The Cambridge Health Alliance's Approach to Antimicrobial Stewardship

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Antimicrobial Stewardship Goals

- Purpose
  - Coordinate the formulation, implementation and assessment of antimicrobial policies
- Primary goal is to optimize clinical outcomes
  - Minimize unintended consequences
  - Ensure appropriate dosing
  - Eliminate redundant therapy
  - Facilitate targeted therapy
- Peripheral goal
  - Reduce healthcare costs


GUIDELINES

Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship

Clin Infect Dis 2007;44:159-77.

CHA Program Components

- Collaborative: ID, Pharmacy, Laboratory
- Formulary management
  - Evidence
  - Internal susceptibility data
  - Structured decision-making tools
  - Antibiotic order form (required)
  - Restriction policies
- Process and outcomes monitoring
  - Internal and external economic benchmarking
  - Drug usage evaluations
  - Antimicrobial resistance tracking

Multi-Attribute Utility Theory (MAUT)

- Specify variables:
  - Antimicrobials of interest
  - Microorganisms of interest
  - Relevant adverse drug reactions
  - Cost
- Create utility scores for variables (consensus)
- Collect data
- Calculate outcomes
- Validate and choose

Example: MAUT for CAP

		Attribute Utility Score				
Attribute / Factor	**Assigned Weight (%)**	**Levofloxacin**	**Moxifloxacin**	**Ceftriaxone + Azithromycin**	**Ceftriaxone + Doxycycline**	**Ampicillin / Sulbactam + Doxycycline**
Efficacy	**61**	**58.5**	**58.3**	**58.6**	**59.1**	**56.7**
S. pneumoniae	30	29.1	29.1	28.8	28.8	27.0
H. influenzae (B'ase -)	7	7.0	7.0	7.0	7.0	7.0
M. pneumoniae	4	4.0	4.0	4.0	4.0	4.0
C. pneumoniae	4	4.0	4.0	4.0	4.0	4.0
S. aureus (MSSA)	4	3.7	3.7	4.0	4.0	4.0
H. influenzae (B'ase +)	3	3.0	3.0	3.0	3.0	3.0
M. catarrhalis	3	3.0	3.0	3.0	3.0	3.0
Legionella	2	2.0	2.0	2.0	2.0	2.0
K. pneumoniae	2	1.8	1.6	1.8	1.8	1.6
S. aureus (MRSA)	1	0.0	0.0	0.0	0.5	0.5
E. coli	1	0.9	0.8	1.0	1.0	0.6

Example: MAUT for CAP (Cont'd)

Attribute / Factor	Assigned Weight (%)	Attribute Utility Score: Levofloxacin	Moxifloxacin	Ceftriaxone + Azithromycin	Ceftriaxone + Doxycycline	Ampicillin / Sulbactam + Doxycycline
Pharmacokinetics	**11**	**8.0**	**9.0**	**8.8**	**7.6**	**3.0**
Dosing interval / # doses	6	6.0	6.0	4.8	3.6	0.0
Drug interactions	4	2.0	2.0	3.0	3.0	3.0
Renal dosing adjustment	1	0.0	1.0	1.0	1.0	0.0
Adverse Drug Reactions	**14**	**9.0**	**8.8**	**11.0**	**10.8**	**11.0**
Cardiovascular	4	3.0	3.0	4.0	3.0	4.0
C. difficile diarrhea	3	1.5	1.5	2.3	2.3	1.5
Central nervous system	2	1.0	1.0	1.5	1.5	2.0
Glucose dysregulation	2	1.5	1.5	2.0	2.0	2.0
Antibiotic associated diarrhea	1	0.5	0.5	0.5	0.5	0.5
Hypersensitivity	1	0.8	0.8	0.8	0.8	0.5
Phlebitis	1	0.8	0.5	0.0	0.8	0.5
Miscellaneous	**14**	**10.5**	**14.0**	**7.0**	**10.5**	**7.0**
Daily cost of drug therapy	14	10.5	14.0	7.0	10.5	7.0
TOTAL UTILITY SCORES	**100**	**86.0**	**90.0**	**85.4**	**88.0**	**77.7**

Clinical Pharmacist Role at CHA

- Pharmacist-managed antimicrobial protocols (intravenous vancomycin)
- Antimicrobial dose optimization and streamlining (empiric → definitive therapy)
- Detection and reduction in medication errors related to antimicrobial use
- Administration of antimicrobial restrictions
- Feedback to physicians

Elements of CHA Vancomycin Protocol

- Approved by Medical Executive Committee
- Vancomycin “per pharmacy protocol”
- Clinical pharmacist will:
  - Confirm appropriateness of use
  - Initiate vancomycin dose/frequency/infusion rate
  - Order serum concentration and BUN/Scr, if necessary
  - Adjust dose &/or frequency
  - Hold vancomycin dose, if necessary
  - Document all activities in patient-care record
  - Regular communication with the health-care team

Antimicrobial Streamlining

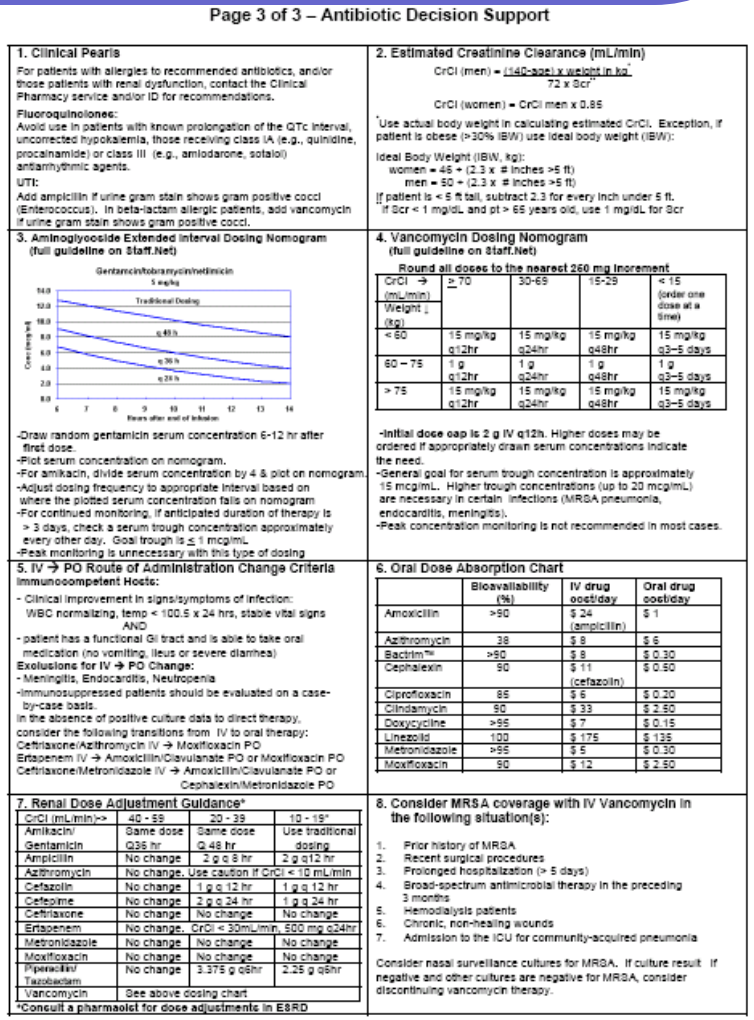
- Considerations for IV to oral switch:
  - Clinical improvement in signs/symptoms of infection (WBC normalizing, afebrile, stable vital signs)
  - Functional GI tract (no vomiting, ileus, severe diarrhea)
- Exceptions to Oral Transition Therapy (or at least think twice before doing it…)
  - Deep-seated infections – acute osteomyelitis, septic arthritis, endocarditis, meningitis
  - Septic patients with hemodynamic instability
  - Necrotizing soft tissue infections
  - Severe infections in immunocompromised patients

Elements of the Antibiotic Order Form

- Mandatory
- Page 1 – Standard Empiric Therapy
- Page 2 – Customized Therapy
  - Definitive therapy (culture-driven)
  - Oral therapy
  - Empiric therapy for a condition not listed on Page 1
  - Any therapy (empiric or definitive) requiring renal dose adjustment
  - Patients with allergies to suggested standard empiric therapy
  - Antibiotics / infections requiring Infectious Disease approval
    - Treatment of any healthcare-associated pneumonia
    - Use of non-formulary antibiotics
    - Use of restricted antimicrobials: tigecycline, linezolid, oral vancomycin, intravenous fluconazole

Decision Support

- Clinical pearls
- Aminoglycoside dosing nomogram
- Transition therapy
- Renal dosing adjustment
- Creatinine clearance
- Vancomycin dosing nomogram
- Oral drug absorption info
- Risks for MRSA



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1. Clinical Pearls

For patients with allergies to recommended antibiotics, and/or those patients with renal dysfunction, contact the Clinical Pharmacy service and/or ID for recommendations.

Fluoroquinolones:
Avoid use in patients with known prolongation of the QTc interval, uncorrected hypokalemia, those receiving class IA (e.g., quinidine, procainamide) or class III (e.g., amiodarone, sotalol) antiarrhythmic agents.

UTI:
Add ampicillin if urine gram stain shows gram positive cocci (Enterococcus). In beta-lactam allergic patients, add vancomycin if urine gram stain shows gram positive cocci.

2. Estimated Creatinine Clearance (mL/min)

$$\text{CrCl (men)} = \frac{(140 - \text{age}) \times \text{weight in kg}^*}{72 \times \text{Scr}}$$

CrCl (women) = CrCl men x 0.85

*Use actual body weight in calculating estimated CrCl. Exception, if patient is obese (>30% IBW) use ideal body weight (IBW):

Ideal Body Weight (IBW, kg):
women = 46 + (2.3 x # inches >5 ft)
men = 50 + (2.3 x # inches >5 ft)

If patient is < 5 ft tall, subtract 2.3 for every inch under 5 ft.
If Scr < 1 mg/dL and pt > 65 years old, use 1 mg/dL for Scr

3. Aminoglycoside Extended Interval Dosing Nomogram (full guideline on Staff.Net)

-Draw random gentamicin serum concentration 6-12 hr after first dose.
-Plot serum concentration on nomogram.
-For amikacin, divide serum concentration by 4 & plot on nomogram.
-Adjust dosing frequency to appropriate interval based on where the plotted serum concentration falls on nomogram
-For continued monitoring, if anticipated duration of therapy is > 3 days, check a serum trough concentration approximately every other day. Goal trough is ≤ 1 mcg/mL
-Peak monitoring is unnecessary with this type of dosing

4. Vancomycin Dosing Nomogram (full guideline on Staff.Net)

Round all doses to the nearest 250 mg increment

CrCl → (mL/min) / Weight ↓ (kg)	≥ 70	30-69	15-29	< 15 (order one dose at a time)
< 60	15 mg/kg q12hr	15 mg/kg q24hr	15 mg/kg q48hr	15 mg/kg q3–5 days
60 – 75	1 g q12hr	1 g q24hr	1 g q48hr	1 g q3–5 days
> 75	15 mg/kg q12hr	15 mg/kg q24hr	15 mg/kg q48hr	15 mg/kg q3–5 days

-Initial dose cap is 2 g IV q12h. Higher doses may be ordered if appropriately drawn serum concentrations indicate the need.
-General goal for serum trough concentration is approximately 15 mcg/mL. Higher trough concentrations (up to 20 mcg/mL) are necessary in certain infections (MRSA pneumonia, endocarditis, meningitis).
-Peak concentration monitoring is not recommended in most cases.

5. IV → PO Route of Administration Change Criteria

Immunocompetent Hosts:
- Clinical improvement in signs/symptoms of infection: WBC normalizing, temp < 100.5 x 24 hrs, stable vital signs AND
- patient has a functional GI tract and is able to take oral medication (no vomiting, ileus or severe diarrhea)

Exclusions for IV → PO Change:
- Meningitis, Endocarditis, Neutropenia
-Immunosuppressed patients should be evaluated on a case-by-case basis.

In the absence of positive culture data to direct therapy, consider the following transitions from IV to oral therapy:
Ceftriaxone/Azithromycin IV → Moxifloxacin PO
Ertapenem IV → Amoxicillin/Clavulanate PO or Moxifloxacin PO
Ceftriaxone/Metronidazole IV → Amoxicillin/Clavulanate PO or Cephalexin/Metronidazole PO

6. Oral Dose Absorption Chart

	Bioavailability (%)	IV drug cost/day	Oral drug cost/day
Amoxicillin	>90	$ 24 (ampicillin)	$ 1
Azithromycin	38	$ 8	$ 6
Bactrim™	>90	$ 8	$ 0.30
Cephalexin	90	$ 11 (cefazolin)	$ 0.50
Ciprofloxacin	85	$ 6	$ 0.20
Clindamycin	90	$ 33	$ 2.50
Doxycycline	>95	$ 7	$ 0.15
Linezolid	100	$ 175	$ 135
Metronidazole	>95	$ 5	$ 0.30
Moxifloxacin	90	$ 12	$ 2.50

7. Renal Dose Adjustment Guidance*

CrCl (mL/min)>>	40 - 59	20 - 39	10 - 19*
Amikacin/ Gentamicin	Same dose Q 36 hr	Same dose Q 48 hr	Use traditional dosing
Ampicillin	No change	2 g q 8 hr	2 g q12 hr
Azithromycin	No change. Use caution if CrCl < 10 mL/min		
Cefazolin	No change	1 g q 12 hr	1 g q 12 hr
Cefepime	No change	2 g q 24 hr	1 g q 24 hr
Ceftriaxone	No change	No change	No change
Ertapenem	No change. CrCl < 30mL/min, 500 mg q24hr		
Metronidazole	No change	No change	No change
Moxifloxacin	No change	No change	No change
Piperacillin/ Tazobactam	No change	3.375 g q6hr	2.25 g q6hr
Vancomycin	See above dosing chart		

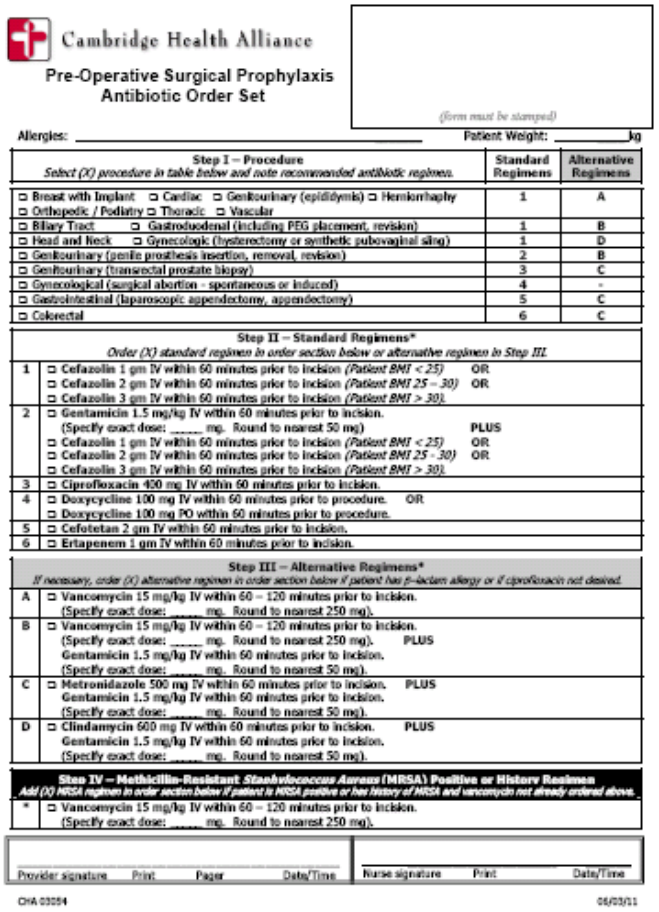
*Consult a pharmacist for dose adjustments in ESRD

8. Consider MRSA coverage with IV Vancomycin in the following situation(s):

1. Prior history of MRSA
2. Recent surgical procedures
3. Prolonged hospitalization (> 5 days)
4. Broad-spectrum antimicrobial therapy in the preceding 3 months
5. Hemodialysis patients
6. Chronic, non-healing wounds
7. Admission to the ICU for community-acquired pneumonia

Consider nasal surveillance cultures for MRSA. If culture result if negative and other cultures are negative for MRSA, consider discontinuing vancomycin therapy.

Surgical Prophylaxis Order Set



Cambridge Health Alliance

Pre-Operative Surgical Prophylaxis Antibiotic Order Set

(form must be stamped)

Allergies: _____ Patient Weight: _____kg

Step I – Procedure *Select (X) procedure in table below and note recommended antibiotic regimen.*	Standard Regimens	Alternative Regimens
☐ Breast with Implant ☐ Cardiac ☐ Genitourinary (epididymis) ☐ Herniorrhaphy ☐ Orthopedic / Podiatry ☐ Thoracic ☐ Vascular	1	A
☐ Biliary Tract ☐ Gastroduodenal (including PEG placement, revision)	1	B
☐ Head and Neck ☐ Gynecologic (hysterectomy or synthetic pubovaginal sling)	1	D
☐ Genitourinary (penile prosthesis insertion, removal, revision)	2	B
☐ Genitourinary (transrectal prostate biopsy)	3	C
☐ Gynecological (surgical abortion - spontaneous or induced)	4	-
☐ Gastrointestinal (laparoscopic appendectomy, appendectomy)	5	C
☐ Colorectal	6	C

Step II – Standard Regimens* *Order (X) standard regimen in order section below or alternative regimen in Step III.*	
1	☐ Cefazolin 1 gm IV within 60 minutes prior to incision *(Patient BMI < 25)* OR ☐ Cefazolin 2 gm IV within 60 minutes prior to incision *(Patient BMI 25 – 30)* OR ☐ Cefazolin 3 gm IV within 60 minutes prior to incision *(Patient BMI > 30).*
2	☐ Gentamicin 1.5 mg/kg IV within 60 minutes prior to incision. (Specify exact dose: _____ mg. Round to nearest 50 mg) PLUS ☐ Cefazolin 1 gm IV within 60 minutes prior to incision *(Patient BMI < 25)* OR ☐ Cefazolin 2 gm IV within 60 minutes prior to incision *(Patient BMI 25 - 30)* OR ☐ Cefazolin 3 gm IV within 60 minutes prior to incision *(Patient BMI > 30).*
3	☐ Ciprofloxacin 400 mg IV within 60 minutes prior to incision.
4	☐ Doxycycline 100 mg IV within 60 minutes prior to procedure. OR ☐ Doxycycline 100 mg PO within 60 minutes prior to procedure.
5	☐ Cefotetan 2 gm IV within 60 minutes prior to incision.
6	☐ Ertapenem 1 gm IV within 60 minutes prior to incision.

Step III – Alternative Regimens* *If necessary, order (X) alternative regimen in order section below if patient has β-lactam allergy or if ciprofloxacin not desired.*	
A	☐ Vancomycin 15 mg/kg IV within 60 – 120 minutes prior to incision. (Specify exact dose: _____ mg. Round to nearest 250 mg).
B	☐ Vancomycin 15 mg/kg IV within 60 – 120 minutes prior to incision. (Specify exact dose: _____ mg. Round to nearest 250 mg). PLUS Gentamicin 1.5 mg/kg IV within 60 minutes prior to incision. (Specify exact dose: _____ mg. Round to nearest 50 mg).
C	☐ Metronidazole 500 mg IV within 60 minutes prior to incision. PLUS Gentamicin 1.5 mg/kg IV within 60 minutes prior to incision. (Specify exact dose: _____ mg. Round to nearest 50 mg).
D	☐ Clindamycin 600 mg IV within 60 minutes prior to incision. PLUS Gentamicin 1.5 mg/kg IV within 60 minutes prior to incision. (Specify exact dose: _____ mg. Round to nearest 50 mg).

Step IV – Methicillin-Resistant *Staphylococcus Aureus* (MRSA) Positive or History Regimen *Add (X) MRSA regimen in order section below if patient is MRSA positive or has history of MRSA and vancomycin not already ordered above.*	
*	☐ Vancomycin 15 mg/kg IV within 60 – 120 minutes prior to incision. (Specify exact dose: _____ mg. Round to nearest 250 mg).

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Nurse signature Print Date/Time

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Questions / Answers