Introduction to antimicrobial stewardship and Principles of Antimicrobial prescribing

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Emergence of Antimicrobial Resistance

- Resistant Bacteria
- Susceptible Bacteria
- Resistance Gene Transfer
- Mutations
- New Resistant Bacteria
Selection of Antimicrobial-resistant Bacteria

Resistant Strains
Rare

Antimicrobial Exposure

Resistant Strains
Dominant
Antimicrobial Stewardship

Bacteria are generous they give each other gifts of resistance elements and humans too
Implementing an Antibiotic Stewardship Program:
Guidelines by the Infectious Diseases Society of America
and the Society for Healthcare Epidemiology of America
What is antimicrobial stewardship?

- Coordinated interventions designed to improve and measure the **appropriate use of antibiotics by**
- Promoting the **selection of the optimal antibiotic, correct dose, duration and route of administration**
- Leading to improved patient outcomes and decreased adverse events – *C. difficile* infections and AMR rates

- Increasing resistance with a dry antibiotic pipeline
- In 2010 WHO recognized antimicrobial resistance as one in top three threats to human health
- Single center studies, show that up to 1/3 of antimicrobial use in acute care settings is inappropriate
Principles of antimicrobial stewardship

• Step 1: Make a diagnosis using multiple data points (Treat patients not blood tests) AND Send confirmatory tests – cultures etc........

• Step 2: Limit empiric antibiotic therapy to life threatening situations

• Step 3: Know the local antibiotic resistance patterns

• Step 4: Use the correct choice, dose and route of antibiotic (Pk-Pd parameters of antibiotic prescribed should be known)

• Step 5: De-escalate once diagnosis and antibiotic susceptibility is known
Start smart and focus

**Start Smart**

- Do not start antibiotics in the absence of evidence of bacterial infection
  - Take history of relevant allergies
  - Initiate prompt effective antibiotic treatment within one hour of diagnosis (or as soon as possible) in patients with life threatening infections
  - Comply with local prescribing guidance
  - Document clinical indication and dose on drug chart and clinical notes
  - Include review/stop date or duration
  - Ensure relevant microbiological specimens taken

**Clinical review & decision** at 48 hours

- Clinical review check microbiology, make and document decision*

  1. STOP
  2. IV/oral switch
  3. Change: to narrow spectrum agent
  4. Continue and review after 4 hours
  5. OPAT**

**DOCUMENT DECISION**

- Antimicrobial Prescribing Decision
- Outpatient Parenteral Therapy

Dr Nathwani et al.
Define clinical situations where antibiotics can be stopped

Table 13. Specific Situations where Antibiotics should be withheld

- Respiratory tract syndromes
  - Viral pharyngitis
  - Viral rhinosinusitis
  - Viral bronchitis
  - Noninfectious cardiopulmonary disorders misdiagnosed as pneumonia
- Acute Otitis Media (AOM) (for selected cases, refer to article)
- Skin and Soft Tissue Infections (SSTI)
  - Subcutaneous abscesses (for selected cases, refer to article)
  - Lower extremity stasis dermatitis
- Asymptomatic bacteriuria and pyuria, including catheterized patients
- Microbial colonization and culture contamination
- Low-grade fever

# Duration of antibiotic therapy

### Table 14. Practice Guideline Recommendations regarding duration of therapy

<table>
<thead>
<tr>
<th>Condition</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community-acquired pneumonia (CAP)</td>
<td>5 days</td>
</tr>
<tr>
<td>Health care-acquired pneumonia</td>
<td>8 days</td>
</tr>
<tr>
<td>Skin and Soft Tissue Infections (SSTI)</td>
<td>5 days</td>
</tr>
<tr>
<td>Urinary Tract Infections (UTI)</td>
<td></td>
</tr>
<tr>
<td>- Cystitis</td>
<td>3-5 days&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>- Pyelonephritis</td>
<td>5-14 days&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>- Catheter associated</td>
<td>7 days&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td><em>S. aureus</em> bacteremia</td>
<td></td>
</tr>
<tr>
<td>- Low risk of complications</td>
<td>2 weeks</td>
</tr>
<tr>
<td>- High risk of complications</td>
<td>4-6 weeks</td>
</tr>
<tr>
<td>Intra-abdominal infection</td>
<td>4-7 days</td>
</tr>
<tr>
<td>Surgical antibiotic prophylaxis,</td>
<td>1 dose&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Depending on antibiotic  
<sup>b</sup> Prolonged to 10-14 days for delayed response  
<sup>c</sup> Up to 24h, without exception

Table 7. The Golden Rules of Antimicrobial Prescribing “MINDME”.

M

Microbiology guides therapy wherever possible

I

Indications should be evidence based

N

Narrowest spectrum required

D

Dosage appropriate to the site and type of infection

M

Minimise duration of therapy

E

Ensure monotherapy in most cases

AMSP team – roles and responsibilities

- Physician leader with ID training
- Co-led by Pharmacist leader with ID training
- Clinicians and HODs: Prescriber led
- Infection preventionists or hospital epidemiologists – Monitor, audit, analyze and report facility wide data
- Quality management staff: Medical quality and patient safety issue
- Microbiology lab: Antibiograms to guide empiric therapy
- IT staff: integrate stewardship protocols into existing workflow
- Nurses: ensure cultures are taken before starting antibiotics
Eight key components of an ASP

• Leadership commitment
• Accountability
• Drug expertise
• Multidisciplinary approach and team
• Prioritized introduction of policies
• Measure
• Report
• Provide ongoing education
Keys to success of a AMSP

1. Clear aim/vision that stewardship is a “Patient safety” priority
2. Management support and accountability
3. Multi-professional AMS team with a strong influential clinical leader
4. Effective communication structures
5. Evidence based stewardship interventions and plan measurement
6. Education and Innovation
7. Ensure early or short term wins and then consolidate success/gains
Strategies of AMSP
Interventions to Improve Antibiotic Use

1. **Persuasive**
   - Education
   - Guidelines
   - Reminders
   - Audit & feedback

2. **Restrictive**
   - Formulary restriction
   - Compulsory order forms
   - Expert approval
   - Automatic stop orders
Two core ASP strategies

• **Front-end strategies:** where antimicrobials are made available through an approval process (formulary restriction and pre-authorization)
  - Immediate reduction in use and expenditure of restricted antibiotics

• **Back-end strategies:** are where antimicrobials are reviewed after antimicrobial therapy has been initiated (prospective audit and feedback)
  - Timely de-escalation of antibiotics
  - Reduction in inappropriate use
<table>
<thead>
<tr>
<th>Core Strategies</th>
<th>Supplemental Strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formulary restrictions and preauthorization*</td>
<td>Streamlining / timely de-escalation of therapy*</td>
</tr>
<tr>
<td>Prospective audit with intervention and feedback*</td>
<td>Dose optimization*</td>
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<tr>
<td>Multidisciplinary stewardship team*</td>
<td>Parenteral to oral conversion*</td>
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<td>Guidelines and clinical pathways*</td>
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<td>Antimicrobial order forms</td>
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<td></td>
<td>Education</td>
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<td>Computerized decision support, surveillance</td>
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<td>Laboratory surveillance and feedback</td>
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<tr>
<td></td>
<td>Combination therapies</td>
</tr>
<tr>
<td></td>
<td>Antimicrobial cycling</td>
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</tbody>
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Adapted from Dellit et al. Clinical Infectious Diseases 2007; 44:159-77.
• 30 year old previously healthy male presents with a H/O abdominal pain, vomiting and high grade fever
• On examination febrile, BP=100/80 , HR=100/min
• P/A: Tenderness in the RIF, guarding and rigidity
• The treating physician writes an order for Inj Meropenem 1g IV Q8H
• How will pre-authorization work vs prospective audit and feedback ?
Pre-authorization

• Shows a decrease in use of antibiotics and antibiotic resistance
• No adverse effects
• White et al.
  - 32% decrease in total parenteral antibiotic expenditures
  - Susceptibilities ↑ to all β-lactam and quinolones

• ↑ in frequency of susceptible isolates among in-patients
• Direct chart review and senior physician approval improved acceptability

Prospective audit and feedback

- Reduced antibiotic use
- Reduced CDI
- Led to a 22% ↓ in use of broad spectrum antibiotics
- Reduced infection due to antibiotic resistant Enterobacteriaceae
- Ellingsen M et al
- Abx use ↓ from 644 → 503 days of therapy

- CDI ↓ from 11 → 6 cases
- Overall susceptibility to Meropenem ↑
- Length of stay and mortality did not change

Comparison of pre-authorization and prospective audit and feedback

• **Advantages of PA**
  - Reduces empiric initiation of inappropriate Abx
  - Encourages early and frequent review of culture data
  - Reduces costs

• **Disadvantages of PA**
  - May delay therapy
  - Loss of prescriber autonomy
  - Impacts only restricted agents

• **Advantages of PAF**
  - ↑ the visibility of the AMSP
  - ↑ More data is available and hence uptake is better
  - Educative and collaborative effort which could address de-escalation and duration of therapy
  - Prescriber autonomy is maintained

• **Disadvantages of PAF**
  - Labor intensive
  - Compliance voluntary and prescriber reluctance to change if patient better
Didactic education

- Passive educational activities like lectures, information pamphlets – *(low quality evidence, weak recommendation)*

  - **Cannot be relied upon as a sole means of reducing inappropriate antibiotic use**

- Integrated education on antibiotic stewardship into clinical and pre-clinical curricula

Facility specific clinical guidelines

- Clinical practice guidelines and algorithms should be developed for common infectious disease syndromes *(weak recommendation, low quality evidence)*

  - This can be an **effective way to standardize prescribing practices, based on local epidemiology**
Prescriber led review of antibiotic prescription without an active AMSP team

- **Antibiotic time-outs, stop orders to encourage prescribers to perform routine review of antibiotic regimens to improve antibiotic prescribing**
  - Weak recommendation, low quality evidence
  - Success requires a persuasive or enforced prompting

Computerized clinical decision support systems integrated into the electronic health record

- **Weak recommendation, moderate quality evidence**
- Streamline the work of ASPs by identifying the opportunities for interventions

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Stratified vs Non stratified antibiograms

- **Antibiograms**: Tables showing how susceptible a series of organisms are to different antibiotics
- Summarise the cumulative proportions of pathogenic organisms that are susceptible to antimicrobials
- **Key strategy as it informs the antibiotic choice and tracks patterns of resistance**

Antibiograms stratified by population, age or hospital units may have more potential to influence appropriate antibiotic Choice – *Weak recommendation, low quality evidence*
Case History

• A 57 yr old man presented with fever and dry cough for 3 days
• He is known to be diabetic, hypertensive, hypothyroid with chronic kidney disease stage 5 on hemodialysis
• **Vitals**: HR =96/min, RR =22/min, BP= 140/90, SpO2:93 %
• **Labs**: Hb=7.6g%; Platelets = 60,000/cu.mm; Urea =121mg%; Creatinine:6.42 mg%; Na/K/Cl/Ca = 133/4.6/106/4.20 mmol/l, Lactate:1.5
• **Microbiology**: C/S Blood: No growth so far, Dengue Serology= IgM, IgG- Negative;
• Rapidly worsened and is on a ventilator
• Started on Inj Meropenem 500mg IV Q 12H
• **QUESTIONS TO THE PANEL**

• What do you think are the diagnostic possibilities and what is inappropriate here in management?

• What are the laboratory tests that could confirm these diagnoses?

• What tools could be employed in diagnostic stewardship to reduce antimicrobial resistance?
A rapid diagnostic point of care can reduce antibiotic use.
Employing biomarkers like Procalcitonin and rapid diagnostic tests reduced initiation, duration and total exposure of antibiotics.
Case

• A 75yr old male, diabetic presents with a 7 day history of swelling of the left lower limb with pain, bullae and pus discharge
• Patient also has NSTEMI during admission with mild respiratory distress
• Shifted to ICU, required intubation
• He undergoes a debridement and a plantar fasciotomy on the day of admission

- **Vitals:** HR:89/min, RR:18/min, BP:173/88 mmHg, SpO₂ :95%, P/F ratio: 307, Lactate: 0.8
- **Labs:** Hb:9.7 g%; TC:13,400 /cu.mm; Plt:464,000 /cu.mm; Procalcitonin:0.208
- Na/K/Cl/Ca:134/3.5/106/1.14; Urea/Creatinine:32/0.87 mg%; CKMB:3.2;
- Trop T:131.5
- **CXR:** Peri-hilar opacities
Microbiology

• Cultures:
  • C/S Urine: no growth
  • C/S Blood: no growth
  • C/S Sputum(ETA): no growth
  • Influenza PCR: negative for A&B
  • C/S Superficial pus swab: polymicrobial (MRSA, Pseudomonas, Streptococcus)

• Necrotizing skin and soft tissue infection
  • Started Inj.Piptaz 4.5g Q6H(8 days) & Inj.Clindamycin 600mg Q8H(5 days)

• Afebrile by 3rd day, CRP and Procalcitonin come down remarkably

Subsequently the patient was changed to
  • T Linezolid 600mg po bd (D14)
  • T Azithromycin 500mg po od(D14)
Questions to the panel

- What is the most likely causative organism?
- What are the risk factors for a polymicrobial infection?
- What are the stewardship intervention opportunities available with antibiotic management in this patient?
- What are the clues to differentiating between a colonizer and a true pathogen?
“Shorter is better”

- Numerous RCTs have demonstrated that shorter regimens are clinically efficacious in
  - Cellulitis
  - Acute bacterial sinusitis
  - Community acquired pneumonia
  - Ventilator associated pneumonia
  - Complicated urinary tract infections
  - Intra abdominal infections

P: 518 patients with complicated IAI
I/C: 10 days vs 4 days after adequate source control
O: No difference in the two groups with regard to SSI, recurrent IAI and death
Duration of treatment in VAP

- Comparison of 15 days vs 8 days of antibiotic therapy in adults
- Mortality was 18.8% vs 17.2%
- Recurrent infections 28.9% vs 26%
- MDR pathogens 62% vs 42.1%
- Antibiotic free days 8.7 vs 13.1
- No. of mechanically ventilated, organ failure free days did not differ

Recurrences did occur with NFGNB including P. aeruginosa when treated for 8 days only (40.6% vs 25.4%)

Duration of antibiotic treatment for acute pyelonephritis and septic urinary tract infection—7 days or less versus longer treatment: systematic review and meta-analysis of randomized controlled trials

Shorten duration of antibiotic therapy when possible
Case history

- A 45 yr old with history of analgesic abuse for osteoarthritis, presented with
- Sudden onset abdominal pain for 1 day and septic shock with ARDS
- She was diagnosed with duodenal ulcer perforation
- She was started on Inj. Meropenem 1g iv q8h(D4), Inj Gentamicin at 5mg/kg and Inj.Flagyl 500mg iv q8h(D4)
- **Vitals:** HR:93 /min; RR:25 / min; SpO₂:98 %; BP:112/70
- Systemic exam reveals a rigid abdomen
- Hb:9.3 g%; TC:5600 /cu.mm; Plt:135,000 /cu.mm; S. procalcitonin: 32.03
- Urea/Creatinine :29/0.6 mg%, Total/Direct Bilirubin: 0.4/0.2 mg/dL
- **Blood culture:** no growth, Pus C/S: ESBL *E.coli* sensitive to Piperacillin-Tazobactam
- Chest X ray- opacity left lower lobe
- Undergoes emergency laparotomy with omental patch repair and shifted to ICU
Questions to the panel

• What are the common organisms which cause an intra-abdominal infections?
• What are the likely resistance mechanisms of these organisms?
• Was the empirical therapy appropriate? What would have been your choice of antibiotic?
• Is de-escalation possible now that culture results are available?
Spectrum of activity

- **Meropenem**: Covers most gram positives [except MRSA and enterococcus], most gram negatives and anaerobes

- **Anaerobic activity**: The most effective antimicrobials against anaerobes are: metronidazole, the carbapenems (imipenem, meropenem, doripenem, ertapenem), chloramphenicol, the combinations of a penicillin and a beta-lactamase inhibitors (ampicillin or ticarcillin plus clavulanate, amoxicillin plus sulbactam, piperacillin plus tazobactam), tigecycline, cefoxitin and clindamycin

Avoid redundant double coverage - gram negative/ anaerobic
• Inoculum effect: ≥ 8 fold MIC increase on testing with higher inoculum, was most consistently detected with cefepime, cefotaxime, and ceftriaxone and Piperacillin-tazobactam.

• This an in vitro laboratory phenomenon, however corroborates increased risk of therapeutic failure in serious infections in clinical studies as well.
Clinical efficacy of antibiotics in ESBL *E.coli*

- 85 consecutive episodes of ESBL *K.pneumoniae* bacteremia in 12 hospitals in 7 countries

- 3.7% (1/27) mortality with Carbapenem therapy vs 64.5% (7/11) with non carbapenems [1](https://doi.org/10.1086/420816)

- 331 patients with ESBL bacteremia - 103 (48%) patients received PTZ empirically and 110 (52%) received carbapenems empirically.

- Risk of death was 1.92 times higher for patients receiving empiric PTZ vs empiric carbapenem therapy (95% confidence interval, 1.07-3.45) [2](https://doi.org/10.1086/680848)
Case history

• 44 year old, Banker, came to hospital for suture removal. She was operated for umbilical hernia last week

• H/o Short Term Foley’s Catheterisation while getting operated for Inguinal Hernia, 1 week back and removed post surgery

• No known co-morbidities (No Diabetes, hypertension).

• No history of fever, urinary complaints

• **Vitals** –

  • BP-120/70mmHg; PR- 90/min; Afebrile

  • No Pallor, icterus, cyanosis, clubbing, lymphadenopathy or Pedal edema

  • PA- Soft Nontender, no organomegaly, No suprapubic/renal angle tenderness

• Other systemic examination - normal
# Labs

**Urine Routine**
- WBC - 14/HPF
- RBC - Nil
- Protein - Nil
- Glucose – Nil

**USG Abdomen** - Normal Study

**CBC**
- TC - 7400, P78/L20/E1/M1

**RBS** - 121

**LFT and Renal Parameter** normal

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### C/S URINE COMMON
- Moderate pus cells, many GNB, occasional Gram positive bacilli
- >100,000 CFU/ML. Significant E.coli ESBL+

### E.coli Sensitivity Test

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin/clavulanic acid</td>
<td>Resistant</td>
</tr>
<tr>
<td>Amikacin</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Cefoperazone + sulbactam</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Meropenem</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Co-Triamoxazole</td>
<td>Resistant</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>Resistant</td>
</tr>
<tr>
<td>Netilmicin</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Piperacillin/Tazo</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Cefpodoxime</td>
<td>Resistant</td>
</tr>
<tr>
<td>Imipenem</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Resistant</td>
</tr>
</tbody>
</table>

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### Treatment
- Inj Meropenem 1 gm IV Q8h for 10 days
Questions to the panel

- Was the treatment choice here appropriate?
- What precautions need to be taken prior to collecting a urine sample?
- How do you differentiate between a colonizer and true pathogen

Do not treat colonizers/contaminants
Urine Culture

- Bacteriuria is **NOT** a disease
  - Does not establish diagnosis
  - Rarely an indication for antibiotics
- Sample
  - Gold standard: bladder urine obtained by SPA
  - MSCC sample **does not** decrease contamination*
- Significant bacteriuria
  - $>10^5$ cfu/ml, single organism
  - SPA $>10^2$ cfu/ml
  - Symptomatic women $>10^2$ cfu/ml
- Antibiotic susceptibility

28 year lady a case of subcutaneous panniculitis like T cell lymphoma in August was given the first cycle of chemotherapy on 3/9/16

Given CHOP-E – Cyclophosphamide, Adriamycin, Vincristine, Etoposide and Prednislone

Presented on 14/9/16 with fever, cough with expectoration and loose stools for 2 days

She also complained of some odynophagia and ENT ruled out a peritonsillar abscess

No history of breathlessness, oliguria and hematuria
On examination

• Vitals: Febrile, Pulse-160/min RR - 22/min, BP-76/40 mmHg
• General exam: Pallor++, Icterus + ,
• Skin: Erythema and swelling observed on medial aspect of the thigh
• P/A- soft, non tender, Liver just palpable, spleen not palpable.
• RS- bilateral conducted sounds present.
• CVS-S1 and S2 present.
• CNS - conscious and oriented

• In ICU for observation, requiring small dose of inotropes and oxygen by mask
Labs

• Hb = 7.5g%,
• T.WBC = 100 cells/cu.mm
• Platelets = 20,000/cu.mm
• Creatinine = 0.99 mg%

Risk assessment

• Febrile neutropenia for 6 days
• Septic shock
• Clinical and microbiological documented infection

• She was started on Meropenem initially and then escalated to Colistin within 5 hours

• Qualitative PCR influenza PCR positive for Influenza B
<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Susceptible</th>
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<tbody>
<tr>
<td>E.coli</td>
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</tr>
<tr>
<td>Cefoper + sulbact</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Amikacin</td>
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</tr>
<tr>
<td>Rifampicin</td>
<td>--</td>
</tr>
<tr>
<td>Oxacillin</td>
<td>--</td>
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<tr>
<td>Teicoplanin</td>
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</tr>
<tr>
<td>Meropenem</td>
<td>Susceptible</td>
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<tr>
<td>Cefoxitin</td>
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<td>Tigecycline</td>
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<td>Linezolid</td>
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</tbody>
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**Questions to the panel**

- What are the common organisms encountered in Hematology patients – either post chemotherapy and post transplant?
- Would you de-escalate and if so to what and why?
- Is it safe to de-escalate in this hypotensive neutropenic patient?
- When would you consider adding gram positive cover?
De-escalation of empirical therapy is associated with lower mortality in patients with severe sepsis and septic shock

- **P** – Patients with septic shock or severe sepsis
- **I** – Intervention was de-escalation defined as discontinuation of an antimicrobial agent or change of antibiotic to one with a narrower spectrum once culture results are available
- **C** – No de-escalation
- **O** – In hospital mortality and 90 day mortality

1. Factors associated with in-hospital mortality were septic shock, SOFA score on the day of culture results and inadequate empirical antimicrobial therapy

2. **De-escalation was protective [OR = 0.58 (0.36 -0.93)]**

3. Independent analysis where only adequate empirical therapy was used de-escalation was still protective [ OR= 0.54 (0.33-0.89)]
Antibiotics are not harmless

• Can predispose to C.difﬁcile colitis and Candidemia
• Wipe out the good bacteria in the gut leaving the multi-resistant bacteria to proliferate
• This multi resistant infection can be passed on to other people in the hospital/ community
• These MDR resistance genes can be transferred to other bacteria making other infections difﬁcult to treat as well
• Increased hospital and drug costs
# Antibiotic prescribing

<table>
<thead>
<tr>
<th>Do ‘s</th>
<th>Don’ts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do make a clinical diagnosis</td>
<td>Don’t give antibiotics for just a fever, make a diagnosis</td>
</tr>
<tr>
<td>Do send appropriate lab tests to confirm a diagnosis</td>
<td>Don’t treat colonizers or contaminants</td>
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<tr>
<td>Do know about local susceptibility patterns and PK-PD of antibiotic prescribed</td>
<td>Don’t give antibiotics for a duration longer than necessary</td>
</tr>
<tr>
<td>Do de-escalate, discontinue or modify once culture results available</td>
<td>Don’t give antibiotics without checking if it will work at the site of infection</td>
</tr>
<tr>
<td>Treat urgently if shock, necrotizing fasciitis, bacterial meningitis, community or hospital acquired pneumonia, febrile neutropenia</td>
<td>Don’t assume failure to respond to the antibiotic immediately is drug resistance</td>
</tr>
</tbody>
</table>
COMBAT DRUG RESISTANCE

No action today, no cure tomorrow

Thank you