

Ventilator Associated Pneumonia in PICU

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Definition

1. CAP - Acute infection (less than 14 days) acquired in the community, of the lower respiratory tract, leading to cough or difficulty breathing, tachypnoea or chest-wall indrawing
2. HAP – Pneumonia developing more than 48 hours after admission to hospital
3. VAP – Nosocomial infection occurring in patients receiving mechanical ventilation that is not present at the time of intubation and develops more than 48 hours after initiation of ventilation

Epidemiology

- Pneumonia = 2nd most common nosocomial infection
- Accounts for 18 – 26% of nosocomial infections
- Children aged 2 – 12 months most affected
- 95% of nosocomial pneumonia occurs in ventilated children

Risk Factors for VAP

- Immunodeficiency
- Immunosuppression
- Neuromuscular blockage
- Septicaemia
- TPN
- Steroids
- H2-blockers
- Mechanical ventilation
- Re-intubation
- Transport while intubated

Microbiology

➤ Early-onset HAP:

- Strep pneumoniae
- Haemophilus influenzae
- Moraxella catarrhalis

➤ Late-onset HAP:

- Staph aureus - MRSA
- Pseudomonas aeruginosa/Aceni**to**bacter - MDR
- Gram-negative Enterobacteriaceae - ESBL

Often more
resistant
organisms

Criteria for VAP for Infants Younger than 12 Months of Age

Clinical Criteria / Radiographic Criteria

Worsening gas exchange with at least 3 of the clinical criteria:

- Temperature instability without other recognized cause
- White blood cells $<4,000/\text{mm}^3$ or $>15,000/\text{mm}^3$ and band forms $>10\%$
- New onset purulent sputum or change in the character of sputum or increased respiratory secretions
- Apnea, tachypnea, increased work of breathing, or grunting
- Wheezing, rales, or rhonchi
- Cough
- Heart rate <100 beats/min or >170 beats/min

plus radiographic criteria

- At least 2 serial chest x-rays with new or progressive and persistent infiltrate, consolidate, cavitation or pneumatocele that develops >48 hours after initiation of mechanical ventilation

Wright ML, et al. Semin Pediatr Infect Dis 2006;17:58-64

Prevention Strategies

- **Infection control**
- Head of bed elevation
- Daily sedation holidays
- Stress ulcer prophylaxis
- DVT prophylaxis
- In-line suctioning
- Oropharyngeal toilet
- Orotracheal intubation
- Change in ventilator circuits only when dirty
- Avoidance of re-intubation

Management

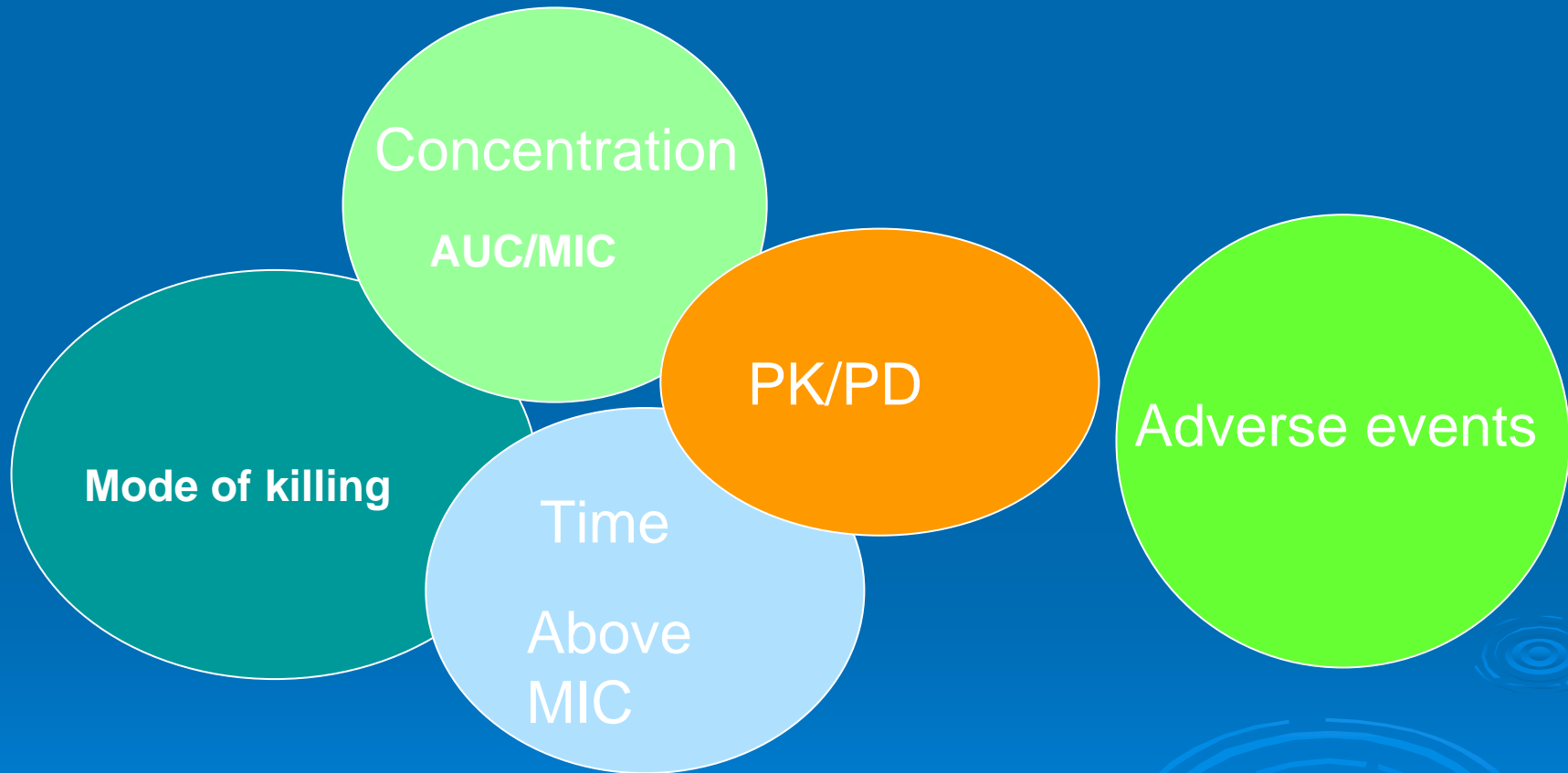
ANTIBIOTICS

- Antibiotic selection policies
- Antibiotic rotation ??
- Regular microbiology fora – Antibiotic Stewardship: designed to
 - optimize antimicrobial therapy administered to hospitalized patients,
 - to ensure cost-effective therapy,
 - improve patients' outcome while containing bacterial resistance.

Antibiotic Stewardship

- A multidisciplinary team including at least an infectious disease physician and a clinical pharmacist is required.
- Feedback to the provider, education and antimicrobial restriction

Selecting Antibiotics



Dosage

- Intervene early and appropriately
- Consider antibiotic for relevant organisms
- Consider dosage interval and total dose depending on the antibiotic mode of killing
- PK = Effect of body on drug (absorption, availability, metabolism, excretion)
- PD = Effect of drug on body (receptor binding, tissue penetration)

PK = Dosage + Concentration

- Correct antibiotic dosages and duration
- Correct antibiotic administration
- Concentration dependent antibiotics (Aminoglycosides, quinolones) = single daily concentration
- Time dependent antibiotics (B-lactams, vancomycin, pip-taz, carbapenems, linezolid) = continuous infusion over 24 hours (3-4 hours for carbapenems, TDS for linezolid)

Duration

- No culture = 3 days
- URTI = 3-5 days
- Positive culture = 5-7 days or 3-5 days after clinical improvement
- Seldom need 10 days
- Exceptions
 - Staph 2-3 weeks
 - PCP 3 weeks
 - Fungal 2-3 weeks

Decontaminate

- Hand washing – the most effective strategy to prevent resistance
- All personal and parents must hand wash
- Use notices and wall mounted sprays
- Anti-inflammatory strategies of Macrolides/Linezolid

Dont

- Use third generation cephalosporins routinely (except meningitis)
- Use inappropriate antibiotics
- Use a long course
- Use too low a dose
- Routinely combine antibiotics
- Routinely use probiotics

Reduced use of third-generation cephalosporins decreases the acquisition of ESBL-producing *Klebsiella Pneumonia*

Infect Control Hosp Epidemiol 2004;25: 832-7

TABLE 2. Univariate Analysis of ESBL-EK Infection and Antimicrobial Use in the 30 Days Before Infection

| Antibiotic, n (%) | ESBL (n = 35) | Non-ESBL (n = 105) | P Value |
|----------------------------------|------------------|-----------------------|---------|
| Third-generation cephalosporins* | 19 (54) | 18 (17) | .000 |
| Ceftazidime only | 15 (43) | 12 (11) | .000 |
| Extended-spectrum penicillins† | 6 (17) | 6 (6) | .073 |
| Carbapenems‡ | 3 (9) | 0 (0) | .015 |
| Anti-anaerobes§ | 13 (37) | 25 (24) | .131 |
| Aminoglycosides | 24 (69) | 50 (48) | .034 |
| Quinolones (ciprofloxacin) | 2 (6) | 1 (1) | .154 |
| Trimethoprim/sulfamethoxazole | 16 (46) | 15 (14) | .000 |

* Includes ceftazidime, ceftriaxone, and cefotaxime.

† Includes ticarcillin/clavulanate, piperacillin, ampicillin, amoxicillin/clavulanate, and ticarcillin.

‡ Includes imipenem, meropenem.

§ Includes ticarcillin/clavulanate, piperacillin, ampicillin/sulbactam, imipenem, meropenem, metronidazole, clindamycin, and ceftriaxone.

|| Includes gentamicin, tobramycin, and amikacin.

TABLE 3. Adjusted Risk Factors for ESBL-EK Infection in Hospitalized Children

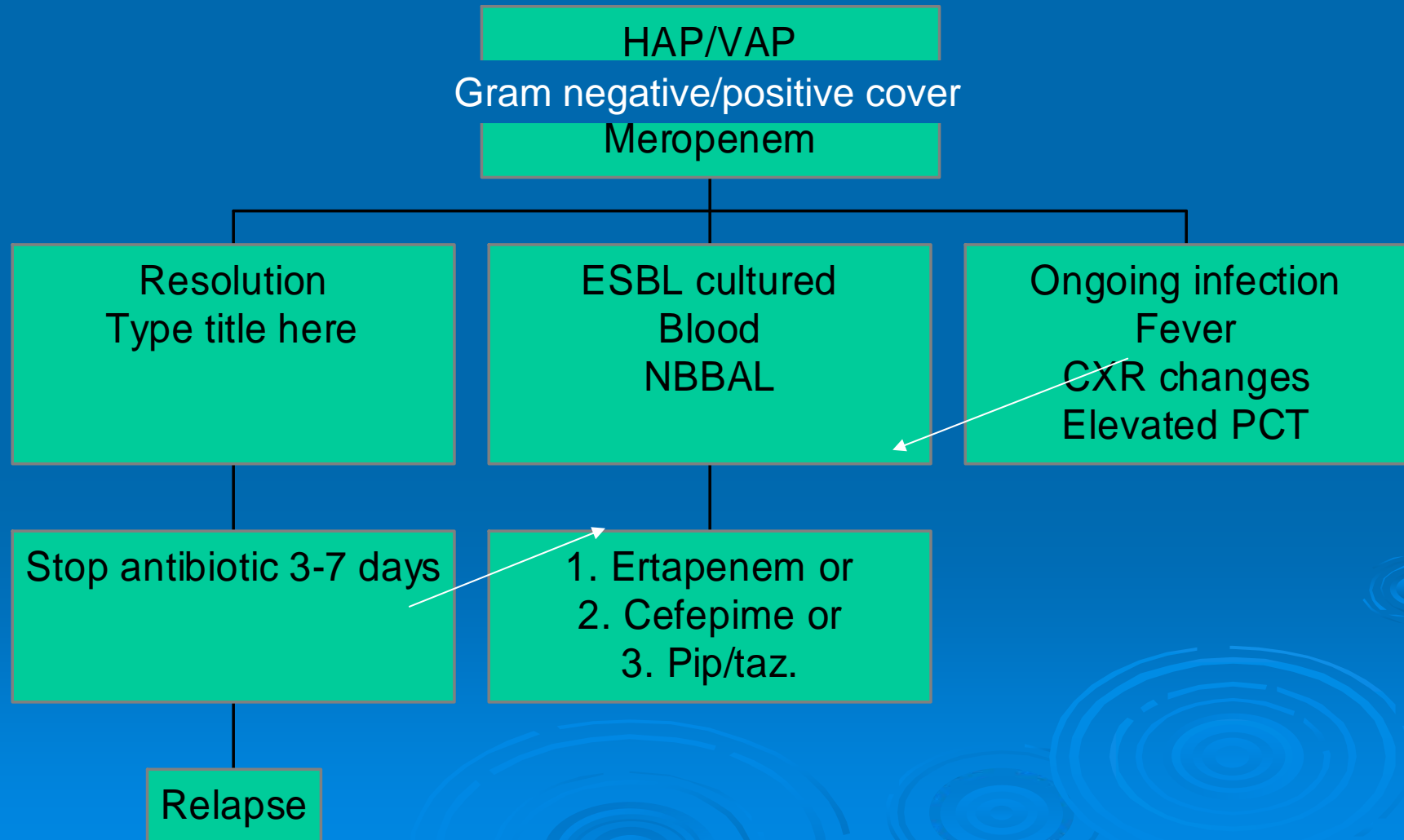
| Variable | Adjusted OR (95% CI) | P Value |
|--|----------------------|---------|
| Third-generation cephalosporin* use in previous 30 d | 5.82 (1.92–17.68) | .002 |
| Female | 4.49 (1.49–13.51) | .008 |
| Infecting organism† | 3.48 (1.07–11.32) | .039 |
| Steroid use in previous 30 d | 4.04 (1.30–12.50) | .016 |

OR indicates odds ratio; CI, confidence interval.

* Third-generation cephalosporins include: cefotaxime, ceftazidime, and ceftriaxone.

† *E coli* as the reference.

Use of Ertapenem



Antibiotics for ESBL (lactose fermenters)

- Carbapenem +/- Aminoglycoside
- - Meronem
- - Imipenem
- - Ertapenem (Invanz)
- Cefepime (Maxipime)
- Piperacillin/tazobactam
- Never – Ciprofloxacin/Rocephin

Other Possible Indications for Ertapenem

- ? First line PICU choice – when low *Pseudomonas* prevalence
- PICU sepsis – especially abdominal surgery – anaerobe cover
- All HIV-infected PCP PICU admissions – higher risk of community acquired multi-resistant gram negatives

Antibiotics for MRSA

➤ Vancomycin – Concerns:

- Unfavourable PK/PD – Dose close to MIC break point (2)
- Highly plasma protein bound – poor lung penetration (14% penetration to epithelial surfaces) – unsuitable for HAP
- Adverse events – kidney/ear/histamine release (anaphylaxis)

➤ Teicoplanin

➤ Linezolid (Zyvoxid)

A Brink Personal communication

Why Linezolid is Best for MRSA

- MIC break point = 4mg/L
- Excellent lung penetration
- Quorum sensing ability =
- Anti-inflammatory effects
- Favourable safety profile

Percentage of Bacteria at each MIC value (mg/L) (n=40)

| Antibiotic | 0.25 | 0.5 | 1 | 2 | 4 | 8 |
|-------------|------|------|------|------|-----|---|
| Linezolid | 0 | 42.5 | 52.5 | 2.5 | 2.5 | 0 |
| Teicoplanin | 0 | 5 | 12.5 | 72.5 | 10 | 0 |
| Vancomycin | 0 | 0 | 27.5 | 70 | 2.5 | 0 |

Conclusion

- Do I need an antibiotic
- Select the most appropriate antibiotic
- Use the correct dose and interval
- Short courses are better
- Avoid 3rd generation cephalosporins for RTI's – except more severe disease
- Always think of Linezolid for Staph pneumonia

Thank You

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