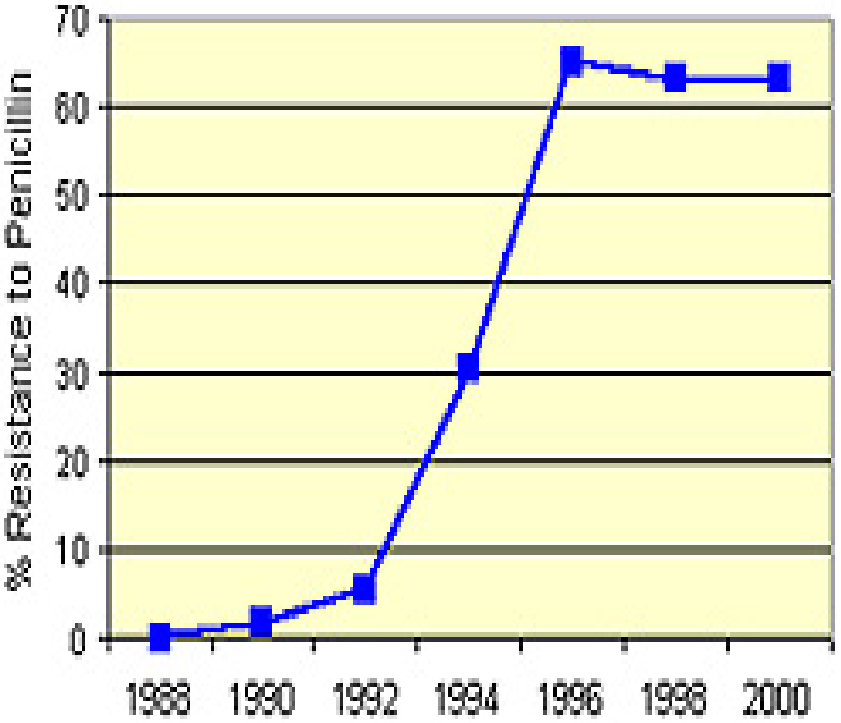
Antibiotics Use in ICU

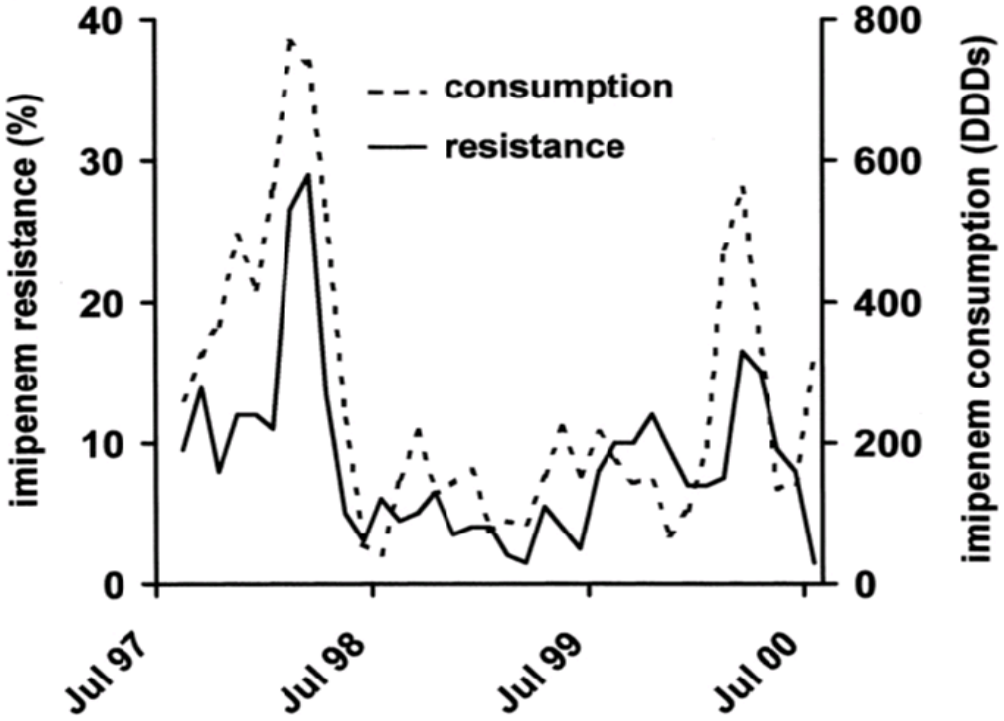
WK To

April 2010

Antibiotics resistance is inevitable & Total consumption is a critical factor in selecting resistance organisms

S. Pneumoniae: Resistant Rate





Source: HA, Hong Kong

Antibiotics are specialized drug!

- Effectiveness
  (Local epidemilogy)
- Pharmaco-kinetic
- Resistance mechanism
- Action mechanism
- Adverse reaction
- Cost

Table 7. Recommended empirical antibiotics for community-acquired pneumonia.

Outpatient treatment

1. Previously healthy and no use of antimicrobials within the previous 3 months

   A macrolide (strong recommendation; level I evidence)

   Doxycyline (weak recommendation; level III evidence)

2. Presence of comorbidities such as chronic heart, lung, liver or renal disease; diabetes mellitus; alcoholism; malignancies; asplenia; immunosuppressing conditions or use of immunosuppressing drugs; or use of antimicrobials within the previous 3 months (in which case an alternative from a different class should be selected)

   A respiratory fluoroquinolone (moxifloxacin, gemifloxacin, or levofloxacin [750 mg]) (strong recommendation; level I evidence)

   A β-lactam **plus** a macrolide (strong recommendation; level I evidence)

3. In regions with a high rate (>25%) of infection with high-level (MIC ≥16 μg/mL) macrolide-resistant *Streptococcus pneumoniae,* consider use of alternative agents listed above in (2) for patients without comorbidities (moderate recommendation; level III evidence)

Inpatients, non-ICU treatment

A respiratory fluoroquinolone (strong recommendation; level I evidence)

A β-lactam **plus** a macrolide (strong recommendation; level I evidence)

IDSA guideline, CID 2007:44 (Suppl 2)

Local epidemiology

S. pneumonia:

% sensitive (HA)

Erythromycin	30
Levofloxacin	96

Treatment of S. pneumoniae

New CLSI interpretation:

Penicillin MIC:	MIC (μg/ml) ≤ 0.06	Amoxil 250mg tds, Augmentin 375mg tds, other b-lactam
≤ 0.06 – 2 μg/ml	MIC (μg/ml) = 0.12 – 1	Amoxil 500mg tds, Augmentin 750mg tds
"Sensitive"	MIC (μg/ml) = 2	Amoxil 750mg-1g tds, Augmentin 1g tds
MIC (μg/ml) = 4	"Intermediate"	Amoxil 1g tds, Augmentin 2g BD
MIC (μg/ml) ≥ 8	"Resistant"	Quinolone / Vancomycin / Cefotoxime (depend on MIC)

Empirical Tx: a. Cover H. influenza, b. **>50% MIC up to 1 μg/ml**

Choice: iv: Augmentin 1.2g Q8H or Ceftriaxone 1g Q24H

Oral: Augmentin 750mg tds or Augmentin 375mg tds + Amoxil 250mg tds

Pharmoacokinetic

Some examples:

- **Quinolones, Linezolid, Metronidazole, Fluconazole**, etc have excellent oral bio-availibility, therefore, PO=IV unless the patients cannot eat or are in shock
- **Aminoglycosides** (if use as mono-therapy) have limited clinical effectiveness for certain infections:
  - Pneumonia: as they have poor penetration in infected airway;
  - Abscess: as activity is diminished in acid conditions
- **Nitrofurantoin**: An excellent alternatives for ESBL+ UTI, however, can be used for UTL only as only urine can achieve adequate drug level for clinical effectiveness.

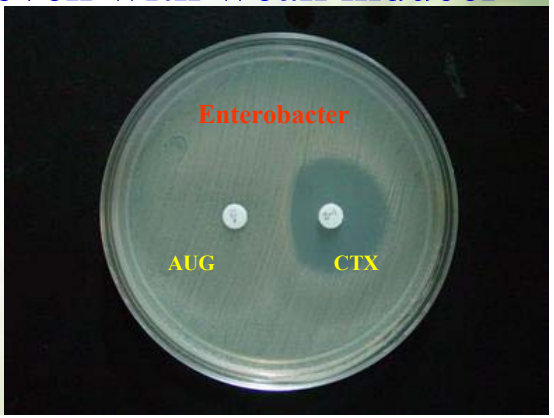
Resistance mechanism: 1. What is ICBL/AmpC

Inducible Enterobacteriaceae

- Organisms with inducible Chromosomal β lactamases /AmpC β lactamases : Enterobacter, Serratia, Morganella morganii,Citrobacter freudii, Providencia Some Klebsiella, E.coli: Plasmid mediated AmpC β lactamases
- Points to notice :
  - (1) AmpC BL are **NOT** inhibited by β lactamase inhibitor
  - (2) AmpC BL has activity against Cephalosporins (1st, 2nd, 3rd gen but **NOT** Cefepime) & Penicillins
  - (3) Enzyme is induced by an inducer
    In vitro test may appear sensitive, especially for weak inducer

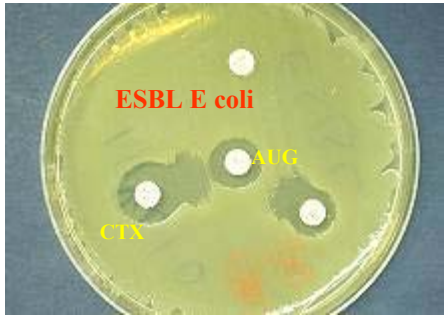
Strong inducer	Ampicillin, Clavulanic acid, Cefoxitin
Weak inducer	2nd, 3rd gen Cephalosporins, Pipericillin

  - (4) Derepressed mutant can be selected during therapy even with weak inducer
- Treatment option :
  - (1) β lactam: a) Carbapenems, b) Cefepime (4th gen.)
  - (2) Non-β lactam : e.g. Quinolone, Aminoglycoside



Phenotypic test suggests presence of AmpC beta-lactamase. Resistance may develop during prolonged therapy with 3rd generation cephalosporins

2. ESBL: Do all infections caused by ESBL-producing organisms require carbapenems?



For **severe infection** with a high bacterial load, e.g. bacteremia, or in sequestered site, e.g. inadequately drained loculated intra-abdominal abscesses, **carbapenems are considered to be the treatment of choice**

β lactam/ β lactamase inhibitor combination drugs are excellent alternatives for most of the milder and uncomplicated infections. e.g. Augmentin, it is highly concentrated in urine and its excellent bioavailability (~80%) allows outpatient treatment. In addition, with anaerobic coverage, it is particular useful to treat polymicrobial infections such as bite wounds and diabetic foot infections.

For deep seated infection or serious infections, although β lactam/ lactamase inhibitor combination drugs are generally not suggested as they may be subject to the inoculum effect in case of high bacterial load, we don't have to step up to carbapenem in all cases if the clinical responses to the empirical treatment are good.

- **Fluoroquinolones**, similarly, have excellent bioavailability (70-90%), and in addition to attaining high level in urine, penetrate prostate tissue well. If being tested sensitive in-vitro, they are considered as alternatives in the treatment of bacteremia and pneumonia caused by ESBL producing organisms.
- Other options for uncomplicated UTI include **Septrin** and **Nitrofurantoin**. Considering that E coli remains highly susceptible to **Nitrofurantoin (PMH data: over 95% sensitive) and its good bioavailability (80%), it should be given as first line empirical treatment for most uncomplicated UTI, except in patients with renal impairment** as reduced urinary excretion would result in sub-therapeutic urine concentration.
- Concerning newer options, such as **tigecycline**, clinical data is still lacking. Moreover, bearing in mind of its low urinary excretion (only 10-15%), its bacteriostatic property and low serum concentration, its role in treating infections caused by ESBL producers is rather limited.

Meropenem(MER) Vs Imipenem(IMI)

Meropenem is the better choice as imipenem is less effective and has much greater chance of seizure?

FDA label: MER: Overall seizure rate being 0.7%.

IMI: Possibly, probably, or definitely related: 0.4%

Imipenem is the **more cost effective choice** of carbapenem with the following exceptions:

- Impair renal function: ≤20mL/min/1.73 m2
- Patients with CNS disorders (e.g., brain lesions or history of seizures)
- Patients on hemodialysis
- Patients (especially paediatric) with CNS infections

Remark: Close adherence to the dosing guidelines for Imipenem needed

Antibiotics S% / Organisms	MEM	IPM
Ps. Aeruginosa	98	98
E-coli	100	100
Klebsiella	100	100
Proteus	100	100
Enterobacter	100	100
Acinetobacter	62	67

Tienam	IV	500 mg Q8H	234
	IV	500 mg Q6H	312
Meropenem	IV	500 mg Q8H	397.14
	IV	1 g Q8H	609.6

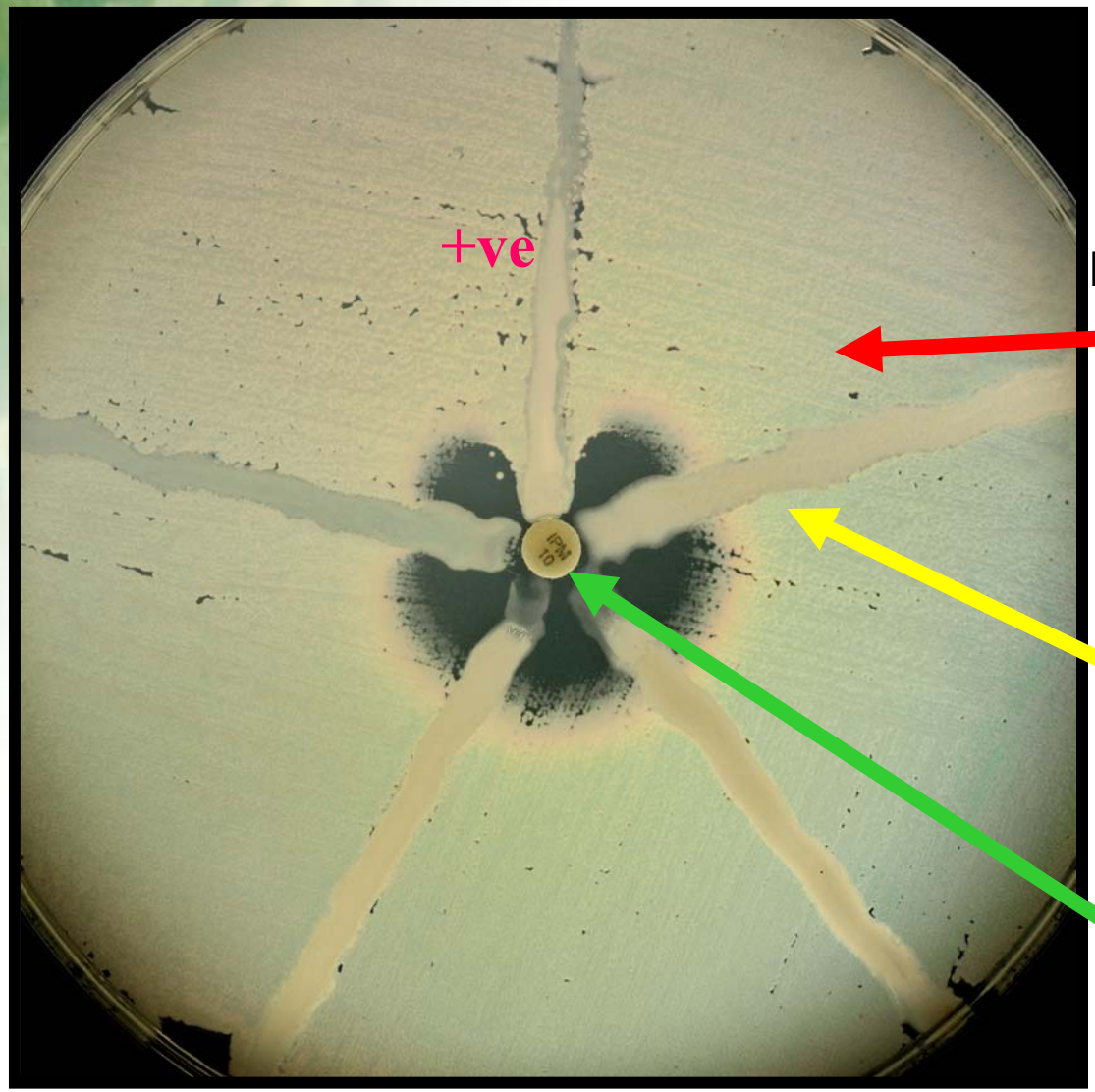
3. Klebsiella Pneumoniae Carbapenemase (KPC)

- KPC is a class A β-lactamase
  - Confers resistance to all β-lactams including extended-spectrum cephalosporins and **carbapenems**
- Occurs in Enterobacteriaceae
  - Most commonly in *Klebsiella pneumoniae*
  - Also reported in: *K. oxytoca*, *Citrobacter freundii*, *Enterobacter* spp., *Escherichia coli*, *Salmonella* spp., *Serratia* spp.,
- Also reported in *Pseudomonas aeruginosa* (Columbia)
- Treatment options: Colistin (nephrotoxic) and tigecycline (low blood level)

When to Suspect a KPC-Producer

- Enterobacteriaceae – especially *Klebsiella pneumoniae* that are resistant to extended-spectrum cephalosporins:
  - MIC range for 151 KPC-producing isolates
    - Ceftazidime 32 to >64 μg/ml
    - Ceftriaxone ≥ 64 μg/ml
    - Cefotaxime ≥ 64 μg/ml
  - Variable susceptibility to cefoxitin and cefepime

Modified Hodge Test



Lawn of *E. coli* ATCC 25922
1:10 dilution of a
0.5 McFarland suspension

Test isolates

Imipenem disk

Described by Lee et al. CMI, 7, 88-102. 2001.

Common fallacies about use of antibiotics

Fallacy 1: Big guns are required for all cases of neutropenic fever

IDSA

2002 Guidelines for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer

Table 3. Factors that favor a low risk for severe infection among patients with neutropenia.

Absolute neutrophil count of ⩾100 cells/mm^3
Absolute monocyte count of ⩾100 cells/mm^3
Normal findings on a chest radiograph
Nearly normal results of hepatic and renal function tests
Duration of neutropenia of <7 days
Resolution of neutropenia expected in <10 days
No intravenous catheter–site infection
Early evidence of bone marrow recovery
Malignancy in remission
Peak temperature of <39.0°C
No neurological or mental changes
No appearance of illness
No abdominal pain
No comorbidity complications[a]

NOTE. Data are adapted from [4, 42–49, 51–53].

[a] Concomitant condition of significance (e.g., shock, hypoxia, pneumonia or other deep-organ infection, vomiting, or diarrhea).

Table 4. Scoring index for identification of low-risk febrile neutropenic patients at time of presentation with fever.

Characteristic	Score
Extent of illness[a]	
No symptoms	5
Mild symptoms	5
Moderate symptoms	3
No hypotension	5
No chronic obstructive pulmonary disease	4
Solid tumor or no fungal infection	4
No dehydration	3
Outpatient at onset of fever	3
Age <60 years[b]	2

NOTE. Highest theoretical score is 26. A risk index score of ⩾21 indicates that the patient is likely to be at low risk for complications and morbidity. The scoring system is derived from [50].

[a] Choose 1 item only.

[b] Does not apply to patients ⩽16 years of age. Initial monocyte count of ⩾100 cells/mm^3, no comorbidity, and normal chest radiograph findings indicate children at low risk for significant bacterial infections [46].

CID 2002:34 (15 March)

2002 Guidelines for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer

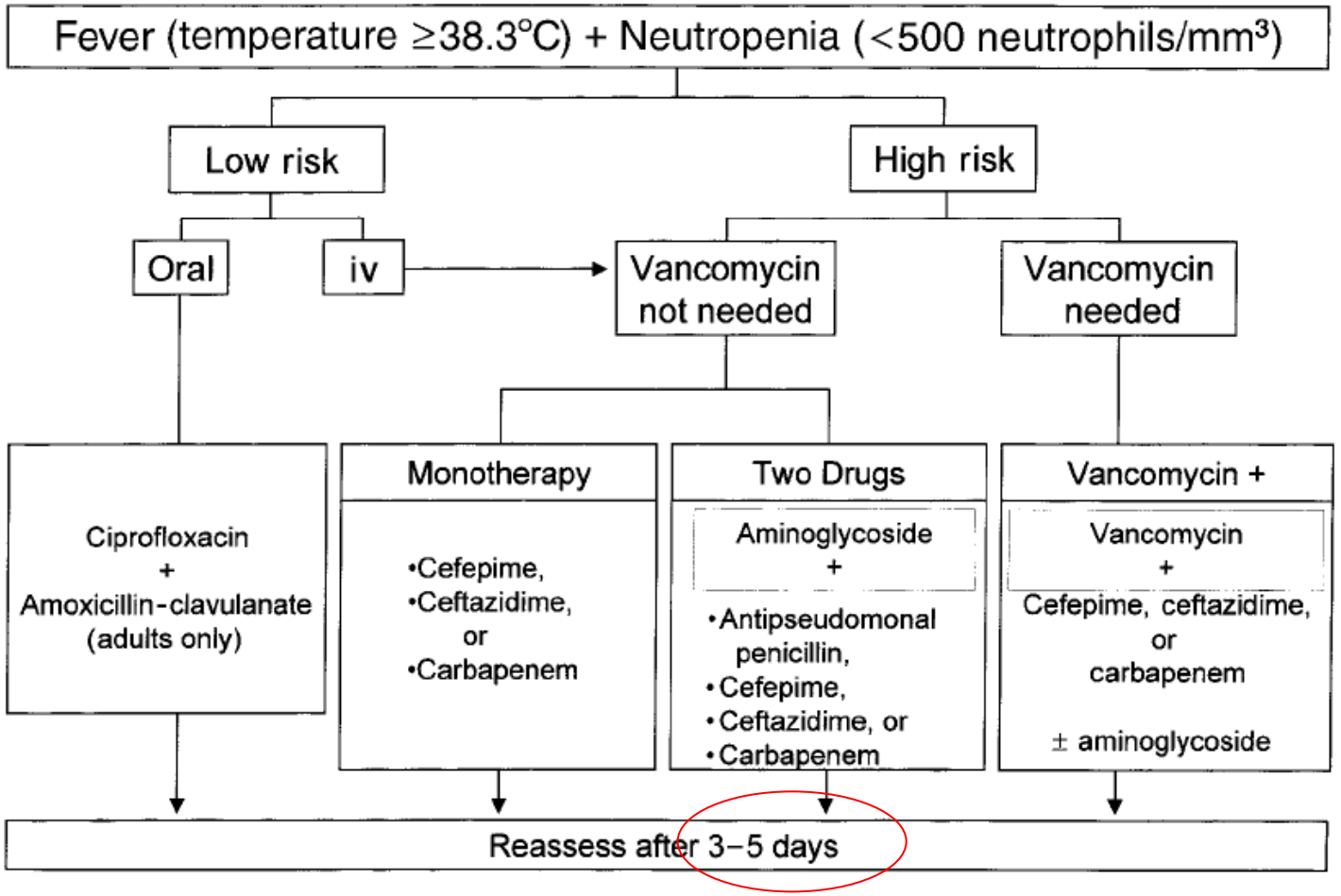


Figure 1. Algorithm for initial management of febrile neutropenic patients. See tables 3 and 4 for rating system for patients at low risk. Carbapenem, imipenem or meropenem.

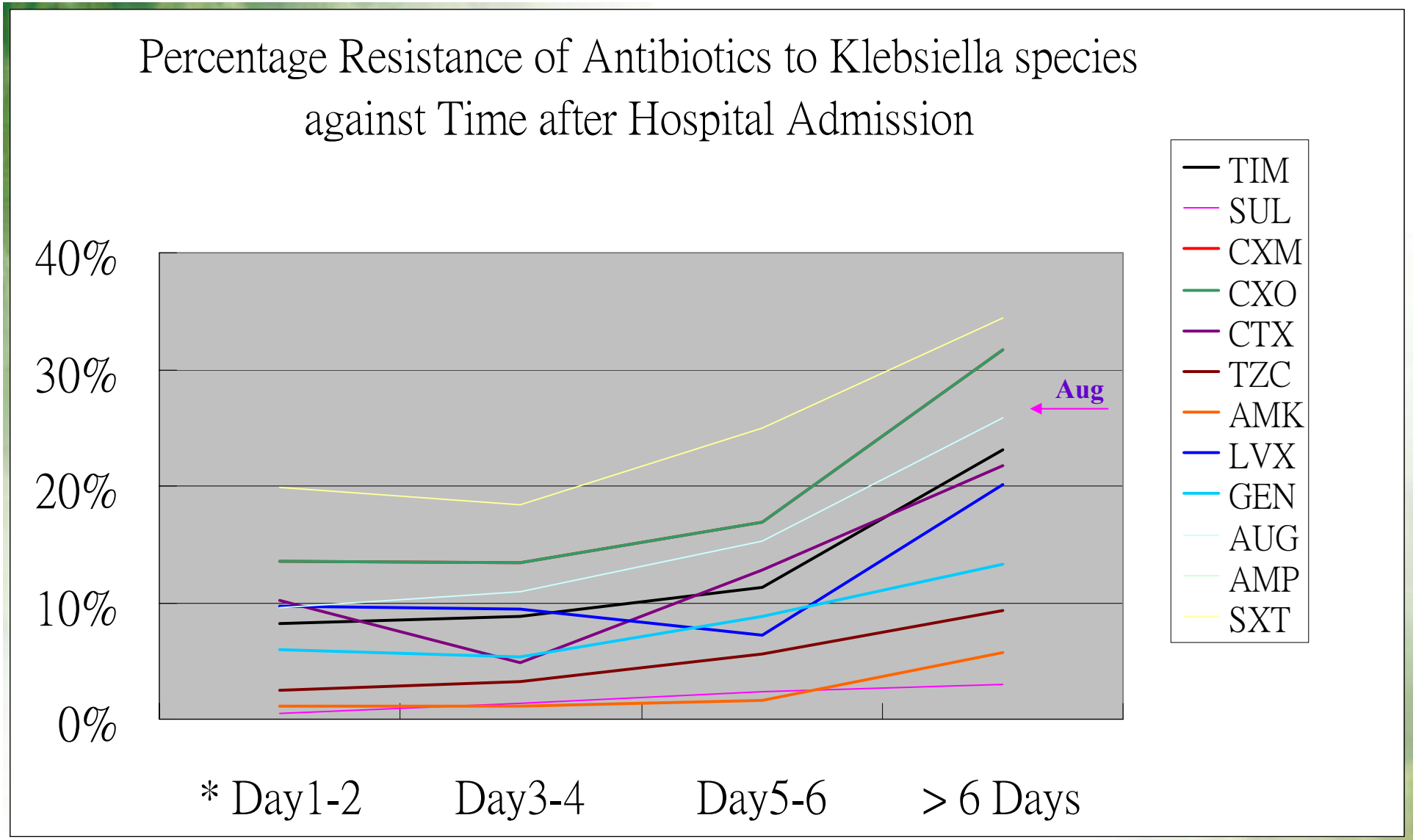
CID 2002:34 (15 March)

Fallacy 2: Big guns are required for all cases of hospital acquired pneumonia

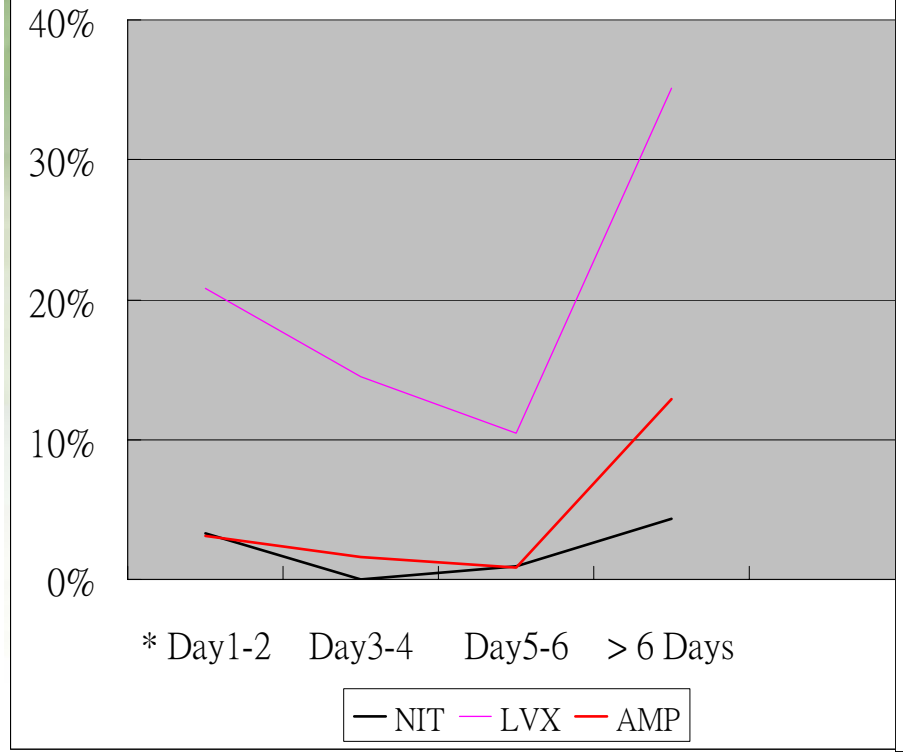
For patients with early-onset infections (fewer than 5 days following admission to hospital) who have not previously received antibiotics and in the absence of other risk factors, the use of co-amoxiclav or cefuroxime would be appropriate.

For patients with early-onset infections (fewer than 5 days following admission to hospital) who have recently received antibiotics and/or who have other risk factors, a third-generation cephalosporin (cefotaxime or ceftriaxone), a fluoroquinolone or piperacillin/tazobactam would be appropriate.

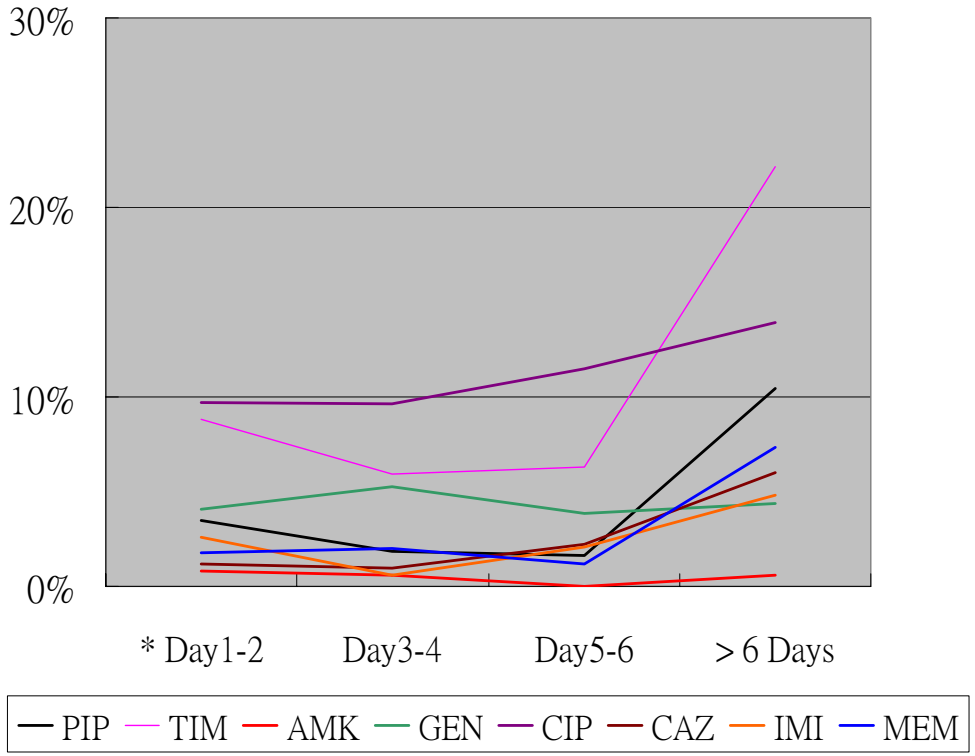
Report of the Working Party on Hospital-Acquired Pneumonia of the British Society for Antimicrobial Chemotherapy. Journal of Antimicrobial Chemotherapy (2008) 62, 5–34

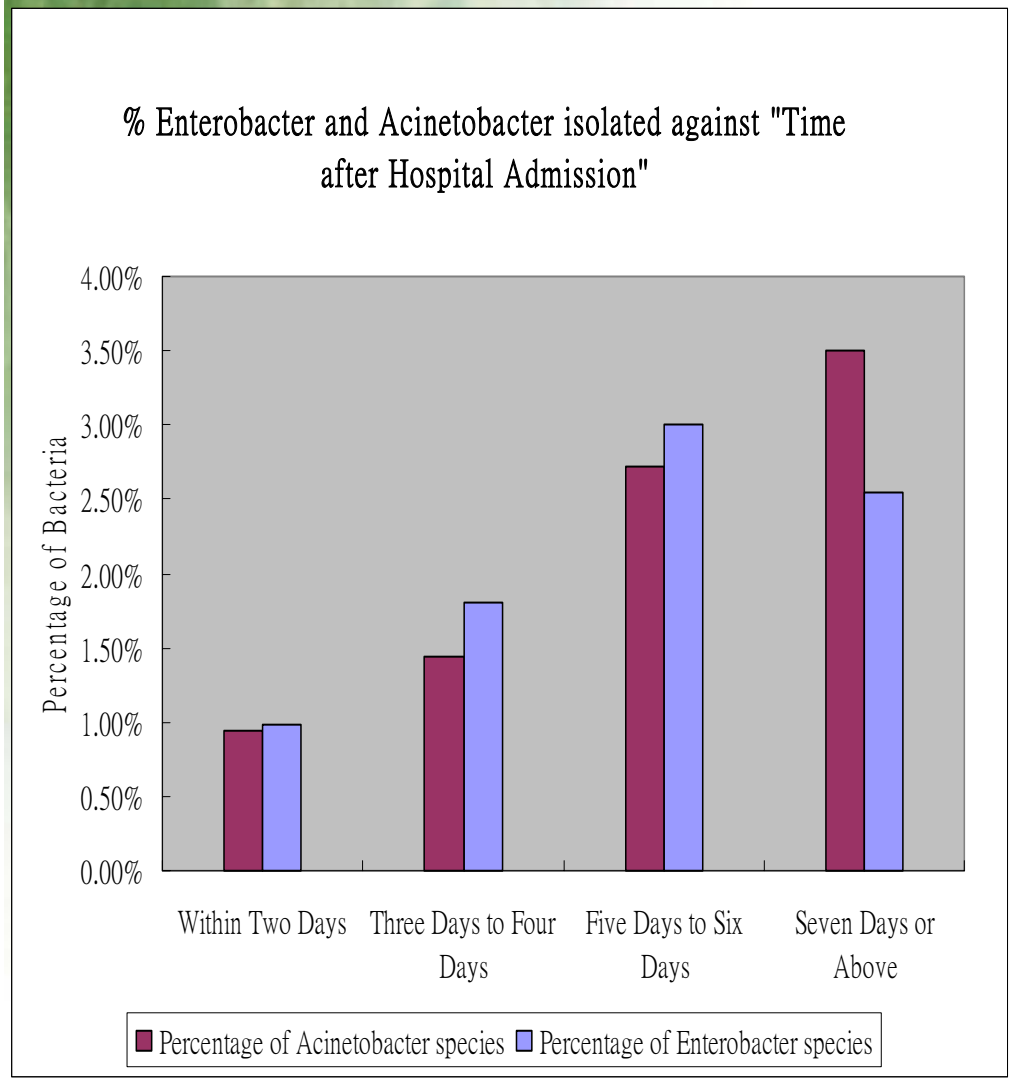

Percentage Resistance of Antibiotics to Klebsiella species against Time after Hospital Admission
40%
30%
20%
10%
0%
Aug
TIM
SUL
CXM
CXO
CTX
TZC
AMK
LVX
GEN
AUG
AMP
SXT
* Day1-2
Day3-4
Day5-6
> 6 Days

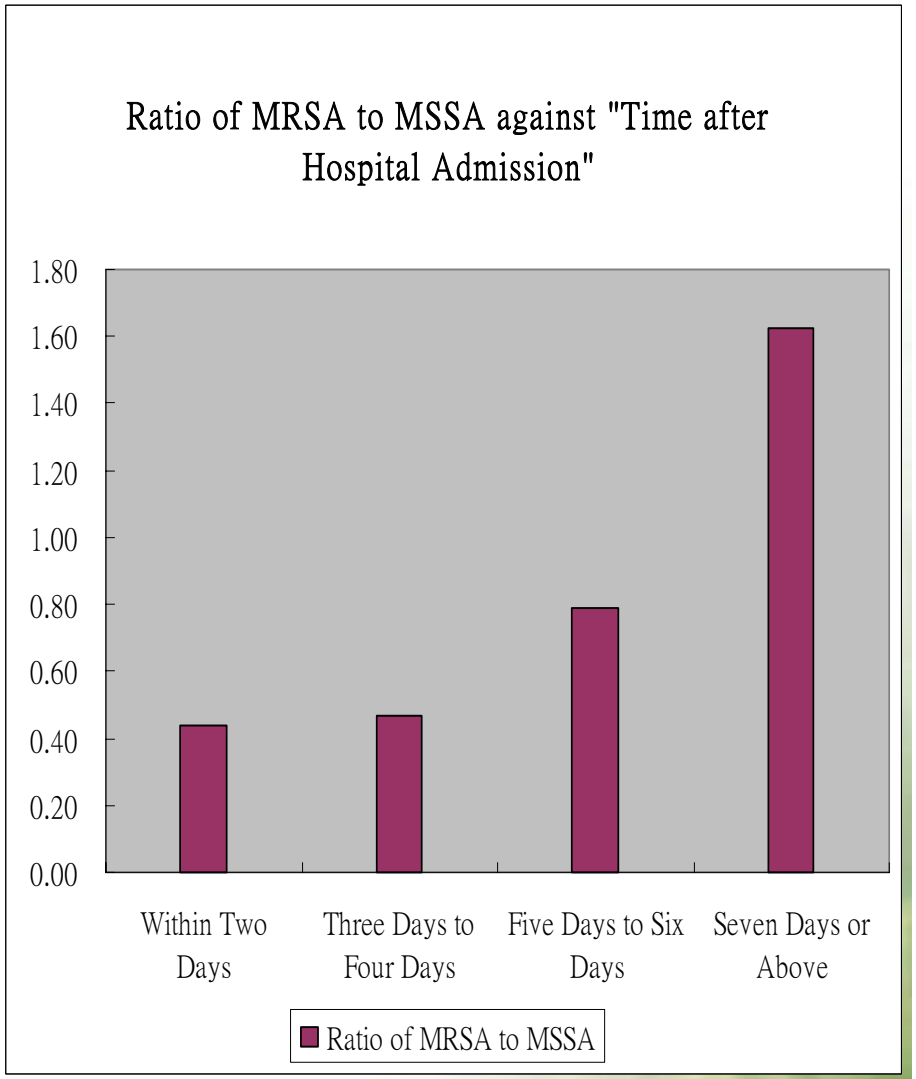
Percentage Resistance of Antibiotics to Enterococci against Time after Hospital Admission



Percentage Resistance of Antibiotics to Pseudomonas aeruginosa against Time after Hospital Admission




% Enterobacter and Acinetobacter isolated against "Time after Hospital Admission"
Percentage of Bacteria
4.00%
3.50%
3.00%
2.50%
2.00%
1.50%
1.00%
0.50%
0.00%
Within Two Days
Three Days to Four Days
Five Days to Six Days
Seven Days or Above
Percentage of Acinetobacter species
Percentage of Enterobacter species


Ratio of MRSA to MSSA against "Time after Hospital Admission"
1.80
1.60
1.40
1.20
1.00
0.80
0.60
0.40
0.20
0.00
Within Two Days
Three Days to Four Days
Five Days to Six Days
Seven Days or Above
Ratio of MRSA to MSSA

In most instances:

- Early onset (within 4-5 days) HAP: Augmentin, Ceftriaxone
- Late onset HAP:
  - No recent antibiotics exposure and,
  - Clinically stable
    - ➢ Consider Augmentin, Ceftriaxone

Fallacy 3: Don't change a winning team & big guns are always more effective than 1st line antibiotics

Streamline the antibiotics when laboratory result available

The patient should be reassessed at 48–72 h and antibiotic therapy should be de-escalated based on the micro-biological results and clinical response. De-escalation includes changing from the broad-spectrum antibiotic to an agent with a narrow focus, based on the culture data; changing the focus from multiple antibiotics to a single drug; and shortening the course of therapy to 5 days in cases with negative culture results and $\geq$ 48 h without fever.

EUROPEAN RESPIRATORY REVIEW2007; 16: 103, 33–39

able 3

ffectiveness and mortality analyses for each treatment group as defined per bacteriologic documentation (visit 2)

Crit Care. 2006; 10(3): R78

	Group I	Group II	Group III	Group IV	Group V	Overall
Effectiveness response rates						
Modified intention-to-treat population	(*n* = 113)	(*n* = 14)	(*n* = 38)	(*n* = 56)	(*n* = 23)	(*n* = 244)
End of therapy (visit 3) (%)	81.4	78.6	68.4	75.0	56.5	75.4
Final evaluation (visit 4) (%)	54.0	64.3	44.7	50.0	34.8	50.4
Patient-evaluable population	(*n* = 100)	(*n* = 11)	(*n* = 36)	(*n* = 48)	(*n* = 18)	(*n* = 213)
Final evaluation (visit 4) (%)	61.0	81.8	47.2	58.3	44.4	57.7
Mortality rates						
Patient-evaluable population	(*n* = 100)	(*n* = 11)	(*n* = 36)	(*n* = 48)	(*n* = 18)	(*n* = 213)
Overall mortality (%)	19.0	18.2	25.0	14.6	33.3	20.2
Nosocomial pneumonia-attributable mortality (%)	15.0	9.1	8.3	8.3	33.3	13.6

Forward stepwise logistic regression analysis (cut-off *P* value of 0.05) was used to determine the relationship between mortality and independent baseline variables previously identified in univariate analyses ($P < 0.05$), including: age, mechanical ventilation, Acute Physiology, Age, and Chronic Health Evaluation (APACHE) II score, treatment group, and adequacy of initial empiric therapy. Group I, patients with an unknown aetiology and unmodified therapy; Group II, patients with resistant organisms, who had unmodified therapy; **Group III, patients with susceptible organisms, who had unmodified therapy; Group IV, patients who had susceptible organisms and whose therapy was modified accordingly**; and Group V, patients who initially received inadequate antibiotic therapy, which was later modified on the basis of cultures

Spectrum VS Effectiveness

Example 1: Cloxacillin VS Cefuroxime (Zinnat)

	Cloxacillin	Cefuroxime
Coverage	S. aureus	Strept., S. aureus, Gram negative bacilli
MIC 90 (S. aureus)	1 μg/ml	4 μg/ml

Spectrum : Cefuroxime > Cloxacillin

Activity against S. aureus: Cefuroxime < cloxacillin

Example 2: Augmentin vs Tazocin

	Augmentin	Tazocin
Coverage	MSSA, enterobacteriacea,	MSSA, ESBL, enterobacteriacea, Pseudomonas
MIC50 (E.coli) (Break point)	2 μg/ml 8 μg/ml	4 μg/ml 16 μg/ml

Spectrum : Tazocin > Augmentin

Activity against E.coli: Tazocin = Augmentin

Fallacy 4: Step up antibiotics immediately when there is no clinical response

Clinical response do take time!

"Receipt of antibiotic treatment for at least 3–5 days is usually required to determine efficacy of the initial regimen." **CID 2002:34 (15 March)**

- **Early switch in deteriorating life threatening diseases**
- **Sepsis workup before you step up your antibiotics!**

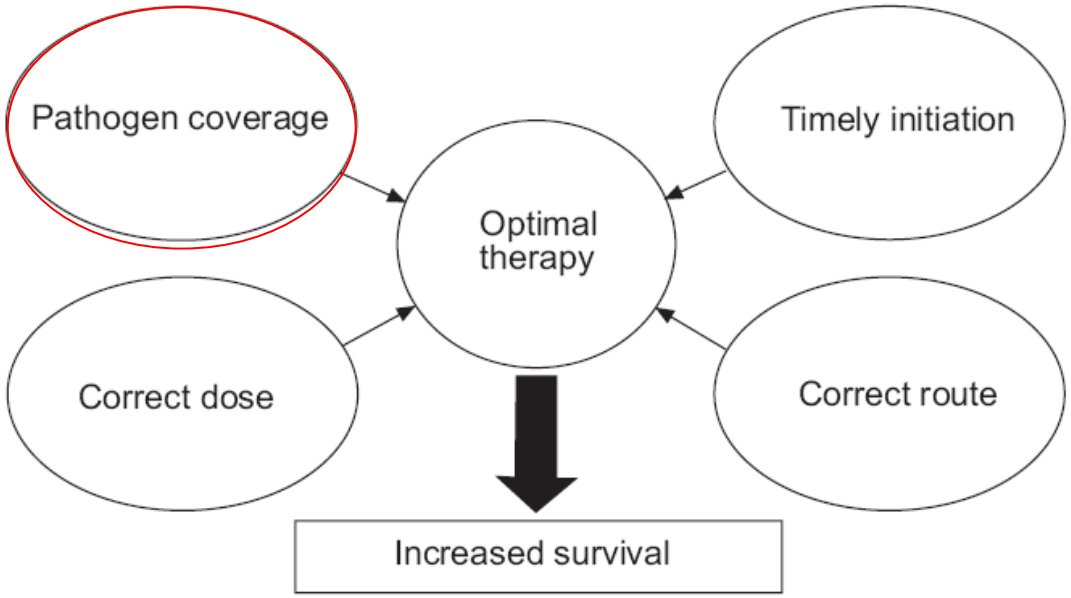


FIGURE 2. Factors involved in optimal initial antibiotic therapy.

Pathogen coverage is just one of the factors that determine the clinical response of a treatment regimen.

Other causes of appearance failure

- Treating colonization
- Inadequate tissue level
- Penetration problems: Undrained abscess; foreign bodies
- Non-infective diseases, e.g, adult still, SLE,…
- Non-bacterial infection: viral, fungal.
- Drug fever

We should determine the causes instead of routinely adding/changing antibiotics!

Fallacy 5: Culture report interpretation:
i: Treatment is required for all positive culture;
ii: Persistence positive culture = Treatment failure →
Prolong treatment or stepping up antibiotics

Colonization/contamination:

- Treatment are not required for colonization/ contamination.
- Even in doubt, sepsis work up before empirical Tx.
- Duration/ Effectiveness of treatment should base on clinical response but not culture result for some infections as most antibiotics are not good for eradicating colonizers.

Fact or Fallacy?
Allergy means whole class of antibiotics cannot be used

If the reaction is an allergy or side effect? Vancomycin: infusion related reaction

If the rash is MP rash or urticaria rash?

For type I hypersensitivity:

1. Skin testing: Highly accurate for the identification of penicillin allergy but false negative result may be obtained for other antibiotics. (NA)
2. Whole class should be avoid unless in life threatening situation with no other alternatives.
3. Drug desensitization & ICU monitoring required when use of B-lactam.

   Oral desensitization appears to have fewer reactions and the starting dose should be very small, usually 1/10,000 of the therapeutic dose. The dose is then doubled every 15 minutes till the full therapeutic dose is achieved.

For non-type I allergy: May try cephalosporins with a **test dose*** with close monitoring and documentation when there is no alternatives.

***Test dose challenge** might be done by using 1/100 of the therapeutic dose followed by 1/10 of the dose and then the full therapeutic dose if there is no reaction.

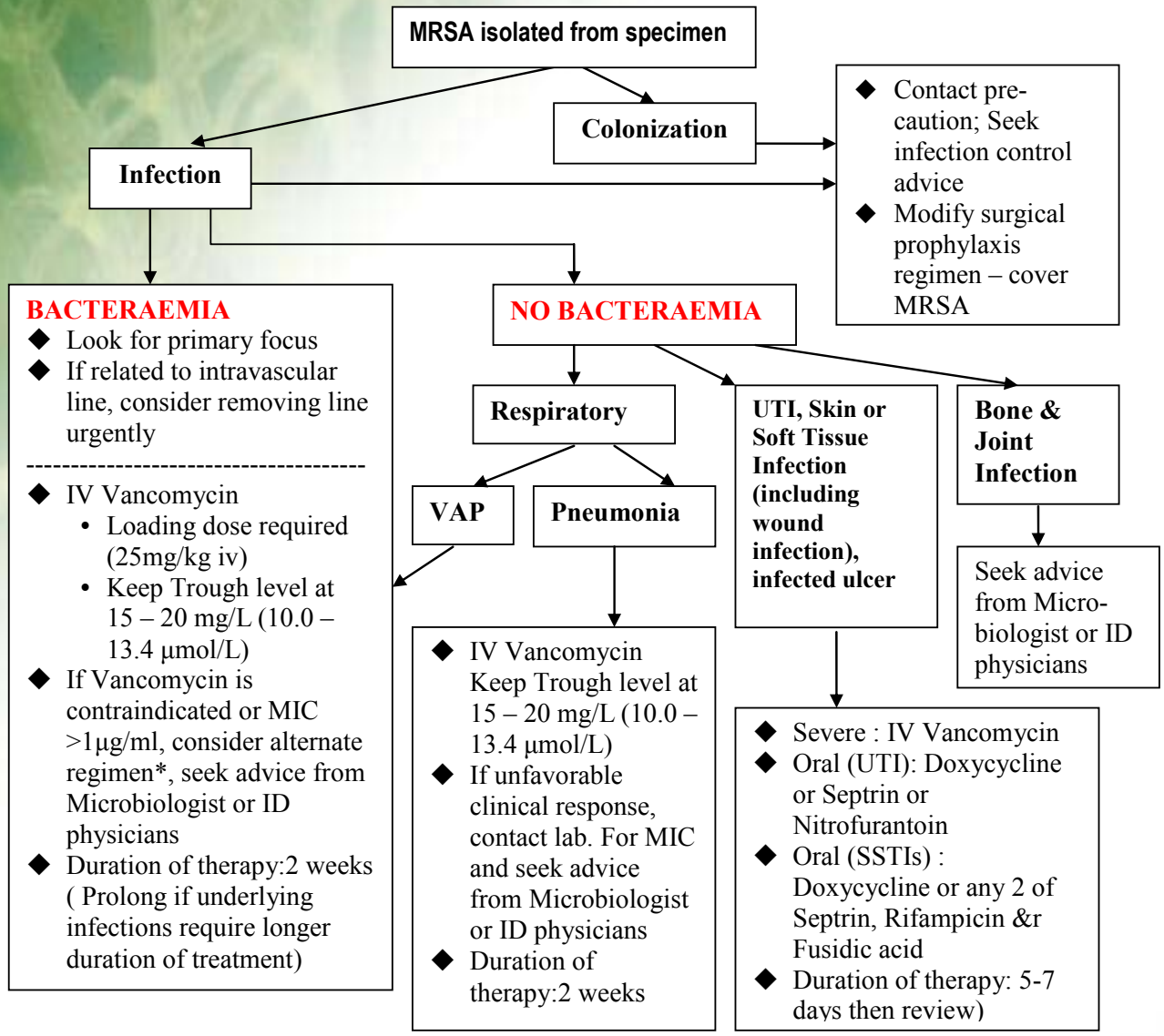
Clearly describe the case whenever you label a drug allergy history of a patient

Treatment of specific organisms

- S. pneumoniae
- ICBL
- ESBL
- KPC
- **MRSA**
- **Acinetobacter**

MRSA TREATMENT PROTOCOL

(Modified from recommendations of the BSAC Guidelines 2005 & 2008 www.bsac.org.uk)



Colonisation: MRSA is present in or on a body site but no clinical signs or symptoms of illness or infection are present.
Infection: Isolation of an organism accompanied by clinical signs of illness or sepsis, eg fever, inflammation, increase WCC, etc.

***Alternate regimens**: Linezolid, Daptomycin (Not for Pneumonia)
Combination treatment: Vancomycin + Septrin/ Rifampicin / Fusidic acid

Antimicrobial Subcommittee, KWC April 10

Use of vancomycin

Early reports of "vancomycin nephrotoxicity" were apparently related to the impurities in the solution and not to vancomycin per se. Therefore, **impaired renal function is not a contraindication of using vancomycin although we have to adjust the dose of vancomycin for patients with renal insufficiency.**

Common misconception: "step up" to vancomycin if the clinically response of MSSA is poor after treating with cloxacillin.
However, if we compare the pharmacokinetic properties and bactericidal activities of these 2 drugs, **cloxacillin is the preferred drug than vancomycin for MSSA infection.** Therefore, if the clinical response of cloxacillin is not good, we may consider other reasons.

Drug Monitoring:

1. **Vancomycin peaks have no clinical significance**
2. **Indications for vancomycin troughs:** (Trough levels should be obtained within 30 minutes before 4th dose of a new regimen or dosage change):
    1. Patients on continuous or intermittent hemodialysis
    2. Patients with unusually high volumes of distribution (e.g. morbid obesity, significant edema, burns)
    3. Initial and definitive therapy of suspected central nervous system infections, endocarditis,ventilator-associated pneumonia, bacteremia or osteomyelitis (Higher trough level needed)

Dosing:

Because of its large molecular size, vancomycin does not penetrate well into many tissues such as lung and bone. Therefore, **higher dose (15-20mg/kg Q8-12H)** of vancomycin may be required to achieve the **adequate trough level of 15 – 20 mg/L (10.0 – 13.4 μ mol/L))** for treating these infections. However, if the MIC of vancomycin is >2mcg/ml, we have to consider alternative therapy.

Acinetobacter

- Current guidelines for the treatment of *A. baumannii* VAP recommend combination therapy with a betalactam plus an aminoglycoside
- However, we start to see emergency of resistant.

2009 Hospital C

Antibiotics	% sensitive
Imipenem/meropenem	53
Tazocin	37
Levofloxacin	38
Septrin	50
Gentamicin	61
Amikacin	83
Sulparzon/unasyn	58

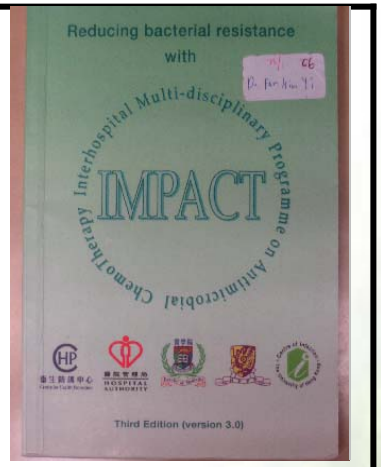
Treatment of Multidrug or pan-drug resistant Acinetobacter baumannii

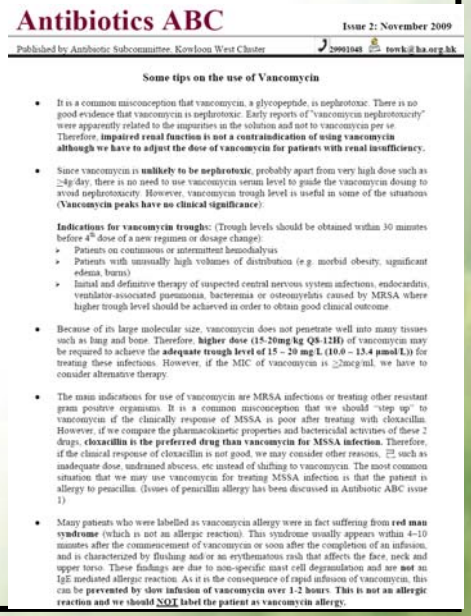
- No standard definition
- HA: concomitant resistant (not including Intermediate resistant) to all the following classes: Fluoroquinolones, Aminoglycosides, Cephalosporins, & Beta-lactam /beta-lactamase inhibitor combinations. Carbapenems are not included in the MDRA criteria.
- High dose of Sulbactam: 4g/day or even higher (8g/d *(Pharmacotherapy. 2002;22(4))*)??
- Colistin +/- rifampicin or amikacin
  - main adverse effects of colistin are nephrotoxicity (acutetubular necrosis) and neurotoxicity
- Tigecycline

Rational use of antibiotics

Antibiotics stewardship program (ASP)

- **Administrative Control**
  1. Drug Formulary
  2. Restricted prescription
  3. Autostop system
  4. Restricted reporting
- **Surveillance**
  1. Antimicrobial susceptibility
  2. Antibiotics consumption
- **Audit: HA** – 7 Big gun
  1. Drug order form
  2. Immediate concurrent feedback
- **Guidelines**
  1. Update
  2. User agreement
- **Education**
  1. Talk
  2. Forum,
  3. Newsletter




Antibiotics ABC

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Some tips on the use of Vancomycin

- It is a common misconception that vancomycin, a glycopeptide, is nephrotoxic. There is no good evidence that vancomycin is nephrotoxic. Early reports of "vancomycin nephrotoxicity" were apparently related to the impurities in the solution and not to vancomycin per se. Therefore, **impaired renal function is not a contraindication of using vancomycin although we have to adjust the dose of vancomycin for patients with renal insufficiency.**
- Since vancomycin is **unlikely to be nephrotoxic**, probably apart from very high dose such as ≥4g/day, there is no need to use vancomycin serum level to guide the vancomycin dosing to avoid nephrotoxicity. However, vancomycin trough level is useful in some of the situations (**Vancomycin peaks have no clinical significance**):

  Indications for vancomycin troughs: (Trough levels should be obtained within 30 minutes before 4th dose of a new regimen or dosage change):
  - Patients on continuous or intermittent hemodialysis
  - Patients with unusually high volumes of distribution (e.g. morbid obesity, significant edema, burns)
  - Initial and definitive therapy of suspected central nervous system infections, endocarditis, ventilator-associated pneumonia, bacteremia or osteomyelitis caused by MRSA where higher trough level should be achieved in order to obtain good clinical outcome.
- Because of its large molecular size, vancomycin does not penetrate well into many tissues such as lung and bone. Therefore, **higher dose (15-20mg/kg Q8-12H)** of vancomycin may be required to achieve the **adequate trough level of 15 – 20 mg/L (10.0 – 13.4 μmol/L))** for treating these infections. However, if the MIC of vancomycin is ≥2mcg/ml, we have to consider alternative therapy.
- The main indications for use of vancomycin are MRSA infections or treating other resistant gram positive organisms. It is a common misconception that we should "step up" to vancomycin if the clinically response of MSSA is poor after treating with cloxacillin. However, if we compare the pharmacokinetic properties and bactericidal activities of these 2 drugs, **cloxacillin is the preferred drug than vancomycin for MSSA infection.** Therefore, if the clinical response of cloxacillin is not good, we may consider other reasons, such as inadequate dose, undrained abscess, etc instead of shifting to vancomycin. The most common situation that we may use vancomycin for treating MSSA infection is that the patient is allergy to penicillin. (Issues of penicillin allergy has been discussed in Antibiotic ABC issue 1)
- Many patients who were labelled as vancomycin allergy were in fact suffering from **red man syndrome** (which is not an allergic reaction). This syndrome usually appears within 4–10 minutes after the commencement of vancomycin or soon after the completion of an infusion, and is characterized by flushing and/or an erythematous rash that affects the face, neck and upper torso. These findings are due to non-specific mast cell degranulation and are **not** an IgE mediated allergic reaction. As it is the consequence of rapid infusion of vancomycin, this can be **prevented by slow infusion of vancomycin over 1-2 hours**. **This is not an allergic reaction and we should NOT label the patient as vancomycin allergy.**

Microbiology Lab. Support

- Streptococcus pneumoniae, M.I.C. of Penicillin : 2 ug/ml
  Suggested doses for adults with normal renal function:
  Amoxicillin 1g TDS or equivalent
- ESBL producing strains are clinically resistant to all Cephalosporins and Aztreonam.
- Phenotypic test suggests presence of AmpC beta-lactamase. Resistance may develop during prolonged therapy with 3rd generation cephalosporins.
- For Enterococcal infection, cephalosporins, clindamycin and trimethoprim- sulfamethoxazole (Septrin) are not effective clinically.
- Coagulase negative Staphylococci is probably a contaminant.
- Oropharyngeal contamination. Suggest repeat if clinically indicated.
- For CSU, treatment needed only if patient has symptoms.
- Multi-resistant organism isolated, please perform "CONTACT ISOLATION" to prevent spreading of the organism.

Conclusion

Aim: To optimize selection & use of antibiotics so that:

- Emergence and spread of antibiotic resistance can be controlled and hospital costs can be reduced
- To achieve best clinical outcomes, with minimal toxicity to the patient.
- NOT to restrict the autonomy of doctor-in-charge

Microbiology / ID consultation

Concurrent feedback

Welcome!

Thank You

Question?

Table 3. Number of cases and national estimates of the rate of emergency department (ED) visits for adverse events associated with a single systemic antibiotic class, by adverse event condition—United States, 2004–2006.

	Adverse event condition									
	Moderate-to-severe allergic reaction[b]		Neurologic and/or psychiatric		Gastrointestinal		Mild allergic reaction[c]		Other or unspecified effect	
Drug class[a]	No. of cases	Estimated no. of ED visits per 10,000 OPV (95% CI)	No. of cases	Estimated no. of ED visits per 10,000 OPV (95% CI)	No. of cases	Estimated no. of ED visits per 10,000 OPV (95% CI)	No. of cases	Estimated no. of ED visits per 10,000 OPV (95% CI)	No. of cases	Estimated no. of ED visits per 10,000 OPV (95% CI)
Penicillins	420	2.2 (1.7–2.7)	66	0.4 (0.3–0.6)	212	1.1 (0.6–1.6)	1528	7.6 (6.0–9.1)	175	0.7 (0.4–0.9)
Cephalosporins	184	1.3 (0.9–1.7)	39	0.3 (0.2–0.5)	88	0.7 (0.3–1.0)	357	2.8 (2.0–3.5)	58	0.4 (0.2–0.6)
Fluoroquinolones	212	2.4 (1.8–3.1)	100	1.2 (0.9–1.6)	83	1.1 (0.6–1.5)	228	2.8 (1.9–3.7)	75	0.7 (0.4–0.9)
Sulfonamides and trimethoprim	163	4.3 (2.9–5.8)	55	1.7 (0.9–2.4)	61	2.0 (0.8–3.1)	355	8.3 (5.8–10.7)	57	1.2 (0.6–1.9)
Macrolides and ketolides	120	1.1 (0.7–1.4)	39	0.3 (0.2–0.4)	111	1.0 (0.6–1.4)	190	1.7 (1.2–2.2)	59	0.4 (0.3–0.6)
Lincosamides (clindamycin)	32	2.8 (1.3–4.2)	11	…	34	3.0 (1.5–4.6)	80	8.4 (5.1–11.7)	18	…
Tetracyclines	38	1.2 (0.6–1.8)	11	…	28	0.7 (0.4–1.0)	66	2.0 (1.3–2.6)	22	0.4 (0.2–0.6)
All other antibiotic classes[d]	80	1.9 (1.2–2.7)	52	1.4 (0.8–1.9)	66	1.7 (0.9–2.4)	171	4.0 (2.9–5.1)	58	1.2 (0.6–0.8)

NOTE. Estimates of the number of adverse events are based on the National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance project (2004–2006). Estimates of the number of outpatient prescription visits (OPV) are based on the National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey (2004–2005). Adverse events were categorized into 1 condition. Adverse event conditions are mutually exclusive and were assigned hierarchically (left to right). For example, a case in which a patient experienced both a severe allergic reaction and gastrointestinal effects would be categorized as a moderate-to-severe allergic reaction.

[a] Only cases in which drugs from a single systemic antibiotic class were implicated in the adverse event are included (5802 cases). Estimates with coefficient of variation >30% or based on <20 cases were not calculated.

[b] Includes anaphylaxis, angioedema, erythema multiforme, exfoliative dermatitis, facial-pharyngeal-genital edema, hypersensitivity vasculitis, red man syndrome, respiratory distress or arrest, serum sickness, and Stevens-Johnson syndrome.

[c] Includes dermatitis, drug eruption, erythema, flushing, localized edema, pruritus, rash, rash morbilliform, and urticaria.

[d] Includes metronidazole, nitrofurans, vancomycin, linezolid, unspecified, and other antibiotic classes.

FDA approved labelling - Meropenem

- **Seizures** and other adverse CNS experiences have been reported during treatment with MERREM I.V.
- These experiences have occurred most commonly in patients with CNS disorders (e.g., brain lesions or history of seizures) or with bacterial meningitis and/or compromised renal function.
- During clinical investigations, 2904 immunocompetent adult patients were treated for non-CNS infections with the overall seizure rate being 0.7% (based on 20 patients with this adverse event). All meropenem-treated patients with seizures had pre-existing contributing factors. Among these are included prior history of seizures or CNS abnormality and concomitant medications with seizure potential. Dosage adjustment is recommended in patients with advanced age and/or reduced renal function.
- Close adherence to the recommended dosage regimens is urged, especially in patients with known factors that predispose to convulsive activity. Anticonvulsant therapy should be continued in patients with known seizure disorders. If focal tremors, myoclonus, or seizures occur, patients should be evaluated neurologically, placed on anticonvulsant therapy if not already instituted, and the dosage of MERREM I.V. re-examined to determine whether it should be decreased or the antibiotic discontinued.

FDA approved labelling – Imipenem-cilastatin

- **CNS adverse experiences** such as confusional states, myoclonic activity, and seizures have been reported during treatment with PRIMAXIN I.V., especially when recommended dosages were exceeded.
- These experiences have occurred most commonly in patients with CNS disorders (e.g., brain lesions or history of seizures) and/or compromised renal function.
- When recommended doses were exceeded, adult patients with creatinine clearances of ≤20mL/min/1.73 m2, whether or not undergoing hemodialysis, had a higher risk of seizure activity than those without impairment of renal function. Therefore, close adherence to the dosing guidelines for these patients is recommended.
- Patients with creatinine clearances of ≤5mL/min/1.73 m2 should not receive PRIMAXIN I.V. unless hemodialysis is instituted within 48 hours.
- For patients on hemodialysis, PRIMAXIN I.V. is recommended only when the benefit outweighs the potential risk of seizures.
- PRIMAXIN I.V. is not recommended in pediatric patients with CNS infections because of the risk of seizures.
- The most frequently reported systemic adverse clinical reactions that were reported as possibly, probably, or definitely related to PRIMAXIN I.V. were nausea (2.0%), diarrhea (1.8%), vomiting (1.5%),rash (0.9%), fever (0.5%), hypotension (0.4%), seizures (0.4%)