Appropriate Antimicrobial Use

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Principle

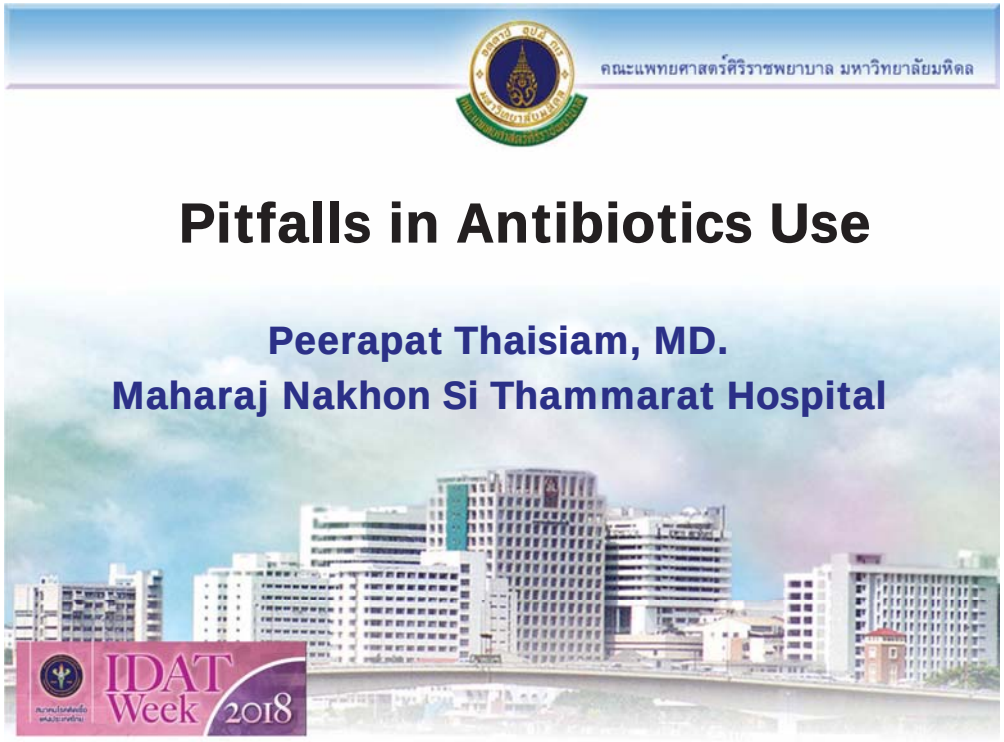
- Accurate diagnosis of infection
- Do not use ATB for colonizer or contaminant organism
- Microbiological investigation
- Likely causative agents
- Consider if ATB is needed
- Risk factors for resistant organisms
- Empiric ATB therapy vs. specific ATB therapy

Principle

- Urgency of initiating ATB
- Appropriate choice, dose, duration of ATB
- De-escalation/discontinuation of ATB when appropriate
- Source control and non-ATB therapy of infection

Principle of appropriate ATB use

- **Consideration of host**
- **Consideration of organisms**
- **Consideration of drugs**



Pitfalls in Antibiotics Use

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IDAT Week 2018

Outline

- Introduction
- Common pitfalls in antibiotics use
- Actions to optimize antibiotic prescribing

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Introduction

- A 47-year-old man
- No underlying disease
- Came to ER at 8.10 a.m.
- History
  - Fever with productive cough for 4 days
- Physical examination
  - BT 36.5 °C, PR 130/min, RR 40/min, BP 68/48 mmHg
  - Crepitation at right upper lung

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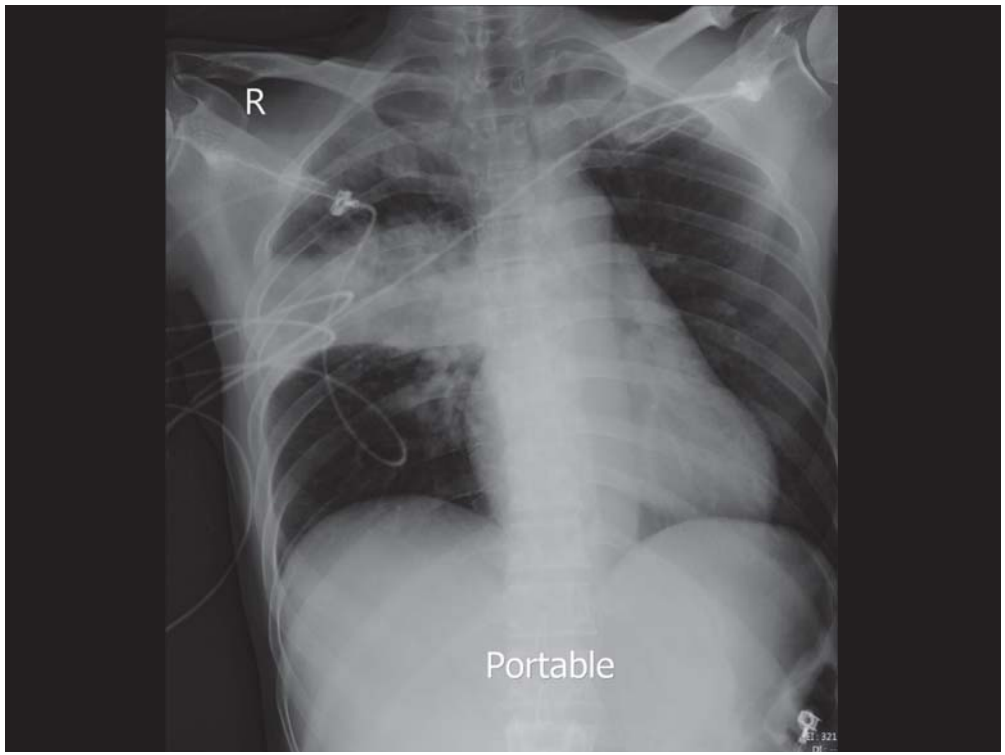
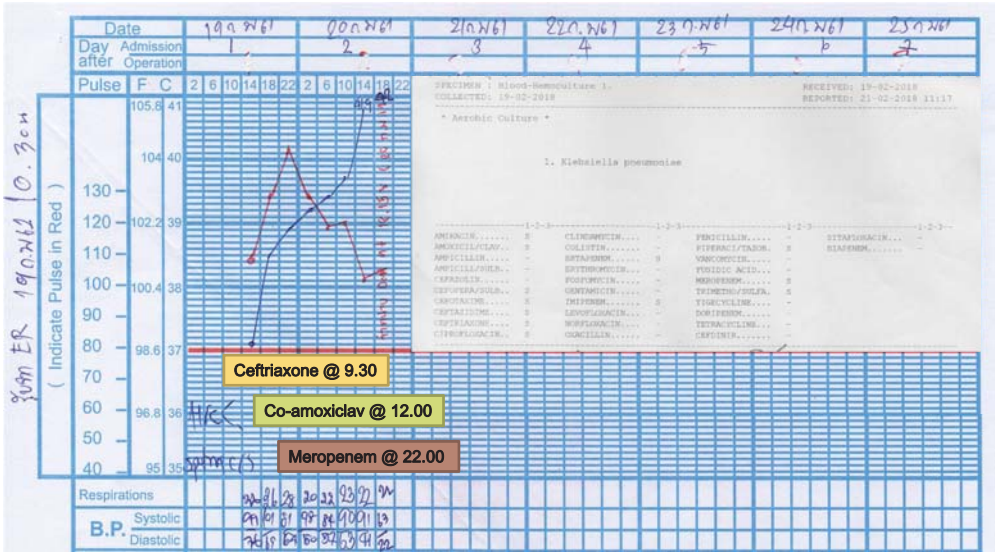
Introduction

- Investigation
  - Hb 13.7 g/dL, Hct 40.5%, WBC 1500/mm^3(N 54%), Platelet 59,000/mm^3
  - BUN 32 mg/dL, Cr 2.16 mg/dL
  - Chest X-ray as figure



Introduction

- Diagnosis
  - Lobar pneumonia with septic shock
- Treatment
  - Fluid resuscitation + norepinephrine
  - Empiric antibiotic: Ceftriaxone 2 g IV at 9.30 a.m.
  - Admit at 10.25 a.m.



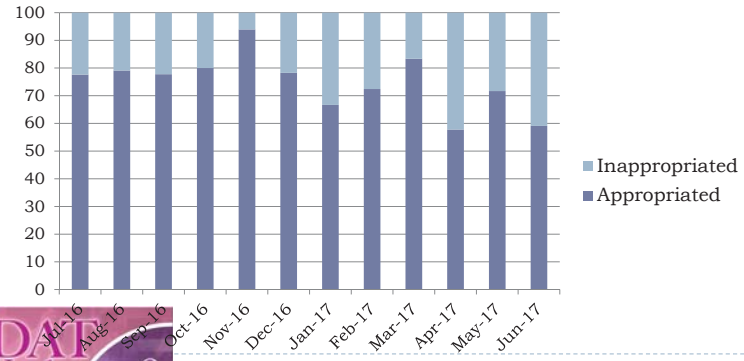
Introduction

- Inappropriate use of antibiotics
  - enhances the development of antibacterial resistance
  - undesirable side effects or toxicity
  - increased patient morbidity and mortality
  - increased hospital length of stay

Chest 1999; 115: 462–74.
Lancet 2005; 365: 579-87. Emerg Infect Dis 2000; 6: 552-6.

Introduction

- Drug Use Evaluation (DUE): Maharaj Nakhon Si Thammarat Hospital, 2016-2017
  - meropenem, imipenem, ertapenem, cefoperazone/ sulbactam, colistin, fosfomycin



Common pitfalls in antibiotics use

1) Prescribing antibiotics unnecessarily
2) Delaying administration of antibiotics
3) Spectrum: too narrow or too broad
4) Dose: too low or too high
5) Duration: too short or too long
6) Inappropriate antimicrobial for surgical prophylaxis and early post-operative fever

J Antimicrob Chemother 2011; 66: 2441-3.

1) Prescribing antibiotics unnecessarily

- Non-bacterial infection: URI and acute diarrhea

	Number (%)
Throat swab culture	
No	1,058 (85.2%)
Yes	183 (14.8%)
Group A streptococci	7 (3.8%)
Non-group A streptococci	7 (3.8%)
Normal throat flora	140 (76.6%)
No growth	5 (2.7%)
Rejected specimen	24 (13.1%)
Stool culture	
No	169 (80.5%)
Yes	41 (19.5%)
Salmonella group B	4 (9.8%)
Salmonella group E	2 (4.9%)
No pathologic agents	35 (85.3%)

J Med Assoc Thai 2014; 97 Suppl 3: S13-9.

1) Prescribing antibiotics unnecessarily

- Antibiotic prescription rate
  - 74% in URI and 78% in acute diarrhea
- Type of antibiotic prescription

	% of ATB prescription	
	General OPD	Private OPD
URI		
Amoxicillin	32.5%	10.4%
Co-amoxiclav	28.8%	31.5%
Roxithromycin	11.4%	8.0%
Clarithromycin	8.2%	14.5%
Azithromycin	5.9%	11.3%
Acute diarrhea		
Norfloxacin	68.0%	33.6%
Ciprofloxacin	22.4%	45.6%
Ceftriaxone	7.4%	-
Cefdinir	-	11.1%

J Med Assoc Thai 2014; 97 Suppl 3: S13-9.

1) Prescribing antibiotics unnecessarily

- Contamination: Coagulase-Negative Staphylococcus (CoNS) blood culture

	Ward			
	ED	ICU	Hemato	Ward
No. of blood culture contamination	62	8	5	26
% of contamination*	3.3%	1.8%	1.2%	2.0%
No. of antibiotic prescription				
- Beta-lactam	-	3	-	-
- Vancomycin	5	4	6	14

* % of contamination = No. of CNS contamination / No. of blood culture taken

Scand J Infect Dis 2008; 40(6-7): 551-4.

1) Prescribing antibiotics unnecessarily

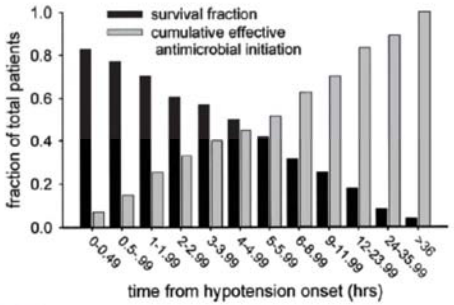
- No infection: Fever of Unknown Origin (FUO)

Inflammation (10% - 30%)	Malignancy (20% - 30%)	Miscellaneous (10% - 20%)
- Adult Still disease	- Leukemia	- Drug-induced
- SLE	- Lymphoma	- Thyroiditis
- Sarcoidosis	- Hepatocellular carcinoma	- Thromboembolic disease
- Giant cell arteritis	- Renal cell carcinoma	- Factitious fever

Am Fam Physician 2014; 90(2): 91-6.

2) Delaying administration of antibiotics

- Timing and survival
  - within the 1st hour: 79.9%
  - every additional hour survival dropped: 7.6%
  - on the 6th hour: 42.0%



Crit Care Med 2006; 34(6): 1589-96.

2) Delaying administration of antibiotics

- Cause of delay
  - did not have sepsis as initial: 268 minutes
  - waited investigations: 320 minutes
  - assessed initially by a resident: 180 minutes

Emerg Med Australas 2013; 25(4): 308-15.

3) Spectrum: too narrow or too broad

- Too narrow: pharmacokinetic properties

	Hydrophilic	Lipophilic
Pharmacokinetic	- Low Vd - Cleared in kidneys - Lower intracellular and tissue penetration	- High Vd - Cleared in liver - Higher intracellular and tissue penetration
Antibiotics	- Beta-lactams - Aminoglycosides - Vancomycin - Colistin	- Fluoroquinolones - Macrolides - Tigecycline
Site of infection	**Bacteremia** **Urinary tract infection**	**Pneumonia** **Intra-abdominal infection** **Skin & soft tissue infection**

Curr Opin Infect Dis 2014; 27(2): 165-73.

3) Spectrum: too narrow or too broad

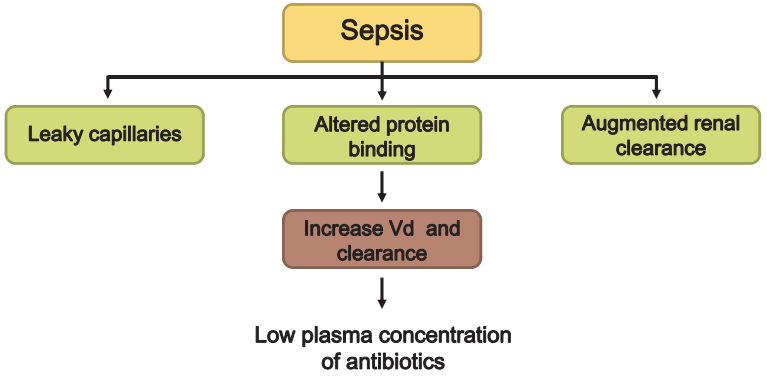
- Too broad: non-de-escalation
  - a single-center, open-label, RCT
  - age > 18 years with ESBL-producing *Enterobacteriaceae* infection: 40% is UTI
  - group 2 carbapenems vs. ertapenem

Outcomes	De-escalation (N = 32)	Non-de-escalation (N = 34)	P-value
Clinical outcomes			
Clinical cure rate	30 (93.8%)	24 (79.4%)	0.09
Microbiological eradication rate	20/20 (100%)	23/24 (95.8%)	0.36
28-day mortality rate	3 (9.4%)	10 (29.4%)	0.05
Superimposed infection rate	6 (18.8%)	12 (35.3%)	0.13

BMC Infect Dis 2017; 17(1): 183.

4) Dose: too low or too high

- Too low: critical illness patient in 24-48 hour



"Treatment failure"

J Intensive Care Soc 2015; 16: 147-53.

4) Dose: too low or too high

- Too low: critical illness patient – dosage (1)

Category	Antibiotic	Dosage
Aminoglycosides*	Gentamicin	7 mg/kg (ABW) IV 24 hourly
	Amikacin	30 mg/kg (ABW) IV 24 hourly
Beta-lactams	Ceftriaxone	1 g IV 12 hourly (2 g IV 12 hourly for CNS infection)
	Cefepime	2 g IV 8 hourly
	Ceftazidime	2 g IV 6-8 hourly
	Imipenem	0.5-1.0 g IV 6-8 hourly
	Piperacillin/tazobactam	4.5 g IV 4-6 hourly
	Meropenem	1 g IV 6-8 hourly (2 g IV 6-8 hourly for CNS infection)
	Ertapenem	1 g IV 12 hourly
Glycopeptides*	Vancomycin	35 mg/kg (TBW) IV loading then 30 mg/kg/day IV continuous infusion

* Dose adjusted by therapeutic drug monitoring

Intensive Care Med 2013; 39(12): 2070-82.

4) Dose: too low or too high

- Too low: critical illness patient – dosage (2)

Category	Antibiotic	Dosage
Fluoroquinolones	Ciprofloxacin	400 mg IV 8 hourly
	Levofloxacin	750-1000 mg IV 24 hourly
	Moxifloxacin	400 mg IV 24 hourly
Miscellaneous	Linezolid	600 mg IV 12 hourly
	Daptomycin	8-12 mg/kg IV 24 hourly
	Lincosamides	600-900 mg IV 8 hourly
	Tigecycline	100 mg IV loading then 50 mg IV 12 hourly (200 mg IV loading then 100 mg IV 12 hourly in borderline susceptibility)
	Colistin	300 mg IV loading then 150 mg IV 8-12 hourly

Intensive Care Med 2013; 39(12): 2070-82.
Clin Infect Dis 2017; 64(5): 565-71.

5) Duration: too short or too long

- HAP: short (7-8 days) vs. prolonged (10-15 days) course in ICU patient

Outcome	Short-course	Prolonged-course	OR (95% CI)
28-day mortality	201 per 1000	175 per 1000	1.18 (0.77 to 1.80)
- NF-GNB	255 per 1000	265 per 1000	0.95 (0.39 to 2.27)
- MRSA	286 per 1000	238 per 1000	1.28 (0.32 to 5.09)
Recurrence rate	237 per 1000	180 per 1000	1.41 (0.94 to 2.12)
- NF-GNB	417 per 1000	247 per 1000	2.18 (1.14 to 4.16)
- MRSA	479 per 1000	370 per 1000	1.56 (0.12 to 19.61)

Cochrane Database Syst Rev 2015; 8: Cd007577.

5) Duration: too short or too long

- Bacteremia: short (5-7 days) vs. long (7-21 days) duration
  - primary bacteremia, 2nd bacteremia from pyelonephritis and pneumonia
  - clinical cure

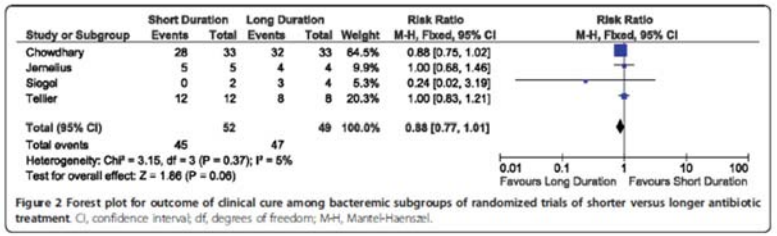


Figure 2 Forest plot for outcome of clinical cure among bacteremic subgroups of randomized trials of shorter versus longer antibiotic treatment. CI, confidence interval; df, degrees of freedom; M-H, Mantel-Haenszel.

Crit Care 2011; 15(6): R267.

6) Antimicrobial prophylaxis for surgery

- Optimal time for administration
  - within 60 minutes before surgical incision
  - fluoroquinolones and vancomycin: within 120 minutes before surgical incision
- Shortened post-operative course
  - a single dose or
  - continuation for less than 24 hours

Am J Health Syst Pharm 2013; 70(3): 195-283.

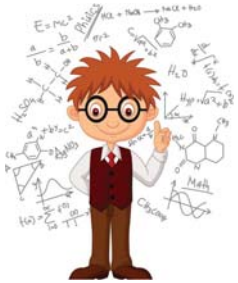
6) Early post-operative fever

- Defined as BT > 38 °C within 72 h after the surgical procedure
- 82% non-infectious cause
- 18% infection cause e.g.
  - surgical site infection
  - pneumonia
  - urinary tract infection
  - *Clostridium difficile* colitis

J Surg Res 2011; 171(1): 245-50.

Actions to optimize antibiotic prescribing

Start smart → Then focus



J Antimicrob Chemother 2011; 66: 2441-3.

Actions to optimize antibiotic prescribing

- Start smart
  - Initiate effective antibiotic
  - Send appropriate specimens (prior to treatment)
  - Prescribe in accordance with local and national policies and guidelines

J Antimicrob Chemother 2011; 66: 2441-3.

Actions to optimize antibiotic prescribing

- Start smart (cont.)
  - Document indication(s), route, dose and duration for antibiotic prescription
  - Prescribe the shortest antibiotic
  - Select agents with minimizing collateral damage

J Antimicrob Chemother 2011; 66: 2441-3.

Actions to optimize antibiotic prescribing

- Start smart (cont.)
  - Monitor antibiotic drug levels
  - Use single dose antibiotic surgical prophylaxis

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J Antimicrob Chemother 2011; 66: 2441-3.

Actions to optimize antibiotic prescribing

- Then focus
  - At 48 h review the need for on-going antibiotic therapy
    - Stop antibiotics if no evidence of infection
    - If antibiotics need to be continued
      - moving to a narrow-spectrum
      - switch from IV to PO
      - consider outpatient parenteral antibiotic therapy (OPAT)

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J Antimicrob Chemother 2011; 66: 2441-3.

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