Gentamicin/Tobramycin		Amikacin	
	Peak	Trough	Peak	Trough
Uncomplicated UTI, synergy	3 - 5 mcg/mL	< 1 mcg/mL	15-20 mcg/mL	< 4 mcg/mL
Moderate gram (-), soft tissue infections, open fracture prophylaxis, pyelonephritis	6 – 8 mcg/mL	< 1 mcg/mL	20-35 mcg/mL	< 4 mcg/mL
Gram (-) sepsis, PNA, life-threatening infections	8 – 10 mcg/mL	< 2 mcg/mL	30-35 mcg/mL	< 8 mcg/mL

AMINOGLYCOSIDES TRADITIONAL DOSING

- **Select Appropriate Loading and Maintenance Doses Based on Estimated CrCl**

Drug	Goal Peak Concentration (mcg/mL)	Loading Dose*	Maintenance Dose	Dosing Interval Based on Estimated CrCl (mL/min)			
			CrCl > 80 mL/min	65 – 80	35 – 65	20 – 35	< 20 or dialysis
Gentamicin or Tobramycin	3 – 5	1 mg/kg	1 mg/kg q8h	q12h	q24h	q48h	Based on Concentration
	6 – 8	2 mg/kg	1.5 mg/kg q8h				
	8 – 10	2 – 3 mg/kg	2- 2.5 mg/kg q8h				
Amikacin	15 – 20	-	4 mg/kg q8h	q12h	q24h	q48h	Based on Concentration
	20 – 35	-	6 mg/kg q8h				
	30 – 35	-	10 mg/kg q8h				

**Loading dose only needed in life-threatening infections or in dialysis patient to achieve steady state levels more rapidly*

AMINOGLYCOSIDES TRADITIONAL DOSING

- **Trough/Peak Concentrations**
  - Obtain when the concentrations are at steady state (with the 4th or 5th dose)
  - Concentrations should be obtained no earlier than:
    - Troughs → 30 minutes prior to dose for
    - Peaks → 30 minutes after the end of the infusion
  - For dosing intervals ≥ 48 hours, obtain trough/peak with the 3rd dose or within 72 hours
  - Reorder new trough/peak concentrations after each change in dosage
  - Once stable on a dosing regimen, monitor every 5 to 7 days
  - If renal function is unstable consider checking every 3 days
- **Random Concentrations**
  - May be necessary in: acute renal failure or steadily rising SCr, dosing the antibiotic by concentration, if patient is experiencing significant fluid status changes, and critically ill patients.
    - Generally ordered with AM labs. Situations may warrant specifically timed concentrations (e.g. 12 or 24 hours after a dose is administered)

AMINOGLYCOSIDES INTERMITTENT HEMODIALYSIS

- Initial loading dose should be based on indication
- Obtain a peak concentration 30 minutes after the end of the first infusion
- Random concentration should be obtained prior to each dialysis session
- Repeat doses should be administered post-dialysis if pre-dialysis concentrations of tobramycin/gentamicin are < 2 mcg/mL or amikacin concentrations < 8 mcg/mL
  - Approximately 25 -30 % of pre-dialysis concentration is removed by hemodialysis

AMINOGLYCOSIDES PERITONEAL DIALYSIS

- Initial loading dose should be based on indication
- Obtain a peak concentration 30 minutes after the first infusion
- A trough concentration is recommended before the second dose
- Repeat doses should be administered once tobramycin/gentamicin concentrations are <2 mcg/mL or amikacin concentrations < 8 mcg/mL
- Intra-peritoneal aminoglycosides are not recommended in patients with IV access

AMINOGLYCOSIDES
DOSE AND FREQUENCY IN DIALYSIS

Drug	Goal Peak Concentration (mcg/mL)	Dose and Frequency in Dialysis Patients	
		Hemodialysis	Peritoneal Dialysis
Gentamicin or Tobramycin	3 – 5	1 mg/kg x 1	
	6 – 8	2 mg/kg x 1	
	8 – 10	2 – 3 mg/kg x 1	
Amikacin	15 – 20	4 mg/kg x 1	
	20 – 35	6 mg/kg x 1	
	30 – 35	10 mg/kg x1	