Impact of Antimicrobial Stewardship on MDR-Pathogens

Anucha Apisarnthanarak, MD

Division of Infectious Diseases

Thammasat University Hospital, Thailand

Adjunct Visiting Professor

Washington University School of Medicine

Saint Louis, MO, USA

Outlines

- Understanding antibiotic use in Asia Pacific Regions
- Environment where antibiotic resistant develops and spreads
- Incidence and patterns of inappropriate antimicrobial use
- What work, not work in Thailand
- Implementing antibiotic stewardship programs
- Long-term success of antibiotic stewardship program
- Integration of antifungal stewardship program
- Role of physicians

Inappropriate antibiotic use: Asia-Pacific region vs. USA

Country	Results	Reference
Philippines (OTC purchase)	Manila: 66%	Lansing et al. J Clin Epidemiol 1990
China Prescribing for viral infections	›Beijing Children's Hospital: 98% of cold ›Taiwan: 30% of all "colds" (45% aged ≤ 15 yrs)s and "RTIs	Yang et al. PIDJ 1993 Chang et al. Int J Ant Ag 199)
Malaysia	53% inappropriate Rx in hospital	Lim Singapore Med J 1993; 1994
Hong Kong False diagnostic indicators and attitudes	Older, more senior, private practice = > AB Rx	Lam. Int J Clin Pract 2001/3
Thailand	Overall 80% inappropriate prescribing in drug store setting	Apisarnthanarak et al. ICHE, 2008
US	›Antibiotics for common cold 36% ›Antibiotics for acute resp infection 51%	Gilberg, J Man Care Pharm 2003 Huang et al, J Clin Epidem 2005

Environment where antibiotic resistance develops and spreads

Nursing Homes

Daycare

Homecare

Tertiary Hospitals

Foreign

Community

Community Hospitals

Feedlots

Scenario and Overview of the Problems

Dispensing antibiotics at Thai Drug Stores

- Six interns trained as patients with common syndromic ailments presented to all drug stores in Pratumthani (central Thailand) from July-December 2006.
- Six presentations were simulated.

Apisarnthanarak A, et al. Non-judicious dispensing of antibiotic by drug store in Thailand. ICHE, 2008

Antibiotic Dispensing at Thai Drug Stores


ขายยา
จ่ายยาตามใบสั่งแพทย์
ขายและแนะนำยา
อ่านฉลากให้ครบถ้วน
อ่านฉลากปรึกษา-สั่ง


รับปรึกษายากับเภสัชกร
วิตามินรวม
ธรรมชาติ
มีขายแล้ว


ยาปฏิชีวนะ, ยาฆ่าเชื้อ
Zinnat suspension 250 mg
Each 5 ml contains 250 mg Cefuroxime as cefuroxime axetil when prepared as directed
Granules for 50 ml
60 ml
No. L950
KLACID
CLARITHROMYCIN
Granules for oral suspension
CEDAX
Ceftibuten
CEDAX
Ceftibuten
Pfizer
ZITHROMAX
Oral suspension 200mg/5ml
ZITHRO
Augmentin
amoxycillin + clavulanate potassium
156 mg/5 ml
60 ml syrup in powder form
156 mg
Augmentin
amoxycillin + clavulanate potassium
156 mg/5 ml
60 ml syrup in powder form
156 mg
Miotin
DRY SYRUP
60 mL
200 mg
BANAN
DRY SYRUP
BANAN
Forte
DRY SYRUP

Presentation and Treatment Guidelines

Presentation	Diagnosis	Treatment
Acute low grade fever and sore throat	Viral pharyngitis	No antibiotic
Acute fever, myalgia, rhinorrhea, cough	Influenza	No antibiotic
Acute fever, tender maxillary sinus with d/c	Viral sinusitis	No antibiotic
Acute watery diarrhea, no abdominal pain	Viral diarrhea	No antibiotic
Skin abrasion without exudate	Non infected wound	No antibiotic
Acute dysuria with suprapubic pain	Urinary tract infection	Quinolones

Slavin RG, et al. The diagnosis and management of sinusitis. J Allergy Immunology, 2005.
Bisno AL. Pharyngitis. In: Principle and Practices in Infectious Diseases, 6th ed, 2005.
Treanor j. Influenza virus. In: Principle and Practices in Infectious Diseases, 6th ed, 2005.
Guerrant RL, et al. Practice guidelines for the management of infectious diarrhea. Clin Infect Dis, 2001
Stevens DL, et al. Practice guidelines for the diagnosis and management of SSTI. Clin Infect Dis, 2005
Gupta K, et al. Increasing antimicrobial resistance and the management of Uncomplicated CAUTI. Ann Intern Med , 2001

Results

- 315 first-class drug stores were identified; 35 were no longer in business
- 280 were surveyed
- Appropriate antibiotic dispensed for all six indications at 56 (20%) drug stores

Dispensing of antibiotics at drug stores for 6 common syndromic ailments

Clinical Syndrome	Stores that prescribed antibiotics (N=280) No. (%)	Antibiotic Dispensed[a] (%)							Other(%)
		Pen V	Amoxi cillin	Amoxi clav	TCN	Erythro	Azithro mycin	Rifam pin	
Acute low-grade fever & sore throat	207 (74)	18	32	15	8	5	11	-	Cefu(8), Cefd(7)
Acute fever, myalgia, rhinorhea, cough	182 (65)	23	38	25	3	2	4	-	Cefd(5), Cefu(5)
Acute fever, tender maxillary sinus with non-purulent discharge	224 (80)	-	37	35	2	2	16	-	Nor(23), Olf(20)
Acute watery diarrhea without fever or abdominal pain	213 (76)	-	6	14	12	8	14	-	Cefu(4), Cefd(4)
Skin abrasion without exudates	179 (64)	14	24	18	8	6	4	-	Mupi(8), Fus(6), Cefp(10)
Acute dysuria & suprapubic pain	280(100)	3	14	15	17	-	-	12	Olf(13), Cipro(30), Cefp(6)

Correlations of outpatient antibiotic use and drug resistance

- Inappropriate use of rifampin: primary rifampin resistance approached 15%

  Riantawan P, et al. Resistant of MTB to anti-tuberculosis *in Central Thailand. Int J Tuberc Lung Dis, 1999*

- Inappropriate use of 2nd & 3rd cephalosporins

  Apisarnthanarak A, et al. Clinical and molecular epidemiology of CO-ESBL E. coli in Thailand. Am J Infect Control 2008

Table 1. Dispensing of antibiotics by drug stores for six common syndromic ailments

Clinical Syndrome	No.(%) Drug stores that prescribed antibiotics (N=280)	Antibiotic Dispensed[a] (%)							Other(%)
		Pen V	Amoxi cillin	Amoxi cillin/ Clavulonic acid	Tetra cycline	Erythro mycin	Azithro mycin	Rifam pin	
Acute low-grade fever and sore Throat	207 (74)	18	32	15	8	5	11	-	Cefu(8), Cefd(7)
Acute fever, myalgia, rhinorhea, cough	182 (65)	23	38	25	3	2	4	-	Cefd(5), Cefu(5)
Acute fever, tender maxillary sinus with non-purulent discharge	224 (80)	-	37	35	2	2	16	-	Nor(23), Olf(20)
Acute watery diarrhea without fever or Abdominal pain	213 (76)	-	6	14	12	8	14	-	Cefu(4), Cefd(4)
Skin abrasion without exudates	179 (64)	14	24	18	8	6	4	-	Mupi(8), Fus(6), Cefp(10)
Acute dysuria and suprapubic pain	280(100)	3	14	15	17	-	-	12	Olf(13), Cipro(30), Cefp(6)

Emergence of mupirocin resistance in Thailand

- Point prevalence survey in January 2010 detected 3.8% (9/250 pts) with MRSA nasal carriage.
- Low level mupirocin-resistance detected in 22% (2/9 pts); all had history of skin abrasion and self-purchase mupirocin and fluoroquinolone from a local pharmacy within 3 months prior to admission.

Apisarnthanarak A, et al. Prevalence of nasal carrier with mupirocin-resistant MRSA in Thailand. ICHE 2011 (in press)
Harbarth S, et al. Risk factors for persistent carrier of MRSA. Clin Infect Dis 2000

Antibiotic prescription is so easy?

Sale of antibiotics according to the clinical case and statement made to obtain the drug.

Result and level of demand (statement)	Clinical case presented, no. (%) of pharmacies visited			
	UTI (n=69)	Sore throat (n=69)	Acute bronchitis (n=59)	Total (n=197)
Antibiotic obtained				
1. (Can you give me something to alleviate the symptoms of the infection?)	52 (75.4)	12 (17.4)	1 (1.7)	65 (33.0)
2. (Can't you give me something stronger?)	2 (2.9)	10 (14.5)	5 (8.5)	17 (8.6)
3. (I would like an antibiotic.)	1 (1.4)	2 (2.9)	4 (6.8)	7 (3.6)
All	55 (79.7)	24 (34.8)	10 (16.9)	89 (45.2)
Antibiotic not obtained	14 (20.3)	45 (65.2)	49 (83.1)	108 (54.8)

Llor C, et al. Sale of antibiotic without prescription in Spain. CID 2009.

Explanation and questions from the pharmacist to the simulated patient in the pharmacies in which the antibiotic was obtained.

Pharmacist statement	Clinical case presented, no. (%) of pharmacies providing antibiotic			
	UTI (n=55)	Sore throat (n=24)	Acute bronchitis (n=10)	Total (n=89)
Explained how often to take the antibiotic	52 (94.5)	17 (70.8)	5 (50.0)	74 (83.1)
Explained how long the antibiotic should be taken	52 (94.5)	9 (37.5)	1 (10.0)	62 (69.7)
Asked patient about other symptoms	38 (69.1)	17 (70.8)	6 (60.0)	61 (68.5)
Asked patient about possible drug allergies	5 (9.1)	17 (70.8)	6 (60.0)	61 (68.5)
Asked patient whether she might be pregnant	2 (3.6)	…	…	2 (3.6)
Recommended that patient see a physician if there is no improvement	1 (1.8)	3 (12.5)	0 (0)	4 (4.5)

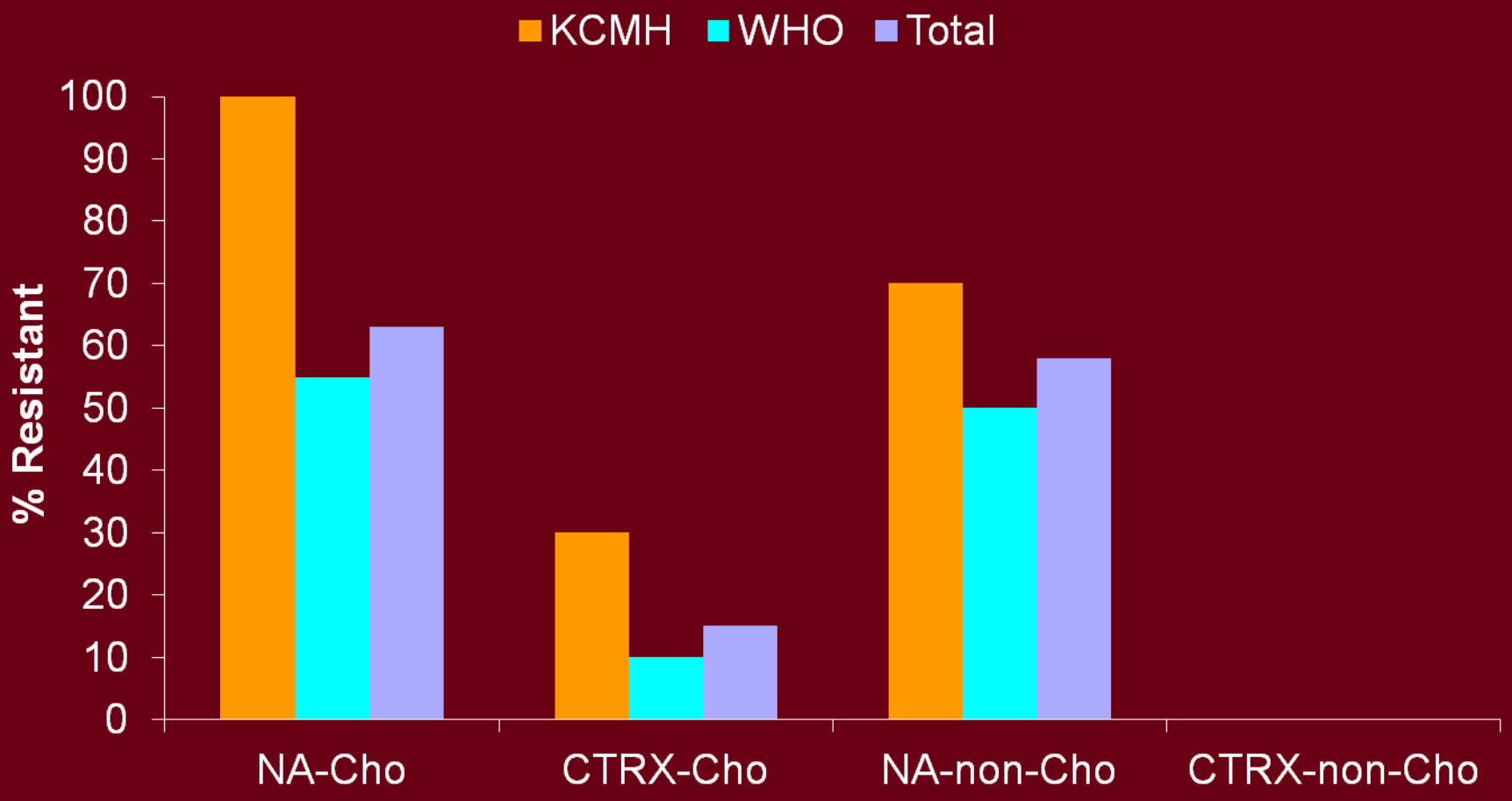
Llor C, et al. Sale of antibiotic without prescription in Spain. CID, 2009

This is a global issue!

- Tangden T, et al. Foreign travel is a major risk factor for colonization with *Escherichia coli* producing CTX-M-type extended-spectrum {beta}-lactamases. AAC 2010
- Leverstein-van Hall MA. Carbapenem resistant *K. pneumoniae* following foreign travel. Ned Tijdschr Geneeskd. 2010
- Emergence of new antibiotic resistant mechanism in India, Pakistan and the UK. Lancet Infect Dis 2010
- Rolain JM, et al. New Delhi metallo-beta-lactamase (NDM-1): towards a new pandemia? CMI 2010

Salmonella spp.
E. coli
Clostridium difficile
Vancomycin-resistant Enterococci

Drug Resistant Non-Typhoidal Salmonella Bacteremia in Thailand



Kulwichit W, et al. EID, 07

International Spread of Multidrug-resistant *Salmonella Schwarzengrund* in Food Products

Country/ source	No. isolates tested/ total no. isolates	No. isolates resistant to antimicrobial drugs*							
		AMP	CHL	CIP	GEN	NAL	STR	SUL	TET
Denmark									
Humans	14/14	8	3	1	6	8	11	9	8
Pigs on farm	22/22	0	2	0	0	0	4	2	2
Pork	4/4	0	0	0	0	0	0	0	0
Chicken meat of unknown origin	7/7	4	1	0	4	5	5	6	4
Imported chicken	13/13	11	0	0	11	11	12	13	13
Imported turkey	9/9	1	0	0	1	1	4	4	4
Others	0/4	-	-	-	-	-	-	-	-
Thailand									
Humans**	46/57	30	13	10	27	42	45	41	35
Chicken meat	44/48	23	16	2	28	39	39	36	23
Turkey meat	2/4	0	0	0	0	0	0	0	0
United States									
Humans	38/390	13	08	16	4	17	4	20	22
Chicken meat	0/3	-	-	-	-	-	-	-	-
Turkey on farm	0/1	-	-	-	-	-	-	-	-
Pigs on farm	2/2	0	0	0	0	0	0	1	1
Imported food	3/3	1	2	1	2	3	2	3	3
Total	204/581	91	45	30	83	126	126	135	115

Aarestrup FM, et al. Emerg infect Dis 2007

This is a global issue!

"CTX-M-type beta-lactamases non-Typhi Salmonella were detected in 2.5% in US during 2007"

Sjölund-Karlsson M, et al. CTX-M producing non-Typhi Salmonella spp. isolated from humans, United States. Emerg Infect Dis 2011

Al-Mashhadani M, et al. Foreign travel and decreased ciprofloxacin susceptibility in *Salmonella enterica* Infections. Emerg Infect Dis 2011

Environment where antibiotic resistance develops and spreads

Nursing Homes

Daycare

Homecare

Tertiary Hospitals

Foreign

Community

Community Hospitals

Feedlots

Incidence/Prevalence and Patterns of Inappropriate Antibiotic Use in Thailand

Prevalence/Incidence, and Patterns of Inappropriate Antibiotic Use in Thailand

Apisarnthanarak A, et al. ICHE, 2006

Reasons: inappropriate surgical prophylaxis, use of antibiotic in absence of clinical evidence of infection, use of antibiotic where narrow spectrum is still available and effective.

Patterns: 3GC were used inappropriately and commonly.

			Patients		
R					
Udo et al					,[b] no
Asw al.[9]					e te
Tha al.[10]					,[b] l atory
					tract infections
Present study	Prevalence	502	63.5	24.8	No indication of use, inappropriate surgical prophylaxis,[b] inappropriate antibiotics for resistant microorganisms, use of broad-spectrum antibiotics where narrow spectrum antibiotic is still available and effective, or other reasons

Factors Associated with Inappropriate Antibiotic Use

Variables	aOR	95% CI
Admission to surgery	2.0	1.1-3.4
Admission to OB &GYN	2.0	1.1-4.1
ID Consultation	0.15	0.03-0.65

Apisarnthanarak A, et al. Inappropriate antibiotic use: an incidence study and review of Thailand experience. Infect Control Hosp Epidemiol, 2006

What works & What doesn't work in Thailand?: Lessons Learned

Antimicrobial Stewardship Program in Thailand: Lessons Learned

- Education
- Formulary restriction
- Antibiotic approval program using Drug Use Evaluation (DUE) Form
- Comprehensive programs

Education Works

- Thamlikitkul V, et al. Impact of an educational program on antibiotic use in a tertiary care hospital in
  D
  S
  S
  D
  %

Interventions were performed in less than a year, so long-term outcome cannot be drawn from these interventions

- Udomthavornsak B, et al. "Intervention of inappropriate antibiotic use at a university teaching hospital, 1991.

Antibiotic Approval Program

- Suwangool P, et al. Effect of a selective restriction policy on antibiotic expenditure and use: an institutional model. *J Med Asso Thai,* 1991.

  Reduction in IAU (pre vs post) 33% vs 18% (*P*<0.001)

  Hospital expense on antibiotics (pre vs post) 2.2 mB vs 1.9 mB (13%)

- **May or May Not Work**

- Ayuthaya S, et al. Utilization of restricted antibiotics in a university hospital in Thailand. *Southeast Asian J Trop Med Public Health*, 2003.

  AOF, closely monitored, enforcement 75% of appropriate antibiotic use

What Doesn't Work?

- Aswapokee N, et al. The failure of a preprinted order form to alter physicians' antimicrobial prescribing pattern. *J Med Assoc Thai*, 1992

AOF alone	Fail

Implementing Antimicrobial Stewardship Program

- Introduction of Antibiogram, Antibiotic Guideline and Prescription Forms

- Interventions:

1. Monthly Education Target High-Risk Units
2. Introduction of Antibiotic Order Form
3. Presence of Clinical Pharmacist
4. Real-time Feedback
5. Encourage ID Consultation

แบบบันทึกการสั่งใช้ยา Ceftazidime/Ceftriaxone/Cefotaxime/ Cefoperazone-sulbactam/Piperacillin-Tazobactam/Cefrom

1. ข้อมูลผู้ป่วย ชื่อสกุล.....HN.....Ward.....

อายุ.....ปี น้ำหนักตัว.....kg CrCl.....ml/min ประวัติการแพ้ยา.....

โรคพื้นฐาน(underlying disease).....

เคย admit หรือเคยได้รับ 3rd generation Cephalosporins ในช่วง 3 เดือนก่อนหน้านี้ ☐ YES ☐ NO

2. ข้อบ่งใช้หรือตำแหน่งติดเชื้อที่จะใช้ยาต้านจุลชีพ หมายเหตุ CAP=Community Acquired Pneumonia , HAP= Hospital Acquired Pneumonia

☐ Bone & joint infection ☐ Meningitis or CNS infection ☐ Skin & soft tissue infection

☐ Febrile neutropenia ☐ Pneumonia (☐ CAP ☐ HAP) ☐ UTI or Pyelonephritis

☐ Intra-abdominal infection ☐ Sepsis or bacteremia ☐ Other.....

3. ลักษณะการใช้ยา ☐ Prophylactic Antibiotic ก่อนการผ่าตัด(procedure).....(ไม่ต้องกรอกข้อมูลในข้อ4และ 5)

☐ Empiric therapy เชื้อที่น่าจะเป็นสาเหตุ → ( ) Gram + ( ) Gram - ( )Mixed organism

○ Clinical stable(ถ้ามีข้อมูลเพียงพอ กรุณากรอกข้อมูลในข้อ 4 และในข้อ 5) ○ Clinical unstable within 72 hr. on admission

○ Clinical deteriorate and on > 3 days of Anti-pseudomonal ATB or Anti-pseudomonal β-lactam-β lactamase inhibitor (βL/βI)*
(ถ้ามีข้อมูลเพียงพอ กรุณากรอกข้อมูลในข้อ 4 และในข้อ 5)

☐ Specific therapy (กรุณากรอกข้อมูลในข้อ 4 และในข้อ 5)

4. ตารางการตรวจ (สามารถเลือกได้มากกว่า 1 ตัวเลือก)

Specimen	By Gram stain	Organism
☐ Blood	☐ Gram + ve bacilli	☐ *P. aeruginosa*
☐ Sputum	☐ Gram – ve bacilli	☐ *S. pneumoniae*
☐ CSF	☐ Gram + ve cocci	☐ *E. coli + K. pnuemoniae* (non-ESBL)
☐ Urine	☐ Gram – ve cocci	☐ *Enterobacter spp.*
☐ Pus	☐ Mixed organism	☐ *E. coli + K. pnuemoniae* (previous ESBL or suspected ESBL)
☐ Not done	☐ Not done	☐ *Acinetobacter spp.*
☐ Other.....	☐ Negative gram strain	☐ No growth / Unknown

5. ผลความไวของเชื้อจากห้องปฏิบัติการ ( ) NOT AVAILABLE ( ) AVAILABLE AS BELOW

Antimicrobial	S	I	R	Antimicrobial	S	I	R	Antimicrobial	S	I	R	Antimicrobial	S	I	R
Penicillin				Ceftriaxone				Gentamicin				Cefotaxime			
Amox/Clav				Ceftazidime				Amikacin				Cefpirome			
Piperacillin				Cefo/sulb				Ciprofloxacin				Erythromycin			

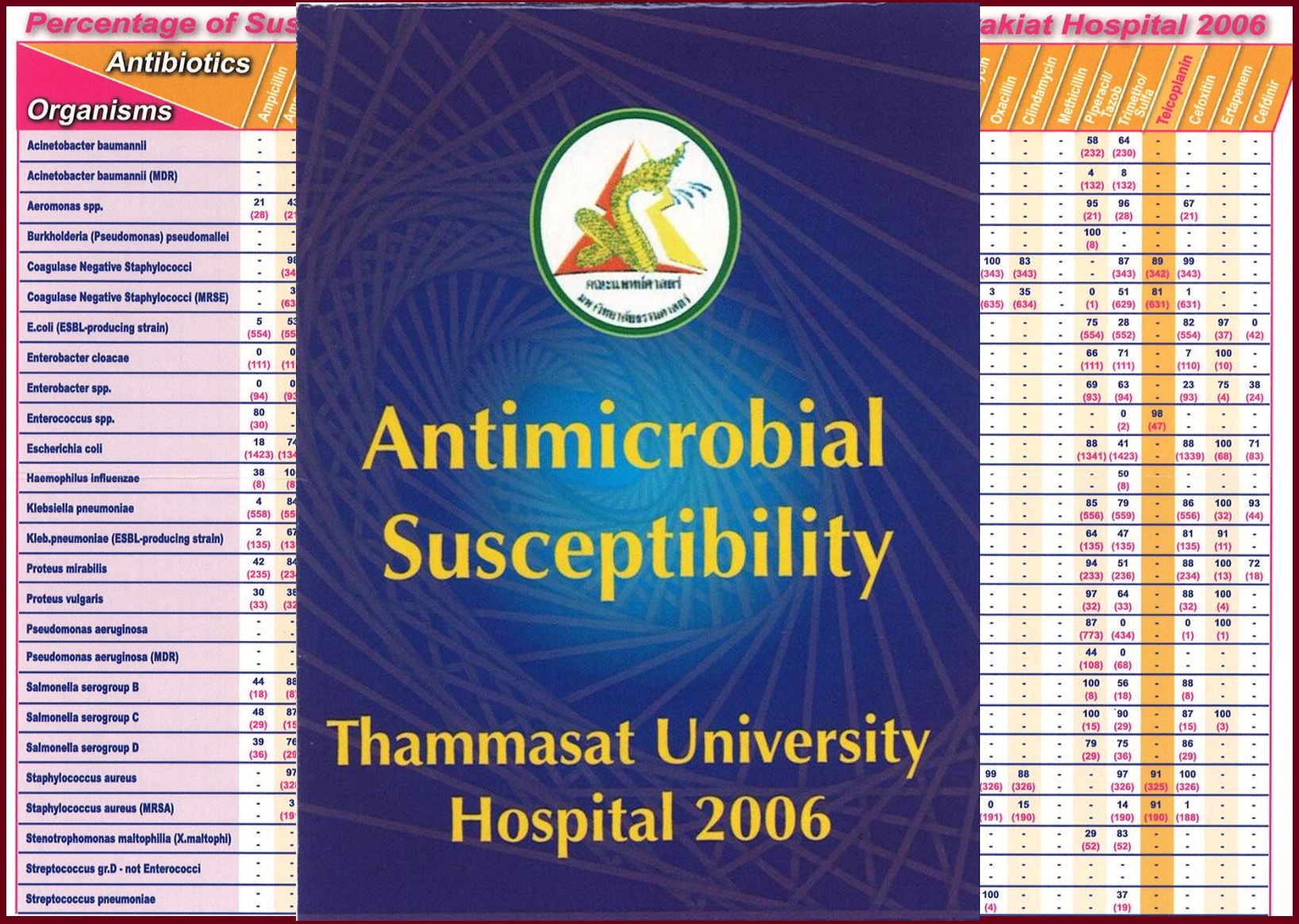
แบบบันทึกนี้ 1 ใบ ใช้สำหรับยา 1 รายการ ควรใช้ได้ไม่เกิน 7 วัน

ยาที่ใช้.....**ขนาดยาที่ใช้**.....**ระยะเวลาที่ใช้(จำนวนวัน)**.....

แพทย์ผู้สั่งใช้ยา..... แพทย์เจ้าของไข้(Staff).....

วันที่สั่งใช้ยา...../...../.....

Pocket size antibiogram



Combination Antibiogram of *A. baumannii*

Drug	Percents of Isolates Susceptible to at Least 1 of the combination agents, by drug												
	GEN	AMI	NET	CEFP	CEFZ	CP/SB	AM/SB	CIP	IMI	MER	PIP/TZ	COL	CP/SB +NET
GEN	…	…	…	28	21	39	34	21	31	30	36	100	…
AMI	…	…	…	30	23	42	36	24	34	32	35	100	…
NET	…	…	…	31	34	54	39	31	40	39	35	100	…
CEFP	28	30	31	…	…	…	…	25	…	…	…	100	…
CETZ	21	23	34	…	…	…	…	20	…	…	…	100	…
CP/SB	39	42	54	…	…	…	…	31	…	…	…	100	…
AM/SB	34	36	39	…	…	…	…	31	…	…	…	100	…
CIP	21	24	31	25	20	31	31	…	29	30	24	100	49
IMI	31	34	40	…	…	…	…	29	…	…	…	100	65
MER	30	32	39	…	…	…	…	30	…	…	…	100	61
PIP/TZ	36	35	35	…	…	…	…	24	…	…	…	100	…
COL	100	100	100	100	100	100	100	100	100	100	100	…	100
CP/SB +NET	…	…	…	…	…	…	…	49	65	61	…	100	…

NOTE: 560 A. baumannii isolates were identified

Apisarnthanarak A, et al. The Role of Combination Antibiogram for Empiric Treatment of Multidrug Resistant *A. baumannii*. ICHE, 2008

Antibiotic Guideline

- Guidelines for empirical therapy
- Guidelines for documented infection in specific organ system
- Guidelines for surgical/OB-GYN prophylaxis

- **All Guidelines are agreed and accepted by all department**

Antimicrobial Stewardship at Thammasat University Hospital

- **Educations to intern, residents, staffs**
  - Five-sessions education for all intern, residents and staffs in the hospital
  - One on one feedback to externs, interns and residents
- **Intervention target at specific units**
  - Structured teaching on medicine, surgery and OB-GYN
  - Monthly education for medical students, interns and residents
  - Presence of clinical pharmacist on medicine, surgery and OB-GYN units
- **Encourage Infectious Diseases consultation**

Initiated in July, 04

Apisarnthanarak A, et al. Effectiveness of Educational and Antibiotic Control Program in a tertiary care hospital in Thailand, Clin Infect Dis, 2006

Table 3. Incidence of inappropriate antibiotic use, reasons for inappropriateness, and departments associated with inappropriate antibiotic use during the pre- and postintervention periods.

Variable	Preintervention period (*n* = 4305)	Postintervention period (*n* = 2830)	*P*
Inappropriate antiobiotic use	1808 (42)	566 (20)	<.001
Reason for inappropriateness[a]			
Inappropriate sugical prophylaxis[b]	452 (25)	115 (20)	.02
Use of antibiotic without any evidence of infection	723 (40)	200 (35)	.04
Redundant spectrum	217 (12)	50 (9)	.03
Bacterial resistance[c]	235 (13)	91 (16)	.07
Narrow spectrum was available[d]	181 (10)	41 (7)	.04
Department[e]			
Surgery	633 (35)	170 (30)	.01
Obstetrics and gynecology	452 (25)	125 (22)	.17
Internal medicine	416 (23)	113 (20)	.14
Other[f]	307 (17)	113 (20)	.12

Bacterial resistance rates during the pre and post intervention periods

Microorganism	Resistance rate % [a]		Associated antibiotic class	Type of variation	R [b]	*P*
	Pre intervention period	Post intervention period				
MRSA	48	33.5	Glycopeptides 3rd gen. Cephalo.	Decrease Decrease	0.55 0.93	<.001 <.001
ESBL *E.coli*	33	21	3rd gen. Cephalo.	Decrease	0.74	<.001
ESBL *K.pneumoniae*	30	20	3rd gen. Cephalo.	Decrease	0.69	<.001
3rdGC-resistant *A. baumanii*	27	19	3rd gen. Cephalo.	Decrease	0.78	<.001
Imipenem-resis *P. aeruginosa*	5	4	None	-	-	
MDR *A.baumanii*	4	5	None	-	-	

[a] Calculated using the total number of strains.
[b] Linear regression analysis between evolution in the resistance rate and antibiotic use throughout the study

What components are needed for long-term success?

Long-Term Outcomes of Antibiotic Control Program With vs. Without Education

- Period 1: July 1, 2004-June 30, 2005

  Introduced obligatory antibiotic order form, monthly education, bed-side discussion

- Period 2: July 1, 2005-June 30, 2006

  Similar activities to period 1, but without education

- Period 3: July 1, 2006-June 30, 2007

  Similar to both period 1 and 2; educational program was re-introduced

Apisarnthanarak A, et al. Long-term outcomes of antibiotic control program with vs. without education. Clin Infect Dis, 2007

Long-Term Outcomes of Antibiotic Control Program With vs. Without Education

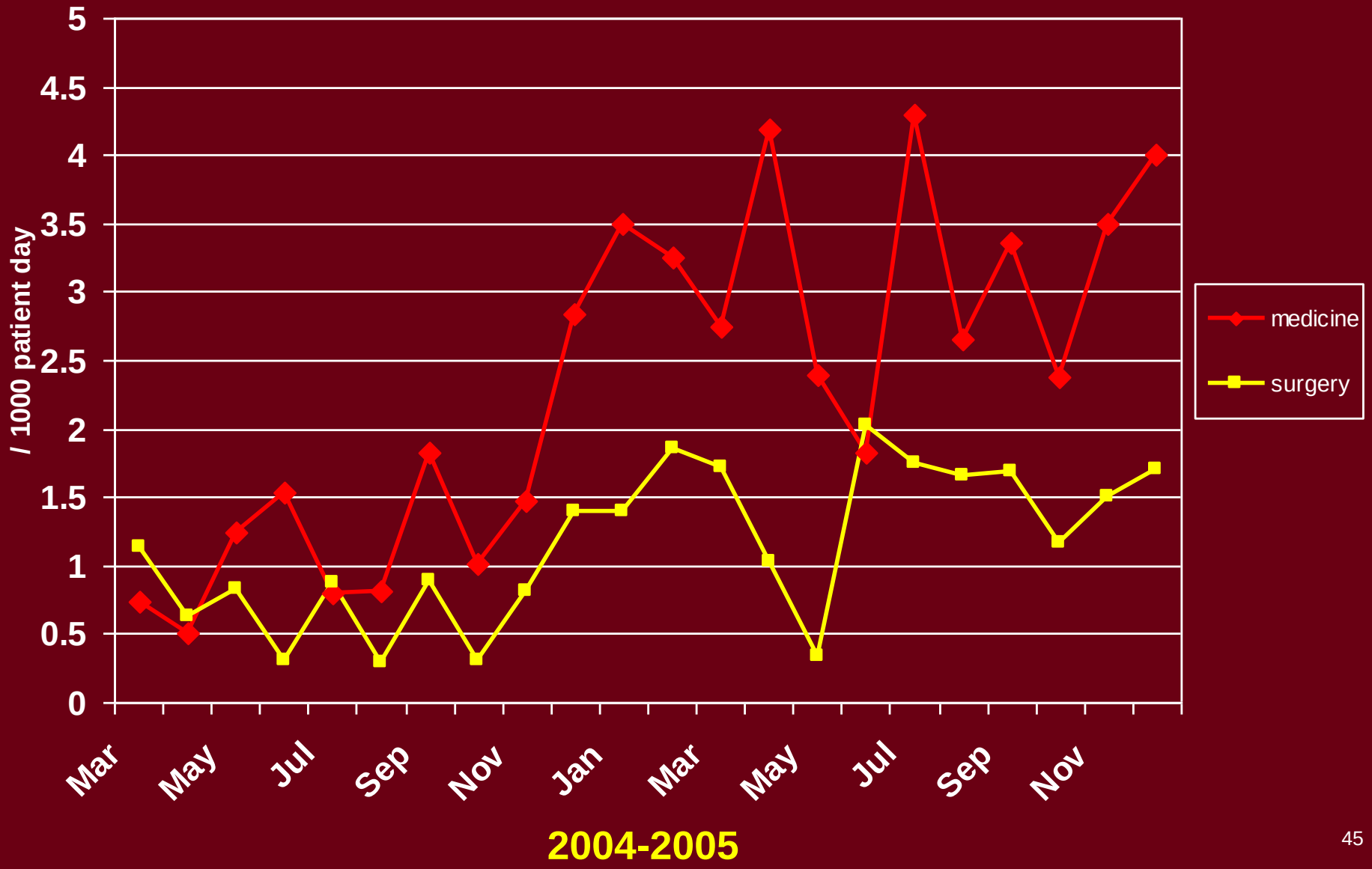
Characteristic	Period 1 (n=2830)	Period 2 (n=2915)	Period 3 (n=2714)
Inappropriate antibiotic use	566 (20)	654 (23)	515 (19)
Reason for inappropriate antibiotic use Inappropriate surgical prophylaxis	115 (20)	170 (26)	93 (18)
Use of antibiotic without evidence of infection	200 (35)	235 (36)	175 (34)
Redundant spectrum	50 (9)	52 (8)	46 (9)
Bacterial resistance	91 (16)	98 (15)	77 (15)
Narrow spectrum available	41 (7)	39 (6)	28 (5)

Controlling Antibiotic Use and Resistant (Editorial Note)

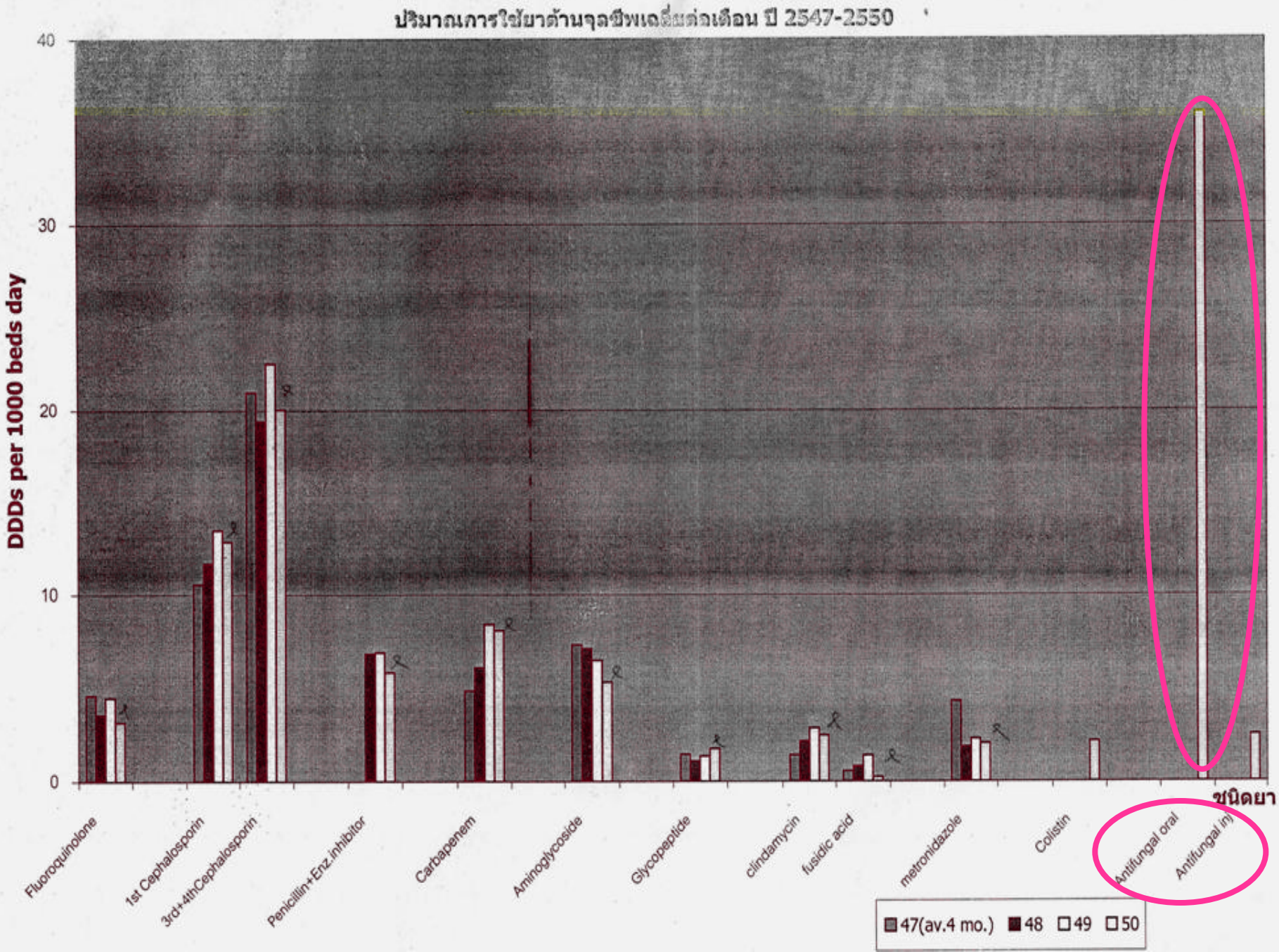
"…..To sustain or even further improve these results, lasting and repeated efforts will be needed. Integrating infection-control efforts into this education and antibiotic-control program is warranted."

Nouven JL, Clin Infect Dis, 2006

Despite effective antimicrobial stewardship program, *PDR-A. baumannii* was emerged….



Integration of Antifungal Stewardship Program


ปริมาณการใช้ยาต้านจุลชีพเฉลี่ยต่อเดือน ปี 2547-2550
DDDs per 1000 beds day
40
30
20
10
0
ชนิดยา
Fluoroquinolone
1st Cephalosporin
3rd+4thCephalosporin
Penicillin+Enz.inhibitor
Carbapenem
Aminoglycoside
Glycopeptide
clindamycin
fusidic acid
metronidazole
Colistin
Antifungal oral
Antifungal inj
47(av.4 mo.)
48
49
50

Inappropriate Use of Antifungal Medications in a Tertiary Care Center in Thailand: A Prospective Study

Anisada Sutepvarnon, MD;

Most mistakes occur in treatment of candiduria and inappropriate antifungal dose adjustment

an-

The

incidence of inappropriate antifungal use was 74% (in 42 of 57 patients). Isolation of *Candida* species from urine ($P = .004$) was a risk factor, whereas receipt of an infectious diseases consultation ($P = .004$) was protective.

Infect Control Hosp Epidemiol 2008; 29:370-373

Interventions Incorporated to Existing Antimicrobial Stewardship Program

- Education on antifungal treatment and prophylaxis for Physicians/Resident/Intern
- Intervention to reduce inappropriate urinary catheterization
- Implement the clinical care practices for Candidemia
- Implement renal dose adjustment for antifungal dose as a poster
- Implement antifungal DUE and encourage ID consultation for complicated cases

Apisarnthanarak A, et al. Impact of education and antifungal control program. ICHE, 2010

Pocket Size for Invasive Candidasis a Care Map

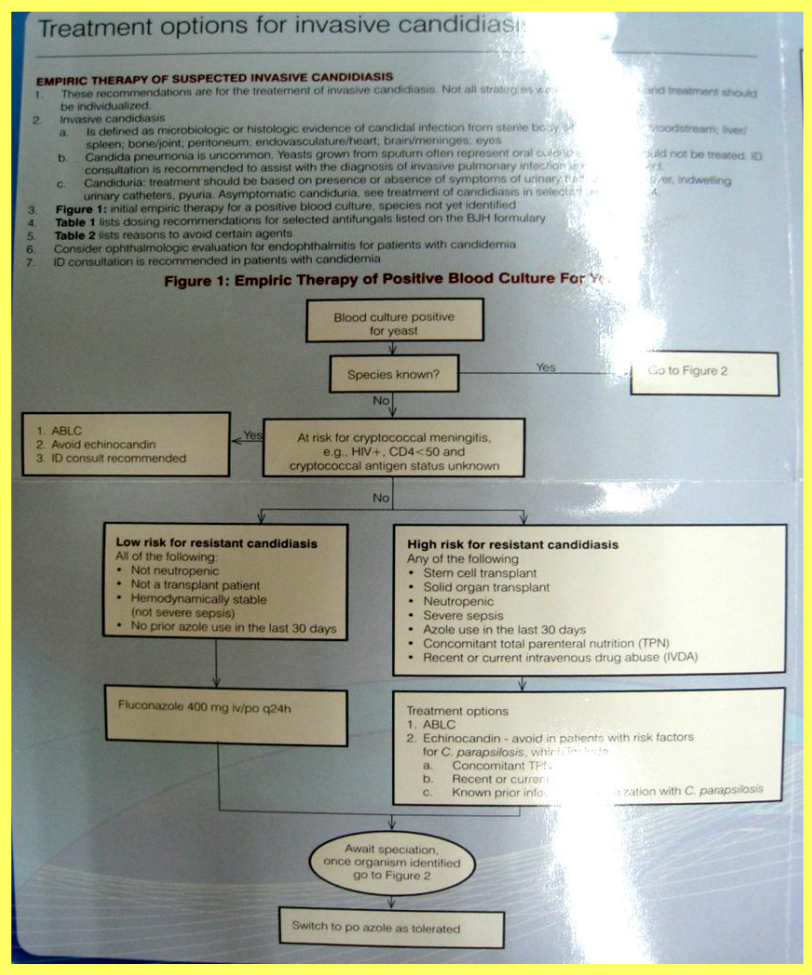
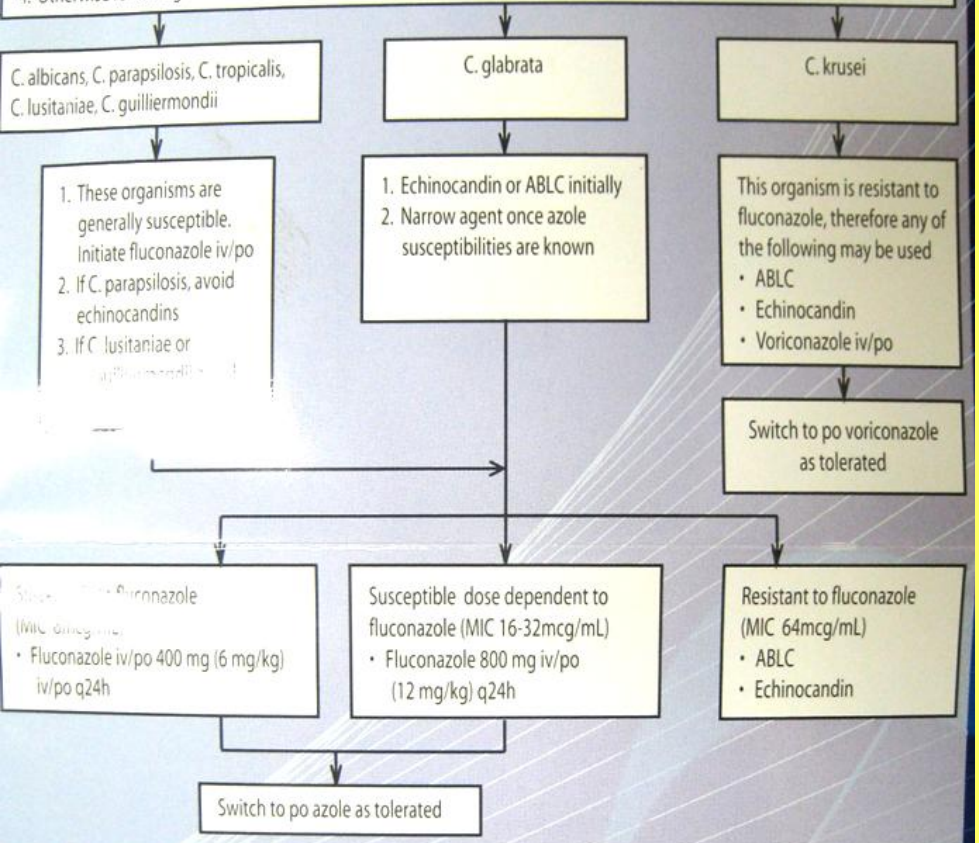


Figure 2: Species-Specific Therapy

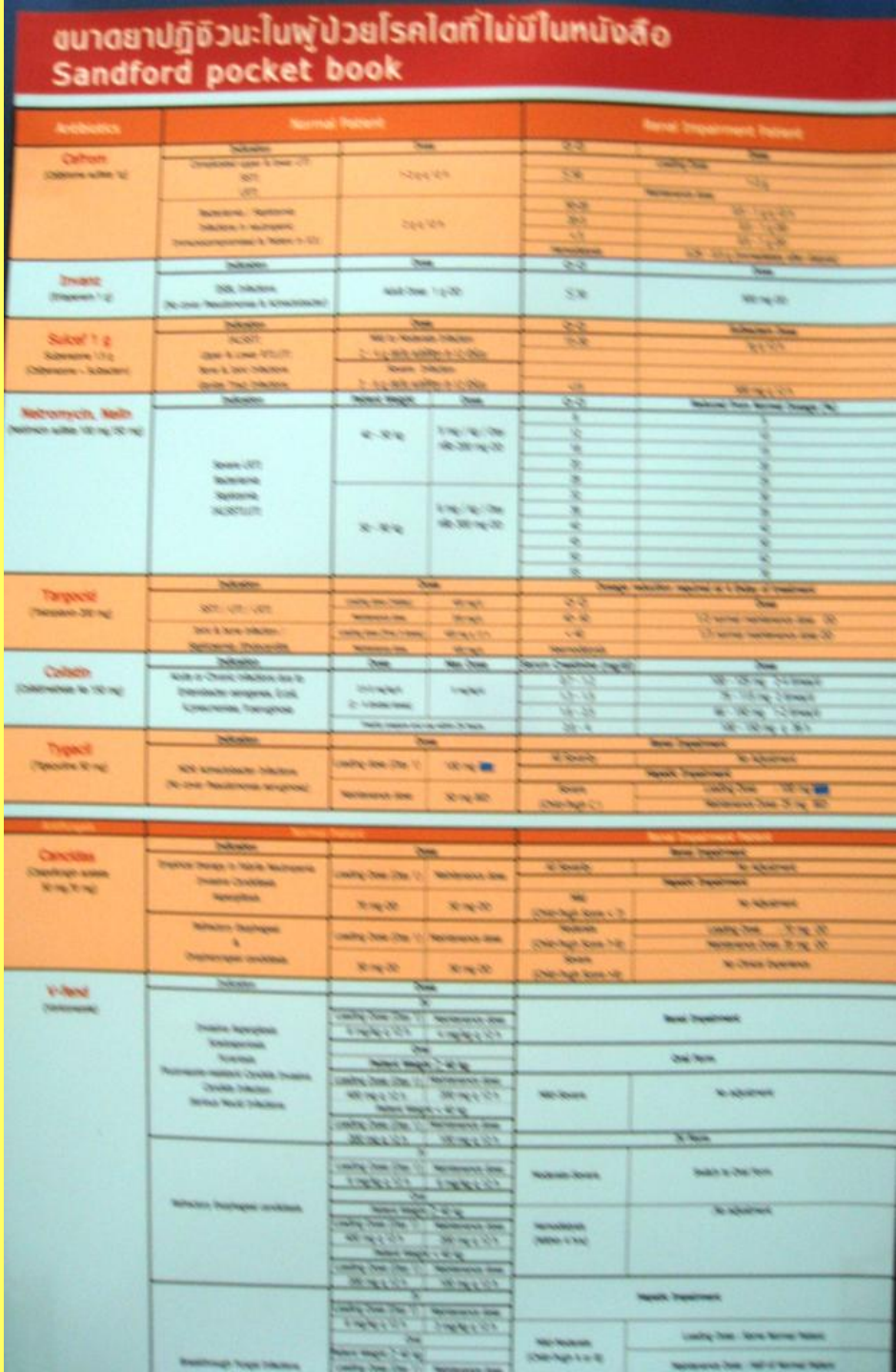
1. If severe sepsis or persistantly neutropenic, use echinocandin or ABLC until these conditions resolve.
2. If patient on azole in last 30 days or bloodstream growing non-albicans species, review antifungal susceptibilities before switching to azole.
3. If history of colonization with C. lusitaniae or C. guilliermondii. Avoid amphotericin.
4. Otherwise follow algorithm below



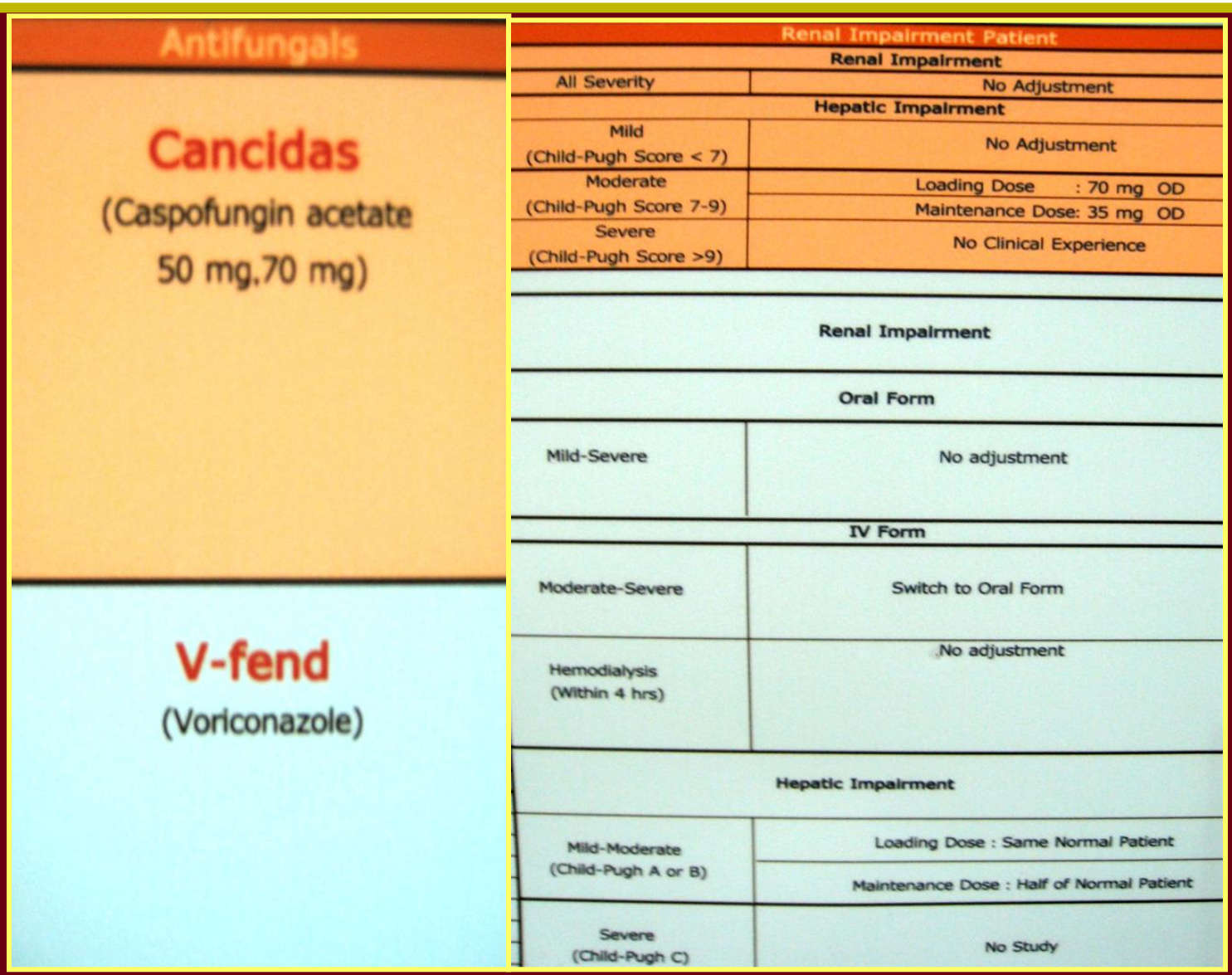
SPECIES-SPECIFIC THERAPY

1. After initial cultures are drawn and empiric therapy has been started, all patients should be re-evaluated in 2-3 days when the fungal species has been identified and when anti-fungal susceptibilities are known
2. **Figure 2** lists species-specific treatment options. Note that fluconazole exhibits variable activity against C. glabrata and is ineffective against C. krusei.
3. For uncomplicated, line-related candidemia, fluconazole 400-800 mg iv/po q24h is preferred. Decrease dose to 400 mg iv q24h if C. albicans or susceptible C. glabrata is identified.
4. If C. glabrata is identified from blood, caution is warranted since this organism exhibits three fluconazole susceptibility patterns. Interpretive breakpoints for each pattern are:
   a. Fluconazole susceptible: MIC 8 mcg/ml
   b. Fluconazole susceptible, dose dependent: [illegible]6-32 mcg/ml. High dose (800 mg q24h) fluconazole is effective for these isol[illegible]
   c. Fl[illegible]

ขนาดยาปฏิชีวนะในผู้ป่วยโรคไตที่ไม่มีในหนังสือ Sandford pocket book



Renal Dose Adjustment Poster



Antifungals

Cancidas

(Caspofungin acetate 50 mg,70 mg)

V-fend

(Voriconazole)

Renal Impairment Patient	
Renal Impairment	
All Severity	No Adjustment
Hepatic Impairment	
Mild (Child-Pugh Score < 7)	No Adjustment
Moderate (Child-Pugh Score 7-9)	Loading Dose : 70 mg OD Maintenance Dose: 35 mg OD
Severe (Child-Pugh Score >9)	No Clinical Experience

Renal Impairment	
Oral Form	
Mild-Severe	No adjustment
IV Form	
Moderate-Severe	Switch to Oral Form
Hemodialysis (Within 4 hrs)	No adjustment
Hepatic Impairment	
Mild-Moderate (Child-Pugh A or B)	Loading Dose : Same Normal Patient Maintenance Dose : Half of Normal Patient
Severe (Child-Pugh C)	No Study

Antifungal DUE

แบบบันทึกการสั่งใช้ยา Fluconazole/Caspofungin/Voriconazole

1. ข้อมูลผู้ป่วย ชื่อสกุล.....HN.....Ward.....

อายุ.....ปี น้ำหนักตัว.....kg Cr=.....mg/dL CrCl : ☐ < 20 ☐ 21-50 ☐ > 50 ml/min

โรคพื้นฐาน(underlying disease).....ประวัติการแพ้ยา.....

เคย admit หรือเคยได้รับ Fluconazole ในช่วง 3 เดือนก่อนหน้านี้ ☐ YES ☐ NO

2. ข้อบ่งใช้หรือตำแหน่งติดเชื้อที่จะใช้ยาต้านเชื้อรา

☐ Bone & joint infection	☐ Meningitis or CNS infection	☐ Skin & soft tissue infection
☐ Febrile neutropenia	☐ Candidemia	☐ Peritonitis
☐ Intra-abdominal infection	☐ Catheter-associated infection	☐ Other.....

3. ลักษณะการใช้ยา ☐ Prophylactic Antifungal ก่อน ( ) Transplantation หรือ ( ) Chemotherapy (ไม่ต้องกรอกข้อมูลในข้อ 4)

☐ Empiric therapy เชื้อที่น่าจะเป็นสาเหตุ .....

◯ Clinical stable (ถ้ามีข้อมูลเพียงพอ กรุณากรอกข้อมูลในข้อ 4) ◯ Clinical unstable within 72 hr. on admission

◯ Clinical deteriorate (ถ้ามีข้อมูลเพียงพอ กรุณากรอกข้อมูลในข้อ 4)

☐ Specific therapy (กรุณากรอกข้อมูลในข้อ 4)

4. ตารางการตรวจ (สามารถเลือกได้มากกว่า 1 ตัวเลือก)

Specimen	Organism
☐ Blood	☐ *Aspergillus spp.*
☐ Sputum	☐ *Candida albican*
☐ CSF	☐ *Candida non-albican*
☐ Urine	☐ *Cryptococcus spp.*
☐ Pus	☐ *Coccidioides imitis*
☐ Not done	☐ *Pseudoallescheria boydii*
☐ Other.....	☐ *Fusanum spp.*
	☐ No growth / Unknown
	☐ Other .....

แบบบันทึกนี้ 1 ใบ ใช้สำหรับยา 1 รายการ ควรใช้ได้ไม่เกิน 7 วัน

ยาที่ใช้.....ขนาดยาที่ใช้.....ระยะเวลาที่ใช้(จำนวนวัน).....

แพทย์ผู้สั่งใช้ยา..... แพทย์เจ้าของไข้(Staff).....

วันที่สั่งใช้ยา...../...../.....เวลา.....

ความเห็นเภสัชกร ☐ เป็นไปตามคู่มือการใช้ยาต้านจุลชีพ รพร.2547-2548 ☐ ส่งปรึกษาแพทย์โรคติดเชื้อ

เนื่องจาก.....

เภสัชกรผู้รับใบ DUE..... วันที่ได้รับใบ DUE ...../...../.....

ความเห็นแพทย์โรคติดเชื้อ ☐ เห็นสมควรให้ใช้ ☐ ไม่เห็นสมควรให้ใช้

เนื่องจาก.....

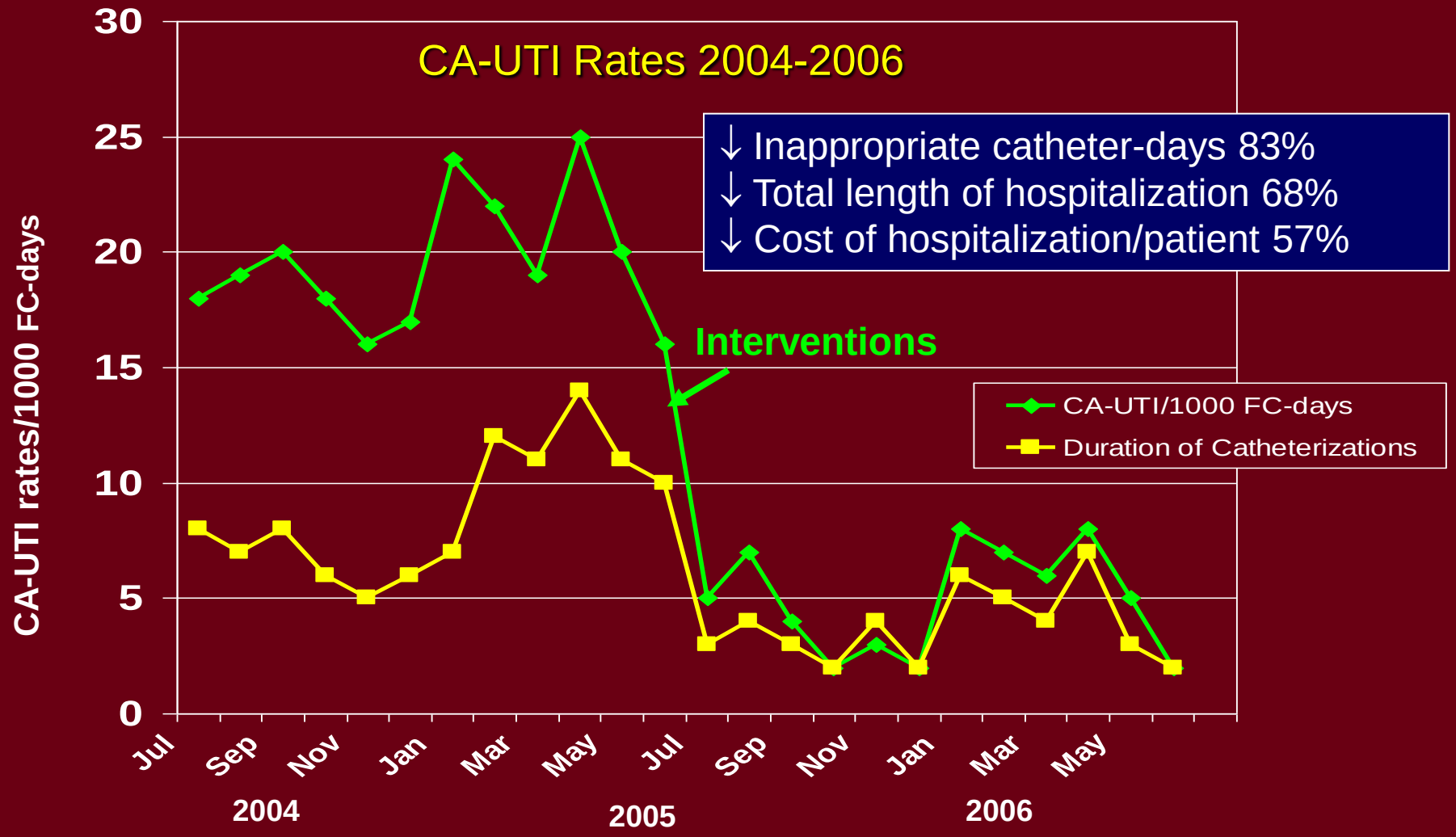
.....

แพทย์โรคติดเชื้อ.....

(.....)

กรุณาดูคู่มือการใช้ยาต้านจุลชีพเพื่อประกอบในการพิจารณาเลือกยาและขนาดยาที่ใช้

Urinary Tract Infection Intervention



Apisarnthanarak A, et al. Effectiveness of multifaceted hospital wide quality improvement program featuring intervention to remove IUC in a tertiary care center in Thailand. ICHE, 2007

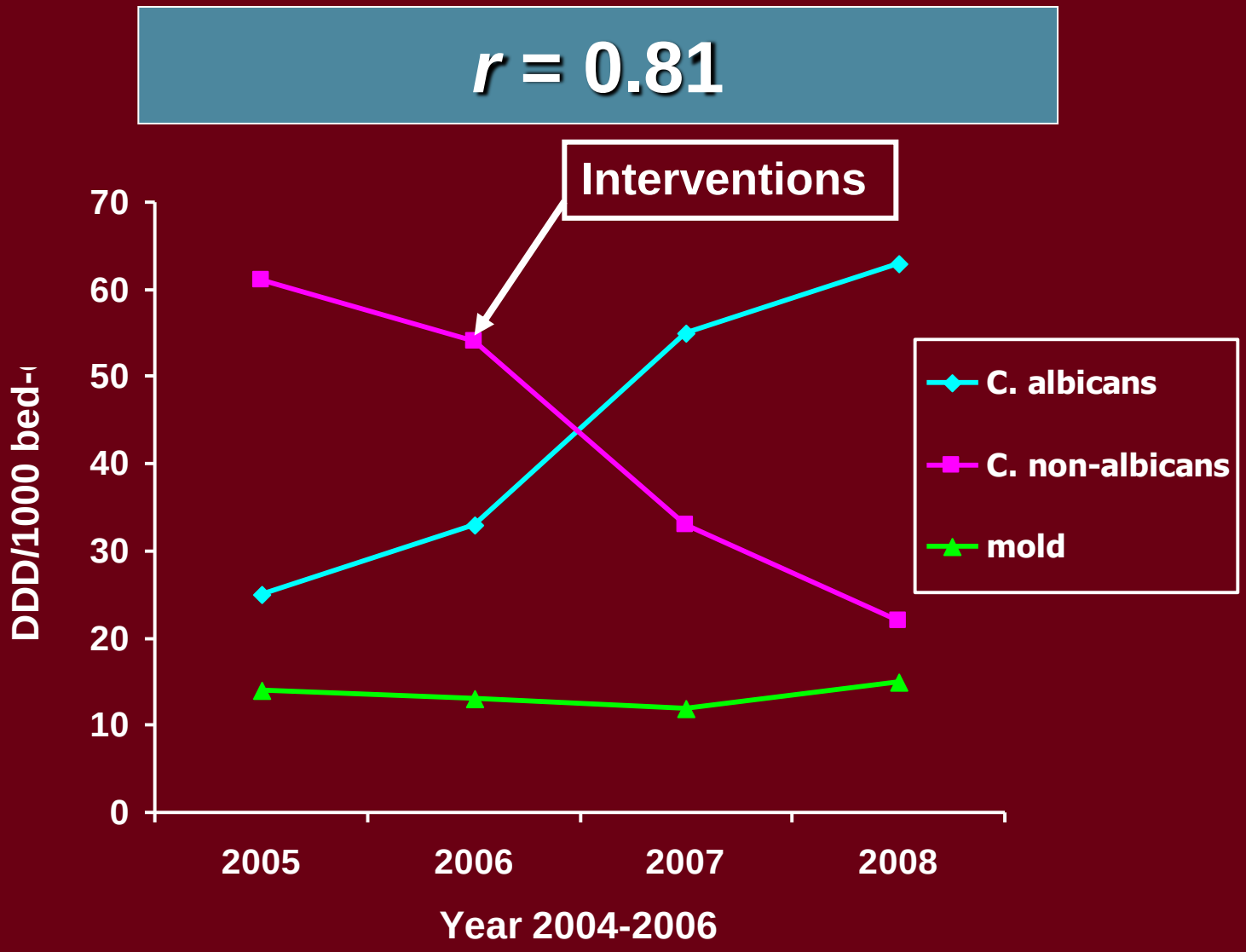
Table 4. Summary of antifungal prescribing practices for 1,106 patients by hospital service, drug and evidence of appropriate use during a three-years study period.

Variables	Pre-intervention period (n=694)	Post-intervention period (n=412)	*P* Value
Inappropriate antifungal use	493 (71)	98 (24)	<0.001
Department			
Medicine	153 (31)	28 (28)	0.42
Surgery	74 (15)	17 (18)	
Intensive care unit	217 (44)	38 (39)	
Others	49 (10)	15 (15)	
Antifungal agent			
Polyenes	128 (26)	23 (24)	0.64
Azoles	335 (68)	62 (63)	
Echinocandins	30 (6)	13 (13)	
Antifungal regimen			
Empiric therapy	30 (6)	7 (7)	0.86
Documented therapy	375 (76)	71 (73)	
Prophylaxis	74 (15)	16 (16)	
Other	15 (3)	4 (4)	
Inappropriate antifungal criteria			
Unnecessary	217 (44)	34 (35)	0.009
Lack of hepatic/renal dose adjustment	118 (24)	20 (20)	
Inappropriate dose or duration	118 (24)	20 (20)	
Inappropriate prophylaxis	89 (18)	16 (16)	
Others	104 (21)	21 (21)	

Table 2. Antifungal prescribing practices, sites of ingections, and Candida species detected during a three-year study period.

Characteristics	Pre-intervention	Post-intervention	*P* Value
Isolations positive for *Candida* spp.	796	799	NA
Site of specimen source			
Urine	430 (54)	439 (55)	0.91
Bloodstream	287 (36)	288 (36)	
Other[a]	79 (10)	72 (9)	
Yeast isolated			
Candida albicans	430 (54)	591 (74)	0.04
Candida glabrata	207 (26)	112 (14)	
Candida krusei	111 (14)	48 (6)	
Other[b]	48 (6)	48 (6)	
Antifungal prescription	694	412	NA
Site of antifungal prescription			
Urine	350 (55)	112 (27)	<0.001
Bloodstream	287 (41)	278 (67)	
Other[a]	57 (8)	22 (6)	
Yeast isolated			
Candida albicans	382 (55)	309 (75)	<0.001
Candida glabrata	173 (25)	41 (10)	
Candida krusei	83 (12)	25 (6)	
Other[b]	56 (8)	36 (9)	

Antifungal Consumption (iv and oral)



Apisarnthanarak A, et al. Impact of education and antifungal control program. ICHE, 2010

Antimicrobial Stewardship: Can physicians help?

- Physicians play an important roles for successful antimicrobial stewardship program
- Potential role of physicians: *input for antibiotic guidelines, consultation with infectious diseases, comply with policies*
- Involvement of ID specialists in the program is more likely associated with successful outcomes
- Patterns of antibiotic use among different physicians will have an impact on how you select appropriate intervention
- Target physicians responsible for IAU in the group that likely comply with the program
- Additional studies to evaluate physicians behaviors that likely comply with antibiotic policy would help strengthen the antimicrobial stewardship program

Acknowledgement

- ICNs & Pharmacist at Thammasat University Hospital
- CCU, MICU, SICU staff
- Panudda Srichomkuan, M.D.
- Pattarachai Kiratisin, M.D., Ph.D.
- Somwang Danchaivijitr, M.D.
- Piyaporn Apisarnthanarak, M.D.
- Victoria J. Fraser, M.D.
- Thomas C. Bailey, M.D.
- Linda M. Mundy, M.D., PhD


Thank you very much for
your attention
“Kob-Koon-Krub”
ขอบคุณครับ

Can antimicrobial stewardship help reduce MDR-pathogens in hospitals where MDR-pathogens are highly prevalent?

Molecular epidemiology of 71 extended-spectrum bete-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae* infections.

Bacteria	Molecular typing	No (%)
Escherichia coli	CTX-M-14	32 (63)
(n = 51)	CTX-M-15	7 (14)
	CTX-M-15, VEB-1	4 (8)
	CTX-M-55	8 (16)
Klebsiella pneumoniae	CTX-M-14	4 (20)
(n = 20)	CTX-M-14, SHV-12	7 (35)
	CTX-M-15	2 (10)
	CTX-M-15, SHV-12	2 (10)
	CTX-M-15, VEB-1	2 (10)
	CTX-M-55	1 (5)
	SHV-12, VEB-1	2 (10)

Apisarnthanarak A, et al. ICHE, 2008

Molecular Epidemiology, Risk Factors and Outcomes of HA-ESBL with Multiple ESBL-genes

Variable	Patient in entire cohort (N = 71)	HA-ESBL with multiple ESBL genes (n =17)	HA-ESBL with single ESBL gene (n =54)	P Value
Age (years): median (range)	58 (15-89)	56 (15-80)	58 (15-89)	0.83
Male, sex	36 (51)	9 (53)	27 (50)	0.43
Underlying disease				
Diabetes	23 (32)	8 (47)	16 (30)	0.18
Cerebrovascular accident	22 (31)	7 (41)	15 (22)	0.30
Other	15 (21)	5 (30)	10 (19)	0.34
Admission APACHE-II score: median (range)	17 (4-23)	18 (6-23)	17 (4-22)	0.71
Time at risk (days): median (range)	10 (0-27)	12 (6-27)	5 (0-14)	0.005
Source of infection				
Urinary tract	44 (62)	10 (59)	34 (63)	0.75
Pneumonia	12 (17)	4 (24)	8 (15)	0.40
Bloodstream infection	6 (8)	2 (12)	4 (7)	0.57
Other	9 (13)	2 (12)	7 (13)	0.89
Previous exposure to ≥3 class of antibiotics	45 (63)	15 (88)	30 (67)	0.01

Molecular Epidemiology, Risk Factors and Outcomes of HA-ESBL with Multiple ESBL-genes

Variable	Patient in entire cohort (N = 71)	HA-ESBL with multiple ESBL genes (n =17)	HA-ESBL with single ESBL gene (n =54)	P Value
Empirical antibiotic regimen				
Third/fourth generation cephalosporins	40 (56)	9 (53)	31 (57)	0.74
Quinolones	12 (17)	4 (24)	8 (15)	0.40
β-lactam /β-lactamase inhibitors	12 (17)	3 (18)	9 (17)	0.92
Other	8 (11)	2 (12)	6 (11)	0.48
Inadequate antibiotic treatment	60 (85)	17 (100)	43 (80)	0.04
Outcomes				
Failure of initial antimicrobial therapy	44 (62)	16 (94)	28 (52)	0.001
Crude mortality	22 (31)	5 (30)	17 (31)	0.87
Length of hospitalization: median (range)	24 (1-48)	25 (1-48)	24 (1-40)	0.71
Hospital costs accrued after Infection (SUS):median (range)	2,145 (45-3,225)	2,155 (85-3,225)	2,089 (45-2,990)	0.83