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Pitfalls in antibiotic use

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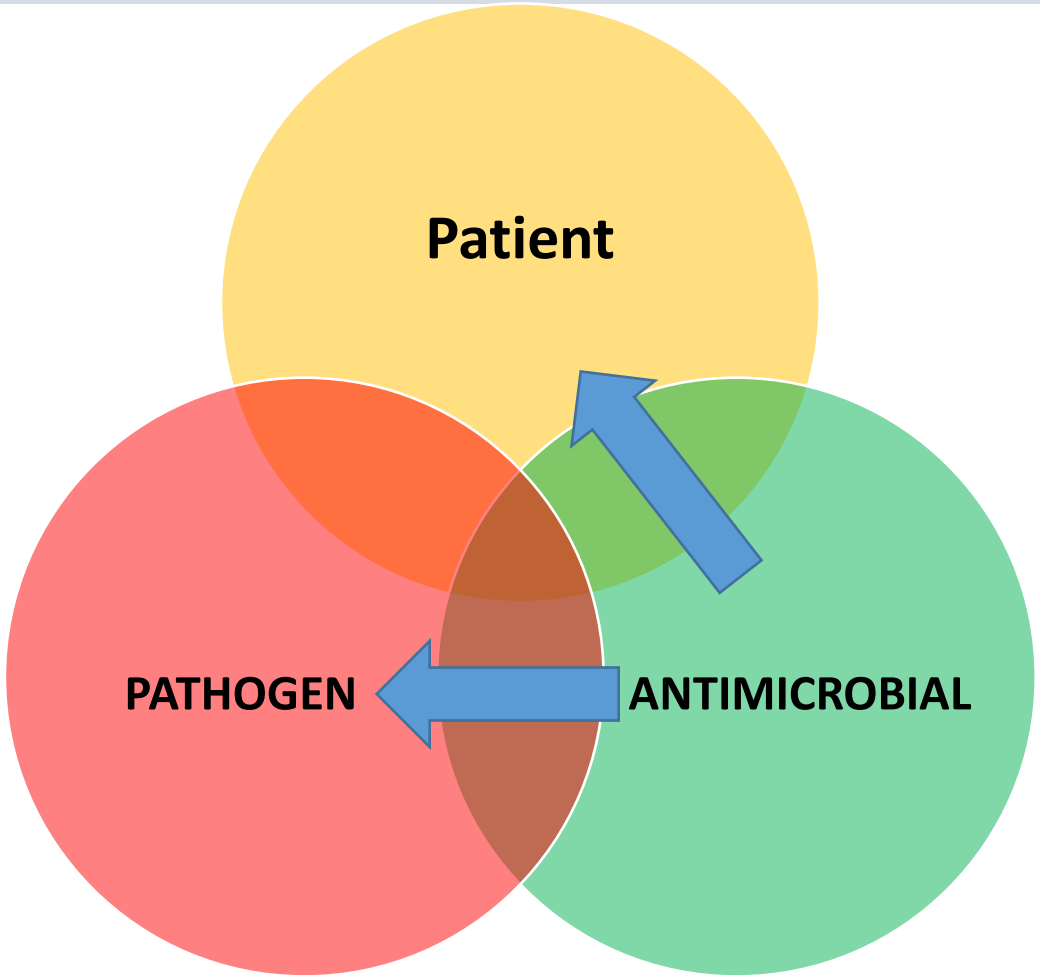
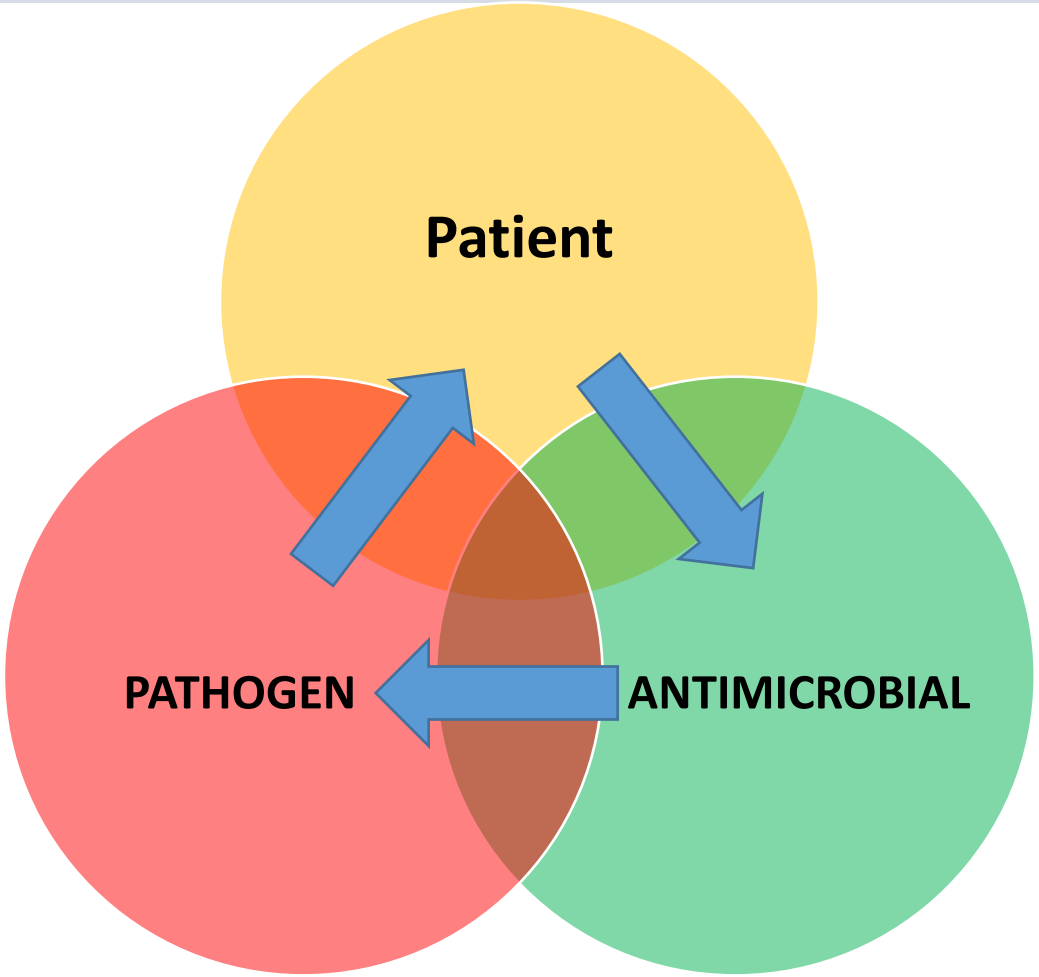
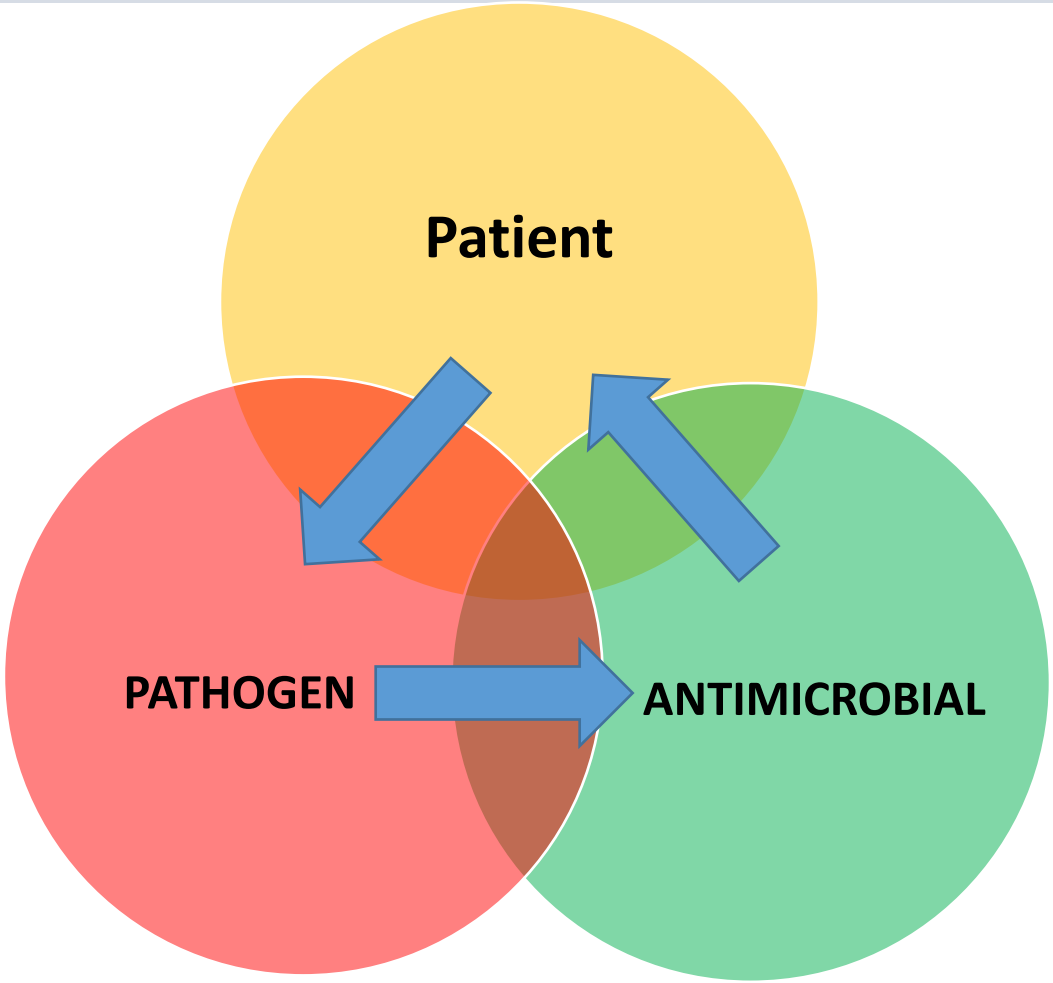
Principles of antimicrobial therapy



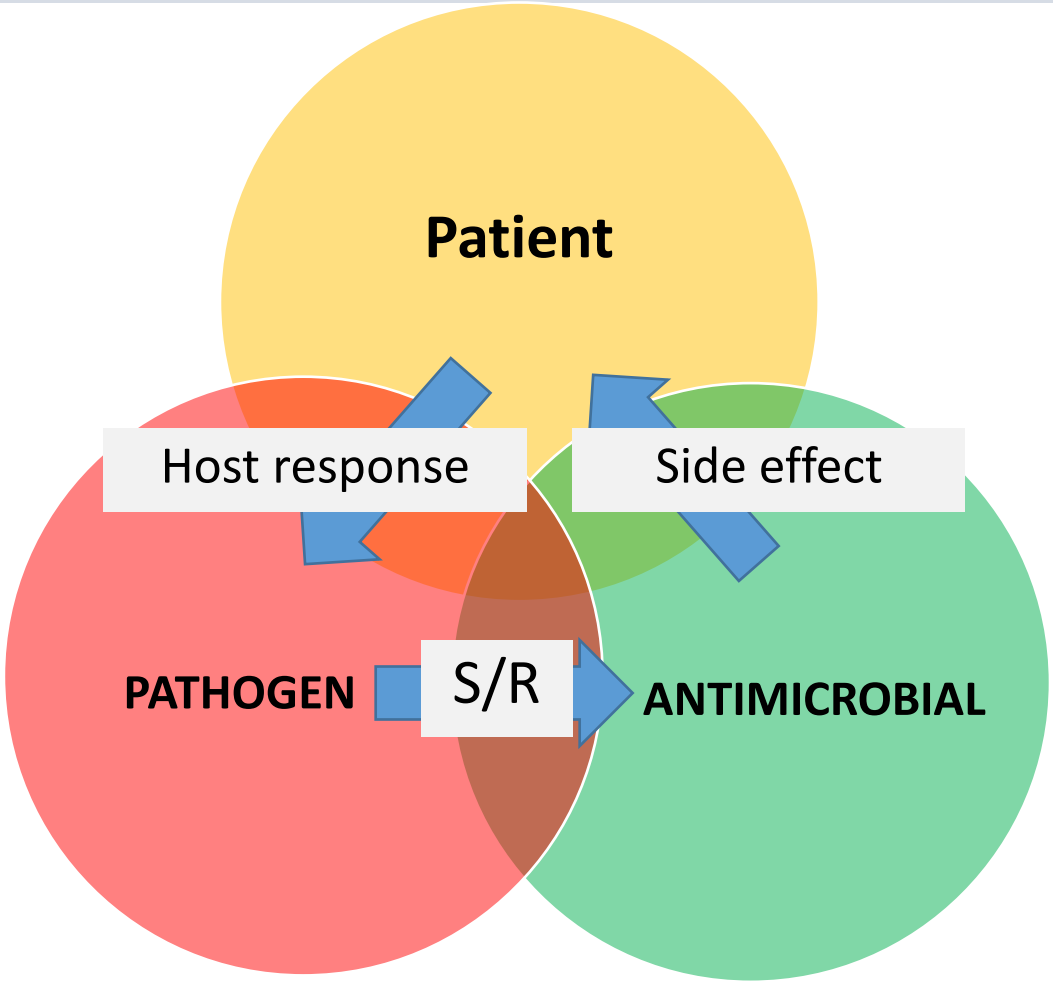
Principles of antimicrobial therapy



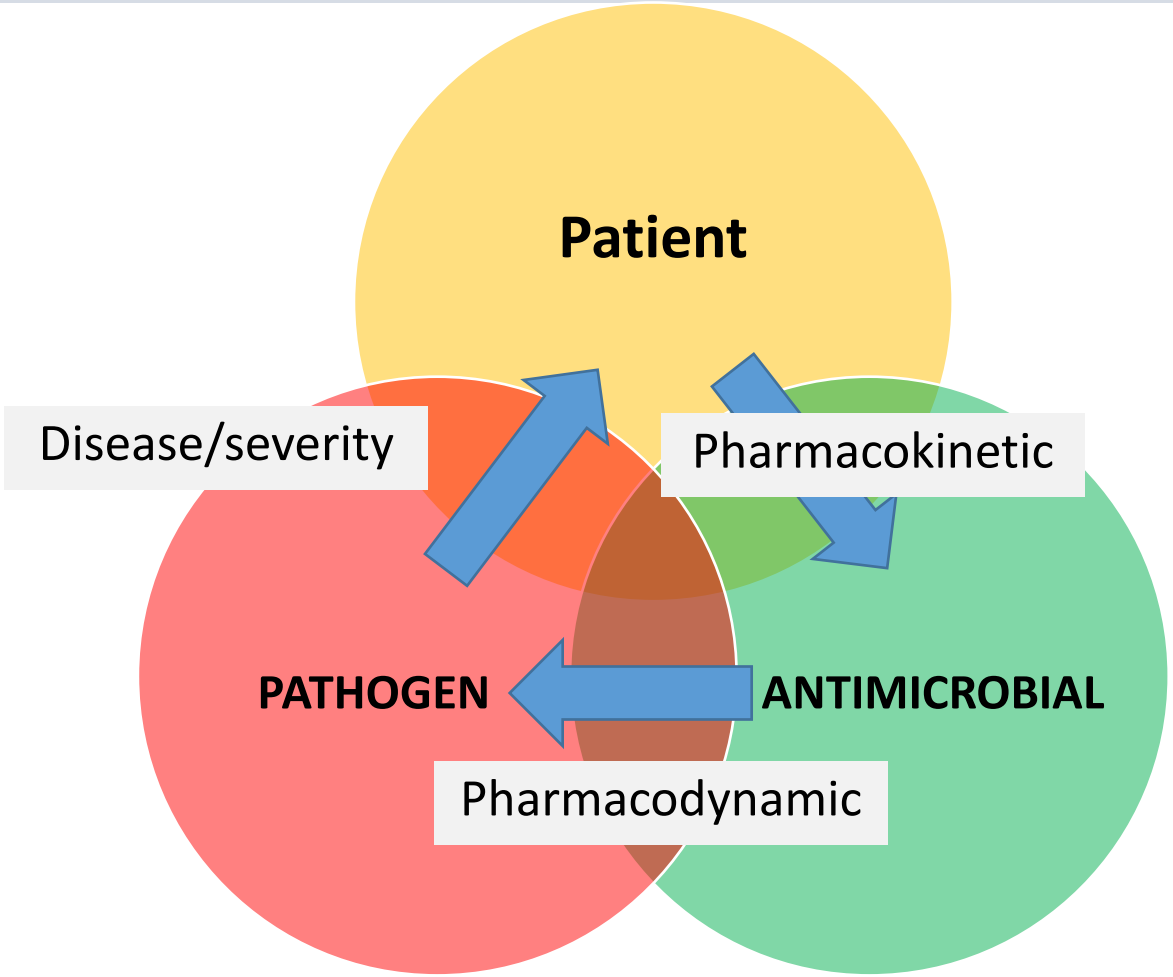
Principles of antimicrobial therapy



Principles of antimicrobial therapy



Principles of antimicrobial therapy



Pitfalls in antibiotic use

- **In community**
- Treat no infection – prophylaxis
- Treat non-bacterial infection – viral
- **In hospital**
- Treat contamination/colonization
- Treat too much, too more, too long

- Right drug
- Right dose
- Right duration

Common Inappropriate Use of Antibiotics: IPD

- TREAT CONTAMINATION OR COLONIZATION
- CHOOSING ANTIBIOTIC THERAPY BASED SOLELY ON SPECTRUM
- TOO MUCH, TOO MORE
- PROLONGED USE OF IV ANTIBIOTICS
- USE OF COMBINATION THERAPY TO PREVENT ATB RESISTANCE
- OVERRELIANCE ON MICROBIOLOGY RESULTS
- USE OF ATB FOR PERSISTENT FEVERS
- INADEQUATE SURGICAL THERAPY AND LACK OF NON-ATB THERAPY OF INFECTION
- PROLONGED ATB THERAPY OR PROPHYLAXIS

Pathogens-antimicrobials

Pathogens	antimicrobials
• Bacteria	• Antibacterial (antibiotic)
• Mycobacteria	• Antimycobacterial
• Virus	• Antiviral
• Fungus	• Antifungal
• Parasite	• Antiparasitic

Prescribing antibiotic unnecessary: OPD

- **Non-bacterial cause: URI, 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.

Prescribing antibiotic unnecessary: OPD

Antibiotic prescription rate: 74% in URI and 78% in diarrhea

	% 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.

Prescribing antibiotic unnecessary: IPD

Contamination: Coagulase negative staphylococci, Bacillus, Diptheroides

	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.

Prescribing antibiotic unnecessary

- **Non-infectious cause of fever**

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

Am Fam Physician 2014;90(2);91-2

Principal of antimicrobial therapy

- **Right drug**
- Right dose
- Right duration

Spectrum of activity

	S. aureus MSSA	Strept gr A	Strept gr B	Enterococci
cephalexin	xxxx	xxxx	xxxx	R
cefuroxime	xxxx	xxxx	xxxx	R
cefixime	R	xxxx	xxxx	R
cefdinir	xxxx	xxxx	xxxx	R
cefpodoxime	R	xxxx	xxxx	R
cefditoren	xxxx	xxxx	xxxx	R

Antibiogram

Antimicrobial Susceptibility Patterns Of Gram Negative Bacilli Organisms, 2016

ORGANISMS	Total	Penicillins	b-Lactam/Inhibitor			Cephalosporins					Aminoglycosides			Fluoroquinolones				Carbapenems								
		Ampicillin	Amoxic./Clavulanate	Ampic./Sulbactam	Pipera/Tazobactam	Cephalothin	Cefotaxime	Ceftazidime	Ceftriaxone	Cefoper./Sulbactam	Amikacin	Gentamicin	Netilmicin	Norfloxacin	Ofloxacin	Levofloxacin	Ciprofloxacin	Imipenem	Meropenem	Ertapenem	Trimetho/Sulfa.	Tetracycline	Doxycycline	Colistin	Tigecycline	Fosfomicin
Acinetobacter baumannii (All)	3032			24 (2870)	17 (2989)		2 (3032)	18 (3032)		28 (2995)	79 (3032)	27 (2961)	26 (490)		18 (2903)	22 (2655)	17 (3032)	4 (2331)	4 (2344)		37 (3032)			98 (2344)	90 (2360)	
Acinetobacter baumannii	666			85 (548)	73 (653)		8 (666)	73 (666)		86 (657)	97 (666)	92 (656)	94 (68)		80 (623)	83 (601)	79 (666)	76 (87)	79 (100)		85 (666)			100 (90)	97 (94)	
Acinetobacter baumannii (MDR/CORO)	2366			9 (2322)	1 (2336)		0 (2366)	2 (2366)		11 (2338)	31 (2366)	6 (2305)	16 (422)		1 (2280)	4 (2054)	8 (2366)	1 (2244)	1 (2244)		24 (2366)			98 (2254)	89 (2266)	
Acinetobacter lwoffii	140			57 (111)	71 (139)		29 (140)	57 (140)		74 (140)	69 (140)	53 (140)			58 (140)	63 (113)	57 (140)	14 (37)	21 (43)		51 (140)			98 (40)	38 (40)	
Burkholderia pseudomallei	129							100 (129)		100 (129)										99 (129)		100 (129)			
Edwardsiella tarda	27	59 (22)	84 (27)			72 (18)	100 (27)	100 (27)	100 (9)		100 (27)	96 (27)			85 (13)		93 (27)				93 (27)					
Enterobacter spp. (All)	1011	0 (1011)	6 (1011)	6 (356)	52 (356)	1 (1011)	62 (1011)	67 (1011)		56 (356)	97 (1011)	83 (1011)	1		76 (1011)	86 (65)	79 (1011)	78 (87)	91 (357)	80 (435)	70 (1011)				77 (335)	91 (335)
Enterobacter spp.	864	0 (864)	7 (864)	10 (209)	62 (209)	0 (864)	72 (864)	77 (864)		68 (209)	98 (864)	93 (864)		86 (90)	88 (864)	87 (53)	9 (864)	97 (37)	100 (207)	100 (291)	79 (864)				81 (197)	95 (197)
Enterobacter spp. (MDR/CRE)	147	0 (147)	2 (147)	0 (147)	36 (147)	0 (147)	2 (147)	6 (147)		42 (147)	87 (147)	23 (147)	55 (38)	15 (40)	63 (147)	83 (12)	14 (147)	64 (50)	76 (150)	49 (144)	16 (147)				71 (138)	87 (147)
E.coli (ALL)	4394	12 (4394)	55 (4394)	28 (2163)	80 (2163)	27 (4394)	49 (4394)	59 (4394)	62 (469)	73 (2163)	99 (4394)	64 (4394)	86 (297)	31 (2195)	34 (3033)	36 (110)	37 (3994)	73 (397)	90 (2181)	90 (4394)	39 (3494)			100 (181)	98 (2096)	96 (2066)
E.coli	3417	15 (3417)	76 (3417)	43 (1204)	90 (1204)	35 (3417)	64 (3417)	76 (3417)	74 (388)	85 (1204)	99 (3417)	81 (3417)	99 (150)	40 (1699)	44 (2056)	46 (78)	47 (3017)	99 (197)	100 (1204)	100 (3417)	44 (3417)			100 (92)	3982 (1119)	98 (1163)
E. coli (MDR/CRE)	977	0 (977)	27 (977)	10 (959)	70 (959)	0 (977)	0 (977)	3 (977)	1 (81)	62 (957)	99 (977)	6 (977)	76 (147)	1 (496)	1 (977)	3 (32)	1 (977)	79 (182)	88 (977)	85 (977)	22 (977)			100 (89)	97 (977)	95 (923)
Kleb.pneumoniae (ALL)	3372	(0) (3372)	(52) (3372)	(8) (1736)	(32) (1736)	(43) (3372)	(48) (3372)	(51) (3372)	(57) (1228)	(33) (1736)	(96) (3372)	(81) (3372)	(75) (224)	(44) (581)	(53) (1128)	(64) (223)	(50) (3372)	(66) (272)	(66) (1736)	(70) (3372)	(49) (3372)			(86) (251)	(70) (1689)	(67) (1689)
Kleb.pneumoniae	1973	0 (1973)	81 (1973)	21 (360)	64 (360)	73 (1973)	81 (1973)	84 (1973)	88 (145)	62 (360)	99 (1973)	95 (1973)	100 (43)	68 (318)	79 (646)	88 (146)	80 (1973)	100 (61)	100 (360)	100 (1973)	75 (1973)			100 (33)	74 (350)	95 (350)
Klebsiella pneumoniae (MDR/CRE)	1399	0 (1399)	12 (1399)	5 (1376)	23 (1376)	0 (1399)	0 (1399)	4 (1399)	4 (83)	25 (1376)	91 (1399)	62 (1399)	69 (181)	15 (263)	19 (482)	17 (77)	8 (1399)	58 (211)	60 (1376)	52 (1376)	12 (1399)			83 (218)	69 (1339)	85 (1339)
Klebsiella spp.	290	0 (290)	51 (290)	5 (128)	49 (128)	37 (290)	52 (290)	58 (290)		34 (128)	96 (290)	83 (290)		39 (57)	54 (290)		82 (290)	40 (55)	68 (152)	96 (290)	57 (290)				73 (128)	82 (128)
Morganella morganii	278	2 (278)	4 (278)	30 (26)	93 (26)	7 (278)	87 (278)	91 (278)		93 (26)	100 (278)	82 (278)		76 (111)	80 (153)		77 (278)		96 (26)	100 (278)	86 (189)					
Plesiomonas shigelloides	165	7 (41)	94 (165)	67 (6)	100 (145)	92 (12)	98 (165)	100 (165)			64 (165)	74 (165)		90 (30)	90 (165)		83 (165)				80 (147)	87 (2)	96 (132)			
Proteus spp.	778	52 (778)	90 (778)	53 (54)	100 (54)	75 (778)	90 (778)	96 (778)	65 (34)	91 (54)	100 (778)	86 (778)		75 (250)	77 (353)		88 (778)		98 (54)	100 (167)	61 (778)					
Providencia spp.	119	30 (119)	28 (119)			24 (119)	93 (119)	96 (119)			100 (119)	96 (119)		90 (41)	87 (54)		88 (19)			100 (119)	87 (119)					
Pseudomonas aeruginosa (All)	2855			7 (477)	78 (2855)			74 (2855)		72 (2855)	86 (2422)	77 (998)				73 (2547)	76 (2835)	20 (594)	17 (597)					100 (657)		
Pseudomonas aeruginosa	2312			16 (206)	92 (2312)			93 (2335)		87 (2312)	98 (1987)	95 (455)				89 (2079)	93 (2292)	71 (127)	75 (127)					100 (131)		
Pseudomonas aeruginosa (MDR)	543			1 (271)	19 (543)			0 (543)		8 (543)	33 (435)	20 (543)				1 (468)	2 (543)	6 (523)	3 (526)					100 (526)		
Serratia spp.	107	1 (107)	1 (107)			98 (107)	89 (107)	95 (107)			98 (107)	98 (107)			97 (34)		91 (107)			100 (107)	95 (107)					
Stenotrophomonas maltophilia (All)	1055			(9) (868)	(47) (1055)		(6) (1055)	(55) (1055)		(82) (1055)	(17) (1055)	(20) (1055)			(80) (1055)		(73) (1055)				(93) (1055)			(85) (192)	(58) (197)	
Stenotrophomonas maltophilia	793			11 (626)	50 (793)		7 (793)	64 (793)		86 (793)	19 (793)	19 (793)			93 (793)	95 (751)	89 (793)				93 (793)			94 (33)	82 (33)	
Stenotrophomonas maltophilia (MDR)	262			5 (242)	10 (262)		1 (262)	29 (262)		49 (262)	11 (262)	18 (262)			39 (262)	52 (231)	23 (262)				82 (262)			84 (159)	53 (164)	
Shigella spp	15	75 (15)	86 (15)				80 (15)	93 (15)			100 (15)	100 (15)			33 (15)		43 (15)				12 (15)					
Salmonella spp.	248	39 (142)	98 (227)			89 (28)	94 (246)	96 (248)	76 (33)		99 (95)	90 (92)		97 (70)	96 (238)		84 (160)				80 (259)		79 (111)			
Vibrio cholera	47	84 (19)	87 (46)				98 (47)	98 (47)			100 (47)	100 (47)			96 (47)		90 (47)				80 (47)					
Vibrio parahaemolyticus	127		100 (127)				95 (127)	99 (127)			87 (127)	94 (127)			99 (127)		97 (127)				99 (127)					

จำนวนเลขตัวบนในแต่ละบรรทัด แสดง % sensitivity

Antimicrobial Susceptibility Patterns of Gram Positive Cocci And Fastidious Organism, 2016

ORGANISMS	Total	Penicillins			Amoxi./Clavulanate	Cephalosporins		Fluoroquinolones			Macrolides									
		Ampicillin	Penicillin	Oxacillin/Cefoxitin		Cefotaxime	Ceftriaxone	Ofloxacin	Levofloxacin	Ciprofloxacin	Erythromycin	Clarithromycin	Trimetho/Sulfa.	Clindamycin	Gentamicin	Tetracycline	Fosfomycin	Fusidic acid	Vancomycin	Tigycycline
Staphylococci coagulase negative	1005		8 (814)	29 (1005)				47 (73)			33 (901)		61 (1005)	39 (901)	59 (1005)		60 (1005)	73 (1005)	100 (1005)	99 (982)
Staphylococci aureus (All)	1816		10 (1498)	76 (1816)							68 (1776)		92 (1816)	69 (1776)	78 (1816)		92 (1816)	95 (1816)	100 (1816)	95 (1816)
Staphylococci aureus (MSSA)	1374		13 (1125)	100 (1374)							87 (1334)		99 (1374)	88 (1334)	99 (1374)		98 (1374)	97 (1374)	100 (1374)	95 (1374)
Staphylococci aureus (MRSA)	442		0 (373)	0 (442)							7 (442)		71 (442)	7 (442)	62 (442)		73 (442)	89 (442)	100 (442)	96 (442)
Enterococcus spp.	235	72 (235)	60 (235)							45 (235)					77 (235)		71 (235)		100 (235)	99 (197)
Enterococcus faecium (ALL)	1026	(11) (1026)	(10) (1026)							22 (1026)					(72) (1026)		(29) (1026)		(78) (1026)	(98) (1026)
Enterococcus faecium (Non VRE)	795	14 (795)	12 (795)							23 (795)					77 (795)		31 (795)		100 (795)	99 (795)
Enterococcus faecium (VRE)	231	0 (231)	0 (231)							2 (231)					53 (231)		19 (231)		0 (131)	96 (321)
Enterococcus faecalis	1104	96 (1104)	69 (1104)												52 (1104)		91 (1104)		100 (1104)	98 (1104)
Streptococcus agalactiae	199		99 (199)			95 (199)					83 (120)			83 (120)					100 (199)	
Streptococcus pyogenes	139		90 (139)			100 (139)					90 (133)			95 (133)					100 (139)	
Streptococcus pneumoniae	13		100 (13)			100 (13)	100 (13)	100 (13)			46 (13)			92 (13)					100 (13)	
Viridans Streptococci	150		88 (150)			88 (150)					57 (140)			64 (140)					100 (150)	
Haemophilus influenzae	75	60 (75)			97 (75)	99 (75)		100 (75)	99 (75)			95 (75)	47 (75)							

จำนวนเลขตัวบนในแต่ละบรรทัด แสดง % sensitivity
จำนวนเลขตัวล่างในวงเล็บแต่ละบรรทัด แสดงจำนวนเชื้อที่ใช้ทดสอบ

PITFALL: CHOOSING ANTIBIOTIC THERAPY BASED SOLELY ON SPECTRUM

- Correct ATB spectrum does not assure clinical effectiveness
- **Tissue is the issue!**
- *Antibiotics that are effective against a microorganism in-vitro but unable to reach the site of infection are of no benefit to the host*
- Areas that are difficult to penetrate or abscesses require surgical drainage
- Implanted foreign materials associated with infection usually need to be removed

Principal of antimicrobial therapy

- Right drug
- **Right dose**
- Right duration

Pharmacokinetics

How patient effects drug level

- A = absorption
- D = distribution
- M = metabolism
- E = elimination

Pharmacodynamics

How drug level effects the pathogens – static, cidal

Dosing: too little or too much

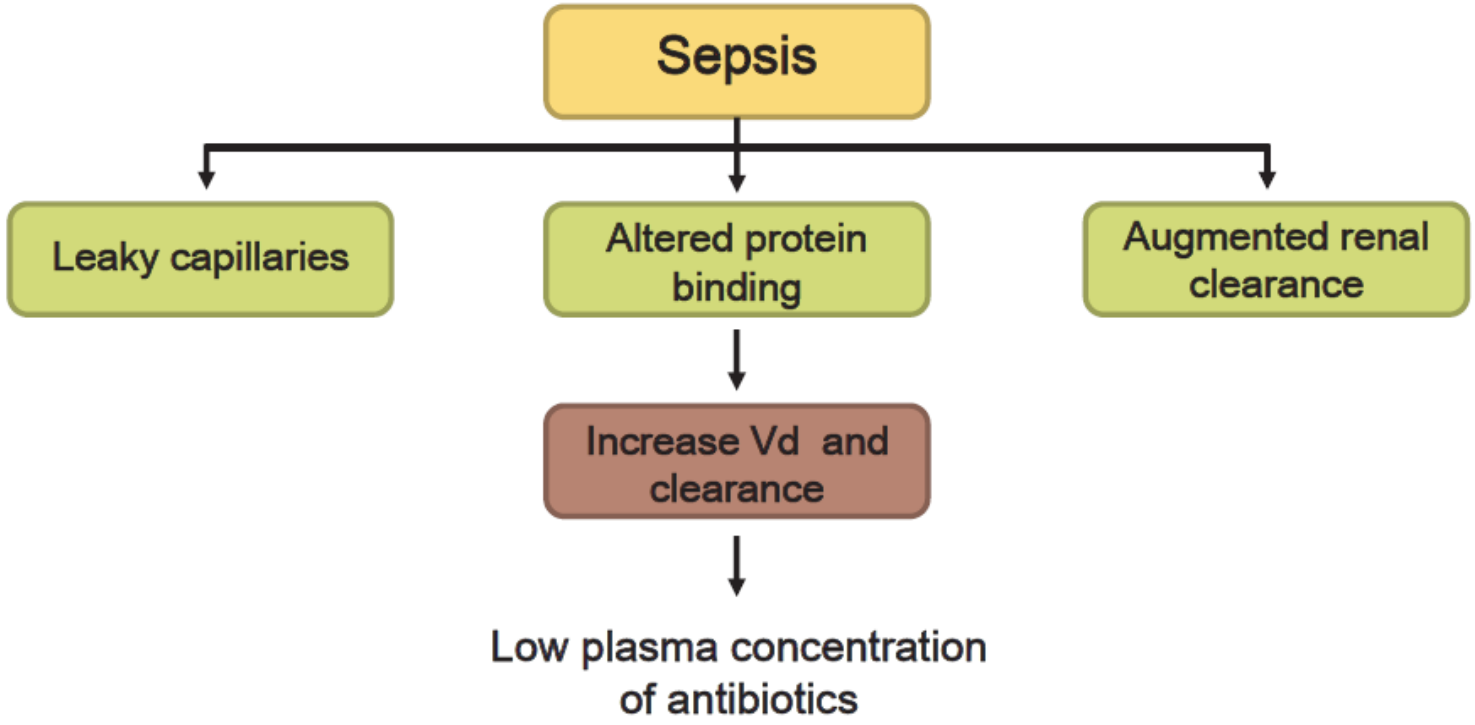
- Pharmacokinetic/pharmacodynamics properties

	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.

Dosing: too little or too much

- Septic patient: too low



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

Dosing: too little or too much

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

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

Dosing: too little or too much

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.

PITFALL: OVERRELIANCE ON MICROBIOLOGY SUSCEPTIBILITY TESTING

- In-vitro data do not differentiate between colonizers and pathogens.
- In-vitro data do not necessarily translate into in-vivo efficacy.
- In-vitro susceptibility testing is dependent on the microbe, methodology, and antibiotic concentration.
- In-vitro susceptibility testing by the microbiology laboratory *assumes* the isolate was recovered from *blood,* and is being exposed to *serum* concentrations of an antibiotic given in the *usual* dose.

PITFALL: USE OF ANTIBIOTICS FOR PERSISTENT FEVERS

- The most common error in the management of apparent antibiotic failure is changing/adding additional antibiotics instead of determining the cause.
- For patients with persistent fevers on an antimicrobial regimens that appears to be failing, it is more important to reassess the patient than add additional antibiotics.
- Causes of prolonged fevers include non-infectious medical disorders (e.g., SLE); drug fever; in-vitro susceptibility but inactive in-vivo; antibiotic tolerance with gram-positive cocci; inadequate coverage/spectrum; inadequate antibiotic blood levels; inadequate antibiotic tissue levels (undrained abscess, foreign body-related infection, protected focus, e.g., cerebrospinal fluid); organ hypoperfusion/diminished blood supply (e.g., chronic osteomyelitis in diabetics); drug-induced interactions (antibiotic inactivation, antibiotic antagonism); decreased antibiotic activity in tissue; fungal superinfection; treating colonization; and antibiotic-unresponsive infectious diseases (most viral infections).
- Undiagnosed causes of leukocytosis/low-grade fevers should not be treated with prolonged courses of antibiotics.

PITFALL: USE OF ANTIBIOTICS FOR PERSISTENT FEVERS

- **Causes of prolonged fevers**
- non-infectious medical disorders (e.g., SLE)
- drug fever
- in-vitro susceptibility but inactive in-vivo
- antibiotic tolerance with gram-positive cocci
- inadequate coverage/spectrum
- inadequate antibiotic blood levels
- inadequate antibiotic tissue levels (undrained abscess, foreign body-related infection, protected focus, e.g., CSF
- organ hypoperfusion/diminished blood supply (e.g., chronic osteomyelitis in diabetics)
- drug-induced interactions (antibiotic inactivation, antibiotic antagonism)
- decreased antibiotic activity in tissue
- fungal superinfection
- treating colonization
- antibiotic-unresponsive infectious diseases (most viral infections)

PITFALL: PROLONGED USE OF IV ANTIBIOTICS IN HOSPITALIZED PATIENTS

- Most hospitalized patients on IV therapy able to take PO medications should be switched to PO equivalent therapy soon after clinical improvement (usually < 72 hours).
- Advantages of early IV-to-PO switch programs include early hospital discharge, virtual elimination of IV line infections, cost saving.
- Drugs well-suited for IV-to-PO switch or for treatment entirely by the oral route include clindamycin, metronidazole, amoxicillin, trimethoprim-sulfamethoxazole, levofloxacin, and linezolid.
- Consider antibiotic spectrum, bioavailability and tissue penetration

Bioavailability

	%
PEN V	60-70
amoxicillin	80
ampicillin	60
cloxacillin	50
dicloxacillin	37
Amoxy/clavulanate	80/30
cephalexin	90
cefuroxime	52

	%
azithromycin	37
clindamycin	90
TMP/SMX	85
metronidazole	100
levofloxacin	99
Moxifloxacin	98
ciprofloxacin	70
linezolid	100

Spectrum: to narrow or too broad

- **Too broad: non-de-escalation**
- A single-center, open-label, RCT
- Age > 18 years with ESBL-producing Enterobacteriaceae: 40% UTI
- De-escalate to Ertapenem vs continue imipenem/meropenem

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.

Principal of antimicrobial therapy

- Right drug
- Right dose
- **Right duration**

Dosing: too short or too long

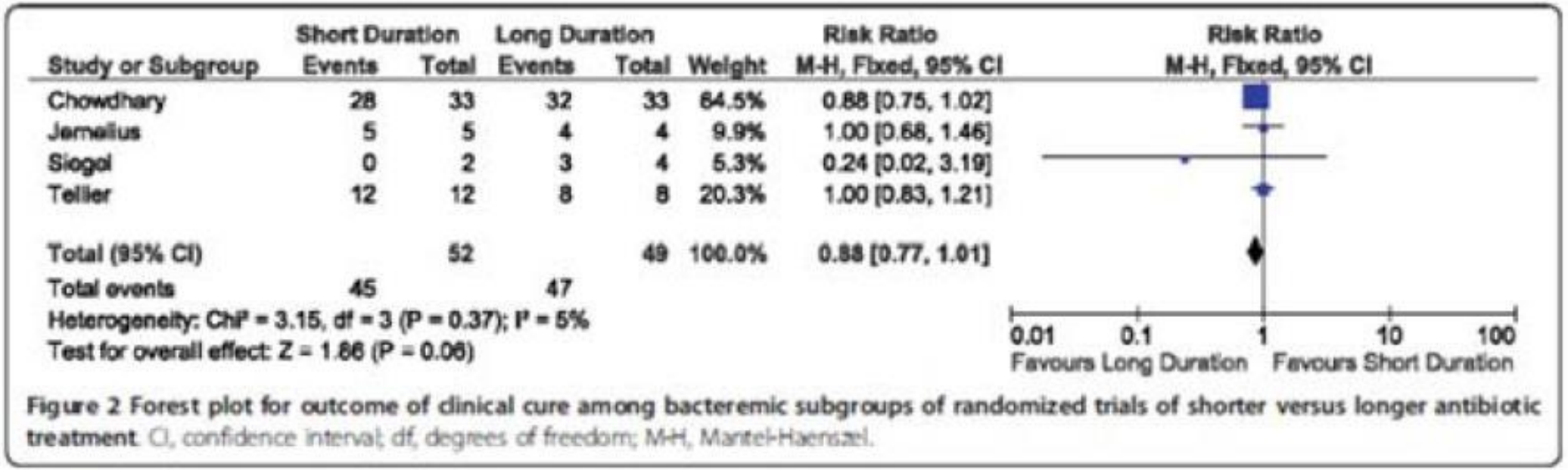
- HAP/VAP in ICU: short (7-8 days) vs prolonged (10-15 days)

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

Dosing: too short or too long

- **Bacteremia**: short (5-7 days) vs prolonged (7-21 days)
- Primary bacteremia, secondary bacteremia from acute pyelonephritis and pneumonia
- Clinical cure



Study or Subgroup	Short Duration Events	Total	Long Duration Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chowdhary	28	33	32	33	64.5%	0.88 [0.75, 1.02]
Jernelius	5	5	4	4	9.9%	1.00 [0.68, 1.46]
Siogol	0	2	3	4	5.3%	0.24 [0.02, 3.19]
Tellier	12	12	8	8	20.3%	1.00 [0.83, 1.21]
Total (95% CI)		52		49	100.0%	0.88 [0.77, 1.01]
Total events	45		47			

Heterogeneity: Chi² = 3.15, df = 3 (P = 0.37); I² = 5%
Test for overall effect: Z = 1.86 (P = 0.06)

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.

PITFALL: USE OF COMBINATION THERAPY TO PREVENT ANTIBIOTIC RESISTANCE

- Monotherapy is preferred over combination therapy
- Monotherapy reduces the risk of drug interactions, medication errors, missed doses and side effects, and is usually less expensive
- Combination therapy is not effective in preventing antibiotic resistance, except in very few situations

PITFALL: INADEQUATE SURGICAL THERAPY

- Infections involving infected prosthetic materials or fluid collections (e.g., abscesses) often require surgical therapy for cure.
- For infections such as chronic osteomyelitis, surgery is the only way to cure the infection
- antibiotics are useful only for suppression or to prevent local infectious complications.

Surgical antibiotic prophylaxis

- Optimal time for administration
  - ➢ within 60 minutes before surgical incision’
  - ➢ Fluoroquinolones and vancomycin: within 120 minutes before surgical incision

- Shortened post-operative prophylaxis
  - ➢ A single dose or
  - ➢ Continuation for less than 24 hours

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

Early post-operative fever

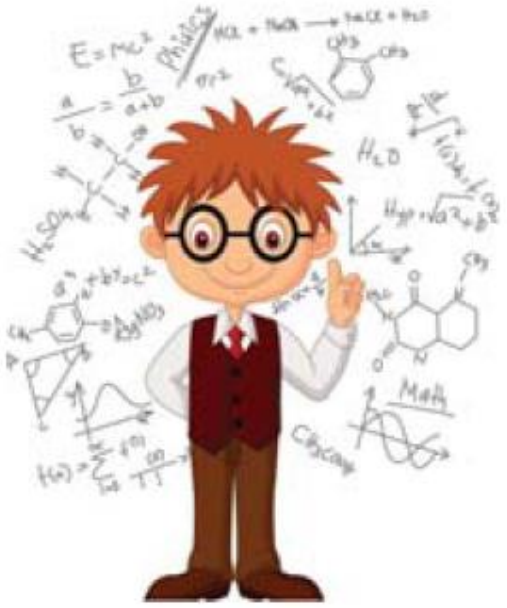
- Defined as BT > 38 C within 72 hours after surgical procedure
- 82% non-infectious cause
- 18% infectious cause
- - surgical site infec
- - pneumonia
- - UTI
- - AAC

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

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

Action to optimize antibiotic prescribing

Start smart → Then focus



J Antimicrob Chemother 2011;66:2441-3.

Action to optimize antibiotic prescribing

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

J Antimicrob Chemother 2011;66:2441-3.

Action to optimize antibiotic prescribing

Then focus

- ❑ At 48 hours review the need for ongoing 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 ATB therapy (OPAT)

J Antimicrob Chemother 2011;66:2441-3.