Integrated Activities and Tools for Antimicrobial Stewardship

ANTIMICROBIAL STEWARDSHIP: NEPAL GUIDELINES

Rajesh Dhoj Joshi, MD

Kathmandu Model Hospital

Presentation Outline

1. Basic Overview
2. Empiric Antibiotic Therapy
3. Stewardship Tips
4. Duration of Therapy
5. Prophylaxis Pearls
6. Transition to Oral Therapy
7. Renal Dosing

What is a Guideline?

- Created as statements and recommendations with the intent to **guide decisions** in order to optimize patient care
  - Based on review of evidence

- Intended to fit the majority of patients
  - **Individualization** of each patient should still be addressed

Purpose of Guidelines

- Improve patient outcome & quality of care
- Reduce inappropriate variation on practice
- Encourage proven treatments
- Educate providers
- Improve efficiency of healthcare

Empiric Antibiotic Therapy

- Used when culture results are **not available**
- Based on the **site of infection** and **organism** most likely to colonize that site
- **Individualize**:
  - Must also look at prior knowledge of bacteria known to colonize the patient, and the likelihood of drug resistance
- Use the local bacterial resistance patterns/ antibiograms available in the hospital

De-escalation

- Evaluate for the possibility of changing antibiotics when new data becomes available
- Look to de-escalate from broad spectrum to narrow spectrum
- Take away any unnecessary components of the antibiotic regimen
- Discontinue antibiotics if the patient does not appear to have an infection
- Convert from IV to PO when possible

Duration of Therapy

- Deleterious effects of prolonged courses
  - Adverse reactions
  - Adherence issues
  - Selection of resistant organisms
  - High cost
- Attempt to use the **shortest effective duration**
- Individualize duration based on clinical, laboratory, and radiologic findings of response to treatment

Colonization

- Do **not** treat colonization!
- Positive culture in absence of infectious symptoms
  - **Example**: bacteria or white cells in the urine with no symptoms (asymptomatic bacteriuria) should not be treated
- Common populations for colonization
  - Indwelling urinary catheter
  - Endotracheal tubes in mechanically ventilated patients
  - Colonization of chronic wounds

EMPIRIC ANTIBIOTIC THERAPY

Intra-abdominal infection – community acquired

Suspected Pathogens	Empiric Therapy	Note
Enterobacteriaceae, Bacteroides sp., Enterococcus, Streptococcus Consider fungi if recent course of antibiotics	Preferred: Ceftriaxone + Metronidazole Alternative: Pip/tazobactam • Cefepime + Metronidazole +/- gentamicin • Imipenem IV Oral options for outpatient therapy: Ofloxacin + Metronidazole • Moxifloxacin PO	E.g. cholecystitis, cholangitis, diverticulitis, abscess 1. **NOTE**: pancreatitis without necrosis does not require antibiotics 2. **NOTE**: Add gentamicin if MDRO suspected or identified

COPD Exacerbation (inpatient)

Suspected Pathogens	Empiric Therapy	Note
H. influenzae, *S. pneumoniae*, *M. Catarrhalis* Respiratory viruses are most common	Preferred: • Azithromycin • Doxycycline	Use antibiotics when: 1. Increased sputum volume and/or purulence OR 2. Acute respiratory failure requiring ICU admission

Gastroenteritis

Suspected Pathogens	Empiric Therapy	Note
Salmonella spp *Shigella spp* *Campylobacter spp*	Preferred: • Ciprofloxacin • Ofloxacin • Trimethoprim/ Sulfamethoxazole • Alternative: Azithromycin	1. *Salmonella* and *Campylobacter:* treat if protracted or comorbidities 2. *Shigella:* always treat **Duration varies according to antibiotic used

Meningitis

Suspected Pathogens	Empiric Therapy	Note
S. pneumoniae, *N. meningitides*, *Listeria monocytogenes*	Ceftriaxone (+/-Vancomycin) +/- Ampicillin (if risk factors for Listeria spp. present)	1. Risk factors for *Listeria* spp.: EtOH abuse, age >50, pregnancy 2. TB Meningitis: Anti-tuberculosis medicine (non-IV therapy)

Pneumonia, community acquired Inpatient

Suspected Pathogens	Empiric Therapy	Note
S. pneumoniae *H. influenza* *Mycoplasma sp.* *Chlamydophila sp.* *Legionella sp.*	• Ceftriaxone + Clarithromycin • Amox/clav • Moxifloxacin	5 days

Pneumonia, community acquired Outpatient

Suspected Pathogens	Empiric Therapy	Note
S. pneumoniae *H. influenza* *Mycoplasma sp.* *Chlamydophila sp.* *Legionella sp.*	• 1st - Amoxicillin OR phenoxymethylpenicillin • 2nd - Amox/clav OR doxycycline	5 days

Pneumonia, MDR Risk, HAP or VAP

Suspected Pathogens	Empiric Therapy	Note
Enterobacteriaceae *P. aeruginosa,* *A. baumannii*	• Cefepime +/- Vancomycin OR Linezolid • Pip-tazo + Gentamicin +/- Vanco OR Linezolid • Imipenem/Cilistatin or Meropenem +/- Vanco OR Linezolid	If suspect *Acinetobacter*: Colistin +/- Tigecycline Add gentamicin or amikacin in patients with severe sepsis or septic shock

Skin and skin structure infections: Cellulitis

Suspected Pathogens	Empiric Therapy	
Staphylococci, Streptococci	Preferred PO: • Cloxacillin • Flucloxacillin • Cephalexin • Cefadroxil Preferred IV if no MRSA history: • Cefazolin • Cloxacillin • Flucloxacillin	Purulent cellulitis OR After failure of IV beta-lactam therapy OR MRSA: Vancomycin OR Linezolid

Skin and skin structure infections: Abscess

Suspected Pathogens	Empiric Therapy	
Staphylococci, Streptococci	Surgical consultation for drainage • Cefazolin • Amoxiclav • Flucloxacillin	If failure of IV beta-lactam therapy OR MRSA: Vancomycin OR Linezolid

SSTI: Polymicrobial (burns, open wounds)

Suspected Pathogens	Empiric Therapy	
Staphylococci, *Streptococci*, Enterobacteriaceae	Cefepime + metronidazole +/- Gentamicin +/- Vancomycin OR Linezolid Pip-tazo +/- Gentamicin +/- Vanco OR Linezolid	If suspect *Acinetobacter*: Colistin +/- Tigecycline Add gentamicin or amikacin in patients with severe sepsis or septic shock

Urinary tract infection uncomplicated cystitis

Suspected Pathogens	Empiric Therapy	
Enterobacteriaceae	Preferred: • Nitrofurantoin (ONLY for CrCl > 40 to 60 mL/min or age < 65 years) • Trimethoprim-Sulfamethoxazole	Pregnant women ONLY: Cefixime

Urinary tract infection Complicated/ Pyelonephritis

Suspected Pathogens	Empiric Therapy	
Enterobacteriaceae	IV Preferred: • Ceftriaxone or Cefotaxime • Cefepime PO options: • Ofloxacin • Cefixime for Pregnant women ONLY	Add gentamicin or amikacin in patients with suspected Pseudomonas spp. and severe sepsis or septic shock. Stop after 3 day

STEWARDSHIP TIPS

Antibiotics on reserve

- This group of antibiotics was created by WHO in 2017.
- They are recommended to be used as "last resort" options when alternative options have failed.
- The aim is to **preserve** the effectiveness of these antibiotics.

Aztreonam	Fosfomycin (IV)
Cefepime	Linezolid
Daptomycin	Tigecycline
Polymixins (polymyxin B, colistin)	

Useful Stewardship Tips

- Always attempt to get bacterial **cultures**
- Stay up to date with your hospital's antibiogram
- **Avoid** empiric quinolone for most infections due to high resistance rates
- **Avoid** using duplicate antibiotics that cover the same organism unnecessarily (e.g. carbapenems or pip-tazo with metronidazole, which both retain anaerobic bacteria coverage)

Useful Stewardship Tips

- Always **de-escalate** to the narrowest antibiotic therapy possible when susceptibility results are available
- Continue to assess if the patient is truly infected, and treat only for the **minimum duration necessary** to cure the patient from infection
- Utilize **oral** agents whenever possible to prevent catheter-associated infections
- **Avoid** treating asymptomatic bacteriuria

Definitive Antibiotic Therapy

- De-escalate based on culture results
- Narrow therapy to decrease side effects and reserve broad spectrum antibiotics
- IV to PO

DURATION OF THERAPY

Remember: treating infections longer is not always better!

Suggested Duration of Antimicrobial Therapy

Diagnosis	Duration of Therapy
Intra-abdominal Infection, community-acquired (Cholecystitis, cholangitis, diverticulitis)	5 days with adequate source control 5-7d ruptured

Diagnosis	Duration of Antimicrobial Therapy	Key References
Asymptomatic bacteriuria (ASB)	**o days!** • **ASB treatment is harmful for most patients** • **Treatment is only routinely indicated in patients who are pregnant or undergoing a urologic procedure**	**Infectious Diseases Society of America Guidelines**

Diagnosis	Duration of Antimicrobial Therapy	Key References
Candidemia	**If no ocular involvement or other metastatic complications:** • *Non-neutropenic:* 14 days from first negative blood culture • *Neutropenic:* minimum of 14 days from first negative blood culture and resolution of neutropenia and symptoms **If ocular involvement:** • 4 to 6 weeks	**Infectious Diseases Society of America Guidelines**

Diagnosis	Duration of Antimicrobial Therapy	Key References
COPD exacerbation	5 days According to the GOLD guidelines, antibiotics are indicated for patients with increased sputum purulence PLUS increased dyspnea and/or sputum volume. Antibiotics are also indicated if COPD exacerbation requires mechanical ventilation.	GOLD Guidelines

Diagnosis	Duration of Antimicrobial Therapy	Key References
Meningitis, community-acquired	**N. meningitidis:** • 5-7 days **S. pneumoniae:** • 10 to 14 days **L. monocytogenes:** • ≥ 21 days neonate **Pathogen not identified:** • 10 days	**Infectious Diseases Society of America Guidelines**

Diagnosis	Duration of Antimicrobial Therapy	Key References
Pneumonia, community acquired	**Prompt clinical response** • 5 days **Delayed clinical response** • 7 to 10 days Patients should be: **afebrile** for at least 48-72 hours and have **no more than one** CAP associated sign of clinical instability before discontinuing antibiotics.	**Infectious Diseases Society of America Guidelines**

Diagnosis	Duration of Antimicrobial Therapy	Key References
Pneumonia, hospital-acquired, ventilator-associated	**If empiric therapy was active and prompt clinical response:** • 7 days	**Infectious Diseases Society of America/ American Thoracic Society Guidelines**

Diagnosis	Duration of Antimicrobial Therapy	Key References
Skin and skin structure, cellulitis	**If prompt clinical response:** • 5-7 days **If delayed clinical response or during a neutropenic fever episode** • 7 to 14 days	**Infectious Diseases Society of America Guidelines**

Diagnosis	Duration of Antimicrobial Therapy	Key References
Urinary tract infection, uncomplicated cystitis **(Uncomplicated: young, female patients with normal genitourinary anatomy)**	**3 days:** • Sulfamethoxazole/trimethoprim or urinary quinolone **5 days:** • Nitrofurantoin **7 days:** • Beta-lactams	**Infectious Diseases Society of America**

Diagnosis	Duration of Antimicrobial Therapy	Key References
Urinary tract infection, pyelonephritis or complicated infection (including bacteremic pyelonephritis)	7 days	Infectious Diseases Society of America Guidelines

PROPHYLAXIS PEARLS

Antibiotic Prophylaxis

Condition	Empiric Regimen	Duration of Therapy
Chronic wound treatment	None	None
Burn treatment	None	None
Pre-operation treatment (if infection suspected)	Ceftriaxone (or other third-gen cephalosporin)	1-3 doses
Post-operation treatment (if infection suspected)	Ceftriaxone (or other third-gen cephalosporin)	1-3 doses

TRANSITION TO ORAL THERAPY

Intravenous to Oral Dose Conversion

For an intravenous to oral conversion, the following criteria must be met:

- **Inclusion Criteria:**
  - Patient is admitted to a non-intensive care unit (ICU)/general practice unit (GPU)
  - Patient has received and is tolerating at least 1 dose of a medication administered enterally or is tolerating an enteral diet
  - Patient has received the medication to be converted intravenously for at least 24 hours
  - Afebrile (T <38°C, 100.4°F) for at least 24 hours
  - Resolving/normalizing WBC (unless on oral or injectable steroids)

Intravenous to Oral Dose Conversion

- **Exclusion Criteria:**
  - Nonfunctioning gastrointestinal tract
    - Gastric obstruction or ileus
    - Persistent nausea and vomiting
  - Strict NPO (for a procedure or other medical reason)
  - Patients receiving treatment for an active GI bleed
  - Neutropenia (ANC <1000)
  - Endocarditis
  - Meningitis or brain abscess
  - MRSA bacteremia
  - Feeding tubes with intestinal access only (applies to fluoroquinolones only)
    - Ex. J-port, J-tube, PEJ (percutaneous endoscopic jejunostomy) tube or any feeding tube accessing the small bowel

Intravenous to Oral Dose Conversion

IV Drug Order	Bioavailability	Oral Conversion
Azithromycin 250-500 mg IV daily	< 50%	Azithromycin 250-500 mg PO daily Convert to identical dose orally
Clindamycin 600 mg IV q8h	~90%	Clindamycin 300 mg PO q6h
Clindamycin 900 mg IV q8h	~90%	Clindamycin 450 mg PO q6h
Ciprofloxacin 400 mg IV	60 – 80%	Ciprofloxacin 500-750 mg PO - Use 750 mg for administration via gastric-access feeding tube Schedule dose 4 hours before or 8 hours after medications that chelate with fluoroquinolones, including antacids, calcium, iron, magnesium, multivitamins, meals, supplements and tube feeds, didanosine, and sucralfate. Do not administer through intestinal access feeding tubes

RENAL DOSING

Antibiotic Renal Dosing

- How are antibiotics usually dosed?

- **Cockcroft-Gault Creatinine Clearance Equation**
- **CrCL = $\frac{(140 - \text{Age}) \times \text{weight}}{(72 \times \text{SCr})} \times 0.85$ (if female)**

Antibiotic Renal Dosing - Amoxicillin

Creatinine Clearance (mL/minute)	Standard Regimen	Community-acquired pneumonia (in combination with a macrolide)
> 30	500 mg PO every 8 hours OR 875 mg PO every 12 hours	1000 mg PO every 8 hours
10 to 30	500 mg PO every 12 hours	1000 mg PO every 12 hours
< 10	500 mg PO every 24 hours	500 mg PO every 24 hours
Hemodialysis	500 mg PO every 24 hours, schedule after HD on HD days	500 mg PO every 24 hours, schedule after HD on HD days

Guidelines Summary

- Important to avoid variance in prescribing
- Help to standardize therapy
- Avoid unneeded antibiotic use
- Improved patient outcomes

THANK YOU!