SHS + UHN ASP ANTIMICROBIAL STEWARDSHIP PROGRAM

Double vs. Single Coverage in Management of *Pseudomonas aeruginosa* Infections

EMPIRIC CHOICE

Choice of antibiotic regimen should be guided by prior exposure and local susceptibility data.
Antibiotic regimens active against *P. aeruginosa* at MSH and UHN include:

- Piperacillin-tazobactam 4.5 g iv **Q6H**
- Ceftazidime **2 g** iv Q8H
- Meropenem 1g iv Q8H (exception: CNS infection—Consult ID)
- Aminoglycosides: gentamicin *or* tobramycin 5 mg/kg IV daily; amikacin 15 mg/kg IV daily
- Ciprofloxacin 400 mg iv Q8H or 750 mg p.o. Q12H

DOUBLE VS. SINGLE COVERAGE

- In patient care areas where *P. aeruginosa* susceptibility is high, routine double coverage with anti-pseudomonal agents is not warranted.
- Multi-drug resistant (MDR) *P. aeruginosa* is associated with prior antibiotic exposure.
- During critical illness (e.g. septic shock), and in those vulnerable to severe infections due to immunocompromised state, "upfront" double anti-pseudomonal coverage may improve the probability of having *at least one active regimen* until susceptibility is known. Most commonly studied regimens include an antipseudomonal beta-lactam plus an aminoglycoside.
- SHS-UHN Ventilator-Associated Pneumonia algorithm recommends the addition of an aminoglycoside (gentamicin or tobramycin) to a beta-lactam agent (piperacillin-tazobactam or meropenem) in patients with septic shock.
  Link: http://www.antimicrobialstewardship.com/sites/default/files/msh-uhn_vap_algorithm_0.pdf
- *High Risk* Febrile Neutropenia Protocol for Malignant Haematology patients recommends gentamicin plus piperacillin-tazobactam combination empirically for up to 72 hrs. Empiric therapy for febrile neutropenic patients should always have activity against *P. aeruginosa*.
  Link: http://www.antimicrobialstewardship.com/sites/default/files/asp_fn_protocol_secured_edition.pdf
- Once susceptibility is **known** for the *P. aeruginosa* isolate, antibiotic therapy should be de-escalated to monotherapy accordingly and at adequate dosing. Ongoing double coverage has not been supported in clinical trials and may have been associated with adverse events such as nephrotoxicity.

CURRENT RESISTANCE ISSUES

- Local *P. aeruginosa* susceptibility data (courtesy of Dr. Sue Poutanen) should be used to determine the most appropriate empiric approach:

	Site (Date: Jan 1 2011-Dec 31, 2011)			
Specimen source	**TG ICU**	**TW ICU**	**MSH ICU**	**PMH (all units*)**
Respiratory	• Tobramycin; amikacin: ≥80% susceptible • Meropenem; piperacillin-tazobactam: 70-79% • Gentamicin; ciprofloxacin: <70%	• All regimens: ≥80% susceptible	• Piperacillin-tazobactam; tobramycin; amikacin: ≥80% • Rest of alternatives: 70-79%	ALL regimens: ≥80% susceptible EXCEPT ceftazidime (74%)
Blood	No isolates	• All regimens: ≥80% susceptible	• Piperacillin-tazobactam; amikacin: 100% • Rest of alternatives: ≤69%§	All regimens: ≥80% susceptible EXCEPT ceftazidime (75%)

*To be interpreted with caution as it included *all* oncology patients and not just those with malignant haematological diseases, who may have higher risk of MDR *P. aeruginosa* due to frequent antibiotic exposure.
§To be interpreted with caution – based on a small number of isolates

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IMMUNOCOMPROMISED HOST CONSIDERATION

- Upfront double coverage may improve the probability of adequate empiric therapy but, once susceptibility is known, antibiotic regimen should be de-escalated to monotherapy accordingly. See also above comments on *High Risk* Febrile Neutropenia Protocol.

Reference:

Tamma PD, Cosgrove SE and Maragakis LL. Combination therapy for treatment of infections with gram-negative bacteria. Clin Microbiol Rev 2012;25:450.